

MED+PECS



**MEDICAL CONFERENCE FOR PHD STUDENTS
AND EXPERTS OF CLINICAL SCIENCES**

17TH OCTOBER 2020

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Clinical Sciences
17th of October 2020
Book of Abstracts**



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Presidential Welcome Speech

Dear Doctoral Students, Doctoral Candidates and Young Researchers,

I warmly welcome you on the pages of the MedPECS 2020 Conference's Book of Abstracts.

This year, the whole world is facing a huge challenge due to the pandemic. This challenge also affects the University of Pécs, together with all its students, lecturers, and staff. Not only is our free time affected by our current situation, but we also face many challenges and problems to solve in the case of our work. This is also true for the research carried out during the doctoral training, which also puts the doctoral student community to the test. It tests the resilience of each member of the community during this difficult time, tests the maintenance of a healthy mindset, tests the commitment to doctoral research, and tests the researcher's self-belief. I am confident that my young colleagues will not deviate from the path they have chosen and will go down this difficult albeit even more colorful and interesting path.

The Doctoral Student Association is committed, more than ever, to support doctoral students and our organization continues to operate in this spirit and this moral compass leads us further each day on our way. One important cornerstone of this is the support of doctoral students. As in previous years, even in such difficult times, we are committed to supporting the scientific and professional progress of doctoral students, contributing to the successful completion of doctoral training, and facilitating and memorizing the time spent in the doctoral student community in Pécs. This goal is also served by our present event, the main goal of which has never been obscured during the online implementation, which is to provide doctoral students with an opportunity to develop the excellence inherent in them.

I am confident that unusually organizing our event will take nothing away from your professional level and, as in previous years, will provide a great opportunity to present the latest research results and high-quality professional exchanges.

I would like to thank all our dear participants for honoring the MedPECS 2020 conference with their presence.

Best regards,



Bence Závodi
president
University of Pécs
Doctoral Student Association

I sincerely welcome all the participants of the Conference!

It is an honour for me to greet all the visitors in the abstract volume of the highly successful MedPECS Conference, held for the third time.

There is something in the air in Pécs. Perhaps this is not only the truth of the mainstream Hungarian pop hit. In Pécs, the community of doctoral candidates has always been very strong. In recent year, in addition to the basic tasks of PhD students, the Doctoral Student Union has raised the organization of scientific conferences to a professional level.

For years now, PTE DOK has evidenced a level of professionalism, regarding MedPECS as well, which is unprecedented in the long history of the organisation, even at the national level.

Looking at the programme offer, the progress in organisation, the invited speakers, I see the progressivity of development confirmed.

The difficult period behind us, caused by an unexpected pandemic, has deranged many things concerning MedPECS, as well. At the same time, I can tell you from experience that, by organising and holding the Scientific Students' Association Conference organised by our Faculty, it has been proven that an online conference loses nothing of its splendour, if its content and message are unquestionable.

Trusting in the work of PTE DOK, I believe that MedPECS 2020 to be held in Microsoft TEAMS will exceed all expectations, thus, I encourage everyone to give in to the temptation of science and not to set bounds to their interest!

Best regards,

Pongrác Ács, Prof.
professor, acting dean
University of Pécs
Faculty of Health Sciences

Welcome Speech - Faculty of Pharmacy, University of Pécs

Dear MedPECS2020 Participant,

On behalf of the Faculty of Pharmacy University of Pécs, I warmly welcome you to the MedPECS 2020 event.

A high-quality conference will be held for the fourth time this year to create a platform to present the scientific results of the professional work of PhD students and young researchers. In 2017, the Doctoral Student Association of the University of Pécs organized a hungarian scientific forum for doctoral students in clinical research, which can be considered as the antecedent of the MedPECS.

The leadership of the Faculty of Pharmacy attaches great importance to events where young Hungarian researchers, including doctoral students, are given the opportunity to present and discuss the results of their scientific work, and to establish personal and professional relationships. We find particularly valueable the initiative to involve companies in the Hungarian healthcare sector as an industrial partner to the conference.

We wish you a lot of success and high-quality presentations for this year's MedPECS conference.

Best regards,

Györgyi Horváth
associate professor
vice-dean for science and
student welfare
University of Pécs
Faculty of Pharmacy

Welcome Speech - Medical School, University of Pécs

Dear Participants,

The Medical School of the University of Pécs would like to thank both the organizers and the presenters for making this high-quality event possible despite the epidemic, as an online conference.

The original idea of bringing together different health-related disciplines in a forum for PhD students to present their research findings shows a great collaboration. The fact that this can only be achieved online in the current period does not take away from this original goal. In this difficult situation the importance of scientific research has come to the fore even more. Everyone, regardless of profession, realizes that in order to protect ourselves and our health, we need to keep up with the changing world, and we need scientifically trained researchers. The fact that students present their research findings to each other can mean practice and competition. On the other hand, further collaborations can be established even in the virtual world.

Adapting to the challenges of the present situation also means that the education and partly the medical attendance moved to virtual platform as well. Therefore, as the part of this collective adaptation, the young researchers should be able to present their research findings in an online forum.

The conference provides an excellent opportunity to improve presentation skills, to learn the mode of professional performance and it means a platform to get an insight into each other's work, which can bring fruitful collaborations in the future.

We wish good luck for everyone!

Best regards,

Dóra Reglódi, Prof.
*professor, vice-dean for
science
University of Pécs
Medical School*

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**Basic Biomedical Sciences and
Translational Medicine**



Immunostimulant effect of bitter melon (*Momordica charantia*) extract on Immunoglobulin M (IgM) and Immunoglobulin G (IgG) activity of male mice (*Mus Musculus*)

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Abstract: In emerging of alternative medicine for tropical disease, traditional or herbal medicine mainly being a prime option recently. Herbal medicine can be a treatment modality in which actively as immunomodulatory agent. One of traditional herbs that mostly used as immunostimulant is Bitter Melon leaves. Research about the effect of extract of bitter melon leaves for immunomodulatory activity had been done. In this research we used 48 mice which randomly into sixteen groups, 8 groups for immunoglobulin M (IgM) test and 8 groups for immunoglobulin G (IgG) test. Four different group, negative control, 0.5% w/v, 1% w/v, and 1.5% w/v of ether extract and undissolved ether extract bitter melon leaves, with 1 ml/30 g body weight given orally once a day for five days. Then each male mice was immunized 1 ml/ 30 g body weight of 2 % Sheep Red Blood Cells (RBC) as the antigenic challenges. The haemagglutination was conducted at the day 6th and 11th, using haemagglutinating antibody titer (HAT) method. The result of statistical analysis will show the significantly all of the treatment and these improvements were statistically significant ($P>0.01$) in ANNOVA test followed by Duncan Multiple Range Test (DMRT). The result shows the significant different between treatment ether extract and undissolved ether extract bitter melon leaves. The highest immunoglobulin activity was achieved by 1% w/v of undissolved ether extract bitter melon leaves (*Momordica charantia* Linn.)

Keywords: Bitter melon leaves, haemagglutinating antibody titer (HAT), immunoglobulin M (IgM), immunoglobulin G (IgG), sheep Red Blood Cells (RBC).

Nuclear regulation of myosin phosphatase by Mg²⁺-dependent protein phosphatase 1B in tumor suppressor pathways

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Introduction: Myosin phosphatase (MP) holoenzyme is a protein phosphatase-1 (PP1) type Ser/Thr specific enzyme that consists of a PP1 catalytic (PP1c) and a myosin phosphatase target subunit-1 (MYPT1). MYPT1 is an ubiquitously expressed isoform and it targets PP1c to its substrates. We identified several novel nuclear MYPT-interacting protein such as the protein arginine methyltransferase 5 (PRMT5) enzyme of the methylosome complex uncovering the nuclear MYPT1-interactome of hepatocellular carcinoma cells. One of the potential upstream regulatory element of MP is the Mg²⁺-dependent protein Phosphatase 1B (PPM1B) that was identified as a MYPT-binding protein by coimmunoprecipitation and pull down assay followed by mass spectrometry analysis. [1]

Aim: Our research aims to investigate the regulating effect PPM1B exercises over MP in nuclear localization, focusing mainly on downstream effectors of MP.

Methods: Overexpression of Flag-PPM1B in HeLa cell line, along with the opponent experiment as inhibiting PPM1B with sanguinarine. Samples will be analyzed by Western Blot technique.

Results: Overexpression of Flag-PPM1B decreased the inhibitory phosphorylation of MYPT1, the decreased stimulating phosphorylation of PRMT5 and the parallel with the decreased symmetric demethylation of histone 2A and 4 suggesting the activation of gene expression of tumor suppressor genes. The silencing of PPM1B as well as the inhibition of PPM1B by sanguinarine resulted opponent effects clarifying the mechanism between PPM1B and MP, revealed that PPM1B activates MP indeed, along with its tumor protective effects. Our results suggest the tumor suppressor role of PPM1B via dephosphorylation of MP and indirectly modulating the activity of PRMT5 thereby regulating gene expression through histone arginine dimethylation.

References:

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Acknowledgements: The work/publication is supported by the EFOP-3.6.1-16-2016-00022 project. The project is co-financed by the European Union and the European Social Fund.

Keywords: myosin phosphatase, PRMT5, tumorigenesis

Possible therapeutic effects of activators of non-genomic estrogen-like signaling in the 3xTg Mouse Model of Alzheimer's Disease

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Introduction: Alzheimer's disease (AD) is the foremost cause of dementia and is characterized by a progressive decline in cognitive function [1]. Preclinical studies are necessary considering there is no cure for AD. Estrogen has neuroprotective effect on AD cases, however, it might have serious side effects [2]. Therefore, two novel Activator of Non-Genomic Estrogen-Like Signaling (ANGELS) compound have been developed and tested using triple-transgenic (amyloid precursor, presenilin-1 and tau) AD mice (3xTg-AD).

Aim: To reveal possible beneficial effect of ANGELS on cognitive and metabolic disturbances of 3xTg-AD mice.

Methods: Two ANGELS compounds -with different molecular structure- were subcutaneously administered to 6-month-old 3xTg-AD and B1/6 control male mice. 24h later mice were tested in sociability and y-maze tests evaluating locomotion (first 5 min of sociability, open field (OF)), social interest (third 5 min of sociability) and short-term memory (fourth 5 min of sociability and y-maze). Additionally, magnetic resonance imaging (MRI) based fat and water quantification was carried out before and after 14 days of treatment to monitor metabolic reactions towards agents.

Results: During 5 min OF the 3xTg-AD mice moved significantly less than their age-matched controls, however, the time spent in the centrum (reflecting anxiety) was not different between groups. Single dose treatment was not able to significantly influence these parameters. All mice preferred social partner above empty box during sociability. 3xTg-AD mice tended to be less interested, while compound 1 enhanced the tendency for social interest. The short-term memory of 3xTg-AD mice were worse than the controls both for the frequency of social discrimination and y-maze based spatial orientation. However, only the latter was improved 24h after a single dose of both compounds. Despite similar body weight 3xTg-AD animals had lower fat and higher water content than their age-matched controls. 14-day treatment resulted in a bit smaller body weight in all groups without significant effect of the treatment.

Conclusions: After a single treatment with ANGELS compounds cognitive function improved in 3xTg-AD mice. Furthermore, MRI results suggest that chronic treatment with ANGELS did not have any negative effect on body composition of mice. Therefore, ANGELS might be a promising agent with neuroprotective effect without peripheral side effects.

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[2] Xu, H., Gouras, G et al. *Estrogen reduces neuronal generation of Alzheimer β – amyloid peptides*. *Nat Med* 1998; Apr;4(4):447-51

Keywords: Alzheimer's disease, estrogen receptor agonist, 3xTg mouse model, y-maze, sociability

Investigation of systemic amyloid deposition in the absence of endogenous PACAP and its receptor

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Introduction: PACAP (pituitary adenylate cyclase activating polypeptide) is a neuropeptide expressed in many organs that has been shown to have general cytoprotective, anti-inflammatory, and antiapoptotic effects. However, we only have little data on its role in the aging process.

Aim: In our previous experiments, we observed accelerated systemic senile amyloid deposition in PACAP KO mice. The aim of the present experiment was to investigate the effect of partial PACAP deficiency in PACAP heterozygous (HZ) mice and PACAP receptor inefficiency in PAC1 receptor KO animals on amyloid deposits.

Methods: In our experiment, we sampled more than 20 organs from PACAP HZ (n = 4) 12-18 months and 1-year-old PAC1 receptor wild (n = 9) and KO (n = 2) mice. Haematoxylin-eosin and Congo red staining were used to examine the amyloid deposits. The amyloid content of the organs was rated on a scale of 0 to 3 according to severity.

Results: In our histopathological analysis, the same or more severe deposits were observed in HZ mice with partial PACAP deficiency as in PACAP KO mice. The organs most severely affected were the kidneys, spleen, liver, skin, thyroid, trachea, esophagus, and intestines. No signs of amyloid deposits were found in any of the PAC1 receptor WT and KO mice.

Conclusions: Based on our results, we can say that systemic amyloidosis develops not only due to the complete but also partial absence of PACAP, in contrast, the lack of its receptor does not lead to pathological protein deposits.

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Acknowledgements: Nemzeti Kiválóság Program TÁMOP 4.2.4.A/2-11-1-2012-0001, GINOP-2.3.2-15-2016-00050 „PEPSYS”, MTA-TKI Lendület Program.

Keywords: PACAP, amyloid, systemic amyloidosis, aging

Comorbidity of depressive-like symptoms and cognitive decline in triple transgenic mouse model of Alzheimer's disease

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Introduction: Alzheimer's disease (AD) is a progressive neurodegenerative disorder, which is the most common cause of dementia in the elderly. Approximately 50% of AD patients develop depressive symptoms and anxiety, contributing to the cognitive decline [1]. This comorbidity was in the focus of our study. Triple-transgenic mouse model of AD (3xTg-AD) is used, that expresses human mutated presenilin-1, amyloid precursor and tau protein. This is considered as the most relevant in vivo model of typical behavioural dysfunctions of AD [2].

Aim: According to the literature the main histological hallmarks of AD appear around 6 months of age in this model [3]. The main aim of our study was to compare the anxiety- and depressive-like behaviour before and after the appearance of the histopathology.

Methods: A behavioural test battery was used to examine anxiety- (open field (OF) and social interaction (SI) tests), and depression-like symptoms (splash test) as well as the cognitive decline (Morris Water Maze (MWM) test). 3xTg-AD were compared to age-matched B1/6 male control mice at 4 and 8 month of age.

Results: In the MWM latency to find the platform was higher for 3xTg-AD mice compare to controls, the difference was more pronounced in the 8-month-old cohort. In the OF test, both age groups of 3xTg-AD mice moved significantly less than controls. Difference in SI of 3xTg-AD and controls appeared at the age of 8 months: 3xTg-AD animals spent less time with friendly social behaviour than controls. Splash test showed depressive-like behaviour as 3xTg-AD mice spent significantly less time with grooming than controls in both ages.

Conclusions: Cognitive decline and asocial behaviour of 3xTg-AD mice are progressive. Some anxiety- and depressive-like symptoms are present in 3xTg-AD mice, therefore this model could be a good choice to explore the comorbidity of AD and depression as well as a great help to develop new possible treatments.

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Acknowledgements: We are thankful to Balázs Hangya for providing the 3xTg-AD mice.

