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SLOVAK RESEARCH AND DEVELOPMENT AGENCY

MINISTRY OF EDUCATION, SCIENCE, RESEARCH AND SPORT OF THE SLOVAK REPUBLIC

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EXCELLENCE IN SCIENCE

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FOREWORD

Dear friends,
we feel honoured to invite you to read the fourth publication The Excellence in Science by which the Agency presents the implementation of projects achieving outstanding level. The publication should meet the needs of everybody who is interested in finding more information on research support in Slovakia.

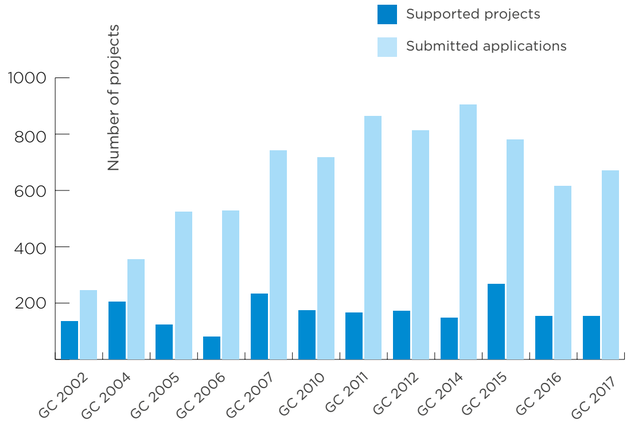
The publication informs about the implementation and results of several years lasting work of Slovak experts on projects from 2015 up to 2019 in the basic and applied research of natural, technical medical, agricultural, social sciences and humanities. Of course, the publication and its content cannot compete with the electronic sources of latest information that are much faster and updated. However, it definitely has certain positives, it enabled us to sum up all the activities conducted by project teams and co-operating institutions within a scientific community in Slovakia. As we have already published the fourth publication, we believe it can clearly present the progress achieved in particular fields of science in which the projects presented in this publication ware implemented. Since its establishment the Slovak Research and Development Agency has been a significant part of the state aid for basic and applied research and development in Slovakia. We are very pleased by the fact you can hardly find anyone from research and development that does not know the name of our Agency.

Finally, our deepest thank you belongs to all solvers of the projects presented in the publication as well as to those who contributed to the preparation of the fourth publication of the research projects with excellent level 2020.

JUDr. Stanislav Mydlo
Director

prof. RNDr. Jozef Masarik, DrSc.
Chairperson

INTRODUCTION



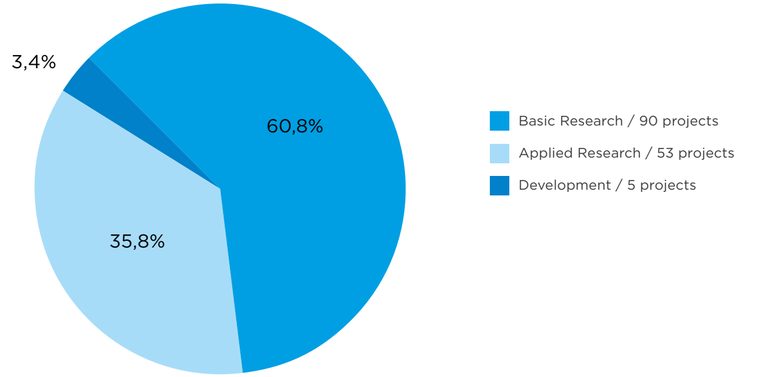
SUMMARY OF APPLICATIONS SUBMITTED AND SUPPORTED PROJECTS IN THE GENERAL CALLS IN THE YEARS 2002 – 2017

The projects presented in this publication have been submitted within the general call to the Slovak Research and Development Agency marked GC 2014. General Call GC 2014 had no limitations on the substantive focus of the projects. Specific focus, objectives and contents of the research and development were determined by the applicants themselves. Applications could be submitted by legal entities as well as natural persons – entrepreneurs without limitation as per sector of research and development. 896 applications for funding were received and registered as part of the general call GC 2014, in order to resolve research and development projects and 148 applications were supported. Start of the project solution was 1. 7. 2015. Latest date of completion of project solutions was 30. 6. 2019. In 2019 subsequently completed projects were evaluated by different scientific councils on the basis of the final reports on projects submitted by the principal investigator within 30 days of the end of solution.
In this publication the Slovak Research and Development Agency presents the selection of the most successful completed and subsequently evaluated projects from the general call GC 2014 in all sectors of Slovak science and technology.

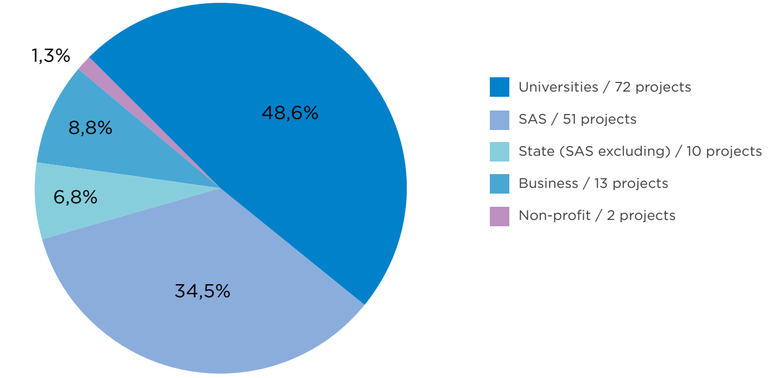
Success rate of applications supported by GC 2014 as per scientific departments.

Department of Science and Technology	Registered applications	Financed projects	Success Rate (%)
Natural sciences	213	36	16,9
Technical sciences	293	46	15,7
Medical sciences	93	15	16,1
Agricultural sciences	119	19	16,0
Social sciences	126	22	17,5
Humanities	52	10	19,2
Total	896	148	16,5

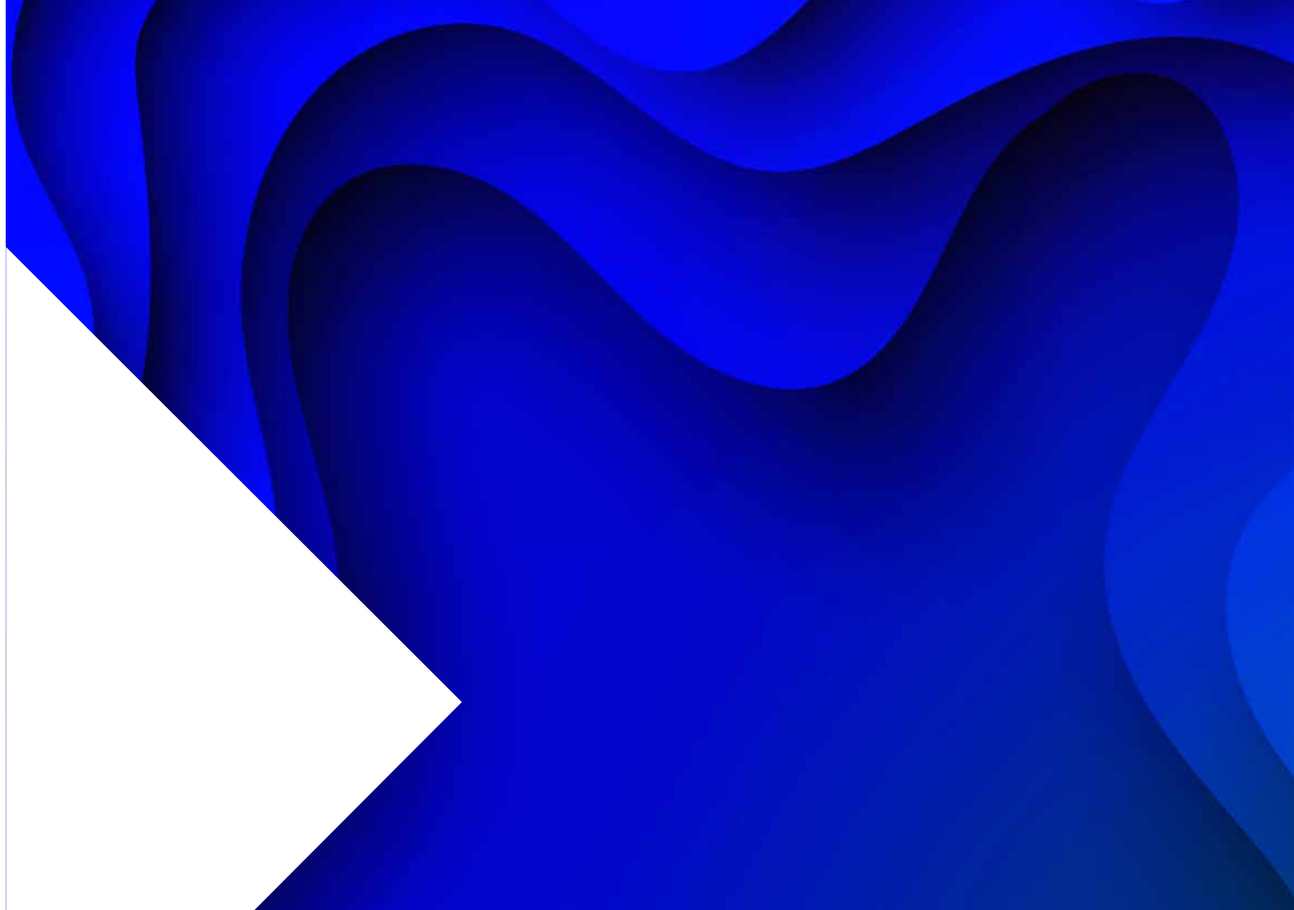
PERCENTAGE RATE OF PROJECTS SUPPORTED AS PER THE NATURE OF THE RESEARCH



BREAKDOWN OF FUNDED PROJECTS AS PER SECTOR



NATURAL SCIENCES



ADVANCED METHODS OF UNCERTAINTY MODELING FOR DECISION PROBLEMS AND THEIR APPLICATIONS

Principal investigator: prof. RNDr. Radko Mesiar, DrSc.
Applicant organisation: Faculty of Civil Engineering, Slovak University of Technology in Bratislava
Term of solution: 7/2015 – 6/2019
Budget from agency: 229 880 €
Project ID: APVV-14-0013

SUBJECT OF RESEARCH

This project was devoted to the development of modern methods for modelling several types of uncertainty. It was focused on copulas in the case of the probabilistic modelling, when the stochastic structure of random vectors was considered. Non-additive measures allow to model the interaction, however, then several new types of integrals should be introduced and studied. Aggregation on different scales, including the lattice scales, belongs to the necessary theoretical background of decision problems. Concerning the applications, we have focused mainly on the advanced modelling of hydrological and financial time series, as well as on the image processing.

OBJECTIVES OF THE PROJECT

Our objectives have considered the proposal and study (with subsequent presentation at distinguished conferences and publishing in top journals) of new valuable results, and application of our recent results in the next domains:
Proposal of new construction methods for 2- and n-dimensional copulas, including the study of properties and dependence parameters of newly constructed ; Proposal of fitting methods and verification of model choices in the framework of multidimensional probability, including the modeling of real financial and hydrological data; Deep study and development of the aggregation theory on lattices; Development of the advanced general measure and integral theory on unipolar and bipolar real scales, including the proposal of new types of measures and integrals, investigation of their properties such as integral inequalities or convergence properties; Generalization of integration on finite universes replacing measures by (partially defined) aggregation functions; Application of theoretical results of the project in image processing.

ACHIEVED RESULTS

We have succeeded to realize all expected objectives, attaining many new valuable results. Our results were published in 78 papers in distinguished impacted journals (most of then being in the first decil of JCR), and they were cited in more than 380 citations in WoS database. Based on our earlier results, we were invited to publish overview papers dealing with expected values of fuzzy sets, and dealing with the latest developments and trends in aggregation. Among the most valuable results of the project, one should mention the construction methods for copulas based on ultramodularity, thus generalizing some recent results based on the product copula, and yielding a new original approach to copulas constructions. Our new concept of moderate deviation functions have attracted the aggregation scientific community, leading to a new approach to comparison of alternatives (based on score vectors) and to a new construction of aggregation functions. Rather interesting and well accepted is also our original idea and subsequent study of sub- and superadditive transformations of aggregation functions, and of new types of monotonicity (directional monotonicity, ordered directional monotonicity), with interesting applications in image processing. Our characterization of Sugeno integrals as the only aggregation functions on lattices preserving congruences is considered as a breaking result in the aggregation theory. We recall also the integral characterization of the necessity and possibility measures, several results concerning the coincidence of different types of decomposition integrals and application of copulas in monotone measures based integrals constructions. One of our major results is the significant extension of the fitting software "acopula" and its application in several outcomes of the project.

BENEFITS FOR PRACTISE

Our results have significantly expanded the theoretical background of different branches of informatics, including the image processing, of a more appropriate stochastic modelling of multidimensional processes, including the multidimensiona time-series modelling, as well as of different decision areas, including the multicriteria decision support and optimization. Our international collaboration have attracted distinguished researchers from several countries, including Australia, Austria, Brasil, Czech Republic, China, India, Iran, Italy, Poland, Spain and USA. This fact has a big positive impact also on the further development of the young investigators participating on this project. The top quality of the results of our team was awarded in 2017 when, based on the evaluation of the National Acreditation Committee, we became an Excellent team.

Fig. 1 / Graphs of different dependence parameters for generalized FGM copulas.

Fig. 2 / Image processing application.

Fig. 3 / 3-D graph of an overlap function applied in image processing.

Fig. 4 / 3-D illustration of parameters determining bivariate polynomial copulas of degree 5 in PQD and NQD classes.

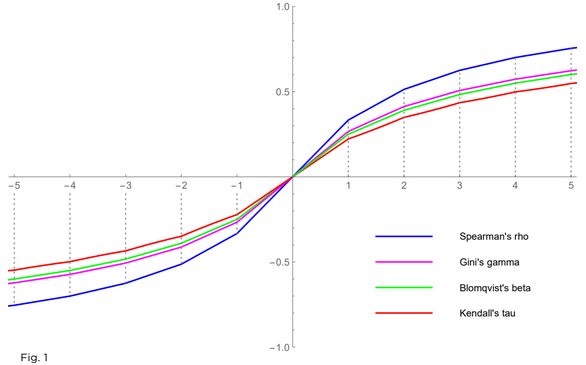


Fig. 1

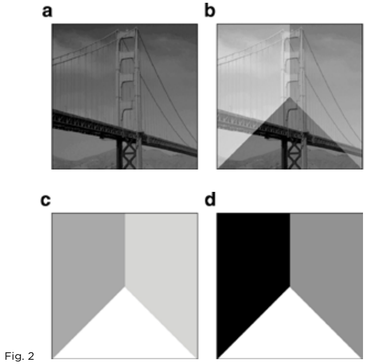


Fig. 2

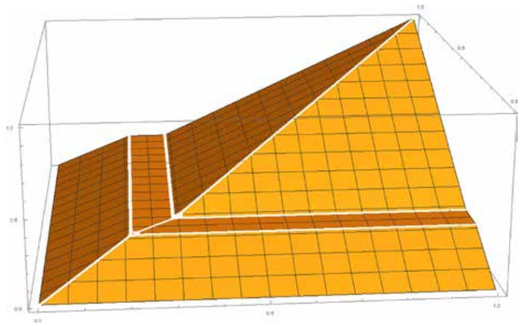


Fig. 3

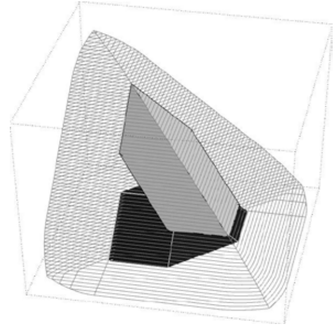


Fig. 4

MAGNETOCALORIC EFFECT IN QUANTUM AND NANOSCOPIC SYSTEMS

Principal investigator: prof. Ing. Martin Orendáč, CSc.
Applicant organisation: Faculty of Science, P. J. Šafárik University
Participating organisations: University of SS. Cyril and Methodius in Trnava – Faculty of Natural Sciences of UCM, Slovak University of Technology in Bratislava – Faculty of Chemical and Food Technology.

Term of solution: 7/2015 – 6/2019
Budget from agency: 249 777 €
Project ID: APGC 14-0073

SUBJECT OF RESEARCH

The investigation of low-energy excitation modes in selected quantum and nanoscopic systems focused on the response of the systems on temperature and magnetic field change.

OBJECTIVES OF THE PROJECT

Synthesis, complex theoretical and experimental study of novel quantum and nanoscopic systems, clarifying the role of spin, crystal – field anisotropy, size, composition of particles on magnetic and magnetothermal properties of the investigated systems. Design of practically applicable novel magnetic coolants with enhanced efficiency on the basis of the study of thermodynamic quantities combined with the investigation of transport and relaxation properties.

OBTAINED ACHIEVED RESULTS

Study of magnetocaloric effect in S = 1 Heisenberg chains with Haldane gap led to the observation, to the best of our knowledge, of the largest inverse magnetocaloric effect in magnetic fields up to 9 T (*M. Orendáč et al., Phys. Rev. B (2017)*). One of the largest rotational magnetocaloric responses up to 2 T was found in KEr(MoO4)2 (Fig. 1) (*V. Tkáč et al., Phys. Rev. B (2015)*). Pronounced effect of phonon bottleneck effect on dynamic response was proved in frustrated planar antiferromagnet Er2Ti2O7 (*M. Orendáč et al., Phys. Rev. B (2016)*) and dynamic spin ice Pr2Sn2O7 (*V. Tkáč et al., J. of Al. and Compd. (2019)*). Appearance of magnetization plateau was theroetically investigated in S = 1/2 dimer and octahedral Heisenberg chains (*T. Verkholyak et al., Phys. Rev. B (2016), J. Strečka et al., Phys. Rev. B (2017)*). Adopting litography and electrodeposition techniques two – dimensional micromagnetic structures have been prepared and their magnetocaloric properties have been optimized (Fig. 2) (*S. Vorobiov et al., J. Magn. Magn. Mat. (2019)*).
Research effort was focused also on the preparation and characterization of transition metal coordination compounds showing the magnetic bistability based on the spin crossover (Fig. 3) or single molecule magnet phenomena (*I. Šalitroš et al., Inorganic Chemistry (2019)*). Term of magnetic bistability can be explained as a unique property of the material/molecule to exist in two stable magnetic states which have different physical properties (projection or/and value of magnetic moment, color, electric conductivity...). The corresponding magnetic states can be altered between each other by the external triggers. The light switchable magnetic materials are the most promising in the sense of technological application due to the possibility to control the magnetic states at the single molecule level (*B. Brachňáková et al., Chemical Papers (2017)*).
The attention has also been devoted to the study of magnetocaloric properties of fine (6–8 nm) Gd2O3 nanoparticles encapsulated in a periodic nanoporous SiO2 silica matrix with hexagonal and cubic symmetry, where the structure of nanocomposites were confirmed by experimental and theoretical methods (A. Zeleňáková et al., Scientific Report (2019). The prepared composite combines the advantages of nanoporous silica with gadolinium oxide in the form of nanoparticles. The combination of the unique porous structure of amorphous silica with fine gadolinium oxide nanoparticles and a high value of magnetic entropy change enables to extend the application of the Gd2O3@SiO2 composite, to cryomagnetic refrigeration (Fig. 4) (*A. Zeleňáková et al., Appl. Phys. (2016)*).

BENEFITS FOR PRACTISE

The effort in searching for potential new magnetic coolants stimulated interest of Slovak companies as well as foreign partners in the obtained results. More specifically, the company B.S.H. s. r. o., belonging to Bosch group, expressed its interest in magnetic cooling and discussions about common collaborative endevaour have been initiated. The observed anomalous magnetocaloric effect in a spin chain with Haldan-gap stimulated testing of the high-quality single crystals of the chain materials as potentional cooling elements in high B/T facility, National High Magnetic field Laboratory, University of Florida, Gainesville. Considering our results led to the invitation to participate in a wide consortium of universities, research institutions and companies in project ESTEEM – "Novel Technologies for Efficient Thermal and Energy Management" submitted in call H2020-MSCA-ITN-2019. In addition, common project „Centre for magnetic cooling and heating " in call OPVaI-VA/DP/2016/1.2.1-01 was submitted in collaboration with the Slovak company Cryosoft s. r. o.

Fig. 1 / Rotational magnetocaloric effect in KEr(MoO4)2 and its potential application.

Fig. 2 / Manufacturing and characterization of man-made two-dimensional magnetic structures.

Fig. 3 / Spin crossover in selected Fe based polynuclear compounds.

Fig. 4 / Manufacturing and magnetothermal properties of nanocomposites Gd2O3@SiO2 for cryomagnetic cooling.

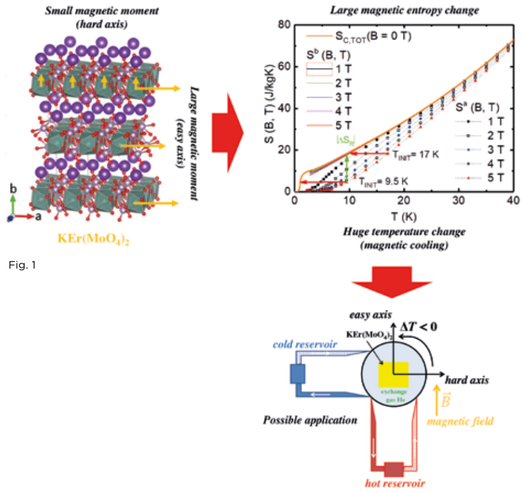


Fig. 1

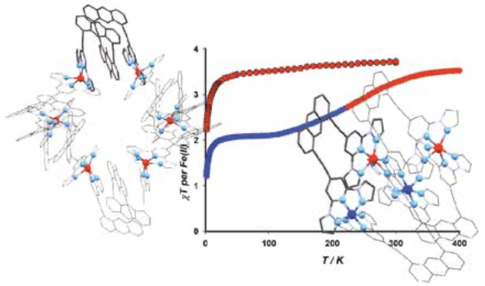


Fig. 3

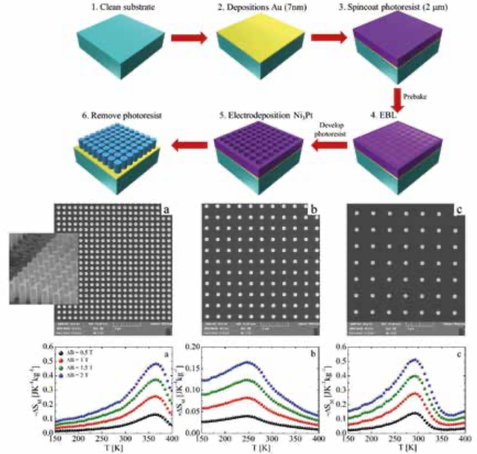


Fig. 2

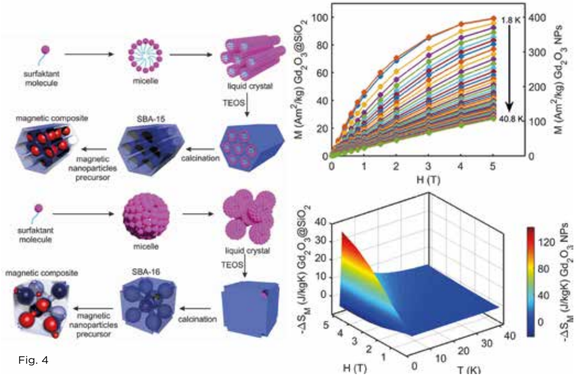


Fig. 4

REGIONAL STRATOTYPES FOR GENETIC, EARTHTIME AND PALEONVIRONMENTAL PROPERTIES OF THE WESTERN CARPATHIAN SEDIMENTARY BASINS

Principal investigator: doc. RNDr. Ján Soták, DrSc.
Applicant organisation: Earth Science Institute, Slovak Academy of Scienses Bratislava
Participating organisation: Comenius University Bratislava – Faculty of Natural Sciences

Term of solution: 07/2015 – 06/2019
Budget from agency: 249 855 €
Project ID: APVV-14-0118

SUBJECT OF RESEARCH

The project has been focused on a critical events in the Earth's history, which provided a record in timescale standards and sedimentary archives of the Western Carpathians. Therefore, the main project objective was a research of boundary stratotypes of the Mesozoic and Cenozoic formations, which were calibrated to the international geological timescale and global changes of the Earth.

OBJECTIVES OF THE PROJECT

The aim of the research was intended in application of a multidisciplinary approach and high-resolution analysis in stratigraphic dating and identification of paleoenvironmental changes in sedimentary formations of the Western Carpathians. The research aimed to improvement of the data from the study of regional stratotypes to the level of international correlation programs IGCP / UNESCO and to integrate into research teams for the definition of global stratotypes and events.

ACHIEVED RESULTS

The research of the Mesozoic formations has provided some discovering results (e.g. the first finding of reptiles of the genus *Pachypleurosaurus* in the Carpathian region), but mainly progress in definition of boundary stratotypes and oceanic anoxic events. The most significant results were obtained from the study of stratotypes of the Jurassic-Cretaceous boundary in the Western Carpathians, which were upgraded to a level of international GSSP reference standards. The results of the project proved a great importance of calpionellids, which like a pelagic microorganisms became of a strategic group of Jurassic and Lower Cretaceous biostratigraphy applied not only in the research of the Western Carpathians, but also with collaboration of project investigators around a whole Tethyan realm (e.g. stratotype sections in France, Ukraine, Crimea, Bulgaria, Mexico, etc.). In biostratigraphic research of younger formations, a similar importance possess a group of foraminifera, which outputs became a main topic of the international micropaleontological conference IWAF 2017 in Smolenice, which programme and logistics was performed by the research team of the project APVV-18-0118 (including the publication of monography issue).
Another very important result of the project is unravelling of an impact event at the Cretaceous- Tertiary boundary (K/T), which is registered worldwide, but has been missing in the Western Carpathians, so far. Now, the K/T boundary has been recorded by extinction events and evolution of a new forms of planktonic life, indices of stress conditions, changes of Earth's paleomagnetism, impact-derived fragments, etc. From the beginning of the Paleogene (65 Ma), the project findings imply a new radiation of organisms and instability of the Earth's climate systems. This process tend to gradual warming and onset of extreme hyperthermal conditions at the Paleocene-Eocene boundary (55 Ma), which were substituted by continual climatic cooling up to first glaciation during the Eocene terminal event (33 Ma). The sedimentary records of these conditions are inferred in temperature and nutrient preferences of organisms, basinal bioproductivity, isotope composition of shells and carbonates, weathering products, etc. Timescale of these changes has been dated by guiding fossil species, magnetozones, and geochronological methods. All knowledge together with those from the Neogene basins allow to reconstruct a sedimentary development of the Western Carpathian basins during 50 million years. Their models has been published, providing an interpretations of life conditions, climatic changes, depositional systems, carbon cycles, hydrographic regimes, but mainly paleogeography within orogenic development of the Alpine-Carpathian-Pannonian belt.

BENEFITS FOR PRACTISE

The APVV-14-0118 project contributed mainly to basic research, providing a topical level of scientific outputs. This is documented by almost a hundred published scientific papers in domestic and foreign peer-reviewed journals (91), two monographic publications (IWAF 2017, Jurassica 2019), a number of conference presentations, participation of researchers in international working groups and programmes, several doctoral graduates from among researchers, and etc.).
Nevertheless, the project also has a significant application in practice, as sedimentary complexes build most of the mountain passages on the highway construction route. Resolution of stratigraphy directly helps to interpret their geological structure in the processing of geotechnical works and tunnels, which in the years 2016 – 2019 has been practically realized on the projects of tunnels Soroška, Čebrať and Korbelka (also with relevant publications).

Fig. 1 / Western Carpathian sections revealing a potential of regional stratotypes but also international parastratotypes of the Jurassic-Cretaceous boundary (145 Ma). Graphics disply a quantitative changes and abundance maxima of calcareous microplankton, clastic admixture, distribution of zonal species of calpionellids and magnetic polarity polarity (Michalík et al., 2016, Geologica Carpathica; 2020, Cretaceous Research).

Fig. 2 / Cretaceous-Paleogene boundary in stratotype section Žilina-Hradisko established on the basis of last occurrences of extinctted species and appearance of new taxa of planktonic foraminifera. For the first time in the Western Carpathianns, there was defined the timescale boundary related to asteroid impact in the Gulf of Mexico 65 million years ago (Chicxulub crater). Soták et al. 2017, Veda, ISBN 978-80-224-1574-3.

Fig. 3 / Paleogeographic and paleotectonic model of sedimentary basins of the Alpine-Carpathian-Pannonian area during the Middle Eocene time (40 – 50 Ma). The model integrates a subsidence centres of the oceanic basins and raised elevations of orogenic zones (Kováč et al. 2016, Global and Planetary Change).

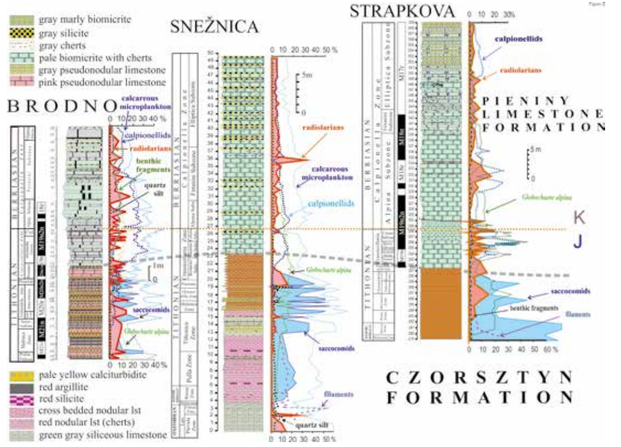


Fig. 1

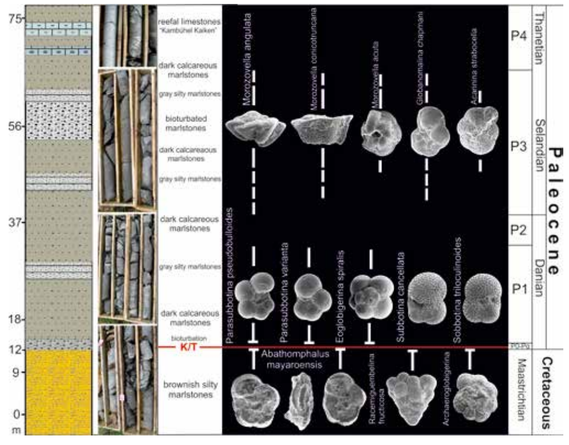
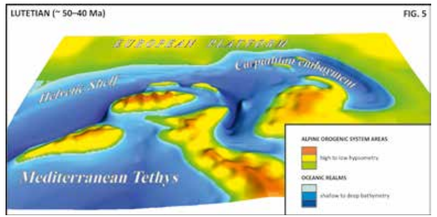


Fig. 2



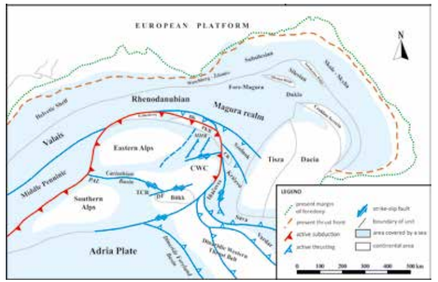


Fig. 3

TRANSCRIPTOME, METABOLOME AND SIGNALOME OF BIOACTIVE COMPOUNDS WITH ANTICANCER EFFECTS IN THE GENUS HYPERICUM

Principal investigator: prof. RNDr. Eva Čellárová, DrSc.
Applicant organisation: Pavol Jozef Šafárik University in Košice
Participating organisation: Comenius University in Bratislava

Term of solution: 7/2015 – 6/2019
Budget from agency: 231 887 €
Project ID: APVV-14-0154

SUBJECT OF RESEARCH

Unexplored species of the genus *Hypericum* represent a huge potential of unique compounds for pharmaceutical industry. From among them the groups of naphthodianthrones and phloroglucinols are the most attractive. In spite of their potential for diagnostics and treatment of cancer, neither the pathways they are synthesized *in planta* were unambiguously validated nor were the genes coding for the key biosynthetic enzymes identified. The project was aimed at complex study of natural compounds – anthraquinones, especially hypericin and its derivatives. The complexity resided in the study of biosynthesis regulation of these compounds, their potential genotoxic effects on biological models and mechanisms of action on some cancer cell lines. In an effort to contribute to better understanding of biosynthesis, the newest sequencing, analytical and imaging technologies enabling to gain and correlate transcriptomic and metabolomics data with those on their localization *in situ* were employed. We hypothesized that *Hypericum*-originated compounds which demonstrate anticancer effects per se or in combination with other drugs could help to overcome some known drawbacks or even lead to enhanced synergic effects, especially in case of photodynamic therapy. A necessary prerequisite for prospective use of these compounds in cancer therapy and diagnostics is their unbiased or even protective effect on normal cells. Therefore, the selected combinations of bioactive compounds were tested for their genotoxicity/antigenotoxicity.

OBJECTIVES OF THE PROJECT

The project was aimed at search for candidate genes involved in biosynthesis of bioactive substances with anticancer effects, hypericins and phloroglucinols in the genus *Hypericum* on the basis of analysis of transcriptomic data and their correlation with the metabolome, and validation of their function for prospective biotechnological production. Synergic or antagonistic effects of hypericin and its combination with other drugs was studied on selected tumour cell lines for improved efficacy in treatment of malignant diseases.

ACHIEVED RESULTS

Complex metabolome and transcriptome analysis of natural sources of pharmacodynamics anticancer compounds from the genus *Hypericum* led to design of new alternative biosynthetic pathway of the photoactive pigment hypericin and enabled to identify a set of candidate genes in biosynthesis of hypericin, hyperforin and melatonin. These results form a basis for design of perspective biotechnological alternative of these compounds. The research aimed at determination of anticancer mechanisms of hypericin revealed an unknown properties both, the light activated and non-activated hypericin alone and/or in combination with other natural agents on several experimental in vitro models. We confirmed the antimetastatic potential of hyperforin and light activated hypericin, and the chemosensitising and immunostimulatory effect of light-activated hypericin and manumycin A. Besides, we documented an important role of BCRP protein in resistance of cancer cells to hypericin-mediated photodynamic therapy. Experiments aimed at analysis of genotoxic/antigenotoxic effect of non-photoactivated or photoactivated hypericin, hyperforin and manumycin A applied alone or in combination showed that these phytocompounds do not have phototoxic effect. Moreover, hyperforin showed anticlastogenic effect against benzo(a)pyrene and cisplatin. This finding is very important for practical application in medicine as hyperforin can eliminate the effect of cisplatin when used as antidepressant for oncological patients.

PROSPECTIVE APPLICATION

The results and outputs of this project should be considered for application in the field of plant biotechnology for pharmaceutical industry and design of new effective preparations of natural origin for photodynamic therapy and diagnostics of cancer. Recently, the „*Herba hyperici*", the aboveground part of *H. perforatum*, is ranked on the world market among the top crude remedies for pharmaceutical industry. Metabolomic studies within this project enabled to recommend other representatives of the genus Hypericum as suitable candidates for biotechnological alternative of their production. Validation of antimutagenic character of the studied metabolites along with a substantial contribution to understanding of the mechanism of their action on the cancer cells are a promising prerequisite of their use in clinical oncology.

Fig. 1 / Hypericum humifusum – dark nodules on sepals filled with hypericin.

Fig. 2 / Hypericum perforatum in vitro.

Fig. 3 / Localization of secondary metabolites by MALDI-HRMS (Kusari et al. 2015).

Fig. 4 / Project meeting (Mýto pod Ďumbierom, Slovakia 2016).

Fig. 1

Fig. 2

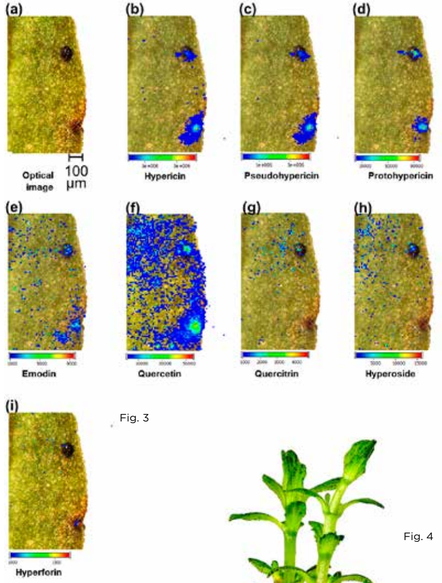


Fig. 3

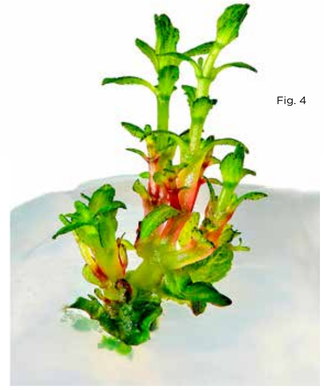


Fig. 4

DECIPHERING THE LIGAND-RECEPTOR INTERACTIONS INVOLVED IN CENTRAL NERVOUS SYSTEM INVASION BY PATHOGENS AND DEVELOPMENT OF TARGETED THERAPEUTIC STRATEGY AGAINST NEUROINFECTIONS

Principal investigator: doc. MVDr. Mangesh Bhide, PhD.
Applicant organisation: University of Veterinary Medicine and Pharmacy in Košice
Term of solution: 7/2015 – 6/2019
Budget from agency: 218 986 €
Project ID: APVV-14-0218

SUBJECT OF RESEARCH

The subject of the research was to unfold interaction between surface ligands of neuropathogens and receptors on the cells of neurovascular unit. The second aim was to produce nanobodies to block ligand-receptor interactions.

OBJECTIVES OF THE PROJECT

i) The first aim was to identify surface proteins (ligands) of neuropathogens (*Borrelia, Neisseria, Streptococcus*) interacting with the cells of the neurovascular unit.
ii) Second objective was to map signalling events triggered in the cells of neurovascular unit when challenged with neuropathogens or their ligands.
iii) The third aim was to identify receptor-binding domain of ligands.
iv) The last aim was to develop nanobodies against receptor-binding domains identified in point iii. Nanobodies could be used further as therapeutic agents against invading neuropathogens.

