POSTER PRESENTATIONS

Vapor or liquid form? Differences in the antibacterial activity of essential oils against respiratory tract pathogens

ÁCS, K.[1], BALÁZS, V.L.[1], KOCSIS, B.[2], BENCSIK, T.[1], BÖSZÖRMÉNYI, A.[3], HORVÁTH, G.[1]

[1]Department of Pharmacognosy; [2]Department of Medical Microbiology and Immunology, University of Pécs, Pécs; [3]Department of Pharmacognosy, Semmelweis University, Budapest

Background: Essential oils (EOs) are complex, volatile substances, which antibacterial application via inhalation is becoming more frequent nowadays. Their antimicrobial potential was confirmed by in vitro methods, which investigated this effect in liquid medium instead of in the vapor phase. In the treatment of respiratory tract infections (RTIs), the patients usually inhale these volatile components. Hence, the investigation of the antibacterial activity of EOs in the vapor phase should be reasonable as well.

Aims: Therefore, our aim was the antibacterial evaluation of clove, cinnamon bark, eucalyptus, thyme, scots pine, peppermint, and citronella oils in liquid medium and vapor phase against respiratory tract pathogens.

Methods: Before the microbiological assays, the EOs were analyzed with GC-MS and GC-FID. The antibacterial activity was tested against *Staphylococcus aureus* (MRSA, 4262), *Pseudomonas aeruginosa* (ATCC 27853), multidrug-resistant *P. aeruginosa* (RPA, 34205), Streptococcus spp., Haemophilus spp., and *Moraxella catarrhalis* (DSM 9143) with macrobroth dilution (BD), and vapor phase (VP) technique. In the BD method, a serial twofold dilution of the EOs was prepared with Polysorbate 80 or DMSO. Four-section Petri dish containing the proper medium was used in VP tests. As a result, the minimum bactericidal concentrations (MBC) and minimum inhibitory concentrations (MIC) were determined. All tests were carried out in triplicate.

Results: Against Haemophilus spp. cinnamon bark oil was the most effective (MIC: 0.06mg/ml) followed by thyme and clove in BD. Clove oil also produced the best inhibition against MRSA (0.1mg/ml). In the case of Streptococci besides cinnamon, clove and thyme produced the lowest MIC in liquid form. In VP test cinnamon bark was the most potent against all investigated pathogens (MIC: 15.62-125µl/l). Besides, thyme, peppermint, and citronella showed activity as well. Eucalyptus and scots pine oil produced moderate activity in our test systems.

Conclusion: On the whole, it should be highlighted that cinnamon, thyme, peppermint, and citronella were effective in both assays; in contrast, clove oil was more effective in the liquid phase. Therefore, they could be promising alternatives to support the treatment of RTIs. We must also note that further studies are required to determine their mode of action and toxicity for their safe application.

In vitro and *in vivo* investigations for the oxidative metabolism of the 4-nitrophenol

ALMÁSI, A.[1], SIKÓ, M.[2], VERKMAN, N.[1], FISCHER, E.[3], PERJÉSI, P.[1]

[1]Institute of Pharmaceutical Chemistry, University of Pécs, Pécs; [2]Sandoz Romania Ltd., Targu-Mures, Romania; [3]Institute of Pharmacology and Pharmacotherapy, University of Pécs, Pécs

Background: Our experiments were planned to investigate the oxidation of 4-nitrophenol in vivo in physiologic and pathologic (experimental diabetes) conditions, and to test the in vitro oxidation of the compound as well. 4-nitrophenol is mainly excreted to the bile and the small intestinal lumen as its glucuronide and sulfate conjugates, although as a minor metabolite the oxidative 4-nitrocatechol can also appear.

Aims: The investigation and confirmation of applicability of 4-nitrophenol as a model compound to study the activity of the CYP2E1 enzyme through quantitation of 4-nitrocatechol in the small intestinal perfusate and the bile. In vitro oxidation and enzyme activity tests were made for the estimation of the measure of the spontaneous and enzymatic oxidation of the 4-nitrophenol.

Methods: Buffered solution of 4-nitrophenol was recirculated through the proximal segment of the jejunum of a male Wistar rat and samples were collected from the intestinal perfusate and the bile. The samples were quantitated by HPLC method. The enzyme activity was measured from the homogenates of the liver and the small intestine. To estimate the

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spontaneous oxidation, the Fenton test was applied. The experimental diabetes was induced by intravenous administration of streptozotocine to rats.

Results: During the measurements, a continuous presence of 4-nitrocatechol was detected in the small intestinal perfusate, while it was undetectable in the bile extracts. The level of the CYP2E1 activity showed an elevation in both the liver and the small intestine.

Conclusion: The performance of the applied analytical method was suitable for quantitation of 4-nitrocatechol and its parent compound. The activity of the CYP2E1 was well measurable and showed an increase in the investigated organs of the hyperglycemic rats. The results of the Fenton tests raise the possibility of the parallel non-enzyme catalyzed oxidation.

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The effect of ethanol on aerosolization properties of spray-dried inhalation powders

AMBRUS, R., BENKE, E., SZABÓ-RÉVÉSZ, P.
Institute of Pharmaceutical Technology and Regulatory Affairs, University of Szeged, Szeged

Background: In recent years, near the disintegrating methods, there are three types of integrative processes – spray drying, spray freeze drying, and supercritical fluid technology – for the preparation of dry powder inhalation systems (DPIs). Spray drying is a frequently applied method because of its favorable properties. The use of organic solvents in this process is also widespread, but few publications have investigated how their application to the formulation affects the properties and effectiveness of the formulations using various active ingredients [1, 2].

Aims: The purpose of this work was to investigate spray-dried DPIs of ciprofloxacin hydrochloride (Cip) containing different concentrations of ethanol (EtOH) in the stock solution, to determine how different EtOH concentrations influence the physicochemical and thus aerosolization of the samples.

Methods: Cip was applied as a model drug. The stock solutions contained 0%, 5%, 10%, 20% and 30% EtOH – by the water – under the same production conditions. Particle size distribution, morphology, density, cohesivity, structure was studied in the case of the samples as physical tests. The in vitro aerosolization properties were investigated with the Andersen Cascade Impactor.

Results: The prepared samples were spherical, their average size was less than 5μm, their density was almost the same, and their structural change was similarly compared to the starting drug. However, there was a difference in morphology, with the increase in the percent of used EtOH, more and more dimples appeared on the surface of the particles. Furthermore, the cohesion test also showed differences between the samples. Therefore, the fine particle fraction results showed lower by 5, 10% EtOH and remarkable increase by 30% EtOH compared to the EtOH-free product.

Conclusion: Based on the results, it can be concluded that the mixture of the initial solution solvent used in spray drying – in this case the amount of EtOH used – notable influences the aerosolization results, thus besides the spraying parameters using this investigation is well-founded.

Acknowledgment: This project was supported by the UNKP-19-3-SZTE New National Excellence Program of the Ministry for Innovation and Technology and by the EFOP-3.6.3-VE-KOP-16-2017-00009 project.

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Compounded medicines in oncology care

ÁROK, R., CSONTOS, D., HIGYISÁN, I.
Hospital Pharmacy, Bajcsy-Zsilinszky Hospital, Budapest

Background: Although the selectivity of anticancer treatments has been significantly improved through the appearance of new modern therapies, the management of new types of side effects has become another challenge. Furthermore, conventional chemotherapeutic drugs are still not excluded from therapeutic practice, which almost certainly leads to cell and tissue damage with high proliferative activity. The resulting deterioration in quality of life can be significantly improved by the use of various supportive treatments.

Aims: Some of the side effects of anticancer treatments can be prevented and treated with external topical formulations. Experience has shown that, due to the variety of therapies and the individual differences between patients, the range of factory-made products is not wide enough for the clinic or unaffordable for patients in the long run. Therefore, the use of compounded medicines in individual supportive treatment is widespread. Our goal is to create a collection of prescriptions of external compounded medicines, which are applied and applicable in oncology care.

Methods: We collected the compounded formulations prescribed by our Institute's oncologists from the Novodata software data between November 1, 2018 and October 31, 2019, and compared them with the prescriptions of the standard collection by the

Hospital Pharmacy (Formulae Nosocomiales). In addition, we evaluated which side effects require new formulations. Subsequently, adverse events and related formulations were classified according to the CTCAE classification (similar to the FoNo VII medical edition), indicating which anticancer therapies are expected to occur.
Results: The most common indications are related to side effects on the skin (eg. dry skin, acne, dermatitis, erythema, urticaria, phototoxicity, nail disorders, hand-foot syndrome) and the gastrointestinal mucositis. Ointments, creams and solutions account the largest ratio of applied pharmaceutical forms. It should also be noted that, in the absence of a uniform collection of prescriptions, the formulations proposed by the attending physician show significant variation and prescription errors are common.
Conclusion: A selection of prescriptions helps clinicians, pharmacists and patients manage side effects by making easier to prescribe, to prepare and to redeem the compounded medicine. The uptaking of routine formulations in FoNoVIII should be considered.

In vitro streptozocin treatment: cytotoxicity without alteration in insulin sensitivity

BAGAMÉRY, F., VARGA, K., KECSMÁR, K., SZÖKŐ, É., TÁBI, T.
Department of Pharmacodynamics, Semmelweis University, Budapest

Background: Alzheimer's disease is a common neurological disorder worldwide with rapidly increasing prevalence. Among several factors cerebral insulin resistance, i.e. the uncoupling of insulin receptor and its downstream signaling pathway has been suggested to contribute to the disease. Therefore, in vivo and in vitro experiments aiming to explore the correlations between neurodegenerative and metabolic disorders are of high importance. In animal and cell culture studies streptozotocin (STZ) is widely used to induce neurodegeneration, however its direct impact on inulin sensitivity of neural cell line has not yet been shown.
Aims: To examine the protective effect of insulin on STZ-induced cytotoxicity and the potential alteration of insulin sensitivity on molecular level in human neuroblastoma cell line.
Methods: The effect of insulin on cell viability and the phosphorylation of glycogen synthase kinase-3 (GSK3) were studied on STZ-treated SHSY5Y cells. Cells of the control group were treated with low serum (LS) medium.
Results: STZ dose-, and time-dependently exerted cellular damage, low, gradual toxicity was induced by 1 mM concentration of the compound. Insulin was found to be similarly cytoprotective in both STZ and LS groups. Also insulin-induced GSK-3 phosphorylation was alike in the STZ and LS treated cells.
Conclusion: According to our results STZ is an appropriate compound to induce slowly developing, non-specific neural toxicity in *in vitro* experiments. However, as insulin showed similar protection and GSK-3 phosphorylation in the LS and STZ groups we can assume that insulin resistance does not play a pivotal role in its action in SHSY5Y neuroblastoma cells, thus it is not a good tool to study the role of insulin resistance in neural death and to study the effect of protective substances that are acting mainly by improving insulin sensitivity.

Antibiofilm effect of pickering nano-emulsion of clove essential oil against *Pseudomonas aeruginosa* and *Streptococcus pneumoniae*

BALÁZS, V.L.[1], HORVÁTH, B.[2], SIMONICS, D.[1], VARGA, A.[3], KEREKES, E.[4], ÁCS, K.[1], KOCSIS, B.[3], KRISCH, J.[5], SZÉCHENYI, A.[2], HORVÁTH, GY.[1]
[1]Institute of Pharmacognosy; [2]Institute of Pharmaceutical Technology and Biopharmacy; [3]Department of Medical Microbiology and Immunology, University of Pécs, Pécs; [4]Institute of Clinical Microbiology, Albert Szent-Györgyi Health Center; [5]Department of Food Engineering, University of Szeged, Szeged

Background: Biofilms are highly-structured communities of cells that produce an extracellular matrix and adhere to abiotic or biological surfaces, therefore they cause outstanding problems in the health care system. The essential oils (EOs) and their components are becoming increasingly popular in medical applications, because of their proven antibacterial effect. Clove (*Syzygium aromaticum (L.)* Merr. & L.M. Perry) which belongs to the Myrtaceae family is a commercially cultivated tree in tropical and sub-tropical countries. Clove oil is frequently inhaled to prevent respiratory tract diseases or due to its pleasant smell, but evidences are rare related to its mode of actions.
Aims: Our aim was to investigate the biofilm inhibiton effect of clove EO against *Pseudomonas aeruginosa* (ATCC 27853) and *Streptococcus pneumoniae* (DSM 20566). Unfortunately, due to its lipophilic character and low water solubility, the direct use of the EOs, in microbiological experiment is limited.
Methods: Because of this, we prepared O/W type Pickering nano-emulsions stabilized with silica nanoparticles, the nanoparticles were synthesized by Stöber method [1]. Firstly, the MIC [Minimum Inhibitory Concentration] was determined with broth

macrodilution test (*P. aeruginosa*: 1.6mg/mL, *S. pneumoniae*: 0.25mg/mL). The biofilm inhibition experiments were performed on the base of Peeters and coworker's study, with the crystal violet assay [2].

Results: Our results showed that the clove EO had anti-biofilm activity against *P. aeruginosa* and *S. pneumoniae* too, because it reduced the biomass of the bacterial biofilm. It is important to highlight that the Pickering nano-emulsions was more effective (P. aeruginosa inhibitory rate: 76.15%; *S. pneumoniae* inhibitory rate: 66.93%) than the conventional Tween80 stabilized emulsions (*P. aeruginosa* inhibitory rate: 69.23%; *S. pneumoniae* inhibitory rate: 60.77%).

Conclusion: In this study, the antibiofilm effect clove EO was investigated against *P. aeruginosa* and *S. pneumoniae*. We can conclude that O/W type Pickering nano-emulsions of clove EO provide a new possibility for biofilm inhibition.

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Practices of portable and disposable, elastomeric pump use in oncology care

BALOGH, A.G., CSONTOS, D., HIGYISÁN, I.
Hospital Pharmacy, Bajcsy-Zsilinszky Hospital, Budapest

Background: Administration time of cytostatic infusions can vary in cancer care, it can be one or two days regarding the therapy. Because of limited capacity of oncology departments and patients' preference, there is an opportunity to administer chemotherapy by a portable and single-use elastomeric pump, which infuses the medication at a controlled flow rate over the prescribed amount of time. Therefore, it isn't obligatory for the patients to stay in the hospital. However inadequate use of elastomeric pumps may increase the risk of adverse events.

Aims: The preparation of cytostatic infusions is centralized in our institute and done under pharmacist surveillance. We experienced an increased need for portable, elastomeric infusion pumps with the active ingredient 5-fluorouracil at our oncology departments. Our goal is to review the national and international practices of pump use and related patient education if it's provided.

Methods: We created an anonymized questionnaire in Hungarian and English, which was sent to 35 Hungarian oncology departments' clinical pharmacists and to 60 member countries' ESOP (European Society of Oncology Pharmacy) delegates as well. Beyond the general questions about the capacity of the oncology departments, we asked about whether the patients receive education about the portable, disposable elastomeric infusion pump and if yes, is it in written or verbal form, who is it performed by, and what topics are included.

Results: We received 17 answers from Hungary, and 7 from foreign countries, which are more or less similar in one way and different in others. Answers came from universities and general hospitals as well, therefore the reported capacity and the number of the elastomeric pumps used by month shows differences. Many institutes experienced an increasing tendency of elastomeric pump use in the recent years, similarly to our situation. It's a positive result that patients receive education, but it is not comprehensive at every site, and it is rarely written. The education should point out not just how to change the daily routine but the danger of contamination too. It is also an important fact, that in the elastomeric pump the active ingredient is not as much diluted as in an infusion, so thrombophlebitis may occur more often.

Conclusion: In summary, the fact is that portable and disposable elastomeric pumps are widely used and part of everyday practice, therefore this should be followed by proper patient education. With this questionnaire hopefully, more institutions' attention will be raised to this topic and a patient education material might be introduced about the use of elastomeric pump.

Potentiation of the uterus relaxing effects of magnesium-sulfate with terbutaline and nifedipine: studies on pregnant rat myometrium

BARNA, T., SZŰCS, K.F., HAJAGOS-TÓTH, J., GÁSPÁR, R.
Department of Pharmacology and Pharmacotherapy, Universety of Szeged, Szeged

Background: Tocolysis is one of the greatest challenges in obstetrical practice. Magnesium-sulfate ($MgSO_4$) is an expansively used tocolytic agent, as it has better side-effect profile compared to other agents. However, the efficacy of this drug has been questioned.

Aims: Our aim was to investigate the uterus-relaxing effect of magnesium-sulfate in combination with other tocolytic drugs in vitro and in vivo.

Methods: Contractions of uterine rings from 22-day-pregnant Sprague-Dawley rats were measured in an organ bath. The contractions were stimulated with 25mM KCl and cumulative-dose response curves were elicited in the presence of $MgSO_4$ (10^{-8}–10^{-1}M), nifedipine (10^{-10}–10^{-6}M) or terbutaline (10^{-9}–10^{-5}M). The uterus relaxing effects of nifedipine and terbuta-

line were also investigated in the presence of magnesium-sulfate (10^{-7}M). The in vivo studies electromyographic studies were carried out during ketamine (36mg/kg) and xylazine (4mg/kg) induced anesthesia with the subcutaneous implantation of and electrode pair. The rats were treated with 10mg/kg $MgSO_4$ intravenously, then 0.05-0.15-0.5-1.5-5-15-50μg/kg terbutaline or 0.05-0.15-0.5-1.5-5-15-50μg/kg nifedipine were given in cumulative bolus injection.

Results: Both terbutaline and nifedipine caused myometrial relaxation in vitro, which was further enhanced by administration of $MgSO_4$. The $MgSO_4$ increased the maximal relaxing effect of terbutaline ($p \leq 0.001$), while it shifted the dose-response curve of nifedipine to the left ($p \leq 0.5$). In the in vivo studies $MgSO_4$ increased the uterus-relaxing effect of terbutaline, however it could not enhance the effect of nifedipine.

Conclusion: The combination of $MgSO_4$ and terbutaline may have a clinical significance, that must be justified in clinical trials. Additionally, this combination is supported by the fact that the pharmacodynamic, pharmacokinetic parameters and risks of these two agents are well-known separately. However, the combination of magnesium-sulfate and nifedipine may have not any therapeutic benefit. We suppose that $MgSO_4$ closes the voltage dependent Ca^{2+}-channels and therefore could not potentiate the effect of nifedipine.

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Model development for assessing cost-effectiveness and prepare reimbursement dossier of RTMS in patient population with treatment-resistant depression in hungary

BELLA, R.[1], KOVÁCS, S.[2], VINCZE, G.[2], ERDŐSI, D.[2], BOTZ, L.[3], ZEMPLÉNYI, A.[2]

[1]*Department of Pharmaceutics Division of Pharmacoeconomics;*
[2]*Chancellery, Center of Health Technology Assessment;*
[3]*Department of Pharmaceutics and Central Clinical Pharmacy, University of Pécs, Pécs*

Background: Major depressive disorder (MDD) is a common mental illness as being the second leading cause of disability worldwide. Treatment-resistant depression (TRD) amounts to 45% of total MDDs, however the definition is not yet standardized. Repetitive Transcranial Magnetic Stimulation (rTMS) has a rich literature for the treatment of TRD-patients.

Aims: The aim of this study was to define an appropriate model concept for the cost effectiveness analysis of rTMS intervention in the TRD subpopulation of MDD in Hungary from payer perspective, to support the reimbursement process initiated by a tertiary healthcare provider.

Methods: A systematic literature review was conducted and reported in compliance with the PRISMA Statement. After the screening, potentially relevant articles were analyzed in full text, and data were systematically extracted by use of explicit methodology.

Results: The search query resulted in 61 articles, which after the deduplication and title abstract screening were narrowed down to six from which information about models employed in full economic analyses of rTMS were extracted. In general, within these articles a model time equal or shorter than 1 year were applied to cover the acute phase and a short maintenance period, however no relapse was implemented due to short model time. From methodological perspective decision tree and Markov models were used to assess the effect of rTMS during the acute and maintenance phase respectively. TMS provided a net cost saving of US$1123 per QALY when compared with the current standard of care [1].

Conclusion: Based on the identified conceptual challenges we developed a model in line with the HTA guideline of Hungary. The model applies the combination of decision tree in the acute and Markov model in the maintenance phase with medical management as comparator. The suggested model time is 3 years, which enables to model relapse, aligned with the natural history of the disease.