Keywords: Alzheimer's disease, depression, 3xTg-AD mice

The role of Urocortin 1 neurons of the centrally projecting Edinger-Westphal nucleus in the development of non-motor symptoms of Parkinson's disease in the rat

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Abstract: Parkinson's disease (PD) is a neurodegenerative disorder characterized by destruction of dopaminergic neurons in the substantia nigra (SN) and the presence of Lewy-bodies (LB), which cause motor control deficiencies, such as tremor, rigor and hypokinesia. In addition to these well-known manifestations, people suffering from PD describe non-motoric symptoms like depression and anxiety. Both affects their quality of life in a more significant manner, than the above-mentioned deteriorating motor functions. It is known, not only SN is affected in PD, morphological changes were described in various brainstem nuclei, including the centrally projecting Edinger-Westphal nucleus (cpEW). It has already been confirmed that Urocortin 1 (Ucn1) expressing neurons of cpEW contribute to stress adaptation response and to emotional reactions.

We assumed, that besides neurodegenerative alterations in SN, morphological changes on Ucn1 neurons will occur, which contribute to mood disorders.

Rats were exposed to six week-long subcutaneous rotenone treatment in order to induce PD and its symptoms. Rotarod, open field (OFT), and sucrose preference tests (SPT) were used regularly to evaluate the changes in mood-condition and motoric responses. Morphological changes were assessed by multiple immunofluorescence labeling.

Rotenone treated rats exhibited anxiety-, and depression like behavior as well as declined motor functions. The model's validity was confirmed by the loss of dopaminergic cells in SN, correlated with decreased number of urocortinergic cells, and the appearance of alpha-synuclein aggregates in the cpEW. Results showed an elevated *Ucn1* immunoreactivity with a decreased *Ucn1* mRNA expression.

Based on our results, Ucn1 neurons of the cpEW may contribute to non-motor symptoms of Parkinson's disease in the rat.

The linkage of genomic stability to breast cancer chemoprevention by rexinoid-based drug combinations

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Introduction: Previously we determined that the RXR selective retinoid bexarotene and carvedilol (B+C), a non-selective beta-blocker represent a combination that is synergistic to suppress cell proliferation and suppressed Her2-induced breast cancer formation in a hormone-independent way, even at low doses. However, the mechanisms behind their effect are yet to be elucidated. Proteomic data (RPPA) showed increased protein levels of ARID1A, a SWI/SNF subunit, in primary human mammary epithelial breast cells (HME-hTert) treated with the combination of bexarotene and carvedilol. ARID1A is a tumor suppressor that is mutated in 8% of breast cancer patients [1].

Aim: We hypothesized that the elevated level of ARID1A alters nucleosome organization to modulate the expression of genes related to genomic stability and proliferation. Our goal was to identify the role of chromatin remodeling behind the anti-proliferative effects of B+C through the actions of ARID1A.

Methods: We validated RPPA results with Western-blot and Immunocytochemistry. ARID1A binding regions were identified through chromatin immunoprecipitation followed by sequencing (ChIP-Seq) and the results were validated with ChIP-qPCR. HME-hTert and MCF-7 breast cell lines were used and the latter was considered a model for ChIP assay optimization.

Results: ChIP-Seq results on HME-hTert and MCF-7 cells showed that ARID1A mainly occupied genomic regions distal to the transcription start site. In addition, we found that about 80% and 60% of ARID1A binding sites in the B+C treated samples were unique compared to the control in HME-hTert and MCF-7 cells, respectively. We found an enrichment of ARID1A in the regulatory regions of genes related to DNA damage repair, differentiation and proliferation regulation. In order to select ARID1A target genes we overlapped ChIP-Seq and gene expression data and identified a number of genes including MAL2 and FOXQ1 which are related to cell growth regulation.

Conclusions: We validated some ARID1A binding regions detected in ChIP-Seq with ChIP-qPCR in normal and tumor cells. We could identify some genes that might be regulated by ARID1A including MAL2 and FOXQ1.

References:

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Acknowledgements: Stipendium Hungaricum.

Keywords: cancer prevention, rexinoids, breast cancer, genomic stability, SWI/SNF

Amiodarone's major metabolite, desethylamiodarone inhibits proliferation and *in vivo* metastasizing property of B16-F10 melanoma cells.

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Introduction: Melanoma is the most lethal form of skin cancer accounting for 132,000 cases a year, with a very poor prognosis [1]. Despite the inflation of therapeutically approaches, metastatic melanoma is highly resistant to chemotherapy.

Aim: Previously, we demonstrated the *in vitro* anti-tumor effects of desethylamiodarone (DEA) in bladder and cervix cancer cell lines [2][3]. In the present study, we intended to establish its potentiality in B16-F10 metastatic melanoma cells *in vitro* and *in vivo*.

Methods: We assessed cell proliferation, apoptosis and cell cycle by using sulforhodamine B assay, Muse™ Annexin V & Dead Cell and Muse® Cell Cycle assays, respectively. We determined colony formation after crystal violet staining. For studying mechanistic aspects, immunoblotting analysis was performed. We used a C57BL/6 experimental lung metastasis model for demonstrating *in vivo* anti-metastatic potential of DEA.

Results: DEA inhibited *in vitro* proliferation and colony formation, and *in vivo* lung metastasizing properties of B16-F10 cells. It arrested the cells in G0/G1 phase of their cycle likely via p21 in a p53-dependent fashion, and induced caspase mediated apoptosis likely via inversely regulating Bcl-2 and Bax levels, and reducing Akt and ERK1/2 activation.

Conclusions: In this study, we provided *in vitro* and *in vivo* experimental evidences for DEA's potentiality in the therapy of metastatic melanomas. Since DEA is the major metabolite of amiodarone, a worldwide used antiarrhythmic drug, safety concerns could be resolved more easily for it than for a novel pharmacological agent.

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Clinical Sciences

Initial results of a novel exoskeleton therapy in a chronic spinal cord injury patient

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Introduction: Traumatic spinal cord injury (SCI) is a devastating condition mostly affecting the young adult population. The therapeutic goal is significantly different in case of incomplete and complete SCI lesions. Following an incomplete injury, there is probability to restore previous functions, therefore supportive rehabilitative robotic devices are useful tools to assist the healing and plasticity by providing high frequency continuous passive movement. However, low level complete SCI patients are forced to use wheelchairs and activity of daily living is severely affected. For chronic complete SCI patients, the robotic exoskeletons are novel solutions in rehabilitation and could be adopted as assistive walking devices for home use to reinforce mobility and avoid long term medical complications due to immobility. Our aim is to introduce a ReWalk P6.0 exoskeleton to clinical practice in Hungary and evaluate the long term effect of the robotic training on general health, bladder and bowel functions following complete SCI.

Methods: The patient suffered complete SCI injury on Th11 level, 26 months ago. According to the training protocol the team performed preparative physiotherapy to improve the trunk balance. The exoskeleton training session is performed five days a week since March 2019. General rehabilitation outcomes measured and movement analysis performed in every milestone to track the posture changes during the therapy.

Results: The preparative physiotherapy was successful, trunk control improved significantly. During the first period of the training, the Berg Balance scale and Trunk Control Measurement values improved by 25% respectively. By the second and third milestone, further progress was found on balance and trunk control, also Timed up and go (84% of improvement) and 10 meter walking test performance (40% of enhancement). These dynamic parameters were further supported by the movement analysis results. The bone density values did not show significant change during this period of training.

Conclusions: The initial system set up and clinical protocol is feasible. There is a considerable demand for long term follow up trials with more patients with standardized outcomes and movement analysis measures, thus we plan to extend our research to multicenter research with National Institute of Medical Rehabilitation in Hungary.

Ticagrelor for Stroke Prevention in Patients at High Risk for Cardiovascular or Cerebrovascular Events: A Systematic Review and Network Meta-Analysis of Randomized Controlled Trials

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Introduction: Preventive antiplatelet therapy is recommended for patients with cardiac and/or cerebrovascular atherosclerosis. Ticagrelor has an improved safety and efficacy profile in patients with acute coronary syndrome, however, data regarding stroke prevention remain controversial.

Aim: To compare ticagrelor with other P2Y₁₂ inhibitors and aspirin in monotherapy or combination in the treatment of patients with high risk for cardiovascular and/or cerebrovascular disease, defined as coronary artery disease, acute coronary syndrome, stroke or transient ischemic attack, or peripheral artery disease.

Methods: Systematic searches of MEDLINE, EMBASE, and Cochrane Library were conducted until 1 Aug 2020. Search terms included *ticagrelor*, *AZD 6140*, and *stroke*. PROSPERO registration number: CRD42020170746. Randomized clinical trials comparing ticagrelor with or without aspirin versus aspirin and/or clopidogrel or prasugrel among patients with established cardio-and/or cerebrovascular disease were included. Data were extracted from original publications. The risk of bias was assessed using the Cochrane Collaborations assessment tool. Random effects model was used to combine risk estimates across trials and risk ratio (RR) with 95% confidence intervals (95% CIs) served as summary statistics. The influence of individual components was evaluated in an additive network meta-analysis model.

Results: Twenty-six randomized clinical trials comprising 124,495 patients were analyzed. When compared to controls ticagrelor plus aspirin significantly reduced the risk of ischemic stroke by 20% (RR 0.80; 95% CI 0.71-0.89). Treatment with ticagrelor monotherapy did not significantly affect ischemic stroke (RR 0.88; 95% CI 0.77-1.00, p=0.05). Compared with aspirin alone major bleeding was in similar ranges with antiplatelet monotherapies while the relative risk was twice higher with combined antiplatelet therapies. There was no considerable difference in the risk of mortality with ticagrelor plus aspirin (RR 0.99; 95% CI 0.91-1.07).

Conclusions: Ticagrelor on top of aspirin may provide more favorable outcomes on secondary stroke prevention in patients with vascular risk factors, however, this benefit may come with the price of increased bleeding risk.

Acknowledgements: This work was supported by the GINOP-2.3.3-15-2016-00031 grant of the Hungarian Government. Dr. Komócsi reports personal fees from Bayer Pharma AG, Pfizer, Krka, d. d., Merck & Co., and Servier, outside of the submitted work. The other authors report no conflicts of interest.

Keywords: *ticagrelor, stroke, acute coronary syndrome, network meta-analysis, prevention*

Multidimensional ROI-level combination of micro- and macrostructural measures in lesion detection

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Introduction: In a recent publication [1] we showed that the voxel-wise Mahalanobis-distance is a suitable metric of dissimilarity for the detection of malformations of cortical development (MCD), using the three dimensional distribution of diffusion tensor (DTI) eigenvalues. While the method proved sensitive to the abnormal tissue microstructure related to MCDs, specificity was constrained by the inaccuracies of spatial coregistration when comparing to control subjects. In the current work, the method was amended in two ways: a) by including cortical volumetry and morphology measures, and b) by performing the statistical analysis on the ROI-level.

Aim: The aim of the current study was to test the multidimensional approach, using the extended parameter space and ROI-level-statistics on healthy controls and individuals with MCDs; and to find the optimal parameter set to maximize the efficiency of lesion detection.

Methods: Diffusion and T1-weighted imaging data of 45 healthy subjects and 13 individuals with MCDs (16 lesions) were processed with ExploreDTI and the Freesurfer software suite. Using the 360 labels of the multi-modal cortical atlas of the Human Connectome Project (HCP-MMP, Glasser, Coalson [2]), ROI-level average DTI-eigenvalues, volumetry, and morphology measures were exported. The multidimensional Mahalanobis-distance was used to identify regions of abnormal tissue micro- and macrostructure using in-house software with all possible combinations of measures.

Results: MCD-related lesions were identified in 14 out of 16 cases, detection performance was improved using measures of cortical morphology (average cortical thickness, rectified mean curvature, and folding index) with reduced number of false positives. DTI-derived measures resulted in more false positives in regions usually affected by susceptibility and EPI-related distortions.

Conclusions: The surface-based approach was efficient in registering the cortical labels to each individuals' image space, and the combination of DTI, volumetry, and morphology measures improved the detection of MCDs in the multidimensional framework.

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Keywords: Lesion detection, Multidimensional statistics, DTI, Morphology, Volumetry, Mahalanobis-distance

Relation of Right Atrial Mechanics to Functional Capacity in Patients With Systemic Sclerosis

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Introduction: Cardiac involvement in systemic sclerosis (SSc) implies a worse prognosis[1]. Little is known about the right atrial (RA) mechanics in this disease, but recent data suggest that it correlates well with the functional capacity of the patients in conditions with known right heart involvement[2].

Aim: We aimed to investigate the abnormalities of the RA function as compared with healthy subjects and to assess the potential correlations between RA mechanics and the functional capacity in SSc patients using 2D speckle tracking technique.

Methods: A total of 70 SSc patients (age: 57±12 years) were investigated. Functional capacity was measured with 6-minute walk test (6MWT). Echocardiographic parameters of the right ventricular (RV) systolic function (TAPSE, RVFAC), parameters of the tricuspid inflow (E, A), and tricuspid annular systolic (S), early- (e') and late- (a') diastolic myocardial velocities were measured. RV wall thickness was obtained. RA reservoir (ϵ_R), conduit (ϵ_{CD}), and contractile (ϵ_{CT}) strain were measured. RA stiffness was calculated as ratio of E/e' to ϵ_R . Echocardiographic data were compared with an age- and gender-matched group of 25 healthy volunteers.

Results: RA ϵ_R (49.29±10.67 vs. 59.6±9.94%, p=0.000) and ϵ_{CD} (26.79±8.09 vs. 34.29±7.33%, p=0.000) were significantly lower in the SSc population. No significant difference was found in ϵ_{CT} (22.93±5.76 vs. 25.31±5.72%, p=0.082). RA stiffness was significantly increased in SSc patients (0.11±0.04 vs. 0.08±0.02, p=0.001). 6MWT distance was 391±95 m. In step-wise multiple linear regression analysis RV wall thickness (r=-0.289, p=0.030) and RA stiffness (r=-0.418, p=0.002) became independent predictors of 6MWT distance.

Conclusions: RA ϵ_R and ϵ_{CD} are impaired, while RA stiffness is increased in SSc compared with healthy subjects. Speckle tracking-derived RA stiffness is turned out to be one of the main determinants of the functional capacity in SSc patients.

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Keywords: systemic sclerosis, speckle tracking, right atrial strain, atrial stiffness, functional capacity

Zero-fluoroscopy strategy for catheterablation of paroxysmal supraventricular arrhythmias: single-center study

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Introduction: Data regarding the comparison of the minimal/zero fluoroscopy and the conventional fluoroscopy-assisted approach in the treatment of paroxysmal supraventricular tachycardias (PSVTs) are limited, furthermore data regarding the impact of electroanatomic mapping systems (EAMSs) on the procedural time are controversial. We aimed to compare the conventionally fluoroscopy-assisted with the minimal/zero fluoroscopy approach guided by electroanatomic mapping systems in the treatment of paroxysmal supraventricular tachycardias.

Methods: 98 consecutive patients undergoing electrophysiologic study with or without ablation due to PSVT were included in our retrospective single-center study. 36 patients underwent an EAMS-guided procedure (Group 1), while in the cases of 62 patients the procedure was performed conventionally (Group 2).

Results: In Group 1 25 AV nodal reentrant tachycardia (AVNRT), 4 atrioventricular reentrant tachycardia (AVRT), 3 atrial tachycardia (AT) and 4 diagnostic electrophysiologic procedure (EPS) were included. Group 2 comprised 37 AVNRT, 5 AVRT, 2 AT and 18 EPS. In Group 1, 91.7% of the procedures were performed without the use of radiation. The success rate was 100% in both groups without any complication. The use of EAMS reduced radiation time (0 [0-0] vs 2.2 [0.1-13.3] min, $p < 0.0001$), with longer procedure time (70.0 [33-190] vs 52.5 [31-160] min, $p = 0.035$). There was no difference either in the number of RF applications (7 [2-29] vs. 7 [3-40]), or in the ablation time (218 [33-851] vs 224 [range: 38-748] s, $p = 0.80$ each).