ACHIEVED RESULTS

First aim was to map surface proteins of neuropathogens (*N. meningitidis, B. bavariensis and S. pneumoniae*) that interacts with cells of neurovascular unit (NVU). Using highthroughput proteomics and bioinformatics, we successfully mapped surface protein interactome of neuropathogens. Interaction of several novel surface proteins to cells of NVU was validated with ELISA and cytochemistry. Second aim was to assess the ability of the surface ligands to evoke signaling events, which help translocation of pathogens across blood-brain barrier (BBB). MafA and NadA of Neisseria, OspA and Erp23 of *Borrelia* and Adhesion lipoprotein of *Streptococcus* were selected to challenge hBMECs and astrocytes. Cell response was assessed at a transcriptomic level using RNA-seq NGS. Selected ligands induced signaling event that can alter the permeability of the BBB. In third aim, we identified binding pockets on the ligands involved in ligand-receptor interactions using limited proteolysis of the ligand-receptor complex and mass spectrometry. Binding pockets (domains) were used in the fourth aim to produce domain-specific VHH nanobodies. "In vitro immunization of llama B-cells" was established to prepare domain-specific VHH-phage or VHH-ribosome libraries (patented). With phage display several VHH nanobodies were produced against neuropathogens. Nanobodies were successfully tested for their ability to block adhesion of ligand and pathogens to hBMECs and abate neuroinflammation. We delivered: 16 papers, 63 abstracts, 1 patent, 1 chapter, 5 invited speeches, 17 oral presentations, 3 EU projects, 7 national projects, 2 brain gain (2 post-docs) and several PhD students finished/ing their PhD.

BENEFITS FOR PRACTISE

1. Unfolding of the complete interactome between neuropathogens and cells of neurovascular unit has created very important database, which is helpful for further study of each ligand of the pathogen. This database will also be helpful for researchers in understanding basic principles of biological processes that undergo during infection. This understanding is important during the drug development.
2. We produced nanobodies with the help of ribosome display. For that, a unique expression cassette was constructed and patented (patent C12N 15/00 (50080-2016). Along with the ribosome display we also established phage display technique for production of nanobodies. Nanobodies developed in the project were able to reduce significantly an adhesion of neuropathogens to the cells of neurovascular unit. Similarly, phage display was used for production of antimicrobial peptides with therapeutic potential against neuropathogens.
3. We standardized a technique "*in vitro* immunization of camelid B-lymphocytes", which replaces classical immunization of animals. The technique was used for production of highly specific nanobodies against ligands of the neuropathogen. This method has unique advantages as follows: i) there is no need of multiple animals to produce antibodies against several antigens; 2) animals do no suffer from toxic and anaphylactic stress due to classical immunization, 3) it is possible to immunize B-lymphocytes with live infectious pathogens (which is practically difficult in case of live animals). With these advantages in vitro immunization can be used widely for raising antibodies in routine practice.
4. Developed nanobodies have high potential in the therapeutic application against neuroborreliosis or meningitis caused due to the *Neisseria*. The pipeline established by is for production of nanobodies can be used seamlessly for production therapeutic antibodies against other pathogens.

Fig. 1 / Mapping of the receptor-binding domain on the ligand of pathogen. In figure NadA ligand of the *Neisseria* is presented, which interacts with endothelial cells of the brain microvasculature. Receptor-binding site is identified with limited proteolysis coupled with mass spectrometry.

Fig. 2 / Recombinant ligand (MafA) of *Neisseria meningitidis*. Important role of MafA during the translocation of meningococcus across blood-brain barrier was identified in the project.

Fig. 3 / Photo presents adhesion of the ligand (major outer membrane protein P.IB, of *Neisseria meningitidis*) on human brain microvascular endothelial cells (green color). Ligands interacts directly with the receptors on the endothelial cells and induce pathological processes in the cells.

Fig. 4 / Neuroinvasive *Borrelia garinii* stained with acridine orange. This strain was used in the the project to develop anti-Borrelia therapeutics.

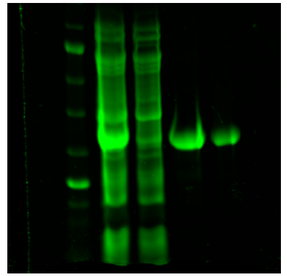
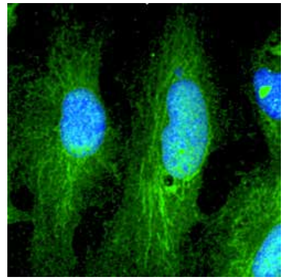


Fig. 2



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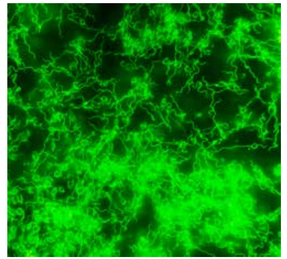
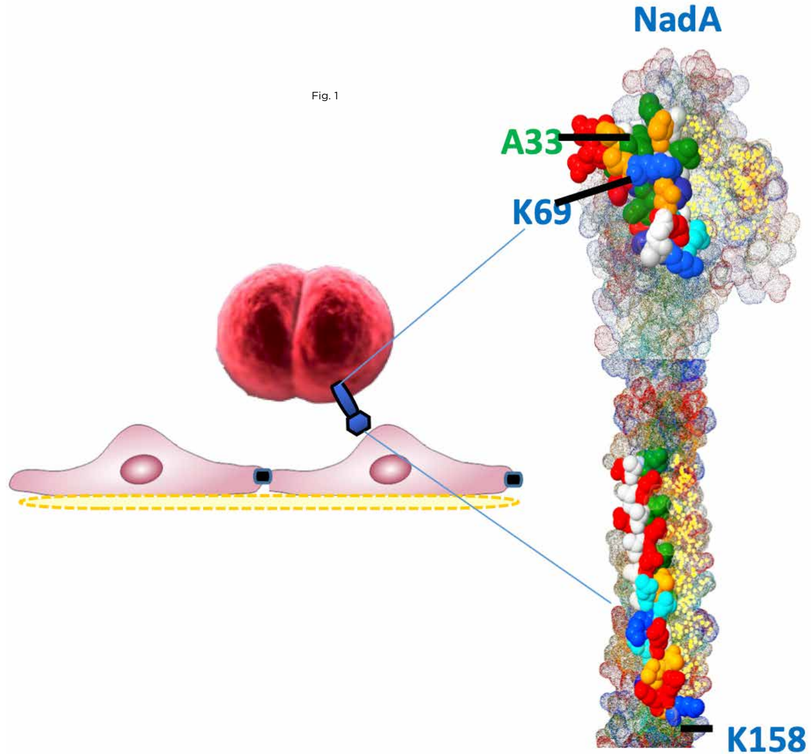


Fig. 4

Fig. 1



COMPARATIVE AND FUNCTIONAL ANALYSIS OF NON-CONVENTIONAL YEAST GENOMES

Principal investigator: prof. RNDr. Jozef Nosek, DrSc.
Applicant organisation: Faculty of Natural Sciences and Faculty of Mathematics, Physics and Informatics of Comenius University in Bratislava
Term of solution: 7/2015 – 12/2018
Budget from agency: 220 000 €
Project ID: APVV-14-0253

SUBJECT OF RESEARCH

The research has been focused on analysis of genomes of non-conventional yeast species, which due to their diversity represent an excellent platform for the study of interesting biological phenomena by means of comparative and functional genomics, bioinformatics, biochemistry, genetics, molecular, and cell biology.

OBJECTIVES OF THE PROJECT

The goal of the project was to determine the genome sequences of several arthroconidial yeasts from the genus *Magnusiomyces/Saprochaete* by combination of the second and third generation sequencing technologies, their comparative and functional analysis, and development of new bioinformatics methods.

ACHIEVED RESULTS

The most important outcomes of the research activities include the determination of highly contiguous genomic sequences of 18 arthroconidial yeast species, including pathogenic (*i.e., Magnusiomyces capitatus, Saprochaete clavata*) and biotechnologically interesting species (*e.g., M. ingens, S. ingens, S. suaveolens*). The genome sequences of several species were annotated using transcriptomic data and public genome browsers were built for them. Several genomic regions have been characterized (*e.g.*, mating-type loci, telomeres). A total of 175 mobile genetic elements have been identified in the mitochondrial genes of the yeasts M. capitatus, M. spicifer and S. clavata, which are ignored during the gene expression by mechanism of programmed translational bypassing. Bioinformatic and proteomic analyses of the components of mitochondrial translational machineries of magnusiomycete species differing by the presence of these elements identified several differences presumably associated with the process of translational bypassing. Moreover, several software tools were developed within the project (*e.g.,* DeepNano, which enables the processing of data obtained by nanopore sequencing technology). The results were published in 24 scientific studies in international scientific journals and proceedings, presented in the form of several lectures and posters at scientific conferences, as well as in the form of master and PhD dissertation theses..

BENEFITS FOR PRACTISE

The sequences of annotated yeast genomes, protocols for isolation of genomic DNAs and preparation of sequencing libraries, genome browsers, as well as developed software tools will be applied in biomedical research and/or biotechnologies. The results of genome analysis of the pathogenic species can be used in designing molecular markers for clinical diagnostics or identification of molecular targets suitable for therapeutic intervention in patients with yeast infections. The project also contributed to the interdisciplinary training of young researchers, undergraduate and PhD students of the Comenius University in Bratislava (in Biochemistry, Genetics and Informatics), who actively participated in the research tasks.

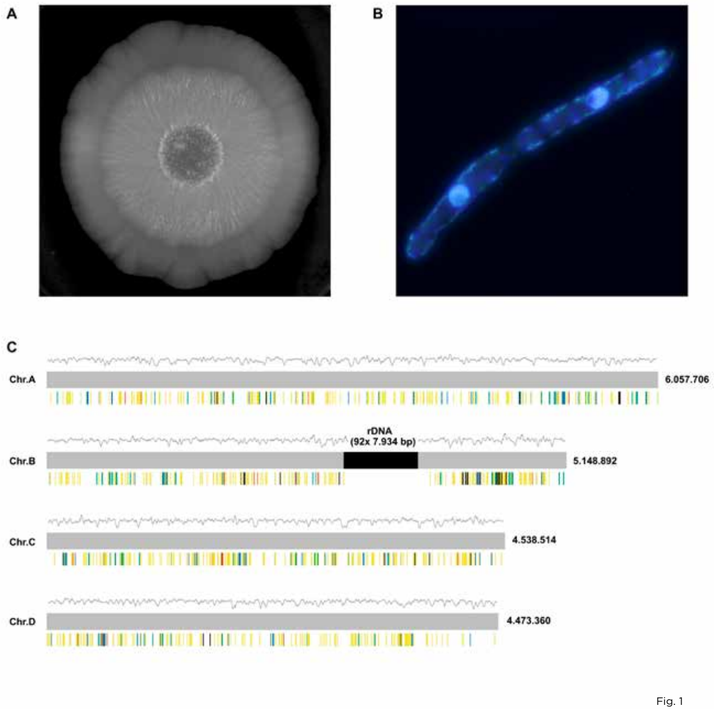


Fig. 1 / Pathogenic yeast *Magnusiomyces capitatus*. (A) Morphology of a cell colony grown on a complex medium (Hodorová, unpublished). (B) Cells with DAPI-stained DNA (Hodorová, unpublished). (C) Organization of the nuclear genome (20.2 Mbp) consisting of 4 chromosomes (Brejová a kol. (2019) *Current Genetics* 65: 539–560).

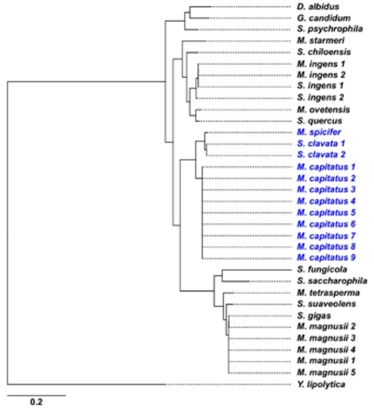


Fig. 2 / A phylogenetic tree of arthroconidial yeast species classified into the genus Magnusiomyces/Saprochaete investigated in the project (Brejová et al., unpublished).

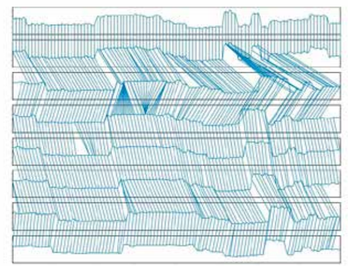


Fig. 3 / An example of variability in the raw signal from nanopore sequencing. The sequencing signals corresponding to the same segment of DNA were aligned using tools developed within the project (Barbora and Vinař, unpublished).

SMALL MAMMALS AS A POTENTIAL SOURCE OF ZOONOTIC BACTERIA AND RESISTENCE TO ANTIBIOTICS

Principal investigator: Doc. RNDr. Michal Stanko, DrSc.
Applicant organisation: Institute of Parasitology Slovak Academy of Sciences (SAS), Košice
Participating organisations: Institute of Zoology SAS, Bratislava
Institute of Animal Physiology, SBs SAS, Košice

Term of solution: 07/2015 – 06/2019
Budget from agency: 168 032 €
Project ID: APVV-14-0274

SUBJECT OF RESEARCH

Small mammals, especially rodents, represent suitable model group of organisms for ecological, parasitological and epidemiological studies. This is due to the fact that the most small rodent species have shorter life span than 2 years. This rapid change of generations allows for the rapid application of mutations. Many species of rodents are typical r-strategists, under favorable biotic and abiotic conditions their populations can grow exponentially, which is manifested in nature by gradation. From a parasitological and epidemiological point of view, it is important that small mammals host a number of groups and species of ectoparasites (ticks, mites, fleas, lice), which are vectors of many pathogens – viruses, bacteria and protozoa. In addition to a fast life cycle and exceptional reproductive capacity, small mammals have the property of living in small home ranges, and therefore the individuals studied reflect the local and current epidemiological situation.

OBJECTIVES OF THE PROJECT

The aim of the project was to obtain new and significantly broaden the existing knowledge about the structure and composition of natural foci in model localities with varying degrees of anthropogenic use, especially in the urban and suburban environment of Košice and partly in Bratislava. The Protection Zone of the Slovak Karst National Park was proposed as a control area. The main aim of the project was to study parasite-host relationship between small mammals, several groups of ectoparasites (especially ticks and fleas) and important bacterial pathogens (genera Anaplasma, Borrelia, Bartonella and Rickettsia) that can cause serious animal and human diseases. We monitored changes in genetic variability and prevalence of these pathogens among the studied localities, during individual years, as well as in model groups of hosts and parasitic arthropods. An important goal of the project was the diagnosis of zoonotic bacteria of the intestinal and cutaneous microflora of wild rodents and the detection of antibiotic resistance in the so-called indicator bacteria (Escherichia coli and enterococci) and staphylococci.

ACHIEVED RESULTS

All the proposed goals of the project were achieved. The research team from the three Institutions of the Slovak Academy of Sciences obtained significant results on the structure and dynamics of natural foci in urban (Košice Botanical Garden), suburban (Košice, Čermeľská dolina) and in the Protection Zone of the Slovak Karst National Park (Hrhov). Teriological research and parasitological examination of rodents and insectivores confirmed the relatively rich fauna of ectoparasites in studied mammals. The obtained results indicated their potential reservoir competence of viral, bacterial and protozoan pathogens. We recorded 10 species of small mammals in the studied localities, 6 species of ticks parasitizing on them, 12 species of parasitic mites and 12 species of fleas. Several years of research on reservoir animals and their ectoparasites, as well as ticks from vegetation, confirmed the existence and activity of natural foci of borreliae, anaplasmae, rickettsiae, bartonellae, neoehrlichiae, babesia, etc. We confirmed the active foci of these zoonoses by multi-year monitoring of the occurrence of ticks and their infestation with pathogens both in the Košice agglomeration and in several localities in Bratislava. The genotyping of pathogens was performed, while in active natural foci we confirmed the circulation of 8 borrelia genospecies, 2 genotypes of anaplasma, 3 genotypes of rickettsiae, 5 bartonella species, and 2 genotypes of babesia. In the faeces of small mammals, we confirmed 6 species and genotypes of cryptosporidia and 5 species of coccidia (Eimeria spp.) by molecular methods. Some of these pathogens can also cause significant diseases in humans and pets. The microbiome of ticks Ixodes ricinus and Dermacentor reticulatus was analyzed by the NGS method. Research has confirmed that small mammals and ticks are important bioindicators of resistant staphylococci. We have found that even antibiotic-sensitive strains of Escherichia coli isolated from the intestine of small mammals can be dangerous to humans. Two new species of cryptosporidia (Cryptosporidium apodemi, C. ditrichi) and the genetic diversity of Dermacentor reticulatus ticks in Europe have been described in international collaboration.

PRACTICAL OUTCOME

The research results have the practical outcome in further epidemiological monitoring to provide public health authorities and the public with information on the current distribution and population densities of ticks in the Košice agglomeration, on the infection of ticks and small mammals with several epidemiologically important pathogens. The results have been published in 12 foreign and 2 domestic peer-reviewed journals and in 1 monograph. The research team also included doctoral students, 4 PhD theses thematically related to the solved project were successfully defended.

Fig. 1 / Capitulum of nymphal *Ixodes frontalis* depicted by scanning microscope

Fig. 2 / Questing female *Dermacentor marginatus* on vegetation (Slovenský kras Karst)

Fig. 3 / Black-striped field mouse (*Apodemus agrarius*)

Fig. 4 / Next-generation sequencing microbiome prepared from pooled females *Ixodes ricinus* collected in the surroundings of Košice city. The letters size proportional to quantity of symbionts and pathogens

Fig. 5 / Ticks larvae sucking on mouse ear (*Apodemus sp.*)

Fig. 6 / Borrelia erythema on human hand around sticking of an infected tick

Fig. 1

Fig. 2

Fig. 3

Fig. 4

Fig. 5

Fig. 6

NONLINEAR PHENOMENA IN EVOLUTION EQUATIONS FROM SCIENCE AND TECHNOLOGY

Principal investigator: prof. RNDr. Marek Fila, DrSc.
Applicant organisation: Faculty of Mathematics, Physics and Informatics, Comenius University in Bratislava
Term of solution: 07/2015 – 06/2019
Budget from agency: 209 440 €
Project ID: APVV-14-0378

SUBJECT OF RESEARCH

The project focused on the development of the theory of nonlinear evolution equations with an aim to understand nonlinear phenomena in nature. The results achieved relate to the qualitative behavior of solutions. The members of the research team investigated a priori estimates and asymptotic behavior of solutions of nonlinear parabolic and elliptic problems; oscillations, chaos and stability for nonlinear differential equations of integer and non-integer order; models of chemical kinetics, gene expression and incompressible fluid flow.

OBJECTIVES OF THE PROJECT

The main aim was to achieve new results in fundamental research in the field of nonlinear evolution equations, which are motivated by continuous mathematical models from science and technology.

ACHIEVED RESULTS

The results of the project were published in 6 monographs, 67 publications in international journals indexed in the Current Contents database and in 21 publications published in international peer-reviewed scientific journals, and were presented at many invited lectures at international scientific events. Member of the research team prof. M. Fečkan was recognized by the HighlyCitedResearchers ranking for the year 2019. The ranking is compiled by ClarivateAnalytics from the Web of ScienceGroup.

BENEFITS FOR PRACTISE

In addition to the publication activity of the research team in prestigious scientific journals, the most important results of the project include the education of graduates and PhD students. There were 12 diploma theses and 4 dissertations related to the project. The contribution of the project also includes the organization of seminars and guest lectures by scientists from leading foreign universities. The financial support received from the APVV agency facilitated the further development of the international links between the members of the research team and leading scientists abroad.

Fig. 1 / The phase transformation of ternary alloys in the gravitational field is accompanied by liquid phase flow or convection. The figure illustrates two modes of convective flow: steady flow in the area under the solid red curve and oscillatory flow in the area between the dashed and solid red curves. The axes represent the degree of initial concentration of the two components of the ternary alloy (so-called Rayleigh numbers).

Fig. 2 / Oscillatory convection results from a complex interaction between convective and diffusive transfer of heat and ternary alloy components. It arises in a wide range of experimental parameters, as illustrated by the dark gray area in the figure. The axes represent the scaled coefficient of concentration diffusion of the two components of the ternary alloy (so-called Lewis numbers).

Fig. 3 / Phase portraits were used to model gene expression. The figure shows an example of such a portrait, in which we see a limit cycle, marked in red. The axes represent the concentrations of transcription factors; the arrows indicate the change in concentrations over time.

Fig. 4 / Randomness also plays a very important role in gene expression. The displayed graph shows a specific measure of randomness, the so-called Fano factor. The axes correspond to the parameters of a model for the expression of an mRNA molecule in the presence of an antagonist microRNA molecule.

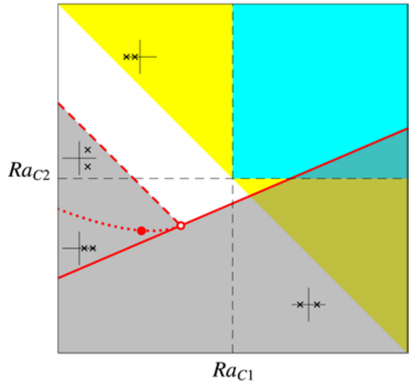


Fig. 1

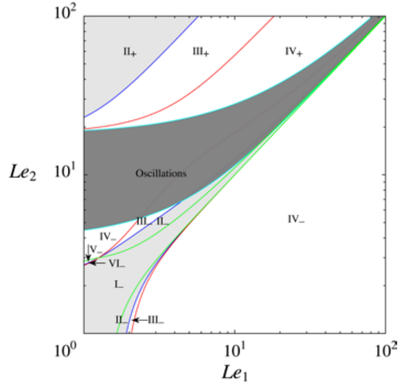


Fig. 2

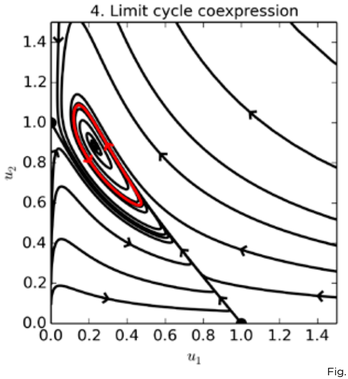


Fig. 3

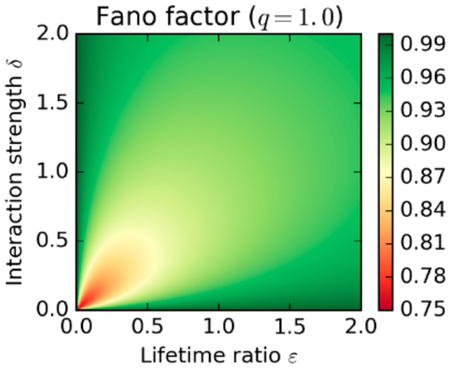


Fig. 4

THE ROLE OF NEUROPEPTIDES AND RECEPTORS IN REGULATION OF PATHOGEN TRANSMISSION FROM TICKS TO THEIR HOSTS

Principal investigator: RNDr. Dušan Žitňan, DrSc.
Applicant organisation: Institute of Zoology, Slovak Academy of Sciences
Participating organisation: Institute of Virology BMC Slovak Academy of Sciences

Term of solution: 7/2015 – 6/2019
Budget from agency: 211 985 €
Project ID: APVV-14-0556

SUBJECT OF RESEARCH

Ticks are important vectors of dangerous pathogens, but mechanisms for transmission of these pathogens into the host are not understood. Very little is known about physiological processes controlling functions of the salivary glands, gut and gonads during life cycle of ticks. In this project we used immunohistochemical, molecular and physiological approaches to identify hormones and their receptors important for regulation of these organs in ticks *Ixodes ricinus* and *I. scapularis*. Using various experiments we found that specific neuropeptides and receptors control activity of these organs and transmission of pathogens during tick feeding on the host. Our results may serve in developing tools for better protection against pathogen transmission and in more efficient suppression of tick reproduction as dangerous ectoparasites of humans and animals.

OBJECTIVES OF THE PROJECT

1. Identification of neuropeptides and expression of neuropeptides in neurons innervating salivary glands, gut and gonads
2. Identification and expression of neuropeptide receptors in the salivary glands, gut and gonads.
3. The role of neuropeptides in regulation of pathogen transmission from the tick internal organs into the host.

ACHIEVED RESULTS

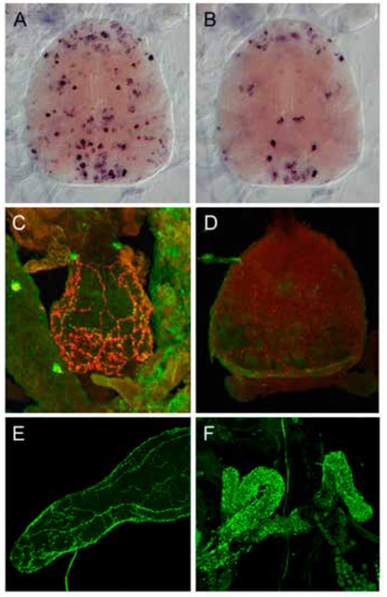
We mapped neuropeptide expression in the brain, salivary glands, gut and reproductive organs of ticks using immunohistochemistry and *in situ* hybridization (Fig. 1). We also determined timing of their release to better understand their possible function during pathogen transmission into the host. We found that neuropeptides are accumulated during starvation and released from innervation and endocrine cells of the gut during feeding (Figs. 1C,D). Specific neuropeptides are accumulated in innervation of the reproductive organs (Figs. 1E,F), indicating their role in tick reproduction. Time course of mRNA expression for neuropeptides and their receptors was determined using qRT-PCR. We found that high expression levels of neuropeptides and receptors at the beginning of feeding continually decrease and reach the background levels at the end of feeding and in depleted animals (Figs. 2, 3). These results indicate important role(s) of neuropeptides and their receptors in the gut and salivary glands during blood feeding. We also confirmed expression of AST-A and its receptors in reproductive organs by qRT-PCR.

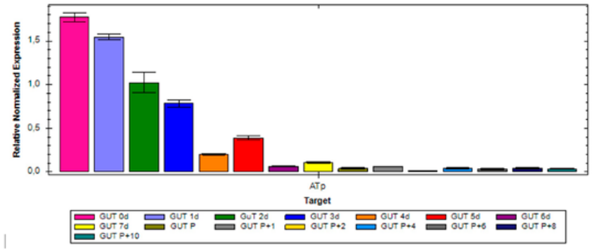
Tick receptors for AT, AST-A and sNPF have not been functionally characterized, so we used chemiluminescent *in vitro* method for characterization of receptors in CHO cells with aequorin. We succeeded to characterize a receptor for AT, four receptors for AST-A and two receptors for sNPF (Fig. 4).

For RNA interference (RNAi) experiments we used five groups of neuropeptides (allatotropin, AST-A, sNPF, SIFa, MIP) and their receptors which are produced or released from the salivary glands, gut and gonads. Using RNAi we successfully suppressed expression of these neuropeptides and receptors. RNAi for allatotropin, AST-A and their receptors induced suppressed feeding, increased mortality and defects during egg laying. These results indicate important role(s) of allatotropin, AST-A and their receptors in regulation of feeding and reproduction of ticks.

We also clarified long disputed transmission mechanisms of European spirochetes *Borrelia afzeli* and American *B. burgdorferi* from ticks to their hosts. Older reports claimed that *B. burgdorferi* must migrate from the gut into the salivary to switch expression of surface proteins from Osp-A to Osp-C. Spirochetes expressing Osp-C are then transmitted from the salivary glands into the host. Our observations using immunohistochemistry revealed that spirochetes never leave the gut and switch from Osp-A to Osp-C occurs in the midgut during blood feeding. Salivary glands are not needed for this process. Our experiments also clearly showed that spirochetes are reproducing in the gut from where they are transmitted into the mice (Fig. 5).

Fig. 1





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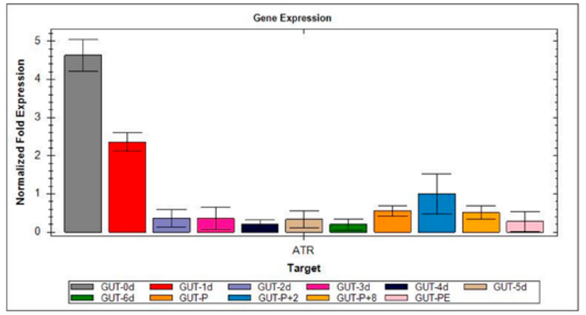

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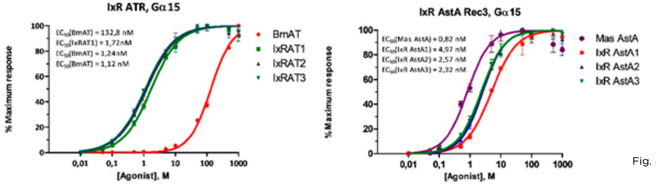

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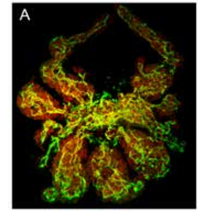


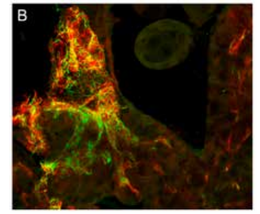


Fig. 5

Fig. 1 / Expression of neuropeptide AST-A in brain neurons of the tick *I. ricinus* (A,B). Some neurons innervate the hindgut (C,D) and accessory glands of males (E) and females (F). Strong immunoreactivity in the gut innervation and endocrine cells of starving ticks disappears during 1–3 day of feeding that indicates the release of neuropeptides at this time (C,D).

Fig. 2 / Time course of mRNA expression for allatotropin in the gut of *I. ricinus*. 0d – unfed, 1-7d – feeding, P+1-10 – depleted ticks.

Fig. 3. / Time course of allatotropin receptor expression in the gut of *I. ricinus*. Increased expression levels were only observed in unfed and early stages of feeding ticks indicating that allatotropin may initiate feeding processes.

Fig. 4. / Chemiluminescent characterization of receptors AT (ATR) a AST-A (AST-A Rec 3) in *I. ricinus*. ATR is equally activated by three AT peptides derived from *at* precursor of *I. ricinus* (Ixr AT1-3) and less efficiently by AT from the silkmoth *Bombyx mori* (Bm AT). AST-A receptor activated by AST-A1-3 encoded by *ast-a* precursor of the tick and AST-A from the hawkmoth *Manduca sexta*.

Fig. 5 / *Borrelia burgdorferi* in the midgut of tick *I. scapularis*. A) Unfed nymph *I. scapularis* infected with *Borrelia burgdorferi immunostained* with antibody to flagellin (green) and Osp-A (red). B) Feeding nymph (36h) *I. scapularis* infected with *Borrelia burgdorferi* immunostained with antibody to Osp-A (red) and Osp-C (green).

SUPERCONDUCTOR-INSULATOR TRANSITION

Principal investigator: Mgr. Pavol Szabó, CSc.
Applicant organisation: Institute of Experimental Physics, Slovak Academy of Sciences, Košice
Participating organisations: Faculty of Mathematics, Physics and Informatics, Comenius University Bratislava
Institute of Physics, Faculty of Science, P.J. Šafárik University, Košice

Term of solution: 07/2015 – 06/2019
Budget from agency: 248 998 €
Project ID: APVV-14-0605

SUBJECT OF RESEARCH

The Superconductor – insulator transition (SIT) project brought together three Slovak research teams with the aim of studying the topic of SIT (objective 1), the topic of topological phenomena in superfluid Helium-3 (objective 2) and in SmB_6 (objective 3). The research team at the IEP SAS and IoP FS UPJŠ provided the experimental infrastructure of the Centre of Low Temperature Physics in Košice while the team at the FMPI UC in Bratislava provided the theoretical support in addition to their technological facilities. The project resulted in 41 publications, 25 of which were published in the highest ranked journals – 1 x Advanced Materials (IF 25), 2 x ACS nano (IF 13.9), 1 x Nature Comm. (IF 12.3), 1 x Appl. Surf. Sci. (IF 5.15), 14 x Phys. Rev. B (IF 3.7), among others.

OBJECTIVE 1 – SUPERCONDUCTOR INSULATOR TRANSITION

The mechanism of the SIT was studied in MoC thin films and in granular Boron doped diamond (BdD). By studying the MoC thin films we found that the bosonic scenario of the SIT is not universal. Our transport and low – temperature Scanning Tunneling Microscopy (STM) experiments demonstrated that the SIT in MoC thin films follows the Fermionic scenario, instead [1]. Moreover, we observed that the spectral smearing increases substantially with the increasing disorder (decreasing film thickness) [1,2]. We developed the theory of Dynes superconductors [3] which explains the smearing by considering local magnetic moments emerging at the interface between the thin film and the substrate [2]. This theory was then successfully applied in the characterization of the complex conductivity in disordered 10 nm thin MoC superconducting films [4]. The theory was elaborated throughout the whole duration of the project [3].

In BdD we studied the bosonic scenario of the SIT. We found that in this case, the suppression of superconductivity is associated with the loss of global coherence in the Cooper pair condensate [5]. Besides, our magnetization, transport and STM experiments revealed a unique coexistence of superconductivity and ferromagnetism in polycrystalline BdD with hydrogenated grain surfaces [6].

OBJECTIVE 2 – SURFACE BOUND STATES IN SUPERFLUID 3HE-B

As a part of our study of the interaction of mechanical resonators with surface bound excitations in superfluid ^{3}He-B at ultra low temperatures, we observed a new phenomenon. It manifests itself as an anomalous, magnetic field-dependent damping of the motion of this resonator, which we interpreted as a nuclear magnetic resonance generated by mechanical motion observed at the anisotropic magnetic moment of surface bound Andreev states in a topological superfluid ^{3}He-B [7].

OBJECTIVE 3 – SmB_6 – TOPOLOGICAL INSULATOR?

Electron band structure of the strongly correlated Kondo insulator SmB_6 was studied by the direct method of ARPES down to temperature of 1 K, at which theoretical predictions expect the existence of topological surface states. We have observed in measuring energy spectra only trivial surface states without characteristic/typical behavior/features for topological insulators [8]. STM measurements, which were carried out at milikelvin temperatures, have confirmed the trivial origin of surface states, too [9]. It was shown, that SmB_6 appears as trivial surface conductor and not as topological insulator.

BENEFITS FOR PRACTISE

The project had the character of basic research, but the achieved results can be applied in quantum nanotechnologies.

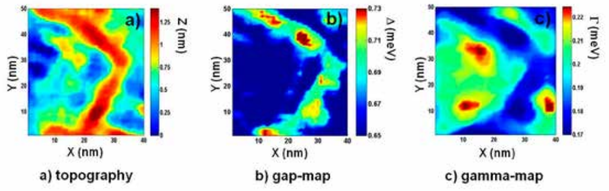
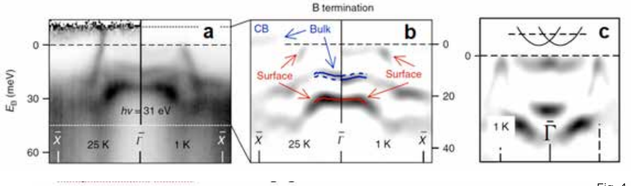


Fig. 1



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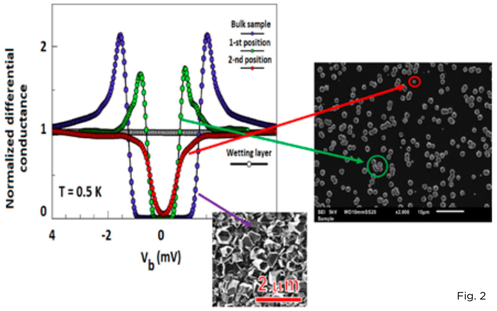


Fig. 2

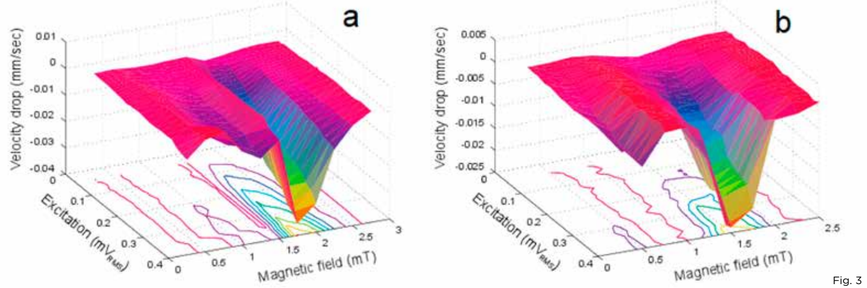


Fig. 3

Fig. 1 / a) STM topograph of 3nm MoC film on Si substrate with a protruding "boomerang" structure b) superconducting energy gap map c) spectral smearing map. Maps b) and c) were obtained by fitting the Dynes modified BCS density of states on the tunneling spectra acquired at each point of the topograph. By comparing the images, it is evident that thinner regions feature higher spectral smearing and smaller gap, contrary to the thicker regions, i.e. the superconductivity is suppressed by proximity to the substrate. This evidences, that the substrate – film interface acts as a local source of Cooper pair breaking [2]. Hence, the ultrathin MoC films behave as Dynes superconductors [3].

Fig. 2 / BdD tunneling spectra for various grain separations: single grain (red), cluster of grains (green) and dense polycrystal (blue) [5]. The topographs were acquired by SEM. The total suppression of coherence peaks (red curve) is a direct consequence of the loss of global coherence in the Cooper pair condensate in isolated BdD nanocrystals.

Fig. 3 / Dependence of velocity of mechanical resonator on the applied magnetic field and excitation measured experimentally (a) and calculated based on theory (b) [7].

Fig. 4 / Band structure (dispersion relation E(k)) of SmB6 at temperatures of 25 K and 1 K, respectively, measured by ARPES method. Surface states, identified at temperature of 1 K near Fermi energy (b), are split around Gama point (c), what shows evidence of trivial nature.