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The influence of the suboptimal body mass index (BMI) on the use of healthcare resources in post-surgical patients: a clinical database study

BELLA, R.[1], KOVÁCS, S.[2], SOMOGYI-VÉGH, A.[3], HARMAT-VINCZE, P.[3], ZEMPLÉNYI, A.[2], BOTZ, L.[3]

[1]*Department of Pharmaceutics Division of Pharmacoeconomics;*
[2]*Health Technology Assessment Center of Pécs, Chancellery;*
[3]*Department of Pharmaceutics and Central Clinical Pharmacy, University of Pécs, Pécs*

Background: Malnutrition is associated with higher complication rates and increased hospital costs. Electronic Medical Record (EMR) systems collect large amounts of data, which were made accessible for research purposes after pseudonymisation. This is a pilot study in a project addressing the secondary use of clinical data asset of our institution.

Aims: Our goal is to determine the impact of malnutrition, as measured by the Body Mass Index (BMI), on healthcare resource utilization in surgical patients using EMR data collected in our Medical Center.

Methods: Relevant patient data was extracted from the hospital information system, rearranged, and transformed to the goals of the study. Study population consisted of adult inpatients who underwent surgery between November 2016 and August 2018, had no previous surgery within 30 days, and for whom a preoperative BMI score was available. The duration of hospitalization after surgery, the number of readmissions within 30 days, and the number of outpatient visit up to 30 days after hospitalization were analyzed in patients with low (<18.5, n=137) and normal (18.5-26, n=1904) preoperative BMI by linear regression analysis.
Results: The mean age of the low BMI group was 52.2 years compared to 61.03 ($p < 0.001$) of normal group. The proportion of women in the low and normal BMI group was 66.4% and 55.7%, respectively ($p < 0.05$). Using a simple linear regression model, the average length of stay in the low BMI group was 1.4093 days longer ($p = 0.0129$), while after controlling for age, gender and ICD codes the difference increased to 1.6002 ($p = 0.005$). However, the preoperative BMI showed no significant effect on the other two variables observed.
Conclusion: The results suggest that after data transformation of EMR useful information on patient risk factors can be retrieved. Even with such a simple indicator as BMI, the impact of malnutrition on patient outcomes can be quantified. Even though, further studies on the applicability and generalizability of this method, using more data from a wider range of healthcare providers are needed, nutrition therapy indicated by clinical pharmacist may lead to reduction of healthcare resource use.

Current practice of online drug distribution in Europe – a panoramic view of the internet pharmacy markets of the eu member states

BELLA, R.[1], MOHAY, Á.[2], FITTLER, A.[3]
[1]Department of Pharmaceutics Division of Pharmacoeconomics; [2]Department of International and European Law; [3]Department of Pharmaceutics and Central Clinical Pharmacy, University of Pécs, Pécs

Background: Since the launch of the first European internet pharmacy, member states have adopted different national regulations on online pharmacy services and the dispensing of drugs over the Internet. EU and national authorities recognised the potential threats associated with the illegal internet pharmacy market. Five years ago the European Commission adopted the common logo for legally operating online pharmacies and member states are required to develop and maintain a register of all legal online drug stores.
Aims: The aim of this study was to provide an overview of these public registers of national medicines authorities and summarize the current landscape of the European internet pharmacy market.
Methods: Based on the existing regulations of Directive 2011/62/EU, we collected the publicly available information related to each member state from national authority websites like the number of internet pharmacies, community pharmacies, inhabitants, and territory of the states and the legally tradeable product range. European Commission documents and EU case law databases were reviewed to determine whether infringement procedures had been initiated in connection with the relevant obligations in the Directive.
Results: Only 21 of the 28 states (77.8%) have publicly available registries for legitimate online sellers. In 14 states (50%) only OTC products are tradeable; 7 states (25%) were found where both OTC and POM can be distributed; in 3 countries (10.7%) POM can be distributed only with restrictions and in 4 countries (14.3%) no information was found related to tradeable products. The research had found that save for some infringement procedures started by the European Commission for late implementation, no substantive infringement of the Directive had been ascertained; these infringement procedures were also resolved without a Court procedure.
Conclusion: The online distribution of medicines has undergone tremendous change in the past and is still in the process of shaping. The current results show that compliance with the regulations is not complete and shows some difficulties in practice. The European online pharmaceutical market is complex due to member states' different legislative, pricing and reimbursement backgrounds. A unified formal requirement or recommendation adopted at the EU level could make it easier for Member State authorities to fulfill their obligation regarding the public registry of online retailers.

Prevalence and antibacterial resistance among predominant bacteria

BENKŐ, R.[1,3], GAJDÁCS, M.[2], MATUZ, M.[1], BODÓ, G.[3], LÁZÁR, A.[4], HAJDÚ, E.[5], PAPFALVI, E.[5], HANNAUER, P.[6], ERDÉLYI, P.[6], PETŐ, Z.[6]
[1]Department of Clinical Pharmacy; [2]Department of Pharmacodynamics and Biopharmacy; [3]Central Pharmacy; [4]Institute of Clinical Microbiology; [5]Infectious Disease Ward, Depertmant of Internal Medicine; [6]Department of Emergency Medicine, Albert Szent-Györgyi Health Center, University of Szeged, Szeged

Background: Antibacterial resistance is one of the most important threats to public health. The knowl-

edge of local epidemiology and resistance patterns are essential for antibacterial stewardship programs.
Aims: To map the prevalence, the source and bacterial resistance profile of predominant bacterial isolates.
Methods: The study was performed at the level I Emergency Department of University of Szeged. Data on positive microbiological isolates were retrieved for the period between 1st July 2014 and 1st July 2019. Duplicate isolates were removed. Bacterial identification was performed using MALDI-TOF MS. Antibiotic susceptibility-testing, phenotypic detection of resistance mechanisms and interpretation of drug resistance (MDR/XDR) categories were based on ESCMID/EUCAST standards.
Results: Overall 6887 bacterial isolates were recovered of which 66.7% were Gram-negative species. The most frequent clinical specimens were blood culture (35.6%), urinary catheter (23.1%), midstream urine (12.1%) or deep wound or abscess samples (14.0%). *Escherichia coli* was the most frequent Gram negative isolate (2191), followed by members of the Klebsiella genus (664, most frequently *K. pneumoniae*) and the Proteus spp. (526, most frequently *P. mirabilis*). Among Gram-positives, the most frequent isolate was *Staphylococcus aureus* (561) and Enterococcus spp. (471). The top five bacterial family/species accounted for nearly 65% of positive clinical isolates. The resistance of *E.coli* and *K. pneumoniae* for penicillin combinations (with beta-lactamase inhibitors) and different cephalosporins ranged between 13.3% and 18.2 % and 23.4% and 32.5%, respectively, while ciprofloxacin-resistance level exceeded 30% for both species. Similar resistance profile was shown for *P. mirabilis*. Methicillin-resistant *S. aureus* (MRSA) was detected in 16.1%, while vancomycin-resistant *E. faecium* was detected in 33.3% of isolates overall.
Conclusion: We identified the most frequent bacteria and revealed the current resistance patterns of bacterial isolates. Some of the data (e.g. fluoroquinolone resistance) raises concerns that may pose therapeutic challenges in the most frequently isolated bacteria. These results should be taken into consideration when updating local antimicrobial guidelines.

Teicoplanin and vancomycin derivatives with perfluorilated alkyl groups are active against influenza and coronavirus

BERECZKI, I.[1], CSÁVÁS, M.[1], SZŰCS Z.[2], RŐTH, E.[1], LŐRINCZ, E.B.[2], BATTA, GY.[3], OSTORHÁZI, E.[4], NAESENS, L.[5], BORBÁS, A.[1], HERCZEGH, P.[1]

[1]Department of Pharmaceutical Chemistry; [2]Doctoral School of Pharmaceutical Sciences; [3]Department of Organic Chemistry, University of Debrecen, Debrecen; [4]Department of Medical Microbiology, Semmelweis University, Budapest; [5]Rega Institute for Medical Research, KU Leuven, Leuven

Background: As we have seen in the last six months, emerging and re-emerging viruses could be the biggest threat for the human population nowadays in our modern, accelerated and globalized world. Both of influenza and coronaviruses have the potential to cause serious pandemics worldwide. Unfortunately, there are no effective enough medications against most of these viruses.
Aims: As some glycopeptide antibiotics and their derivatives proved to be effective against several viruses1, therefore we planned to synthesize some new derivatives equipped with highly fluorinated lipophilic groups.
Methods: Perfluorobutyl and perfluorooctyl groups were conjugated to the N-terminus of teicoplanin pseudoaglycone and vancomycin aglycone derivatives through ethylene glycol and tetraethylene glycol linkers by means of photoinitiated addition and azide-alkyne click reaction. The effect of the derivatives were evaluated against several viruses including influenza and human coronavirus.
Results: Vancomycin aglycone derivatives were inactive against all of the studied influenza strains, while 3 out of the 4 perfluorobutyl and perfluorooctyl derivatives of teicoplanin pseudoaglycone displayed very good activity against influenza H1N1, H3N2 and B strains. Two of the derivatives were active against human coronavirus as well.
Conclusion: We hope that these results can open a new way in finding more effective antivirals based on glycopeptide antibiotics.

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The influence of stearic acid in water removable cream bases with moisturizing properties

BÎRSAN, M.[1], ANTONOAEA, P.[2], VLAD, RA.[2], WRÓBEWSKA, M.[3], SOSNOWSKA, K.[3], TODORAN, N.[2], CIURBA, A.[2]

[1]Department of Pharmaceutical Technology, "Grigore T. Popa" University of Medicine and Pharmacy of Iasi, Iași, Romania; [2]Department of Specialty Pharmaceutical Sciences, „George Emil Palade" University of Medicine, Pharmacy, Science and Technology of Târgu Mureş, Târgu Mureş, Romania; [3]Department of Pharmaceutical Techolongy, Medical University of Bialystok, Bialystok, Poland

Background: Water removable bases are oil-in-water cream bases and there are the most used types of

creams because they have a texture nongreasy and therefore aesthetically pleasing.
Aims: Our study aims the formulation and characterization 4 types of bases with Polyglyceryl-3-methylglucose distearate (PGMGds) as emulsier and stearic acid in different concentration
Methods: Cream bases were manufactured using the following componets: PGMGds, Olea Europaea Fruit Oil cold pressed, stearic acid, cetyl palmitate and distilled water. The emulsions were prepared by using different methods and and their stability was determined. Pharmacotechnical parameters and skin moisture level were studied [1,2].
Results: pH of creams was between 5.70-7.40. The thixotropy is emphasized in all the formulas, making exception the last formulation who has the highest consistency with contain the maximum quantity of stearic acid and PGMGds. The addition of 1% stearic acid causes the pH to decrease by 0.8 units (5.7 – 6.5), without affecting the adhesion (which is kept at 0.0016 N/mm^2); The first formulation which contain the minimum quantity of stearic acid shows the highest increase in hydration level 4 hours after a single application. All types of thease cream bases have a very good stability in different types of preparing.
Conclusion: According to the pharmacotechnical analysis performed the most optimal formula contain 3-3.5% PGMGds and stearic acid 3%. If the formula contains 3% PGMGds and stearic acid 4% the pharmacotechnical analysis are performed but the moisturizing is very lower. The formulas that has all the desired characteristics are those with contain only 3% stearic acid.

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Off-label in neonatology – creative therapy solutions

BUDAI, K.A.
University Pharmacy Department of Pharmacy Administration, Semmelweis University, Budapest

Background: Off-label drug use (use of medicines other than in the summary of product characteristics [SmPC]) is considerable in the pediatrics, as special in neonatology.
Aims: Investigation of the reasons for various therapies used in neonatological practice.
Methods: Relevant literature research in databases (Pubmed, Cochrane, Uptodate).
Results: Paracetamol is suitable for close the patent ductus arteriosus (PDA) and the quality of evidence is moderate. It inhibits prostaglandin synthesis. Its side-effect profile is more favorable than that of ibuprofen, and paraceramol has the same efficacy as ibuprofen and indomethacin. There is no difference from ibuprofen in neurodevelopmental outcome, but the evidence for this is low, and in view of concerns after prenatal and postnatal exposure of paracetamol 18-24 months' postnatal follow-up should be required [1]. In the treatment of neonatal sepsis and necrotizing enterocolitis (NEC), intravenous pentoxifylline may be an adjuvant therapy in addition to antibiotics. Pentoxifylline is a phosphodiesterase inhibitor and it suppresses TNF-α production, thereby reducing inflammation, tissue damage, and has a positive effect on endothelial cell function and coagulation. With low-quality evidence, in combination with antibiotics, it reduces mortality and length of hospital stay for newborn sepsis. No adverse effects were identified. Further better quality evidence and studies are needed to support its use in NEC [2]. Recombinant human erythropoietin has promising neuroprotective effects. In a meta-analysis, prophylactic erythropoietin improved cognitive development, reduced the incidence of mental developmental index (MDI) <70 in infants, but had no effect on other neurodevelopmental outcomes. Further controlled, randomized trials are needed to schedule and dose the treatment adequately [3].
Conclusion: Off-label therapies can help the recovery, but the evidence of effectiveness is moderate or low, and further studies are needed to assess their efficacy and safety.

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Development and evaluation of amlodipine/ atorvastatin immediate release tablets

CIURBA, A.[1], ANTONOAEA, P.[1], VLAD, R.A.[1], TODORAN, N.[1], RÉDAI, E.[1], BÎRSAN, M.[2]
[1]*Pharmaceutical Technology and Cosmetology, George Emil Palade University of Medicine, Pharmacy, Science, and Technology of Targu Mures, Targu Mures;* [2]*Grigore T. Popa University of Medicine and Pharmacy, Iași*

Background: Increased blood pressure and dyslipidemia are two diseases which can be found associated in elderly patients. The association of two active ingredients in one tablet can increase the patient's compliance.
Aims: This study aims in developing and evaluation of new formulation of tablets with a content of amlodipine besylate (AB) and atorvastatin (AT) (10/10mg).
Methods: In this study were developed 3 formulations FI, FII and FIII in which the concentration of ac-

tive ingredient, disintegrant (pregelatinized starch) and lubricant (colloidal silicon dioxide) were maintained constant; the quantity of the diluent (microcrystalline cellulose) and the association between the superdisintegrants (croscarmellose sodium-CCS and sodium starch glycolate-SSG) has been varied. The tablets were prepared by direct compression having a 10mm diameter. The following pharmacotechnical properties were evaluated: variation of mass, friability, mechanical hardness and disintegration time. The releasing study of the two APIs was realized in phosphate buffer (pH6.8). The concentration of AB and AT were determined spectrophotometrically.

Results: For the proposed formulations, uniformity of mass showed a deviation by the average mass less than 5% and the friability was less than 1%. The results of the disintegration test depended on the type and concentration of superdisintegrant. The superdisintegrant determined a twice lower mechanical resistance compared with FI formulation. The lack of superdisintegrant in FI formulation conducts in a released concentration of 79.49% AB after 30 minutes and 82.18% AT after 60 minutes. The presence of sodium croscarmellose determined a released concentration of 67.89% AB after 40 minutes and 86.49% AT after 25 minutes. The use of sodium starch glycolate determined a released concentration of 79.58% AB after 35 minutes and 96.87% atorvastatin after 45 minutes.

Conclusion: Pharmacotechnical properties of the three formulations are in the range limits provided European Pharmacopoeia 8th Edition. The release of AB and AT from the 3 formulations is directly corelated with the presence/absence of the superdisintegrant, but not with the type of the superdisintegrant used.

Utilization of lipid modifying medications in Hungary between 2008 and 2018

CSATORDAI, M., SCHVÁB, K., MATUZ, M., BENKŐ, R., DORÓ, P.

Department of Clinical Pharmacy, University of Szeged, Szeged

Background: Morbidity and mortality rate of cardiovascular diseases are very high in Hungary and lipid lowering drugs have an important role in prevention and treatment.

Aims: Our aim was to analyse the trends of lipid modifying agents use focusing on statin utilization in Hungary between the period of 2008 and 2018.

Methods: Reimbursed national drug utilization data for the entire population of Hungary were obtained from the National Health Insurance Fund. Data were analysed using the WHO's ATC/DDD system and were expressed in Defined Daily Dose per 1000 inhabitants per day (DDD/TID), and in percentage of the total use.

Results: The use of lipid lowering agents (ATC: C10) grew from 69.7 DDD/TID in 2008 to 110.1 DDD/TID in 2018. 91.2% of the total use was statins (also including combination products) and 6.4% of the total use was fibrates and 2.4% of the total use was ezetimibe in 2018. During the study period the statin use was emerging, 87.2% of the total use was statin monocomponent products (95.9 DDD/TID) and 3.9% of the total use was combined statin products, mainly atorvastatin or rosuvastatin with amlodipine (4.4 DDD/TID) in 2018. While in 2008 the most consumed drug was atorvastatin, rosuvastatin has showed a growth and overtook atorvastatin use by 2014. These two agents accounted for 94.0% of total statin use in 2018.

Conclusion: Lipid modifying drug use considerably grew, and statin use was the highest throughout the 11-year study period.

Possibility of an anti-adhesion based therapy and prophylaxis in the treatment of pseudomonas aeruginosa infection

CSÁVÁS, M.[1], MALINOVSKÁ, L.[2], VASKOVA MICHAELA[3], HODEK PETR[3], WIMMEROVÁ MICHAELA[2], BORBÁS ANIKÓ[1]

[1]Department of Pharmaceutical Chemistry, University of Debrecen, Debrecen; [2]Central European Institute of Technology, Brno; [3]Charles University, Prague

Background: Lectins are specific carbohydrate-binding proteins of a non-immune origin. Lectins could be important virulence factors, involved in recognition and adhesion processes, moreover promising therapeutic targets which could be inhibited by carbohydrate ligands. Lectins are usually multimeric proteins, containing several binding sites per molecule and/or forming oligomers. Consequently, the multivalent carbohydrate moieties are considered to be potential drugs for anti-adhesion therapy [1]. The Gram-negative bacterium P. aeruginosa (PA) is an important opportunistic pathogen, it produces soluble, galactose-specific lectin PA-IL [2]. Specifically, PA-IL displays toxicity to respiratory epithelial cells in primary culture. Due to its importance, several multivalent inhibitors were designed and tested against PA-IL.

Aims: The aim of this research was to synthesize oligovalent D-galactose presenting glycoclusters via click-strategy and the potency of glycomimetics with lectin PA-IL was investigated.

Methods: The methods of classical organic chemistry, mainly the azide-alkyne click-reaction was used

for the syntheses. The interaction of glycomimetics with lectin PA-IL was examined by biophysical methods. Inhibition of PA (isolated from a cystic fibrosis patient) adhesion to epithelial bronchial cells was tested by ex vivo bacterial adherence assay.

Results: Novel tetravalent galactose-presenting ligands were synthesized, biophysical assays proved that all compounds were suitable ligands of the lectin in vitro, with significantly better inhibitory effect than simple galactose. Two candidates were able to decrease adhesion of PA cells to bronchial human cells in the ex vivo adhesion assay.

Conclusion: The anti-adhesion therapy with glycomimetics and the application of multivalent glycoclusters might be novel tools and supporting methods in the treatment of P. aeruginosa infection. In conclusion, some ligands are promising candidates for testing using a mouse cystic fibrosis model with potential future utilization as prophylactic agents against bacterial colonization of lungs.

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Antioxidant and antimicrobial investigation of *Lysimachia Nummularia L.* applied in the Transylvanian Ethnomedicine

CSEPREGI R.[1], KERÉNYI M.[2], KŐSZEGI T.[1], FODOR-GRISNIK I.[3], DAS SOURAV[1], PAPP N.[3]

[1]Department of Laboratory Medicine, [2]Department of Medical Microbiology and Immunology; [3]Department of Pharmacognosy, University of Pécs, Pécs

Background: In folk medicine in Transylvania several plants are used nowadays frequently mentioned for skin problems.

Aims: Based on our earlier collection, among plants applied for wounds, *Lysimachia nummularia* was selected for antioxidant and antimicrobial tests.