Conclusions: The EAMS-guided approach for the treatment of PSVTs is a feasible and safe method that reduces fluoroscopy time and does not influence the number of applications, ablation time, success or complication rates.

Keywords: zero fluoroscopic, electrophysiology, paroxysmal supraventricular tachycardia

Measuring the efficacy of lower extremity exoskeletons in the rehabilitation of spinal cord injury patients

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Introduction: The effects of spinal cord injury (SCI) have intense consequences, such as the loss of sensory or motor functions. Recent times have showed an increasing number of patients suffering SCIs, thus the rehabilitation of locomotion is becoming more and more of a key element for patients with SCI. Numerous devices have been developed in aid to assist gait and locomotion rehabilitation, one of the technologies being exoskeletons. In the past two decades lower extremity exoskeletons (LEE) have shown a growing interest among health professionals, SCI patients, industrial and military stakeholders.

Aim: The aim of the study is to include the gait training with LEEs into the rehabilitation process, comparing the parameters of functional and physiological changes to SCI patients receiving standard rehabilitation.

Methods: The study is conducted according to the terms and conditions of prospective, controlled studies. The control group will be of individuals with SCI meeting the inclusion criterias, but solely receiving standard rehabilitation.

Protocol and therapy: At least two certified therapists will work with one patient at a time. The therapy is divided into four stages, the first three stages being more intense, five times of 60-90 minutes training per week. The training and follow-up for both group's patients will be for a period of 6 months. The therapy is tailor-made, the fourth stage being a lower intensity, sustaining gait therapy. Psychologists will be available during the study and the follow-up period to monitor any psychological issues.

Present state of the study: Due to the pandemic the study could not commence, although all procedures were lined up and 6 SCI patients were going to be tested along the inclusion criterias. Therefore there are no results and conclusions as of present.

Keywords: exoskeleton, rehabilitation, spinal cord injury



Health Sciences and Health Economics

Choice architecture interventions to promote healthy eating on Warwick Campus - Original research study

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Introduction: Obesity and overweight are a global crisis. They increase the risk of chronic and psychosocial diseases. While attractive food becomes more accessible. Nutrition-friendly Schools Initiative emphasised that health campus environment plays a vital role in healthier diet. Research has shown that choice architecture interventions can modify eating choices and behaviour. The food label is one of the accessible architecture interventions. However, its function has not been confirmed in different type.

Aim: This study aims to explore the relationship between label architecture interventions and healthy eating on the Warwick University.

Methods: Four kinds of labels were used in three intervention places. Poisson regression analysis was employed to assess the consumption of food. Kruskal Wallis test was applied to compare the difference among label groups. Multivariate Analysis of Variance was used to exam the impact of labels in different calorie groups.

Results: The consumption of foods in label groups was different with a no-label group, but its residual ratios were no different. Label interventions could decrease customers' choice of cakes and increase that of fruit. Furthermore, Per piece calorie with sports label increased the consumption of fruit.

Conclusions: Label interventions can promote customers' healthy eating on the Warwick campus. Per piece calorie with sports label was recommended.

Keywords: Architecture Intervention, Label, Healthy Eating, Campus

Prevalence and Correlates of Caries Experience and the Quality of Life of Children Enrolled in Governmental Schools in Jordan: A Cross-Sectional Epidemiological Survey.

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Aim: Caries experience has negative effects on the functional, physical psychosocial well-being, and the quality of life of children. The study aimed to assess the prevalence of caries experience and its impact on the quality of life of school children between the ages of six to twelve in Amman.

Methods: A cross-sectional study of 343 (female = 204, male = 139) schoolchildren aged between 6 and 12 years enrolled in governmental schools in Amman, using a modified reliable and valid instrument, Oral Health-Related Quality of Life (OHRQoL-29). Cronbach's alpha was used to test the instrument reliability, Pearson Correlation was assessing the internal validity within each domain of the instrument. The prevalence of caries experience among study groups was analyzed through the latest clinical examination of oral health records. The visual Analogue Scale (VAS) method was used to evaluate the quality of life weight of the students. Spearman Correlation Coefficient test used to assess the correlation between Decayed Missing Filled Teeth (DMFT) index and OHRQoL-29 dimensions. Independent samples Mann Whitney U Test of the demographic variables regarding the questionnaire dimensions were tested.

Results: The prevalence of caries experience was 89.4% in 6-year-olds and 74.5 % in 12-year-olds, however, 75%, 91.8% among females and males, respectively. Sixty-one percent of students responses ' Fair' health of the teeth, lips, jaws, mouth and 'A lot of effects' on life overall, where only 11.4% of student responses 'Excellent' health of the teeth, lips, jaws, mouth and 'Not at all' effect of life overall. A statistically significant correlation of DMFT/dmft index was founded with the functional limitation, oral hygiene practices, and oral health quality of life domains with p values: 0.048, 0.003, 0.001 respectively.

Conclusions: The prevalence of caries experience is high and significantly correlated with the students' quality of life, the validated OHRQoL- 29 Arabic version of the untreated dental caries among school-age children can be reliably used to assess children's OHRQoL in the Arabic speaking population, and it is considered a matter of urgency to establish an effective and cost-effective school oral health program.

Acknowledgements: The author would like to acknowledge, the school principals and teachers of the government schools in Amman for the support, patience and the time been provided in the data collection phase, besides, the thanked efforts go to 1st grade, 7th-grade students and their parents. As well as being grateful to Dr Hekmat Abu Alfoul, Dr Mahmoud Alzreqat and Dr. Yousef Abu al-Shaar for facilitating the research area and the data collection.

Keywords: Decayed Missing Filled Teeth (DMFT), Quality of life (QoL), Oral health-related quality of life (OHRQoL), Visual analogue scale (VAS).

Is prescriptions non-redemption a source of poor health of Roma? Cross-sectional analysis on drug consumption data from the National Health Insurance Fund of Hungary

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Introduction: Primary medication nonadherence (PMNA) refers to patients not redeeming new medications written by health professionals and a global major public health issue [1,2].

Aim: Our study aimed to investigate prescription redemptions or PMNA in segregated Roma colonies (SRC) and complementary area (CA) in northeastern Hungary.

Methods: A cross-sectional study was carried out on data obtained from the National Institute of Health Insurance Fund Management (NIHIFM) with inclusion of 67,017 residents from both settlements of all age groups. Crude and standardized (indirect) redemption ratios were calculated for each and total Anatomical Therapeutic Chemical Classifications (ATC) group redemptions. Relative redemptions (RR) with 95% confidence intervals were calculated.

Results: Higher RR for alimentary and cardiovascular drugs but lower for anti-infective drugs were found in the SRC. Overall, RR was 2.8% (RR = 1.028, 95% CI: 1.018–1.038) higher in SRC than CA with extra 919.75 prescription redemptions attributed to the area.

Conclusions: Redemption of prescriptions was significantly higher among Roma living in SRC and these findings contradict stereotyping that Roma do not use health services properly.

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Keywords: prescription non-redemption, complementary area, segregated Roma colonies, indirect standardization, metabolism drugs, cardiovascular drugs

Pesticide use, related health risks and their management in Ethiopia

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Introduction: Pesticide use has become a major public health problem worldwide, following the intensification of agriculture and the promotion of agrochemical use in low- and middle-income countries that resulted in widespread exposure, even severe pesticide poisoning episodes.

Aim: The study aimed to investigate pesticide use, knowledge, and perception of health risks and their management among extension officers providing advisory service for farmers in the eastern Hararge zone, Ethiopia.

Methods: A cross-sectional study was conducted using a structured survey questionnaire. Descriptive analysis and multivariable logistic regression model fitted to control confounding factors and ascertain the independent predictors of outcome variables was applied in SPSS Version 25. Crude and adjusted odds ratios (AORs) were calculated to assess the strength of association between outcome and explanatory variables. The significance of statistical associations was accepted at 5% significance level.

Results: A total of 234 respondents have participated in the study with a 100% response rate. Malathion, 2-4-D, Diazinon, Glyphosate, and Deltamethrin, were the five most frequently reported pesticides from the study area. Based on the WHO classification, 70% of the reported pesticides were moderately hazardous (WHO class II). The study indicated that 66% and 58% of the respondents had good knowledge about pesticide products and routes of exposure, respectively. 78% of the respondents deemed pesticides risky, 42% of them experienced pesticide poisoning among farmers in the past, and 85% thought that farmers poorly used personal protective equipment (PPE). The perceived health risk of pesticides was found to be statistically significantly associated with respondents' educational status (AOR=4.70, 95%CI: 1.36-16.29, p=0.044), with their opinion that the pesticide management system was ineffective (AOR=3.77, 95%CI: 1.12-12.69, p=0.05) and with their opinion that farmers are rarely trained about the health risks of pesticides (AOR=8.42, 95%CI: 2.62-27.08, p<0.001).

Conclusions: Insecticides and herbicides were the mostly used pesticides in the study area, and the majority of them are moderately hazardous. A considerable proportion of extension officers reported that there is unsafe use of pesticides, poor utilization of PPE by farmers, inadequate training, and they experienced pesticide poisoning among farmers. The extension officers' knowledge about pesticides and the routes of entry, as well as their risk-aware attitude are still insufficient. This impairs the quality of advisory service provided by them and a threat to pesticide applicators. Further investigation of the health risks of occupational pesticide exposure is important.

Acknowledgements: We would like to thank the Stipendium Hungaricum Program of the Tempus Public Foundation for the provision for funding of this study. Our great appreciation goes to extension officers for their time in participating in the study.

Keywords: pesticide, risk perception, knowledge, exposure, risk management

Kinematics Characteristic of lower limbs in patients with non-contact anterior cruciate ligament reconstruction

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Aim: This study aim to analyze the characteristics of lower limb kinematics in patients after anterior cruciate ligament (ACL) reconstruction, so as to lay a theoretical foundation for the rehabilitation of ACL injuries and prevention of secondary injuries.

Methods: Ten patients (5 males and 5 females) were selected with ACL reconstruction. Their healthy lower limbs were in group NI, the affected lower limbs were in group I, and 10 healthy persons (5 males and 5 females) were selected in group H. Using Vicon three-dimensional motion capture system to collect the kinematics data when participants take-off from a box which height is 30cm.

Results: There was significant difference in hip flexion angle between group H and group I ($p < 0.05$, $p = 0.037$). There was extremely significant difference among group H and group I ($p < 0.05$, $p = 0.008$).

Conclusions: After ACL reconstruction, knee flexion angle and hip flexion angle of the affected knee were lower than those healthy people when taking off from 30cm box.

Keywords: anterior cruciate ligament, non-contact injury, kinematics, Vicon three-dimensional motion capture

Association of single nucleotide polymorphisms with taste and food preferences of the Hungarian general and Roma populations

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Introduction: It is reasonable to suppose that poor diet [1] underlies the unfavorable health status of the disadvantaged Roma population of Europe and Hungary.

Aim: Eating habits may be influenced by genetic factors [2]; so we aimed to evaluate the potential associations of genetic variants with taste and food preferences in our study samples.

Methods: Fruit and vegetable consumption, bitter, salty, sweet and fat taste preferences of Hungarian (HG, n=410) and Roma (HR, n=387) subjects were tested with TAS1R3, CD36, SCNN1B, TRPV1, TAS2R38, TAS2R19 and CA6 polymorphisms.

Results: In HG, rs1527483 was associated with fat taste preference; rs2274333 with dark chocolate preference; rs10772420 with white cabbage preference; and rs713598 with vegetable consumption. In HR, rs713598 and rs8065080 showed significant associations with salting frequency; rs8065080 and rs2274333 with salty taste preference; rs2274333 with kohlrabi preference; rs10772420 with grapefruit preference; and rs713598 with quantity of sugar added.

Conclusions: Our results suggest that genetics may mediate food preferences in our study samples. Individuals with different ethnic background may require personalized interventions to modify diet.

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Keywords: genetics, taste preference, food preference, diet, Roma population, Hungarian population

Budget Impacts of Transparent Procurement of Medicines in Healthcare - A Conceptual Model

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Introduction: There is evidence that healthcare is among candidates for budget cuts potentially reversing gains made towards universal health coverage (UHC) as countries globally are confronted with limited resources. Budgets for medicines in most healthcare systems are limited [1] which may lead to constrained access to medicines. On the other hand, confidentiality in pharmaceutical transactions create opportunism that may result in misuse of funds and inefficiencies [2,3].

Aim: The current paper aims at conceptualizing a model for analysing the mediated effects of procurement transparency on budget impact in the provision of medicines in healthcare.

Methods: The conceptual framework is developed from review of existing literature and centred on agency theory [4].

Results: The paper proposes a theoretical model postulating that clinical governance has a direct positive effect on procurement transparency of medicines. While transparent procurement leads to a reduced budget impact. Further, the model proposes that the relationship between transparent procurement is mediated by clinical governance.

Conclusions: This paper presents a first attempt at modelling both the effect of clinical governance on procurement transparency and the mediating effect of clinical governance on the relationship between procurement transparency and budget impact. The model has policy implications on the level of clinical governance adoption.

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Keywords: clinical governance, transparent procurement, budget impact, medicine, agency theory, conceptual model



Psychology and Mental Health



Linguistic Analysis of Schizophrenic Patient Communication in Guided Interviews

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Introduction: The case study focuses on the preliminary results of an interdisciplinary research related to the genre of doctor-patient communication. Discourse analysis is particularly relevant in the context of psychotherapeutic consultations. The success of the communication and the therapy largely depends on the patient's mental capacity to adequately interpret the interlocutor's inner mental states. This capacity is referred to as mentalization [1].

Aim: The study aims to present the preliminary results of an interdisciplinary research based on guided interviews related to Hemingway's short story entitled *The End of Something* [2]. The primary purpose of the research is to describe and categorize schizophrenic patients' language use in terms of their mental capacities with a special focus on deictic elements.

Methods: The case study consists of guided conversations between a PhD student and a schizophrenic patient and a control participant, respectively. The research is based on an interdisciplinary analytic method enabling the description and categorization of supposedly recurring linguistic patterns present in schizophrenic patients' speech. The qualitative analysis focuses on deictic phrases reflecting the linguistic patterns of mentalization included in the corpus.

Results: Based on the results to date, it can be suggested that schizophrenic patients' language use reflects mild microlinguistic disturbances, and from a pragmatic aspect, tends to display even more severe macrolinguistic deficiencies in their discourses, especially when employing deictic elements [3].

Conclusions: Hopefully, the findings can contribute to more successful psychotherapeutic sessions by offering further linguistic methods and a somewhat deeper understanding of patients with mental disorders.

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Keywords: doctor-patient communication, conversation analysis, functional pragmatics, mentalization, deixis

Detection of acute mental fatigue based on heart-rate variability: a machine learning approach

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Introduction: Declined cognitive performance induced by acute mental fatigue (MF) has significant implications for medical work and safety monitoring. Previous studies have shown that machine learning algorithms using physiological data (e.g. heart-rate variability, HRV) can be applied for effective MF detection in order to prevent the negative consequences of MF [1-2].

Aim: We aimed to increase the generalizability of previous findings by using variable MF induction methods and a larger sample size to train machine learning models that can detect MF.

Methods: The data of three MF experiments applying different cognitive tasks lasting 1-2 hours to induce MF were analyzed: a working memory task (n=20), a switching task (n=38) and a Stroop-task (n=27). In each experiment, electrocardiogram was continuously recorded, and 21 HRV indices were calculated for two 5-min intervals: one at the beginning (non-fatigued block) and one at the end of the tasks (fatigued block). Logistic regression, K-nearest neighbors (KNN) and random forest classifiers with 5-fold stratified cross-validation (CV) were used to detect MF.