TECHNICAL SCIENCES

MULTICOMPONENT NANOCOMPOSITE COATINGS PREPARED BY HIGHLY IONIZED DEPOSITION TECHNOLOGIES

Principal investigator: doc., RNDr. František Lofaj, DrSc.
Applicant organisation: Institute of Materials Research of SAS
Participating organisations: Faculty of mathematics, physics and informatics, Comenius University in Bratislava
Institute of Materials and Machine Mechanics of SAS

Term of solution: 7/2015 – 9/2018
Budget from agency: 245 700 €
Project ID: APVV-14-0173

SUBJECT OF RESEARCH

In engineering, thin coatings are applied on bulk materials to improve their properties at the level well above the properties of the substrate material. During the last decade, main trend in the hard coatings is to form and control the structure at nanometer (atomic) scale. Nanostructured (nanocomposite) coatings belong to a group of materials consisting of at least two separated phases with nanocrystalline or amorphous structure and their combination. Because of very small grain size and thin amorphous matrix at their boundaries, the properties of nanocomposite materials exhibit different, often improved properties and behavior in comparison with conventional materials. However, having nanocomposite structure with high hardness may not be sufficient, novel coatings have to combine high hardness with high oxidation resistance above 1000 oC, exhibit low friction, high wear resistance and improved toughness. Therefore, the focus of the research is oriented toward the development of ternary-, quaternary- and multicomponent nanocomposite systems, involving also theoretical approaches (e.g. *ab initio* models) to describe the formation of metastable phases, mutual interactions among atoms, chemical bonds, etc.
The most promising direction in nanostructured coatings with high hardness, thermal stability and toughness seems to be doping of various ternary and multicomponent nitride or carbide systems by sufficient amounts of noble metals.
From the viewpoints of effectivity of the deposition process and practical applications of the coatings, the deposition of high performance nanocomposite coatings on the substrates at relatively low deposition temperatures while keeping adhesion sufficiently high are required. These requirements led to the introduction of new deposition techniques with high energy plasma and high degree of ionization of sputtered material for the coatings, deposition without additional substrate heating, ion cleaning, higher target utilization, etc. The current highly ionized plasma methods which are represented by two novel technologies:

1. HiPIMS – High power Impulse Magnetron Sputtering, and
2. HiTUS – High Target Utilization Sputtering.

Although HiPIMS technology has already been used for the deposition of various hard coatings, the use of HiTUS is very limited. However, neither of these technologies has been applied to nanocomposite multicomponent coating systems with controlled structure and properties. Thus, the project is focused on this area.

OBJECTIVES OF THE PROJECT

The general aim of the project was an increase of thermal stability, structural and oxidation resistance, wear resistance, lifetime and toughness application of the hard three- and multicomponent nanocomposite coatings based on Ti-, Cr-, Al- W-nitrides by means of doping by the additional reactive elements (, e.g. Ta, V, Y, W, Nb, Si, B, etc.) and using novel deposition technologies based on HiPIMS a HiTUS.

ACHIEVED RESULTS

The main scientific results include:
- understanding of the mechanisms of formation of nanostructured multicomponent coatings consisting of metastable, stable and amorphous phases;
- determination of the influence of selected doping elements on thermal stability, structural and oxidation resistance and mechanical properties of these coatings;
- understanding of their behavior at high temperatures;
- determination of the effect of enhanced ionization of sputtered material on the formation and properties of the studied systems.

The main technological results encompass:
- determination of the basic relationships among the PVD parameters and resulting structure and final properties of the studied systems;
- successful testing and introduction of HIPIMS and HiTUS among PVD technologies for hard coatings.

The deliverables of the project were fulfilled and in some areas even exceeded. Within the project, 9 publications in the respected international journals included in Current Content database were published; they were cited more than 34 times in WoS and Scopus databases. Simultaneously, together with our foreign partners, 2 patent applications were submitted (Ukraine). The results were presented at international conferences as presentations, including 5 invited presentations (F. Lofaj – Coatings and Layers 2017, Rožnov p. Radhoštem, Czech Republic, 2017; F. Lofaj – Annual Meeting of Japan Tribology Society, Tokushima, Japan, 2017; F. Lofaj – Instrumented Indentation Workshop, Sapporo, Japan, 2018; M. Mikula – Vadstena, Sweden, 2018) at specialized scientific meetings. Special attention should be paid to the invited talk (B. Grančič, key note speaker) on our research activities in the field of hard ternary and quaternary coatings entitled „Tantalum alloying – improvement of thermal stability and mechanical properties of ternary and quaternary transition metal nitrides" at the world conference ICMCFT 2019 in San Diego, USA.
Within the project, 4 Master works and 3 PhD works (P. Hviščová – 2016, D. Németh – 2017, M. Pleva – 2018) were prepared and successfully defended. Currently, additional 3 PhD students continue the research activities based on the project topic (the first defense will be at the end of 2018).

BENEFITS FOR PRACTISE

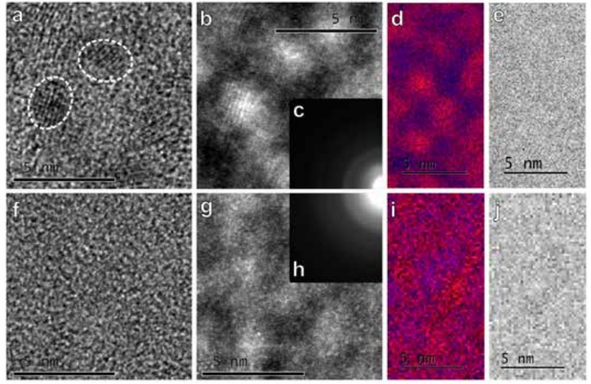
The main results and contribution of the project is the development of:
- novel multicomponent nanostructured coatings with improved thermal stability, oxidation resistance, elastic properties and toughness;
- demonstration of suitability of HiPIMS and HITUS technologies for the deposition of hard multicomponent nanostructured coatings;
- introduction of additional deposition, testing and analytical methods for the characterization of novel coating systems.

These results represent a database for faster acceptance of HiPIMS and HiTUS technologies for hard coatings in industry.
Based on these results, our industrial partner Staton, s.r.o. Turany, started to test the developed systems on cutting tools in industrial conditions. AT the same time, the works on the projects were a basis for the collaboration with the research institutions abroad, incl. Linkoping University, Sweden and Erich Schmid Institute, Leoben, Austria.

Fig. 1 / M. Pleva, B. Grančič, M. Mikula, et al., Thermal stability of amorphous Ti-B-Si-N coatings with variable Si/B concentration ratio, Surface and Coatings Technology, 333, (2018) 52-60. https://doi.org/10.1016/j.surfcoat.2017.10.063

Fig. 2 / Cross-sectional a, f) dark-field STEM, b, g) bright field STEM, c, h) SAED pattern, EELS mapping of d, i) Ti (red) and B (violet) and e, j) N atoms of sample a, b, c, d, e) A – $Ti_{0.12}B_{0.33}Si_{0.03}N_{0.51}$ and f, g, h, i, j) C – $Ti_{0.12}B_{0.23}Si_{0.12}N_{0.51}$ annealed to 800 °C.

Fig. 3 / Hardness and b) effective Young's modulus of as-deposited and annealed Ti-B-Si-N coatings.



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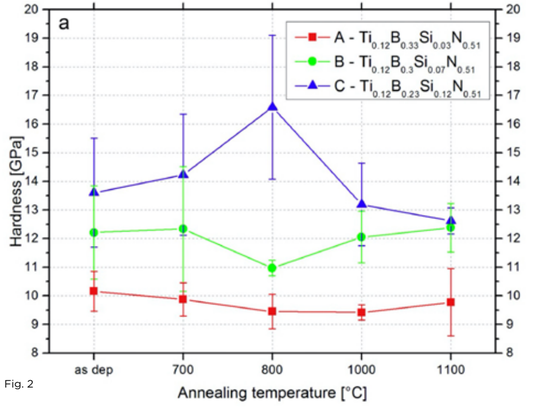


Fig. 2

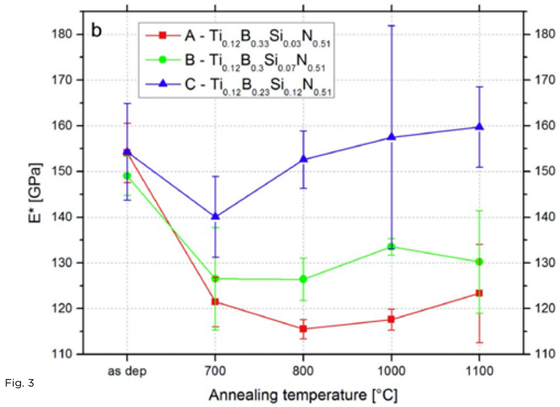


Fig. 3

UTILIZATION OF FIBER OBTAINED FROM WASTED AGGLOMERATED WOOD BASED MATERIALS

Principal investigator: Ing. Henrich Lübke
Applicant organisation: Pulp and Paper Research Institute
Term of solution: 7/2015 – 6/2018
Budget from agency: 246 869 €
Project ID: APVV-14-0243

Tab. 1: Composition of chips from waste PB after treatment by the 30 min cooking and subsequent chipping using longitudinal slits.

Tab. 2: Distribution and properties of fiber obtained from PB bonded with urea-formaldehyde glue after grinding on a Sprout-Waldron mill and grinding in Valley Holland.

SUBJECT OF RESEARCH

The project deals with the use of waste agglomerated wood-based materials. Wood recycling is a topic based on EU directives and the Act of the Slovak Republic 79/2015. Unnecessary furniture and demolition construction waste are the main sources of waste with a chemical load, such as chipboards, fibreboards and oriented strand boards (OSB). The ultimate goal of material recovery of wood based agglomerated materials is the re-production of chipboard and medium density fibreboards (MDF) and their recycling for fluting for the production of less demanding cartons.

OBJECTIVES OF THE PROJECT

The scientific goal of the project was to propose methods to increase the recycling rate of difficult-to-recycle wood-based materials with hardened resins, which were added during their production as a binder. As part of the project solution, the method of initial destruction of individual waste sources, the method of preparation of recovered wood particles and the method of preparation of pulp from the obtained particles were determined. The application goal of the project was to determine the conditions for the re-production of agglomerated wood-based materials and also to design methods for their recycling using known paper technologies.

ACHIEVED RESULTS

As part of the project, three patent applications were submitted, six impacted and several professional publications were published. Pilot-scale tests were carried out and, based on the results of the project, cooperation was established with the Wilhelm-Klauditz Institute based in Braunschweig (Germany) in the field of a new method of pressing of agglomerated wood-based materials.
Laboratory tests have shown that at least 40% relative humidity is required for chipping the waste material. Waste particleboards (PB) and oriented strand boards (OSB) treated in this way and chipped on an equipment with longitudinal slits have a chip composition suitable for the new production of PB and also for the production of fiber for middle density fiberboards (MDF).

Sieve	8 mm	4 mm	2 mm	1 mm	0,25 mm	Rest	Total
Portion (%)	0	19,3	20,3	20,65	25,6	14,15	100,0

°SR		40	24	13
Dewatering (sec)	500 ml	19,47	2,46	2,47
	700 ml	49,19	11,38	4,70
	800 ml	74,92	18,00	9,50
Brecht-Holl (%)	16 (mesh 40)	4,175	25,90	42,52
	50 (mesh 120)	49,330	47,48	40,56
	100 (mesh 240)	19,490	13,47	10,13
	Over 100 (mesh 240)	26,805	13,15	6,79

Chips prepared over 2 mm were heated to 80°C with steam. The obtained fiber, prepared using Sprout-Waldrone, with a grinding fineness of 5°SR (Schopper-Riegler) was insufficient for preparation of new MDF boards and it was necessary to set it at Valley Dutch at 13°SR and 24°SR. Grinding to a higher degree increases the consumption of glue in the preparation of the board.

Similarly, the preparation of wood pulp from waste MDF boards bonded with urea-formaldehyde glue was optimized. Waste OSB and PB boards bonded with melamine-urea-formaldehyde glue for further processing must be treated by cooking and subsequent crushing. They can be chipped in this way using longitudinal slits. The chips obtained have a composition suitable for fiber production and also for new PB production. The amount of formaldehyde in the prepared chips from waste PB after treatment with water is reduced depending on the processing method.

BENEFITS FOR PRACTICE

The patented particleboard production technology enables the production of formaldehyde-free products with energy savings of 381 kWh per 1 tonne of PB produced. Old waste recycling saves pulp wood in amount of about 58.8 EUR per tonne of PB produced, while allowing 100% recycled use. The increase in production due to the pressing time shortening to 1.5 to 2 min corresponds to an increase in efficiency of 33% to 55%. In the case of an annual production of 500 ths m³ of PB, at a price level of 179 EUR/m³, production will increase from the value of 89 mil EUR to 119 mil up to 138 mil EUR.
In the preparation of fluting by chemical recycling of wood based agglomerated waste, two methods of delignification were used, namely a slightly alkaline sulfur-free process and an alkaline one. Particles over 2 mm prepared according to our proposed technology were used for chemical processing. The best results were obtained with alkaline delignification with 16% a.a. Already at a total cooking time of 80 min, the strength parameters of the semi-pulp required for the production of "Semi Chemical Fluting 2" and "Brown Testliner 2" were achieved.

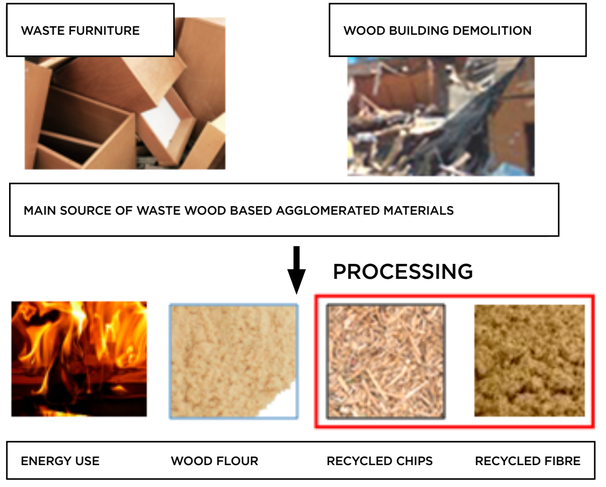


Fig. 1

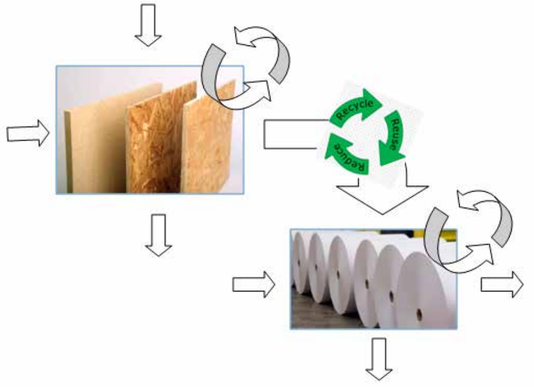


Fig. 2

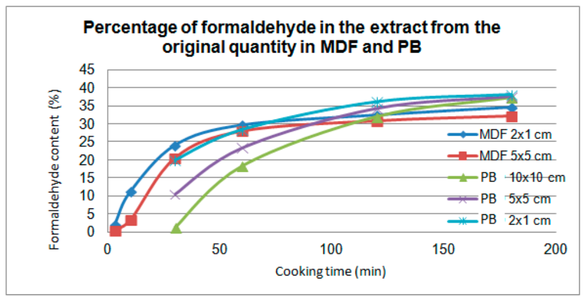


Fig. 3

Fig. 1 / Segment of cascade recovery of wood mass, so-called downcycling, creating a product with a lower added value.

Fig. 2 / Material recovery of waste wood based agglomerated materials with a hardened binder.

Fig. 3 / Method for determination of formaldehyde in extracts from waste agglomerated materials.

DEVELOPMENT OF SOFTWARE SUPPORT BY USING PHYSICAL SIMULATION FOR OPTIMIZATION OF CONTINUOS CASTING PROCESSES OF STEEL AS DISTRIBUTED PARAMETER SYSTEMS FOR ŽELEZIARNE PODBREZOVÁ, A.S.

Principal investigator: Prof. Ing. Gabriel Hulkó, DrSc.
Applicant organisation: Slovak University of Technology in Bratislava, The Faculty of Mechanical Engineering
Participating organisation: Environment Research and Development Center Ltd.

Term of solution: 7/2015 – 6/2019
Budget from agency: 248 000 €
Project ID: APVV-14-0244

SUBJECT OF THE RESEARCH AND OBJECTIVE OF THE PROJECT

Continuous casting of steel is one of the fundamental technologies of our civilization – more than 1,5 billion tons of steel semi products are produced in the world annually using this technology. In the process of continuous casting, the liquid steel from the ladle and tundish is sequentially cooled in a continuous casting machine (CCM) according to the set geometry – the format of the continuous casting, Fig. 1.

The cooling process significantly determines the course of solidification of steel and thus the quality and efficiency of production. The cooling process of continuous castings is optimized and controlled mainly in the secondary cooling zone, where cooling water with flow rates U1 (k) – Un (k) flows through independent sections of nozzles 6.1 – 6.n to the surface of the hot semi-finished product. Fig. 1.

The control task is to provide the required temperature profiles on the surface of the casting strand with changes in the cooling water flow rates, U1 (k) – Un (k). In common engineering practice, the secondary cooling zone is divided into 5-10 parts, and in control the dynamics of the individual parts are described on the basis of ordinary differential equations.

Within the solved project for Železiarne Podbrezová, a.s. the controlled system was interpreted as a continuum and on the basis of describing partial differential equations as a distributed parameter system, where the results of long-term research activities of the research team in the field of control of distributed parameter systems were used.

Physical simulations were performed in Plastometric laboratory of Regional Materials Science and Technology Research Centre VSB – TU Ostrava.

Numerical models of CCM in Železiarne Podbrezová, a.s. were set up in a virtual software environment ProCAST and transformed to lumped input and distributed parameter output systems for purposes of control tasks solution. To optimize control tasks, the OPTIexpert software product was created, Fig. 2 along with OPTIcontrol for solution of control tasks, Fig. 3. while the software product of research team DPS Blockset for Simulink elaborated in the CONNECTIONS program of The MathWorks Inc., as third-party software product of this company, was used.

Examples of the control process in the secondary cooling zone within OPTIcontrol are shown in Fig. 4-6. In Fig. 4 is a transition between the specified near steady temperature profiles in a linearized operating mode, where the SCZ denotes the spatial distribution of the secondary cooling zone. Fig. 5 shows the control process during sudden changes in casting speed, and Fig. 6 shows a controlled transition between remote operating modes in the segmentation of nonlinear transition dynamics. The possibilities of Slovak Grid – Slovak infrastructure for high-performance computing were also used in the simulation calculations.

BENEFITS FOR PRACTICE

The results of the solution were continuously handed over in Železiarne Podbrezová, a.s. Physical and numerical simulation studies together with OPTIexpert and OPTIcontrol software products have been used to optimize operating modes with implications for improvements of production quality and efficiency. In general, the proposed control concept based on the results of the theory of distributed parameter systems represents an innovation with respect to commonly used secondary cooling control systems in current engineering practice in the world.

Fig. 1 / Scheme of Continuous Casting Machine (CCM) – radial type: (M) mould area, 1. ladle, 2. tundish, 3. refractory submerged entry nozzle, 4. mould wall, 5. liquid core of the casting, 6. secondary cooling area, 6.1 – 6.n independent secondary cooling zones with water flow rates U1(k) – Un(k), 7. tertiary cooling zone, 8. cutting of castings.

Fig. 2 / Hierarchy of the OPTIexpert system for the investigation of steady-state conditions in the continuous casting of the 205R40 support format.

Fig. 3 / Hierarchy of the OPTIcontrol system for the control of thermal processes as distributed parameter systems in the continuous casting of steel of the 205R40 primary format.

Fig. 4 / Transition between specified near steady temperature profiles in linearized mode, where the SCZ denotes the spatial distribution of the secondary cooling zone.

Fig. 5 / Control process at sudden changes in casting speed, where the SCZ denotes the spatial distribution of the secondary cooling zone.

Fig. 6 / Controlled transition between remote operating modes in segmentation of nonlinear transition dynamics, where the SCZ denotes the spatial distribution of the secondary cooling zone.

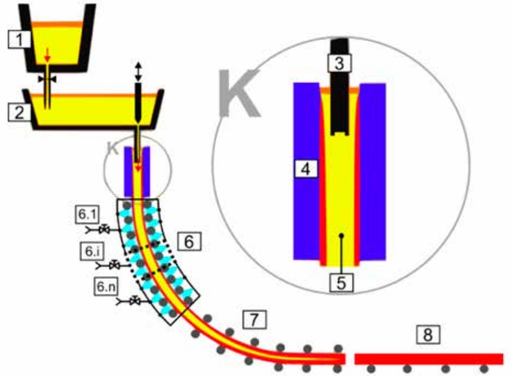


Fig. 1

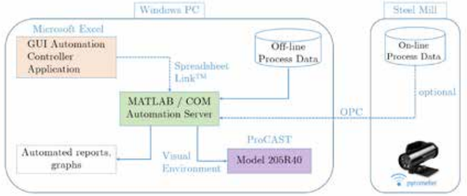


Fig. 2

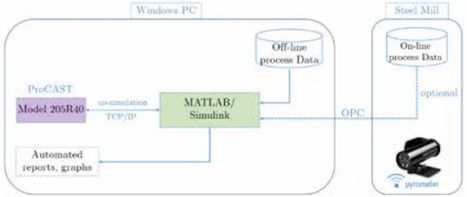


Fig. 3

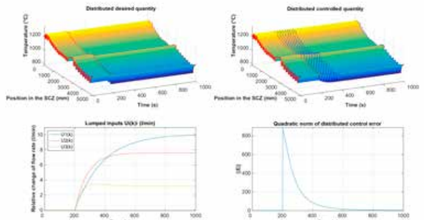


Fig. 4

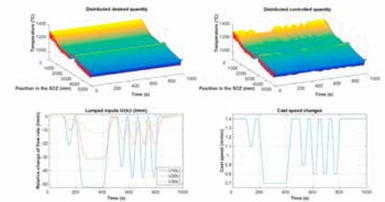


Fig. 5

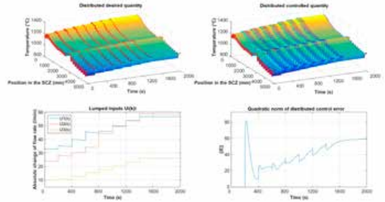


Fig. 6

MANUFACTURE AND TESTING OF HYDROXYAPATITE (HA) CUSTOM HARD TISSUE REPLACEMENTS USING THE 3D PRINTING TECHNOLOGY

Principal investigator: prof. Ing. Radovan Hudák, PhD.
Applicant organisation: Technical University of Košice
Participating organisations: Comenius University in Bratislava
ICARST, n.o.

Term of solution: 7/2015 – 6/2018
Budget from agency: 235 000 €
Project ID: APVV-14-0294

INVESTIGATION SUBJECT AND OBJECTIVES OF THE PROJECT

The key objective of the project was to manufacture ceramic implants made of hydroxyapatite (HA) and tricalcium phosphate (TCP), or a mixture of these two materials, while applying two different technologies (LCM – Lithography-based Ceramic Manufacturing and FDM – Fused Deposition Modelling). The manufactured samples were tested for their biomechanical, biomaterial and biological properties. Based on the available expert knowledge, it was observed that it is beneficial to combine hydroxyapatite (HA) and tricalcium phosphate (TCP) in order to achieve required biomechanical properties and adjust biodegradability parameters of the material. For the purpose of further manufacture and testing, the HA/TCP ratios excluding pure HA and TCP were determined as follows: 30/70; 70/30; and 50/50 (HATCP37, HATCP73, HATCP55). In order to accelerate or optimise osteointegration, the samples were manufactured with the porosities of 200 μm, 400 μm and 600 μm. Various combinations of porosity, a HA/TCP ratio and a shape (cubic and cylindrical) were applied to manufacture 900 samples which were then tested and analysed.

ACHIEVED RESULTS AND BENEFITS FOR PRACTICAL APPLICATIONS

The project implementation included the measurement and identification of basic sample parameters, such as weight and total dimensions; the evaluation of homogeneity, density and cross-sectional area using the industrial computed tomography (CT); mechanical tests under uniaxial pressure; and tests of biocompatibility of bioceramic scaffolds made of HA and TCP, or a combination of the two, in in-vitro conditions. Fig. 2 presents a cylindrical bioceramic sample and analysis outputs obtained using the industrial computed tomography (CT).
In order to facilitate a biomechanical analysis of samples manufactured using the additive technology, a computer simulation was carried out and its results were compared with the results of the mechanical compression test. The test results were then used in the testing of bioceramic materials defined in terms of their clinical applications (hard tissue replacement types). Fig. 3 shows the differences between the mechanical properties of five analysed materials with the porosity of 200 μm, compared with mechanical properties of selected human bones.
Successful implementation of an implant is conditioned by fast osteointegration and mechanical stability of the implant. Therefore, microroughness of bioceramic samples was identified using the Plu neox Optical Profiler microscope (SensoFar, Spain) based on interferometry and confocal microscopy. The process of microroughness identification was carried out in the SensoMap environment (SensoFar, Spain) which facilitated 2D and 3D surface analyses. A cytotoxic effect was tested using a model of human stem cells isolated from subcutaneous fat while applying a direct contact method. The isolated cells (in the concentration of 1 x 105) were embedded on bioceramic scaffolds placed in a 6-well culture plate. The culture medium was continuously replaced and the cell proliferation in the culture on the bioceramic matrix was identified (after 24, 48 and 72 hours). The proliferation activity of fat tissue stem cells was identified through identification of the solution absorbance using the BioTek EL 800 spectrophotometer (Biotek, USA) at the wave length of 490 nm. The data obtained by measurements (Fig. 4) indicated that bioceramic scaffolds do not have a negative proliferation effect on stem cells and, therefore, that a potential application of bioceramic implants should not negatively affect a human organism; however, this conclusion must be further validated in clinical trials. The most significant results include identification of the material which is most suitable for clinical applications, primarily in terms of its strength. On the basis of the performed testing and analyses, the material most appropriate for the manufacture of implants was the mixture of the two tested materials combined in the ratios of 30/70 or 70/30 with the pore sizes of 200 μm or 400 μm, as these two samples exhibited the highest compressive strength and no negative effects on mesenchymal stem cells. Another observation was that the bioceramic material prepared using the additive technology had no negative proliferation effect on stem cells. Moreover, the methodology was developed for implant manufacture and subsequent postproduction processing for the purpose of transferring the obtained outputs to clinical practice.
The key benefit of the achieved results for practical applications is the verification of the use of LCM technology in the production of bioceramic samples, including porous implants, of similar dimensions. Porous bioceramic materials may be used as an alternative to metal and polymer materials. Their great advantages are support of osteointegration and partial biodegradability; on the other hand, their disadvantage is their fragility. The use of these materials, especially in areas with less mechanical load (Fig. 5), is also supported by the results of chemical and biological analyses.

Fig. 1 / Equipment for additive manufacturing from ceramic materials and the LCM technology principle (Lithoz, Austria).

Fig. 2 / Bioceramic cylindrical sample and the analysis of the internal structure using the industrial computed tomography.

Fig. 3 / Comparison of compressive stresses of five tested materials with mechanical properties of selected bones with porosity 200 μm.

Fig. 4 / Proliferation activity of stem cells isolated form subcutaneous fat on a bioceramic scaffold.

Fig. 5 / Ceramic cranial implants and bioceramic cranioplasty.

Fig. 1

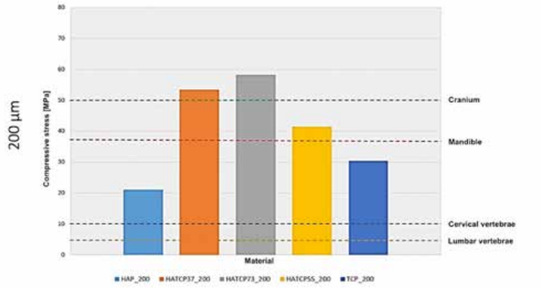
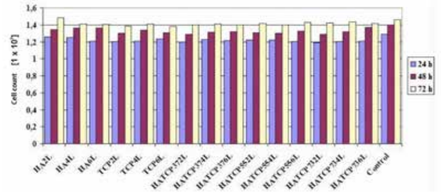


Fig. 3



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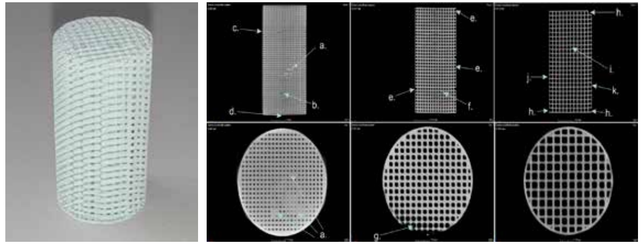


Fig. 2

Fig. 5

LOWERING OF FORMALDEHYDE EMISSION FROM WOOD BASED PANELS BY ENVIRONMENTAL PROGRESSIVE MODIFICATION OF POLYCONDENSATION ADHESIVES WITH BIOPOLYMERS FROM LEATHER WASTE, NATURAL NANOFILLERS, ADDITIVES AND ACTIVATORS

Principal investigator: prof. Ing. Ján Sedliačik, PhD.
Applicant organisation: Faculty of Wood Sciences and Technology, Technical University in Zvolen
Participating organisation: VIPO a.s., Partizánske

Term of solution: 07/2015 – 06/2019
Budget from agency: 249 941 €
Project ID: APVV-14-0506

SUBJECT OF RESEARCH

In woodworking industry, gluing of wood belongs to very important technological operations. It contributes significantly to the improvement of quality of products, but also is the basis for creation of new progressive wood products. In this context, there are the adhesive bonded board materials, such as plywood, blockboard, particleboard and fibreboard, production of which enables to utilise economically the secondary sources of wood raw material. The proper combination of auxiliary substances used in a wood-based product creates a modern ecological material, parameters of which correspond to the demands of the present time. In woodworking industry, the most often used adhesives for wood gluing are polycondensation urea-formaldehyde (UF) resins. Their use is widespread thanks to their relatively low price, high reactivity, easy applicability and transparent joint after hardening process. The great disadvantage is the adhesives' low resistance against water and moisture, and mainly toxicity caused by hydrolysis of hardened resin and subsequent release of formaldehyde from finished products. The current widespread use of products bonded with formaldehyde resins is the reason why formaldehyde has become the integral part of testing of quality of the adhesives and bonded products.

OBJECTIVES OF THE PROJECT

The strategic aims of the project were oriented to the preparation of environmentally friendly wood-based panels with low formaldehyde content and formaldehyde emission and with required mechanical and physical parameters. This objective was achieved by modification of polycondensation adhesive mixtures with functional biopolymers from leather waste, natural mineral fillers, ligno-cellulosic additives and chemical activators.

ACHIEVED RESULTS

The most effective biopolymers for these applications were collagen and keratin hydrolysates. The formaldehyde content in UF cured adhesive compositions decreased in all tested formulations, and this effect was enhancing with the increasing concentration of biopolymers. For both biopolymers, the 20% decrease in formaldehyde content was recorded, from 0.35 mg fd/g (reference sample) to 0.28 mg fd/g. The research continued by testing these biopolymers with addition of other activators based on glutaraldehyde and its pre-condensates with urea. The most significant reduction of formaldehyde emission up to 45% was achieved by the addition of 2.5% methylol pre-condensate and 5% keratin to the UF standard. Modification of UF adhesives with the amino acids cysteine and cystine, prepared from sheep's wool, resulted in a decrease in formaldehyde up to 44% when 0.5% of cysteine was added. All samples have a great potential for use as the formaldehyde scavengers. After evaluating the results, the following transformation of knowledge into the industrial practice in production of particleboard has begun in the company Kronospan Zvolen.
In another part of the research, the use of lignocellulosic waste fibres was tested. Four main types of fibres were applied: primary wood fibre sludge from the production of fibreboard, sludge from primary cellulose from the production of pulp, fibre sludge from waste paper, and disintegrated beech bark. The use of these types of fibres in the UF resin compositions reduced formaldehyde emissions from the plywood by 27, 25, 19 resp. 42%.
In the research of specific natural additives for applications into UF adhesives, the physical and chemical properties of three mineral nanoporous sorbents: zeolite, montmorillonite and palygorskite were tested. The sorbents were activated by the action of heat, pulsed magnetic field or microwave field. Microwave activation has been found to be the most effective method of activation. After the activation of sorbents in the microwave field, montmorillonite increases its adsorption capacity 8.7 times, zeolite about 5 times and palygorskite 4.2 times.

The results of experiments showed that the activation of sorbents significantly increases their adsorption capacity for formaldehyde, which ensures lower emissions and lower content of free formaldehyde up to 22% in the adhesive and in the glued product, while the quality of the glued board is standard.

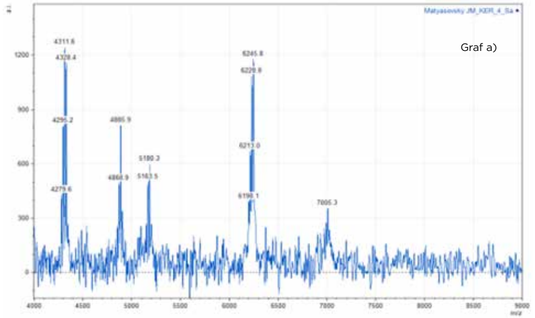
BENEFITS FOR PRACTISE

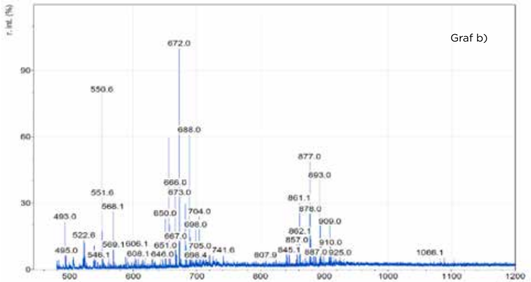
The result of the project is the knowledge about the possibilities to use progressive modifiers, biopolymers, natural nanofillers, additives and activators to reduce the free formaldehyde content and formaldehyde emissions from bonded wood-based materials, so that the panels would obtain properties meeting the current and forthcoming European legislation after 2020.

Mass spectrum of collagen and keratin hydrolysates, which most significantly reduced formaldehyde emissions.
Graph a) Sample of collagen prepared by acid hydrolysis with minimal degree of deamination (decrease of isoelectric point from 7.5 to 6.9 with distribution of molecular weight within 4300-7000 Da.
Graph b) Sample of keratin with wide distribution of mole weight within 500-900 Da, with the highest share 550, 670 Da and has significantly lower molecular weight as a sample of collagen.

Fig. 1 / Antioxidant efficiency in the PEG matrix as a function of temperature.

Fig. 2 / The most significant decrease in fd emission up to 39% was achieved with modifications of MOD-I + Cysteine = 0.223 (mg/l) and MOD-II + Cysteine = 0.225 (mg/l) according to EN ISO 12460-4.





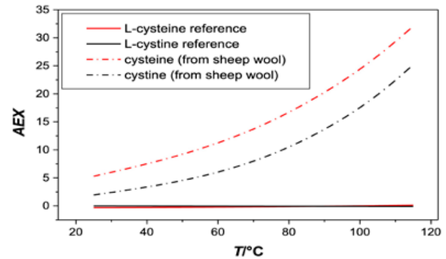


Fig. 1

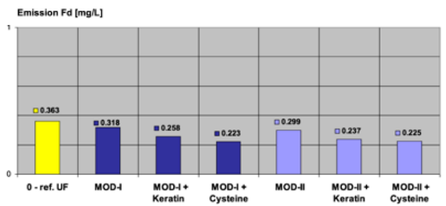


Fig. 2

The project has achieved 4 patents and 28 CC publications 5 of them in the prestigious "The Journal of the American Leather Chemists Association".

ULTRA LIGHT COMPOSITE SUPERCONDUCTOR BASED ON MG, B, TI AND AL

Principal investigator: Ing. Pavol Kováč, DrSc.
Applicant organisation: Institute of Electrical Engineering of SAS

Term of solution: 7/2015 – 12/2018
Budget from agency: 246 805 €
Project ID: APVV-14-0522

SUBJECT OF RESEARCH

The theme of this research was to make extra-light superconducting wire applicable for windings generating strong magnetic fields at the temperature close to 20 K which is built on the idea to combine the lightest superconducting compound MgB_2 having the specific weight of 2.55 gcm^{-3} with very light metallic elements: titanium diffusion barrier (4.5 gcm^{-3}) and aluminium outer sheath (2.7 gcm^{-3}).

OBJECTIVES OF THE PROJECT

The of research is to have extra-light MgB_2 superconducting wire with high current densities at external magnetic 0 – 5 T, strain tolerance to mechanical stresses and also low AC losses at frequencies 1 – 100 Hz. For reaching these aims the method of magnesium infiltration and diffusion into dense boron powder with subsequent creation of inter-metallic MgB_2 phase around 650°C has been selected.

ACHIEVED RESULTS

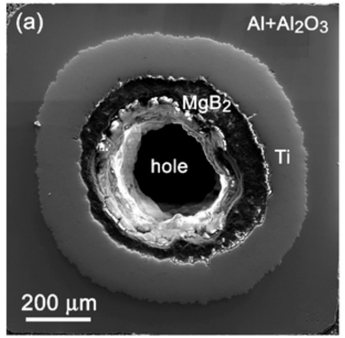
The results follow our many year's experiences with filamentary superconductors. We have verified experimentally that mostly used metallic material used for diffusion barrier Nb (8.5 gcm^{-3}) can be replaced by lighter and well formable titanium (4.5 gcm^{-3}), which is not reacting with Mg and B during the final heat treatment. The mechanical softness of pure aluminium did not allow to make composite wire by rolling or drawing. Therefore, constructional material (Al+Al_2O_3) called HITEMAL® developed by the institute of materials of SAS by powder metallurgy has been tested. Extruded Al+Al_2O_3 rods were deformed into wires and characterized mechanically and electrically at room temperature and also at low temperatures and after that used for making of the lightest superconducting MgB_2 wire. The manufacturing process was based on the deformation of central Mg wire surrounded by fine boron powder inside the Ti tube inserted into outer one made of Al+Al_2O_3, which was groove rolled up to the wire size of ~1 mm. Several heat treatment profiles with maximal temperature 646°C (wA), 642°C (wB) and 640°C (wC) were used for wire heat treatment of duration 10-30 min. The highest current densities (10^4 Acm^{-2} at 4.2 K and magnetic field 5.8 T) were measured for annealing at 646.5°C, however the best tolerance of composite to tensile strain has been found for temperature 640°C. Heat treatment at temperatures close to melting one resulted in re-crystallization of Al+Al_2O_3 sheath and consequently the strain tolerance is affected, see Figure. 1.

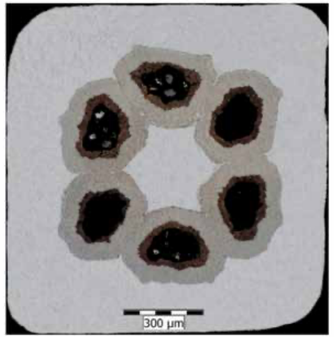
The mentioned above results were stimulating for using of sheaths with different content of Al+Al_2O_3 phase (1.3 – 3.1 vol%) and their application for cabled conductors and multi-core wires with excellent tolerances to tensile stress, see Figure 2.