Methods: Plant extracts were prepared by methanol, hexane, chloroform, ethyl acetate, butanol and water according to Lee et al. (2014). Mueller-Hinton broth and agar were used for microdilution methods and evaluation of minimum inhibitory and bactericidal concentration. Tested strains were the following: *Staphylococcus aureus* ATCC 23923, MRSA ATCC 700698, *Escherichia coli* ATCC 25922, *E. coli* ESBL, *Klebsiella pneumoniae* ATCC 13883, *K. pneumoniae* ESBL, *Pseudomonas aeruginosa* ATCC 27853, *P. aeruginosa* MDR, *Salmonella typhimurium* ATCC 14028, and *Acinetobacter baumannii* MDR. Enhanced chemiluminescence (ECL), Oxygen Radical Absorbance Capacity (ORAC), 2,2-diphenyl-1-picrylhydrazyl (DPPH), and Trolox Equivalent Antioxidant Capacity (TEAC) assays were used for the study of antioxidant potential of ethanolic and water extract of the plant (Kőszegi et al. 2017). In ECL and ORAC tests, results were calculated by the calibration curve using the net area under curve based on Trolox dilutions. The total antioxidant activity was given as Trolox equivalent referred to 1 g (in μmol/g). In DPPH and TEAC tests, radical scavenging activity was expressed as the inhibitory concentration at 50% (IC50; in μg/mL), which was calculated by a linear regression analysis of % scavenger activity.

Results: In the microbiological study, methanol and butanol extracts showed inhibition on E. coli ATCC 25922, both *K. pneumoniae* strains, MRSA, and *S. aureus*. Hexane and ethyl acetate extracts were effective in the lowest concentration against *S. aureus* and MRSA. Water extract had antimicrobial activity against each strain except for *P. aeruginosa* and *A. baumannii* which were not inhibited by any tested phases. In antioxidant tests, ethanolic extract showed higher total antioxidant capacity than water extract in each assay, which can be related to the higher polyphenol content in ethanolic phase.

Conclusion: Our preliminary data give new records for *L. nummularia* which will be further analysed for phytochemical profile and medicinal use.

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Effect of particle size on dissolution: a study on micro- and nanosized drugs

CSICSÁK, D.[1], TAKÁCS-NOVÁK, K.[1], SINKÓ, B.[2], VÖLGYI, G.[1]

[1]Department of Pharmaceutical Chemistry, Semmelweis University, Budapest; [2]Pion Inc., Billerica, USA

Background: The bioavability of a drug is largely determined by the physico-chemical properties of the active ingredient. Among these, the solubility, the rate of dissolution and the membrane permeability are the most important ones. Poor solubility, low dissolution rate and poor permeability may result in improper absorption. Is it known, that the particle size of a compound or the different excipients can influence the dissolution rate.

Aims: The aim of this study was to investigate the equilibrium solubility and the dissolution kinetics of different model compounds under in vitro conditions. We also conducted measurements in a biomimetic medium. The selected active compounds were available in macro crystalline, micronized, and nanonized (with various excipients) forms, thus ena-

bling the study of the role of particle size on the dissolution kinetics.
Methods: The equilibrium solubility of the drugs was determined using the saturated shake-flask method, where the concentration of the supernatant was measured by spectroscopy using a Jasco V-550 UV/VIS spectrophotometer. In-situ UV probes were used to monitor the dissolution in real-time, so it was possible to obtain precise information on the time needed to achieve the equilibrium, and the rate of supersaturation.
Results: Measurements were performed using different solvents: stimulated gastric fluid (SGF), fasted state simulated intestine fluid (FaSSIF), fed state simulated intestine fluid (FeSSIF) and the blank buffers (FaSSIF blank and FeSSIF blank). In the case of macrocrystalline and microsized drugs the measurements were performed in the presence of the excipients used at the nanonized drugs, so we can eliminate their effect on the solubility and the dissolution.
Conclusion: Our results show that the particle size can influence the dissolution of a drug. Nanonized drugs reach the highest concentrations, but the solubility and the dissolution of the micronized drugs were also better than the macrocrystalline forms. We observed that in most cases the excipients used by us did not have a solubility increasing role.

Synthesis and evaluation of quinoline photocages with improved aqueous solubility

DUNKEL, P.
Department of Organic Chemistry, Semmelweis University, Budapest

Background: Photolabile protecting groups ('photocages') allow the temporary inactivation/masking of biologically active agents and their subsequent spatiotemporally controlled re-activation upon light irradiation (UV – one-photon or NIR – two-photon) via cleavage of the blocking group. Appropriate photolabile moieties open up several potential experimental and eventual therapeutic applications. Of the various photocage families described in the literature, quinolines being synthetically available and having interesting one- and two-photon uncaging quantum yields were selected as core protecting group scaffolds [1-3].
Aims: For biological applications, photocages should comply with several criteria [4]. In particular, photocages should be reasonably water-soluble (ideally at least in the 50-100mM range), a real challenge as typically chromophores favoring two-photon absorption are characterised with extended conjugation, therefore higher lypophilicity. In the present study we assessed structural modifications for improving this critical aspect. Several small-molecule quinoline cages were studied with various substituent patterns previously. In the present work we set out to prepare novel derivatives with substituents confering better aqueous solubility without hampering the uncaging efficiency.
Methods: A novel set of quinoline photocages were prepared using palladium-catalysed coupling or N-alkylation reactions and further side chain functionalisations. The novel photocages were characterised by standard methods for one- and two-photon uncaging quantum yield, fluorescence, UV-absorption, aqueous solubility and stability.
Results: Synthetic pathways for a small library of novel quinoline photocages were developed. A comparative study of aqueous solubility was accomplished using both computational and experimental methods.
Conclusion: The effect of modifications with various hydrophilic substituents on the photophysical and photochemical properties was evaluated on a small set of quinolines, helping the design of future improved photocages.

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Treatment of obesity in pharmaceutical care

EKÉS-KRETOVICS, J., HÁZMAN, Z.
Halmy Telepi Pharmacy, Vecsés

Background: Obesity – which is not only a Hungarian, but also a world phenomenon – puts the appearance of some serious diseases at high risk, such as intense heart muscle load, hypertension, diabetes, atherosclerosis, gall diseases, musculoskeletal system diseases, sleep apnea, tumor.
Aims: There are possibilities to direct patients in the direction of a healthier way of life within the confines of pharmaceutical consultation. We offer the Premium Diet program, a long and continuous diet, which together with the necessary exercises treats obesity. Mental health control, regular consultation are also extremely important.
Methods: At the start of each nursing consultation process the following measurements take place: body weight, abdomen circumference and blood pressure, blood sugar level, cholesterol level and triglycerides level. With the help of a BIA instrument body cell weight, extracellular liquid, fat weight, fat-

less weight and hydration values are also determined. After these measurements a consultation query is filled out – target weight, use of the formulas, full value lunches, the necessary exercise and the consultation appointments are discussed. The district doctor of the patient is advised of the patient's involvement in this program, with special attention to the proper drug administration.
Results: Based on the results of the measurements it can be said that significant body weight decrease (10-24%) is always accompanied by great amount of fat reduction and abdomen circumference decrease. The determined values were found in the normal range. It is important to mention that during the diet the patients hadn't reported any negative mental effects. The Premium products are suitable for body weight and body fat reduction without the reduction of the skeletal muscles.
Conclusion: The results of the diet with the Premium program has clearly convinced us that by losing weight, applying appropriate diet and customized exercising patients can be helped fighting overweight. Moreover, diseases in connection with obesity can also be improved this way. The new available instrument gives us the possibility to make pharmaceutical consultation even more comprehensive.

Opioid utilisation in Hungary between 2006 and 2019

ENGI, ZS., BENKŐ, R., SCHVÁB, K., DORÓ, P., VIOLA, R., SOÓS, G., MATUZ, M.
Department of Clinical Pharmacy, University of Szeged, Szeged

Background: Analgesia is a fundamental human right and an extremely important task in patient care. Severe pain can be successfully treated with opioid analgesics. In ambulatory care, the main indications for opioid drug prescriptions are cancer and musculoskeletal pain.
Aims: To gain comprehensive knowledge on the national opioid utilisation trends in ambulatory care over the last 14 years in Hungary.
Methods: Raw national drug utilization data on reimbursed medicine for the entire population of Hungary were obtained from the National Health Insurance Fund. The study period was set from 2006 to 2019. The data were analysed using WHO's ATC/DDD system and were expressed in DDD per 1000 inhabitants per day (2020 version). We focused our analysis on the N02A ATC subgroup.
Results: During the study period, there was a monotonic increase in opioid use from 3.05 DDD per 1000 inhabitants per day in 2006 to 5.09 DDD per 1000 inhabitants per day in 2019. Tramadol and tramadol combination prescriptions steadily covered approximately 75% of the opioid use throughout the study period. Fentanyl products were the second most prescribed opioids while other opioid drugs (oxycodone, codeine, dihydrocodeine, hydromorphone, morphine, buprenorphine) amounted to less than 10% of dispensation. There was an increase (0.02 vs. 0.29) in fentanyl use in the indication-linked 90% reimbursement category, which means that musculoskeletal pain is becoming a more and more frequent indication. Increase in the consumption of 25μg/h fentanyl patches also supports this assumption since that is the most potent patch that can be prescribed for musculoskeletal pain. In the final year, the amount of prescriptions in this reimbursement category was more than half of the amount of prescriptions in the category of cancer pain management.
Conclusion: Opioid utilisation gradually increased over the last 14 years in Hungary. Tramadol consumption was persistently dominant, with an increase in the use of combinations.

First steps of introducing antimicrobial stewardship

ERDÉLYI, L., KNAUSZ, M., SOMOGYI, A.
Petz Aladár Country Teaching Hospital, Győr

Background: Spreading of antibiotic resistance of pathogens is a real problem not only in Hungary, but in most parts of Europe as well, in the emergence of which irresponsible or nontargeted use of antibiotics plays a crucial role. Continuous monitoring of the use of antibiotics in inpatient care facilities is also governed by regulations to restrain this problem. Since September 2019, also an Antibiotic Stewardship (ABS) Team has been operating in Petz Aladár County Teaching Hospital based on the Methodological Guideline for Antimicrobial Stewardship in Inpatient Care Facilities. Our opportunities are seriously limited by the fact that we currently have enough professionals with adequate qualification for the setting up of only one ABS.
Aims: In the 1438 bedded Petz Aladár County Teaching Hospital, clinical audits of antibiotic use have been being carried out in inpatient units since 2014. In 2018, the method was improved, the results of which established the way of further improvements. In the course of an ABS consultation we go through patients' relevant antibiotic treatments together with their physicians and discuss patients' further antibiotic therapies.
Methods: This is based on the following data: the antibiotic use on a given ward in the preceding 12 months, antibiotic resistance map and the rate of the emergence of multiresistant pathogens. During our work, we draw our colleagues' attention to the im-

portance of that sampling should always be performed properly and timely. By our contribution, we are aiming to increase the numbers of successful empirical and targeted antibiotic therapies.
Results: First part of our work started at the diabetology department. We are studying the antimicrobial therapy of the patients for three months along.The evaluation has been done in the month of January. In total of 17 patients received antibiotic therapy. 14 patients left the ward, 3 died, but not due to bacterial infection. Examining the therapy of 14 cured patients, we can say that 5 therapies were adequate and 8 were defective. There were two errors in the 8 failed therapy. Incorrect dosing was observed in 3 patients. No dose adjustment was made for renal function. Bacterial infection could not be confirmed in 5 patients. Probably due to inappropriate sampling. We would like to evaluate our February and March results in the same way. Then compare it to the typical antibiotic use in the first half of 2019.
Conclusion: On the base of the numeric data, we summarise our work and find out whether we managed to put our plans into action, and whether it is necessary to alter the methods of our consultations.

Investigation of gastric juice resistance of probiotic microcapsules in different formulations

ERDÉLYI, L.[1], KOVÁCS, R.[2], GAÁL, B.[3], FENYVESI, F.[3], BÁCSKAY, I.[3], VECSERNYÉS, M.[3], VÁRADI, J.[3]
[1]Petz Aladár Country Teaching Hospital, Győr; [2]Institue of Medical Microbiology; [3]Department of Pharmaceutical Technology, University of Debrecen, Debrecen

Background: Generally, probiotics are used in treatment for a variety of gastrointestinal disorders, however, their beneficial properties are not only useful in the sick organisms. They help digestion even in healthy gastrointestinal tract; reduce overproduction of gas producing and bile salt deconjugating species, thereby improving the digestion of food. They also increase the amount of nutrients that can be utilized, which is true for both the human and the animal body.
Aims: Our collaborative work is the microencapsulation of bacterial species used as probiotics for veterinary purposes: Lactobacillus plantarum, Bifidobacterium bifidum. The purpose of microencapsulation of bacterial species is to increase their survival at higher temperatures during feed pelleting and protect against the inactivating effect of gastric acid.
Methods: The probiotic strains were suspended in alginate solution and microencapsulated using a Büchi Encapsulator B-395 apparatus, than the microcapsules were precipitated in calcium chloride solution. In order to increase survival, biofilms of both bacterial species were formed by keeping the wet microcapsules of each bacterium for one day at room temperature. Groups of microcapsules were chitosan coated and lyophilized for further stabilization. Subsequently, dissolution testing was performed in artificial gastric juice. The microcapsules containing the bacteria were dissolved in peptone water, inoculated into the appropriate medium. After culturing, the effect of the treatments on viability (log N/N0) and the survival rate after acidic lysis was determined on the basis of CFU values.
Results: According to our results, the chitosan coating provided better protection against the acidic effect for bacteries. Among the probiotic strains, Lactobacillus plantarum showed higher survival compared to Bifidobacterium bifidum according to the pH optimum.
Conclusion: The probiotic strains were successfully microencapsulated, but the different formulations provided different degrees of protection against the acidic environment.

Prospect of image analysis in the evaluation of propellant-free foam characteristics

FARKAS, D., KÁLLAI-SZABÓ, N., ANTAL, I.
Department of Pharmaceutics, Semmelweis University, Budapest

Background: For decades the use of pharmaceutical foams was limited to dermal drug delivery. Not only are they proven to be sufficient drug carrier systems but the excellent patient compliance also makes them outstanding. Although the use of foams is becoming increasingly favored, the evaluation methods of this dosage form are yet far from extensive. Several properties, like stability or spreadability are related to the structure of the foam, therefor its investigation is largely informative.
Aims: This research aims to show the various ways image analysis can be used in the evaluation process of foams. Apart from the macroscopic attributes, like the height of foam and microscopic parameters, as the number, size and shape of the foam cells (bubbles) are similarly describable along with the size distribution of foams. The information allows assumptions on important foam characteristics, like bubble and foam-forming ability and stability.
Methods: Various propellant-free foam formulations were investigated in this study. Foams were produced in propellant-free pump devices from simple and complex surfactant solutions with and without active ingredient, as well as essential oil-containing microemulsions. Photos and videos were processed and analysed with image analysis software (ImageJ; Wayne Rasband, National Institute of Health, USA).

For stability assessment, dynamic light scattering and laser diffraction (Mastersizer 2000TM with Hydro SM instrument. Zetasizer Nano ZS; Malvern Instruments Ltd., UK) measurements were also carried out. Additionally, a test was carried out to examine the bubble forming ability of the initial liquids.
Results: The difference in the shape and size of bubbles in foams is clearly visible from the microscopic images. This deviation is also apparent at the characteristics of the foams. Further connection was found between the single bubble forming ability and the foaming.
Conclusion: Image analysis is an entirely applicable method for the investigation of macroscopic and microscopic foam characteristics consequently for the evaluation of pharmaceutical foams.

International illegitimate online pharmacy networks manipulate and dominate search engine Results:

FITTLER, A.[1], IVÁNYI, P.[2]
[1]*Department of Pharmaceutics and Central Clinical Pharmacy;* [2]*Department of Systems and Software Technologies, University of Pécs, Pécs*

Background: The internet pharmacy market is dominated by illegal vendors selling unauthorized and counterfeit medicines. These products pose significant patient safety issues globally. Illegitimate pharmacy networks utilize abusive/underground marketing techniques including e-mail spam, forum abuse and search engine manipulation to attract customers. Although search engines typically refer consumers to relevant online resources quickly, search-redirection attacks refer consumers and patients from hacked websites appearing among top search results, to illegal online pharmacies operated by illegitimate actors.
Aims: We aimed to measure the prevalence of search-redirection attacks (hacking) among popular search engine results (SER) appearing in Google.hu for erectile dysfunction medications. Furthermore, to map and document redirection chain elements, and propose a methodology for closing down manipulated web links in collaboration with the national drug authority.
Methods: The four major active pharmaceutical ingredients: sildenafil, tadalafil, vardenafil and avanafil were searched on the most popular search engine Google.hu in August and October 2019. First 20 search engine query results were documented and evaluated manually, including SER ranking, link, redirect in source code, final destination website, and website relevancy.
Results: A total number of 111 links were evaluated during our two-month study period. The majority (n=72, 64.8%) offered erectile dysfunction medications for sale, while links promoting dietary-supplement accounted for 9.9% of SER, the rest being benign, irrelevant or not working. In August out of 55 relevant links 47 links were hacked and delivered visitors to 5 final international online pharmacies, while in October out of 46 links 35 were hacked, promoting 8 final destination pharmacy websites. These final destinations were all international illegitimate pharmacies operating in English.
Conclusion: Majority of the search results are illicit and within them compromised websites are dominant. The number and the SER position of websites affected by search-redirection attacks dynamically evolve over time, hacked links significantly outnumbering traditional unlicensed pharmacies. Shutting down such links in collaboration with authorities will likely clean up SER pages and prevent patients from accessing potentially dangerous pharmaceuticals.

Development of a complex visualization and quality management tool for the pharmacy curriculum

FITTLER, A.[1], SZABÓ, I.[2], VIDA, R.G.[1], STORCZ, T.[3]
[1]*Department of Pharmaceutics and Central Clinical Pharmacy;* [2]*Registrar's Office of the Medical School and Faculty of Pharmacy;* [3]*Department of Systems and Software Technologies, University of Pécs, Pécs*

Background: Current electronic administration systems do not collect and summarize prerequisites of obligatory subjects, data on student dropout rate, and integrate all relevant information in a visual map.
Aims: Development of a decision support and quality management tool supporting Faculty management and subject directors to further develop curriculum and optimize prerequisite subject structure.
Methods: Commercially available tools were tested, prerequisites of obligatory subjects were exported to various software aiming to visualize the networks. Dropout rates were collected from the electronic administration system (Neptun). A Windows Forms application was developed using C#.net.
Results: A curricular system can be considered as a graph containing nodes (subjects) and edges (prerequisites). The 10 semester curriculum is highly complex, as nearly 70 obligatory subjects have more than 110 prerequisites. Visualization in MS Project as a Gantt chart makes visual interpretation difficult. Network analysis and visualization software (eg.: Gephi), was also an inadequate tool to visualize the

timeline of education. 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.
Conclusion: A network analysis and visual presentation of subjects require an individual software developed to meet our expectations and needs. Novel information technology methods will likely improve curriculum structure and reduce dropout rate by identifying critical subjects and affected students (e.g. by artificial intelligence).

New approaches to discover and evaluate pharmacy networks on the Internet

FITTLER, A.[1], IVÁNYI, P.[2], HAHIGHI, R.[3]
[1]Department of Pharmaceutics and Central Clinical Pharmacy; [2]Department of Systems and Software Technologies; [3]Department of Pharmaceutics and Central Clinical Pharmacy, University of Pécs, Pécs

Background: Due to the uncontrolled nature of the internet large number of illegal online pharmacies exist globally, violating international laws and distributing falsified medications. International and national authorities lack efficient tools to discover and close rogue websites down. Manual mapping and evaluating internet pharmacy website networks is incomplete, and wasteful for human resources. Thus, advanced computational methods are needed to detect and mitigate cybercriminal activity.
Aims: We aimed to develop a specific web crawler to better detect and classify illicit online pharmacies through text mining, content and link structure analysis.
Methods: The currently developed computer tool starts from a set of initial web sites determined from Google, where illegal pharmacies selling erectile dysfunction medications were searched for. The crawler downloads the web sites, determines it's and in the newt step downloads them. Again from these level 2 web pages the links are determined, and the process can be repeated infinitely. To avoid this exponential explosion of the number of web pages, conditions determine whether the page is relevant and whether the web page will be processed. The three basic conditions for relevance were: text of the web page must be in Hungarian, the domain of the web page should not be in a banned list, and four of eight keywords must occur on the web page at least once. The banned list of domains contained general 43 social web sites. The eight keywords were related to erectile dysfunction (tadalafil, cialis, vardenafil, levitra, sildenafil, viagra, avanafil, spedra).
Results: The 7 starting points were selected manually from the top 20 relevant search results from Google.hu in July 2019. A nine-level network of relevant web pages has been discovered, scanning lasted for approx. 150 minutes. The tool visited 6972 pages belonging to 289 domains, including 35 redirection pages, 488 duplicates, 199 non-Hungarian, 56 pages belonged to banned domains, while 1567 not contain the eight keywords. A total of 4253 pages were relevant, belonging to 94 websites found to be illegally selling erectile dysfunction drugs.
Conclusion: Due to the changing environment of search engines, and the changing behavior of illegal sites such novel computer tools are required. Further enhancement of the algorithms determining relevancy of the web pages, and an automatic classification tool estimating web site legality will increase sensitivity and specificity for the crawler.