Results: Using the best set of features, the highest classification score was achieved by logistic regression, which had a CV accuracy of 78.16%. The KNN (k=9) and random forest (number of estimators = 100) algorithms achieved CV accuracies of 75.8% and 73.8%, respectively.

Conclusions: In line with previous research, our results suggest that machine learning algorithms can effectively detect MF based on HRV measures. However, since the data was obtained from a larger and more heterogeneous sample in terms of MF-induction, it gives us more confidence that the findings can be generalized to a broader population.

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Keywords: *mental fatigue, machine learning, classification, heart-rate variability*

Dealing with Early Dementia Symptoms in Studies related to the Environment

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Introduction: There is an urgent need of conceptual and building modifications to cope with the needs of people with dementia in a better way [1]. Many studies are being conducted in order to create better environments that could improve the quality of life and well-being of the elderly living with dementia. However, most of the researches do not include them as active participants. Although people with dementia have been perceived to be incapable of eliciting their personal accounts as a consequence of verbal communication disability and memory deficits [2] recent studies proved otherwise.

Aim: This study provides evidence on dealing with early dementia symptoms that, according to the literature, could affect the inclusion of people with dementia as active participants in studies related to the environment. It investigates early dementia symptoms most cited in the literature and it analyzes the chosen research methods.

Methods: A literature review was adopted to explore the topic. Full-text english papers included in the review were found at PubMed, Springer and PsychINFO database platforms.

Results: Although there are a range of symptoms associated with dementia, three main symptoms were considered: memory loss, communication impairment and behavioral disturbances. The results reinforce the fact that the person with dementia have the ability to collaborate as potent informant. Methods of data collection should be adapted for their inclusion.

Conclusions: The stigma created around dementia and the complexity of the inclusion of people with dementia as active participants was probably the main reason of the notable smaller amount of studies related to the built environment that actually include people living with dementia as active informants in the literature. Even though it can be a complex task, all the reviewed studies could manage the adversities of their inclusion.

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Keywords: People with dementia, environment, literature review, social inclusion

Spiritualism and personal hygiene

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Introduction: Spiritualism serves an important role in the mental health of the individuals. [1] But how does it affect physical health, and what role does it have in personal hygienic behaviour? Is it possible to give space to religions in awareness raising for personal hygiene? What possible role could they have in the light of the COVID-19 pandemic?

Aim: The aim of this study is to identify linkages between spiritualism, faith and health with highlighting religious customs relevant to personal hygiene.

Methods: We applied an extended literature review of religious and public health studies including 27 relevant publications covering seven major religions.

Results: Based on the academic literature and the religious texts reviewed, we present the connection between spiritualism and hygiene to draw attention on this less represented research area. With the ritual of handwashing in the centre of this paper, we illustrate that handwashing is an established custom in many religions, which has a potential for the better planning of public health interventions and hygiene promotion activities. As main part of this study we review the ritual handwashing practices (ablution) of seven religions, including Christianity, Judaism, Islam, Hindu, Shintoism, Buddhism and Bahá'í.

Conclusions: After the review of these considerations, we phrase recommendations reflecting the contemporary multicultural environment of public health interventions. We argue that professionals involved in health promotion should establish an intercultural awareness, including knowledge on religious customs of beneficiaries, which might have a positive effect on the success of their programmes. We also suggest to involve religious leaders in hygiene promotion activities as they might be able to utilize religious rituals as examples for good hygienic behaviour.

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Keywords: hand hygiene, spiritualism, washing hands, personal hygiene, COVID19



Pharmaceutical Sciences

Investigation of the receptor-ligand complexes of TRPA1 receptor by computational approaches

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Introduction: Transient receptor potential channel subfamily A member 1 (TRPA1) is a Ca²⁺-permeable cation channel [1]. TRPA1 is a primary sensor of environmental irritants, expressed by nociceptive neurons. TRPA1 is a validated target in the treatment of inflammatory pain diseases [2].

Aim: The aim of the current study is to investigate the structure of TRPA1 and its receptor-ligand complexes by computational approaches. An accurate knowledge of the molecular structure of the receptor and specific binding positions of the ligands plays a key role in drug development.

Methods: During the work, molecular mechanics and molecule dynamics simulations were applied to study the atomic resolution structure of TRPA1 receptor and the ligand binding mechanisms. The target-ligand complexes might prove helpful in understanding the accurate binding mechanisms of the ligands.

Results: TRPA1 structures available in the Protein Data Bank were evaluated, and the convenient structure was identified and prepared for further analysis. The whole ligand-bound target structure was produced based on molecular docking calculations, in the case of the ligand dimethyl-trisulfide (DMTS). The calculated binding free energy and position of the ligand were *de novo* determined in this study.

Conclusions: TRPA1 is an important target for drug design, that is in the highlight of research groups. In the past 5 years intensive research was conducted regarding TRPA1. However, there is a lack in computational studies of the ligand binding mechanisms of TRPA1 in the literature. The present study surveys the applicability of available computational approaches to study the atomic resolution target-ligand complexes of TRPA1.

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Keywords: TRPA1, DMTS, ligand binding, molecular docking

Peptide docking to protein targets: challenges and applications

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Introduction: In the past few decades, molecular docking methods have been widely used in academia and the pharmaceutical industry as a valuable tool for drug design and development. Since protein-peptide interactions have been known to play central roles in most cellular processes, peptides and peptidomimetics has become increasingly attractive for developing new drug entities and an increasing number of new methods for protein-peptide docking have been developed. Although molecular docking methods are proven to provide fast and accurate results for small molecule interactions, peptide docking is significantly challenging due to high conformational flexibility of peptides and often extensive, shallow binding sites.

Aim: We evaluated the general performance of twelve fast docking methods on a test set of pharmaceutically relevant and yet structurally challenging protein-peptide complexes primarily by comparing their ability to reproduce experimentally determined binding poses of peptide ligands.

Methods: In this study, a diverse test set of 40 protein kinase-peptide and reader protein-histone peptide complexes was used to evaluate the performance of twelve fast docking methods in terms of docking and ranking accuracy. In order to perform a fair comparison, the input structures are prepared in a universal manner without considering specific factors and the “default” settings are employed for the docking assays.

Results: Based on their top-ranked binding modes, HPEPDOCK and GalaxyPepDock performed the best with average RMSD_{top} 10.81 Å (±5.8) and 11.21 Å (±9.8), respectively. When the best docked poses are considered, HPEPDOCK and GalaxyPepDock outperformed again with average RMSD_{min} 6.32 Å (±3.4) and 7.59 Å (±7.9), respectively. In terms of ranking accuracy, PEP-FOLD3, ClusPro, Gramm-X, and SwarmDock showed better performances with a success rate of 22.5-31.25 %.

Conclusions: Docking methods examined in this study failed to produce accurate and statistically reliable results indicating that docking highly flexible peptide ligands is still challenging for current fast docking methods and need further improvement.

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Keywords: molecular docking, protein-peptide interactions, protein-peptide docking

Orally active somatostatin 4 receptor agonists as novel analgesic candidates

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Introduction: Current therapy of neuropathic pain is unsatisfactory, thus there is a great effort to develop analgesics with novel mechanism of action. Somatostatin released from capsaicin-sensitive peptidergic nociceptors at the periphery and GABAergic interneurons in the brain has analgesic and anti-inflammatory effects mediated by its sst₄ receptor without influencing the endocrine system. Therefore, sst₄ might be a promising target for drug development [2]. We investigated the effects of our four novel small molecule sst₄ receptor agonists in mouse models of neuropathic pain and neurogenic inflammation.

Methods: The binding abilities of our pirrolo-pyrimidine compounds were determined by in silico modelling and by G-protein activation assay on sst₄-expressing CHO cells. The effects of the two most potent and most efficacious agonists were tested in the partial sciatic nerve ligation-induced traumatic mononeuropathy (Seltzer-model) and resiniferatoxin-evoked acute neurogenic inflammation in mice.

Results: All four of our novel compounds bind to the same high affinity binding site of the sst₄ with similar interaction energy and induce G protein activation. Compound 1 exerts 60-66% maximal anti-hyperalgesic effect in the neuropathy model after a single oral administration of 500 µg/kg dose and Compound 1 also reduces neurogenic inflammatory pain.

Conclusions: Our sst₄ agonists are promising analgesic drug candidates for chronic neuropathic and neurogenic inflammatory pain.

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Keywords: somatostatin, neuropathic pain, neurogenic inflammation, analgesic drugs

Cannabis: safe source of food or efficient medicine?

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Introduction: The importance of *Cannabis sativa* as medicine for different types of diseases has been increasing in the last couple of years. Research has been focused on elucidating the mechanism of action and clinical efficacy of cannabinoids. Although the safety and efficacy of pure compounds and especially those of different herbal extracts have not been discovered fully yet, the use of dietary supplements and food products containing cannabis is becoming more and more popular [1].

Aim: The purpose of this work was to review the aspects of *Cannabis* as recreational drug, medicine and food source. A short overview on the pharmacological effects of the main cannabinoid compounds was provided and based on our analytical experiment the diversity of the extracts in various matrices was demonstrated. The cardiovascular effects of certain cannabinoids were studied.

Methods: The overview of the pharmacological profiles was based on the overview of literature. The chemical profiles of food supplements available on the Hungarian market were analyzed by HPLC. The effects of cannabinoids on cellular cardiac electrophysiological properties were assessed *in vitro* and *in vivo*.

Results: The current legal situation of *Cannabis* is controversial worldwide. Although certain, THC-containing preparations are considered as illicit drugs in several countries, less attention is paid to products rich in other cannabinoids, although some of these compounds are characterized by remarkable pharmacological effects. Certain cannabinoids are available as approved medicines, but their use as food is only poorly regulated. The products analyzed by us were chemically diverse, and cannabidiol, as one of the most popular cannabinoids in food supplements, exerted proarrhythmic effects in our experiments [2].

Conclusions: The chemical diversity of *Cannabis*-based food supplements, together with the cardiovascular risk associated with certain cannabinoids raises severe safety issues regarding the use of uncontrolled products as food.

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Keywords: cannabis, cannabinoids, safety, efficacy, pharmacognosy

Lipid raft disruption as a novel approach in pain management

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Introduction: Transient Receptor Potential (TRP) Vanilloid 1 and Ankyrin 1 (TRPV1/TRPA1) are nociceptors expressed in primary sensory neurons. Capsaicin, resiniferatoxin, noxious heat activate TRPV1, while formaldehyde, noxious cold, mechanical stimuli activate TRPA1. Lipid rafts - specialized microdomains of the plasma-membrane, which are rich in cholesterol, sphingomyelins and gangliosides - form functional complexes with several receptors including TRP channels. Sphingomyelinase (SMase), myriocin (Myr), or synthetic products, as our carboxamido-steroid (C1) and methyl β -cyclodextrin (MCD) are useful tools to disrupt rafts and investigate their effect on TRP channels.

Aim: The aim of the present study is to investigate the antinociceptive effects of lipid raft disruptors in mouse models of pain with different mechanisms based on our earlier *in vitro* results. To prove the potential mechanism of action we also tested some *in vitro* properties.

Methods: Animals were pretreated locally with 50 mU SMase, 1 mM Myr, 100 or 500 μ M C1 and 15 mM MCD. Eye-wiping movements were counted after 30 μ g/ml capsaicin instillation into the right eye of the animals. Resiniferatoxin (0,1 μ g/ml) was injected into the right hindpaw, and the development of thermal allodynia and mechanical hyperalgesia was measured with an increasing temperature Hot Plate and Dynamic Plantar Aesthesiometer, respectively. Intraplantar administered formalin (2,5%) evoked nocifensive behavior time were measured in two phases. The *in vitro* properties were tested by fluorescent spectroscopy.

Results: In the “eye-wiping” test all compounds reduced the number of wipings, furthermore Myr and C1 had prolonged effect. SMase and Myr alleviated the RTX-induced thermal allodynia, moreover SMase and C1 diminished mechanical hyperalgesia. Only Myr did not reduce duration of nocifensive behaviour after formalin injection in the second phase. In the fluorescent spectroscopy only SMase did not modified Laurdan spectra.

Conclusions: We proved that not only cholesterol but also sphingolipids have important role in the lipid raft integrity and targeting them might be a novel pharmacological method in the pain management.

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Keywords: lipid raft, methyl β -cyclodextrin, myriocin, sphingomyelinase, Transient Receptor Potential



Pharmaceutical Technology



A Design of Experiment (DoE) approach for the chitosan/thiolated chitosan and hyaluronic acid nanoplexes for the pulmonary drug delivery in tuberculosis

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Introduction: Although, tuberculosis is the curable disease, however, the current therapies fail to deliver the drug to the alveolar macrophages (where causative agent resides) in lung. The ineffective drug delivery approaches lead to the drug toxicity and organ damage [1].

Aim: Currently, the dry powder inhalers (DPIs) are being explored for the site specific drug delivery in infectious diseases [2]. Biocompatible polymers; chitosan (CS), thiolated chitosan (TC) and hyaluronic acid (HA) were used because of their affinity for oral mucosa and alveolar macrophages to achieve higher drug deposition in deeper tissues of lungs.

Methods: Nanoparticles based DPIs loaded with isoniazid (CS/HA and TC/HA NPs) were synthesized by using the Design of Experiment (DoE) approach. The nanoparticles were prepared by ionic gelation method and later optimized by Box-Behnken screening design prior to freeze-drying to obtain nano-DPIs [3].

Results: The size, morphology, physico-chemical properties, *in-vitro* release profile, *in-vitro* permeation, aerodynamic profile, *in-silico* drug deposition of the nano-powders were promising. *In-vitro* aerodynamic profile and *in-silico* deposition profile, were correlated in terms of results.

Conclusions: Altogether, DPIs showed promising results based on the preliminary fundamental outcomes with enhanced drug encapsulation efficiency and drug deposition.

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Keywords: Andersen cascade impactor, Box-Behnken, thiolated chitosan, *in-silico*, dry powder inhaler

Release Control of Levodopa methyl ester hydrochloride by loading into modified silica

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Introduction: The levodopa methyl ester hydrochloride (LDME) is a dopamine precursor active ingredient for Parkinson's disease treatment. During the off period of the disease, the drug concentration is below the desired level which can be an end-of-dose (*wearing-off*) effect or an immediate seizure when the formulation does not have a quick enough onset (*delayed on*). The former can be treated by prolonged, the latter by accelerated drug dissolution. The mesoporous silicas are non-toxic per os, have high special surface area causing that they can adsorb a large amount of material. The drug release can be tuned based on the adsorbent wettability [1]. Our aim was to regulate the LDME release by controlling the hydrophobicity.

Methods: Mesoporous silica powder was dispersed in n-hexane, the hydrophobization agent was chloro(trimethyl)silane with different concentrations to achieve surfaces with different level of hydrophobization. The wetting properties of the hydrophobized silica was characterized by contact angle measurement. LDME was loaded into the silica, then pastilles were formulated using Box-Benken 3³ factorial design (varying factors: the hydrophobization extent, the LDME:excipient ratio and the compression force). The LDME-content, the secondary interactions and the *in vitro* release properties were investigated.

Results: The hydrophobization extent was proportional to the reactant concentration based on the contact angle measurements. The release properties of the LDME could be regulated by varying factors. There were products with quick release and with slow-release, as well.

Conclusions: LDME-containing silica products were formulated. The products with immediate release create the opportunity to treat the *delayed on* effect. The ones with slow-release can provide constant blood level potentially treating the *wearing-off* effect

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Keywords: mesoporous silica, release control, hydrophobization reaction, levodopa methyl ester

Formulation of dry powder inhalers using nano spray dryer

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Introduction: The lung, as an alternative way of drug delivery, has lots of advantages such as rapid onset of action, large surface for absorption, limited drug degradation, and high solute permeability. The appropriate inhalable nanoparticle engineering technique is the most important factor to get enhanced aerosolization properties and improved therapeutic effect. The non-steroidal anti-inflammatory meloxicam (MX) was used as a model active ingredient. It could be effective for the treatment of non-small cell lung cancer, cystic fibrosis and chronic obstructive pulmonary disease [1].