Al+Al_2O_3 material has worse electrical conductivity in comparison to pure Al and also lowered melting temperature ~652°C. Lowered conductivity of Al+Al_2O_3 offers to reduce the eddy current losses for alternating windings, but lowered melting point makes the final heat treatment more complicated. The interesting advantage of wire with A sheath is a simple possibility to insulate it by the surface oxidation and creation of thin layer (~µm Al_2O_3) withstanding the heat treatments and having good thermal conductivity as well. Such unique insulation has been successfully used for superconducting coil wound of MgB_2/Ti/Al+Al_2O_3 wire on the stainless steel former, see Figure 3. This light coil design has very good insulation and especially very high space (over 90 %), which allows to considerably minimize the volume and mass of winding.

BENEFITS FOR PRACTISE

The obtained results clearly demonstrate the real possibility of production of ultra-light superconducting MgB_2 wire with high current densities and stain tolerances, which allows to design superconducting magnets with small inner diameters of coils wound before final heat treatment. Very high space factor of such winding (over 90 %) allows to generate desired magnetic fields with minimised coils mass. These conductor properties can be utilized for high power wind turbines (over 10 MW), light airborne electro-motors and also for potential space applications, e.g. magneto-spherical plasma propulsion and an active magnetic shielding for long period missions to Mars.





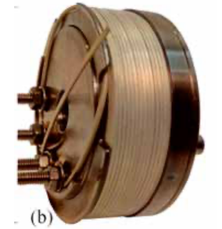


Fig. 3

Fig. 1 / The cross-section of superconducting wire with MgB_2 phase, Ti barrier and Al+Al_2O_3 sheath (left) and effect of tensile strain on the critical currents of wires annealed at temperatures: 646°C (wA), 642°C (wB) and 640°C (wC).

Fig. 2 / The cross-section of 6-core wire of 1.16 x 1.16 mm^2 and its tensile stress tolerances at room temperature (300 K) and liquid He temperature (4.2 K).

Fig. 3. / Stainless steel former (a), coil wound of Mg/B/Ti/Al+Al_2O_3 wire insulated by thin aluminium oxide (b) and heat treated coil with MgB_2 phase (c).

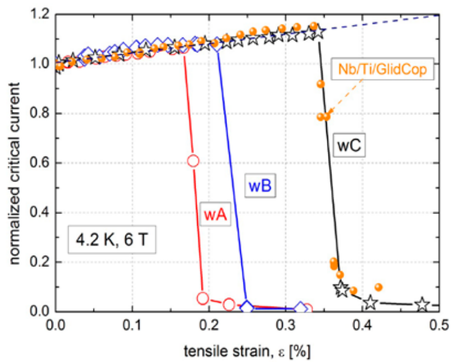


Fig. 1

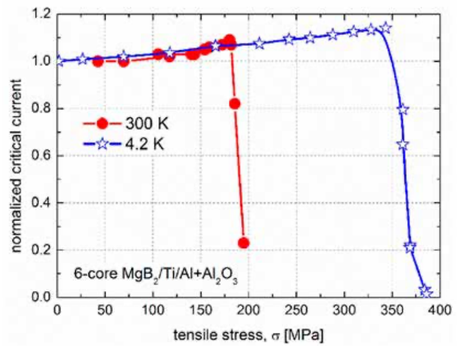


Fig. 2

PROCESSING OF INDUSTRIAL WASTES WITH THE AIM TO OBTAIN ZINC, TIN AND LEAD – BASED MARKETABLE PRODUCTS

Principal investigator: prof. Ing. Tomáš Havlik, DrSc.
Applicant organisation: Technical university of Kosice, Faculty of materials, metallurgy and recycling

Term of solution: 7/2015 – 6/2019
Budget from agency: 214 204 €
Project ID: APVV-14-0591

SUBJECT OF RESEARCH

The research objective was the development of recycling processes for industrial wastes containing zinc, tin and lead and recovery of marketable products based on Zn, Sn and Pb.

OBJECTIVES OF THE PROJECT

The project goals were specified as follows:

1. Proposal, development and testing processes/know-how for hydrometallurgical treatment of selected industrial wastes containing Zn, Pb a Sn on laboratory scale;
2. Construction of pilot-scale line for hydrometallurgical treatment of above mentioned industrial wastes;
3. Testing of proposed processes on pilot plant scale;
4. Recovery of marketable products based on metals Zn, Sn a Pb.

For the applied research project APVV-14-0591 after foregoing analysis of different industrial wastes with the content of Zn, Sn and Pb available at Slovak market three types of wastes were selected for the experimental study, namely: a) electric arc furnace (EAF) dust from steel production with the content of Zn; b) converter dust from copper production containing Pb, Sn and c) tin sludge from steel plating. Mentioned wastes belong to hazardous wastes but at the same time they are deficient and valuable source of secondary metals and raw materials. The intention of the project was in the harmony with the EU and national waste economy priorities and initiatives for critical raw materials. Those initiatives encourage and support increasing level of metals and materials recycling, prefer recycling of hazardous wastes and reduce their disposal and decrease of the EU dependency on raw materials import.

ACHIEVED RESULTS

At first, by laboratory scale experimental investigation, the significant process parameters of proposed hydrometallurgical methods of recovery of metal/compounds for selected wastes were adjusted and optimized. For the research a sophisticated tools and methodics have been applied including thermodynamic calculations, software and analytical innovative solutions. After completion of the pilot plant line the pilot plant scale test with selected wastes have been performed. Outputs from those pilot plant tests represented marketable products based on ZnO, $ZnSO_4xH_2O$, Sn and Pb concentrate. Proposed verified technologies and products (ZnO a $ZnSO_4.7H_2O$) have been presented and discussed with industrial partner (Železiarne Podbrezová, a.s.) and other potential customers with positive attitude. In the harmony with circular economy principles the attention was paid also to the waste water and spent leaching agents in order to reduce environmental impacts and improve material and economy balance. The complex regeneration methods for waste waters and leaching media was developed and applied in the pilot plant line. Based on the pilot plant test data the material and economy balance of the recycling process using SuperPro Designer software was calculated. The general outputs represent know-how and verified recycling processes for three industrial wastes on pilot plant scale, functional pilot plant line in operation able to process industrial wastes containing Zn, Sn, Pb. Added value of the project results is that pilot plant line is highly flexible and able to process different kind of solid as well as liquid wastes with metal content (dust, sludge, slags or municipal scrap etc.) and obtain valuable metals or compounds. Unique hydrometallurgical pilot plant line is possible to use for testing and verifying of various recycling processes/technologies with products recovery. Within the project 6 scientific paper in journals registered in Current Contents or Scopus database, 1 textbook, 1 audiovisual work (presentation video at Youtube (https://www.youtube.com/watch?v=E5mNMXsDMY0) and Institute website, urt.fmmr.tuke) were published and 2 patent applications are in preparation.

CONTRIBUTION TO THE PRACTICE

1. Developed and on pilot plant scale verified process (know-how) for processing of waste based on Zn, Sn and Pb, exploitable in practice within the frame of SR or EU.
2. Built up of functional flexible pilot plant line, applicable for processing and recycling of various solid or liquid industrial wastes.
3. Outputs – products, recovered by processing of selected waste – EAF dust in constructed pilot plant line (e.g. ZnO a $ZnSO_4.7H_2O$) are on the basis of performed analysis, product presentation and discussion with customers (Železiarne Podbrezová,a.s. and others subjects) commercially utilizable and satisfy a qualitative requirements.
4. Results confirmed that pilot plant line is capable to treat different wastes like sludge, dusts, slags or even municipal waste or scrap with the aim to recover metals or compounds.
5. Added value of the project results is that pilot plant line is suitable to serve as testing line for different processes/technologies verifying and marketable products recovery in broader measures.
6. Results gained by recycling of EAF dust in pilot plant line and economy balance calculation using SuperPro designer software showed that process is from energy and economy point of view effective and return of investments counting at the capacity of 7 000 ton per year around 10 years. By execution of proposed processes in practice the raw materials would be saved and returned back to the market, increased an employment, reduced landfilling at the preserved interesting financial benefits.

Fig. 1

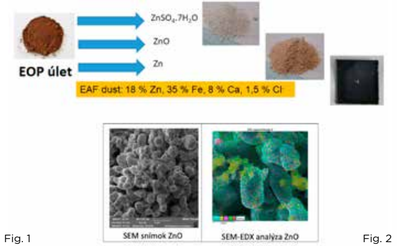


Fig. 2

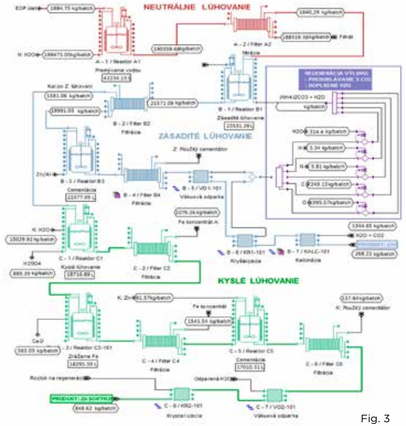


Fig. 3

Fig. 1 / View of pilot plant line for hydrometallurgical processing of waste located at Institute of recycling technologies, Faculty of materials, metallurgy and recycling at the Technical university of Kosice, Slovakia.

Fig. 2 / Treated EOP dust and recovered products achieved by their recycling in hydrometallurgical pilot plant line built up in the frame of the project and details of ZnO product (75 % Zn, 0.32 % Fe).

Fig. 3 / Flowsheet and material balance of developed process of EAF dust recycling simulated by software SuperPro Designer (SPD) based on data achieved from pilot plant tests.

Fig. 4 / Flowsheet of proposed processing of converter Cu dust and recovery of valuable Pb products (Pb or $PbSO_4$); detail of product (Pb metal concentrate).

Fig. 5 / Flowsheet of proposed process for tin sludge treatment and Sn recovery (gained Sn at electrode; SEM scan and SEM-EDX microanalysis of recovered Sn (purity of 97 %).

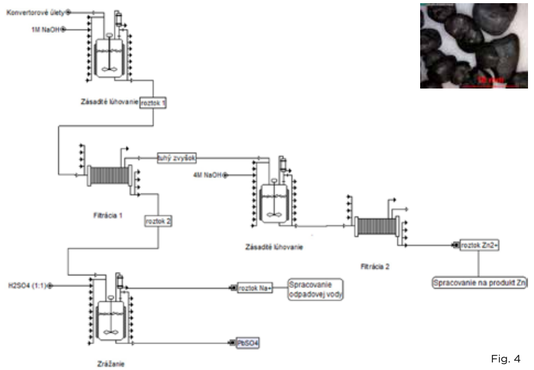


Fig. 4

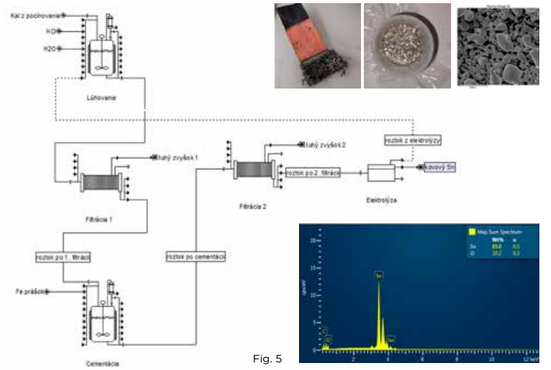


Fig. 5

RECONFIGURABLE LOGISTIC SYSTEM FOR NEW GENERATION OF FACTORY OF THE FUTURE MANUFACTURING SYSTEMS (RLS_FOF)

Principal investigator: prof. Ing. Milan Gregor, PhD.
Applicant organisation: Faculty of Mechanical Engineering, University of Žilina
Term of solution: 7/2015 – 6/2018
Budget from agency: 248 194 €
Project ID: APVV-14-0752

SUBJECT OF RESEARCH

The objectives of the applied research project addressed were oriented towards the field of reconfigurable systems. The developed solution in the project is currently the most progressive global trend, and so far it is addressed by only a small group of leading research sites in the world (University of Chicago – the USA, University of Windsor – Canada, IML FhG Dortmund – SRN). The ambition of the researchers was to design and develop a new practical concept of the reconfigurable logistics system and on prototype verify the possibilities of its deployment in the automotive and electrical industries.

OBJECTIVES OF THE PROJECT

The main objective of the project was to design, create and test a prototype of a low-cost, modular, reconfigurable logistics system for the next generation manufacturing systems for factories of the future.
The aim was to develop a solution that can be rapidly adapted through reconfiguration to the new requirements for the functionality and capacity of the logistics system and ensure its direct integration with the interoperative transport system and the interoperative handling system. Such solutions have not yet been developed, and solutions are needed, particularly in sectors where there is high competition, such as the electrical and automotive industries.

ACHIEVED RESULTS

We consider the creation of models and prototypes for the RLS_FoF: – RMS data model; – Set of 3D models of individual agents; – Simulation model for MAS; – Mobile Robotic System – MRS; – Modular Platform – MP; – Workspace for MRS and MP.
As a part of the research project solution, a prototype of a new multiagent control system (MAS) has been developed that, using agents, can plan MRS and MAP activities (virtual path plan), using genetic algorithms to dynamically allocate segments of the required pathway and dynamically allocate tasks to individual agents through the MAS core and control the current state of their performance. Such a solution makes it possible to distribute direct control to individual, autonomous mobile robotic systems, which can independently react to changes in the environment and coordinate their activities with other entities in the production system.
To simulate developed solution, multiagent control system modules are used, developed as part of a research project solution that uses the services of the Ella® software platform.
The results achieved include a new concept of adaptive logistics systems (ALS). The methodology for designing such systems includes a module for determining the number of available configurations and a reasonably extensive system for the capacity calculation of the number of relevant clusters.

BENEFITS FOR PRACTISE

The output of the research solution is original solution that originated is based on the needs of the industry. It is planned to be used by domestic industrial producers, with the primary objective of the researchers, in cooperation with the Central European Institute of Technology, a proposed solution to export as domestic know-how to the world.
Future manufacturing and its organization will gradually approach more of the functioning of living organisms than mechanical machines. Today's "hard" lines will be replaced by a set of autonomous workplaces, for which the functions of inter-operational transport and handling will be provided by mobile robotic systems. Such a solution is currently referred to as the competent islands.

Fig. 1

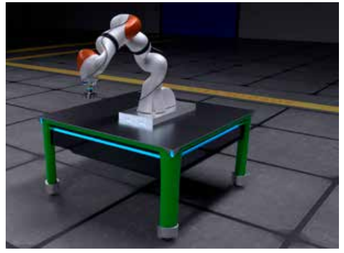


Fig. 2


Fig. 3

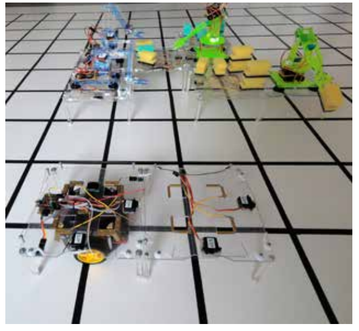


Fig. 4


Fig. 5

Fig. 1 / Simulation of multi-agent control of mobile robots
Fig. 2 / MRS and MAP integration model
Fig. 3 / Model scene RLS_FoF – 3D
Fig. 4 / Model scene RLS_FoF – prototypes
Fig. 5 / Mobile automatic platform MAP – robotic arm and CEIT AGV

RESEARCH AND DEVELOPMENT OF A PLATFORM OF CURRENT SOURCE POWER SUPPLIES FEEDING SUPERCONDUCTING PARTICLE ACCELERATOR MAGNETS WITH DYNAMIC MODE OF OPERATION, WITH POWER FACTOR CORRECTION AND WITH ENERGY REGENERATION TO THE DISTRIBUTION NETWORK

Principal investigator: Ing. Gabriel Kácsor, PhD.
Applicant organisation: EVPÚ, j. s. c. (Electrotechnical Research and Projecting Company)

Term of solution: 7/2015 – 5/2018
Budget from agency: 250 000 €
Project ID: APVV-14-0856

SUBJECT OF RESEARCH

Modern particle accelerators require extremely stable, accurate and energy-efficient power supplies to feed their superconducting magnets. The project was therefore focused on research of a new concept and control algorithms of a power supply for this application area, including the development of a new topology based on modern IGBT modules and control algorithms to achieve extremely strict requirements for accuracy and stability of the power supply output current. Development of a modular concept with a four-quadrant converter in the input part, which is controlled by space vector modulation, allowed to achieve high power factor and low distortion of electrical waveforms, at the power supply input in PFC rectifier mode. This concept met all the criteria for the power supplies needed to excite the main superconducting magnets of synchrotrons, whose powers are already in the order of megawatts.

OBJECTIVES OF THE PROJECT

The main goal of the project was the development and design of a new modular power supply concept for superconducting magnets of particle accelerators with energy recuperation ability. Other goals of the project were development of prototype of 3-phase 4-quadrant converter module with unity power factor, with space vector modulation control for the input part, development of 1-phase 4-quadrant converter module for output part and development of control structure and control algorithm of the modular system to achieve required output current parameters at the both directions of energy flow. Development of a universal basic unit of the power supply, which enables parallel connection of several units and thus achieving megawatt output power levels and compilation of a prototype for verification of the parameters and properties of the developed concept.

ACHIEVED RESULTS

Research and development of a modular power supply concept with a 4-quadrant input converter topology, with space vector modulation control and with the possibility of energy recuperation to the feeding network has expanded the application possibilities of IGBT technology in current source power supplies even at the highest power levels, with all the advantages of IGBT technology. The result of the project is also a modular power supply prototype for feeding superconducting magnets, with the possibility of parallel connection of several basic power supply units to achieve megawatt output power levels, where thyristor technology has been used. The tests confirmed that the waveforms of the input electrical waveforms show minimal harmonic distortion and a unity power factor, so the power supply has a minimal undesirable effect on the feeding network. The dynamic properties of the output current were verified using a 24-bit AD converter. The measured values of dynamic accuracy of the output current were -0.12A / +0.12A, which are significantly better than the target values ±0.6 A. The eight-hour stability of the output current was measured with a precision multimeter (with a DC voltage sensitivity of 100nV and a basic accuracy of 0.002%). The measured value of long-term stability of the power supply was 45 ppm, while the defined target value was max. 50ppm. The power supply was also tested at real operation conditions in the laboratories of the Joint Institute for Nuclear Research, in Dubna, in the Russian Federation. The measured results and other detailed tests on the developed prototype showed that the developed power supply concept is correct, the power supply can meet all the requirements of particle accelerator superconducting magnets generally used at experimental physics or medical applications.

BENEFITS FOR PRACTISE

A new platform for current source power supplies has been developed, which enables energy recuperation ability. A set of control and regulation algorithms was developed to achieve extremely stringent requirements for the accuracy and stability of the power supply output current, including simulation models for adapting parameters and algorithms in other designs of a similar power supplies with different parameters. Research and development of a new modern power supply concept based on IGBT technology, with higher switching frequencies and at high quality input and output currents for the application area of current source power supplies, where high requirements are placed on stability and accuracy of output current significantly contributed to research results in this application area on a global scale.

Fig. 1 / 3D model of the developed 3-phase 4Q PFC module.

Fig. 2 / Photograph of the developed 3-phase 4Q PFC module during the commissioning.

Fig. 3 / Photograph of the PS600-80D prototype power supply during testing, output voltage 80V, output current 600A, dynamic operation mode.

Fig. 4 / Measured waveforms at the input of the prototype current source PS600-80D, Sin = 47kVA, mains voltage $u_i(t)$,) primary current of transformer $i_{TR0}(t)$, input current of 3p4Q converter $i_{4Q}(t)$.

Fig. 5 / Measured dynamic mode accuracy of output current on the prototype, at L=50mH, 10V - 600A, desired current $i_{DEM(t)}$, Output current $i_{OUT(t)}$ overlapped waveforms in the upper part, (Δ) $i_{DIF2(t)} = i_{OUT(t)} - i_{DEM(t)}$, Dynamic accuracy error: -2mV / +2mV < ±10mV.

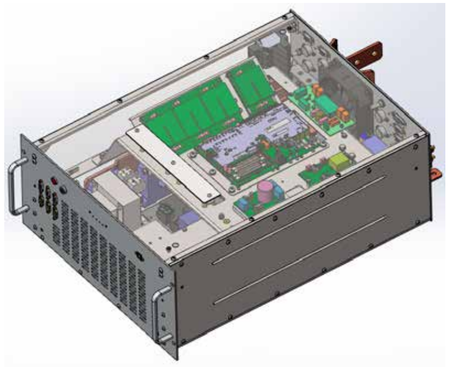
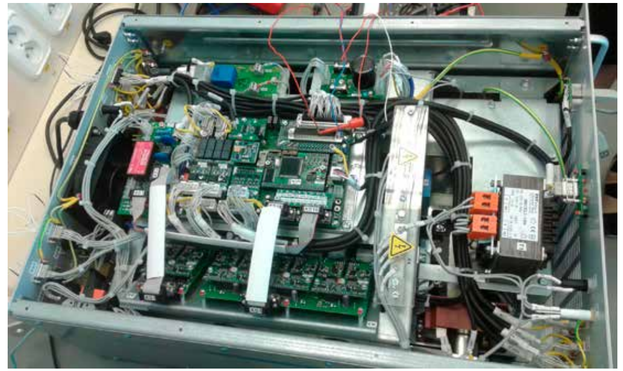


Fig. 1



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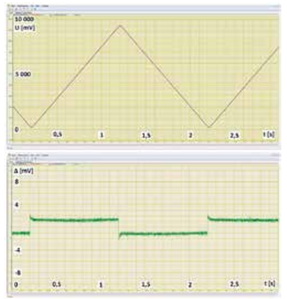

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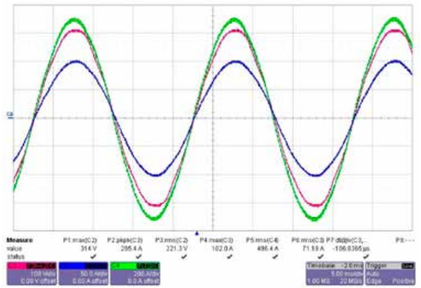


Fig. 4

Fig. 3

RESEARCH OF WELDABILITY OF MODERN PRESSURE-CAST ALUMINUM AND MAGNESIUM ALLOYS BY ELECTRON BEAM AND LASER

Principal investigator: Ing. František Kolenič, PhD.
Applicant organisation: PRVÁ ZVÁRAČSKÁ, a. s.
Term of solution: 7/2015 – 12/2018
Budget from agency: 249 334 €
Project ID: APVV-14-0871

SUBJECT OF RESEARCH

The subject of the project was the research of the weldability of modern pressure-cast aluminium and magnesium alloys by concentrated energy sources such as laser and electron beam. Energy density of laser and electron beam at the focus reaches the values of 10^8 W/cm^2 and thus creates unique conditions for production of demanding weld joints. From the wide range of aluminium alloys, the following were selected for the weldability research: samples of non-hardenable aluminium alloys of the class Al – Mg (AW 5XXX), samples of ternary alloys type Al – Mg – Si of class AW 6XXX that belong among ductile hardenable aluminium alloys, samples of high-strength hardenable aluminium alloys intended for forming of the class Al – Zn – Mg – Cu (AW 7XXX) and samples of aluminium alloys intended for die casting of the class Al – Mg – Si (AC 43XXX). Of magnesium alloys, weldability of Mg – Zn – Al (AZ XX) alloy was researched. These are wrought alloys, alloyed by a combination of zinc and aluminium and they can be deformation-strengthened. Solid-state fibre laser type IPG YLS 5000 with laser technologic head Precitec YW 32 and electron beam welding complex type PZ EB ZH 4 were used during the experiments.

OBJECTIVES OF THE PROJECT

The main project aim was gaining new knowledge regarding the weldability of the selected types of aluminium and magnesium alloys by laser and electron beam. The experiments were focused on the research of the influence of the welded sample production method, their surface conditions and the relevant technologic parameters of welding on the structural and mechanical properties of the welded joints. The influence of the welding heat cycle gradient and technological oscillation of the electron beam to the mechanism of the creation of pores, voids and creation of hot cracks in welded joints was researched as well.

ACHIEVED RESULTS

Excellent results were achieved in the research of electron beam welding of pressure-cast aluminium alloys. The proposed original technologic practices allow to significantly reduce the creation of pores and passable defect in welded joints. Sophisticated dynamic electron beam oscillation, welding current pulsing is applied, along with the application of multiple beam passes over the welded joint is applied in the process of making butt welds, end welds and T-joint welds. While researching laser welding of pressure-cast aluminium and magnesium alloys, knowledge of the influence of process parameters on forming of hot cracks, excessive poring and passable cracks in welded joints was gained. The experiments also included the research of the welding heat gradient on the welded joint properties. The possibility of simultaneous pre-heating/subsequent heating of the welded material using arc technology TIG was verified. This application allows achieving high welding speed up to 100 mm.s^{-1}, while maintaining the final quality of the welds. The results show that laser welding is capable of achieving acceptable quality of welded joints of AZ31 type magnesium alloys. While welding formed aluminium alloys by electron beam, focus was paid to minimization of the occurrence of hot cracks. Methods and practices that allow successful suppression of the hot cracking have been proposed.
To reduce the occurrence of hot cracks, modification of the welding metal crystallization mode through suitable selection of welding parameters and the verified method of suppressing the formation of hot cracks by creating suitable thermal stress fields, e.g. using a split electron beam, was used.

BENEFITS FOR PRACTISE

Verified new technologic welding practices that are the direct outputs of the project find adequate application in the industrial practice. The most important and economically most effective contribution is the welding procedure of heat exchangers from die cast alloy AlSi10Mg (Fe). Welded heat exchangers have been integrated into a wide array of modern electric and hybrid cars. Another important project output is the fact that based on this procedure new conception of the highly productive electron beam machine for welding of heat exchangers has been designed with the annual production more than several hundred thousand pieces.

Fig. 1

Fig. 3

Fig. 1 / The experimental laser work station with the IPG YLS 5000 fibre laser for welding aluminium and magnesium alloys.

Fig. 2 / Macrostructure of welded joint of aluminum alloy EN AW 5754, electron beam welding.

Fig. 3 / The experimental electron beam welding work station type PZ EZ ZH 4 for the research of aluminium and magnesium alloy.

Fig. 4/ High-productivity electron beam welding equipment, for welding heat exchangers, designed on the basis of project results.

Fig. 5 / Macrostructure of butt weld joint of aluminum alloy AlSi10Mg (Fe).

Fig. 4

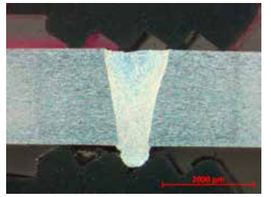


Fig. 2

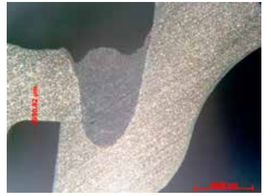


Fig. 5

NONINVASIVE LOCALIZATION OF ECTOPIC ARRHYTHMIAS OF HEART VENTRICLES USING ECG MAPPING AND ITS USE FOR CAUSAL THERAPY

Principal investigator: doc. Ing. Milan Tyšler, CSc.
Applicant organisation: Institute of Measurement Science of the Slovak Academy of Sciences
Participating organisation: National Institute of Cardiovascular Diseases

Term of solution: 7/2015 – 12/2018
Budget from agency: 249 967 €
Project ID: APVV-14-0875

SUBJECT OF RESEARCH

The project focused on the non-invasive localization of areas of the heart in which ventricular arrhythmias occur. These can be caused by conduction disturbances or structural changes in the myocardium and can lead to decreased pumping function and symptoms of heart failure. If pharmacological treatment is not effective, therapeutic intervention is required based on catheter radiofrequency ablation of the arrhythmogenic substrate. However, this requires its exact localization. In conventional therapeutic procedures, this site is sought during the procedure by means of an intracardiac catheter under fluoroscopic control or by means of intracardiac mapping. With the increasing availability of tomographic examinations, procedures are currently being sought to determine the site of the procedure in a non-invasive manner, before it begins.

OBJECTIVES OF THE PROJECT

The main goal of the project was to design and verify the accuracy and robustness of the method for non-invasive localization of areas of the heart in which abnormal ventricular activation occurs. The method is based on multichannel measurement of surface ECGs and an individual model of the patient's torso obtained from a tomographic image. The location in the heart that is the source of the arrhythmia must be calculated using mathematical modeling of the electric field generated by some local source at that location. Other goals included the development of a suitable ECG measurement system and the solution of software for the processing of ECG and tomographic data.

ACHIEVED RESULTS

The project proposed a method for localization of an arrhythmogenic substrate in the heart by solving the inverse problem of electrocardiology using a dipole model of the cardiac electric generator. The method was compared with other approaches in the framework of international cooperation and it was confirmed on simulated and real data that it gives results in good agreement with methods based on other models.

Based on the evaluation of the accuracy, reliability and practical applicability of the method, it was found that it is necessary to measure at least 64, but optimally 96 to 128 ECG leads on the whole chest. The ProCardio 8 measuring system was developed and methods for ECG signal processing, calculation of surface potential distribution and solution of the inverse problem were implemented in its software.

The influence of the used torso model on the inverse solution was investigated. Homogeneous models gave more stable results, while inhomogeneous models (taking into account the different electrical properties of internal organs) should be applied to check the correctness of the solution. To create a chest and heart model from a CT scan, the commercial TomoCon tomographic software was extended to include semi-automatic segmentation of the torso, lungs, and heart surfaces and to identify ECG electrode positions. The exact combination of heart geometries obtained from CT and from the intracardiac catheter of the systems used in the electrophysiology laboratory (Carto or NavX) has proved to be problematic. Differences in some segments of the heart can reach up to 20 mm and thus limit the possibility of accurate localization.

To verify the proposed method, 55 patients were examined, of whom 24 patients underwent ablation and were evaluated. The estimated accuracy of the arrhythmogenic substrate localization was 2 to 24 mm and proves to be sufficiently accurate and robust for the given target. In several patients, the dispersion of the results obtained from different ECG cycles or the resulting localization error were larger and the method should be supplemented to signal such cases.

BENEFITS FOR PRACTISE

The main benefit of the project is a practically applicable method enabling non-invasive finding of the source of ectopic ventricular complexes before the ablation procedure in the electrophysiological laboratory. This allows better planning of the course of therapy, shortening the time of invasive intervention and reducing the burden on the patient and staff associated with exposure to X-rays. Another benefit is the design of the examination procedure using ECG mapping and thoracic CT imaging and the materialization of a special multi-channel ECG measurement system.

During the project, the method was verified and evaluated at the co-research facility – NÚSCH in Bratislava, where measurements were performed on a group of 37 selected patients, in 14 of them ablation was applied. Another 18 patients were measured at the Královské Vinohrady Hospital in Prague, 10 of whom underwent ablation. In these, it was possible to verify the accuracy of the results of the proposed non-invasive method – the agreement of non-invasive and invasive localization of the source of ectopic ventricular complexes. Examination of patients and evaluation of the method continues after the end of the project and the aim is to obtain a more extensive set of data for its clinical evaluation.

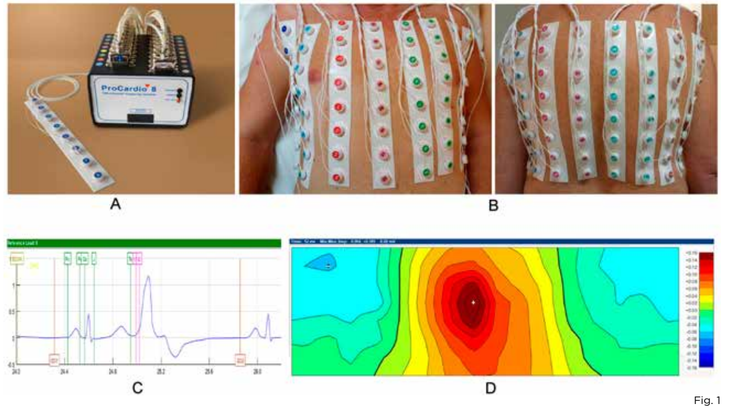


Fig. 1

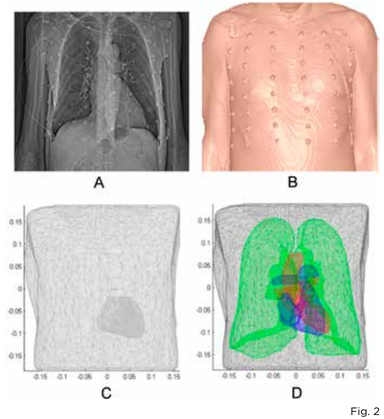


Fig. 2

Fig. 3

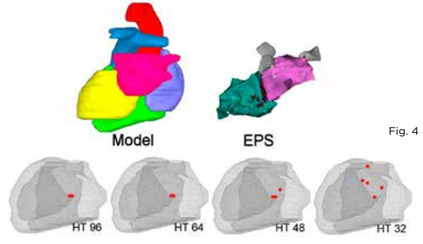


Fig. 4

Fig. 1 / Multichannel ECG measurement using the developed ProCardio 8 system (A) with 128 ECG electrodes placed on the chest (B). During ECG processing, the initial extrasystole time interval (C – points marked in purple) is identified and maps of body surface potential distribution in this interval are calculated (D). The left half of the map represents the front of the chest, the right half represents the back.

Fig. 2 / Tomographic imaging of the patient's chest with ECG electrodes loaded (A) is used to determine the exact positions of the ECG electrodes (B) and to create a homogeneous (C) and inhomogeneous (D) model of the chest and heart.

Fig. 3 / Example of localization of the initial area of arrhythmia in the right ventricular outflow tract (RVOT) in a patient of NÚSCH in Bratislava looking at the heart antero-lateral from the left. Intracardiac electroanatomical mapping (EPS) using the NavX system identified the area in the antero-lateral part of the RVOT. Non-invasive localization using 128 ECG leads and a homogeneous (HT) and inhomogeneous (IT) torso model correctly identified the source of the arrhythmia in the RVOT but more laterally to the left. When using the IT model, the variance of the results obtained from the selected 10 extrasystoles was higher than when using the HT model.

Fig. 4 / Results of localization of the source of arrhythmia in the basal inferior region of the left ventricle in a patient of the Královské Vinohrady hospital in Prague when looking at the heart from behind (posterior). The left ventricle is marked in yellow in the CT model (Model), in the output from the Carto intracardiac mapping system in the electrophysiology laboratory (EPS) in green. The sites of successful ablation (marked in red) were in the basal inferior part of the left ventricle. The results of the inverse solution with a homogeneous chest model (HT) obtained from selected 5 extrasystoles and using different numbers of ECG leads are at the bottom of the figure. Using 96 leads, all results were correctly in the basal inferior part of the left ventricle. Using a smaller number of 64, 48 and 32 leads, the results gradually deteriorated and for 32 leads the accuracy of the solution was already insufficient.

ECONOMIC PREPARATION OF MAGNESIUM HYDRIDE POWDER FROM MOLTEN MAGNESIUM

Principal investigator: Dr. Ing. František Simančík
Applicant organisation: Institute of Materials and Machine Mechanics of the Slovak Academy of Sciences
Participating organisation: Institute of Physics of the Slovak Academy of Sciences

Term of solution: 7/2015 – 9/2018
Budget from agency: 241 770 €
Project ID: APVV-14-0934

SUBJECT OF RESEARCH

Hydrogen is considered an ideal energy carrier for both mobile and stationary applications, which minimizes adverse effects on the environment and reduces dependence on oil and natural gas imports. Due to its low density, it is practically stored either at high pressure (- 70 MPa) or in a liquefied cryogenic state. Both methods are very energy and financially demanding. However, a small hydrogen atom also allows it to be stored in the free spaces of the crystal lattice of suitable metals, so that it can be stored safely and for a long time at normal ambient temperature and pressure (Fig. 1). Magnesium, which forms magnesium hydride MgH_2 when saturated with hydrogen, with a theoretically possible content of up to 7.7% by weight of hydrogen, which represents almost 9 MJ of hydrogen energy stored in 1 kg of hydride, appears to be very promising for this purpose. Hydrogen can be dissolved in magnesium at a pressure of 10 bar, which is the typical outlet pressure of the electrolyser, and released at a pressure of 2 bar, which is the inlet pressure of the fuel cell turbine.
However, the preparation of MgH_2 is relatively complicated and expensive due to the formation of a passivation layer on the surface of magnesium (impermeable to hydrogen even at a thickness of ~ 30 nm), as it requires intensive mechanical grinding of Mg powder with the addition of various elements (Ti, Fe, Cr, V) in order to disrupt passivated surfaces and create suitable pathways in the microstructure for the diffusion of hydrogen to the depth of the material. Technological limits (material is milled for more than 10 hours, the amount of Mg in one batch is limited) significantly increase the price of magnesium hydride and thus prevent its wider applicability in practice.

OBJECTIVES OF THE PROJECT

The aim of the basic research project was therefore to explore alternative processes for the production of magnesium hydride, which would allow its economic preparation in large quantities required practically. Two fundamentally different approaches were examined. The first consisted in the preparation of a rapidly solidified strips of alloyed Mg alloy, in the structure of which a suitable alloying element creates diffusion paths for hydrogen to Mg grains which are not larger than 100 nm. The strips can be produced in large quantities in a relatively simple manner and at low cost by means of known technologies for casting on a rotating cooled disk or the like. The IP SAS was responsible for this part of the project. The second method consisted in the preparation of MgH_2 from Mg vapors which, when condensed under hydrogen pressure, form solid particles directly in the form of MgH_2 (the "bottom-up" method, when active hydrogen acts on the surface of just condensing Mg atoms). The IMMS SAS was responsible for this part of the project.

ACHIEVED RESULTS

The thermodynamic and kinetic principles of Mg hydrogenation as well as the influence of additive elements and morphological and structural effects on it were determined in the project. Model compositions of alloys were proposed, which could be effective in the subsequent process of hydrogen storage (Fig. 2). In parallel, a new economically undemanding method for the preparation of MgH_2 powders directly from magnesium vapors was experimentally tested, which succeeded to produce extremely fine powders with a high hydrogen content at the level of 30% of the theoretical value. In addition, the project tested several alternative technological processes for the processing of Mg powders after the release of hydrogen. As a by-product, a new BIACOM® material for the production of dental implants has been developed that consists of the extruded mixture of Ti and Mg powders, in which magnesium forms a biodegradable component in the form of fine mutually contacted fibers. The empty spaces remaining from biologically dissolved Mg fibers improve then mechanical compatibility of implant with the bone as well as the bone integration into the implant (Fig. 3). The concrete result of the project are 3 independent patent applications and a total of 5 impacted publications.