Evaluation of the Hungarian pharmacy curriculum: results of a comprehensive national survey among pharmacists

FITTLER, A.[1], GUTAY, T.[2], GYIMESI, N.[3], FÜSTÖS, K.[1], VIDA, RG.[1]
[1]Department of Pharmaceutics and Central Clinical Pharmacy, University of Pécs, Pécs; [2]Integration and Youth Committee of the Hungarian Chamber of Pharmacists, Budapest; [3]Youth Committee, Organization of Hospital Pharmacists, Hungarian Society for Pharmaceutical Sciences, Budapest

Background: There is an on-going change and progression in societal and professional expectations towards pharmacist, simultaneously role of pharmacists in healthcare are increasingly. Accordingly, modification of the 'Training and qualification requirements' has become an issue of the decade. Numerous professional bodies have identified areas for improvement.
Aims: We aimed to collect the opinions of practicing pharmacists (especially those who graduated in the near past) about Hungarian pharmacy education. Furthermore, to explore which areas and modules need to be changed based on their practical experience.
Methods: A 19 items online questionnaire was promoted nation-wide on professional forums and social media in November 2019. Questions were constructed, based on a previous survey of Hungarian Society for Pharmaceutical Sciences Youth Committee in 2014 as well as publications and suggestions from professional organizations. Graduates from the four universities were recruited to comment on the items and participate in the pilot of the questionnaire. We differentiate the respondents by the year and place of graduation, and area of practice. The

questions focused on the different modules and knowledge requirements needed to obtain a master's degree, as well as educational techniques and other training related topics.
Results: Numerous responses arrived (n=222) by the endo of November 2019, with 117 of those who have graduated between 2014 and 2019, representative for all areas of practice and universities. Majority of the responders answered that basic module's weight in education should be at least slightly reduced, and profession specific knowledge weight should be increased. The weight of education of pharmaceutical care, pharmacological and therapeutic knowledge must be increased according to the respondents, which is in accordance with the changed requirements towards pharmacists. Regrading the relationship of training to daily practice, most of the responders indicated that the training does not equip them with problem-solving skill, and the final exam does not assess the real employment demands.
Conclusion: Education in those topics which helps to prepare for patient and therapy-focused pharmaceutical service are much more needed in pharmacist training. Also, the answers provide guidance on which items in the curriculum may need focused attention.

Integration of pharmacist communication in English programs offered by European universities

FITTLER, A.[1], NAGY, G.[2]
[1]*Department of Pharmaceutics and Central Clinical Pharmacy;*
[2]*Department of Languages for Biomedical Purposes and Communication, University of Pécs, Pécs*

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.
Aims: 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 14 universities of 11 different EU member countries, where 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 web sites.
Results: Pharmacist communication is an individual obligatory course only in 2 (in Debrecen and Prague) universities evaluated in our study. Another two institutions electively offer individual courses of communication and counseling (Szeged and Brno). Communication is integrated into Pharmaceutical Care in 3 universities, while into other obligatory courses in 3 other cases. In one institution academic English communication courses run for several years without integrating specialist language. In Denmark, training modules are used, in which communication skills are evaluated and integrated into pharmacy project assignments. Based on course descriptions and syllabus available from the university websites, communication skills are not an integral element of pharmacy education in 6 (42.8%) institutions.
Conclusion: Data reflect that the education of communication skills for pharmacy students show significant differences, while only a minority of faculties of pharmacy with English educational program in the EU integrate communication as an essential segment of pharmacist training today; nevertheless, its significance has been more widely recognized.

Antioxidant and antimicrobial activity of lyophilized flower extract of *Rosa damascena* L.

GAVRA, D.[1], JURCA, T.[1], MARIAN, E.[1], PALLAG, A.[1], VICAS, L.[1], BOTA, S.[1], BÁCSKAY I.[2]
[1]*Departament Pharmacy, University of Oradea, Oradea;*
[2]*Department of Pharmaceutical Technology, University of Debrecen, Debrecen*

Rosa damascena L. with origin in the Middle East, has medicinal functions that are partly attributed to their abundance of active compounds as flavonoids, glycosides, anthocyanins, terpenes. The constituents of this plant are responsible for antioxidant, anti-inflammatory, hypnotic, analgesic, anticonvulsant effect.
The aim of this study was to investigate the bioactive compounds, antioxidant capacity and antimicrobial activity of the extract. Using HPLC method was investigated the composition of phenolic compounds and the identification was achieved by comparison with retention times of standards. Determination of antioxidant activity of samples was made by DPPH, FRAP, CUPRAC and ABTS methods. The antimicrobial activity of the extract was determined by the disk diffusimetry method.
The result of total phenolic compounds using Folin-Ciocalteu assay was 321 mg GAE/100 g DW. The total flavonoid content determined by the colorimetric method AlCl3 was 32.4 mg QE/100 g DW.
Regarding the antimicrobial activity, the most sensitive antimicrobial effect was on the reference and the

clinical isolate of Pseudomonas aeruginosa strain. The high total polyphenols, flavonoids and anthocyanins content revealed that lyophilized rose petals represent a promising source of phenolic compounds which might be used as functional food ingredients and might be implicated in different antioxidant activity and therapeutic applications of this plant.

Brain activation pattern changes after acute citalopram administration during pharmacological magnetic resonance imaging (phMRI)

GECSE, K.[1,2], ÉDES, A.E.[1,2], SZABÓ, E.[1,2,3], KOCSEL, N.[1,2,3], KÖKÖNYEI, G.[1,2,3], BAGDY, G.[1,4], JUHÁSZ, G.[1,2]

[1]Department of Pharmacodynamics, Faculty of Pharmacy, Semmelweis University, [2]SE-NAP2 Genetic Brain Imaging Migraine Research Group; Institute of Psychology, Eötvös Loránd University, [4]SE-NAP2 New Antidepressant Target Research Group, Budapest

Background: Citalopram, a selective serotonin reuptake inhibitor (SSRI) is widely used to treat several mental disorders such as depression. It takes 2-3 weeks to reach the full effect, but an acute citalopram administration increases synaptic serotonin content immediately and has a modulatory effect on information processing.
Aims: The aim of this study was to investigate alterations in brain activations pattern which can bring us closer to understand why altered serotonergic neural transmission leads to different neuropsychiatric disorders.
Methods: 32 (19 women and 13 men) healthy volunteers participated in two separate 30-minute scanning sessions, where they received normal saline or 7.5mg citalopram infusion in a randomized, double-blind trial. Data analyses was carried out in SPM12 software using flexible factorial method.
Results: After 7.5mg of acute citalopram administration a significant increased activation was detected in several areas of major brain networks such as the default mode network (posterior cingulate cortex, precuneus, MTG) the visual network (fusiform gyrus, lingual gyrus) and the sensorimotor network (postcentral gyrus). These activated brain regions show similarities with areas activated during an increased arousal.
Conclusion: The citalopram-induced increased synaptic serotonin content generate an arousal-like brain state. These neural changes can play a role in the acute side effects of citalopram and, in addition, induce downstream neuroplastic changes. Further investigations are needed to determine the exact therapeutic effects of increased synaptic serotonin among patients.

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Optimization of capillary electrophoresis conditions for the separation of gangliosides

GEDA, O., TÁBI, T., SZÖKŐ, É.

Department of Pharmacodynamics, Semmelweis University, Budapest

Background: Gangliosides are glycolipids that are present in microdomains in the outer leaflet of cell membranes where they are involved in the regulation of membrane-associated signaling proteins. According to recent studies, altered concentration of gangliosides has a potential role in the development of insulin resistance by modulating insulin receptor signal transduction. Gangliosides are structurally heterogeneous molecules composed of a ceramide portion and an oligosaccharide chain containing at least one sialic acid. They form micelles in aqueous solution, which hinders their separation as monomers by capillary electrophoresis (CE). Disruption of the micelles by cyclodextrins (CDs) was reported in previous studies using CE.
Aims: We aimed at optimizing a CE method for the separation of the most abundant gangliosides in biological samples.
Methods: Separation conditions including pH, buffer concentration and CD type and concentration have been optimized for the separation of gangliosides GM3, GM1, GD1a, GD1b and GT1b. The applicability of the method was demonstrated on biological samples.
Results: RAMEA (randomly methylated beta-cyclodextrin) as buffer additive was found appropriate for the separation of all five studied gangliosides. The best resolution was achieved at 15mM RAMEA in 100 mM sodium borate buffer. Mono-sialylated gangliosides GM3 and GM1 were separated in their native form for the first time by our CE method. Increased concentration of sodium borate buffer resulted in higher resolution due to the increased borate-carbohydrate complexation which results in additional negative charges on the analyte molecule. Increased resolution using more alkaline pH (10.0) where the complexation is most effective was observed, as well. The optimized method was applied on various biological samples, including ganglioside

extracts of rat brain, in which brain-specific gangliosides were identified, namely GM1, GD1a, GD1b and GT1b.
Conclusion: Separation of the studied gangliosides was achieved using the optimized method with RAMEA as buffer additive. This method was found appropriate for the analysis of ganglioside extracts from animal brain samples.

Advantages and disadvantages of the patient-oriented picking systems; How many is the wastage of packaging material?

GULYÁS, E., HALÉDER, ZS., TAKÁCS, H., KEREK, A.
University Pharmacy Department of Pharmacy Administration, Semmelweis University, Budapest

Background: More and more patient-oriented picking systems are used in hospital pharmacies to support the direct patients care of pharmacists. Undoubted advantage of these automated systems the increased drug & patients" safety, but at the same time have to take into consideration the question of pickings.
Aims: To measure the quantity of the unwanted packaging material produced in the course of operation of HD Medi automated patient-oriented picking system what is used in the Semmelweis University Pharmacy Korányi Department since 2018.
Methods: For 14 days all unwanted packaging material – the blisters and paper boxes produced at upset of cassettes, and the empty folia produced by automata during packaging, furthermore the traditional containers were collected on daily basis.
Results: During observational period content of 472 boxes were upset into the cassettes; it represented 1083 blisters plus 85 plastic container plus, 5299 ampullas were distributed from 956 boxes. The automate put in 10 907 bags but 22% of them were blank, that means waste as well. The whole quantity of wastage was 1103 litres, 22.6% of this was the blisters, and 77.4% paper wastage.
Conclusion: Problems we are facing at the moment – a lot of false error messages – time consuming – technical limits of identification and our assessment demonstrated that near 20% blank bags are produced by the automate.
The hope for technical assistance of the vendor could improve this mistake and by this way the wastage could be decreased. It would be a great help for the pharmacy workers if the drug companies provided in loose packages of the frequently used preparation for the hospitals. Further, in the interest of environment launching of the biodegradable drug packaging material would be appreciated.

Traditional uses of medicinal plants in the Southern Plain Region of Hungary

HAJDÚ, Z.[1], HÁZNAGY-RADNAI, E.[1], GELLÉNY, K.[2], CSEH, V.[2], MARGÓCZI, K.[2], MÓD, L.[3], SIMON, A.[3], HOHMANN, J.[1]
[1]Department of Pharmacognosy; [2]Department of Ecology; [3]Department of Ethnology and Cultural Antropology, University of Szeged, Szeged

Background: Traditional medicine is an important part of human health care. The uses of medicinal plants contribute a remarkable part of health care in many developing countries and also in developed countries, increasing their commercial value [1].
Aims: The aim of the present study was the estimation of traditional utilization of plants as medicine in the Southern Great Plain Region of Hungary. Field survey was carried out among the people who live in the affected area, and the ethnobotanical literature survey of the region was evaluated.
Methods: An interview line was created to assess the traditional knowledge of local communities concerning traditional plant utilizations in the affected area. A slideshow of plant photos was prepared and shown to every interviewer to elicit the plant species related knowledge. 25 field interviews were performed using the questionnaire. Population participating in the survey lives in Bács-Kiskun, and Csongrád counties. The ethnobotanical literature survey of the traditionally used plants and the scientifically proven activities and uses of them in medicine today are also collected.
Results: Data on local plant utilizations were processed and summarized, and literature survey was also evaluated. These data were reviewed with special emphasis on confirmed medicinal use, allowing the comparison of local traditional plant use with the scientifically proven data. Documentation of mode of production of several preparations made from plants was involved in the survey. Mainly the gastrointestinal, the respiratory system and skin problems were mentioned as therapeutic indication for which traditional herbal treatment can be applied. 60 plant species are outstanding in the research and the majority of the traditional plant uses are consistent with the scientifically proved uses, however, some specific plant utilisations were also recognised. The safety concerns of the plants were also considered in evaluation the data.
Conclusion: The informants usually proved to have broad knowledge about the plant use. This allowed gathering information about the cultural heritage and traditional uses of the local flora. The traditionally used plants considering the scientifically proven

activities and uses of them in medicine today provides a detailed, practical and research based approach to the use of modern herbal treatments.

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Possible mechanisms of drug-drug interactions in the medication of kidney transplant patients

HORVÁTH, I.

University Pharmacy Department of Pharmacy Administration and Department of Transplantation and Surgery, Semmelweis University, Budapest

Background: In Hungary there are a growing number of renal transplant patients. Due to their immunosuppressive therapy and health status, they considered a high risk patient population. Moreover, these patients have various comorbidities, that lead to polypharmacy, which can potentially cause serious drug-drug interactions.

Aims: The aim of the survey was to assess the drug-drug interactions among our kidney transplant patients and to evaluate their clinical significance.

Methods: Within 24 hours of a patient's admission, as the part of the comprehensive drug history, a drug-drug interaction review was performed using Lexicomp® Drug Interactions tool. The interactions were rated by Lexicomp®'s rating system: X – avoid combination, D – consider therapy modification, C – monitor therapy, B – No action needed, A – no known interaction. Group B and A were excluded from the study to focus on the more clinically relevant interactions.

Results: During the pilot study (from 22/Oct/2019 to 25/Nov/2019.) there were 37 patients (51% male, mean age: 51) involved. The average number of concomittantly used medication were 11.78±4.81 per patient. 364 interactions were identified (X: 13, D: 35, C: 316) and classified. 3 problemes were highlighted: 1) The impaired absoprtion of mycophenolate mofetil due to administration of proton pump inhibitor 2) Polyethylene glycol as solvent of Bactrim infusion and metronidazole interaction resulting lactic acidosis 3) The potential vitamin D toxicity as a result of concomittantantly used active and inactive form of vitamin D.

Conclusion: Pharmacists should frequently monitor the immunosuppressant medication therapies, because of the latent absorption deviations. various adverse effects and potential drug-drug interactions. By the contribution of the clinical pharmacist in the medical team, the medication treatment could be more personalized and potential drug related interactions and adverse events could be decreased.

Antiproliferative cyclic C5-curcuminoids without DNA binding: design, synthesis, lipophilicity and biological activity in a SAR analysis

HUBER, I.[1], ROZMER, Z.[1], GYÖNGYI, Z.[2], BUDÁN, F.[2], HORVÁTH, P.[3], KISS, E.[3], PERJÉSI, P.[1]

[1]Institute of Pharmaceutical Chemistry;[2]Institute of Public Health Medicine, University of Pécs, Pécs; [3]Department of Pharmaceutical Chemistry, Semmelweis University, Budapest

Background: The chemical susceptibility of the ß-diketone linker between the two aromatic rings in the structure of curcumin to hydrolysis and metabolism has made it crucial to investigate structurally modified analogs of curcumin without such shortcomings.

Aim: The synthesis of twenty cyclic C5-curcuminoids is described in this study in order to gain more insight into their anticancer structure activity relationship (SAR). The design of their synthesis included four different cyclanones and five substituted aromatic aldehydes to form four, five-membered subgroups.

Methods: These model-compounds were evaluated in vitro for antiproliferative activity in an XTT cell viability assay against MCF-7 human non-invasive breast adenocarcinoma cancer cells and Jurkat human T lymphocyte leukaemia cells in five different concentrations (10nM, 100nM, 1μM, 10μM and 20μM).

Results: The majority of the compounds investigated have shown remarkable cytotoxicity with IC50 values in the range of 120nM and 2μM with very high relative toxicity values to curcumin. The SAR conclusions are drawn and summarized. A method was developed and applied in a TLC based experimental logP measurement, which is new for such C5-curcuminoids. The logP data and structural modifications have shown a strong correlation. The correlation of these experimental logP and the corresponding IC50 values of the model-compounds were calculated according to the Pearson and Kendall correlation coefficient and showed weak concordance. The physicochemical behaviors of the majority of these compounds are in good accordance with the Lipinski rules. The most promising compound is 7a, which is the most active (IC50=0.12-0.32μM), most potent (80 times of curcumin) with the lowest lipophilicity (experimental logP=3.22) which is important also from a pharmacokinetic point of view.

Conclusions: The analysis of experimental logP and computed ClogP values have revealed good agreement. These cyclic C5-curcuminoids, in contrast to

curcumin, do not bind to natural DNA based on their CD spectra.

Support: This study was supported by the European Union, co-financed by the European Social Fund (EFOP-3.6.1.-16-2016-00004).

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Formulation and investigation of creams containing Spirulina powder

JÓZSA L.[1], BÁCSKAY I.[1], UJHELYI Z.[1], SINKA D.[1], VECSERNYÉS M.[1], SZABÓ J.[2], FEHÉR P.[1]

[1]Department of Pharmaceutical Technology; [2]Institue of Medical Microbiology, University of Debrecen, Debrecen

Background: Products containing natural active substances have an increasing role in therapy. Dietary supplements made using Spirulina algae have been in circulation for some time, but their external application is not so widespread, although Spirulina contains valuable ingredients with antioxidant and antibacterial effect.

Aims: The aim of our experimental work was to formulate creams containing Spirulina powder as a natural active substance. Creams containing penetration enhancing excipients were formulated. Various types of nonionic amphiphilic surfactants were used (Polysorbate 60, Cremophor RH 40, sugar-ester SP 50, SP 70). To enchance the penetration of Spirulina, through the skin, Transcutol was also added to our ointments as a solubilizer excipient.

Methods: The release of drug from the vehicle and its penetration through the membrane were determined by Franz diffusion cell. The cytotoxic effect of compositions was evaluated by a colorimetric method (MTT) on HaCaT keratinocyte cell line. The antioxidant effect of Spirulina-containing creams was also investigated on HaCaT cells. The cells were exposed to UV-B radiation, pre-and post-treated with samples containing Spirulina powder in different compositions, and superoxide dismutase (SOD) activity was measured. The antimicrobial activity of Spirulina cream was checked against Propionibacterium acnes with turbidimetric method.

Results: Cream containing sugar-ester SP 70 as emulsifying agent was the most preferred composition according to the diffusion and MTT tests. The penetration rate was the highest from this formulation. With the addition of Transcutol higher release of Spirulina was observed. The diffused amount of active substance thus reaches 40% in the case of a cream containing SP 70 emulsifying agent. Thanks to the Spirulina treatment the activity of antioxidant enzyme was increased in the cells. In those compositions where Transcutol was added to dissolve the Spirulina powder we detected higher increase in the SOD activity. According to the result of antimicrobial test Spirulina cream could be effective against *P. acnes*.

Conclusion: In conclusion, o/w creams with appropriate consistency were formulated. Transcutol with sugar-ester type emulgents elevated the amount of active substance across the diffusion membrane. Sufficient antioxidant activity was measured against UV-induced oxidative stress on HaCaT cells. Spirulina cream showed antimicrobial effect against *P. acnes*, so it can play an important role in the treatment of acne vulgaris.

Formulation development of Telmisartan driven by flux measurements

KÁDÁR, SZ.[1], BORBÁS, E.[1], TŐZSÉR, P.[1], NAGY, B.[1], TSINMAN, O.[2], TSINMAN, K.[2], SINKÓ, B.[2], NAGY, ZS. K.[1]

[1]University of Budapest Technology and Economics, Budapest; [2]Pion Inc., Billerica, USA

Background: Utility of in vitro flux measurements in formulation development and bioequivalence prediction have been explored in a number of recent studies. The benefits of such measurements are based on the fact that they capture the complex interplay between effects of formulation ingredients on solubility, dissolution rate and permeability of an active pharmaceutical ingredient (API).

Aims: The aim of this project is to prove the applicability of instruments and methods as biorelevant tools incorporated in drug formulation development.