Aim: Our aim was to produce inhalable dry powders containing nanoparticles using wet milling and nano spray drying. We expect from our samples rapid dissolution, high permeability and outstanding alveolar deposition.

Methods: We used a two-step preparation method. First, the nanoparticle size pre-suspension was prepared with wet milling technology, using polyvinyl alcohol (PVA) and MX. The powders were produced by nano spray drying from the diluted suspension and leucine (LEU). We measured the following properties: particle size (DLS), morphology (SEM), true density, structure (XRPD), thermoanalytical properties (DSC), *in vitro* dissolution, *in vitro* absorption, *in vitro* lung deposition (Andersen Cascade Impactor) and *in silico* aerodynamic properties (Stochastic Lung Model).

Results: We worked out a nano particle preparation method, using wet milling and nano spray drying for pulmonary administration. We managed to prepare 500-800 nm particles. Thanks to the improved surface area and amorphization, the released and the absorbed amount of MX increased. The alveolar depositions of the samples containing LEU were promising also *in vitro* and *in silico*.

Conclusions: The samples are suitable for pulmonary delivery, therefore our products could treat different respiratory diseases also.

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Keywords: nano spray dryer, dry powder inhalers, meloxicam, Andersen cascade impactor, *in silico* assesment

Investigation of polymer-based nanofibers to modify the physico-chemical properties of ciprofloxacin

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Introduction: The water solubility of a drug can be increased by formulating it into polymer-based electrospun nanofibers [1]. These novel nanocarriers are mostly prepared by the electrospinning (ES) process. Beside the most common single-needle ES there are plenty of other electrospinning methods such as coaxial and needleless ES.

Aim: The study aimed to produce and investigate various polyvinyl-pyrrolidone (PVP) based ciprofloxacin (CIP)-loaded nanofibers and to find the optimal composition and the appropriate technological parameters to improve the physico-chemical properties of CIP. As a result, the *in vitro* dissolution rate could be increased.

Methods: Nanofibrous samples were made in different combinations of ingredients with different ES methods. To characterize the samples the micrometric (SEM) and the structural (DSC, XRPD) properties were investigated. Also, *in vitro* dissolution profiles were examined.

Results: All electrospun nanofibers contained the CIP in its amorphous form. Fine fibers (average diameter 542-645 nm) with smooth surfaces provided immediate-release formulations. However, with the fusion of the fibers, the drug release kinetic changed.

Conclusions: Immediate-release CIP-loaded nanofibrous formulations were developed. Moreover, it has been found that the morphology of the nanofibers plays key role in the dissolution. Therefore, the stability of the formulations' morphology is extremely important and need to be guaranteed.

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Keywords: *electrospinning, nanofibers, ciprofloxacin, dissolution kinetic*

Buccal polymer film as an innovative drug delivery system

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Introduction: Nowadays the pharmaceutical industry is trying to come up with innovative solutions. Oral mucoadhesive systems like tablets, gels, and polymer films are one of these possible products. These systems possess many advantages, one of them is that systemic and local effects are also available and they have fast effect, so we can use these products in case of emergency [1].

Aim: The aim of this work was to formulate polymer films with different compositions from sodium alginate, to investigate the physical and chemical properties of the prepared films with different methods and to find the optimal composition.

Methods: Sodium alginate and hydroxypropyl methylcellulose were used as a film former. Glycerol was added as plasticizer and cetirizine dihydrochloride served as API [2]. The polymer films were prepared by solvent casting method at room temperature.

Results: The physical properties of the films, such as tensile strength, thickness and mucoadhesion were examined. The physical-chemical properties of the films were investigated by FT-IR and Raman spectroscopy, thermal analysis (TG, DSC). We also tested the dissolution of the active substance from the films by a dissolution basket tester and the sample was analyzed by a UV spectrometer. The mucoadhesion test represented adequate force to bind to the mucosa. The results indicated that the material has a notable effect on the properties of polymer films, and the active pharmaceutical ingredient indicated homogeneous distribution. The dissolution test showed that the entire amount of the API dissolved from the polymer films.

Conclusions: Oral mucoadhesive polymer films which can bind to the buccal mucosa were prepared successfully. In the polymer films there is interaction between the film components. The API was distributed homogeneously in the prepared polymer films.

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Keywords: buccal, mucoadhesive film, drug delivery system, sodium alginate, cetirizine

Optimization and Investigation of Structure and In Vitro Behavior of Meloxicam-Loaded Nasal Polymeric Micelles

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Introduction: Intranasal delivery offers many possibilities, exploiting the direct “nose-to-brain” pathway which allows the drug to reach the central nervous system without losing its pharmaceutically active form. With unique properties of polymeric micelles in a proper nasal formulation, a higher bioavailability can be achieved which is important amongst people suffering from neurodegenerative disease associated neuroinflammation.

Aim: The aim was to optimize the formulation of Soluplus[®]-Meloxicam polymeric micelles for the intranasal administration route. The desired product is a solid dosage form powder which can be used to ex tempore formulate a nasal spray by adding water to the system.

Methods: The optimization of the thin film-method was based on Box-Behnken factorial design followed by micelle characterization via DLS, solubility and wettability studies. The interactions in solid state were investigated by vibrational spectroscopy, thermoanalytics and x-ray diffraction. The physical stability and *in vitro* characteristics were also measured.

Results: The MEL-loaded polymeric micelles can be characterized as monodisperse formulations with improved physicochemical attributes contributing to higher water solubility, wettability and encapsulation efficiency. The interactions between Soluplus and MEL showed that a stable product was designed, supplemented by proper *in vitro* characteristics.

Conclusions: The current optimized formulation of MEL-loaded polymeric micelles are a proper basis for further investigations aiming to be tested in the treatment of neuroinflammation [1].

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Acknowledgements: The research was funded by the GINOP-2.3.2-15-2017-00060 project.

Keywords: polymeric micelles, nasal, meloxicam, nanoDDS, neuroinflammation

API – excipient interaction and compressibility studies in solid matrix systems

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Introduction: Solid dosage forms are still the most favoured types of medicines in the pharmaceutical market. A recently emerging trend on personalized medicine, pharmaceutical industry faces a new challenge on providing matrix systems with variable properties. A novel approach of pharmaceutical design may be applied with a more detailed investigation of physico-chemical property-based interactions between the drug and the applied excipients.

Aim: The main aim of this research work is the better understanding of chemical interactions therefore to meet the requirements of the ‘Functionality related properties of materials’ concept of Quality by Design.

Methods: A line of chemically similar APIs and matrix forming agents were mixed and directly compressed with an instrumented IMA Kilian SP300 tablet press. The interactions formed within tablets were studied by FT-IR spectroscopy, and a custom-made device was applied to perform dissolution tests to obtain information about the effects of interactions on the drug liberation kinetics. Kawakita and Walker analysis were made to obtain information about the compositions compressibility.

Results: The spectral information revealed that hydrogen bonds were formed between the drug and excipients even in solid state. The investigations during dissolution tests proved that the strength of interactions have increased due to the formation of polyelectrolyte complexes which affects not just the speed of drug liberation but also the quantity of the liberated drug. Compressibility studies showed that due to chemical interactions particles are attracted to each other causing an increment in the energy value needed for deformation.

Conclusions: According to the findings we assume that in addition to the physico-chemical properties of the drug delivery system, the drug liberation is considerably influenced by the chemical interactions formed between the used API and excipient.

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Keywords: Drug-excipient interaction, polymers, matrix tablet, controlled release, Kawakita analysis, Walker analysis

How can the application of Risk Assessment support the development process of liposomes?

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Introduction: The liposomal formulations, nano-sized drug delivery systems, have a remarkable role in the development of therapeutic and diagnostic techniques. The regulatory authorities need to meet several challenges from the quality, safety and efficacy aspects of the liposome-based products [1]. Dedicated regulatory authorisation processes for liposomes are still missing. The application of the Quality by Design (QbD) quality management procedure in the pharmaceutical developments improves the formulation process via the systematisation of the required knowledge and thus by the rationalisation of the necessary experiments [2]. The key element of this workflow is the Risk Assessment (RA) when the most potential influencing factors are determined.

Aim: Our work aimed to collect and systemise all the relevant factors of the liposome formulation development via the QbD technique, identify the Quality Target Product Profile (QTPP) for a liposome-based formulation, the Critical Quality Attributes (CQAs) of the liposomes, the possible Material Attributes (MAs) and the Process Parameters (PPs) of the traditional thin-film hydration manufacturing method that may influence the key characteristics of the targeted formulation.

Methods: After the aimed QTPP was built and the CQAs determined, due to the knowledge space development, the critical factors (CMAs, CPPs) were chosen from the MAs and PPs. For the evaluation, an initial RA was performed.

Results: The phospholipids, the active pharmaceutical ingredient (API) content, the surface modifiers, the cholesterol content, the ratio between the phospholipids and the cholesterol, the phase transition temperature of the lipophilic phase, the quality of the hydration media and the cryoprotectant were found as the most highly influencing CMAs; and the working temperature, the duration of the sonication and the number of filtrations as the essential CPPs.

Conclusions: The RA draws the researcher's attention for the critical points of a formulation process, and that helps to achieve the aimed quality for the products.

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Keywords: *Quality by Design, Risk Assessment, critical factors, liposome formulation, thin-film hydration method*



Poster sessions

Development of a visualization and analytical method of the pharmacy curriculum

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Introduction: Logical arrangement of the pharmacy curriculum, relevant prerequisite system and monitoring of dropout rates is essential for the effective educational process. To our best knowledge currently no commercially available software that can evaluate and visualize the curriculum.

Aim: We aim to collect and summarize prerequisites of obligatory subjects, data on student dropout rate, and integrate all relevant information in a visual map. We have set the following objectives: (1) capability to support faculty leadership decision making; (2) direct data extraction from the Neptune Unified educational administrative system; (3) user friendly visualization of semesters in a linear, vertically upward direction; (4) in depth analysis of data for a particular object.(5). Our long term goal is the development of a student interface permitting students to see the risks to their educational progress.

Methods: Prerequisites of obligatory subjects were exported to various software aiming to visualize the networks of our curriculum. Dropout rates were collected from the electronic administration system (Neptun). A tailor-made software has been programmed integrating key subject specific components (credit value, subject code, semester, module, prerequisites, etc.) and educational properties (e.g.: failure rate, students' feedback on education), and a graphical user interface was developed for course visualization.

Results: The 10 semester one-tier master pharmacy degree program is highly complex, as the 70 obligatory subjects have more than 110 prerequisites [1]. We have designed and created a software, capable of showing the type failed exams for each course, performing critical path calculations. Further, the estimated value of the expected completion time per item, also in cumulated form, and movement of a subject to an earlier or later recommended semester.

Conclusions: A network analysis and visual presentation of the obligatory subjects of pharmacy curriculum require an individual software developed to meet our expectations and needs. Applying such novel method will likely improve curriculum structure and reduce dropout rate by identifying critical subjects with high number of prerequisites and high failure rate.

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Keywords: Dropout Rate, Curriculum Development, Prerequisites, Progress Monitoring

Application of Ionic Liquid-Based Column for the Analysis of Fatty Acid Composition in Bacteria and its Lipopolysaccharides by GC-MS

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Introduction: The presence of bacteria in the bloodstream causes systemic inflammation (blood poisoning, sepsis), which is a serious problem in medicine. Bacterial endotoxins, also known as lipopolysaccharides (LPSs), are important biomolecules found in Gram-negative bacteria. The chemical structures of endotoxins are closely related to their biological activity, which can be beneficial or harmful to human health, depending on the amount and structure of LPSs in the blood.

Aim: The purpose of our research is to monitor the structure of bacterial surface molecules by external or internal influences. According to our hypothesis, the change in the growth temperature has an effect on LPS biosynthesis, thus the bacteria can appear differently in various host organisms. Such as at room temperature, *i.e.* hospital devices, the human body (37 °C), or a bird body (42 °C), which may also be a potential target of the bacterium.

Methods: The fatty acid composition of Gram-negative bacteria and its LPSs were analyzed by gas chromatography-mass spectrometry (GC-MS) applying an ionic liquid-based column, SLB-IL111. A 26-component Bacterial Acid Methyl Ester mixture was used for the validation process and for qualitative and quantitative determination.

Results: An optimal gas chromatographic method was developed and validated, and the appropriate sample derivatization method was found for the analysis of bacterial acid methyl esters. The proposed method was evaluated to 26 fatty acid components on the ionic liquid column and the results correspond to the general criteria. Analysis of the temperature dependence of the bacteria structures from the *Enterobacteriaceae* and *Pseudomonadaceae* families and their endotoxins were carried out. The fatty acids were identified and the percentage composition were determined.

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Keywords: ionic liquids, bacteria, lipopolysaccharides, fatty acids, gas chromatography

The proteasome activator PA200 resides in the vicinity of mitochondria and regulates mitochondrial dynamics and bioenergetics in a human neuroblastoma cell line

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The conserved Blm10/PA200 family belongs to the proteasome activators. The binding of PA200 to the proteasome core facilitates peptide degradation in an ATP and ubiquitin independent manner. Our knowledge about its exact role in diseased cells, however, is still limited. Here, we show that the stable knockdown of PA200 in human neuroblastoma cells (shPA200) following oligomycin treatment leads to altered mitochondrial morphology including increased compact tubular structure and reduced mitochondrial fragmentation. Western blot analysis of mitochondrial fusion and fission proteins showed an accumulation of L-OPA 1 isoform and a significant reduction in the protease OMA1 in shPA200 cells after oligomycin treatment. Sub-cellular fractionation and immunofluorescence staining demonstrated that PA200 is present in the mitochondrial fraction and it co-localizes with mtDNA. Seahorse data analysis showed that the silencing of PA200 resulted in a significant increase in glycolysis and glycolytic capacity and reduced proton leak and spare respiratory capacity. Flow cytometry analysis revealed a significant reduction of mitochondrial membrane potential and reactive oxygen species (ROS) in shPA200 cells. Furthermore, mitochondrial OXPHOS proteomic profile showed a significant reduction of protein level of mitochondrial complex-I in shPA200 cells. These data suggest that PA200 has a crucial role in metabolic homeostasis, mitochondrial dynamics and biogenesis.

Clinical Effectiveness and Cost-Effectiveness of Oral-Health Promotion in Dental Caries Prevention among Children: Systematic Review and Meta-Analysis

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Introduction: Dental prevention programs and oral health promotion programs rarely receive the same level of attention as medical care among decision-makers when considering the cost-effective allocation of scarce health care resources. However, the economic evaluation of the cost-effectiveness to determine the programs value for money remains unclear.

Aim: The objective of this study was to evaluate the clinical effectiveness and cost-effectiveness of oral-health promotion programs aiming to improve children's knowledge of favorable oral health behavior to lower decayed/-missing/-filled teeth while reducing the financial cost on health institutions.

Methods: An electronic search was performed in seven databases. Studies were restricted to human interventions published in English. The search study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines, and the risk of bias was assessed based on the Drummonds Checklist.

Results: A total of 1072 references were found. Among these, 19 full texts were included. Most studies had a strong quality. The overall pooled impact of OHPPs estimates children suffering from DMFT/S to have 81% lower odds of participating in OHPP (95% CI 61–90%, I²: 98.3%, $P \leq 0.01$). Furthermore, the program was shown to be effective at lowering the cost in 97 out of 100 OHPPs (95% CI 89–99%, I²: 99%, $P \leq 0.01$). Three subgroups analyses (age groups, study countries, studies of the last five years) were performed to evaluate the influence modification on the pooled effect.