BENEFITS FOR PRACTISE

The proposed technology of storing hydrogen in metallic magnesium has great potential for practical application because it does not require energy-intensive processes and is highly productive with the ability to prepare hydride as an intermediate product directly from molten magnesium, while temporarily storing the required amount of hydrogen produced e.g. from excess electricity (Fig. 4). After releasing hydrogen at a suitable time to supply the necessary energy, Mg powder remains available, which can be advantageously used in chemical or engineering industry. One of the possible applications is a newly developed biocompatible material suitable for dental implants, which is currently being tested for practical use.

Fig. 1 / Crystal structure of magnesium hydride, hydrogen atoms are shown in green (source Ben Mills https://commons.wikimedia.org/w/index.php?curid=4576078)

Fig. 2 / X – ray diffraction profiles of selected hydrogenated strips and magnesium hydride.

Fig. 3 / 3D model and macroscopic image of BIACOM® dental implant with detail of its surface.

Fig. 4 / The combination of an electrolyser, a magnesium-based hydrogen storage tank, a fuel cell or a hydrogen-burning engine creates an ideal scheme for efficient use of instable green energy (source McPhy Energy S.A.).

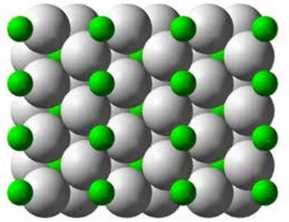
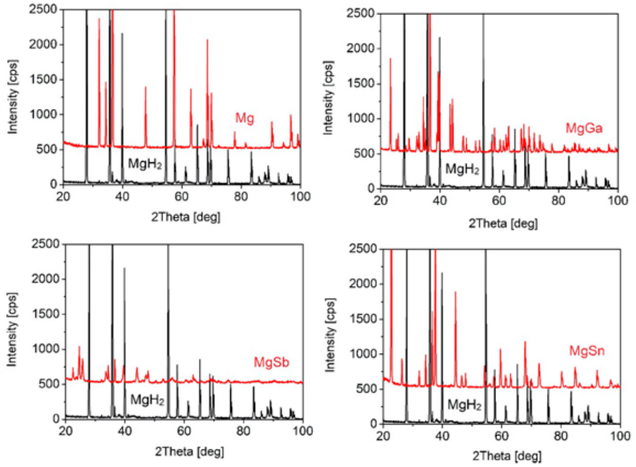


Fig. 1



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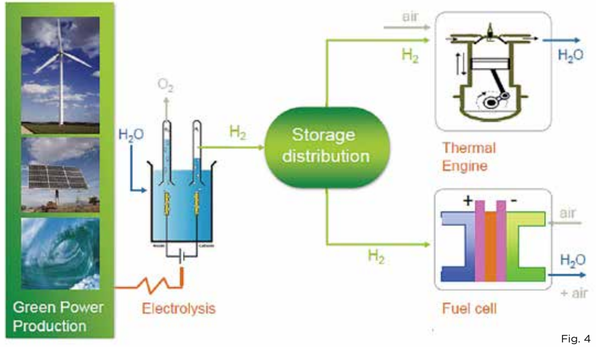


Fig. 4

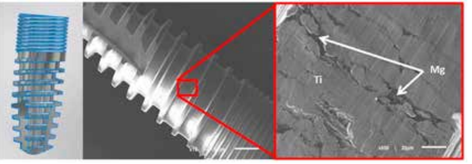


Fig. 3

MEDICAL SCIENCES

NEW BIOMARKERS OF PREMOTOR PARKINSON'S DISEASE

Principal investigator: prof. MUDr. Zuzana Gdovinová, CSc., FESO, FEAN
Applicant organisation: P. J. Šafárik University Košice, Faculty of Medicine
Term of solution: 7/2015 – 6/2019
Budget from agency: 249 915 €
Project ID: APVV-14-0415

SUBJECT OF RESEARCH

Diagnosis of Parkinson's disease (PD) is currently possible only after manifestation of typical motor signs, when dopaminergic neurons loss in the substantia nigra reaches at least 60%, and there is also a significant involvement of other neurotransmitter systems. The pathological process itself at the time of current early diagnosis is estimated to last 15-20 years. It is assumed that PD itself does not start primarily in the brain but in most patients in the peripheral nervous system (intestinal, olfactory), from where it gradually spreads to the brain and specific biomarkers could allow the diagnosis of PD in its very early prodromal stages. Most studies to date which examined potential neuroprotective interventions have not yielded significant positive results, largely due to the progression of pathological changes and the low functional reserves of brain structures that are the target of these therapeutic interventions in the current relatively late diagnosis of PD. The identification of sufficiently sensitive and specific biomarkers of the prodromal stage of PD would therefore be of crucial importance.

OBJECTIVES OF THE PROJECT

The project focused on the investigation and characterization of potential clinical, tissue, neurophysiological and imaging biomarkers of premotor stage of Parkinson's disease in a population of neurologically asymptomatic patients with gastrointestinal disorders, which may represent one of the earliest clinical prodromal manifestations of PD. The project set the following sub-objectives – a) to select a cohort of patients with suspected prodromal PD (pPD) for long-term prospective follow-up based on deep phenotyping, b) to determine the prevalence of non-motor risk factors of PD, substantia nigra hyperechogenicity and the presence of REM sleep behavior disorder in neurologically asymptomatic population of patients undergoing routine screening colonoscopy, c) to determine the prevalence and optimal methodology for the determination of pathological aggregates of α-synuclein in the intestinal nervous system in this population, d) to define quality of life and key non-motor clinical manifestations in these patients and also in early motor stages of PD.

ACHIEVED RESULTS

The most important results achieved during the project can be characterized as follows:

- In our pilot works on prodromal PD we focused mainly on gastrointestinal problems and related pathology in diagnostics. We have proved an increased prevalence of pPD disease in a cohort of patients undergoing colonoscopy for gastrointestinal problems with a prevalence of 5%. These patients may represent an enriched cohort useful for screening and enrolling patients for future studies. We also focused on the detection of pathological alpha-synuclein aggregates in the intestinal mucosa as a diagnostic biomarker of pPD.
- Previous work with several immunostaining methodologies has yielded mixed results, using a new immunostaining method with 5G4 a-synuclein antibodies we have achieved the best diagnostic accuracy with independent and blinded evaluation of intestinal biopsies in top pathological laboratories in Europe, with sensitivity and specificity from healthy controls > 80%.
- We coordinated and published the world's largest study on quality of life and its determinants in patients with PD to date, analyzing data from > 3200 patients from 15 countries. We have shown that non-motor manifestations of the disease such as depression, apathy and fatigue have a more significant impact on patients' quality of life than motor manifestations, what is far from being reflected in the volume of research and intervention studies in this area.
- We have identified a mutation in the ZNF142 gene as a new cause of human disease, dominated by extrapyramidal symptoms, cognition and speech impairment.

BENEFITS FOR PRACTISE

We confirmed that patients with gastrointestinal problems represent an enriched cohort for pPD research, with a significantly higher prevalence of pPD compared to the general geriatric population. We have also published the most specific methodology to date for the determination of α-synuclein from in vivo colonic intestinal biopsies. Within genetic diseases, we have identified a new human disease caused by a mutation in the ZNF142 gene, which is a new significant differential-diagnostic entity in patients with dystonia.

Fig. 1 / Immunohistochemical staining of colon biopsies.
(A) Neurofilament immunostaining (SMI-31) depicting nerve fibers and ganglion cells.
(B–D) Dot-like, globular, and thread-like dark brown 5G4 immunoreactive structures (indicated by arrowheads) independent from an overlap with a cell nucleus (areas indicated by arrows are enlarged in the right upper insets). (B, PD subject; C and D, pPD subjects).
(E) Granular immunoreactivity seen in a mast cell.
(F) Yellowish lipopigment is not considered as specific immunoreactivity.
Bar in (A) indicates 15 micrometers for (A), (E), (F) and right upper insets in (B–D); and 50 micrometers for (B–D).

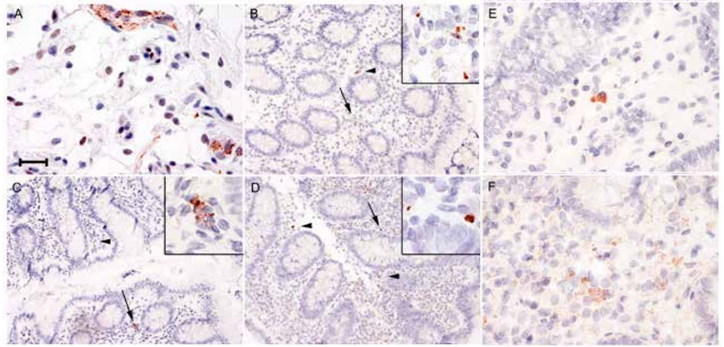


Fig. 1

Fig. 2 / Likely pathogenic variants in ZNF142 are associated with syndromic neurodevelopmental phenotypes in four unrelated pedigrees. (a–d) Pedigrees of four families with syndromic neurodevelopmental symptoms segregating in an autosomal recessive pattern of inheritance. Double lines in pedigrees indicate consanguinity. Filled and unfilled circles/squares represent affected and unaffected individuals respectively, while circle/squares with diagonal lines indicate deceased individuals. Genotypes are represented as either WT/WT (wild type), MX/WT (heterozygous) or MX/MX (homozygous) for individuals with available genotypes. (e–h) Representative chromatograms are shown for each variant. Vertical arrows indicate variant position. (i) Top: schematic of the ZNF142 locus with exons 6–9 harboring likely pathogenic variants. Boxes, exons; black line, introns; white, untranslated regions; blue shaded boxes, coding regions. Bottom: schematic representation of ZNF142 protein; gray rectangles represent predicted C2H2-type domains. Truncating alterations are indicated with black lollipops; missense variants are indicated with salmon-colored lollipops.

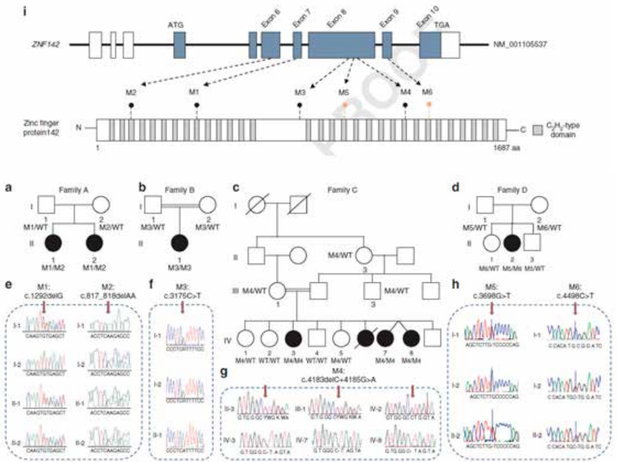


Fig. 2

PREPARATION OF ERYTHROPOIETIN A THERAPEUTIC HORMONE AFFECTING THE PRODUCTION OF RED BLOOD CELLS BY EXPRESSION IN EUKARYOTIC CELL SYSTEM AND ITS FURTHER PURIFICATION

Principal investigator: Ing. Ludovít Škultéty, Dr.Sc.
Applicant organisation: Institute of Virology, Biomedical Research Center of the Slovak Academy of Sciences, Bratislava
Participating organisation: Faculty of Chemical and Food Technology of the Slovak Technical University, Bratislava

Term of solution: 07/2015 – 06/2019
Budget from agency: 249 998 €
Project ID: APVV-14-0474

SUBJECT OF RESEARCH

Human erythropoietin (hEPO) is an essential therapeutic hormone with an antiapoptotic property, which is responsible for controlling the production of red blood cells (erythrocytes). It is mainly used to treat anemia in patients with chronic kidney disease, AIDS, or cancer. The gene encoding hEPO is highly conserved. It is found in a single 5.4 kilobase copy on chromosome 7q11-q22 (Jacobs et al.: Nature 313, 1985, 806-10). After translation, a prohormone is formed, which consists of 193 amino acids. The mature hormone is developed by post-translational modifications, which include the cleavage of 27 amino acids from the N-terminus and an arginyl residue from the C-terminus. The molecular weight of the resulting polypeptide chain is 18 kDa. However, it is usually highly glycosylated. Glycosyl residues make up about 40% of the total molecular weight of hEPO. Therefore, the properly glycosylated molecule has a molecular weight of about 30.4 kDa (Lai et al .: J Biol Chem 261, 1986, 3116-21). The commercial rhEPO preparations are, due to needed glycosylation to maintain biological activity, mostly produces using animal cell lines (especially Chinese hamster ovary cells).

OBJECTIVES OF THE PROJECT

The main aim of the project was to construct a new, highly efficient eukaryotic expression system producing native hEPO and to develop a purification method as a sequence of separation steps based on chromatography and membrane separation processes. Although the production method is known in principle, the whole technology has several critical points that had to be optimized, e.g., preparation of high-producing cells expressing recombinant hEPO (rhEPO), defining the most suitable culture conditions, as well as optimizing purification processes. Therefore, the originality of the project is based on introduction of state-of-the-art molecular biology and separation methods for the production of rhEPO.

ACHIEVED RESULTS

Since hEPO is naturally produced in peritubular cells of the renal cortex, the selection has focused on human renal cell lines. The HEK 293 line appeared to be the most suitable. From this line, the genetic information coding the protein was isolated, which served as a template for the amplification by a polymerase chain reaction. The hEPO gene was then cloned into a eukaryotic expression vector, which was used to transfect (insert the gene into) the HEK 293 cells grown in a serum-free culture medium. Finally, a stable rhEPO-producing cell line (recombinant hEPO) was obtained under geneticin pressure. This system was chosen to ensure the correct post-translational modifications of the protein, similar to the native state. The proportion of rhEPO in this medium achieved 2-2.2% from the total protein content depending on the exact culture conditions.
Subsequently, the development of the purification procedure was launched. Several complexed, albeit seven-step processes are described in the literature, in which various hydrophobic, ion exchange, multimodal adsorbents, or reverse phases are employed. Besides, affinity and size exclusion chromatography were often applied. Some separation procedures also use hydroxyapatite. The system developed by us has only three separation steps, which employ a multimodal resin, chromatography on an adsorbent with phenyl functional groups, and a strong cation exchanger. Especially, the correct choice of multimodal adsorbent ensured the removal of the most contaminating proteins in the first step. A significant advantage of this carrier is a salt resistance allowing direct use of the culture medium for separation without treatment of the raw material (supernatant) by diafiltration. Also, the appropriate arrangement allowed the direct use of the product from the previous in a subsequent separation steps. The developed procedure has resulted in 90 – 95% purity of rhEPO at an overall yield of 13 to 26% (depending on the specific separation conditions).

BENEFITS FOR PRACTISE

The project implementation has increased experimental knowledge, which was passed to younger generation by the researchers during educational activities. Nevertheless, the main benefit for general public is the successful development of a novel procedure for the production and purification of rhEPO (patent application number: 69-2020) that can be used for industrial preparation of this essential therapeutic protein. Thus, the result of the project is an impulse for pharmaceutical industry.

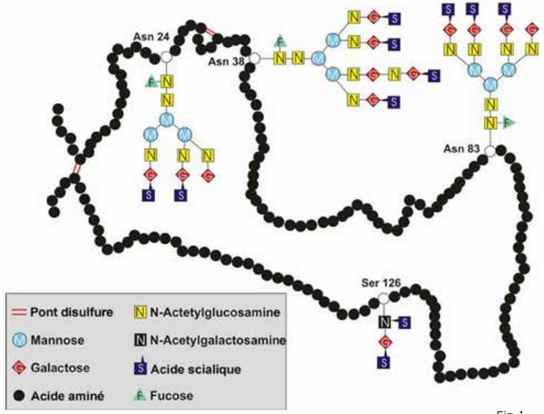
Fig. 1 / Structural formula of ligand Capto MMC ImpRes.

Fig. 2 / Matrix structural formula Capto MMC ImpRes. *Arrows indicate: (A) thiophilic, (B) hydrophobic, (C) hydrogen and (D) electrostatic interactions.*

Fig. 3 / Comparison of Capto MMC chromatography resin's binding capacities for total proteins (A) and EPO (B) at different pH without NaCl (■) and in the presence of 300 mM NaCl (■).

Fig. 4 / Effect of pH and arginine concentration on the recovery of adsorbed EPO.

Fig. 5 / The 2D gel of the main elution fraction after the first purification step on a Capto MMC ImpRes resin. *The labeled spots represent proteins identified by mass spectrometry: 1,2 – isoforms of rhEPO isoforms, 3 – nidogen-1, 4 – nucleoside diphosphate kinase, 5 – peptidyl-prolyl cis-trans isomerase.*



Schematic representation of a human hEPO structure

Fig. 1

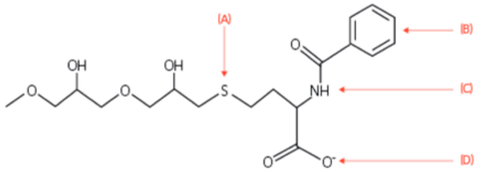
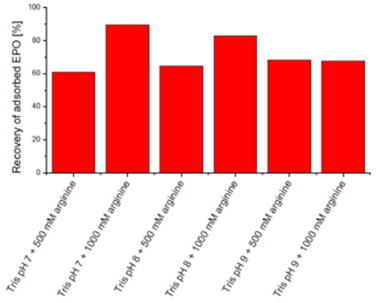


Fig. 2



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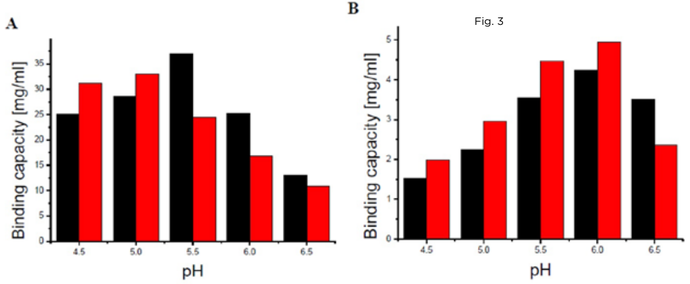


Fig. 3

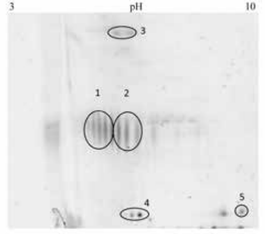


Fig. 5

DEVELOPMENT OF A NEW PEPTIDE SYSTEM FOR DRUG TRANSPORT TO THE BRAIN

Principal investigator: PharmDr. Andrej Kováč, PhD.
Applicant organisation: Institute of Neuroimmunology
of the Slovak Academy of Sciences, Bratislava

Term of solution: 7/2015 – 6/2018
Budget from agency: 244 246 €
Project ID: APVV-14-0547

SUBJECT OF RESEARCH

The blood-brain barrier (BBB) is a highly selective semipermeable border of endothelial cells that protects the brain from harmful substances from the blood. The BBB represents the a bottleneck in brain drug development and is the most critical factor limiting the future growth of neurotherapeutics. Virtually 100% of large-molecule pharmaceutics, including peptides, recombinant proteins, monoclonal antibodies, RNA based drugs, and gene therapies, and 98% of small-molecule drugs do not cross the BBB. Our project was focused on one of the most important parts of brain research, on BBB. Delivery of therapeutics to the brain is often restricted because of the poor transport of these molecules through BBB. To overcome this problem, we developed cell-permeable peptide conjugates that cross the BBB efficiently without compromising its integrity. For this purpose, we used modern methods and procedures from neuroscience, molecular biology, cell biology, proteomics, and analytical chemistry.

OBJECTIVES OF THE PROJECT

The main aims of our project were:

- Identification of transport peptides recognizing primary rat endothelial cells a validation of their transport properties using an animal model
- Identification of specific receptors and transporters mediating peptide transport across BBB

The accomplishment of several objectives fulfilled the project aims. First, we developed a new phage peptide library. At the next step, we used in vitro model of BBB and phage display technology to identify peptides that were able to cross in vitro BBB. Our primary rat BBB model was developed by co-cultivation of primary rat endothelial cells, pericytes, and glial cells. The transport properties of identified peptides displayed on phages were validated by in vivo studies using the Sprague-Dawley animal model and mass spectrometry. Finally, we explored the mechanism involved in BBB transport of identified peptides.

ACHIEVED RESULTS

The results achieved during the project can be summarized as follows:

(1) We created a new peptide phage library using molecular biology and phage display methods.
(2) We set up a platform to measure the passage of potential drug vectors across the blood-brain barrier. The primary rat model of the BBB created by us, consisting of primary rat endothelial cells and mixed glial cultures. This model can also be used in the future in the research of new CNS therapeutics.
(3) Using a cell model of the BBB and a peptide phage library, we identified several transport peptides that selectively recognize primary brain endothelial cells.
(4) We have developed a bioanalytical method for measuring the concentration of identified peptides, which we then used to determine permeability coefficients and select candidate molecules. The permeability obtained for selected peptides was in the same order of magnitude as other known BBB shuttles.
(5) Using high-resolution mass spectrometry in combination with cell experiments, we identified the mechanism of the transport of candidate peptides across the BBB. The results showed that the peptides are internalized and transported by an adsorption mediated transcytosis process.

BENEFITS FOR PRACTISE

The identification of vectors capable of efficiently transporting drugs to the brain across the blood-brain barrier is an important part of modern brain pharmacotherapy research. A pharmacologically active system using peptides, as a vector for drug delivery to the brain has several advantages compared to other systems: simple development, the possibility of modification to increase the pharmacological and pharmaceutical effect.
During the grant assignment, we identified peptides that specifically bind to brain endothelial cells and are efficiently transported across the BBB. Such transport vectors may, in the future, be used to transport drugs and biopharmaceuticals to the brain for the treatment or effective diagnosis of various CNS diseases.

During the project, we published 8 scientific papers in prestigious peer-reviewed journals. The practical benefit of the project was the successful defense of doctoral students and the education of young researchers. The results of the project were presented in the form of a poster or lectures at 11 domestic and international scientific conferences.
Due to the potential of the obtained results in practice, the identified peptides became the subject of a patent application (SK PP24-2019). The data from the project served as a basis for the follow-up project APVV-18-0302, which is currently being addressed at our workplace.

Fig. 1 / Bio-panning experiments. Selection of phages specific for endothelial cells. 12-mer Phage Display Peptide Library was first incubated with neuroblastoma cells to exclude promiscuous binding peptides. The non-bound phages were then screened on primary rat brain endothelial cells. We performed four rounds of bio-panning.

Fig. 2 / In vitro model of the blood-brain barrier. Primary rat brain endothelial cells were cultivated together with mixed glial cells in the Transwell system. After seven days of co-cultivation, the inserts were ready for permeability experiments.

Fig. 3 / The permeability of peptides was assessed using a primary rat in vitro BBB model. Different qualitative and quantitative techniques were used to confirm BBB integrity. The peptide transport to the abluminal compartment was quantified by ultra-high-performance liquid chromatography/mass spectrometry (UHPLC-MS/MS) method.

Fig. 4 / To shed light on the mechanism by which the identified peptides are transported across BBB, we performed internalization assay using primary rat endothelial cells. The biotin-labeled peptides (red) were incubated with endothelial cells stained with laminin specific antibody (green), and the process of internalization was evaluated by confocal microscopy. The results showed that both peptides are effectively internalized by primary endothelial cells.

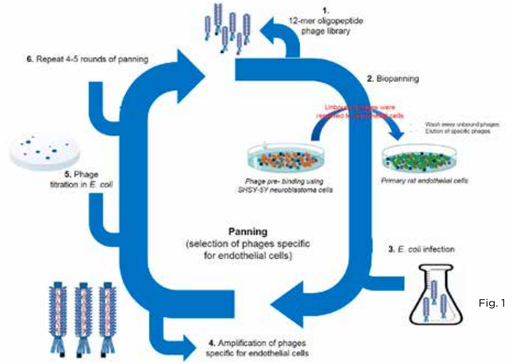


Fig. 1

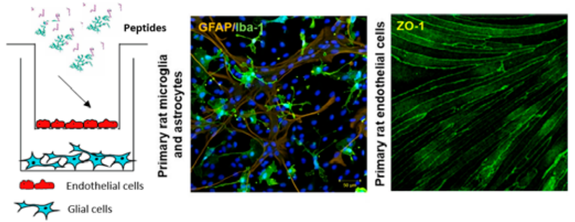


Fig. 2

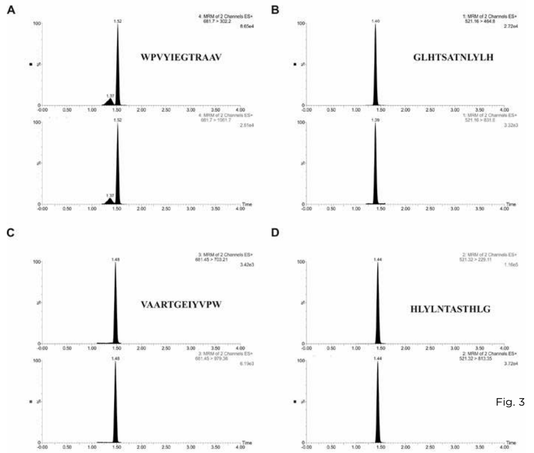


Fig. 3

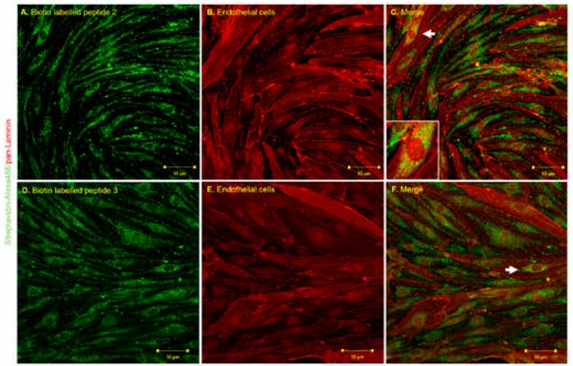


Fig. 4

GALECTINS AS POTENTIAL MODULATORS OF TUMOR/WOUND MICROENVIROMENT

Principal investigator: RNDr. Peter Gál, PhD., MBA
Applicant organisation: East-Slovak Institute of Cardiovascular Diseases, Inc.
Term of solution: 07/2015 – 06/2019
Budget from agency: 194 877 €
Project ID: APVV-14-0731

SUBJECT OF RESEARCH AND OBJECTIVES OF THE PROJECT

Galectins are representatives of endogenous lectins – molecules specifically recognizing distinct sugar motifs. They play an important role in the processes of cell proliferation, differentiation, migration and extracellular matrix formation. Furthermore, galectins are able to transfer cellular signals and to participate in cellular interaction. It has been proven that galectins play an important role in the formation of tumor and/or wound healing microenvironment. This project is focused on studying/comparing biological roles of galectins in wound repair and tumor growth.

ACHIEVED RESULTS

a) Regulation of wound microenvironment – excision and incision wound model in rat

By comparing the healing of excision and the incision wounds, we showed that Gal-1 induces differentiation of fibroblasts into myofibroblasts (Fig. 1) leading to better wound contraction. In contrast, Gal-3 improves organization of collagen fibers (Fig. 1), leading to increased wound tensile strength (Fig. 1).

b) Tumor microenvironment – model of squamous cell carcinoma of the head and neck in human

Fibroblast is the main cell type that produces extracellular matrix (ECM). Since an enormous significance of fibroblasts and ECM in the formation of the tumor and wound microenvironments may be expected, we analyzed the expression profiles of cancer-associated fibroblasts isolated from malignant melanoma (Fib_Mel), basal cell carcinoma (Fib_B5), squamous cell carcinoma (Fib_S4) and skin metastasis of breast cancer compared to healthy fibroblasts isolated from skin following breast reduction surgery (HF/D). The results showed clustering based on the differentiation expression of Fib_Mel, Fib_B5 and Fib_S4 on the one hand and the relative proximity of BCMF and HF/D on the other hand.
Based on analysis all fibroblasts agreed on the expression of 153 genes. 19 genes were unique and could form a common molecular signature of cancer-associated fibroblasts (Fig. 2).
In our experiments, we compared fibroblasts in the insert system (model of an indirect co-culture separated by a membrane) with normal or malignant (FaDu – hypopharyngeal carcinoma) epithelial cells. In those fibroblasts we detected the production of tenascin, fibronectin and galectin-1 (Fig. 3). We have shown that cancer-associated fibroblasts (Fib_S4, SCCF) produce less ECM than normal dermal fibroblasts (HF/D).
The study follows the research of our cooperating laboratory (Zivicova et al. Anticancer Res. 2017;37(5):2275-88). Similarly, we performed expression profiles of squamous cell carcinomas of the head and neck (HNSCC) and compared these data with the margin of surgical resecate (MSR) and normal mucosa (NM) located on the contralateral side of the same patient. We divided patients into two groups based on the expression of tenascin (Ten). Histopathological examination demonstrated that Ten+Fn+Gal-1+ co-expression occurs more frequently in samples of HNSCC (55%) than in NM (9%). Contrary, the Ten-Fn+Gal-1- (45%) and Ten-Fn-Gal-1- (39%) status occurred with higher frequency in NM. In MSRs, different immunophenotypes were distributed rather equally (Ten+Fn+Gal-1+ = 24%; Ten-Fn+Gal-1- = 36%; Ten-Fn-Gal-1- = 33%).
Microarray analysis (Fig. 4) revealed: i) gene expression related to tumor progression in Ten+ tumors and ii) strong up-regulation of genes associated with lipid metabolism in MSR of Ten- tumors.

BENEFITS FOR PRACTISE

Galectin-1 activates myofibroblasts, both in wounds and in tumors. Gal-1 wound treatment accelerates healing and its pharmacological targeting in tumors may increase the efficiency of anticancer therapy. Galectin-3 induces fibrosis leading to increased wound tensile strength.

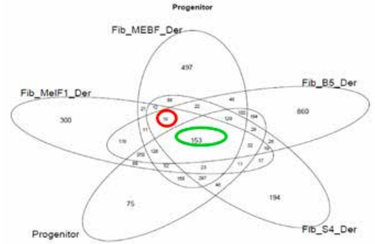


Fig. 2

Fig. 1 / Results from animal experiment of open wound treatment (histological examination of open wounds, VG – Van Gieson, Fibr – fibronectin, SMA – smooth muscle actin) and sutured wounds (wound tensile strength) following Gal-1 and Gal-3 treatment.

Fig. 2 / Venn diagram of overlapping genes in studied fibroblasts.

Fig. 3 / Comparison of ECM production in vitro.

Fig. 4 / Selected genes expression comparison in tenascin expressing (Ten+) / not expressing (Ten-) tumors.

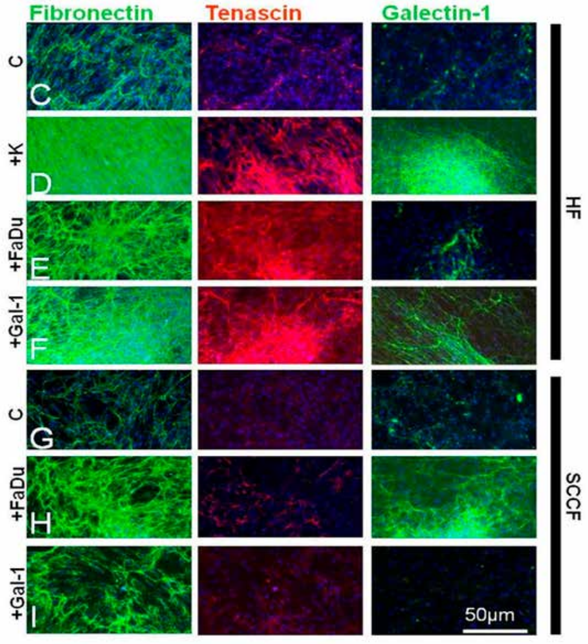


Fig. 3

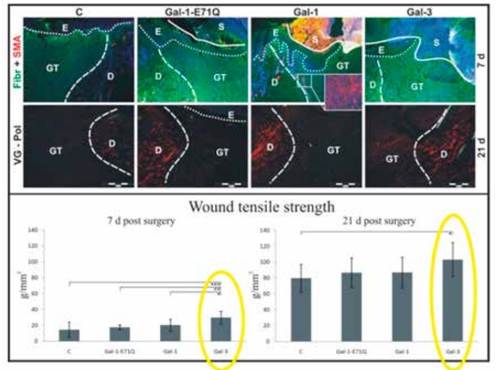


Fig. 1

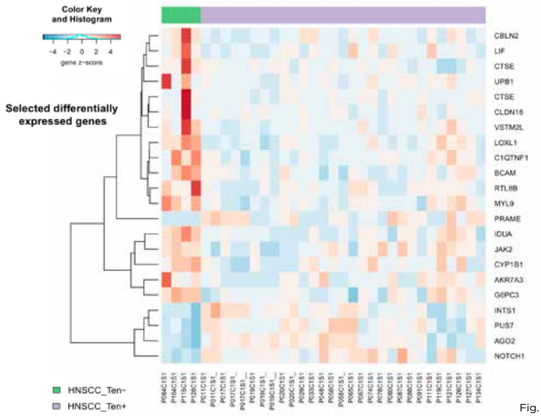


Fig. 4

EFFECTS OF NANOENCAPSULATED SIMVASTATIN ON CARDIOVASCULAR SYSTEM IN EXPERIMENTAL METABOLIC SYNDROME

Principal investigator: doc. RNDr. Oľga Pecháňová, DrSc.
Applicant organisation: Centre of Experimental Medicine SAS, Bratislava
Participating organisations: Institute of Polymers SAS, Bratislava,
Institute of Experimental Physic, SAS, Košice

Term of solution: 7/2015 – 6/2019
Budget from agency: 246 375 €
Project ID: APVV-14-0932

SUBJECT OF RESEARCH

The project addressed the actual topic of treatment of cardiometabolic diseases by an active substance encapsulated in polymeric nanoparticles. The administration of pharmacologically active substances encapsulated in polymeric nanoparticles makes it possible to achieve a significant reduction in the dose of the drug, an increase in its effect in the target tissues, or its controlled release and a reduction in side effects. The project was focused on analyzing the effects of nanoencapsulated simvastatin and coenzyme Q10 in rats with metabolic syndrome.

OBJECTIVES OF THE PROJECT

The main goal of the project was to reduce the side effects of simvastatin (SIM) in an animal model of metabolic syndrome by encapsulation the drug in polymeric nanoparticles and by co-administration of nanoencapsulated coenzyme Q10 (CoQ10), which effectively prevents a decrease in ATP levels. This goal required the preparation of a polymeric nanoparticles, which are increasingly taken up by the liver – the target organ of the effect of simvastatin. The nanoencapsulated and powdered formulations of both drugs were administered to adult obese Zucker (fa / fa) and lean Zucker rats for 6 weeks. Their weight and blood pressure were monitored every week. After finishing the administration, serum lipid profile, glucose level and energy metabolism were determined. Samples of the heart, blood vessels, kidney, liver and skeletal muscle were analyzed at the molecular, biochemical and morphological levels, with an emphasis on determination the oxidative state and the nitric oxide (NO) pathway.

ACHIEVED RESULTS

We have prepared polymeric nanoparticles with simvastatin and CoQ, which were suitable for long-term *in vivo* administration. These biocompatible copolymer nanoparticles, consisted of a crosslinked hydrophobic core and a hydrophilic outer shell, were used to encapsulate mentioned substances (Fig. 1) as well as coumarin – a fluorescent label for the nanoparticles visualization (Fig. 2).

The monomers N-dodecylmethacrylamide (DMAm), N-vinyl-2-pyrrolidone (VP) and poly (ethylene glycol) monomethacrylate (PEG, Mn 360 g mol-1) in an 11:1:14 molar ratio, and the crosslinker methylene- (bis) acrylamide were utilized to prepare the nanoparticles by free-radical copolymerization in an aqueous medium. In the reaction mixture, polymer nanoparticles stabilized by water-soluble PEG chains were formed due to the formation of a dispersion from the hydrophobic core of the particles. The prepared polymer nanoparticles had a number-average size ~200 nm with a narrow distribution (PDI ~0.2). Analysis of the samples showed that CoQ10 and its combination with SIM in nanoparticles were able to increase NO synthase activity in the heart left ventricle and aorta. The same combination significantly increased the expression of eNOS and phosphorylated eNOS in the left ventricle and aorta. CoQ10 in both forms decreased the protein expression of the p22 NADPH oxidase subunit as well as its activity. Only the administration of CoQ10 in both forms had a significant effect on the oxidative state in terms of reducing oxidative damage in the heart, liver and kidney. Analysis of mesenteric artery vasoactivity showed an increase in relaxation after SIM administration in both forms, but with a higher degree of significance for SIM in nanoparticles. These results are in good agreement with blood pressure values, as only SIM in nanoparticles was able to significantly reduce the systolic blood pressure of obese Zucker rats at the end of 6 weeks of treatment. This decrease is probably due to the reduced weight of rats and cholesterol levels after SIM administration in nanoparticles.

Our results showed that only administration of simvastatin in polymeric nanoparticles was able to reduce cholesterol levels, rat weight and systolic blood pressure. Powder form of simvastatin did not demonstrate this ability. However, as revealed by morphological studies and the determination of elastatin and collagen in the aorta, administration of nanoparticles alone had negative effects on the endothelium and vascular wall, as it led to an increase in collagen content. Therefore, further studies are needed to prepare nanoparticles of different sizes from different polymers with positive *in vivo* effects.

BENEFITS FOR PRACTISE

Our results showed that the administration of simvastatin in polymeric nanoparticles had a better effect on most parameters than the administration of the powder form. Nanoencapsulated simvastatin therefore merits further analysis and perspective as well as through clinical studies. Within the project, 26 papers published in impacted journals were created, which are so far cited more than 80 times. So far, 7 PhD students have defended their dissertations, which were closely related to the topic of the project. Several conferences were held with the support of the APVV, including the World Congress of the International Society of Pathophysiology in Bratislava, 2018. The project provoked several collaborations, which resulted in domestic and foreign projects (APVV, VEGA, TUBITAK, COST).

Fig. 1 / Polymeric nanoparticles with simvastatin.

Fig. 2 / Accumulation of polymeric nanoparticles in the spleen, green.

Fig. 3 / Effect of nanoencapsulated simvastatin (SIM) and coenzyme Q10 (CoQ10) on systolic blood pressure in obese Zucker rats during 6 weeks of administration.