Methods: PAMPA Measurements Each well of the top compartment of 96-well STIRWELL PAMPA sandwich was coated with n-dodecane. Before forming the sandwich, the bottom and top plate was prefilled with suitable compounds. After 30 minutes the PAMPA sandwich was separated and 100 μL of both the donor and acceptor compartments were transferred to UV plates. UV absorption was measured with Tecan Infinite M200. FLUX Measurements Electrospun formulations of TEL were tested using MicroFLUX and final forms of TEL were tested with MacroFLUX. Concentration in both chambers were monitored in real time using in situ fiber optic dip probes connected to the Rainbow instrument. An artificial membrane impregnated with n-dodecane to form a lipophilic barrier between the donor and acceptor chamber.

Results: The excipients of the available TEL formulations and widely used standard excipients were in-

volved in the first API-excipient investigations. The surfactants have significant reducing effect, while the polymers have a slight, non-significant increasing effect. Mixed effect were experienced with fillers, where mannitol provided a lower flux and permeability then the others. Due to the permeability decreasing effect of surfactants and increasing effect of polymers, amorphization has been selected as the formulation strategy, which we implemented by electrospinning. To simulate the in vivo conditions, media change was carried out after 30 minutes. During the first 30 minutes of the experiment no flux across the membrane was detected because of the charged state of the API, while after media change TEL started to permeate through the membrane. The developed formulations provided similar flux profile to Micardis.

Conclusion: The described formulation development procedure demonstrated how excipients can be classified in the early stage of excipient selection and the most advantageous ones can be used in the later stages to ensure suitable behavior of the final product.

Synthesis and characterization of novel cyclodextrin-based drug-carriers targeting the central nervous system

KALYDI, E.[1], MALANGA, M.[2], BÁLINT, M.[2], VARGA, E.[2], BÉNI, SZ.[1], BENKOVICS, G.[2]
[1]*Department of Pharmacognosy, Semmelweis University;*
[2]*Cyclolab, Cyclodextrin R&D Ltd., Budapest*

Background: Blood-brain barrier (BBB) segregating the central nervous system (CNS) from the systemic circulation inhibits also the delivery of therapeutics into the brain. As glucose transporters are overexpressed on the surface of the BBB, they provide ideal targets for new drug carrier systems aiming the CNS [1]. Another approach is the use of positively charged carriers to achieve high affinity for the negatively charged endothelial cells of the brain capillaries. It is also evidenced, that organizing monomeric compound to macromolecular systems enhances their transport across the phospholipid membranes [2].

Aims: As cyclodextrins (CDs) are known as ideal drug carriers, our aim was to develop new CD-based drug delivery systems, capable to cross the BBB.

Methods: Based on the aforementioned considerations, we have synthetized two sets of CD derivatives: (1) glucose appended beta-CD (BCD) and hydroxypropyl-BCD (HPBCD) scaffolds using click-chemistry, (2) positively charged polymer by crosslinking (2-hydroxy-3-N,N,N-trimethylamino) propyl-BCD (QA-BCD) with epichlorohydrin.

Results: For the in vitro investigation of the compounds, their fluorescent labeling was necessary. As fluorescent tags, 7-alkylamino-4-nitrobenzofurazan (NBF) and fluorescein-isothiocyanate (FITC) were used. The labelled glucose-modified CDs were synthetized by the simultaneous attachment of the fluorophore and a targeting unit via click-reaction and characterized by NMR and MALDI-TOF-MS. The FITC-labelled polymers were synthetized through a copolymerization of the QA-BCD and 1% FITC-BCD monomer and characterized using NMR and dynamic and static light scattering. The cellular internalization properties of the conjugates will be investigated using isolated human brain microvascular endothelial cells (HBEC-5i). The HBEC-5i monolayer serves as a barrier model. Confocal fluorescence microscopy is used to determine the internalization process and flow-cytometry is used to quantify the cell-penetration. In vitro properties of the conjugates are under investigation.

Conclusion: Various new CD-based drug carriers targeting the CNS have been synthetized and characterized by NMR, MS and microscopy.

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Study of interaction of reduced glutathione (GSH) with some chalcone analogs in vitro and in vivo

KENARI, F.[1], BERNARDES, A.[2], NODA, PC.[2], MOLNÁR, S.[1], KULCSÁR, G.[1], PÉRJESI, P.[1]
[1]*Institute of Pharmaceutical Chemistry, University of Pécs, Pécs;*
[2]*Federal University of Goiás, Goiânia*

Background: Chalcones are intermediary precursors of flavonoid biosynthesis. Both natural and synthetic chalcone analogs are proven to have various biological activities. In our previous experiments, some cyclic chalcone analogs showed a significant effect on GSH status of Jurkat T lymphocyte cells, and most of the investigated chalcones displayed spontaneous GSH-reactivity.

Aims: The aim is to demonstrate A) the relationship between GSH-reactivity of chalcones and their anti-cancer properties; and the influence of this reactivity on their other biological effects. B) How the ring size, substituents, and pH affect the reactivity and stereochemistry of the reaction. C) to compare luminal elimination kinetics and metabolism of our chalcones and their bis-Mannich-base analogs.

Methods: For analyzing the in vitro incubates, proper RP-HPLC-UV-VIS and HPLC-MS methods were

developed. In the case of the in vivo experiment, the isotonic buffer of the two compounds was perfused for 90 minutes in anesthetized rats, and monitored using a validated method of HPLC-DAD as well as HPLC MS.

Results: Most of the compounds showed an intrinsic reactivity towards GSH. This reversible reaction yields two diastereomeric adducts in case of open-chain chalcones (in both in vitro and in vivo), and four ones in the case of cyclic chalcones. The open chain and six-membered chalcone derivatives showed the highest reactivity. The methyl and dimethylamino derivatives displayed the highest and lowest GSH reactivities respectively. Mannich analogs showed more reactivity than their parent compound. In the in vivo experiment, Mannich analogs showed a lower rate of absorption and a higher rate of elimination in comparison to chalcones. In the small intestine perfusates, the chalcone and Mannich analog, and their glucuronide, sulfate and glutathione-conjugates were detected.

Conclusion: The rate and mechanism of the reaction is found to depend on the ratio of deprotonated to protonated GSH. Reactivity of the chalcone derivatives was also found to depend on the aromatic substituent of the A ring. Based on the results, the GSH reactivity does not seem to be a direct determining factor in the cytotoxic effect of the compounds. Our in vivo experiments demonstrated that the GSH-conjugation reaction of chalcones plays a role in the fate of the per os administered compounds.

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Logistic and storage management of cytotsatic infusions

KOCSÁN, R., SZŰCS, Á., BUCHHOLCZ, G.
Central Clinical Pharmacy, University of Debrecen, Debrecen

With the increased occurrence of malignancies in the past decades the demand for cytostatic infusions increasing rapidly. Their centralized production and distribution are a big challenge for hospital pharmacies worldwide.

The preparation of cytostatic infusions by computer aided gravimetric methods (CATO) was introduced in 2017 for Department of Oncology. Since the beginning of 2020 Department of Pulmonology and Gynecology have joined the CATO system.

The protection of the professional staff, the patients and the environment is ensured by the temperature control transport of cytotoxic infusions and the regulations of international guidelines (ESOP).

The cytostatic drugs are stored in separate storeroom equipped with „spill kit" which is available in the transport van also. In addition the containers are marked with international „yellow hand" symbol. The staff is being trained regularly how to manage an accidental contamination.

Cytostatic infusions are delivered by thermo controlled vehicles. The transport packaging guarantees that breakage and contamination cannot occur. The containers are equipped with international symbol, which consist of "yellow hand" pictogram and a short warning message.

Collaborated care, specific instructions and precautions are needed in the handling and transport of chemotherapeutic drugs. In addition to the design of therapies and the preparation of infusions, the logistics, patient safety, protection of employees' health and environment is key task.

Development of oral peptide drug delivery systems

KÓSA, D., PETŐ, Á., FEHÉR, P., VECSERNYÉS, M., BÁCSKAY, I., UJHELYI, Z.
Department of Pharmaceutical Technology, University of Debrecen, Debrecen

Background: Therapeutic proteins have become the treatment of several diseases due to their bioactivity and specificity. At this point, injections mean the most common way for administering proteins and peptides because of their extremely low oral bioavailability. Efforts to improve bioavailability of orally delivered proteins have been intensified over the years and several approaches have been recommended like the chemical modification of the protein, or the formulation of carrier systems.

Aims: The object of our research was to formulate innovative sodium alginate nanospheres of a peptide type API by controlled gelification method. Thus, our aim was the calibration and settings optimization of the encapsulator instrument as well. We have been also evaluated the cytotoxicity of different penetration enhancer excipients.

Methods: Formulation has been performed by controlled polimerisation method with the help of Büchi Encapsulator B-395 Pro. For the formulation, we used 1.5% sodium alginate solution as encapsulating polymer, and 100mM calcium chloride dihydrate solution as hardening solution. In vitro dissolution has been evaluated to characterise drug release from the beads with an average diameter of 200μm. The drug concentration in each sample was analysed by radioimmunoassay. Biological properties of the excipients

had been evaluated as well with MTT assay on Caco-2 cells. To determine swelling behavior of beads, dry beads were weighed and placed in distilled water for an hour, then zhe equilibrium water uptake was determined. Particle size distribution of the beads with an average diameter of 200μm has been performed with laser diffraction technique in a collaboration with Budapest University of Technology and Economics.

Results: Over the last few months, we have successfully determined the optimal parameters and settings for the formulation using 200μm nozzle. According to the results, it can be concluded that the whole amount of the encapsulated API was detected after 60 minutes. The results of MTT assay showed that the selected excipients are safe under in vitro conditions. The physical analysis of the beads proved that real particle size is close to the theoretical water uptake depends on the size of the beads.

Conclusion: Our results suggest that these microbeads may provide a traditional oral pathway for the delivery of peptides.

Enhancing of primycin production by Saccharomonospora azurea with various fatty acids

KOVÁCS, M.[1], SEFFER-SZALAI, M.[1], SEFFER, D.[1], PÉNZES-HŰVÖS, Á.[1], KOVÁCS-VALASEK, A.[2]

[1]*PannonPharma Pharmaceutical Company Ltd., Pécsvárad;*
[2]*Szentágothai Research Centre, University of Pécs, Pécs*

Background: Primycin, produced by a Gram-positive filamentous bacteria *Saccharomonospora azurea* is a 36-membered marginolactone antibiotic, which possesses high antimicrobial activity against several clinically important bacterial pathogens. Like other guanidino marginolactone antibiotics, primycin is biosynthesized through the bacterial modular type I polyketide synthase (PKS) multienzyme, which assembly mechanism is closely related to fatty acid (FA) biosynthesis. Since the biosynthesis of polyketides and FAs share common precursors via acetyl-, and malonyl-CoA, the two pathways may compete for substrate, which can affect the yield of antibiotic production.

Aims: The aim of present study was to determine the impact of various fatty acid substrates on primycin production, thereby find out the fatty acid substrate specificity of the primycin PKS pathway during antibiotic biosynthesis.

Methods: To evaluate their potential to enhance fermentation performance, the effect of stearic acid (C18:0), palmitic acid (C16:0), lauric acid (C12:0), capric acid (C10:0), enanthic acid (C7:0), caproic acid (C6:0), and butyric acid (C4:0) in growth medium were investigated. Among the tested fatty acids, those with highest primycin production inducing ability were selected and further investigated in a time course experiment. In order to determine primycin concentrations of fermentation medium, HPLC-DAD-MSD analysis was performed.

Results: The data demonstrated that stearic acid and palmitic acid possess the highest primycin production inducing ability among the examined fatty acids. Our results clearly show that palmitic acid was a better alternative of the originally applied stearic acid in all tested concentrations, while 4.5g/L proved to be the most effective.

Conclusion: The present study revealed that palmitic acid plays an essential role in primycin biosynthesis and may be used not only as an alternative component of stearic acid in the fermentation media but could serve as a standard component of a newly designed and highly effective primycin producing fermentation media.

Synthesis and analysis of opioid glycine-hapten derivatives

KÖTELES, I., HOSZTAFI, S.

Department of Pharmaceutical Chemistry, Semmelweis University, Budapest

Background: Drugs of abuse are small molecules that typically do not induce an antibody response following injection or inhalation. To induce antibodies against small molecules, structural surrogates of the molecules, which were named "haptens", must be coupled to immunogenic proteins, called "carriers". These structural surrogates are typically drug-linker adducts, in which the linker has a terminal functional group that forms a covalent bond with the carrier. The efficacy of these conjugate vaccines depends on several factors including hapten design, coupling strategy, hapten density, carrier protein selection, and vaccine adjuvant.

Aims: Synthesis and structural analysis of potent hapten-like morphine derivatives.

Methods: We designed N-substituted morphine compounds and for this purpose the normorphine-derivatives were required. Morphine, codeine, their dihydro derivatives, oxymorphone and oxycodone were N-demethylated with alfa-chloroethyl chloroformate. After receiving the appropriate hapten molecules the next step was the coupling phase with glycine ethyl ester. Unfortunately the reactions didn't work or the work-up process was not possible. As an alternative route the normorphine-compounds were reacted with N-chloroacetyl glycine ethyl ester. If purification was needed column chromatography

was used. The structures of the new compounds were determined by NMR and partially mass spectroscopy. These products were hydrolysed in alkaline media and after the work-up process all of the derivatives contained the free carboxylic group of the glycine sidechain, confirmed by NMR measurements. All of the glycine ester and the glycine carboxylic acid derivatives (except the norcodein ones) are under biological tests.

Results: Previously 12 hapten type molecules were synthetized from another 12 ethyl ester precursors. To model the peptide connection 6 glycine ethyl ester derivatives were obtained and all 6 have been hydrolysed to achieve the free acidic forms. 8 of the 12 N-acetyl-glycine-nor-compounds are under biological studies. The other molecules are under physico-chemical measurements. The structures of all of these molecules are confirmed by NMR spectroscopy.

Conclusion: We have developed different reaction ways to obtain 36 hapten-like normorphine derivatives and 32 of them are synthetized for the first time. The most potent compounds are under biological experiments. Right now we are working on new sidechains to change the linker and the amino acid part as well.

How can we improve patient collaboration?

KÖVÉR, B.[1], SZABÓ-SZAKÁL, N.[2]
[1]Szebellédy Pharmacy, [2]Ezüst Kehely Pharmacy, Sopron

Background: The definition of adherence in the WHO's wording is "the behavior of an individual in accordance with recommendations of a health care professional in the field of medication, diet and lifestyle changes". Adherence is when an individual interacts with medication and / or lifestyle modification in accordance with health care recommendations during therapy. This also requires the same quality of information from a healthcare professional, wherever they are available.

Aims: The purpose of the presentation is to highlight two issues that hinder patient collaboration: 1. packaging problems: confusing packaging, changing the usual packaging, empty blisters, hard-to-open containers, incorrectly sized measuring instruments, home-cooking problems. 2. Expedition of suspension formulations from special dosage forms: eg. steroid nasal sprays, steroid eye drops, inhalation suspensions, home-made antibiotic suspensions.

Methods: As a method, we conduct a questionnaire survey with more expeditioners and patients. By presenting individual examples and processing the questionnaire, we would like to draw attention to some problems in the freight forwarding practice. The questionnaire examines the accuracy of the information received and the effect of the "Shake Before Use" instruction for the above mentioned preparations. Another highlight is the problem of packaging. The so-called. since the introduction of the tepee-safe boxes, it has not been possible to check whether the grade prescribed by the prescribed medical instruction is in place. packaged next to an antibiotic suspension, but it is also problematic to dispense formulations that are almost identical in packaging but have different effects.

Results: After evaluating the questionnaires, we will be able to draw the final conclusion.

Conclusion: Finally, we would like to make a recommendation to resolve the issues we have discovered so that we can further improve the safe medication practices for patients.

Transcriptomic studies in animals – TRPV1 and TRPA1 as key players in migraine?

KUMAR, S., BAKSA, D., BAGDY, GY., JUHÁSZ, G., PETSCHNER P.
Department of Pharmacodynamics, Semmelweis University, Budapest

Background: Transcriptomics are gaining relevance for gathering knowledge about diseases more precisely. Migraine is a complex disorder not fully understood and the pathophysiology is still not clear.

Aims: After reviewing transcriptomic studies in migraine the genes transient receptor potential cation channel subfamily V member 1 (TRPV1) and transient receptor potential cation channel, subfamily A, member 1 (TRPA1) emerged as possible contributors to migraine headache.

Methods: I have reviewed some of the latest articles and extracted the most relevant results.

Results: These two genes were differentially expressed in animal studies using a nitroglycerin-induced migraine model. With ADM_12, a TRPA1 antagonist, and ghrelin, a substance tested to influence TRPV1 expression, it was possible to counteract both expression changes. TRPA1 is situated in nociceptive neurons in which TRPV1 channels and neuropeptides such as CGRP or Substance P are expressed. It was also shown that TRPV1 receptor induction releases the neuropeptide CGRP that has neurovascular and proinflammatory effects. Furthermore, the TRP ion channel family could be found surrounding the trigeminal ganglia, trigeminal nuclei and their vessels, regions strongly associated with pain sensation.

Conclusion: These findings suggest that these two channels might be important contributors to migraine headache.

Investigation of solubility and enhancement of biological activity of chrysin

LE PHUONG NGUYEN, T.[1], FENYVESI, F[1], HERMENEAN, A.[2], BÁCSKAY, I.[1], FEHÉR, P.[1], UJHELYI, Z.[1], VASVÁRI, G.[1], VECSERNYÉS, M.[1], VÁRADI, J.[1]

[1]Department of Pharmaceutical Technology, University of Debrecen, Debrecen; [2]Department of Histology, 'Vasile Goldiș' Western University of Arad, Arad

Background: Chrysin is a bioflavonoid that can be found in nature which possesses several biological effects (anti-inflammatory, antioxidant). However, chrysin is poorly soluble in water and so its bioavailability is reduced.
Aims: The aim of this research is to investigate the chrysin solubilization capacity of different β-cylcodextrins derivatives and compare their biological activities to each other's.
Methods: Chrysin-cyclodextrin complexes were produced by liophylisation in different molar ratios. Phase-solubility test was performed with β-, (BCD) Hydroxypropyl-β-, (HPBCD) Sulfobutylether-β-, (SBEBCD) and Randomly-methylated-β-cyclodextrin (RAMEB) and the concentration of dissolved chrysin was determined by HPLC method. Cytotoxicity of the complexes was tested by MTT test and the anti-inflammatory action was studied by immunofluorescence, labelling the p65 subunit the inhibition of NF-κB pathway activation. The antioxidant capacity of complexes was determined by SOD, GPx and ORAC assay.
Results: Phase-solubility experiments showed, that each cyclodextrin increased the solubility of chrysin, but there were significant differences among the derivatives. SBEBCD, RAMEB and HPBCD were able to effectively solubilize chrysin, while BCD showed limited capacity. MTT test revealed that up to 100μM concentration the examined complexes were not cytotoxic on Caco-2 cells. Investigating the NF-κB inflammatory pathway we found that the 1:1 Chrysin-Cyclodextrin complexes decreased more efficiently the TNF-α-induced nuclear translocation of p65. SOD activity in the cytosol after treatment with complexes show the correlation with cell permeability test results in which both 1:1 and 1:2 ratio complexes show the efficacy to improve chrysin permeation. According to ORAC assay results, it is proved that with increasing molar ratio of complexes, the solubilized concentration of chrysin is increasing.
Conclusion: In conclusion, cyclodextrin derivatives can effectively improve the water solubility of chrysin and the formed complexes are not cytotoxic in the tested concentration range. The complexes can inhibit the NF-κB inflammatory pathway, and cyclodextrins had not activated the pathway. The in vitro ORAC antioxidant test and in vivo SOD and GPx assay showed different correlation with molar ratio of complexes.