Conclusions: A comprehensive analysis of the OHPPs confirmed a reduction effect on child DMFT, lowering the financial burden of dental-care treatment on health institution among (Age > 6), however, the program confirmed no clinical effectiveness and cost effectiveness among (Age ≤ 6), studies published before and after the 2015-year revealed the OHPP cost effectiveness, as well as OHPP efficient to reduce dental caries and cost in UK, Finland, Ireland and Japan.

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Keywords: Oral Health Promotion Programs (OHPP); Decayed Missing Filled Teeth (DMFT); Cost-Effectiveness Analysis (CEA); Incremental Cost Effectiveness Ratio (ICER)

The effect of screen media activity on social cognition- an fMRI study

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Introduction: Recent evidences suggest negative effects of Problematic Internet Use (PIU) and Screen Media Activity (SMA, e.g. using social media, playing video games) on social cognition [1], [2]. Growing literature indicates that Internet-related addictions are also associated with breakdown of social functional brain networks [3], but the effect of SMA on brain functions is not well understood.

Aim: Our study aims to investigate the social cognition-related functional connectivity alterations induced by SMA & PIU, using whole brain psychophysiological interaction (PPI) analysis with amygdala seeds.

Methods: To observe functional connectivities, BOLD responses during emotion recognition task (e.g. happiness, angry, etc.) were measured in 69 healthy university students (36 females, mean age= 22.4, SD= 2.68). Self reported questionnaires were used to assess PIU and SMA.

Results: We found significant, positive correlation between PIU and the PPI between the right amygdala and areas related to executive functions (left superior frontal gyrus, right frontal pole). Furthermore, time spent on social media sites correlated positively with the PPI between the amygdala seeds and left and right frontal pole. In addition, time spent with browsing on the web correlated positively with the PPI between the left amygdala and areas related to social cognition (bilateral precuneus and bilateral posterior cingulate gyrus).

Conclusions: According to previous studies, our results suggest negative effects of SMA and PIU on social cognition. Increased time of social media using and browsing on the web alters brain connections with areas related to social cognition, while altered connections with executive brain regions may be the reason for having difficulties in controlling the overuse. Taken together, these findings suggest that overuse of SMA might have negative effect on social cognition in PIU.

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Keywords: problematic Internet use, Internet addiction, functional brain networks, social cognition

Gene-environmental interactions and risk of venous thromboembolism was higher in the Hungarian Roma population than in a general one

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Introduction: Interactions of genetic and environmental risk factors contribute to the increased risk of venous thromboembolism (VTE). Understanding how genetics and environmental risk factors were interacting, gives insight for early identification of risk groups of the populations, taking appropriate preventive and curative measures.

Objective: To compare gene- environmental interactions (GxE) and VTE risk in Hungarian general and Roma populations.

Methods: A comparative health survey was employed in 406 Hungarian general and 395 Roma subjects. DNA was genotyped for rs121909567 (SERPINC1), rs1799963 (F2), rs2036914 (F11), rs2066865 (FGG), rs6025 (F5), and rs8176719 (ABO) polymorphisms. Multivariable linear regression analysis was applied to test the impact of GxE on VTE risk after interaction term was created between VTE environmental and genetic risk factors.

Results: The VTE risk increased in the Hungarian Roma ($\beta = 0.280, p = 0.001$) and the general population ($\beta = 0.423, p = 0.001$) as a result of multiplicative interaction between coronary artery diseases (CAD) and rs2036914 (F11). In addition, the risk of VTE was higher among depressive Roma subjects who carried the risk variant of rs2036914 ($\beta = 0.819, p = 0.02$); however, the presence of interaction between depression and rs8176719 (ABO) increases VTE for Hungarian general only ($\beta = 0.342, p < 0.001$). The presence of multiplicative interaction between rs2066865 (FGG) and CAD increased the VTE risk for Roma population ($\beta = 0.143, p = 0.046$), but not for the general one ($\beta = -0.329, p < 0.001$). Our study also identifies the increased risk of VTE as a result of a multiplicative interaction between rs8176719 (ABO) and cancer, which was higher for the Roma population ($\beta = 0.370, p < 0.001$) than that of Hungarian general ($\beta = -0.042, p = 0.6$). Due to the simultaneous presence of diabetes mellitus and non-O blood groups, the VTE risk was higher for Hungarian general ($\beta = 0.194, p < 0.01$), than for the Roma population ($\beta = -0.039, p = 0.63$). The interaction between rs6025 (F5) and smoking also increases VTE risk in the Hungarian general population ($\beta = 0.172, p = 0.008$), but not for Roma population ($\beta = -0.014, p = 0.86$). The joint presence of high level of LDL-C and rs2066865 (FGG) increases the VTE risk in the Roma subjects ($\beta = 0.389, p = 0.002$), whereas the interaction of LDL-C with rs6025 (F5) risk variant increases VTE risk in the general one ($\beta = 0.368, p = 0.001$).

Conclusions: The combination of coronary artery diseases, cancer, diabetes mellitus, smoking, LDL-C, and depression with genetics risk factors increases VTE risks. As a result of dual burden the Roma population were at higher risk of VTE compared to Hungarian general. Thus, to improve the cardiovascular health of this minority, due emphasis should be given for tackling the VTE risk through combating the preventable environmental and personal risk factors that hasten the occurrences of VTE and its consequences among the Roma population.

Keywords: VTE risk, GxE interaction, genetic risk scores, Hungarian, Roma

Structural differences between Gelsolin and Flightless-I proteins and their behavior in the presence and absence of Ca²⁺-ion

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Gelsolin homology (GH) domain proteins are central to the control of the actin cytoskeleton. Its eponymous member; the six-GH-domain gelsolin (GSN) is a calcium-activated multifunctional actin regulator. Recently, a unique member; Flightless I (Fli-I) was identified by the six-GH-segment structure alloying a leucine-rich repeat. Both GSN and Fli-I are implicated in pathologies, including sepsis and tissue regeneration, respectively. Albeit, the structural-functional relation in GSN upon Ca²⁺-dependent activation has been well described the role of Ca²⁺ in the actin activities of Fli-I is unraveled. Our functional analyses indicate that GSN and the GH16 domains of Fli-I respond to Ca²⁺ differently implying different conformational characteristics of the GH domains in the two proteins. We aimed to investigate the structural behavior of GSN and Fli-I in the presence and absence of calcium-ion by using fluorescence spectroscopy and biochemical approaches.

The change in the fluorescence parameters (emission and maximum wavelength) of Trp in GSN upon quenching by acrylamide or guanidine-hydrochloride induced chemical denaturation are consistent with marked conformational rearrangements in response to Ca²⁺. This is in agreement with the high-resolution structural model of GSN activation. In contrast, our data suggest that the microenvironment of Trp residues in Fli-I GH16 is different from that of GSN even in Ca²⁺-free conditions and not markedly affected by the presence of the divalent cation. The hydrophobic properties of GSN and Fli-I GH16 were also found to be different based on the spectral emission changes of 1-anilinonaphthalene-8-sulfonic acid (ANS). Fluorescence spectroscopy data is supported by the different kinetics of limited proteolysis observed for GSN and Fli-I GH16. Our experimental findings are supported by bioinformatics analysis predicting that the sequence elements responsible for Ca²⁺-activation of GSN are not conserved in Fli-I GH16. Altogether, our work reveals different Ca²⁺-response and predicts distinct modes of activation of GSN and Fli-I.

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Are we sure we can make good decisions on health issues?

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Introduction: Health literacy is the ability of people to make appropriate decisions about their own and their family members' health and about the health care system [1]. Every second person in Hungary has limited HL level [2]. Limited HL level can cause higher mortality and morbidity level [3], more frequent use of emergency care [4].

Aim: The aim of the research was to conduct a pilot study among the population of Baranya County in Hungary with different socio-economic statuses.

Methods: In a cross-sectional study conducted in 2019 with 186 participants, socio-economic status, health status, health literacy (HL) level. The questionnaire included the European Health Literacy Survey Questionnaire (HLS-EU-Q47) to monitor the HL level. Descriptive statistical analysis and mathematical statistical analysis were applied. SPSS 24.0 statistical software was used to analyse the data. Relationships were considered significant at the $p < 0.05$ level.

Results: 186 people were involved in the research, but 45 of them were excluded (N=141). There were significant differences in HL levels by gender and educational level ($p=0.017$), health education ($p=0.032$) and presence of children in the household ($p=0.049$). Educational level ($p=0.002$) and type of settlement ($p=0.01$) had strong impacts on economic status. We found that 46.1% of the participants had limited comprehensive HL (cHL) level. This percentage was slightly lower for the disease prevention sub-index (33.3%). The average cHL index score was 34.8 ± 8.7 points, the average health care sub-index score was 34.6 ± 9.7 points, the average DP sub-index score was 35.8 ± 9.9 points, and the average health promotion sub-index score was 34.2 ± 9.4 points. Much (46.1%) of the examined population in Hungary (46.1%) had limited HL level.

Conclusions: Socio-economic status has a strong influence on HL level. If we would like to improve HL level in our country, we need to concentrate on regions with low average income.

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Keywords: health literacy, emergency care, socio-economic status

Antifungal and antibiofilm effects of caffeic acid phenethyl ester on different *Candida* species

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Introduction: *Candida* species are major human fungal pathogens that cause cutaneous and systemic infections with a high death rate, especially in immunosuppressed people. The emergence of highly resistant strains to the most common antifungal drugs, also due to biofilm formation, needs the development of new antifungal agents [1].

Aim: This study aimed to determine the antifungal and antibiofilm effects of caffeic acid phenethyl ester (CAPE) on nine strains of different *Candida* species (*C. albicans* 001, 1423, 1424; *C. parapsilosis* 8007, 8008; *C. glabrata* 1374, 1378 and *C. tropicalis* 1366, 1512).

Methods: Standard microdilution technique (CLSI M44-A) was used to determine the minimum inhibitory concentration values (MIC₈₀). Crystal violet assay was used both for the quantitative assessment of biofilm formation and mature biofilm eradication in 96-well microtiter plates.

Results: The findings of this study revealed that CAPE has inhibitory effect on different human pathogen *Candida* species. The MIC values were 12.5 µg/ml for *C. glabrata* 1374, *C. glabrata* 1378 and *C. parapsilosis* 8008, 25 µg/ml for *C. parapsilosis* 8007, 50 µg/ml for *C. albicans* 001, *C. albicans* 1424, *C. tropicalis* 1366 and *C. tropicalis* 1512, and 100 µg/ml for *C. albicans* 1423. The results of biofilm formation test showed that CAPE has an ability to reduce the formation of biofilm (*C. albicans* 1424, *C. parapsilosis* 8007, *C. glabrata* 1374 and *C. tropicalis* 1366) in a dose dependent manner. Minimum biofilm inhibitory concentrations (MBIC₈₀) were 50 µg/ml for *C. albicans* 1424, *C. parapsilosis* 8007, *C. glabrata* 1374, and 100 µg/ml for *C. tropicalis* 1366. The study of CAPE on matured biofilms revealed that, *C. albicans* 1424, *C. parapsilosis* 8007 and *C. glabrata* 1374 were partially eradicated (40-48%) by low concentrations of CAPE (3.125 – 25 µg/ml). However, in case of *C. parapsilosis* 8007 and *C. glabrata* 1374 higher (50 and 100 µg/ml) concentrations of CAPE revealed lower effect. On the other hand, matured biofilm of *C. tropicalis* 1366 were partially reduced (10-20%) at the higher concentrations (50 and 100 µg/ml) only. Surprisingly, higher concentrations of CAPE on matured biofilm of *C. albicans* 1424 revealed increased biomass.

Conclusions: It can be concluded that CAPE has antifungal activity against planktonic cells of *C. albicans* and non-*albicans* species. It can inhibit formation of biofilms and also partially eradicate their matured biofilms on a strain-dependent manner. In summary, this study highlights the potential of alternative and/or complementary use of CAPE as an antifungal therapy.

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Keywords: *Candida*, CAPE, biofilm, antifungal effects.

Sense of coherence and health behaviour of high school students – partial Results

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Introduction: The onset of the sense of coherence can be traced back to childhood. From then on, it undergoes a continuous transformation what ends in a positive personality who has goals and problem-solving mechanisms, capable to control his/her own life and consciously influence his/her health.

Aim: Our aim is to map the sense of coherence, health behaviour and mental health amongst sports-, high school- and vocational high school- students. It will be based on the assumption that there is a difference in the mentioned factors for students participating in these different types of education. With our research we aimed to conduct a program-experiment supporting mental hygiene. The effect of this experiment and the differences in its consequences for each type of training will be confirmed by re-measurement at the end of the program.

Methods: Before and after the program-experiment, students' sense of coherence, health behaviour, and mental health will be assessed using self-designed and standard questionnaires. In the case groups selected for the different types of training, we use observation, student self-reflection, and focus group interviews during the program-experiment. Data will be processed using SPSS 20.00 statistical software with a 95% probability level ($p \leq 0.05$).

Results: The average age of the high school students ($n = 49$) participating in the research was 14.73 years. 36.7% of the sample are girls. The largest proportion of the sample considers their current state of health to be good (59.4%). Among the psychosomatic symptoms that appeared during the last six months, it should be noted that nearly half (44.9%) of the sample struggled with tiredness on a daily basis and nearly a third (26.5%) with nervousness. 61.2% of the surveyed high school students does some form of daily exercise. The sample is characterized by a moderate level of well-being as well as life satisfaction. Excellent or good health was associated with a higher level of well-being ($p = 0.011$), average self-esteem ($p < 0.001$), and with a higher sense of satisfaction with life ($p = 0.001$). The sense of coherence was associated with excellent or good health ($p = 0.002$). 79.6% of the responding students use the problem-centric coping mechanism during a certain difficult life situation.

Conclusions: It can be concluded from our partial results that part-of-health well-being, life satisfaction, self-esteem and a sense of coherence are related to each other. From which it can be assumed that if we change or develop any factor, it will have a positive effect on the other factors as well.

Keywords: health behaviour, sense of coherence, mental health, teens.

A quantum mechanical scoring scheme for drug design

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Introduction: Changes of thermodynamic potential functions are primary descriptors of binding strength of drug candidates to their targeted macromolecules. Thus, the determination of target - ligand binding thermodynamics is essential in rational drug design. Besides time consuming, expensive measurements, structure-based calculation of binding thermodynamics parameters is also an alternative, particularly when experiments cannot be carried out.

Aim: Calculation of target-ligand complex structures comes along with problems for large systems. While fast molecular mechanical (MM) optimization can cope with large complexes, it neglects electronic effects of interactions. Thorough quantum mechanical (QM) calculations consider electronic contributions, but they are rather time consuming, especially for macromolecular complexes. Our aim was to combine the the benefits of MM and QM theory in the present method.

Methods: MM-level minimization of complex structures was performed efficiently using the HPC infrastructure and parallelized code of the popular molecular dynamics engine GROMACS. Using the relaxed geometry of the complex interface, a relatively quick QM calculation at PM7 semi-empirical level produces the desired binding thermodynamics data.

Results: Excellent correlation was observed between calculated and experimental values for a relatively large set of systems.

Conclusions: Calculated enthalpy values can be used as a score during the screening of candidate libraries or enthalpic optimization processes of lead compounds. The scores are particularly useful for large peptidic ligands often applied as leads in the pharmaceutical industry.

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Keywords: drug design, scoring function, binding enthalpy, MM/QM

Phytochemical and pharmacological investigation of sea rush

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Introduction: *Juncus* is one of the largest genera of Juncaceae. Juncaceae species accumulate different types of secondary metabolites, the most interesting among them are phenanthrenes. Phenanthrenes compose a small group of aromatic secondary metabolites. Several compounds possessed promising biological activities, e.g. antiproliferative, antimicrobial, anti-inflammatory, antioxidant, spasmolytic, anxiolytic, and antifungal effects [1].