Fig. 4 / Effect of nanoencapsulated simvastatin (SIM)and coenzyme Q10 (CoQ10) on NO synthase (NOS) activity in obese Zucker rats after 6 weeks of administration.

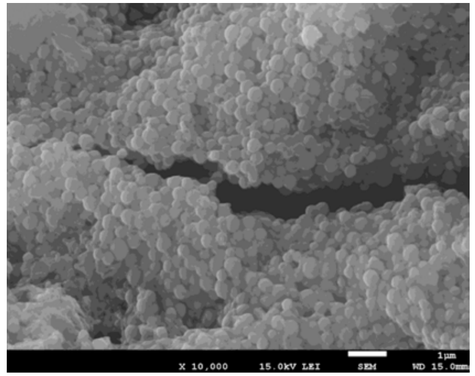


Fig. 1

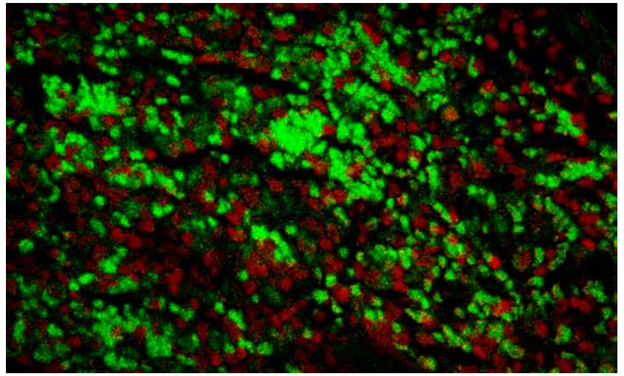


Fig. 2

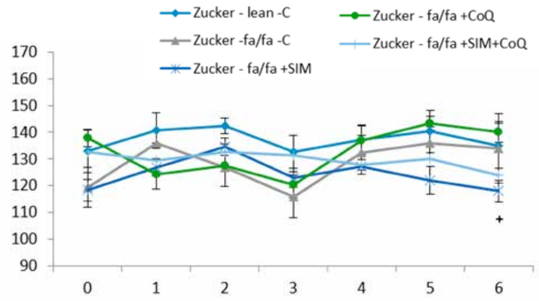


Fig. 3

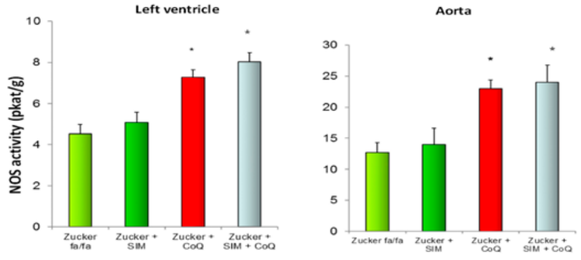


Fig. 4

AGRICULTURAL SCIENCES

THE EGG'S FIBRILLAR SPERE – THE GLOGE FOR LIFE: A FUNDAMENTAL GENETIC AND EPIGENETIC STUDY

Principal investigator: prof. Dr. MVDr. Jozef Laurinčík, DrSc.
Applicant organisation: Constantine the Philosopher University in Nitra
Term of solution: 7/2015 – 6/2019
Budget from agency: 249 200 €
Project ID: APVV-14-0001

SUBJECT OF RESEARCH

The fibrillary spere is the cell organelle responsible for ribosome synthesis and, hence, for protein synthesis. The fibrillar sphere is of utmost importance for the development of the embryo. In this project, porcine oocytes were used to study the content of the fibrillary sphere as well as the developmental competence conveyed by this structure (Fig. 1).

OBJECTIVES OF THE PROJECT

The aim of the project was to increase the developmental capacity of non-ovulatory oocytes by adding (1) an additional fibrillar sphere (spheres; FS), which is a reservoir of maternal RNAs and proteins, or (2) exchanging FS in non-ovulatory oocytes for FS obtained from preovulatory oocytes. In addition, (3) the possibility of using xenotransplantation was tested in order to determine the possibilities of increasing the quality of oocytes of one species by replacing the original FS with quality FS of another species.

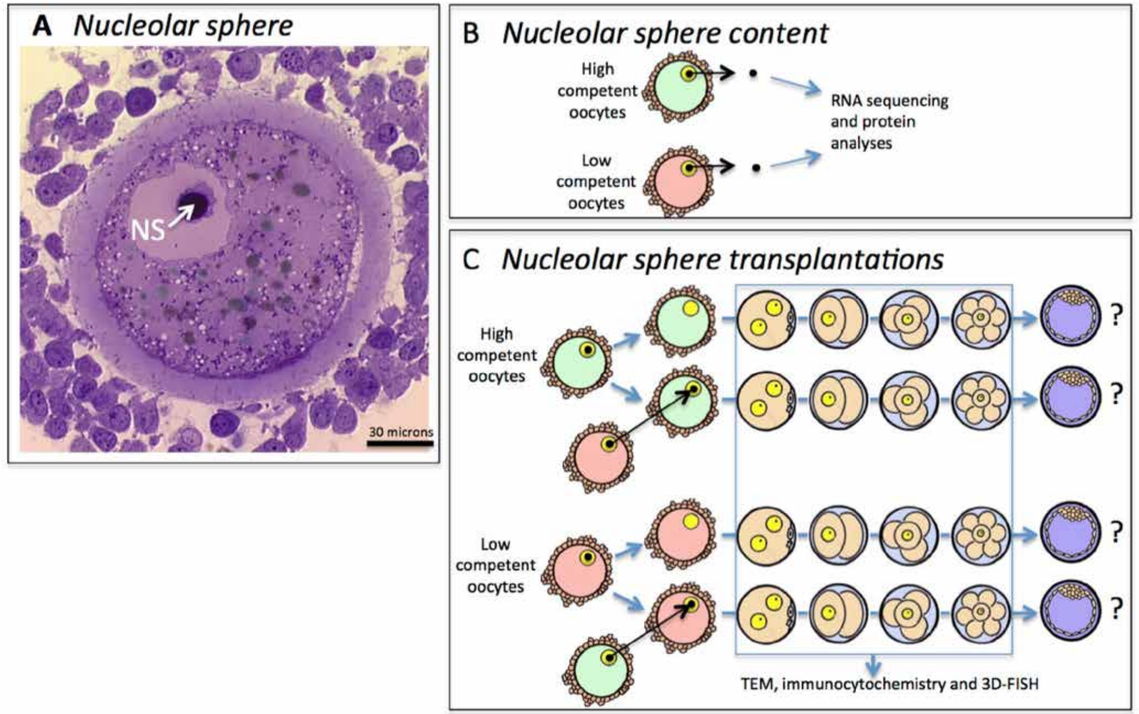
ACHIEVED RESULTS

The study resulted in:

(1) Characterization of HC and LC oocytes with respect to developmental capacity, fibrillary sphere numbers and quality, and chromatin configuration.
(2) Aspiration of fibrillary spheres from HC and LC oocytes and characterization of their composition with respect to RNA and proteins.
(3) Functional characterization of fibrillary spheres from HC and LC oocytes with respect to their ability to sustain embryonic development.

BENEFITS FOR PRACTISE

The scientific clarification of the question if and to what extent the low quality of the oocytes used by ART leads to abnormalities is of eminent and obvious significance not only for future use of animal embryos for biomedical research but also for human assisted reproduction. The results of the project will be relevant as an alternative model to somatic cell nucleologenesis and will increase the number of checkpoints suitable for evaluation and improvement of the normality of the oocytes used in biomedical research and future agricultural application.



(A) Light micrograph of porcine oocyte presenting the nucleolar sphere (NS). (B) Anylyses of the content of nucleolar spheres from high vs. low competent oocytes. (C) Transfer of nucleolar spheres from high competent to low competent oocytes and vice versa and studies of resultant embryo development.

METATRANSCRIPTOME OF EWES' LUMP CHEESE: AN RNA-BASED APPROACH TO DETERMINE THE CONTRIBUTION OF MICROORGANISMS TO ORGANOLEPTIC QUALITY OF BRYNDZA CHEESE

Principal investigator: RNDr. Tomáš Kuchta, DrSc.
Applicant organisation: National Agricultural and Food Centre – Food Research Institute
Participating organisations: Institute of Molecular Biology, Slovak Academy of Sciences; Faculty of Nature Sciences, Comenius University, Bratislava; Faculty of Nature Sciences, University of Ss. Cyril and Methodius, Trnava

Term of solution: 07/2015 – 09/2018
Budget from agency: 248 992 €
Project ID: APVV-14-0025

SUBJECT OF RESEARCH

The research dealt with quality of Slovakian bryndza cheese from the aspect of contribution of microorganisms, in particular lactic acid bacteria, to aroma of ewes' lump cheese as a main raw material in the production of bryndza cheese. Modern methods of metatranscriptome research were used based on reverse transcription, polymerase chain reaction (PCR) and Next generation sequencing.

OBJECTIVES OF THE PROJECT

1. Analysis of genomes of *Lactococcus lactis* a *Lactobacillus* spp. regarding genes responsible for proteolytic activity, development of PCR amplification systems and design of the transcriptomic platform for genes responsible for the cheese aroma.
2. Application of the developed PCR amplification systems to analysis of microbial cultures and identification of microorganisms.
3. Metatranscriptomic analysis of ewes' lump cheese aimed at genes responsible for aroma formation using DNA and RNA extraction, PCR amplification and Next generation sequencing, with identification of microorganisms actively transcribing the given genes.
4. Whole genome sequencing and genome annotation of a panel of lactic acid bacteria regarding genes taken as positive or negative for practical use in cheesemaking.

ACHIEVED RESULTS

New knowledge was obtained on the activity of microorganisms during ripening of ewes' lump cheese as the main raw material for production of bryndza cheese. New polymerase chain reaction-based systems with primers specific for genes *prtP*, *pepN*, *pepX* and *bcaT* were elaborated. These were used, in combination with Next generation sequencing, on RNA and DNA isolated from authentic ewes' lump cheese samples from various ripening stages, as obtained from a traditional manufacturer. In this way, detailed experimentally verified knowledge was obtained on contribution of various groups of lactic acid bacteria to the proteolytic transcriptome, which is a pre-requisite for formation of volatile aroma-active compounds from proteins and modulates the typical organoleptic properties of bryndza cheese. Lactococci were found to play a major role in the process, with lactobacilli being also important in the final stage of ripening. In case of medium chain fatty acids, which are responsible for the „ewes'" aroma and are dependent on lipolysis, results of a series of experiments during cheese ripening based on dynamic microbiological analyses and gas-chromatographic determination of marker compounds showed that both yeasts and lactobacilli played a role in formation of these compounds, while *Galactomyces/Geotrichum* did not play a central role. Using Next generation sequencing, whole genome sequences of 21 strains of lactic acid bacteria were obtained and, based on annotation of genes encoding for bacteriocins, restriction-modifications systems, prophages, CRISPR-Cas systems, antibiotic resistance and formation of biogenic amines, their potential to be used as starter cultures was evaluated.

BENEFITS FOR PRACTISE

The project produced new knowledge on the activity of microorganisms during ripening of ewes' lump cheese as the main raw material for production of bryndza cheese. The results obtained represent a basis for applied research and development of specific starter cultures that will guarantee the typical organoleptic properties of bryndza cheese. Methods and PCR primers developed in frames of the project are useful for microbiological and dairy research and can be universally used to determine presence and transcription activity of *prtP*, *pepX*, *pepN* a *bcaT* genes, while being sequence-specific for species of lactic acid bacteria. The obtained information on whole genome sequences of 21 strains of lactic acid bacteria represents a contribution to international scientific knowledge.

Fig. 1

Fig. 2

Fig. 3

Fig. 4

Fig. 1 / Amplification of DNA fragments by polymerase chain reaction in a cycler.

Fig. 2 / Isolation of strains of lactic acid bacteria from ewes' lump cheese on agar media.

Fig. 3 / Isolation of DNA and RNA from ewes' lump cheese.

Fig. 4 / Microscopic observation of microbial cultures.

CRYOPRESERVATION OF ANIMAL GENETIC RESOURCES IN SLOVAKIA

Principal investigator: prof. Ing. Peter Chrenek, DrSc.
Applicant organisation: Slovak University of Agriculture in Nitre, Faculty of Biotechnology and Food Sciences
Participating organisations: National Agricultural and Food Centre- Research Institute for Animal production in Nitra
University of SS. Cyril and Methodius in Trnava – Faculty of Natural Sciences

Term of solution: 7/2015 – 6/2018
Budget from agency: 249 842 €
Project ID: APVV-14-0043

SUBJECT OF RESEARCH

Availability of the animal genetic resources has an impact on the present and also future life quality and important effect on the food safety. Protection of the animal genetic resources also emerge from the European Biodiversity Action Plan for Agriculture, The Global Strategy for the Management of Farm Animal Genetic Resources FAO OSN, Council Regulation (EC) No 870/2004 establishing a Community programme on the conservation, characterization, collection and utilization of genetic resources in agriculture; Act No. 194/1998 Coll. on breeding and reproduction of farm animals.
The effective cryopreservation of biological material of some livestock species is not currently mastered. This results in lower viability or quality of frozen/thawed sperm, embryos and stem cells of livestock.

OBJECTIVES OF THE PROJECT

The project was realized in three stages:
Stage 1
focused on the optimization of sperm, embryo and stem cells cryoprotection methods of rabbit and cattle.
Stage 2
focused on the optimization methods of isolation, manipulation and cryoprotection of sperm and stem cells (blastodermal and primordial) of poultry.
Stage 3
focused on placing frozen samples of slovak breeds in a gene bank of animal genetic resources, registering them on "www. Efabis" and "www. Cryoweb".

ACHIEVED RESULTS

Stage 1
the result is optimization of methods (specific protocols) confirmed by the evaluation of the quality of the biological material by fluorescence and electrone microscopy, as well as by molecular genetic analyzes.
Stage 2
a major success is the optimization of these methods (specific protocols) and their establishment in Slovakia as the only workplace. The quality of the biological material obtained from the Oravka breed was also analyzed by light, fluorescence and electron microscopy as well as by molecular-genetic analyzes. At this stage, we successfully tested the new marker (ALDH-Aldehyde dehydrogenase) as the first in the world to ensure the originality of primordial poultry stem cells.
Stage 3
Achieving good results is confirmed by several publications in foreign journals and three monographs. The project was also hosted by the International Conference on Animal Genetic Resources (Animal Biotechnology 2017). Last but not least, the project enabled the cryopreservation of biological material of several endangered breeds reared in Slovakia, thus fulfilling the conditions of the contract signed between the Slovak Republic and the FAO in 1994 concerning genetic resources.

BENEFITS FOR PRACTISE

We have successfully optimized methodologies related to cryopreservation of sperm, embryos and stem cells of rabbits and chicken with successful output in WOS – peer-reviewed publications (14 in total) and three monographs. The gene bank of animal genetic resources at VÚŽV NPPC Nitra in cooperation with SPU Nitra was supplemented with insemination doses of all mentioned breeds, as well as embryos and stem cells of rabbits and poultry.
The obtained results are part of archived documentation on genetic animal resources and are available for comparative studies, breeding programs in the Slovak Republic, as well as for foreign workplaces involved in global programs for the protection of animal genetic resources under the auspices of the FAO.

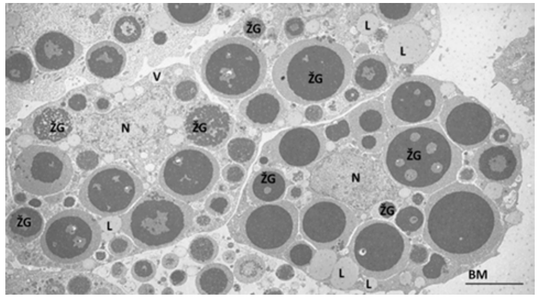


Fig. 1

Fig. 2

Fig. 1 / Zobor rabbit.

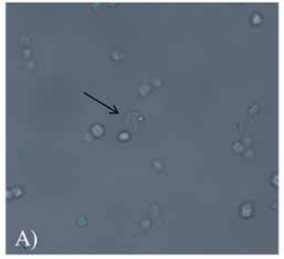
Fig. 2 / Breed „oravka".

Fig. 3 / Fluorescent analysis of primordial stem cells (PGCs).
A – light microscopy
B – DAPI positive cells
C – PI positive cells

Fig. 4 / Freshly isolated sample of BCs.

Fig. 5 / Gene bank of animal genetic resources.

Fig. 4



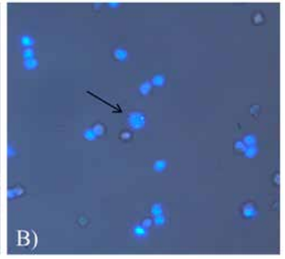


Fig. 3

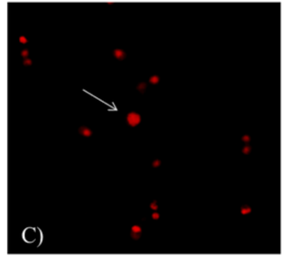


Fig. 5

MOLECULAR GENETIC DIVERSITY AND PRODUCTION POTENTIAL OF ANIMAL GENETIC RESOURCES IN SLOVAKIA

Principal investigator: prof. Ing. Radovan Kasarda, PhD.
Applicant organisation: Slovak University of Agriculture in Nitra, Nitra
Term of solution: 07/2015 – 06/2019
Budget from agency: 248 780 €
Project ID: APVV-14-0054

SUBJECT OF RESEARCH

The project was primarily focused on determining and quantifying the degree of genetic diversity of important breeds of cattle and horses in Slovakia as well as their position concerning the global diversity of animal food resources. The project also enabled the identification of genomic regions defining the uniqueness of specific local populations compared to commercial breeds and a deeper knowledge of specific genetic variants involved in the control of important production, reproductive and functional traits of livestock.

OBJECTIVES OF THE PROJECT

The main goal of the project was to prepare a comprehensive methodology for assessing the diversity of animal genetic resource populations of socio-economic importance, including " higher-level " identifiers. Testing the applicability of the methodology to different livestock and wildlife species was based on several types of data sources (pedigrees and genomic DNA) to assess the risk of diversity loss, optimisation of livestock and horse breeding programs, determination of specific molecular-genetic markers in the form of a panel and evaluation of their relationship to the production and performance potential of important national livestock breeds.

ACHIEVED RESULTS

During the solution of individual phases of the project, complex databases of pedigree and genome-wide information (STR and SNP markers) were prepared to focus on the gene pool of national cattle (Slovak spotted, Slovak Pinzgau, Jersey, Charolais, Limousine) and horse (Lipican, Nonius, Furioso, Slovak warmblood, Norik of Muran) breeds. Within the partial tasks, comprehensive methodologies were compiled based on sophisticated bioinformatics tools to determine the risk of genetic diversity loss for each population, estimate the degree of their differentiation with respect to genetically closely related breeds or subpopulations, identify genomic regions unique to particular breeds and regions significantly affected by artificial and natural selection. Concerning production, reproduction, and functional traits associations between phenotypic and genotypic information were tested. Subsequently, panels of SNP markers were prepared to implement obtained results in genomic selection programs to increase genetic gain. Depending on the evaluated breed, genealogical and genomic information about individuals was also used to develop new or optimise existing mating strategies to preserve animal genetic resources in Slovakia from a long-term view. The methodological approaches applied in particular research activities were also presented to the scientific and professional public in two international scientific conferences and several training courses to enhance the visibility of the project and build or strengthen the existing cooperation with renowned scientific organisations at home and abroad. The results obtained during the project were published in 9 papers in current content journals, 21 papers in journals registered in Web of Science or SCOPUS databases, four scientific monographs, two university textbooks and in more than 40 papers in peer-reviewed scientific journals, non-peer-reviewed professional journals and proceedings from national and international scientific conferences.

BENEFITS FOR PRACTISE

As part of popularisation activities, the results of various studies carried out during the project were presented in professional publications, primarily focused on livestock breeders and the public to popularise and implement new knowledge into common practice. The project results were provided to various organisations involved in the control of the breeding process at the level of state administration – Breeding Services of the Slovak Republic s.e., breeders' organisations and associations as well as farmers and other groups participating in breeding and sustainable use of animal genetic resources in Slovakia. As shown by international studies, the application of obtained knowledge and developed methodological approaches in practice can significantly contribute to successful management and especially sustainable use of animal genetic resources in Slovakia in the future.

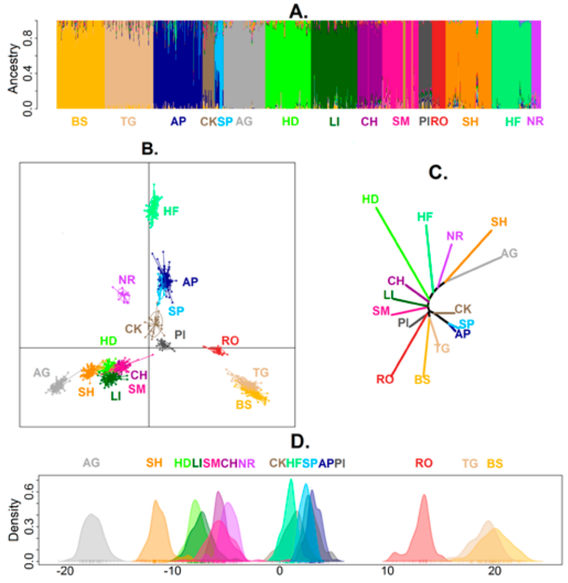


Fig. 1

Fig. 1 / Graphical visualisation of population structure and genetic relationships among 15 European cattle breeds (Angus-AG, Austrian Pinzgau-AP, Brown Swiss-BS, Cika-CK, Hereford-HD, Holstein-HF, Charolais-CH, Limousine-LI, Norwegian Red -NR, Piedmontese-PI, Romagnola-RO, Shorthorn-SH, Slovak Pinzgau-SP, Simmental-SM, Tyrol Gray-TG) based on 34866 SNPs genotyped by Illumina Bovine SNP50 array for 1040 individuals. A. The genetic admixture within analysed populations, B. Genetic differentiation among breeds based on the first and second discriminant function, C. Dendrogram derived from the genetic distance matrix and D. Substructure of the analysed population based on the first discriminant function of DAPC analysis.

Fig. 2 / Differences in the linkage disequilibrium level analysed based on the model of Lipizzan and Norik of Muran breeds, reflecting the difference in their breeding goals and the intensity of selection pressure on specific regions in their genome (the dashed line shows the genome-wide significance threshold).

Fig. 3 / Scientific monograph "Genetic diversity of the Slovak Pinzgau breed".

Fig. 4 / Scientific monograph "Genomic characterisation of Slovak Pinzgau cattle".

Fig. 5 / Scientific monograph "Genetic diversity of the Slovak Spotted and Holstein breeds".

Fig. 6 / Textbook for students at II. level of higher education and subjects Population Genetics, Biodiversity in livestock populations and Breeding programs in animal husbandry.

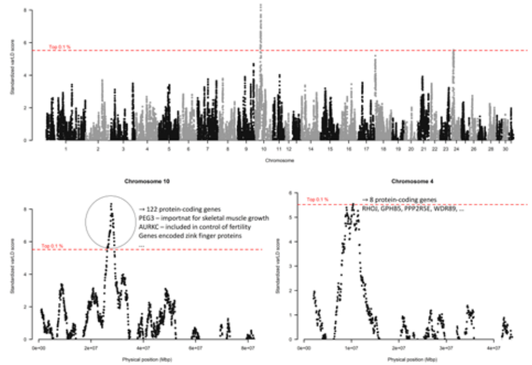


Fig. 2

Fig. 3

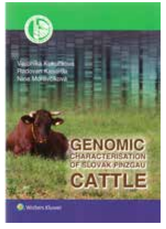


Fig. 4

Fig. 5

Fig. 6

EFFECTIVE DIAGNOSTICS OF VIRUSES THREATENING THE PRODUCTION OF TOMATO IN SLOVAKIA

Principal investigator: Ing. Jozef Gubiš, PhD.
Applicant organisation: National Agricultural and Food Centre – Research Institute of Plant Production
Participating organisations: Biomedical Research Center SAS – Institute of Virology
University of SS. Cyril and Methodius in Trnava – Faculty of Natural Sciences of UCM
University of Žilina – Institute of High Mountain Biology

Term of solution: 07/2015 – 06/2019
Budget from agency: 249 936 €
Project ID: APVV-14-0055

SUBJECT OF RESEARCH

The subject of the research was to evaluate the occurrence and molecular diversity of viral pathogens, the optimization of their detection in the field and experimental conditions on a model crop of tomato (*Solanum lycopersicum L.*) using available and newly developed immunochemical and molecular diagnostic procedures.

OBJECTIVES OF THE PROJECT

The aim of the project was to develop effective and innovative diagnostic methods for the detection of plant viruses, which would improve the currently available methods and clearly confirm the presence of infectious agents in the plants. The goals were realised in the systems of *in vitro, in planta* and in the real field conditions.

ACHIEVED RESULTS

In the project, we compared the composition of 18 mRNA, i.e. capsid proteins of the Tomato mosaic virus (CP ToMV). The analysed collection contained various ToMV isolates. Based on these data, methods for detecting the presence of ToMV in our analysed and collected tomato samples were designed. We identified the presence of tobamoviruses in the plant materials of the project outcomes user, Zelseed company, as well as from various growing areas of Western Slovakia using available immunochemical and molecular diagnostic procedures. Using commercially available tests, we had difficulty to detect the presence of ToMV because the ToMV pathotypes occurring in our area are different from the isolates of this virus detected so far. We analysed selected samples by a combination of Sanger sequencing and Next-Generation Sequencing (NGS) and we identified a new pathotyp of ToMV virus, SL-1 (GenBank: KY912162.1), that is the first identification of ToMV in our territory (Sihelská et al. 2017). Using our identified ToMV SL-1 virus we evaluated the resistance of tomato genotypes by a series of experiments with an artificial infection of plants. We designed 2 oligopeptides from the amino acid sequences of the ToMV pathotypes for the ToMV SL-1 capsid protein, which were used to prepare a polyclonal antibody. We determined the degree of "cross-reactivity" of our antibody to the presence of CP ToMV SL-1. We detected the presence of CP ToMV SL-1 up to 24 hours after the artificial infection in the DAS-ELISA but in Western blot, it was already 2 hours after the artificial infection. Our antibody showed the formation of immunocomplexes with the capsid proteins of the ToMV, TMV and PMMoV viruses. Using Western blot analysis, we further characterised the ToMV-SL-1 pathotype. We confirmed the presence of viral CP ToMV SL-1 in roots, seeds, leaves, as well as in root residues, even after 2 years without the presence of biotic factor. Viable, infectious virus particles have been demonstrated at the proteomic level in the rhizosphere and even in root residues treated by short-term laboratory sterilization. We found that our antibody showed a higher detection sensitivity and a higher rate of immunocomplex formation when compared to commercially available antibodies in ELISA and Western blot procedures. Also, we described the occurrence and molecular variability of Potato virus S (PVS) and Potato virus M (PVM) (Predajňa et al., 2017, Glasa et al., 2019) for the first time in our territory. Finally, primers for RT-PCR detection were designed to capture the regional diversity of Potato virus Y (PVY), Potato virus S (PVS), Potato virus M (PVM), and Cucumber mosaic virus (CMV).

BENEFITS FOR PRACTISE

The project solution was designed and realised in accordance with the needs of special plant production. For the first time, Tomato mosaic virus (ToMV SL-1), Potato virus S (PVS) and Potato virus M (PVM) were described and molecular characterised in the Slovak territory. Transcriptomic-level protocols for the detection of tobamoviruses have been prepared for the needs of the project outcomes user Zelseed company because commonly available diagnostic procedures are based on immunochemical diagnostics that do not guarantee to cross-link with all virus pathotypes. At the proteomic level, user-tailored immunochemical detection was prepared, where the prepared procedures show qualitatively and also quantitatively better parameters than hitherto commercially available diagnostic kits. The obtained results may be useful in the future in the implementation of effective phytosanitary measures and will contribute to the increase of the qualitative and quantitative parameters of tomato production in Slovakia.

Fig. 1 / Graphical illustration of ToMV SL-1 virus quantification of infected samples from roots and seeds of tomato genotypes.

Fig. 2 / The amino acid sequence of ToMV PV-0135 with the designation of our proposed Epi 1 and Epi 2 epitopes using CLC Main Workbench software.

Fig. 3 / n blot analysis of leaf samples from artificially infected plants detecting the presence of ToMV capsid protein with a molecular weight of 17.8 kDa.

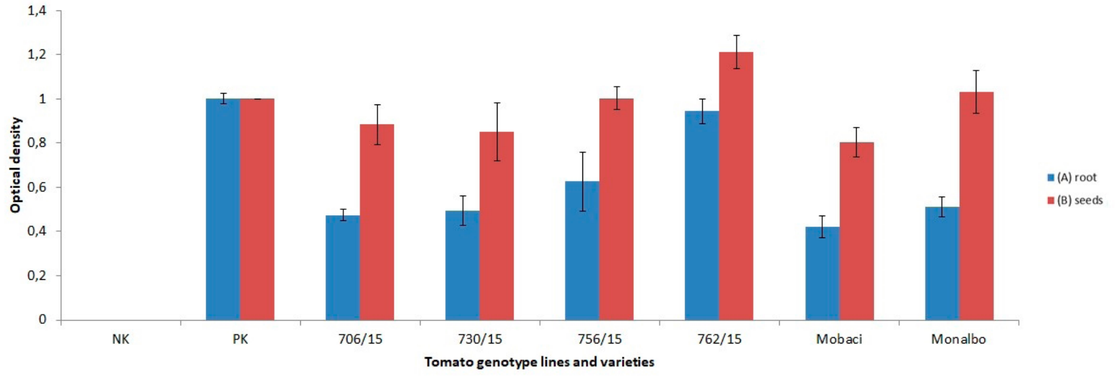


Fig. 1

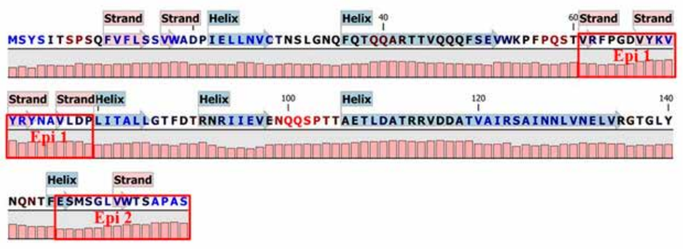


Fig. 2

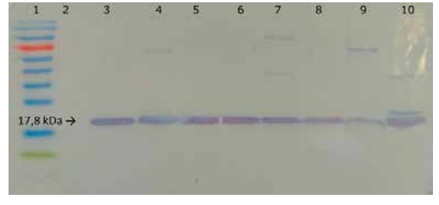


Fig. 3

RESISTANCE OF PARASITES TO ANTHELMINTICS – CHALLENGES, PERSPECTIVES AND SOLUTIONS

Principal investigator: doc. MVDr. Várady Marián, DrSc.
Applicant organisation: Institute of Parasitology SAS
Participating organisation: Centrum of Bioscience SAS – Institute Animal Physiology

Term of solution: 7/2015 – 6/2019
Budget from agency: 247 553 €
Project ID: APVV-14-0169

SUBJECT OF RESEARCH

The subject of the research was to solve the serious problem of resistance to anthelmintics in parasites of small ruminants. In the project, we wanted to map the shortcomings of currently used *in vitro* methods for detection of anthelmintic resistance. In addition, we will investigate the *in vitro* and in vivo efficacy of selected mixtures of medicinal plants in experimentally infected animals.

OBJECTIVES OF THE PROJECT

The main objectives of the project can be summarized in the following points:

1. Genotyping of larval stages of parasites in the *in vitro* Egg Hatch Test
2. Correlation of in vivo, *in vitro* and molecular methods in the detection of resistance
3. Genotyping of parasite larvae during the patent period
4. *In vitro* testing of medicinal plant mixtures on parasites
5. Verification of the efficacy of selected plant mixtures on endoparasites in experimentally infected sheep
6. Comparison of inflammatory parameters in uninfected animals and experimentally infected sheep with subsequent therapy using selected mixtures of plants

ACHIEVED RESULTS

The following are the most significant results achieved within the project solution:

1. When genotyping the developmental stages of parasites in the *in vitro* Egg Hatch Test, we found that only resistant homozygous forms were identified at high test concentrations, indicating that a higher concentration of anthelmintic must be used in the *in vitro* diagnosis of benzimidazole resistance using this test.
2. The results of the second goal confirmed that when estimating the efficacy of an anthelmintic in vivo, or when estimating the proportion of resistant allele in the tested population, we only need to perform an *in vitro* test with a single anthelmintic concentration (e.g. 0.3 µg/ml or 0,5 µg/ml thiabendazole), which will significantly reduce the financial and time required to detect resistant parasites in an unknown population.
3. We found that the genetic information (percentage of resistant/sensitive alleles) on 25 independent days during the patent period of 2 months significantly varies in both resistant and sensitive strains.
4. The results obtained show that the most significant antiparasitic activity (p <0.05) was shown by methanolic extracts of A. absinthium and C. recutita at a concentration of 1024 µg/ml using the *in vitro* Egg Hatch Test and A. absinthium, C. recutita and M. sylvestris using an *in vitro* Larval Development Test. The wider spectrum of aqueous extracts showed stronger ovicidal activity compared to methanolic extracts. A similar trend was observed when evaluating the larvicidal activity of aqueous and methanolic plant extracts.
5. The effectiveness of selected plant mixtures as well as individual plants was investigated in four separate experiments. The plant mixtures were mixed from selected medicinal herbs typical of Central Europe. In total, we used 4 mixtures with 13 different herbs. The experiments did not confirm the direct anthelmintic effect of plant mixtures on the viability of parasites, but the treatment used indirectly contributed to increasing the resistance of lambs to parasitic infections and easier overcoming of the infectious load.
6. When comparing inflammatory parameters, the results showed that serum albumin A is not a suitable parameter for monitoring the course of Haemonchus contortus parasite infection in a longer time interval after infection. In contrast, calprotectin has been shown to be a suitable parameter for monitoring the course of infection by this parasite. At the same time, we conclude that the addition of HERBMIX (herbal mixture No. 1) significantly stimulated the immune system in infected animals, which probably resulted in easier management of the infection in this group of animals.

BENEFITS FOR PRACTISE

The findings, which have been published in ten articles in international journals, clearly pointed to the direct use of our results and the prospects for the use of *in vitro* methods in the field diagnosis of anthelmintic resistance. Based on our results, we found that:

i) in the field diagnosis of resistance using a single concentration in the *in vitro* test, we can precisely estimate the percentage of resistant parasites in the tested population,
ii) on the basis of the result from *in vitro* tests we can precisely estimate the effect of the anthelmintic in vivo and on this basis we can inform farmers and breeders about preventive measures in the herd/farm,
(iii) the enrichment of feed rations by the administration of mixtures of plants with bioactive ingredients may to some extent replace the lack of plant diversity in pastures and at the same time improve the health of the animals themselves as a result of the parasitic infection

Fig. 2

Fig. 1

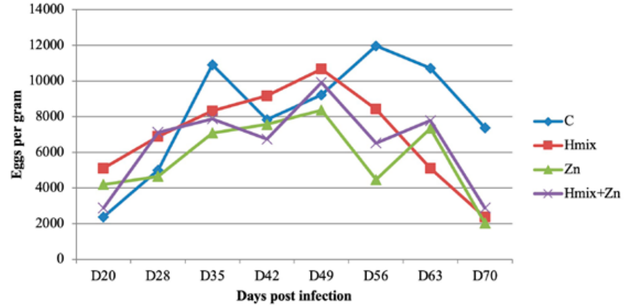


Fig. 3

Fig. 1 / Female Haemonchus contortus – gastro-intestinal parasite of ruminants.

Fig. 2 / Ready to work with our experimental animals on the farm.

Fig. 3 / Mean fecal egg counts of the groups of lambs infected with Haemonchus contortus.

PREPARATION OF SPECIFIC ANTIBODIES FOR THE ISOLATION OF RABBIT HEMATOPOIETIC STEM CELLS FOR THE ESTABLISHMENT OF STEM CELL BANK

Principal investigator: Ing. Jaromír Vašíček, PhD.
Applicant organisation: Research Institute for Animal Production Nitra, National Agricultural and Food Centre

Term of solution: 07/2015 – 06/2019
Budget from agency: 249 528 €
Project ID: APVV-14-0348

SUBJECT OF RESEARCH

The national gene banks that gather animal genetic resources for the preservation of either domestic or whole world biodiversity are recently established all over the world. These banks store genetic information of different significant domestic farm animal breeds (species). Besides the reproductive cells (spermatozoa, oocytes and embryos), also adult stem cells represent an important source of genetic resources. Although, their presence within the organism is very scarce, they can be obtained from different biological sources (blood, bone marrow, adipose tissue etc.)

OBJECTIVES OF THE PROJECT

The aim of the project was preparation of immunospecific antibodies for the detection of rabbit adult hematopoietic (HSCs) stem and progenitor (HPCs) cells and know-how for the establishment of stem cell bank of the domestic rabbit breeds (Nitra and Zobor rabbit) within the National gene bank, as well as the production of commercially available rabbit antibodies for other biomedical applications.