The development of a semi-solid formulation containing natural extracts as a hand-sanitizer preparation

LENDVAI, B.[1], NMAR F.[1], KOCSIS, B.[2], HORVÁTH, GY.[3], PÁL, SZ.[1], TAKÁCSI-NAGY, A.[1]

[1]Institute of Pharmaceutical Technology and Biopharmacy; [2]Department of Medical Microbiology and Immunology; [3]Department of Pharmacognosy, University of Pécs, Pécs

Background: Hand sanitization is an important step in both everyday life and health care. However, it is a general experience that this process is not always correctly performed, moreover many users are reluctant to use preparations containing synthetic materials. According to the results of hand hygiene compliance measurements, in many cases, medical personnel use gloves instead of hand sanitizer.
Aims: Nowadays, the demand for natural, plant-based preparations is increasing. Our work aims to produce a semi-solid composition containing essential oils which in addition to its favorable technological properties and applicability, can be used effectively to sanitize the hand according to European Standards [1]. Some plant-based materials have been shown to have bactericidal activity without the development of bacterial resistance [2]. Thus, the use of such a product provides new possibilities for hand sanitization.
Methods: In the first phase of the work, we designed a gel capable of delivering the components responsible for antimicrobial activity at appropriate concentrations during use without leaving a sticky or tacky residue after absorption. After formulation, examination and physicochemical tests were conducted according to the Hungarian and European Pharmacopoeias including; rheometric, dissolution and diffusion tests, microscopic examination, extensometric test, pH measurements. Next, the evaluation of bactericidal activity was performed. The effect of the prepared gel on the resident bacterial flora of the hand skin and hygiene were monitored by swab sampling for microbiological testing.
Results: Our results show that the physicochemical stability of the formulation appears promising. Moreover, it has good technological properties and applicability and has been proven to be effective against the microorganisms tested (*Staphylococcus epidermidis, Staphylococcus aureus,* and *Candida albicans* among others).

Conclusions: Results suggest that the gel can be used as an adjuvant hand-sanitizer in basic health care. It is easy and fast to use, making it more convenient to sanitize the hand of the health care personnel, for example, between two patient examinations or drug administrations.

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Synthesis of amphiphilic sialic acid derivatives

LŐRINCZ, E.B., BAKAI-BERECZKI, I., HERCZEGH, P., BORBÁS, A.
Department of Pharmaceutical Chemistry, University of Debrecen, Debrecen

Background: Influenza is a widespread disease worldwide and its pathogene is one of the 10 deadliest viruses. In 2019, WHO drew attention to the dangerousness of influenza. It can be the greatest threat for the population of the World. Therefore, development of new medications with new mode of actions against influenza is necessary and inportant. [1]. Influenza has two glycoproteins on its surface: hemagglutinin (HA) and neuraminidase (NA). HA helps the attachment of the virus on the host cell's surface, it recognizes and bonds to the terminal sialic acid molecules of the receptors on the surface of the host cells. After replication NA hydrolyses the glycosilic bond of the sialic acid moieties and helps to release the newly formed viruses. The currently used NA inhibitor are not effective enough.
Aims: Unfortunately, there are no hemagglutinin inhibitor in use, although the usage of these types of drugs could solve the problem of resistance, because if the attachment of the virus on the host cell is inhibited, the infection and mutation can not be occurred. Therefore, we decided to prepare multivalent sialic acid derivatives to trap influenza through hemagglutinin.
Methods: We have synthesized lipophilic sialic acid derivatives. As carrier molecule methyl α-D-glucopyranoside was used, it was equipped with two lipophilic chains (butyls, octyls, and decyls). Into position 6 a tetraethylene glycol chain was introduced bearing azido group and a propargylated sialic acid derivative was conjugated to this azido group by a 1,3-dipolar cycloaddition reaction.
Results: The octyl derivative is proved to be active against *influenza A* and *B viruses*.
Conclusion: In water these molecules can form aggregates, these aggregations may mimic the surface of the host cell, and they may trap influenza viruses. In other way they could inhibit the attachment of the virus by the possible interaction with the lipid bilayer of the host cell or the virus.

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

MERCZEL, S.[1], VIDA, R.G.[2], TASI, T.[3], FITTLER, A.[2]
[1]Institute Pharmacy, Somogy County Moritz Kaposi General Hospital, Kaposvár; [2]Department of Pharmaceutics and Central Clinical Pharmacy, University of Pécs, Pécs [3]MEDICOPUS Nonprofit Health Service Provider Ltd, Kaposvár

Background: 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. Three product samples (multi-dose eye drops, preserved with benzalkonium chloride) were purchased for quality control tests.
Aims: Our aim was to develop a method for the determination of the quality of online purchased multidose 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. Six HPLC methods described in the literature proved to be suitable for the co-examination of active substances and two for the determination of the microbiological preservative in these solutions. 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: We first had to set up the HPLC method and test the eye drops. Subsequently, the total amount of samples were used for sterility testing. Sampling was performed in A grade, aseptic space because of later test of sterility. Liquid chromatography was performed on a WATERS STERISORB ODS1 C18 (5µm, 25cm x 4,6mm) column and the mobile phase consisted of an acetonitrile: phosphate buffer (pH 2.5): methanol (5:85:10 v/v/v) mix and a flow rate of 1.0ml/min and equipped with a Shimadzu SPD-20AV DUAL UV/VIS detector at two fixed wavelengths (210.0 nm and 250.0nm). The retention times for dorzolamide hydrochloride and timolol maleate were found to be 8.5 and 3.2min (250nm). The benzalkonium chloride gave two peaks at 11.5 and 23.4min. Membrane filtration technique was used for sterility testing. Validation of HPLC and microbiological assays was performed using original multi-dose formulations purchased from a community pharmacy in addition to the reference standards according to the ICH guideline. The HPLC and microbiological analysis are in progress.

Conclusion: The HPLC procedure was successfully applied to the simultaneous determination of these compounds in pharmaceutical preparations. Our results will demonstrate the medication safety risks of internet purchased ophthalmic medications and the potential public health concerns of illegal internet market of pharmaceuticals.

Non-genomic actions of steroid hormones on pregnant uterine contractions: an in vitro study

MIRDAMADI, M., GÁSPÁR, R.
Department of Pharmacology and Pharmacotherapy, University of Szeged, Szeged

Background: It has proven the prompt action of steroids is independent of their Genomic pathways, the correct mechanism of this fast-action which called as non-genomic pathway still needs to do more investigation.
Aims: Was investigate these actions of 5 types of steroid hormones on pregnant uterine contraction in rats.
Methods: Uterine tissues from 22-days-pregnant SPRD rats were dissected and mounted in an organ bath. Myometrial contractions elicited with KCl then cumulative dose-response of 17β-estradiol, progesterone, testosterone, fludrocortisone, and dexamethasone were recorded and statistically analyzed with unpaired t-test. In another set of experiments, the samples were pre-incubated with the following drugs before stimulation with KCl: (1) with cycloheximide, a protein synthesis inhibitor and actinomycin D, a transcriptional inhibitor for 30 minutes. (2) with the specific steroid hormone receptor antagonist of different types of steroids for 10 minutes; fulvestrant for 17β-estradiol, spironolactone for fludrocortisone and mifepristone for progesterone, and dexamethasone. (3) with mifepristone for all types of steroids. later, the endothelium of uterine tissues was removed by scratching, the experiment repeated to observe the effect of myometrium alone.
Results: Both 17β-estradiol and testosterone showed 60% while dexamethasone, fludrocortisone, and progesterone had 28, 24 and 40% relaxing effects, respectively. The remove of the endothelium or use of Actinomycin D and cycloheximide did not change the responses of any steroids. Specific antagonists did not block the effects of testosterone, fludrocortisone, and progesterone. Mifepristone (10^{-8}M) inhibited the effect of dexamethasone. Surprisingly, a high concentration of mifepristone (10^{-6}M) blocked the effects of all steroids, except progesterone.
Conclusion: In the 30min period of the experiment, we observe all types of steroids had a relaxing effect. the actions are not related to the genomic pathway and located on the pregnant myometrium. 17β-estradiol and testosterone have the strongest effect, while the actions of dexamethasone, progesterone, and fludrocortisone are moderate. Their actions (except dexamethasone) were resistant to their specific antagonists. Mifepristone seems to be a general blocker of non-genomic action of steroids (except progesterone). Non-genomic, prompt actions of steroid hormones inhibit pregnant uterine contractions, it might be a key for future investigation and be beneficial during preterm birth.

Lipid peroxidation and ibuprofen metabolism in hyperglycemic rats with *in-vitro* oxidative ibuprofen modifications

MOHAMMED, H., ALMÁSI, A., MOLNÁR, S., PERJÉSI, P.
Institute of Pharmaceutical Chemistry, University of Pécs, Pécs

Background: Hyperglycemia considered as a source of diabetic complications via induction of oxidative stress generating a higher rate of reactive oxygen species (ROSs). They have a significant role in the onset of both types of diabetes, and ROSs can oxidize non-enzymatic, endogenous and exogenous molecules. ROSs react with sensitive cellular macromolecules (nucleic acids, lipids, proteins) and exogenous (e.g. drug) molecules to form characteristic products. The latter is not well studied in the diabetic environment.
Aims: This study is an effort to better understanding of how oxidative stress develops diabetic complications in STZ-treated rats, and to what extent oxidative stress modifies the metabolism of ibuprofen (IBP), as an example of an exogenous compound. In addition, in vitro non-enzymatic oxidation of IBP modification was studied.
Methods: STZ-treated (hyperglycemic) rats were studied for four weeks. Then, the level of peroxidation was examined by means of a) UV-Vis determination of malondialdehyde (MDA), and b) HPLC-UV-Vis determination of lipid peroxidation (LP) generated carbonyl compounds. Glutathione (GSH) level was determined by UV-Vis method. For comparison, the oxidative metabolism of IBP was studied by analysis of the intestinal perfusate of the rats. In addition, in-vitro Fenton and Udenfriend tests were performed to evaluate non-enzyme-catalyzed oxidation of IBP. The structure of the investigated derivatives and products was proved by LC-hrMS.
Results: The MDA level was slightly increased in the 1st week of the liver and the small intestine and decreased in the 2nd and 4th week of the small intestine. GSH level of the small intestine and the liver was significantly elevated in all groups, but the 4th-week

initiates to become falling. While MDA and HNE (DNPH-derivatives) could not be identified. In general, chromatograms of the liver and the small intestine extracts were not significantly different from that of the control samples. In vitro, 1-OH-IBP, 2-OH-IBP and IBP-COOH were formed in the Fenton reactions and Udenfriend hydroxylation test.
Conclusion: Hyperglycemia can promote ROS accumulation through different metabolic pathways. The results of the 1st week (increased MDA) gives evidence of increased ROS production. Lack of increase in the secondary carbonyl LP products indicates that the oxidative and reductive enzymes effectively transform them in the liver and small intestine. The increased GSH levels can be the result of the increased ROS formation, which induces GSH biosynthesis.

Do newly initiated drug treatments pose real risk to chronic drug users? Prospective drug-drug interaction survey among hospitalized patients

MOHÁCSI, B.[1], BÁLINT, D.[2], KUPCSIK, Z.[2], BENKŐ, R.[1], SOÓS, GY.[1], MATUZ, M.[1]
[1]*Department of Clinical Pharmacy, University of Szeged, Szeged*
[2]*Bács-Kiskun County Hospital, Kecskemét*

Background: Medical treatment is often initiated in patients admitted to the hospital. Adhere to the „nil-nocere" concept, assessment of drug-drug interactions and avoidance of iatrogenic harm is an important patient and drug safety issue. On the other hand, only minority of drug drug interactions are clinically relevant and some of them are beneficial. Clinical pharmacy services include assessment of drug-drug interactions upon initiation of new medicines.
Aims: Assessment and evaluation of drug-drug interactions between newly initiated drugs and between newly initiated and chronic drugs.
Methods: Thirty-thirty consecutive patients admitted to the orthopaedics and oncology units in 2019 August were included in the study. Medication use were retrieved from patient charts. Interactions between active agent were analysed by the Lexicomp® Drug Interactions module of the UpToDate database. Drug-drug interactions were classified into five categories (A, B, C, D, X) depending on the severity of the possible interaction.
Results: Data of 59 patients were analysed. Overall, study patients took 641 different drugs (on average 10.9 drugs/patient) of which 70% (451 drugs) were chronic drugs. Polypharmacy (use min. 5 drugs concomitantly) was present in 91.5% of patients. We detected 741 possible interactions which belonged to 57 patients. Most drug-drug interactions (389, 52.3%) occurred between chronically used medications. Only 14 interactions were rated as X-category (avoid combination) and affected 11 patients. Out of these 14 interactions, only one interaction affected a newly initiated drug treatment with modest reliability. In the other 13 cases, the two interacting chronic drugs were used parallel without any clinical problem.
Conclusion: Although possible drug-drug interactions affected almost every patient, but number of clinically relevant, possibly severe drug-drug interactions were limited and has not been clinically manifested. Interaction databases detects many irrelevant, insignificant interactions.

Measurement and evaluation of pre- and postoperative pain relief in surgery of herniated disc

MOLNÁR, N., LÉVAI, B., BUCHHOLCZ, G.
Central Clinical Pharmacy, University of Debrecen, Debrecen

Background: Despite the availability of modern analgesic drugs, tools, techniques, the pain management is a major challenge. In the case of surgical interventions, a proper pain relief has an important role in particular the postoperative analgesia. Use of analgesic techniques not only improve the patient's well-being and general condition but also contribute healing by alleviating the body's inflammatory and mechanical reactions.
Aims: All neurosurgical interventions, especially for spinal surgeons, are characterized by the constant presence of increased pain in the preoperative period. Thus, analgesia is important both in the pre-operative and post-operative stages. Our aim was to review, evaluate and optimize the protocol for chronic pain therapy in case of the pre- and postoperative conditions.
Methods: During the 5 months of research, we could chance to approach to he patient interview and medication history. We have been informed about chronic pain and the used pain management techniques, furthermore, measure the pre- and postoperative pain on the day of surgery and for another two days using a visual analogue scale (VAS) and pain-related questions. We have studied the drugs taken by patients previously, the active pharmaceutical ingredients (API), the dose, the administration's time of premedication and analgesics used during the intraoperative and postoperative periods. In addition, we evaluated the effects of drugs taken during the postoperative period and contributed to the development of post-operative pain management techniques.
Results: The patient's pain perception is positively influenced by the appropriate therapy. Continuous,

empathic management of pain sensation improves patient adherence and compliance. Proper pain relief can reduce the days of hospitalization to three or two days. Furthermore, the use of intravenous analgesics could be reduced only for the day of surgery, then pills can be used. These lead to lower costs.

Conclusion: There is no general analgesic solution that can be used by all patients, it needs to be personalized. Initial surveys, clinical pharmaceutical intervention, and ongoing feedback are crucial in the development of individual therapies. This also means that the monitoring and method of questioning, the techniques used and protocols need to be continuously improved.

Analysis of HCTZ use and the skin cancer risk among the patients of Semmelweis University, Dermatological Department

NAGY, D.[1,2], TÓTH, V.[2], TÓTH, B.[2], SOÓS, GY.[3]
[1]University Pharmacy Department of Pharmacy Administration; [2]Department of Dermatology, Venereology and Dermatooncology, Semmelweis University, Budapest; [3]Department of Clinical Pharmacy, University of Szeged, Szeged

Background: A recommendation was issued by the EMA on 1st October 2018 to improve awareness about the increased risk of certain non-melanoma skin cancer (NMSC) types (basal cell carcinoma and squamous cell carcinoma) following higher cumulative doses of hydrochlorothiazide. Various epidemiological observations suggest a correlation between cumulative dose of hydrochlorothiazide (HCTZ) exposure and the increased risk of NMSC. Though results are ambiguous, they support a cumulative dose-dependent assotiation between HCTZ and NMSC.

Aims: This study aims to identify therapeutic HCTZ exposure in the anamnesis of patients with non-melanoma skin cancer (BCC, SqCC) admitted to the Department of Dermatology, of Semmelweis University and also assesses whether HCTZ use imposes an enhanced risk of NMSC.

Methods: Throughout 2019, a case-control study was conducted on patients whose therapy was managed in our Department of Semmelweis University. The study compared patients with non-melanoma skin cancer (BCC, SqCC) with cancer free subjects, who were also HCTZ users.

Results: Over the period 847 patients have undergone surgical procedures, 657 of whom suffer from basal cell carcinoma (BCC) and 190 from squamous cell carcinoma. Those subject to HCTZ treatment after operation amount to 68 in the BCC group and 38 in the spinalioma group. 66 patients of the 1139 numbered control group receive HCTZ treatment, this concludes an odds ratio of 1.87 (95%CI: 1.31 to 2.6) in case of the BCC group and an OR=4.06 (95%CI: 2.63 to 6.27) for the spinalioma group.

Conclusion: In support and confirmation of EMA's safety consideration on medicinal products with the active ingredient hydrochlorothiazide, the study served to justify that an increased risk to developing NMSC can be distinguished among patients on long term treatment of HCTZ.

A pharmacist-led, prospective audit on antibiotic prescribing at traumatology ward

NAGY, E., BOR, A., GYIMESI, N., SÜLE, A.
Péterfy Hospital and Jenő Manninger National Trauma Centre, Budapest

Background: Our institution commenced a pharmacist-led antimicrobial stewardship service at 3 hospital wards in September 2018. After the 3-month pilot phase we extended the service to the traumatology ward.

Aims: Our aims were to document and analyse the prescribed antibiotic therapies, as well as to record the clinical pharmacist interventions and the rate of acceptance.

Methods: The prospective, interventional study was started in January 2019, and has been performed over an 11-month period. Baseline patient data, documentation of allergies, indication of therapies and circumstances of microbiological testing were collected on a paper-based audit form. Patient charts and medical records were applied as data sources. Detailed information on antibiotic therapies and the 48-72-hour revision with outcomes were also documented. Clinical pharmacist interventions (CPIs) were categorised and their acceptance were recorded. Microsoft Excel was used for data management and analysis.

Results: 77 patients were involved in our study, 41 men and 36 women (mean age was 57.7 years ± 19.2 years and 72.4 years ± 17.6 years). Overall, 81 antibiotic therapies (59 empirical and 22 targeted) were evaluated. 16 different antimicrobial agents were prescribed, the most frequent was amoxicillin-clavulanic acid (27 cases). Based on the evaluation by the infectologist and clinical pharmacist, 24 cases (30%) of all antibiotic therapies were inappropriate. Initial antibiotic therapies weren't optimal in 21 cases (26%), mainly due to the unnecessary initiation of antimicrobials in asymptomatic bacteriuria before orthopedic procedures (38% of initial inappropriate therapies). Therapeutic decisions at the revision

point were inappropriate in 28 cases (35%). CPIs were actioned in 36 cases, most frequently discontiunation of the therapy (43%) and parenteral-oral conversion of the therapy (25%). The overall rate of acceptance was 64%.

Conclusion: The audit plays a crucial role to highlight inappropriate practice on antibiotic prescribing and gives the opportunity to the clinical pharmacist to provide continuous and prompt feedback to the prescribers. Their different professional insight can further improve appropriate antibiotic usage.

Anticancer activities of herbal sesquiterpenes of *Neurolaena lobata*

NAGY, N.[1], BÓZSITY, N.[1], SCHELZ, Z.[1], VASAS, A.[2], HOHMANN, J.[2], KRUPITZA, G.[3], ZUPKÓ I.[1]

[1]*Department of Pharmacodynamics and Biopharmacy;*
[2]*Department of Pharmacognosy, University of Szeged, Szeged;*
[3]*Clinical Institute of Pathology, Medical University of Vienna, Vienna*

Background: Cervical cancer is a leading malignancy in women mainly with underlying *human papillomavirus* (*HPV*) infection.

Aims: Sesquiterpene constituents of *Neurolena lobata L. (Asteraceae)* were tested on human cervical malignant cell lines in vitro in order to evaluate their antiproliferative, antimetastatic and proapoptotic effects.

Methods: The antiproliferative effects were investigated with the MTT assay, IC50 values were determined on three cervical cancer cell lines with different *HPV* status (SiHa, HeLa, C33A). Tumor selectivity was examined by using fibroblast cells (NIH, MRC-5). The migratory capacity of tumor cells was analyzed by the wound healing assay, the migration of the cells into the wound site was visualized by phase-contrast inverted microscope. Images were taken by a CCD camera at definite intervals and the rate of migration was calculated according to the rate of wound closure by ImageJ software. Invasive features of the cells were investigated by Boyden-chamber assay on HeLa cells. The number of cancer cells that invaded the Matrigel-coated membrane were assessed after crystal violet staining under phase-contrast microscope. Cell cycle analysis was performed by flow cytometry in order to further elucidate the antitumor effects of the tested sesquiterpenes.

Results: Two of the twelve tested compounds showed pronounced antiproliferative effects with significant tumorselectivity IC50 values varied between 1.83-8.14μM). SiHa, an *HPV* 16-positive epithelial cervical cell line was the most responsive to the treatment. LOB-48, the most effective sesquiterpene component inhibited the cell migration and invasion in concentration dependent manner. According to the cell cycle analysis, LOB-48 slightly elevated the cell number in the hypodiploid phase and altered the distribution of the different subpopulations.