Aim: The aim of our work was the isolation of biologically active secondary metabolites – phenanthrenes – from *Juncus maritimus* (sea rush).

Methods: The methanolic extract, prepared from the aerial parts of the plant, was subjected to solvent–solvent partition with *n*-hexane, chloroform and ethyl acetate. The chloroform fraction was separated by a combination of different chromatographic methods, including column chromatography, vacuum liquid chromatography, gel filtration, medium and high pressure liquid chromatography. The structure elucidation of the compounds was carried out by extensive NMR spectroscopic analysis, and HRMS experiments.

Results: Up to now the results allowed the identification of 11 phenanthrenes from the chloroform fraction of the plant. Four compounds (maritin A-D) are new natural products, while 7 phenanthrenes with the exception of juncusol were isolated for the first time from the plant. The isolated phenanthrenes were tested for their antiproliferative effect against human tumor (MCF-7, KCR, A2780, A2780cis, Hela, HTB-26, T47D) cell lines. Several compounds possessed higher activity than the positive control cisplatin.

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Keywords: *Juncus maritimus*, Juncaceae, phenanthrenes, antiproliferative

The role of limbic forebrain glucose monitoring neurons in the body weight regulation

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Worldwide the occurrence of various nutritional and metabolic diseases is increasing at a higher rate. In their background, peripheral regulatory disturbances were identified, but nowadays it is well known that the central nervous system regulatory mechanisms are affected as well [1].

The target group of our present experiments is the so-called glucose monitoring (GM) neurons, which chemo-sensitive cells have fundamental role in the central regulation of nutrition and metabolism [2, 3] as well. These neurons can be found in several brain areas regulating nutrition and homeostasis, also they can be found in different limbic forebrain structures, which have role in the regulation of learning, motivation, and food intake [4–7].

The GM neurons are known to respond actively and variably to the changes of glucose concentration of the surrounding interstitial fluid [8], and consequently they are respond to the blood glucose level changes as well. The intracerebral bilateral microinjection of streptozotocin (STZ) selectively destroys the GM neurons in the affected area. This selective lesion causes various metabolic changes, among others it causes weight gain by disrupting the regulation of carbohydrate metabolism [9].

The goal of the present experiments, to investigate the relationship of the regulatory mechanisms, related to the GM neurons, blood glucose levels and body weight.

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Protective role of PAC1 receptor in endotoxin-induced endophthalmitis

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Introduction: Endophthalmitis is a rare complication of E. coli-induced septicemia that may result in permanent loss of useful vision in the affected eye. Treatment of endogenous endophthalmitis depends in part on the cause of the condition. One of the most important to get an antibiotic into the eye as soon as possible. PAC1 receptor has been shown to play crucial roles in the nervous system. PAC1 receptor activation can be delay apoptotic events and enhance cell survival therefore it has emerged as a pharmaceutical target.

Aim: Was to investigate the protective role of the specific PAC-1 receptor agonist maxadilan in LPS caused inflammation by using different methods.

Methods: CD-1 IGS mice were injected ip. 6 mg/kg dose of LPS. Right eyes received maxadilan (1 μ M) intravitreally and left eyes injected with PBS. Animals were followed for 5 weeks from LPS administration. Histological changes of the eye (cornea and retina) were investigated by optical coherence tomography (OCT) and to examine the retinal functions we also used dark-adapted electroretinography (ERG).

Results: OCT results demonstrated that corneas exposed to LPS showed significant changes in the structure, edema was observed. The structural changes of the cornea were less in the mice of maxadilan treated group than the LPS injected ones. Additionally, all the retinal layers were significantly thinner in LPS-injected mice compared to maxadilan treated animals. During LPS infection the ERG responses of untreated mice were disturbed (amplitudes of waves and b-wave implicit time) compared to the maxadilan injected animals.

Conclusions: These results clearly show that PAC1 receptor has an important protective role in endotoxin-induced eye inflammation.

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The effects of a smartphone's presence on the attention

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Introduction: Our smartphones have a lot of features and functions that help us in our everyday life. Separation from a smartphone can also cause anxiety, increased heart rate and blood pressure because users feel unable to respond to notifications [1]. University students are considered to be the most sensitive and vulnerable for these. It can be said that a smartphone always carries a kind of interfering effect, even if the individual intend to ignore the device. The biggest problem is that most people are trying to be constantly online because they try to keep connected to their colleagues, family members or friends, and use gaming apps [2].

Aim: We hypothesized that individuals that are connected to the Internet during the task will perform worse than those who are not. We also assumed that those individuals that are characterized by problematic smartphone usage will perform worse than their peers on the vigilance test.

Methods: The sample comprised 47 participants (27 women; mean age = 23.5 years). All of them owned a smartphone. During the study participants had to take part in a psychomotor vigilance (PVT) test while their smartphones were placed next to them on the table with or without (control group) available Internet connection. At the end of the session each participant had to fill out four questionnaires to assess problematic Internet use questionnarrie, Smartphone addiction Scale, fear of missing out scale and ICT tool usage habits questionnarrie.

Results: We found no significant differences between the groups in the terms of their performance on the vigilance test. However, the statistical analysis showed a moderately strong correlation between the questionnaires examining smartphone use and their performance on the PVT test

Conclusions: Although the statistical analysis did not support our hypothesis, we can draw some important conclusions. Based on the questionnaires we can assume that there is a potential connection between the problematic smatphone usage and the decreased attention achievement. Further researches are needed in this topic.

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Keywords: smartphone addiction, attention, psychomotor vigilance task, presence of smartphone

Altered functional networks in problematic smartphone use: resting state fMRI study

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Introduction: The neural mechanisms underlying drug addictions have become recognized in the last decades, but it is still controversial, whether behavioral addictions have the same neurobiological basis. Problematic internet use is a well known behavioral addiction, although there is a lack of agreement surrounding its definition [1]. Smartphones and the internet is available for almost anybody, it is a form of entertainment, communication. The addictive potential of these personal devices is considerable, since the rising tendency of addictive behavior surrounding smartphone use [2].

Aim: This research presents data on problematic smartphone use using resting state functional MRI.

Methods: A sample of 65 people participated in this study, 18 to 30 years, all of them was right handed, neurological or psychiatric disorder were exclusion criterias. Behavioral data was assessed using questionnaires: Smartphone Application-Based addiction Scale, Problematic Internet Use Questionnaire, Screen Media Activity, Beck Depression Inventory, State- Trait Anxiety Inventory. Resting state functional MRI measurements were used to examine the neural networks, especially the default mode network.

Results: As a result, we found many neural networks (e.g. default mode network, visual network, somatosensory network, left frontoparietal network) being affected when problematic smartphone use occurs.

Conclusions: These findings suggest similarities between drug-related and behavioral addiction, and highlights the potential harm of smartphone use.

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Keywords: Problematic smartphone use, fMRI, resting state

New ANGELS compounds discovered with neuroprotective potential in an animal model of Alzheimer's disease

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Introduction: Our previous studies demonstrated that E2-induced non-genomic action on intracellular signaling pathways protects basal forebrain cholinergic (BFC) neurons via estrogen receptor α (ER α) in an animal model of Alzheimer's disease (AD). Recent progress of non-classical estrogen research was the identification of new estrogen-like compounds "Activators of Non-Genomic Estrogen Like Signaling" (ANGELS) [1].

Aim: The aim of our study is to find ANGELS compounds with a neuroprotective potential in an animal model of AD without classical genomic action and uterotrophic effect.

Methods: First, the assortment was achieved by computational docking of the steroids to both the classical and alternative binding sites of ER α [2]. From the top binders, eight molecules were tested for classical effects in vitro, investigating their estrogen responsive element (ERE) activating potential on ERE-luciferase transfected MCF-7 cells. The most effective candidates were tested in vivo for uterotrophic effects on ovariectomized mice, by measuring the uterus weight. Finally, the neuroprotective effects of ANGELS compounds were examined in vivo after A β ₁₋₄₂ microinjection to the nucleus basalis magnocellularis (NBM). The A β ₁₋₄₂-induced cholinergic fiber loss in the somatosensory cortex (SC) and cholinergic cell loss in the NBM were determined with quantitative histochemistry and immunohistochemistry.

Results: From the tested ANGELS we found three molecules without any classical ERE mediated actions and uterotrophic effects. These compounds significantly restored the A β ₁₋₄₂-induced cholinergic fiber loss in SC and they did not affect the number of cholinergic cell bodies in NBM.

Conclusions: Our discovery pathway combining computational screening with in vitro and in vivo testing proved to be useful for selection of potential neuroprotective compounds against A β ₁₋₄₂-induced neurotoxicity. We believe that these compounds provide a novel approach in AD therapy.

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Keywords: estradiol, ANGELS, neuroprotection, Alzheimer's disease

Quality by Design: A Novel Regulatory Approach Used in the Development of Nasal Polymeric Micelles

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Introduction: With the increasing number of people affected by neurodegenerative diseases, a targeted therapy is in need with proper quality. To approach this problem, a novel and an effective regulatory background must be established in the early stages of formulation studies.

Aim: Our research team aimed to formulate intranasally applicable Soluplus® - Meloxicam polymeric micelles in the form of a nasal spray. This needs the so called Quality by Design (QbD) approach where the aim was to find the potential risks in the formulation studies and to establish a design space where the desired product characteristics can be achieved.

Methods: The first step in QbD-based initial risk assessment was the determination of the QTPP of the target product. The identification of CQAs and the CPPs of the formulation method was the second step. A primary knowledge space development was made as part of the QbD methodology and a cause and effect (Ishikawa) diagram was set up. A risk assessment (RA) was prepared via interdependence and probability rating as well.

Results: By evaluating the RA, the main critical factors were determined in the formulation process we aimed to use. The main risks are associated by the particle characteristics such as size (- distribution) and the excipients used to formulate these intranasal polymeric micelles.

Conclusions: Quality by Design can be applied in the formulation of nasal polymeric micelles, which leads to a proper quality assurance background for the product development [1].

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Keywords: *Quality by Design, risk assessment, quality assurance, polymeric micelles, nasal*

Clinical characteristics, treatment and outcome of anti-NMDAR encephalitis patients in Hungary: A multicenter retrospective study

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Introduction: In anti-NMDAR encephalitis, autoantibodies are directed against the GluN1 subunit of NMDARs, leading to development of psychiatric symptoms, cognitive impairment, seizures and movement disorders[1]. Prompt diagnosis relies on clinical symptoms, autoantibody detection and auxiliary examinations (CSF, EEG, brain MRI), leading to early introduction of therapy and favorable outcome in most patients[2, 3].

Materials and methods: In our multicenter retrospective study, a standard online questionnaire was used to collect clinical data of 19 patients with definitive anti-NMDAR encephalitis.

Results: 58% of anti-NMDAR patients were male, median age was 32.5 years. Clinical symptoms were the following: psychiatric symptoms (90%), seizures (74%), movement disorders (47%), memory loss (42%), speech disorder (21%), insomnia (11%). Tumor association was rare (16%). Abnormal CSF was found in 42% of patients, meanwhile EEG abnormalities were more common (53%) and brain MRI findings occurred in 37% of patients. 53% of patients presented without signs of CNS inflammation by MRI and CSF. In most cases, immunotherapy led to clinical improvement and anti-NMDAR patients achieved a good outcome.

Conclusions: Characteristics of anti-NMDAR encephalitis patients in our Hungarian multicenter retrospective study were in accordance with previous findings. However, it was more common among young males in our cohort, and showed no association with ovarian teratoma. Lack of CNS inflammation both in CSF and MRI in half of AE patients emphasizes the importance of clinical symptoms and autoantibody testing in diagnostic workflow for early introduction of immunotherapy which can lead to favorable outcome in AE patients.

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Keywords: Anti-NMDAR encephalitis, neuronal cell surface autoantibody, clinical characteristics, immunotherapy, prognosis

Changes of blood PACAP level in patients with Parkinson's disease

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Introduction: Pituitary adenylate cyclase-activating polypeptide (PACAP) is a neuropeptide with antiapoptotic, antioxidant, regulatory and antiinflammatory effects proved by numerous *in vitro* and *in vivo* studies. In the last few years several studies examined changes of PACAP levels in human samples to show alterations in various physiological and pathological conditions. Plasma PACAP concentrations were significantly increased after acute spontaneous basal ganglia hemorrhage and reduced in the cerebrospinal fluid (CSF) of Alzheimer's disease patients. We showed correlation between patient mortality and PACAP levels in severe traumatic brain injury. Earlier experiments did not show changes of PACAP levels in the CSF of Parkinson's disease (PD) patients.

Aim: Our aim was to examine the PACAP in blood samples of patients with PD (n=107, control=39).

Methods: We measured the plasma PACAP38 level of PD patients with sandwich-type ELISA and searched for correlations with clinical parameters such as gender, age, stage and subtype of disease, type of treatment and specified scores for PD [Hoehn-Yahr, Movement Disorder Society - Unified Parkinson's Disease Rating Scale (MDS-UPDRS)].

Results: We showed significantly decreased PACAP38 levels in PD patients over 50 compared to younger group and in Hoehn-Yahr scale stage 3 compared to HYS2 group. Elevated levels were found after deep brain stimulation. We didn't find significant correlations between plasma PACAP38 levels and the MDS-UPDRS or the type of pharmacological treatment.

Conclusions: Earlier experiments did not find significant changes in CSF PACAP levels of PD patients, however, our experiments showed decreased level in plasma samples. The reduced levels of PACAP found in PD patients and the significant increase after DBS treatment confirm the hypothesis that the neuroprotective effect of PACAP could have a role in PD. Based on our results we assume the possibility of using PACAP as a biomarker to monitor the course of the disease.

Investigation of PACAP1-38 eye drops treatment in glaucoma

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Introduction: Approximately 4.5 million people worldwide are blind due to glaucoma, which makes it the second most common cause of irreversible blindness. This progressive condition develops by the blockage of the aqueous humor drainage system leading to intraocular hypertension. Progression of the condition causes the loss of the retinal ganglion cells and their axons. PACAP has shown protection against retinal degenerations in several diseases, such as excitotoxicity, hypoxia, or diabetic retinopathy. Also we proved that PACAP passes through ocular barriers and so, retinoprotection can be achieved also by eye drops. Accordingly, the aim of the present study was to examine the possible neuroprotective effects of topically administered (eye drops) PACAP in glaucoma.

Methods: We used 20 adult, male *Sprague-Dawley* rats for this study. Polystyrene microbeads (10µl, 10µm) were injected into the anterior chamber of the right eyes with 33G Hamilton syringe, while the control group received the same volume of PBS serving as control. After the microbeads injections we treated the eyes with PACAP1-38 eye drops for 4 weeks. Intraocular pressure (IOP) was monitored with tonometer and retinal morphological changes were followed with Optical Coherence Tomography.

Results: In the PACAP1-38 treated group we observed a lower IOP and less severe damage in the retinal thickness and GCL compared to the microbeads injected, control animals

Conclusions: Based on our results, we proved that topical administration of PACAP is neuroprotective in glaucoma, providing the basis for future therapeutic administration

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TLR analogue (CD180) alters B cell activation and distribution in systemic sclerosis

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Introduction: CD180 is a TLR homologue membrane protein, mainly expressed by B cells and macrophages, but its natural ligand is unknown. Its altered expression and function is associated with the development of several autoimmune disorders [1]. Previously, we have found decreased memory (especially non-switched (NS) memory) B cell ratio in systemic sclerosis (SSc) patients, which indicates the role of B cells in the development of SSc [2]. Our aim was to determine the CD180 expression of B cells and memory B cell subsets in SSc patients and to investigate the effect of stimulation via CD180 on the distribution and activation of memory B cell subsets.