ACHIEVED RESULTS

Since there were no available antibodies that are specific to rabbit CD34, the majority of commercially available CD34 antibodies with different affinity to human, mouse or rat were tested on the human blood (Medical University of Vienna, Austria) and rabbit blood and bone marrow samples. The analyses revealed two antibody clones (AC136 and Qbend-10) that showed higher affinity to tested samples and thus were used for the magnetic separation of CD34 positive cells (HSCs and HPCs) from human and rabbit blood and rabbit bone marrow. However, the results from flow cytometry and PCR analyses demonstrated that used clones are not suitable for the isolation of rabbit HSCs and HPCs. For this reason, it was necessary to generate novel monoclonal antibodies with higher affinity to rabbit CD34. Since, rabbit CD34$^+$ cells that could serve as the immunogen for the antibody generation were not directly available, four synthetic CD34 peptides were designed that were immunogenic enough for the immunization of mice and the antibody generation using hybridoma technology (Institute of Neuroimmunology SAS). Several appropriate subisotypes that detect unknown CD34$^+$ cell population within rabbit blood and bone marrow were chosen from the raised antibodies. It is known that human endothelial cells (ECs) express CD34. As CD34 protein is conserved among mammalian species, it can be assumed that also rabbit ECs might express CD34 and thus be used as control cells for raised antibodies. For this reason, a new methodology for the isolation of progenitor ECs from rabbit blood and bone marrow was optimized. Expression of CD34 by these cells were assessed by above mentioned commercially available CD34 antibodies. However, flow cytometry did not reveal higher CD34 expression and qPCR analysis showed decreasing expression of CD34 with the following passage. The same was noticed in human ECs, when the cell passaging decreased CD34 expression by those cells. Thus, rabbit ECs seem not to be an appropriate sample for the testing of new generated CD34 antibodies. Despite that, these cells present another source of genetic resources of domestic rabbit breeds. Therefore, rabbit ECs from both biological sources were thoroughly studied in terms of their phenotype and morphology using flow cytometry, PCR and microscopic techniques. Those analyses revealed typical endothelial shape and phenotype as well as other stem cell features such as expression of SSEA-4, MSCA-1 and aldehyde dehydrogenase (ALDH). In general, ALDH seems to a suitable mutual marker for different types of rabbit stem and progenitor cells. Besides the mentioned studies, a new methodology for the enrichment of CD34$^+$ cells via the elimination of mature CD45$^+$ hematopoietic cells from rabbit blood and bone marrow was optimized. Separated cells were successfully proliferated in special medium for the expansion of CD34$^+$ cells. Significant increase of CD34 expression and decrease of CD45 expression was noticed after 2 days of culture. Moreover, these CD34 enriched cells showed higher expression of CD117 (marker of human and mice HSCs).

BENEFITS FOR PRACTISE

The results of the project are applicable for basic knowledge as well as in practice in the form of new information about the examined rabbit progenitor ECs derived from blood and bone marrow as well as the cryopreservation of these cells from domestic rabbit breeds (Nitra and Zobor rabbit) in the form of animal genetic resources. In addition, prepared and validated CD34 monoclonal antibodies can be used for the identification and eventual isolation of rabbit HSCs and HPCs as well as for further biomedical research in the field of hematopoietic diseases.

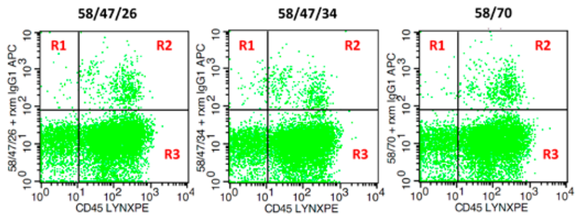


Fig. 1

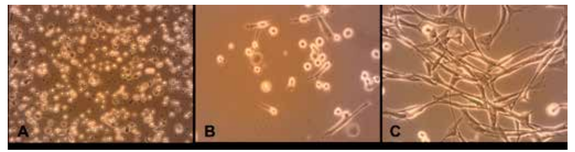


Fig. 2

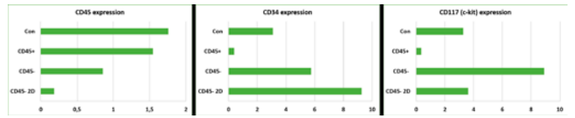


Fig. 5

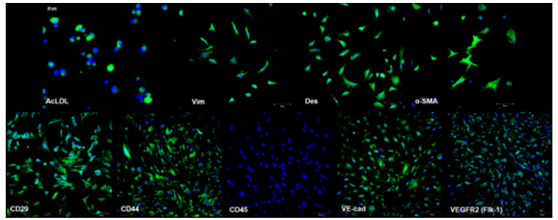


Fig. 3

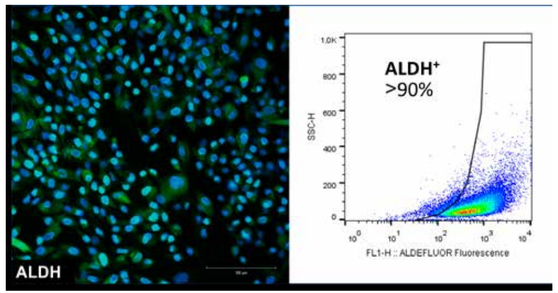


Fig. 4

Fig. 1 / Expression of selected CD34 antibody subclones (58/47/26, 58/47/34 and 58/70) in rabbit bone marrow: R1 – CD34$^+$/CD45$^-$ cells (probably HSCs); R2 – CD34$^+$/CD45$^+$ cells (probably HPCs); R3 – CD34$^-$/CD45$^+$ mature hematopoietic cells.

Fig. 2 / Phase-contrast microscopy of the morphological changes of rabbit blood-derived EPCs after 1–11 days of culture: The cell morphology changed from round (A, B) to the typical spindle-shaped endothelium-like morphology (C) after 2 weeks of culture.

Fig. 3 / Fluorescence confocal microscopy of the specific rabbit EPCs intracellular and cell surface markers: Confocal microscopy revealed positive expression of AcLDL, vimentin (Vim), desmin (Des), actin (α-SMA), CD29, CD44, VE-cadherin (VE-cad) and VEGFR2, whereas CD45 (hematopoietic lineage marker) was not expressed. DAPI – nuclear stain (blue), Positive marker expression (green fluorescence).

Fig. 4 / Expression of aldehyde dehydrogenase (ALDH) in rabbit EPCs proved by confocal microscopy and flow cytometry.

Fig. 5 / qPCR analysis of sorted and cultured bone marrow cells: After 2 days of incubation cultured cells showed increased CD34 expression, whereas CD45 expression decreased in comparison to other samples (control and both fractions). Expression of CD117 increased in CD45$^-$ fraction in comparison to positive fraction or control sample. However, expression of CD117 in cultured cells decreased after short-term incubation in comparison to CD45$^-$ fraction. This might indicate an expansion of progenitor cells over stem cells.

APPLICATION OF ORGANIC FEED IN THE DIET OF POULTRY FOR THE PRODUCTION OF FUNCTIONAL FOODS ENRICHED WITH IMPORTANT POLYUNSATURATED FATTY ACIDS

Principal investigator: doc. MVDr. Slavomír Marcinčák, PhD.
Applicant organisation: University of Veterinary Medicine and Pharmacy in Kosice

Term of solution: 07/2015 – 06/2019
Budget from agency: 249 998 €
Project ID: APVV-14-0397

Fig. 1 / Macroscopic view of the growth of Cuninghamella echinulata during cultivation on wheat bran for 7 days.

Fig. 2/ Slaughtered chicken body.

SUBJECT OF RESEARCH

This project is focused on evaluation the impact of fermented feed in broiler and laying hens nutrition on enrichment of meat and eggs with important polyunsaturated fatty acids (PUFA). We prepared feed enriched with selected PUFA and carotene pigments using solid state fermentation by lower filamentous fungi effectively growing and utilizing agro food by-products. The broilers were fed with prepared fermented bio-feed and the impact on production parameters, broiler´s health status, fatty acids profile and meat and eggs quality was evaluated.

OBJECTIVES OF THE PROJECT

The main aim of the project was to prepare fermented bio-feed enriched with targeted PUFA and pigments by solid-state fermentations using lower filamentous fungi (*Cunninghamella, Mortierella, Umbelopsis*) effectively growing and utilizing agri-food by-products (wheat bran, corn grits). After testing all prepared bio-feeds, three species were selected. The main PUFA was gamma-linolenic acid (GLA) and beta-carotene in two of them and in the third feed the important acids were alpha-linolenic, eicosapentaenoic and arachidonic acid. Bio-feeds were added at a dose of 10 and 15% to the feed of broiler chickens and hens and their effect on increasing the amount of significant PUFA in meat and egg fat as well as the effect of feed on animal production parameters and health during fattening and quality of produced meat and eggs was studied.

ACHIEVED RESULTS

The selection of suitable production strains of filamentous fungi is a basic criterion for culture processes that largely determine the characteristics of metabolites. Therefore, the first step was to verify the production capacity during solid-state cultivations with polyunsaturated fatty acid (PUFA) and carotenoid pigment producers. The results of the project confirmed the positive impact of fermentation processes on the solid phase on the use of by-products as feed in poultry nutrition. Through fermentation processes with lower filamentous fungi (*Cunninghamella, Mortierella and Umbelopsis*), the by-products were enriched with important fatty acids (GLA, eicosapenaenoic – EPA, arachidonic – ARA, alpha-linolenic – ALA) and increased the usability of by-products for fattening. Wheat bran and maize meal are by-products of the milling industry and, due to their high fiber content, are not a suitable raw material for compound feed for poultry. However, the fermentation process reduced the content of indigestible fiber and increased the content of enzymes and other products (pigments, coenzyme Q10), which significantly improved the usability of feed in fattening. The results of our experiments confirmed that when bio-feed was added to commercial feed mixtures at a dose of 10%, it did not significantly reduce the growth parameters of chickens. An important result of the project is the realization of the enrichment of the product during fermentation with important fatty acids (GLA, ARA, ALA, EPA), which will also significantly increase the possibilities of this product in fattening. The results obtained are valuable information that will be used in further research in the application of fermented products and their addition to chicken feed. The production of a new type of feed will help by-products to recover waste.

The results of the project also confirmed that by adding fermented organic feed with a higher proportion of PUFA, it is possible way to increase the proportion of important fatty acids in the fat of produced meat and eggs. In this way, it is possible to produce functional foods with polyunsaturated fatty acids and a beneficial effect on human health. The products produced are oxidatively stable and do not show differences in sensory quality. This type of product brings an economically affordable alternative also for poultry and egg producers who are interested in expanding the range with new functional and healthier products that can appeal to consumers, especially those who believe in a healthier lifestyle.

BENEFITS FOR PRACTISE

By biotechnological processes it is possible to evaluate by-products of agricultural origin for a complete feed in poultry nutrition. The application of fermented feed in poultry nutrition is another way to enrich meat and eggs with significant PUFA, resulting in a functional food with a beneficial effect on human health. For feed manufacturers, organic feed can be a new raw material with a high proportion of PUFA, which will enrich the range of compound feed, and for poultry farmers the opportunity to produce a new type of chicken and eggs with a higher proportion of significant fatty acids in meat and egg fat.

Fig. 2

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BioMed Research International
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Research Article

Effect of Fungal Solid-State Fermented Product in Broiler Chicken Nutrition on Quality and Safety of Produced Breast Meat

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Fatty acids profile of breast and thigh muscle fat after feeding of 5 % of fermented product (Thamnidium ellegans, spelt bran)

FATTY ACID (%)	BREAST MUSCLE C	BREAST MUSCLE FP	THIGH MUSCLE C	THIGH MUSCLE FP
C 14:0, MA	0.42 ± 0.04	0.45 ± 0.01	0.44 ± 0.03	0.44 ± 0.02
C 16:0, PA	24.32 ± 0.68	23.57 ± 0.63	21.32 ± 2.23	20.97 ± 0.53
C 16:1	0.56 ± 0.040	0.49 ± 0.02	0.61 ± 0.05	0.57 ± 0.02
C 16:1 N-7	3.69 ± 0.110	4.45 ± 0.54	5.45 ± 0.19	5.07 ± 0.61
C 18:0, SA	9.73 ± 0.35	9.13 ± 1.21	9.86 ± 0.12	9.58 ± 0.52
C 18:1 N-9, OA	27.44 ± 1.87	28.21 ± 4.30	30.75 ± 0.91	31.38 ± 0.44
C 18:1 N-7, VA	4.80 ± 0.34	4.38 ± 1.06	3.61 ± 0.29	3.12 ± 0.16
C 18:2 N-6, LA	18.16 ± 1.32	19.20 ± 0.26	19.89 ± 0.55	20.75 ± 0.44
C 18:3 N-6, GLA	0.09 ± 0.01	0.16 ± 0.11	0.13 ± 0.03	0.22 ± 0.01
C 18:3 N-3, ALA	0.51 ± 0.04	0.57 ± 0.14	0.67 ± 0.08	0.69 ± 0.07
C 20:2 N-6	1.01 ± 0.12	0.82 ± 0.25	0.38 ± 0.03	0.40 ± 0.08
C 20:3 N-6, DGLA	1,37 ± 0,03	1.32 ± 0.59	0.70 ± 0.12	0.68 ± 0.09
C 20:4-N-6, ARA	4.90 ± 0.19	4.90 ± 1.00	4.28 ± 0.69	4.19 ± 0.34
C 20:5 N-3, EPA	0.35 ± 0.05	0.30 ± 0.09	0.17 ± 0.03	0.18 ± 0.01
C 22:5 N-3, DPA	0.69 ± 0.04	0.59 ± 0.14	0.45 ± 0.12	0.50 ± 0.03
C 22:6 N-3, DHA	0.47 ± 0.01	0.44 ± 0.10	0.25 ± 0.04	0.30 ± 0.02
∑ SFA	34.86 ± 0.99	33.19 ± 1.89	31.82 ± 2.20	31.11 ± 0.91
∑ MUFA	38.42 ± 1.86	39.15 ± 3.42	41.51 ± 1.05	41,19 ± 0.61
∑ PUFA N-3	2.18 ± 0.13	2.13 ± 0.20	1.67 ± 0.22	1.86 ± 0.08
∑ PUFA N-6	24.54 ± 1.43	25.54 ± 1.35	25.00 ± 1.29	25.84 ± 0.29
∑ PUFA N-6/N-3	26.72 ± 1.52	27.67 ± 1.53	26.67 ± 1.46	27.70 ± 0.34
	11.24 ± 0.54	11.98 ± 0.57	14.97 ± 1.50	13.88 ± 0.53

Fig. 1

C – control, FP – fermented product, PA – palmitic acid, SA – stearic acid, VA – vaccenic acid, OA – oleic acid, LA –linoleic acid, ALA – alfa-linolenic acid, GLA – gama-linolenic acid, DGLA – dihomo-gama linolenic acid, ARA – arachidonic acid, EPA – eicosapentaenoic acid, DPA – docosapentaenoic acid, DHA – dokosahexaenoic acid, SFA – saturated fatty acids, MUFA – monounsaturated fatty acids, PUFA – polyunsaturated fatty acids; (Kovalik et al., 2018)

XENOBIOTICS AND PREIMPLANTATION EMBRYO DEVELOPMENT

Principal investigator: prof. MVDr. Juraj Koppel, DrSc.
Applicant organisation: Centre of Biosciences SAS, Institute of Animal Physiology
Participating organisation: National Agricultural and Food Centre – Research Institute for Animal Production Nitra

Term of solution: 7/2015 – 6/2019
Budget from agency: 249 470 €
Project ID: APVV-14-0763

SUBJECT OF RESEARCH

In this project we have investigated the effects of selected xenobiotics on early embryo development. The project was focused on two groups of substances with oral poisoning potential for farm and domestic animals or human: insecticides and food additives. Their impact on early female reproductive capacity was analysed in two laboratory animal models: mouse and rabbit, in which the influence of maternal intoxication on the developmental capacity and qualitative parameters of preimplantation embryos was studied in the in the context of actual maternal physiological and metabolic status.

OBJECTIVES OF THE PROJECT

To analyze the effect of chosen insecticides on preimplantation development

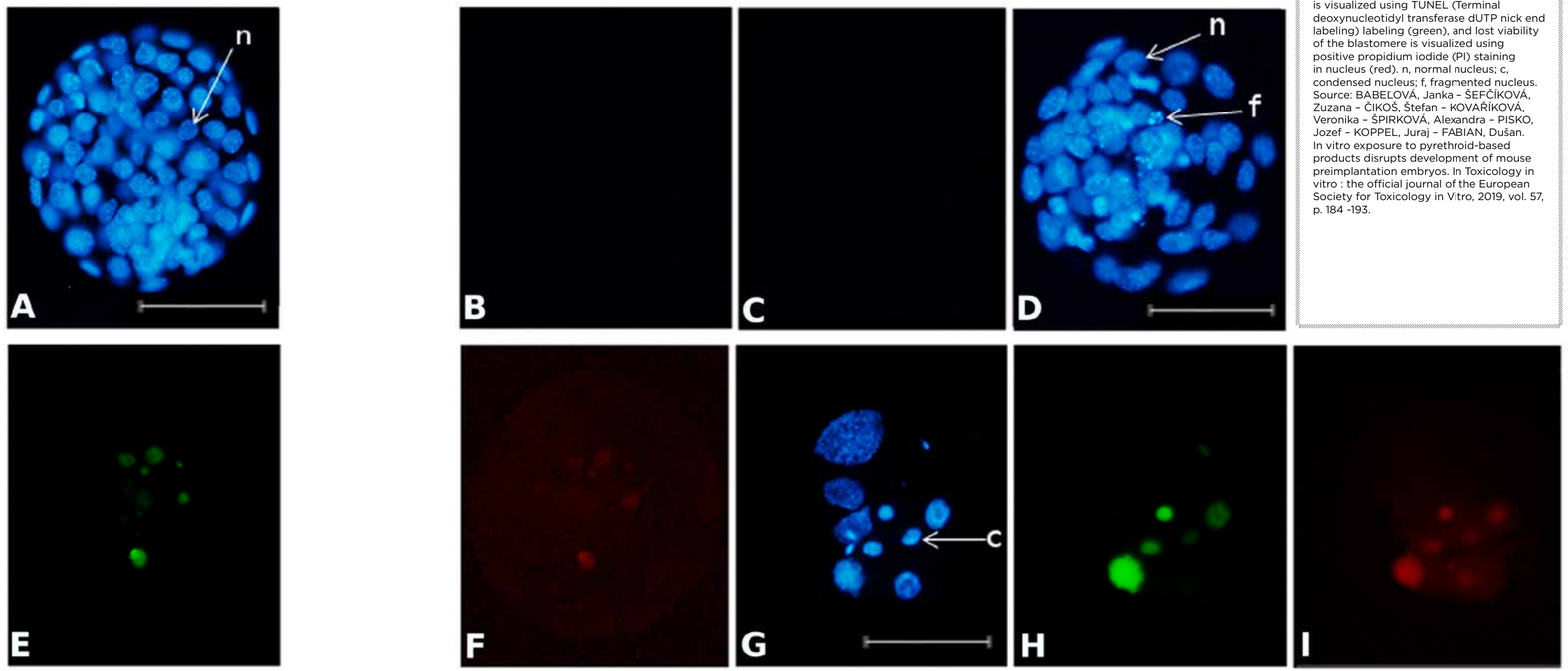
- To analyze the effect of chosen food additives on preimplantation development
- To analyze the effect of xenobiotics on preimplantation development in the context of altered condition of maternal organism

ACHIEVED RESULTS

The main aim of the project was to evaluate the effect of chosen xenobiotics on development of preimplantation embryo. We analyzed: 1. embryotoxic potential of nine active components of insecticides, several randomly-chosen commercial products and known secondary components of such products; and 2. embryotoxic potential of four food additives used for taste enhancement and three antioxidants used for long-time preservation of foodstuff, cosmetics and pharmacological products. Despite the declared minimal danger for mammalian cells and organs, guaranteed by producers of insect-killing products, we identified two insecticides with high embryotoxic potential in our in vitro and in vivo studies: fipronil (phenyl-pyrazole derivate) and thiacloprid (neonicotinoid). Since the presence of these insecticides in the environment of developing mouse (or rabbit) preimplantation embryo had significant negative effect on its developmental capacities and quality (decreased cell number and elevated incidence of cell death), we can conclude that exposure to fipronil- or thiacloprid-based products to female animals in the time of mating might increase the risk of embryonic loss. Interestingly, the presence of some secondary components of commercial insecticidal products (e.g. DECIS EW50) in the environment of developing embryo significantly increased detrimental effect of their active components (pyrethroid deltamethrin). However, the identification of many of such components was difficult, due to the protection of confidential commercial information. Results of our testing of three antioxidants, butylhydroxy-paraben (E209), butylhydroxy-anisol and (E320) butylhydroxy-toluen (E321) that are used for long-term preservation of food, cosmetics and pharmacological products, showed possible negative effects of these antioxidants on preimplantation embryo development as well. On the other hand, results of testing of two food additives used as flavouring agents – sodium nitrite (E250) and aspartam (E951) showed only slight influence on preimplantation embryo.

BENEFITS FOR PRACTISE

Decreased ability of preimplantation embryos to survive during first days of development is a serious problem of animal husbandry. Optimal management of nutrition and health of animals in the time before and after mating could significantly decrease a risk of preimplantation embryo losses. Our results indicate that insecticides (substances aimed to kill insects) belong to the most important detrimental factors potentially directly inducing embryonal losses in farm and wild animals as well as in companion animals. These animals are frequently in the contact with these compounds either in acute high doses (veterinary prevention and therapy of parasitic diseases) or as long-lasting intake of low doses (different feedstuff including grains, vegetables and fruits contaminated by residues of insecticides).



Illustrative fluorescence microphotographs of mouse blastocyst obtained in vitro: control group blastocyst (A, B, C); Permethrin treated group blastocyst (D, E, F); Decis EW 50 treated group blastocyst (G, H, I). Original magnification: x 400; scale bar 50 m. Nuclear morphology is visualized using chromatin staining with Hoechst 33342 (blue), specific DNA degradation in the nucleoplasm is visualized using TUNEL (Terminal deoxynucleotidyl transferase dUTP nick end labeling) labeling (green), and lost viability of the blastomere is visualized using positive propidium iodide (PI) staining in nucleus (red). n, normal nucleus; c, condensed nucleus; f, fragmented nucleus. Source: BABELOVÁ, Janka – ŠEFČÍKOVÁ, Zuzana – ČIKOŠ, Štefan – KOVAŘÍKOVÁ, Veronika – ŠPIRKOVÁ, Alexandra – PIŠKO, Jozef – KOPPEL, Juraj – FABIAN, Dušan. In vitro exposure to pyrethroid-based products disrupts development of mouse preimplantation embryos. In Toxicology in vitro : the official journal of the European Society for Toxicology in Vitro, 2019, vol. 57, p. 184 -193.

SOCIAL SCIENCES

SCIENCE CURRICULUM FOR PRIMARY SCHOOL 2020

Principal investigator: prof. PhDr. Lubomír Held, CSc.
Applicant organisation: Trnava University in Trnava, Faculty of Education
Participating organisations: Comenius University in Bratislava, Faculty of Mathematics, Physics, and Informatics, Faculty of Natural Sciences

Term of solution: 7/2015 – 6/2019
Budget from agency: 199 210 €
Project ID: APVV-14-0070

SUBJECT OF RESEARCH

Applied research carried out within the presented project focuses on science education of Slovak pupils, who according to many indications stay behind the level of education in economically developed countries. It also includes the proposed concept and organization of science curriculum that would ensure a change in science education in line with current European trends.

OBJECTIVES OF THE PROJECT

The stages of solving the project tasks were logically connected with the set goals:

- Mapping the current situation of science education of fifteen-year-old students
- Selection of "big" science ideas and concepts as target categories of science education
- Didactic reconstruction of selected topics of science education
- Construction of an innovated science curriculum for ISCED 2
- Verification of the innovated science curriculum at selected schools
- Optimization of innovated curricular documents
- Presentation of the innovated curriculum to the public – dissemination of the project results

ACHIEVED RESULTS

The aim of the project was to confirm (and possibly question) and specify alarming reports about the situation in science education in Slovakia resulting from OECD PISA measurements about the level of pupils' scientific literacy. When submitting the project, we relied only on the results of OECD PISA measurements from 2012, later even worse results of the measurements in 2015 went public. Deteriorating trend continued in 2018. Our empirical studies have confirmed this trend.
We were looking for different mechanisms for the coordination of curricular documents in the science education than we were used to in our country, in order to bring them into line with current trends in the developed world. The topicality of our applied research proved to be coherent with the elite team of W. Harlen and the elaboration of the so-called Big Scientific Ideas, which is a kind of ideological manifesto for the reform of science education in Europe.
The didactic reconstruction of traditional topics of science education was systematically re-evaluated. The key topics were studied from two perspectives in the process of their reconstruction: students' ideas (preconceptions and misconceptions) about the topics and recapitulation of historical (scientific) development of the scientific topic.

BENEFITS FOR PRACTISE

Partial material of the prepared curriculum was verified directly at schools. Some schools or selected teachers were involved in verifying the proposed activities for pupils. Based on the feedback, these activities were adjusted. About 200 activities have been prepared, which will be gradually published in the journal Biology, Ecology, Chemistry, to be accessible to teachers, experts and public generally. Several activities are being prepared in the form of "working textbooks" and are gradually finding their publishers. We hope they will be ready in the open market of textbooks.
Positive events took place during our work also in the management and legislative sphere, in particular, the possibility of carrying out practical activities with a larger number of pupils and by dividing the science lessons into smaller groups. Conceptual materials in science education are prepared for the changes that can be expected with political changes.
Dissemination of project results is connected with practice. If we take into account the number of researchers (including graduates and doctoral students), teachers involved in verifying activities, participants in various teacher conferences, participants in continual professional programs, members of subject commissions at the National Institute for Education, members of the Scholar Society at Slovak Academy of Sciences (SAS) and evaluators who evaluated partial results, we can state that the ideas of the science curriculum 2020 were discussed and evaluated by a quite large "sample of the experts in the field" and found a positive response here.
In addition to the international scientific conferences organized by the researchers at the beginning and the end of the project (ScienEdu 2016, Didsci + 2019 and IOSTE 2019), they continuously published their results in scientific journals and proceedings, many of which are registered in scientific databases (4 CCC, 9 WOS, 4 SCOPUS).
The results of the project are summarized in a collective monographic study: Held, Ľ., et al.. (2019) *Koncepcia prírodovedného kurikula pre základnú školu 2020. Trnava : TYPI., ISBN 978-80-568-0197-0.*

Fig. 1 / Chemistry can be interesting, too. Pupils are doing inquiry in order to find out properties of matter.

Fig. 2 / The gas can explode but also burn easily. Pupils "doing research" about flammability of gases.

Fig. 3 / Preparing teachers for changes in science education in the last phase of the project.

Fig. 4 / Young teachers getting ready for the demonstration of the Avogadro hypothesis, an original activity developed within the PK 2020 project.

Fig. 1

Fig. 2

Fig. 3

Fig. 4

DIDACTIC MEANS FACILITATING THE IMPLEMENTATION OF SELECTED CROSS-CUTTING THEMES IN THE TEACHING OF ETHICS IN THE SECOND GRADE OF PRIMARY SCHOOL

Principal investigator: prof. PaedDr. Eva Poláková, PhD.
Applicant organisation: Matej Bel University in Banska Bystrica, Faculty of Pedagogy
Term of solution: 7/2015 – 12/2018
Budget from agency: 169 742 €
Project ID: APVV-14-0176

SUBJECT OF RESEARCH

The integration of cross-cutting themes into the content of school subjects is still insufficient in practice. Several researches point out that, although teachers know theory of cross-sectional topics, they lack suitable teaching materials for their effective presentation to students. Because of this, the subject of the applied project APVV-14-0176, became the problem of the lack of didactic materials enabling the effective implementation of cross-cutting themes in Ethics for older school-age pupils.

OBJECTIVES OF THE PROJECT

The main goal of the project was to create such didactic tools based on empirical research of the current state, analysis of professional literary sources and the needs of practice, which would help teachers to continuously integrate selected cross-sectional topics into the teaching of Ethics. The fulfillment of the mentioned partial goals was reflected in the achieved results of the project and their use in educational practice:

- Realize empirical research of the current state at the second grade of primary schools;
- Realize analysis of relevant professional domestic and foreign sources – theoretical and empirical experiences of teachers;
- Create for teachers of Ethics a methodology for the implementation of cross-cutting themes into the content of ethical education and adequate teaching materials;
- Implement didactic workshops for teachers focused on the use of created teaching tools in teaching and test them in everyday educational practice.

ACHIEVED RESULTS

Based on the results of empirical research and theoretical analysis of resources, we specified the thematic units and topics of Ethics, in which we proposed to implement selected cross-cutting themes: personal and social development, media education, multicultural education and environmental education. Gradually, we worked on the creation of methodology, 4 multimedia didactic materials and 2 workbooks for students with differentiated content according to individual cross-sectional topics. Teaching aids were verified in teaching by cooperating teachers who had previously participated in workshops focused on their didactic use. We realized 5 workshops, some in cooperation with methodological centers, at which a total of 168 participants were trained. All didactic materials were published not only on DVDs, but also made available online on the created web portal "Cross-cutting themes in primary school".
We continuously informed the professional public about the results of the project by speaking at conferences (two of them organized within the project with the publication of proceedings), publishing articles, presenting posters, meetings of teachers and principals, organized in cooperation with methodological centers and popularization activities.

BENEFITS FOR PRACTISE

All activities and outputs of the project reflected its application character in the environment of real teaching at primary schools. The created methodological materials and didactic aids were distributed free of charge to primary school teachers at workshops, cooperating schools and methodological centers, thus achieving a wider dissemination of project results in pedagogical practice. The online accessibility of materials for 4 years on the portal www.prierezovetemy.info was very important. Published materials, methodological recommendations, various examples and examples of integration of cross-cutting themes into teaching helped to develop teacher´s didactic creativity in the form of alternative problem-solving strategies presented in cross-cutting themes and should be a motivation for creative implementation of offered forms, methods and audiovisual materials into concrete teaching. Subsequently, the results of the project were taken over by the State Pedagogical Institute on the basis of a concluded contract and published on its website in materials for teaching Ethics.
We therefore believe that the results of the project were maximally beneficial for the pedagogical public and will be permanently used in pedagogical practice.

Fig. 1

Fig. 3

Fig. 2

CONTAGION AMONG INTERNATIONAL MARKETS: REVISITING MODELS AND ANALYZING NETWORKS

Principal investigator: doc. Ing. Eduard Baumöhl, PhD.
Applicant organisation: University of Economics in Bratislava
Term of solution: 7/2015 – 12/2018
Budget from agency: 224 405 €
Project ID: APVV-14-0357

SUBJECT OF RESEARCH

Crashes on financial markets occur infrequently; still they are one of the major risks to policy makers and investors. The recent financial and sovereign-debt crisis showed us that even local market-specific problems might dramatically influence other markets around the world (e.g., Arghyrou – Kontonikas, 2012; Beirne – Fratzscher, 2013). It seems that growing interdependence between economies and different assets classes will only increase contagious tendencies in markets. As a consequence, contagion is a central topic among researchers and policy makers. Without a clear understanding of financial contagion and its mechanism, we can neither assess the problem nor design appropriate policy measures to control it. The main finding stemming from a vast amount of research conducted so far is that the different mechanisms by which a certain crisis can spread differs greatly case by case, both in their causes and implications. Policy measures that do not take these differences into account may do more harm than good (Moser, 2003).

OBJECTIVES OF THE PROJECT

The main goal of the project was to model the contagion between the stock, bond, foreign exchange, money and commodity markets around the world.

ACHIEVED RESULTS

The main results of the project were published in 15 foreign CC journals, such as Finance Research Letters (Elsevier), Journal of International Financial Markets, Institutions and Money (Elsevier), Journal of Financial Econometrics (Oxford Academic), Physica A: Statistical Mechanics and its Applications (Elsevier), The Review of Financial Studies (Oxford Academic), Quantitative Finance (Taylor & Francis).
Based on literature overview and revision of existing models measuring financial contagion, we proposed a concept based on Granger causality, the effects of non-synchronous trading, and graph theory. Apart from examining the topological properties of constructed networks over time, we used a spatial probit model to determine the determinants affecting the existence of oriented edges between individual stock markets. This procedure (combination of financial econometrics, graph theory, and spatial econometrics) has not been used in the literature and brings several new findings. In addition to the usual determinants (e.g., market characteristics), the temporal closeness of trading hours between markets has proven to be a highly significant factor for return and volatility spillovers.

BENEFITS FOR PRACTISE

From a practical point of view, this means that the benefits of international diversification are lower if investors decide to invest in markets whose trading hours are closer together. A similar effect has been demonstrated in relation to the US market – the likelihood of spillovers between markets is higher if their trading hours are closer to the US market. We have also identified markets with higher probability of contagion transmission. Our results also showed that the individual characteristics of markets do not play such a vital role in volatility spillovers between markets, as the overall induced spillover effect propagated by neighboring markets within constructed networks.
We have summarized the achieved results into a practical application focused on the construction of an effective portfolio, which is based on the topological properties of the created financial networks. On a sample of 45 different financial assets (stock indices, bonds and money market instruments, commodities, and currencies), we showed that regardless of the type of network and the degree of centrality used, network-based allocation strategies improve the basic risk-return characteristics of created portfolios.

Fig. 1

Fig. 2

Fig. 1 / Project investigators at the organized conference Slovak Economic Association Meeting 2017 in Košice with the keynote speaker – Nobel Prize in Economics laureate – Robert Engle.

Fig. 2 / The results of the project were presented at SEAM 2017 in a special session "APVV CIMRMAN'S session" in the presence of Robert Engle.

Fig. 3 / Complex network of stock market return spillovers in 2008.

Fig. 4 / Correlation threshold graph of different assets.

Fig. 4

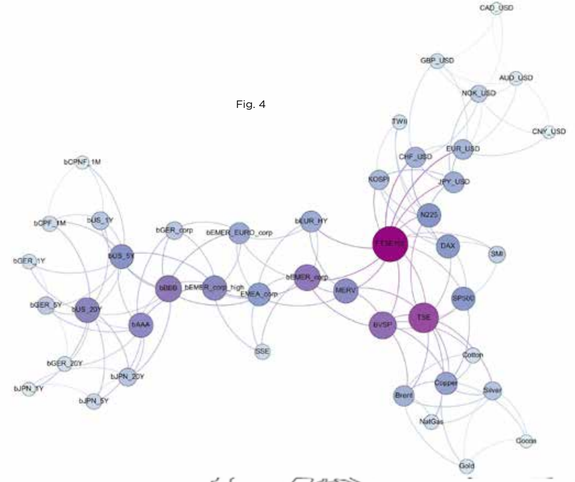


Fig. 3

BETWEEN EAST AND WEST, INTEGRATION OR DIVERGENCE OF VALUES? SLOVAKIA IN CROSS-NATIONAL COMPARATIVE RESEARCH

Principal investigator: Ing. Mgr. Bahna Miloslav, PhD.
Applicant organisation: Institute of Sociology of Slovak Academy of Sciences
Participating organisations: Comenius University in Bratislava, Faculty of Arts, Department of Sociology
Faculty of Social and Economic Sciences, Comenius University in Bratislava

Term of solution: 7/2015 – 6/2019
Budget from agency: 249 244 €
Project ID: APVV-14-0527

SUBJECT OF RESEARCH

In comparative research Slovakia is traditionally analyzed within the group of ex- / post-communist or transforming countries. Via participation in the development and fielding of international comparative research within the *International Social Survey Programme (ISSP)* and *Comparative Study of Electoral Systems (CSES)* the project tested empirically if this classification still applies or if there are other, more adequate, explanations or applicable typologies.

OBJECTIVES OF THE PROJECT

The project had four main objectives. *The first* was to support the continuing participation of Slovakia in international comparative research programs ISSP and CSES by participating in the selection of the research topics and fielding of the modules planned for the time of the project duration.
The second objective was to develop comparative analysis of the Slovak society using the optics of macro-sociological theories of social change.
The third objective was to develop the methodology of comparative research via methodological experiments.
The fourth objective was the expansion of the Slovak Archive of Social Data (SASD) by emergency archiving of several valuable older surveys, mainly from the 1990s, which were made available to the expert public.

ACHIEVED RESULTS

Four modules of the ISSP survey as well as one CSES module were fielded within the project. Team members also participated in the thematic and scientific heading of these programs. In 2016 team members representing Slovakia in the ISSP were elected as ISSP Standing Committee members (for the 2016 to 2020 period). In 2019 the ISSP General Assembly voted Slovakia to become one of the Drafting Group members for the 2022 ISSP module. The ISSP General Assembly will be held in Bratislava in 2022. Within the project the Slovak CSES representative participated in preparation of module 5 focusing on populist politics. This module is being fielded in Slovakia after the 2020 parliamentary elections.

Comparative analyses were presented in the *"Slovakia on Value Maps: Views of the Slovak Public in the Context of the International Comparative Survey ISSP"* publication as well as in several journal articles. Team members were successful at publishing papers in several prestigious international journals (e.g. *East European Politics, Government Information Quarterly, Nationalities Papers, Population Space and Place, New Perspectives or Studies in Higher Education*), most of which also belong to the top 25% most cited journals within their respective disciplines based on Journal Citation Reports. The final results of the comparative analysis will be published in the concluding project monograph which is currently been prepared for print.
Split ballot experiments were part of all surveys fielded within the project. Findings from these methodological experiments widened the knowledge on reliability and sensitivity of international comparisons as well as on the sensitivity of the respondents in Slovakia to minor changes in questions asked within international comparative surveys.
Besides the four surveys fielded and archived within the project, another thirteen so far unavailable older surveys mostly from the 1991 to 1997 period have been archived and were made available via the Slovak Archive of Social Data (http://sasd.sav.sk).

BENEFITS FOR PRACTISE

Thanks to the surveys fielded within the project data from Slovakia became part of the integrated datasets of ISSP and CSES comparative research programs and are globally available to social scientists around the globe via the respective archives of these research programs. This is a precondition for Slovakia to become part of future analyses written by not only the project team members but also of further analyses using data from ISSP and CSES all over the world. Thanks to archiving of older representative survey from the period immediately after the fall of communism in 1989 the whole scientific community gained new analytical material. For these surveys the archiving preserved data as well as methodological documentation. In 2019, the young post-doctoral fellow hired for the post-doctoral position within the project was awarded the post-doctoral stipend from the Štefan Schwarz fund of the Slovak Academy of Sciences and placed second in the young scientists below 35 years awards of the Academy.

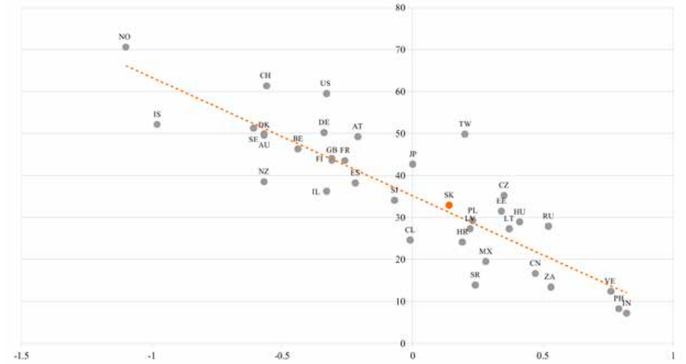


Fig. 4

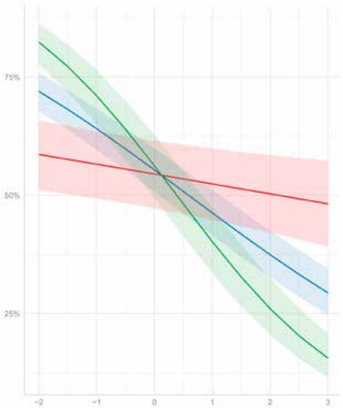


Fig. 3

Fig. 5

Fig. 2

Fig. 1

Fig. 1 / Meeting of national coordinators of the CSES survey in August in Philadelphia, USA.