Conclusion: Our results revealed the in vitro antitumor effects of sesquiterpenes isolated from Neurolaena lobata and confirm its proper utilization in traditional medicine as an anticancer drug. The tested sesquiterpene constituents can be candidates for the design of new anticancer agents.

Chemotherapy extravasation management

NAGY, T.M., KOCSÁN, R., BUCHHOLCZ, G.
Central Clinical Pharmacy, University of Debrecen, Debrecen

Background: Extravasation of chemotherapy which is defined as the accidental leakage of anti-cancer drugs from the vein into the surrounding tissue at the injection site and can result in severe and irreversible local injuries. Multiple factors play a role in the potential occurrence of extravasation, including the volume, contact time, antineoplastic agent properties and individual patient characteristics, such as the condition of peripheral veins.

Aims: The main goal of our present work was to improve patient safety and medical care by reducing the risk of extravasation, to provide evidence-based guidance on all aspects of extravasation and educate staff consistently on early preventative measures.

Methods: Local protocol for the prevention and management of extravasation is in accordance with the latest scientific literature.

Results: Providing an extravasation kit, available at the ward, and by implementing guidelines in the practice setting, nurses' up to date knowledge in the treatment of intravenous cytotoxic chemotherapy is ensured. The extravasation kit – provided by the pharmacy – contains documentation forms, such as instructions for use, extravasation form, antidotes and other necessary materials (e.g. sterile syringes, cannulas, cold-hot packs) for the immediate management of a chemotherapy extravasation.

Conclusion: Keeping in mind that the most important approach in order to minimize the consequences of extravasation is prevention, it is crucial that an extravasation is recognized and diagnosed promptly, since delays in the treatment increase the risk of necrosis. Hence patient awareness, modern port devices, medical team experience and the presence of clinical pharmacists play a key role in reducing frequency and severity of extravasations.

Antibacterial activity of domestic acacia, lime and sunflower honeys

NAGY-RADVÁNYI, L.[1], BALÁZS, V.L.[1], KOCSIS, B.[2], KOCSIS, M.[3], FARKAS, Á.[1]
[1]Institute of Pharmacognosy; [2]Department of Medical Microbiology and Immunology; [3]Institue of Biology, University of Pécs, Pécs

Background: With the unnecessary and irresponsible use of antibiotics the incidence of resistant bacteria strains has increased nowadays, hence also in Hungary, antibiotic resistance poses one of the highest patient safety risks. Honey has been confirmed to inhibit bacteria proliferation, thus it can provide an alternative solution for the treatment of resistant infections. The antibacterial effect of honey is mostly attributed to the presence of H_2O_2 and the bacteriostatic properties of the antioxidant compounds. A large proportion of bacterial infections are due to the formation of biofilms, which need to be reduced or destroyed in order to ensure the effectiveness of the treatment.
Aims: The aims of our research were to verify the botanical origin of the unifloral honey varieties and to determine the extent to which the botanical origin influences their antimicrobial effects, including their anti-biofilm activity.
Methods: The exact botanical origin of the unifloral honeys (purchased as acacia, sunflower and lime honey) was determined by means of microscopic pollen analysis. The antimicrobial effects against bacteria causing upper respiratory tract infections (e.g. *Pseudomonas aeruginosa*, *Streptococcus pneumoniae*, *Haemophilus sp.*) were tested by in vitro microbiological methods. Our pilot experiments were carried out with agar diffusion test, then the biofilms were cultured on 96-well polystyrene microtitre plates and the inhibitory effect of honey on bacterial biofilm formation was revealed with crystal violet assay.
Results: Microscopic pollen analysis confirmed the botanical origin of the various honey samples, the tested honeys corresponded to the variety indicated on the packaging. Different honeys inhibited bacterial growth to a different extent in the pre-experiments, and we received similar results also in hindering biofilm formation. The degree of inhibition was influenced by the composition and botanical origin of the particular honey types.
Conclusion: It has been observed that the tested unifloral honey varieties were able to reduce the biofilm formation in case of a number of bacteria involved in respiratory infections. The introduction of honey, complementary to antibiotics can have a significant role, as it achieves its antibacterial effect on several points of attack.

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The usage of topically administered corticosteroids and their dilutions in different creams and ointments in the Hospital of Szekszárd

NAVRECZKI, Á., HATHÁZI, A., KARAGITY, E.
Hospital Pharmacy, Balassa János County Hospital, Szekszárd

Background: Certain dilutions of topical corticosteroids are part of the most often used treatments in the Department of Dermatology at the Hospital of Szekszárd. These ointments and creams have anti-inflammatory, vasoconstrictive and antiproliferative effects. Due to these properties, "topical steroid dilutions" are used to treat allergic contact dermatitis, psoriasis, atopic dermatitis (eczema) and intertrigo. Physicians prescribe in our region corticosteroids diluted with different types of ointment bases so in spite of the lack of this topic's popularity, it would be really necessary to emphasize its importance.
Aims: The aim of this study is to help dermatologists and pharmacists find their way amongst the uncountable variations of "topical steroid dilutions" by discussing the mixtures used in our Hospital.
Methods: Consultation with dermatologists, reviewing of both English and Hungarian literature, collection and analysis of prescriptions of community pharmacy Ezüst Kígyó.
Results: During the data collection we found that not only the concentrations of these mixtures vary but they are also prescribed in many forms (pastes, ointments, creams, etc.). The most often used vehicle is Cremor refrigerans FoNo VII. The physicians prescribe one or two tube topical corticosteroid (Flucinar, Elocom, etc.) with Cremor refrig grammata 100 or ad grammata 100/200. Sometimes are used borax in order to killing germs. There is a pasta with one tube Elocom to treat the intertigo. A pediatrist prescribe a mixture with Ung. hydrophil. nonion, Ung. emolliens and Advantan 1:1 ratio. To the better penetration physicans use Unguentum glycerini and stearini, sometimes Acidum salicylicum or Ung. ad vulnera FoNo VII. in different concentrations.
The success of the treatment depends on many factors such as the skin problem, the properties of the semi-solid bases that the prescribed corticosteroids are mixed in and the duration of the treatment. According to the latest reports the dilution of ointments containing corticosteroids does not reduce the risk of adverse effects and we also have to consider the fact

that without related clinical studies we can not be certain of the presence of molecular interactions within these new compositions. When it comes to dispensing medications, pharmacists should focus more on providing relevant information to the patients at community pharmacy – in relation to certain preparations. Consulting with dermatologists would be really important in order to clarify any upcoming uncertainty when dispensing these diluted preparations.

Conclusion: Due to the lack of evidence based knowledge in this field we can say that these dilutions of topical corticosteroids are presumably not the best option to treat cutaneous diseases, but years of medical experience seem to prove that some of these preparations have their role in dermatological treatments. But sometimes the best way is applying creams of FoNo as moisturizing products and than the topical corticosteroid in monotherapy.

Quality by Design-based development process of resveratrol-enclosing intranasal liposomes

NÉMETH, ZS., DOBÓ, D.G., PALLAGI, E., CSÓKA, I.

Institute of Pharmaceutical Technology and Regulatory Affairs, University of Szeged, Szeged

Background: Resveratrol, a polyphenolic stilbene, is under investigation to be used for the prevention and treatment of Central Nervous System (CNS) diseases (Parkinson's and Alzheimer's disease) due to its antioxidant property [1]. The chemically unstable compound has poor water solubility and can easily degrade by high temperature, UV lights, pH changes, and enzymes. However, the enhancement of its absorption by the use of liposomes can be an overcome on the low oral bioavailability, delay the drug release and reach better stability. Intranasal application, as an alternate 'nose-to-brain' administration route, means a way to reach the brain without the limitations of the blood-brain barrier. The application of the Quality by Design (QbD) method, a new quality management procedure, is adopted more and more times in the field of pharmaceutical developments to rationalize the study design [2].

Aims: Our research goal was to establish a development process for a liposomal resveratrol-containing formulation for brain target and nasal administration. Our work presents how to apply the risk-focused QbD approach in the development phase of a research project.

Methods: By the application of the QbD-based approach, the quality target product profile was defined, the critical factors were selected and a risk assessment (RA) was performed. Based on the results of the RA, the liposome preparation (lipid-film hydration method) was designed and the necessary instrumental investigations to check the process were planned.

Results: The determination of the important features and parameters (QTTPs, CQAs, and CPPs) provides a holistic network of information that can be useful to achieve a more effective experimental design.

Conclusion: The results proved that the collection of the proper information combining with the optimization and the rationalization of the required experiments and measurements can improve the development process of the liposomal formulations.

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Results of antibiotic policy development at the National Institute of Clinical Neuroscience

NYESTE, ZS.[1], GYURCSÁNYI, A.[1], KOROM, J.[1], BUDAI J.[2]

[1]National Institute of Clinical Neurosciences, [2]South Pest Central Hospital-National Institute of Hematology and Infectology, Budapest

Background: Antibiotic Policy (AP) of the National Clinic of Neuroscience (OKITI) was approved in 2011. In recent years, antibiotic use has been steadily increasing in both days of treatment (DOT) and value cost. The reasons for the increase and the necessary measures were taken in spring 2018 on the recommendation of the Institute for Infection Control and Antibiotics (IIAB). One major change in Antibiotic Policy is the renewal of the antibiotic prescription sheet. The purpose of the poster is to present the results of the period since the introduction of the Antibiotic Policy on May 1, 2018.

Aims: Description of OKITI AB policy owing to improvement of antibiotc therapy.

Methods: Evaluation of OKITI antibiotic use, and processing of antibiotic prescription sheets.

Results: Close cooperation between IIAB members. We were able to control antibiotic orders with the help of a hospital-based infectologist. A pharmacist checks and dispense the antibiotics. As a result of this collaboration, we have been able to stop the increasing use of antibiotics (both both days of treatment and in value) for years. Following the recommendation of the European Medicines Agency (EMA), the use of fluoroquinolone has decreased at institutional level (only an infectologist can initiate fluoroquinolone therapy).

Conclusion: Antibiotic use (in value cost) is a significant part (10 %) of the cost of medicine for hospitals. A well-working antibiotic management team can streamline usage, reduce costs, and stop the rise in antibiotic resistance.

Experiences of implementing antimicrobial stewardship in the University of Debrecen

OLÁH, A., VIRÁG, M., BIRÓ, K., BUCHHOLCZ, G.
Central Clinical Pharmacy, University of Debrecen, Debrecen

Background: In the last two decades the emergence and spread of antibiotic resistance, in other words the ability of bacteria to resist the action of an antibiotic, has become a recognized global problem. Antibiotics are frequently used inappropriately or when they are not needed.
Aims: The primary goal of antimicrobial stewardship is to optimize the use of antibiotics to prevent the development and spread of antibiotic-resistant bacteria and improve clinical outcomes.
Methods: Based on Regulation No 32/2018, the Institutional Infection Control and Antibiotic Committee has determined the list of controlled antibiotics and the multidisciplinary team in charge of antibiotic stewardship was established. 21 out of 47 antibiotics used in Clinical Centre are regulated the physician, the infectologist, the microbiologist, the clinical pharmacist and the representative of management are responsible for the operation of the system. Certain antibiotics can only be used documented approval by the infectologist. It is compulsory to fill out electronic forms to order the restricted antibiotics and after the therapy is over. Antimicrobial pharmacist as key person supervises the therapy including dosing, interactions, incompatibilities and drug allergies to ensure adequate therapy. Members of the antibiotic stewardship team assess the cases, oversee adherence to the local protocol, evaluate the antibiotic consumption (DDD) and monitor the changes of bacterial resistance. The results provide information for further intervention.
Results: Rationalizing the use of antibiotics was successful. Antibiotic prescribing practice, the local resistance conditions and the cost-efficiency were changed which confirm the necessity of antibiotic stewardship.
Conclusions: With the help of evidence-based antibiotic use, therapy can be optimized, and hospital costs can be decreased. The system contributes to preventing development of antibiotic-resistant bacteria and save the efficacy of antibiotics.

Comparative study of the *in vitro* toxicity of artificial tears and ophtalmic preservatives in a human conjunctival cell line

OLÁH, G., HALMOS, G., VASS, A., VINCZE, R.
Department of Biopharmacy, University of Debrecen, Debrecen

Background: Dry eye disease (keratoconjunctivitis sicca, KS) is one of the most common ophthalmic diagnoses. Although the development of KS does not lead to the development of a life-threatening condition, it can significantly impair the patient's quality of life and thus his or her ability to work. In many cases, the composition of KS formulations is determined by market needs rather than by strict professional expectations. There is currently no study comparing the cytotoxicity of artificial tears and their preservatives in community pharmacies on a conjunctival model.
Aims: The aim of our work was to set up a new in vitro experimental model that can compare artificial tears and their preservatives, thus helping the daily work of professionals. As well as analyzing national sales of artificial tear.
Methods: The effects of various treatments were investigated in vitro using the MTT assay on the Chang CCL-20.2 human conjunctival cell line. We compared our results with national sales of teardrops.
Results: As a result, the formulations and their preservatives can dramatically affect the viability of the Chang CCL-20.2 human conjunctival cell line. Analysis of sales data pointed to a serious deficiency in pharmacy patient information.
Conclusion: Based on our findings, many of the currently available artificial tears may cause a long-term risk to patient's health. Therefore, it would be important to review them and optimize their composition.

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The effect of restrictions on fluoroquinolone anitbiotics usage in hospital care

PAP, R., STEFÁNOVITS, E., KASZÁS, I., BEZSILA, K.
Buda Hospital of the Hospitaller Order of Saint John of God, Budapest

Background: In 2019 EMA's human medicines committee (CHMP) confirmed that the use of the fluoroquinolone (FQ) antibiotics should be restricted because of disabling and potentially permanent side

effects. Hungarian National Institute of Pharmacy and Nutrition (OGYÉI) released in April 2019 direct healthcare professional communication (DHPC) for safer use of fluoroquinolone antibiotics and all Summary of Product Characteristics (SPCs) were revised.
Aims: Monitoring and improving fluoroquinolone antibiotics usage in the Buda Hospital of the Hospitaller Order of Saint John of God (Budai Irgalmasrendi Kórház) regarding changes in SPCs and DHPCs.
Methods: Analysis of fluoroquinolone antibiotic usage in the hospital, especially in those units where FQs are frequently used. We made a retrospective analysis of patient documentation before and after DHPC release whether FQ usage was appropriate. We designed a questionnaire to collect all relevant information.
Results: Results show that despite the restrictions on indications, the usage of FQ antibiotics in our hospital is still high. We believe that DHPCs alone may not be effective enough to change strong prescription habits.
Conclusion: We decided to do some training for prescribing doctors to reach appropriate fluoroquinolone antibiotics use, to improve patient safety, save cost and disburden the nurses with the timely switch from parenteral to oral dosage form.

Development and characterization of human serum albumin glycoconjugates containing biopolymers

PÁPAY, ZS.E., KIRÁLY, M., JAKAB, G., KISS, B., LUDÁNYI, K., ANTAL, I.
Department of Pharmaceutics, Semmelweis University, Budapest

Background: Proteins, due to their interfacial structure, are widely used as emulsifiers in the food industry and are gaining interest in the pharmaceutical research. However, proteins are very sensitive to environmental stresses, protein glycoconjugates has improved functional properties such as emulsifying ability, thermal stability and foaming capacity. Glycation, commonly known as Maillard reaction, is a simple, spontaneous and naturally occurring „green" reaction. This non-enzymatic conjugation takes place between reducing sugars and available amino groups of a protein in certain conditions of temperature and humidity. Human serum albumin was chosen as model protein due to its importance in the modern drug delivery systems nowadays. Biopolymers such as polysaccharides derived from plants are widely used in due to their biocompatibility and safety.
Aims: The aim of this study was to prepare glycated human serum albumin with branched and linear chain polysaccharides such as galactomannan (locust bean gum, LBG) and sodium alginate (ALG). The glycated products were further characterized using fluorescence spectroscopy, gel electrophoresis, DSC, XRD and FTIR, furthermore, emulsifying ability was also tested.
Methods: The human serum albumin and biopolymers were added together in distilled water in 1:1, 1:2, 1:3 and 1:6 molar ratios and freeze dried in order to remove water. After that conjugates were prepared by at 60°C and 80% relative humidity for 72 hours.
Results: The Maillard reaction between HSA and polysaccharides was verified by fluorescence spectroscopy. The intensity of amine IR absorptions was increased while that of the amide I and II bands were significantly decreased on the specta of HSA conjugates which is more prominent at the 1:6 molar ratio. The fluorescence emission intensity of Trp 212 residue of HSA was significantly decreased on the specta of both conjugates due to the conformation changes of the protein.
Conclusion: It can be concluded that glycation was successful and the potential use of Maillard reaction in pharmaceutical industry could be assumed.

Histological evaluation of plants based on ethnomedicinal data in Transylvania

PAPP, N., FARKAS, Á.
Department of Pharmacognosy, University of Pécs, Pécs

Background: Although medicinal plants are of primary importance in many regions of Transylvania, we have little information on the histological traits of their drug parts. Based on earlier ethnomedicinal surveys (2007-2019) in Transylvania, four plant species were selected for complex analyses including histological investigation of their parts applied in traditional treatments.
Aims: Our goal was to provide anatomical data of the medicinally important organs of *Anthyllis vulneraria L.*, *Lathyrus tuberosus L.*, *Lysimachia nummularia L.*, and *Tanacetum balsamita L.*
Methods: Plant samples were collected from the typical habitat of each species. Preceding embedding in artificial resin, samples were dehydrated in ascending ethanol series. Cross sections were cut with a rotary microtome, and stained with toluidine blue. Light microscopic investigation was performed with a Motic 102M microscope, and micrographs were taken with Motic Images Plus 2.0.
Results: The tuber of *L. tuberosus* is covered by periderm, below which groups of sclerenchymatous cells are scattered. A substantial portion of the tuber is filled with nutrient storing parenchyma. The cylin-

drical stem of *A. vulneraria* is characterised by the presence of vascular bundles in addition to continuous vascular tissues, a significant portion of pith parenchyma and the presence of calcium oxalate druses. The petiole contains four minor and a single central vascular bundle, the latter one supported by sclerenchyma. The dorsiventral leaf bears uniserial, non-branching cover hairs on the abaxial side. Mesomorphic stomata are located on the adaxial surface. The cross section of the stem in *L. nummularia* is four-cornered; the epidermis is formed by circular, isodiametric cells with papillae, thickened cell walls and cuticle; and vascular tissues form a continuous ring. Mesomorphic stomata and capitate glandular hairs appear on both sides of the dorsiventral leaves. Essential oil cavities can be observed in the mesophyll. The dorsiventral leaves of *T. balsamita* are characterised by the presence of capitate glandular hairs, which are responsible for essential oil secretion.

Conclusion: Our research provided the first detailed histological description of the drug parts of four medicinal plants widely used in Transylvania. Our results can contribute valuable data also to the phytochemical studies of the species, by revealing the exact site of active compound synthesis.

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Comparative ethnomedicinal survey in the Homorod Valley, Transylvania

PAPP, N.[1], MIHALOVITS, F.[1], FILEP, R.[1], PURGER, D.1, CZÉGÉNYI, D.[2]

[1]Department of Pharmacognosy, University of Pécs, Pécs; [2]Hungarian Department of Ethnography and Anthropology, Babeş-Bolyai University of Cluj-Napoca, Cluj-Napoca, Romania

Background: Homorod Valley, region of Székely Land in Transylvania has been studied for ethnobotanical data earlier (e.g. Gub 1994) documented the traditional knowledge of Székely people of 14 villages.

Aims: The aim of our work was to collect and compare ethnomedicinal data obtained from 10 villages of Homorod Valley. In data comparison, similarity and differences were taken into consideration.

Methods: Ethnobotanical survey was conducted in Aldea, Bădeni, Călugăreni, Comănești, Ghipeș, Locodeni, Mărtiniș, Petreni, Sânpaul, and Orășeni (2013-2019). These settlements are 2-15 km far from each other belonging to Mărtiniș as region centre. Semi-structured interviews were performed with ~150 informants aged from 14 to 99. Interviews focused on the local name, collection time and place, used parts, preparation and administration, as well as treated disorders of plants based on traditional elements. Data were arranged in tables comparing terminology, application and indications of the mentioned plants in each village. In addition, our records were compared to those of earlier works to indicate overlapping, disappeared and new records. Plants were also compared to medicinal plants of Pharmacopoeia Hungarica VIII (Ph. Hg. VIII) to highlight scientifically proved data.