Materials and methods: Negative magnetic bead-based selection of peripheral blood B cells of SSc patients and healthy controls were performed, followed by anti-CD180 antibody stimulation. We measured the expression of CD180 at protein and mRNA levels using flow cytometry and qPCR. Distribution and activation (CD69, CD86) of memory B cell subsets, defined by CD27/IgD staining, was analysed with flow cytometry.

Results: We found decreased expression of CD180 at protein and mRNA levels in peripheral blood B cells of SSc patients compared to healthy controls [3]. The percentage of NS memory B cells in SSc patients was further decreased following anti-CD180 antibody treatment. After anti-CD180 stimulation, the ratio of CD69 and CD86 positive switched (S) memory B cells was increased but in NS B cells only the percentage of CD69+ cells was elevated. Furthermore, the proportion of CD69+ cells was lower in NS B cells and higher in S B cells in SSc patients compared to healthy controls.

Conclusions: Our findings show that stimulation via CD180 leads to increased proportion and activation of S B cells in SSc, which may play a role in B cell dysfunction and autoantibody production. Detailed investigation of the mechanisms of B cells activation via CD180 could facilitate the understanding of the pathomechanism of SSc and the identification of currently unknown potential therapeutic targets.

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Keywords: B cells; non-switched B cells; switched B cells, systemic sclerosis; SSc; TLR; CD180

Examination of the non-motor symptoms in Parkinson's disease due to selective elimination of the urocortin-1 cells in the centrally projecting Edinger-Westphal nucleus, in rat.

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Introduction: Parkinson's disease (PD) is a progressive neurodegenerative disorder. Mainly the loss of the dopaminergic cells in the substantia nigra is responsible for the motor symptoms (tremor, rigor, hypokinesia) however the neurological background of the associated anxiety and depression is still unknown. In addition to several other brainstem areas, the disease also affects the Edinger-Westphal nucleus (EW). Based on our previous animal data, the amount of urocortin 1 (Ucn1) cells in the centrally projecting division (cpEW) of the EW expressing leptin receptors also decreased.

Hypothesis: After, the selective elimination of cpEW Ucn1 cells, mood disorders appear without parkinsonian symptoms.

Methods: Using stereotaxic method, rats were intracerebrally (IC) injected with leptin-saporin solution (n=10), while the control group (n=9) received only saporin solution. After the operation behavior tests were performed weakly to follow the developed symptoms of disorder caused by the lesion. Motor coordination was examined by rotarod (RPT), mood status by open field (OFT) and sucrose preference (SPT) tests. Morphological changes were assessed by multiple label immunofluorescence.

Results: Leptin-saporin-treated animals spent longer time near the wall in OFT, suggesting that the levels of anxiety were increased. Since the locomotive ability was intact between the two groups, hypokinesia was excluded.

Conclusions: Based on behavioral tests, selective elimination of cpEW Ucn1 cells increased anxiety, demonstrating a prominent role for these cells in the regulation of mood life. Histological examinations are in progress to determine the measure of cell loss.

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The role of empathic communication in doctor-patient interactions

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Introduction: The study is a presentation of a research project that seeks to identify key linguistic tools through the applied linguistic and psychological analysis of doctor-patient interactions, the development of which enhances the doctor's ability to cooperate and empathize with the patient, thus facilitating the recovery. It focuses on improving the empathy of students while breaking bad news in doctor (student) - patient (actor) simulated role-plays.

Aim: The therapeutic importance of empathy emphasizes the need to help medical students develop their empathetic abilities. The purpose of our research was to identify factors that promote the development and expression of empathy in medical students during doctor and patient communication. This study aims to investigate the language of clinical empathy: how medical students can use the language to build empathetic communication.

Methods: Participants are all undergraduate 3rd-4th or 5th year medical students participating in the course 'Taking medical history with actors, simulation practices in the MediSkillsLab' course at the Medical School of University of Pécs. During simulation of breaking bad news one of the medical students plays the role of a doctor and an actor/actress plays the patient role. Other students take part as observers. During the observed interactions, the communication process focused on the emergence and development of empathy. To measure this, we used an empathy scale. During the study, following the simulated doctor-patient interaction, the participants playing the role of the patient completed the empathy scale that was designed to measure how empathic a dialogue was in a given communication situation. The original Empathy Scale was developed in English, 'The Patient-Professional Interaction Questionnaire (PPIQ) to Assess Patient Centered Care from the Patient's Perspective' (Casu – Sommaruga – Gremigni, 2018).

Results: In the case of effective communication, all patients gave the maximum point. They talked to the patient with respect and attention. In each simulated situation, the student playing the doctor was able to express as much as possible their interest in the patient's views on their current health status and future treatment options. In each case, the patient evaluated his doctor so that he could fully understand his feelings. The lowest scores were given by the actors playing the patient to the question that the doctor could imagine himself in the patient's place. In each situation, the patient felt, he took enough time to ask his questions.

Conclusions: Feedback from the actors playing the patient, the group, the instructor, and the specialist helped students develop their effective, empathetic communication skills throughout the semester. The implementation of effective communication was successful. In case of empathy, we found that in clinical communication, the perception of the patient's feelings by the doctor could not be realized to such an extent as the intelligibility and clear expressing of the information.

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Multiple Antimicrobial Resistance and Molecular Characterization of β -lactamases in enteric bacteria from Hospital Effluents and Wastewater Treatment Plant

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Introduction: Bioactive molecules in untreated hospital liquid waste disposals (especially unmetabolized antibiotics at sub inhibitory concentrations) and the nutrient rich environment in wastewater treatment plants have been reported as hot spots for emergence of antibiotic resistance facilitated by transfer of antibiotic resistant genes among environmental bacteria [1].

Aim: The purpose of our study was to assess the prevalence of multiple antibiotic resistance and to characterize the common β -lactamase encoding genes among enteric bacteria from wastewater.

Methods: Hospital effluents and proximate wastewater treatment plant (WWTP) samples were analyzed for persistence of antimicrobial resistant disease causing enteric bacteria. The targeted bacteria were isolated and identified by Matrix assisted laser desorption ionization-time of flight mass spectrometer MALDI-TOF/MS. The drug susceptibility of 126 identified enteric bacteria belonging to species *Escherichia coli*, *Klebsiella pneumoniae*, *Klebsiella oxytoca*, *Enterobacter cloacae* and *Citrobacter freundii* to four chemical classes of antibiotics were investigated and the presence of β -lactamase encoding genes detected.

Results: The proportion of multiple antibiotic resistant (MAR) enteric bacteria was high in the hospital effluents (73.33%) and the activated sludge (66.7%). *E.coli* isolates showed the highest multiple antimicrobial resistance phenotype, 72.41% (n = 58), *Klebsiella* isolates 69.77% (n = 43) and other enteric bacteria (*Enterobacter* and *Citrobacter* isolates) 40% (n = 25). 86.23%, of *E.coli* isolates phenotypically expressed extended spectrum beta-lactamase (ESBL) enzymes, 76.74%, of *Klebsiella* isolates and 25%, of *Citrobacter* isolates which were predominantly from the hospital effluents. CTX-M and TEM genes were the most prevalent among the ESBL positive strains. VIM was the only carbapenamase encoding gene detected in a *Klebsiella oxytoca* strain.

Conclusions: The hospital effluents present as a vehicle for high fecal carriage of bacteria harboring antibiotic resistant genes to municipal sewage. Disinfection of hospital wastewater would be a reasonable policy to put into practice to slow the spread of resistant bacteria into the environment especially in this era of limited development of new antibiotics.

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Keywords: Hospital effluent, WWTP, enteric bacteria, multiple antibiotic resistance, Beta-lactamases

How long does the protection of personal data „live”?

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Introduction: The main field of the research is the protection of the personal data of the deceased people, including data recorded during their lives, or in the context of their deaths, and the regulation of the prevention of the misuse of the personal data.

Aim: The aim of the research is to detect the faults, gaps of the legislation, and to analyze the rights and obligations of the participants of the data processing. The other goal is to develop a catalog, to help the family members of the deceased, the authorities, especially the medical personnel to understand what actions they can do with the pre-recorded personal data.

Methods: The study examines domestic and European Union law, scientific literature, and focuses to provide expedient conclusion for the legislature, and also for anyone processing personal data, thus improving the usage and future legislation of the domestic data protection law.

Relevance: The topic is important according to the ever growing need to protect ones data, also it is relevant with the data recorded during the pandemic situation of the COVID19. Moreover another field of use of the study could be the medical reasearches where personal data, or organs of the deceased people are used.

Keywords: personal data protection, health data, deceased people

Online Assessment of English for Specific Purposes – The First Steps

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Introduction: The presentation is about the first findings of my research on the online assessment of English for specific purposes (ESP). The focus is on *online approach* as a potential future form of language testing. The study is innovative and its main target is to uncover the intriguing questions of validity of online testing. Due to today's situation, the topic of online assessment has become very important and highly demanded, so it is needless to say that the study has a key role in the field.

Goal: The aim of the presentation is to enlighten the candidates and professional assessors about the advantages and disadvantages of certain types of online test tasks after a thorough experimental process currently being implemented. The test tasks include online tests written in English and Hungarian by the students at the Medical School of the University of Pécs. The same students volunteered to participate in my online survey regarding tests and other possibilities online which truly has a huge importance hence today's situation around the globe. It can unquestionably be used as a perspective in a vast array of contents.

Methods: Material and methods include a survey which has recently been carried out; needs analysis and trial versions of online tests. Surveys do not only question future candidates but also assessors in order to find both perspectives of needs and wants. Surveys are already being carried out focusing on the relevant questions.

Results: The survey hypothesized that the students of the 21st century expect everything available online and not only expects but also would like to be accustomed with online contents and opportunities not only in everyday life possibilities but with studying and testing their knowledge online as well.

Consequences: In this context, the presentation focuses on the possible questions, techniques and approaches of the issue of online assessment which can be used not only in language lessons, a type of classroom techniques but also assessing students after a digital semester, too.

Keywords: assessment, online, English for Specific Purposes, validity, online assessment

End-range Maitland mobilization effecting immediately pressure pain threshold in knee osteoarthritis

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Introduction: Peripheral and central sensitization are the underlying mechanisms of pain in knee osteoarthritis (KOA) [1] [2]. Pressure pain threshold (PPT) measurement is a commonly used method for investigating the magnitude of peripheral and central sensitization in KOA.

Aim: The aim of this trial was to investigate the immediate effect of end-range Maitland mobilization on PPT and different pain-related measures in KOA.

Methods: Randomized, patient-blinded trial was performed with twenty patients in Maitland Group (MG) receiving end-range Maitland mobilization and twenty patients in Control Group (CG) receiving placebo. Measurements were taken before and after 30 minutes. Outcome measures were local PPT of knee, distant PPT at ipsilateral Extensor Carpi Radialis Longus, Timed Up and Go Test (TUG) and associated pain intensity measured with Numerating Pain Rating Scale (NPRS) and passive tension (PT) of knee at beginning of pain. Wilcoxon-signed rank test and Mann-Whitney U test was used for statistical analysis.

Results: Local and distant PPT improved with 16.51% and 24.60%, TUG decreased with 14.66%, NPRS with 53.57% and PT of knee with 58.84% with significant difference after intervention in MG. PT of knee increased and all other outcomes decreased without significant difference after intervention in CG. Between-group comparison revealed significant difference for all outcomes after intervention in MG.

Conclusions: Based on the present results, applying end-range Maitland mobilization may be effective complementary intervention of physical therapy in KOA

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Keywords: knee osteoarthritis, end-range mobilization, pressure pain threshold

Communication Training in Patient-Centered Pharmacist Education

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Background: The roles and responsibilities of 21st century pharmacists are evolving with their active participation in medication therapy management and pharmaceutical care in community, or medication reconciliation and antibiotic stewardship in hospital settings. These new professional competencies can improve therapeutic effectiveness, reduce risks of medication misuse and facilitate the rational use of financial resources. However, the need for advanced communication skills and strategies is essential.

Aim: We aimed to map trends in the education of communication skills and identify academic courses taught in English in European faculties of pharmacy in order to search for shifts towards a more patient centered and practice oriented pharmacist education.

Methods: The study included 17 universities of 10 different EU member countries, in which pharmacy education was offered in English in 2019. Data on curricular information (e.g. title, course description, obligatory or optional course, number of lectures per semester, credit value) were selected and collected from institutional websites.

Results: Pharmacist communication is an individual obligatory course in three universities (Debrecen, Prague, Warsaw) evaluated in our study. One Hungarian institution electively offers two individual courses to develop pharmacist communication skills (Szeged). Communication skills seem to be integrated into obligatory courses of pharmaceutical care or practice in six universities. In two other cases communication skills are integrated into elective courses. Based on course description and syllabus sources available from the university websites, communication skills do not form an element of pharmacist education only in one institute of the study.

Conclusions: Our data illustrate the degree of development and recognition of professional communication skills in pharmacist education demonstrate significant differences among the selected European countries. Many of the institutions incorporated communication as an element of their professional training program. Still, several institutions do not seem to consider communication skills development as a core segment of pharmacist training today. Communication training is a key element in patient-centered pharmacist education.

Keywords: communication, education, patient-centered, pharmacist

Method development for the simultaneous HPLC testing and sterility determination of dorzolamide hydrochloride and timolol maleate containing eye drops preserved with benzalkonium chloride.

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Introduction: After the risk based safety mapping of the internet market of eye drops, the dorzolamide hydrochloride and timolol maleate containing eye drops were selected as products with the highest patient- and medication safety risk. 3 product samples (multi-dose eye drops, preserved with benzalkonium chloride) were purchased for quality control tests.

Aim: Our aim was to develop and apply a complex analytical-microbiological method for the determination of the quality of online purchased multi-dose eye drops and quantify medication safety risks.

Methods: Due to the small amount of samples (5ml), we only designed assay with HPLC and test of sterility. The method for determining the 3 components together was not found in the literature. The sterility testing was completed according to the European Pharmacopoeia.

Results: According to the literature and based on the materials and equipment available to us, the method of Liquid chromatography was performed on a WATERS STERISORB ODS1 C18 (5 µm, 250 mm x 4,6 mm) column, and was equipped with a Shimadzu SPD-20AV DUAL UV/VIS detector. The method was optimized by varying the ratio of organic and inorganic components in the mobile phase (acetonitrile:phosphate buffer (pH=2,50) (20:80 v/v) - Eluent B, acetonitrile: phosphate buffer (pH = 5,65) (70:30 v/v) - Eluent BAC), by varying the detection wavelength (dorzolamide hydrochloride – 250 nm, timolol maleate – 300 nm, benzalkonium chloride – 210nm) and the flow rate 1,0 ml x min⁻¹). The retention times for dorzolamide hydrochloride and timolol maleate were found to be 4,5 and 7,16 min. The benzalkonium chloride has three homologues and gave peaks at 6,24 min, 9,53 min and 16,15 min. System suitability parameters were measured from five replicate injections of standard solutions and the results were within the acceptable limits per EMEA guideline. Membrane filtration technique was used for sterility testing according to Ph. Eur. Validation of microbiological assay was performed using original multi-dose formulations purchased from a community pharmacy according to the ICH guideline.

Conclusions: With the application of our simple, rapid, validated HPLC method, combined with pharmacopoeial microbiological sterility testing, medication safety issues (e.g. inappropriate quality and quantity of active ingredients, excipients and microbiological contamination) can be identified in dubious test purchase samples.

Keywords: HPLC, sterility testing, dorzolamide, timolol, benzalkonium chloride



Keywords



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