Fig. 2 / Press conference on findings from CSES and ISSP 2016 in February 2017.

Fig. 3 / Predicted probability of borrowing money from family and friends (Y axis) depending on respondent's age (X axis, age is standardized) from a multilevel binary logistic regression model. The model based on ISSP 2017 Social Networks and Social Resources III survey demonstrates that the modeled relationship is different in societies with high (red), medium (blue) and low (green) levels of corruption.

Fig. 4 / Positive relationship between utilitarian understanding of work (X axis) and gross domestic product per capita in 2017 in USD (Y axis) based on surveys from 36 countries of the world participating in the ISSP 2015 Work orientation IV module.

Fig. 5 / Cover of the "Slovakia on Value Maps: Views of the Slovak Public in the Context of the International Comparative Survey ISSP" publication.

SOCIAL STRATIFICATION AND SOCIAL MOBILITY IN SLOVAK SOCIETY

Principal investigator: prof. PhDr. Ján Sopóci, PhD.
Applicant organisation: Comenius University in Bratislava, Faculty of Arts, Department of Sociology
Term of solution: 7/2015 – 12/2018
Budget from agency: 249 564 €
Project ID: APVV-14-0639

SUBJECT OF RESEARCH

The project focused on analysis of social stratification and social mobility in Slovakia, as well as analysis of the context and consequences of social inequalities. Research was based on the most recent theoretical findings (neo-Weberian theories of stratification) and methodological approaches that are applied in current sociology. The research team conducted an empirical survey, which addressed the questions of social stratification and mobility, but also precarious work, or societal anomie.

OBJECTIVES OF THE PROJECT

The aim was to generate sociological knowledge about the following issues:

- social inequalities and social differentiation of the Slovak society;
- economic, social and cultural characteristics of social classes and status groups that form the basis of social stratification system;
- intra-generational and inter-generational social mobility, as well as their sources and mechanisms;
- life chances of members of different social classes and status groups;
- the most important societal consequences of social inequalities;
- the most recent trends in social stratification and mobility, as well as consequences of social inequalities in the comparative perspective.

ACHIEVED RESULTS

The analysis of long-term development of social stratification shows that a post-feudal type of stratification, seen at the beginning of the 20th century, was gradually replaced by modern type of social stratification, which is similar to the stratification in the contemporary western societies.
After 1989, following significant changes in social stratification can be identified:

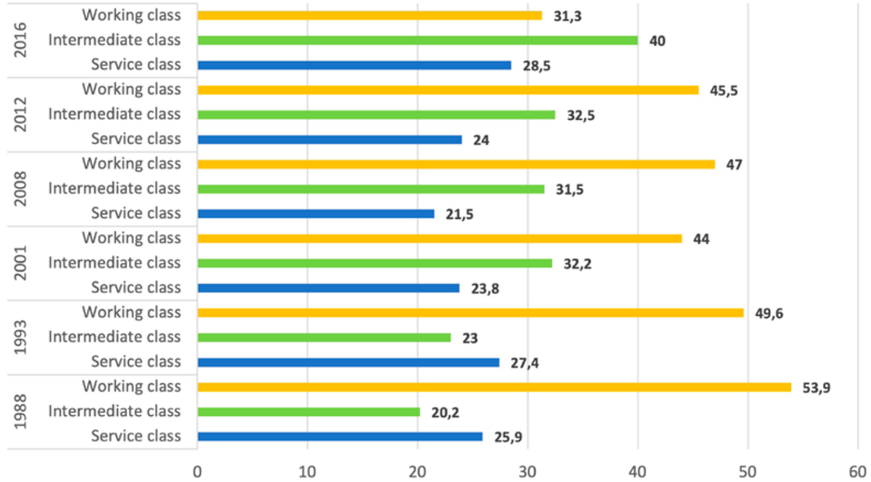
- a significant decrease in the proportion of manual and agricultural workers;
- a continuous increase in the proportion of small entrepreneurs;
- an increase in the proportion of service class and class of routine non-manual workers;
- increasing presence of inter-mediate class and decreasing presence of working class.

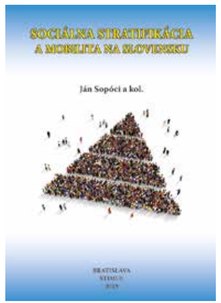
As result, social stratification has no longer the shape of pyramid, but it is shaped like rugby ball, with the strongest presence of intermediate class and more or less the same proportion of service and working class.
When testing the models of relationship between social classes and lifestyles (including cultural consumption), it has been shown that the class homology model is valid for Slovakia. It means that members of different social classes and status groups do have distinct forms of cultural consumption.
Social hierarchy manifests itself not only in class structure, but also in status hierarchy, which can be identified, for example, in relation to the selection of partners with similar employment status (including required education level and content of work). This status hierarchy represents a dimension of social stratification which differs from class structure, as well as from hierarchy based on socio-economic status.
Attention was also paid to patterns of intra- and inter-generational social mobility. It has been shown that in terms of intra-generational mobility, men show a higher mobility than women. But intra-generational mobility in Slovakia is characterized by persistence of class position: the most of people do not change their class position over working life. When it comes to intergenerational social mobility, members of working class and lower middle class have the lowest chances to upward mobility.
Data from the empirical survey confirmed increasing presence of precarious work in Slovakia. However, they show increasing polarization in the labour market and its segmentation, with persisting differences between primary labour market (more stable and better paid jobs with better future prospects), and secondary labour markets (more unstable and worse paid jobs with worse future prospects).

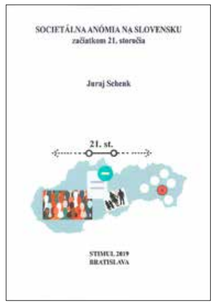
BENEFITS FOR PRACTISE

The research project brought about new findings about the Slovak society, which could be used by social scientists and pedagogues. They may also serve as resources for decision-making process – as basis point for additional analyses of socio-economic issues and problems related to equal opportunities, social inequalities and social mobility, or as reference point for preparing long-term visions and strategies.

Class structure of economically active population in the period 1988 – 2016, based on 3 class EGP scheme (%).







DEVELOPMENT OF INCLUSIVE ENTREPRENEURSHIP OF THE SELECTED DISADVANTAGED GROUPS IN SLOVAKIA: PRAGMATIC APPROACH

Principal investigator: prof. Ing. Anna Pilková,PhD., MBA
Applicant organisation: Comenius University in Bratislava, Faculty of Management (FM UK)
Participating organisation: Slovak Business Agency (SBA)

Term of solution: 7/2015 – 6/2019
Budget from agency: 153 741 €
Project ID: APVV-14-0647

SUBJECT OF RESEARCH

The subject of research was the issue of entrepreneurial inclusivity development in Slovakia. Entrepreneurial inclusivity represents the involvement of disadvantaged groups (e.g. women, seniors, youth, migrants, etc.) in entrepreneurial activities, which unleashes their creative potential and contributes to their economic self-sufficiency as well as to the development of society.

OBJECTIVES OF THE PROJECT

The main aim of the project was to develop a comprehensive methodology for the development of entrepreneurial inclusivity in Slovakia at the national and regional levels for selected disadvantaged groups (women, youth, seniors and migrants) based on the analysis of the current state, the latest theoretical knowledge as well as practical experience (best practices) in Europe and in the world. At the same time, the aim was to verify and test selected components of the methodology in the form of pilot projects and to prepare an analysis of the quantification of potential impacts of selected attributes of the methodology (the so-called impact study).

ACHIEVED RESULTS

The result of the first stage of the project aimed at analyzing the current state of entrepreneurial inclusivity of women, youth, seniors and migrants in Slovakia is a scientific monograph of a ten-member team of the FM UK and SBA entitled "Entrepreneurial Inclusivity in Slovakia: state and development trends". It is a comprehensive document on the entrepreneurial inclusivity of selected disadvantaged groups in Slovakia, which in 12 chapters presents the results of quantitative and qualitative analyzes carried out on the data of the Global Entrepreneurship Monitor (GEM), as well as specially conducted surveys for individual studied groups. The document was published in 150 copies and distributed among relevant stakeholders and members of the academic community. It is one of the main tools for project presentation, its outputs and summary knowledge on the issue of entrepreneurial inclusivity in Slovakia.

The result of the second stage of the project aimed at monitoring the state of entrepreneurial inclusivity in Slovakia from the perspective of individual disadvantaged groups (women, seniors, youth, migrants) using GEM methodology was the creation of a "dashboard", which represents a set of key indicators of the state of entrepreneurial inclusivity of women, young people and seniors in Slovakia. It is based on GEM data as well as available secondary data for which there is a presumption of stable availability and harmonization over time. It contains a total of 49 indicators, while 46 of them can also be obtained at the level of regions (8 self-governing regions) and 31 of them can be monitored (due to their nature) as the inclusion index. The "Dashboard" contains data on an annual basis and is continuously updated in connection with the availability of new data (usually in the first half of the calendar year, data of the previous year are available).
As part of the third stage of the project, a comprehensive methodology for the development of entrepreneurial inclusivity for women, youth, seniors, and migrants in Slovakia was developed. The methodology contains both a general methodology for the development of entrepreneurial inclusivity with universal components (governance, analysis of entrepreneurial inclusivity, strategy formulation and priority setting, action plan, monitoring and evaluation, regional applications, institutional implementation model, work schedule and responsibilities), as well as its specifications for individual disadvantaged groups – women, youth, seniors, and migrants. A special component of the methodology is an impact study in the form of instructions for monitoring and evaluation of programs.
The result of the fourth stage of the project was the verification of the proposed methodology on four pilot projects, namely the project to support women's entrepreneurship through activities within the National Business Center, the project to support youth entrepreneurship through the SBA Microloan Program; the entrepreneurial education project with an element of intergenerational cooperation at FM UK and Centre of further education UK; and the project Training for the start-up or further development of business for foreigners in Slovakia implemented by the IOM (International Organization for Migration) in cooperation with FM UK and SBA.

BENEFITS FOR PRACTISE

The research project had the character of applied research. Each of these results has practical use mainly in institutions focused on the development of entrepreneurial inclusivity in Slovakia. The main coordinator of the use of the main output – a comprehensive methodology for the development of entrepreneurial inclusivity, is the SBA, which was also a cooperating organization of the project. Representatives of ministries were acquainted with the individual outputs at conferences and workshops, which were regularly organized throughout the project.

Fig. 1 / Workshop at SBA in 2018 on the results of the analysis of entrepreneurial inclusivity.

Fig. 2 / Workshop at SBA in 2019 on the key components of a comprehensive methodology for the development of entrepreneurial inclusivity.

Fig. 3 / Workshop with OECD in 2016 on the OECD online tool for entrepreneurial inclusivity analysis.

Fig. 1

Fig. 2

Fig. 3

HUMANITIES

ERROR TYPOLOGY IN MACHINE TRANSLATION INTO SLOVAK AS AN INFLECTIONAL LANGUAGE

Principal investigator: doc. RNDr. Daša Munková, PhD.
Applicant organisation: Constantine the Philosopher University in Nitra

Term of solution: 7/2015 – 9/2018
Budget from agency: 112 681 €
Project ID: APVV-14-0336

SUBJECT OF RESEARCH

Undoubtedly, translation is one of the key tools of human communication. Currently, as translation technologies are almost fully integrated into translation processes, it is essential to know how to utilize them effectively. The growing progress of language and translation technologies has not only changed but continues to change the way people communicate, resulting in a new space for translation research and the development of the translation industry in today's globalized world.
Due to the widespread use of technologies in the translation process, the evaluation of Machine Translation (MT) quality has become increasingly important. When evaluating MT quality, the concept of optimization is closely related to the quality, as the examined MT systems are optimized based on the results of quality evaluation.

OBJECTIVES OF THE PROJECT

The aim of the project was to emphasize the importance of functionality of the theory of artificial intelligence and its interdisciplinary aspect in the context of translation process aiming at its scientific base. Furthermore, it was one of the objectives to point out the legitimacy of machine translation in the translation process. Attention was paid to quality evaluation of machine translation from English and German into Slovak using methods of manual and automatic evaluation, including the identification and classification of MT errors.

ACHIEVED RESULTS

To monitor the dimensions of (factual) accuracy and (linguistic) correctness, a categorical model (Vaňko, 2017) was designed to evaluate machine translation, corresponding with the DFQ Errors Typology for the majority of languages. Accuracy is defined as the degree to which machine translation captures the meaning of the source language, and fluency (intelligibility) is defined as the degree to which machine translation is a "good" example of the target language. Considering the text intelligibility, two types of errors usually occur with machine translation. The first comprises such errors that do not cause the text to be unintelligible, the second category are errors that make a word, a phrase or a paragraph, incomprehensible. A directly proportional dependence with adequacy and fluency was identified for all error categories of the model. Errors in nominal morphosyntax contribute to the reduction of fluency in Slovak.
Although manual evaluation is the most desirable, it is financially demanding and time-consuming. Also, it includes a high level of subjectivity, therefore an automatic evaluation is often used, the metrics of which are reliable and valid, which we, like the first to, proved for Slovak. Since the project was rooted in several academic disciplines, a unique system OSTPERE was designed for teaching translation, post-editing of machine translation, translation revision, and evaluation of translation quality, in detailed cooperation with the Department of Informatics CPU in Nitra.

BENEFITS FOR PRACTISE

This project is of strong interdisciplinary character and of a novel nature within both the Slovak and international research environments. The project research of MT was applied to Slovak as an inflectional type of language comprising a high number of morphological inflections including grammatical polysemy, and homonymy. The issue of MT within Slovak has not yet been researched which makes the project purposeful and innovative.
Currently, numerous language and translation technologies are based on the principles of artificial intelligence. The main benefits delivered by the project are the increase of machine translation awareness as well as developing MT literacy and MT attributes among its users. We want them to become informed and critical users, either before the translation process itself in the form of text pre-editing or after the translation process in the form of text post-editing.

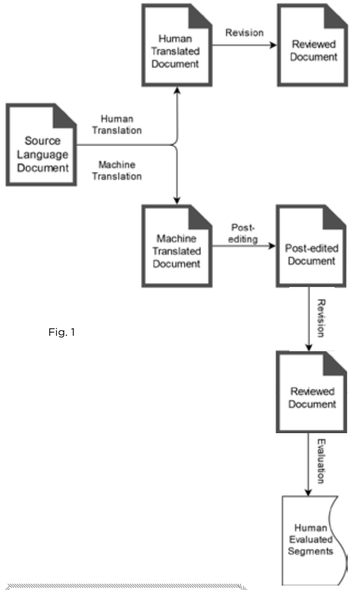
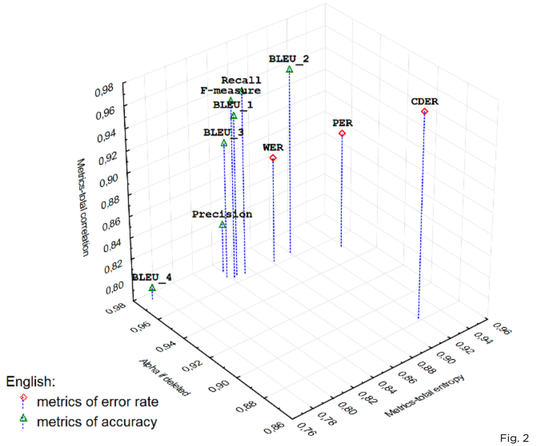


Fig. 1

Fig. 1 / Illustration of the workflow of MT evaluation using OSTPERE.

Fig. 2 / Categorized 3D scatterplot of reliability estimations of examined metrics of MT.

Fig. 3 / Results of residuals analysis of the precision/recall metric of MT and PEMT.



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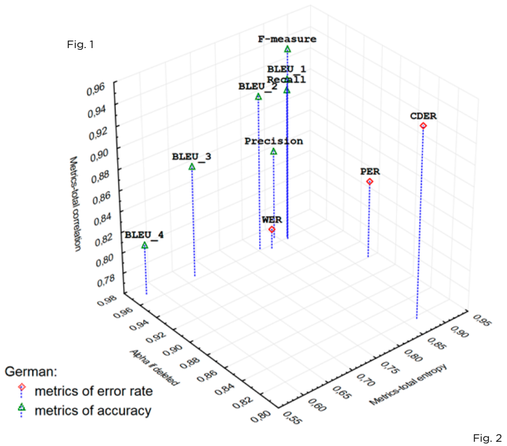

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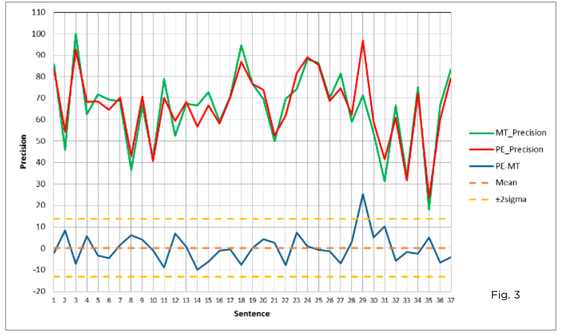

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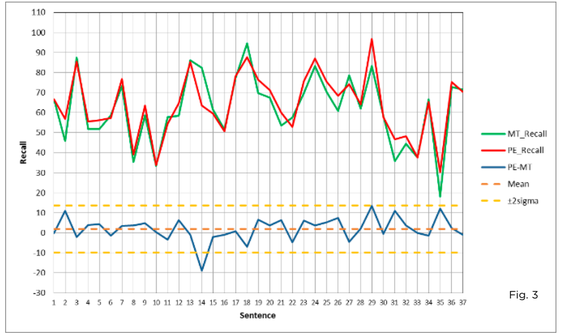


Fig. 3

SCIENCE, SOCIETY, VALUES: A PHILOSOPHICAL ANALYSIS OF THEIR MUTUAL INTERCONNECTEDNESS AND INTERACTIONS

Principal investigator: doc. PhDr. Mariana Szapuová, PhD.
Applicant organisation: Faculty of Arts of Comenius University
Term of solution: 7/2015 – 6/2019
Budget from agency: 217 994 €
Project ID: APVV-14-0510

SUBJECT OF RESEARCH

The subject of the research was the social dimensions of scientific knowledge, i.e. a) the influence of the value-laden social environment on scientific knowledge production, b) the effects of science on human life and values, and c) the value and importance of science in contemporary society. Research attention was also focused on of how some social factors – especially power and gender – intervene in knowledge production and how they enter into the processes of accepting scientific knowledge by society.

OBJECTIVES OF THE PROJECT

The main goal of the project was to examine the forms of relationships and interactions between science, values and the socio-cultural environment, to shed light on the current dynamics of these relationships with special regard to current issues in the relationship "science and society".
We conducted our research as multidimensional philosophical and ethical research aimed at:
a)reconstruction of the traditional view of the relationship between science and social values, based on the principles of objectivity and autonomy of science, and reconceptualization of basic concepts; b) analyzing the value dimension of science and developing a conceptual apparatus that can be used to explain the ways in which values intervene in the knowledge production; c) examination of power techniques acting on and in science, as well as the influence of knowledge on the formation of moral attitudes of the subject; d) examining the ethical issues of science and the ethical issues related to the exploitation of its results.
The basic hypothesis of the project "There is no value-neutral system of scientific knowledge and every social system of (moral, cultural) values depends on the current state of knowledge and technology within the community", was based on the assumption that a) values intervene in the processes of knowledge creation, b) scientific knowledge shapes the value environment and c) science is situated and this characteristic is not something arbitrary, but rather constitutive of science. This hypothesis was tested by a critical analysis of the traditional view of the relationship between science and values, analysis of current philosophical concepts that emphasize the value-ladenness of scientific knowledge, examining how social factors (power, gender) act in the processes of creating scientific knowledge, and analysis of moral consequences of science.

ACHIEVED RESULTS

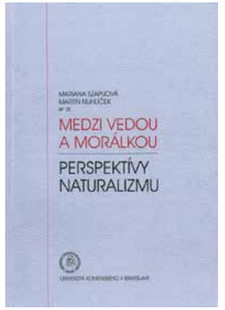
An important result of the research is the demonstration of the inadequacy of the dichotomous understanding of the relationship between facts and values, as well as the traditional assumption of value neutrality of science. The question of whether scientific knowledge is value-neutral needs to be reformulated into the question of which, or what are the values that operate in science. Research focusing on the ethical aspects of science in the context of its changing societal status, on ethical issues related to the exploitation of science results, as well as on power strategies affecting science, has demonstrated the complex nature of the relationship between science and moral values. It has proved appropriate to grasp these issues through the perspective of philosophical naturalism. This perspective allows the creation of concepts exceeding the framework of the classical image of science by integrating into it the reflection of real processes of knowledge production and the results of empirical research on it. The research also confirmed that the ideal of "pure" power-independent truth is unattainable and currently dysfunctional. On the other hand, even if we accept that scientific knowledge is infiltrated with values, it does not make science a sphere of subjectivism, nor leads us to resign from scientific objectivity. The objectivity of science does not have to be understood in the (traditional) sense of value neutrality, but it can also be considered in such a way that does not exclude the value-ladenness of science. Objectivity can be associated with the social, intersubjective and communal nature of the creation of scientific knowledge, with the practice of scientific communities, and with such mechanisms and procedures as e.g. peer review and criticism.

BENEFITS FOR PRACTISE

The results of the project can be applied in both practical and theoretical levels. At the practical level, they can be used in setting science policies, in evaluating science and in creating codes of conduct for scientific and academic institutions. At the theoretical level, the results are to be applied in a follow-up project on naturalism as a universal philosophical program and they can also set the directions of further research in the field of bioethics and ethics of research.

Fig. 1

Fig. 2



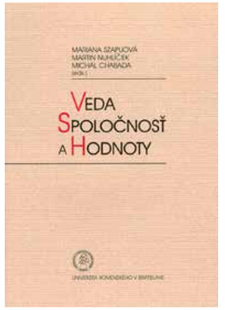


Fig. 1 / The speech by MUDr. Križanová at the 3rd workshop on Science and Ethics, May 22, 2017, on the topic: The Morality of Euthanasia?

Fig. 2 / Poject conference on Science and Values: Naturalistic and Constructivist Approaches, held in Bratislava, May 4, 2017, (Prof. Dr. Ludger Honnefelder (Bonn), Prof. Mgr. Michal Chabada, PhD., the head of the Department of Philosophy and History of Philosophy, Faculty of Arts, CU in Bratislava, Prof. PhDr. Jaroslav Šušol, PhD., the Dean of the Faculty of Arts, CU in Bratislava).

CONTINUITY AND DISCONTINUITY PROJECT OF THE POLITICAL AND SOCIAL ELITES IN SLOVAKIA IN THE 19TH AND 20TH CENTURIES

Principal investigator: PhDr. Valerián Bystrický, DrSc. (do roku 2017), doc. Peter Šoltés, PhD.
Applicant organisation: Institute of History of Slovak Academy of Sciences
Term of solution: 7/2015 – 6/2019
Budget from agency: 207 554 €
Project ID: APVV-14-0644

SUBJECT OF RESEARCH

The project *Continuity and Discontinuity Project of the Political and Social Elites in Slovakia in the 19th and 20th Centuries* has been the first project of the basic research that systematically investigated the long-term impacts of societal ruptures, regime changes and coup d'états on various types of elites.
In every modern society, there is a group of elites with the power and influence to decide the crucial questions. Without understanding the mechanism of the "circulation of elites," it is impossible to describe and analyze the development of society. During the 19th and 20th centuries, the frequent and recurring geopolitical changes significantly affected the composition and functioning of Slovak elites. As a result, the traditional perception of modern Slovak history is based on the perception of the radical and complete replacement of elites after each political change.

OBJECTIVES OF THE PROJECT

Besides the traditional focus on political elites, project comprehensively examined also cultural, intellectual, and economic elites. The research team identified and analyzed strategies utilized by established elites to responded to the new political conditions.
The project paid attention to the social processes among the local elites. The research on Slovak national elites in the Kingdom of Hungary and the political elites of minorities in the interwar and postwar Czechoslovakia was followed by innovative prosopography on the level of local and regional associations and societies as well as executive and financial elites.

ACHIEVED RESULTS

The project results offer new knowledge regarding the survival strategies of the "old elites" and the programs for educating new, loyal intelligentsia. The focuses are on the changes in the relations between the ruling power and the intellectual elites, especially during the "Ludák" regime of the Slovak state (1939 – 1945) and the socialist dictatorship (1948 – 1989). Research has proved that an immediate and complete replacement of elites has never happened in Slovakia. On the contrary, such a process was always long-lasting and had a form of merging old and new cadres. No political change or revolution purged the established elites completely. Various types of elites had different chances to survive the political ruptures. In general, it was easy to replace the political power holders. However, to replace thousands of experts like civil servants or scientists with new, politically loyal, or ideologically fitting ones was nearly impossible. Each new regime had to deal with the dilemma of what is more important loyalty or qualification. In 1918 and 1989 the pragmatism prevailed. In the Ludák and communist regimes, the ideological, class, and racial aspects very often (although not always) played a crucial role.
In 2018, the project team organized an international conference *An Empire within the Empire? The Habsburg Hungary in the 19th century and after the dissolution* attended by renowned historians from the USA, Great Britain, and Hungary (Pieter M. Judson, Mark Cornwall, Gábor Gyáni, Gábor Egry).
The project supported the publication of 13 monographs and 78 academic studies. The main and concluding output of the project is the collective monograph *Elity a kontraelity na Slovensku v 19. a 20. storočí.* Kontinuity a diskontinuity [Elites and Counter-Elites in Slovakia in the 19th and 20th Centuries. Continuities and Discontinuities.] (Veda 2019).

BENEFITS FOR PRACTISE

The history of elites is an established research topic intricately connected with the actual social issues like the accumulation of wealth in the hands of the small group or restricted social mobility. Slovakia is a part of the region where the reproduction of elites did not occur unhindered in a framework of relatively stable nation-states. The cumulative effects of this fact are essential for the understanding of why the selection of potential elites, their behavioral patterns, and the values they represent were/are so often contradictory to those in the more stable parts of Europe. The long-term analysis of the people in the decision-making positions in the broader global context is essential for the comprehension of the current issues shaping society. Many such problems have their roots in the weak, poor-quality, and, therefore, failing elites.
The project team actively participated in the popularization of its research resultsProject members took part in more than 30 TV and radio broadcasts and four documentaries, both as authors and participants.

Fig. 1

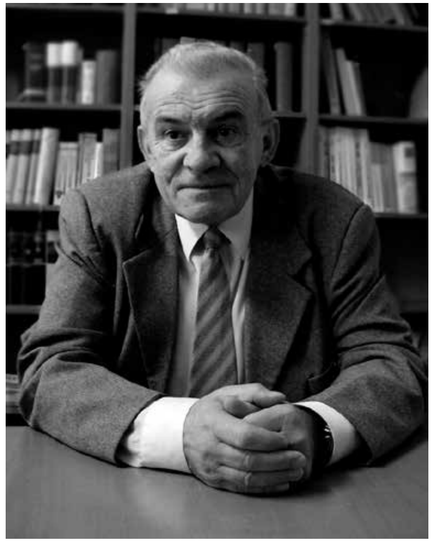


Fig. 2

Fig. 3

Fig. 1 / Scientific publications supported by the project.

Fig. 2 / The principal investigator of the project, Valerián Bystrický, passed away in 2017.

Fig. 3 / Elena Mannová (Institute of History of Slovak Academy of Sciences) presenting her paper at the conference An Empire within the Empire? The Habsburg Hungary in the 19th century and after the dissolution. From the left Pieter M. Judson and Body Zsombor.

MUSIC IN BRATISLAVA

Principal investigator: doc. PhDr. Jana Bartová, PhD.
Applicant organisation: Faculty of Arts of Comenius University
Term of solution: 07/2015 – 06/2019
Budget from agency: 209 187 €
Project ID: APVV-14-0681

SUBJECT OF RESEARCH

The subject of the research was the musical culture of Bratislava, researched in the time range from the oldest existing sources to the present. In terms of content, the musical culture of the city was explored in its broad-spectrum forms of expression, ranging from musical creation through the organization of musical life, activities of individuals and institutions involved in various areas of musical life, to contemporary reflection of creative acts and events and its analysis in historical contexts.

OBJECTIVES OF THE PROJECT

The project objectives were appointed, as follows:

1. to achieve new knowledge about music and musical life in Bratislava from the source research, mainly in these areas, which were not sufficiently investigated until now;
2. to create a new image of the music history of the city from the Middle Ages until today in an integral, systematically outlined and updated form in terms of knowledge and methodology;
3. to analyse and prove the assumption that Bratislava occupied an unique position in respect to the musical life and culture within the network of Central-European urban communities;
4. to present results of the research to the scientifical community as well as wider cultural public by the word (active participation in conferences, organizing lectures and discussion forums), by the text (studies in scientifical journals and monographies, critical score editions, popularizing articles), but also by artistic forms (realisation of concert and recording in the co-operation with the profesional performers).

ACHIEVED RESULTS

The starting point for the implementation of the project was the source research with the aim of concentrating the study on selected thematic areas, which have so far received little attention and to study the sources systematically and comprehensively. The research brought new knowledge to several problem areas and stages of the music history of the city, for example to the activities of the Bratislava Chapter´s scriptorium (investigation of the origin of so-called Buda Antiphonary, E. Veselovská); to the establishing and functioning of the oldest public music school and the development of burgher´s piano culture (E. Szórádová); to the organization of musical life, the management of musical institutions and forms of musical patronage (J. Bartová); to the activities of musical instrument makers in Bratislava, especially that of Carl Schmidt and Franz Schöllnast (E. Szórádová, P. Jantoščiak); to musical production at the Municipal Theater and his position in the musical life of the city's cultural elites (J. Laslavíková). Attention was also focused on musical life and cultural policy in the period of the first Slovak Republic (B. Ladič, Y. Kajanová), but the latest pop, jazz and alternative music scene (Y. Kajanová) was also mapped. Thanks to the study of hitherto unknown sources, it was possible to supplement our knowledge with new facts and contexts, but also to re-evaluate and reinterpret some existing statements. New investigations were reflected in the manuscript of a new extensive monograph on the musical history of Bratislava from the Middle Ages to the present, which has already been partially published in electronic version. New findings, analyzes, critical interpretations of sources were presented also at domestic and foreign conferences, as well as in international indexed journals, or proceedings and in monographs. The scientific outputs also included the publication of source critical editions from the hitherto unpublished works of Bratislava composers (S. Capricornus, J. N. Hummel). As part of the project, there was also cooperation on the development of two important international databases – the cantus database, which captures the repertoire of medieval Latin chant, and the RISM database, which gathers information about the sources of polyphonic music. The organization of the project closing conference "Music in Bratislava" with the active participation of members of the research team and invited experts from abroad provided space for the presentation of research results and the exchange of experiences of the research of the urban communities´ musical culture. The special result and form of the project output was a public concert and audio recording of the music of the 17th century, which originated or was related to the town. Almost all selected and studied works were revived in the world premiere and in top performing of internationally recognized specialists on historically informed interpretation (under the artistic direction of P. Zajíček, leader of the ensemble Musica Aeterna), and therefore the CD recording and the concert were extremely positively received among specialists as well as broad cultural public.

BENEFITS FOR PRACTISE

The results of the project expand knowledge in music historiography and motivate futher research, but also other art and historical disciplines can draw on from them. Source-critical music editions provide an opportunity to enrich the repertoire of professional and amateur performers with works connected with the musical traditions of Bratislava and so to convey them to the general cultural public.

Fig. 1 / Examples of project outcomes in the form of monographs.

Fig. 2 / Shot from the concert of 17th century music originated or related to Bratislava. Performers: Musica Aeterna under the artistic direction of Peter Zajíček, Czech Ensemble Barock Choir and Les Cornets Noirs, Moyzes Hall in Bratislava, 26th of May, 2017.

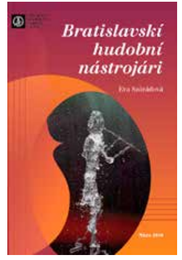
Fig. 3 / Snapshot form recording and title page of CD *Jubilate et plaudite.*

Fig. 4 / Snapshot from the conference Music in Bratislava, 27th and 28th of June, 2019.

Fig. 2

Fig. 4

Fig. 3



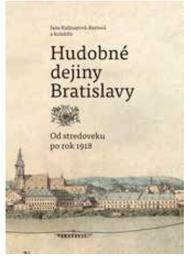


Fig. 1

Fig. 3

HEIDEGGER, METAPHYSICS AND HISTORY OF PHILOSOPHY

Principal investigator: prof. PhDr. Vladimír Leško, CSc.
Applicant organisation: Faculty of Philosophy OF UPJŠ Košice
Term of solution: 07/2015 – 12/2018
Budget from agency: 226 110 €
Project ID: APVV-14-0706

SUBJECT OF RESEARCH

The philosophical work of the German philosopher Martin Heidegger is one of the most important works, which shaped the forms of philosophisation in the 20th century. It takes an extraordinary explorer's effort to understand this history-philosophical *phenomenon* as well as its current metamorphosis. Understanding his theoretical ways of finding answers to the main ontological question of *what* Being is, brought with him many fundamental philosophical inspirations, which are also currently the subject of intensive research efforts. For the above reasons, it is also necessary in our domestic conditions to deal with the Heidegger philosophical heritage in the unity of historically-philosophical and philosophical problems. Heidegger's philosophical work is sui generis, the completion of a *strong model* of history of philosophy and philosophy itself, which has its origins in Hegel's philosophical teachings.

OBJECTIVES OF THE PROJECT

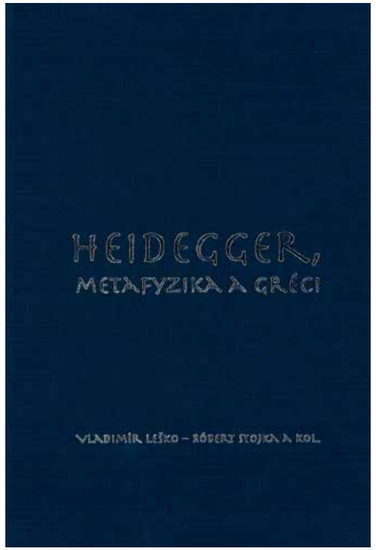
The aim of the project was to reveal Heidegger's philosophical depth and peculiarity of reflecting Western European philosophy – metaphysics, with an emphasis on its exploration in genesis from ancient metaphysics, through the new age *metaphysics of subjectivity* to its completion in Hegel and Nietzsche's philosophy. In his work, Heidegger moves in the space of finding *a jorney from the metaphysics of residence to non-methaphysical thinking – a different mindset.* This journey contains the reflection of both the early and late Heidegger's
work, with the decisive intention of understanding of how to shape the question of Being in determining the unity of metaphysics and the history of philosophy not only through some narrowly defined fragment of his work, but through the complete visor of his entire work. In this definition the grant project is original not only in our domestic, but also international conditions.

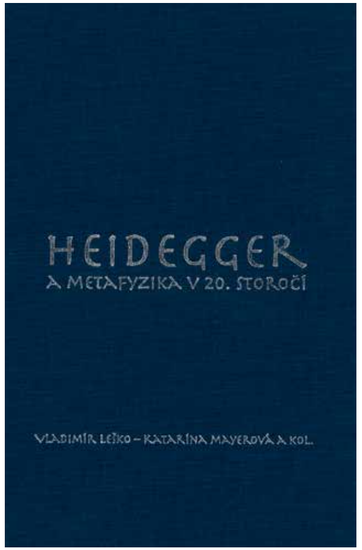
ACHIEVED RESULTS

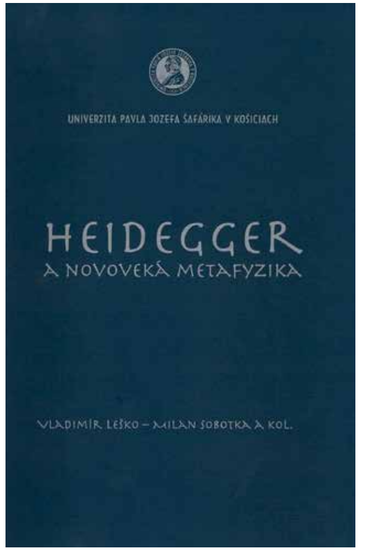
The research activities produced very significant results, which were presented mainly in three very voluminous collective monographs, which totaled 2524 pages. First of all, it should be noted that our examinations have shown convincingly enough that Heidegger's *dialogue* with the history of Western philosophy could not have been positive in conceiving a new understanding of metaphysics as learning *about Being, regardless of the existence* to positively fulfill it. Thinking of Being without of existence is possible, but only on the condition that we inevitably find ourselves again on the on-theo-logical field where *Being* equals *God*. Heidegger's belief in his early creation that only a *way back* from Aristotle to his predecessors would it be possible to talk about *Parmenid's teachings about Being* and to understand him as a decisive step that determined the meaning and fate of Western ontology and logic which proved unfounded. Despite heidegger's extraordinary philosophical efforts, his fundamental hypothesis could not be successfully. The reason is understandable. In the beginnings of Greek philosophical thinking, it is not yet contemplated Being and existing through the prussation of ontological differentiation, as Heidegger did at an early stage of his philosophical development and then later in his entire work. We have examined this in great detail in our most important publications:
Leško, V. – Stojka, R. and col. : *Heidegger and the Greeks.* Košice: Publishing House UPJ Š2016, 693 s.
Leško, V. – Sobotka, M. and col. : *Heidegger and modern period metaphysics.* Košice: UPJŠ Publishing house 2017, 889 s.
Leško, V. – Mayerová, K. and col. : *Heidegger and metaphysics in the 20th century.* Košice: UPJŠ Publishing House 2018, 742 s.

BENEFITS FOR PRACTISE

The results of our project are primarily the starting point for the further development of heideggerological research in Slovakia, which until now have been very weak compared to such initiatives in an international context. This is particularly important because, without knowing Heidegger's work and its impact on the development of philosophisation in the 20th century, we cannot be creatively active in contemporary philosophical activities. Secondly, our achievements in our project will become an integral part of creative higher education, especially in the fields of philosophy history and metaphysics. Through them, university students can penetrate the core of Heidegger's philosophical thinking and critically cope with his theoretical reference.







The most important published publications

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