Results: Total number of records of plants varied from 42 to 73/village. Altogether 12 plants were described as overlapped species in all settlements, and 36 ones official in Ph. Hg. VIII (e.g. *Achillea millefolium*, *Calendula officinalis*, *Plantago lanceolata*). Some species were documented only in 1-1 village, e.g. *Lamium album*, *Morus alba* (Mărtiniş), *Echium vulgare*, *Orchis morio* (Sânpaul), *Helleborus purpurascens* (Orășeni), and *Atriplex hortensis* (Aldea). Altogether 10 plants were mentioned of other origin, e.g. of books and media sources (e.g. Capsella bursa-pastoris, *Silybum marianum*, *Melilotus officinalis*), and 3 new species cultivated from urban environment (Aloe sp., *Lavandula angustifolia, Rosmarinus officinalis*). Compared to earlier data, majority of our records overlaps with those published in 1990s. Among disappeared records, e.g. use of *Aegopodium podagraria, Daphne mezereum*, and *Inula helenium* can be mentioned.

Conclusion: This survey underlines the importance of ethnomedicinal collection in this region, and of data comparison as a case study in ethnobotanical researches.

This work was supported by a grant from the OTKA (Hungarian Scientific Research Fund, K 127944).

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The treatment of anhedoniae with antidepressants and ketamine

PETSZULAT, C.[1], TÖRÖK, D.[1], GONDA, X.[2,3], JUHÁSZ, G.[1,3], BAGDY, GY.[1], PETSCHNER, P.[1]

[1]Department of Pharmacodynamics; [2]Department of Psychiatry and Psychotherapy, Semmelweis University, [3]SE-NAP 2 Genetic Brain Imaging Migraine Research Group, Budapest

Background: Anhedonia is one of the main symptoms of depression, which is generally associated with a decreased ability to feel joy and pleasure. It affects approximately 37% of people with depression and it has different triggers, thus bit's manifestation can be different from patient to patient. Anhedonia is relatively difficult to treat, most antidepressants currently in use are ineffective.

Aims: In most cases, the widely used SSRI treatments are ineffective, often aggravate depressive symptoms. There are new suggestions for ketamine

therapy, which is an antagonist of the NMDA receptor and has an anti-depressive effect. Several studies have mentioned ketamine to treat the symptoms of anhedonia, especially in case of decreased ability to feel pleasure there are also several evidences suggesting that substances that are targeting the glutamatergic system and affect the level of norepinephrine and serotonin are helping in the recovery from anhedonia.

Methods: I have reviewed the latest articles on anhedonia treatment and extracted the relevant results.

Results: The most studies treatment are ketamine, imipramine, fluoxetine, clozapine, and haloperidol. A study approved that fluoxetine had no effect on anhedonia, and while imipramine therapy showed effectiveness but only on certain subgroups of rats that were exposed to chronic stress. The treatment of clozapine had an effect on anhedonia but did not improve the hyporeactivity. Haloperidol also had no influence on the symptoms of anhedonia. Ketamine is proved to be effective but in many cases, there are side effects.

Conclusion: It is hard to find the perfect treatment because the level of anhedonia can be very different among people. There are good approaches in various articles, but there are still not clear enough for targeted therapy. First, we have to find an animal model that is better suited to human anhedonia. In the next step, we need more animal experiments to find new targets, but this is still a hard task. We still do not know enough about anhedonia to find the perfect treatment. Ketamine is a step in the right direction, but we need further research.

Cytotoxicity investigations of different polyethylene glycol (PEG) derivatives

PHAM, H., NEMES, D., BÁCSKAY, I.
[1]Department of Pharmaceutical Technology, University of Debrecen, Debrecen

Background: Polyethylene glycol (PEG) polymers are hydrophilic, water miscible and can solubilize many poorly water-soluble compounds. This compound has variety of applications from chemical manufacturing to medical field, depending on their molecular weight, especially in pharmaceutical industry as an excipient. PEGs are available commercially with wide molecular weight range from 200 to 10.000.000.

Aims: The aim of this study was to investigate the cytotoxicity of PEG with different molecular weight.

Methods: My experiments were performed on the Caco-2 human adenocarcinoma cell line by cytotoxicity assays including MTT and neutral red (NR) methods. They were implemented with different concentration of various PEG derivatives (based on molecular weight).

Results: PEGs with differrent molecular weight were examined at concentrations of 2%, 10%, 30% and 40%, respectively. All tests were carried out with both MTT and NR methods. The cell viability was high at 2% concentration and slighlty decreased to 70% at 10% and 30% concentrations. Finally, PEGs were seriously harmful to cells when increasing the concentration to 40%. The cytotoxicity was elevated to 50% and above at this concentration.

Conclusion: PEG are relatively nontoxic in increasing concentration to 30%. PEGs have severe effect on cell PEG if the concentration is above 30%. According to our results, we can say that PEGs are a good choice for new drug formulation because of their safety. Therefore, PEGylation has become a promising method for the delivery of traditional drugs and biopharmaceuticals due to its bioavaibility improving effect.

Study on interaction of some (E)-2-benzylidenebenzosuberone derivatives with serum albumin by spectroscopic methods and on topoisomerase inhibition

ROZMER, ZS., PERJÉSI, P.
Institute of Pharmaceutical Chemistry, University of Pécs, Pécs

Background: Some cyclic chalcone analogues, (E)-2-(4-X-benzylidene)-1-benzosuberone derivatives showed remarkable biological activity including tumor citotoxic effect.

Aims: Based on preliminary results, the biological activity of the compounds might be partially th result of non-covalent interaction between the compounds and cellular macromolecules (proteins, DNA). For a better understanding of the mechanism of action, interaction with different proteins was investigated.

Methods: The UV-Vis absorption spectra of bovine and human serum albumin titrated by selected (E)-2-(4′-X-benzylidene)-1-benzosuberones analogues solution were monitored in order to explore the structural changes of BSA and HSA caused by addition of the compounds. Their effect on the activity of the nuclear enzyme DNA topoisomerase I and II was also investigated.

Results: The results suggest a non-covalent interaction between the compounds and serum albumin, which occured via the π-π stacking between aromatic rings of chalcone analogues, and Trp residues possessed conjugated π-electrons and located in the binding cavity of serum albumin. The investigated derivatives showed weak dual inhibitory activity against DNA relaxation by topoisomerases I and II.

Conclusion: The interaction with protein and the observed moderate topoizomerase inhibitory effect might be contributing vectors of the observed cytotoxicity. The obtained results provide additional knowledge on pharmacological effect of cyclic chalcone analogues.

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Vapor chamber, a novel method for rat liver perfusion in metabolite research

SAMAVATI, R.[1], KOVÁCS, O.[1], KÖRMÖCZI, T.[2], BERKECZ, R.[2], GÁSPÁR, R.[1]

[1]Department of Pharmacology and Pharmacotherapy;[2]Institute of Pharmaceutical Analysis, University of Szeged, Szeged

Background: Hepatic steatosis in obese or non-obese patients may alter drug metabolism. As an ex vivo simulation model, isolated rat liver perfusion is used for the examination of the liver metabolism. This method has several advantages, such as the architecture of the organ is saved, compare to in vivo model higher dose of drugs can be tolerated and large number of perfusion samples can be collected.
Aims: To investigate the possible alterations of drug methabolism in hepatic steatosis. To develope a new method for rat liver perfusion (ex vivo).
Methods: After the cannulation and removal, the liver of male SPRD rats (300-320 g) was placed into the porous chamber filled with buffer vapor. Oxygenated perfusion buffer was pumped into the organ in a recirculating pattern with constant flow rate. The pressure and pH of perfusion fluid were controlled during experiment continuously. In order to monitor the liver viability, the lactate dehydrogenase (LDH) level was determined in collected samples. The liver function was investigated by pharmacokinetics determination of diclofenac (DF) and its main metabolites via targeted reversed-phase LC-MS/MS method.
Results: The viability of the perfused liver was around 2-4 hours based on the measured LDH level (max. 300U/l) in the perfusion solution and the amount of the produced bile (3-6µl/min). The dynamic alterations of the concentrations of 4′-hydroxydiclofenac (Phase I. metabolite), and diclofenac-1-O-acyl glucuronide (Phase II. metabolite) were determined in the perfusion fluid. The amounts of Phase I and Phase II metabolites were 7.7 and 11.7 folds higher, respectively at 100min as compared with at 10min after starting the perfusion.
Conclusion: A new rat liver perfusion method was successfully developed. The novelty of the method is the lack of hydrostatic pressure on the liver that may provide a more physiological condition for the organ as compared with former methods. This method seems to be proper for the investigation of drug metabolism in different hepatic conditions, including the obesity induced hepatic steatosis.

The effects of leptin, adiponectin and kisspeptin on pregnant rat uterine contractility *in vitro*

SCHAFFER, A.[1], HAJAGOS-TÓTH, J.[1], DUCZA, E.[2], GÁSPÁR, R.[1]

[1]Department of Pharmacology and Pharmacotherapy;[2]Department of Pharmacodynamics and Biopharmacy, University of Szeged, Szeged

Background: It is generally accepted that several adipocytokines are regulators of the reproductive system, since they influence the hypothalamic-pituitary-gonadal axis. Their plasma concentrations have been found to alter during gestation and it is also hypothesized that they take part in pregnancy related complications.
Aims: The aims of this study were to clarify the uterine effects of leptin, adiponectin and kisspeptin on different gestational days in pregnant rats and to identify the myometrial and uterine expressions of their receptors throughout pregnancy.
Methods: KCl-induced contractions of uterine rings from pregnant Sprague-Dawley rats were measured in an organ bath on gestational day 5, 15, 18, 20 and 22. Cumulative dose-response curves were elicited in the presence of leptin (10^{-12}–10^{-8}M), adiponectin (10^{-12}–10^{-8}M) or kisspeptin (10^{-12}–10^{-7}M). The isolated organ bath experiments were also carried out after endometrial removal. The myometrial and endometrial expressions of the adipokine receptors were determined by RT-PCR and Western blot analysis.
Results: We found that the uterus relaxant effect of leptin was strong at the early phase of pregnancy, but it decreased towards the end of gestation. We observed a similar trend in the case of kisspeptin, but its inhibitory effect was still detectable on the 22nd day. The relaxing effect of adiponectin tends to increase from pregnancy day 5 to day 18, but then practically ceases on the last day of gestation. The removal of the endometrium altered the uterine relaxant effects and the expressions of receptor mRNAs and proteins in the uterus.
Conclusion: All the investigated peptides inhibited the contractions of pregnant rat uterus. The effects of leptin and adiponectin ceased towards the end of pregnancy, suggesting that they had no crucial role in the last day contractions. On the other hand, kisspeptin had significant relaxing action during the whole pregnancy. The myometrial and endometrial expressions of the adipokine receptors were confirmed as well.

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Utilization of asthma and COPD medications in Hungary between 2008 and 2018

SCHVÁB, K., CSATORDAI, M., MATUZ, M., ENGI, ZS., BENKŐ, R., DORÓ, P.
Department of Clinical Pharmacy, University of Szeged, Szeged

Background: The prevalence of asthma and chronic obstructive pulmonary disease have considerably grown in Hungary during the past decade.
Aims: Our aim was to analyze the utilization of medicines used for the treatment of obstructive airway diseases (asthma and chronic obstructive pulmonary disease) and their financial burden between 2008 and 2018.
Methods: Data was collected from the National Health Insurance Fund of Hungary containing the reimbursed medication use of the entire population. Data was analyzed using the WHO's ATC/DDD system and expressed in Defined Daily Dose per 1000 inhabitant per day (DDD/TID).
Results: The total use of drugs for chronic obstructive airway disease (ATC: R03) increased from 33.27 DDD/TID in 2008 to 42.30 DDD/TID in 2018. In 2008 the most frequently used medicines were the xanthines with 9.96 DDD/TID, and by the end of the study period their consumption decreased by 29% to 7.08 DDD/TID. In 2018 the most popular drug group was inhaled corticosteroids in combination with long acting beta2-agonists which use rose by 56% from 6.41 DDD/TID in 2008 to 9.98 DDD/TID in 2018. During the study period the total drug expenditure showed a 36% increase reaching 95.1 million Euro in 2018.
Conclusion: As the prevalence of chronic obstructive pulmonary diseases increased the utilization of drugs used for their treatment increased as well. The utilization of preparations containing combination of inhalation medications showed the highest increase during the study period.

The level of mercury in thermal waters

SILAȘI, O.[1], BÎRSAN, M.[2], RÉDAI, E.[1], ANTONOAEA, P.[1], VLAD, R.A.[1], TODORAN, N.[1], CIURBA, A.[1]
[1]Department of Pharmacuetical Technology and Cosmetology, George Emil Palade University of Medicine, Pharmacy, Science and Technology of Targu Mures, Targu Mures; [2]Grigore T. Popa University of Medicine and Pharmacy, Iași, Romania

Background: Thermal waters are the most used in our century for different types of skin. The biggest advantages of the thermal waters are naturally antioxidant, soothes and protects, moisturizes and make a stronger barrier for healthier looking skin. The consumer could use a big quantity of this type of dermatocosmetic daily.
Aims: Our study aims to discover if a quantity of this products could be high level of mercury potential hamfull for skin [1,2].
Methods: A total of 6 samples of thermal water from commercial brands were selected from beauty shop and pharmacy. The equipment used to analyze this samples is AMA 254 Mercury Analyzer (Leco, Czech Republic) which measure mercury concentration in products.
Results: The values of mercury in samples on the market are under the limits allowed by the European Union. The consumer could use a bigger quantity of thermal water than regular cosmetic products and even if the level of mercury is under the limits these products could be a potential risk. But the amount of mercury in thermal waters is in lower concentration to the amount of mercury when exposed to air or even drinking water.
Conclusion: Most cosmetic products have a higher concentration of mercury than thermal water sprays. These thermal waters even if applied to the skin several times per day, they are not a potential risk for our skin's health and safety. When using thermal waters in combination with many other cosmetics, including make-up products, caution is advised as all those products combined may lead to an increase of mercury levels in the body.

References: 1 Tang H et al. Clin Nephrol. 2013;79:326–329; 2 Nohynek G et al. Toxicol. Appl. Pharm, 2010;43:239– 259.

QbD-based formulation of intranasal polymeric micelles

SIPOS, B., AMBRUS, R., CSÓKA, I., SZABÓ-RÉVÉSZ, P.,PALLAGI, E., KATONA, G.
Institute of Pharmaceutical Technology and Regulatory Affairs, University of Szeged, Szeged

Background: Polymeric micelles offer a great way to improve bioavailability, water solubility and the toxicological profile. They can be applied through alternative administration routes such as intranasal targeting the central nervous system directly. Quality by Design is a novel approach in research and industry, therefore it can be applied in the early stages of pharmaceutical developments as well.
Aims: Our goal was to formulate NSAID-loaded polymeric micelles with proper particle properties, material structure and in vitro characteristics which can be used for intranasal administration treating the inflammatory responses in the CNS.
Methods: At first, QTTPs, QCAs and CPPs were determined and a risk assessment was evaluated in

harmony with the ICH guidelines. For API we used Meloxicam and tocophersolan as a micelle-forming amphiphilic graft co-polymer. The formulation is based on solvent extraction and precipitation. We used a 3-level Box-Behnken factorial design to optimize the formulation. We investigated the particle size, polydispersity index, zeta-potential as main three nanoparticle determining parameters. For the material structure investigations, we used XRPD, DSC, TG and spectrophotometric measurements. The encapsulation efficiency was measured via HPLC. In vitro dissolution and permeability studies were carried out in SNES media. The physical stability was investigated monthly after freeze-drying and storing at 5±3°C.

Results: We successfully determined and optimized the main factors using QbD methods for the desired quality. The products show us monodisperse distribution with proper zeta-potential and particle size even after storing for months. The characteristic peaks of the API or the polymer cannot be detected in the products, the material structure investigations indicate that it has amorphous crystalline structure. The in vitro kinetics and the encapsulation efficiency showed us good results which correlates with the criteria of the intranasal administration.

Conclusion: The stable polymeric micelles with the proper quality and quantity parameters can be used for intranasal administration. Quality by design can be applied in researching nanotechnology-based drug delivery systems as well. Tocophersolan can be used as a polymeric micelle-forming excipient.

Potential immunotherapy target identification in glioblastoma and meningioma

SOLTANI, A.
Department of Pharmaceutical Biotechnology, University of Pécs, Pécs

Background: Despite relentless research, survival rates of malignant tumors of the central nervous system (CNS) have not improved significantly. Glioma is categorized as low grade glioma and higher-grade glioma. Glioblastoma (GBM) is the aggressive malignant glioma. In contrast, meningioma is a slow growing, more benign brain tumor originating from the meninges, but can be recurrent and even turn malignant. The primary therapy for both tumor types is surgery and radiotherapy. Temozolomide (TMZ) can increase survival rates, but not all CNS tumors are responsive to TMZ.

Aims: The current study has focused on the immune microenvironment of two types of brain tumors, namely grade IV glioma and grade I meningioma.

Methods: Tissue samples were postoperative primary CNS tumors, grade IV glioma and grade I meningioma. Using quantitative real-time PCR mRNA levels of characteristic immune cell surface markers (CD3, CD4, CD8, CD56 CD19, CD168 etc.), cytokines (TGFβ, IL10, etc.) and Indoleamine 2,3-dioxygenase (IDO) were determined. Immunohistochemistry supported the presence or absence of specific protein levels.

Results: In both CNS tumor types the immune microenvironment has proved to be highly similar. Both cases the immune suppressive elements were highly elevated. This included the presence of immune suppressive regulatory (reg) T cells (CD4+FOXP3+) and tumor associated macrophages (TAMs). The m-RNA level of IDO was also increased in both types of tumors. The metabolic product of IDO-1 is kynurenine which generates metabolites that enhance the activities of CD4+ FOXP3+ T-reg cells and myeloid-derived suppressor cells. IL-10 and TGFβ were also over expressed in both tumor types. In contrast, differential expression of molecules targeted by immune checkpoint inhibitors was detected. CTLA4 mRNA level was elevated over normal control, while expression of PD-1 and PDL1 varied individually.

Conclusion: Our results show a strong immune suppressive microenvironment in both tumor types. However, individually selected immune checkpoint inhibitors in combination with IDO-1 inhibitors might become alternative treatments for certain brain tumor types, or even refractory meningiomas and chemoresistant glioblastomas.

References: 1 de Robles P. et al. Cancer Genet. Cytogenet., 2008;187:25–27; 2 Sherman W. and Raizer J., Expert Rev. Neurother., 2012;12(10):1189–1196

High-priority drug interaction list for use in hospital formulary

SOMOGYI-VÉGH, A., NYAKA, B., BOTZ, L.
Central Clinical Pharmacy, University of Pécs, Pécs

Background: Increasing introduction of electronic prescribing and pharmacist-led prescription order validation in Hungarian hospitals demands improvements to computerized interaction screening. Discrepancies between different drug-drug interaction (DDI) ratings are well-documented. In addition to that, over-alerting and lack of practical recommendations make physicians and pharmacists commonly override DDI alerts. Reaching a consensus on an elementary set of interactions would be a great leap forward in improving patient safety.

Aims: To develop a hospital formulary methodology for selection of high-priority DDIs, the detection of which can be considered as a standard of medical informatics software at our institution.

Methods: Literature searches for similar lists and guidelines on selection and implementation of DDI alerts into clinical systems were performed. A decision model has been developed to identify and select high-priority interactions. As the final list must be achieved by multidisciplinary consensus, candidate DDIs and management recommendations will be discussed by the institutional drug and therapeutics committee.
Results: According to a validated decision algorithm, candidate interactions should be evaluated by the following criteria: evidence, severity of the adverse event, necessity of medical intervention, difficulty of surveillance, availability of suitable alternatives and dose adjustment guidelines, risk-benefit ratio of the combination [1]. Main sources of candidate interactions include (a) consensus-based lists identified in a previous systematic search of the literature [2], (b) DDI databases using a transparent and management-oriented classification system and (c) available evidence-based clinical guidelines on the management of DDIs. Priority should be given to population-based studies as they provide clinically relevant information and are incompletely referenced by DDI databases. Complementary sources include summaries of product characteristics and CYP enzyme databases.
Conclusion: The problem today is not the lack of information on DDIs but to optimally translate it to clinical practice. The presented methodology provides a professionally valid approach for the institutional consensus-based screening of high-priotrity drug interactions in a unit-dose distribution system.

References: 1 Far, E. et al. BMC Pharmacol Toxicol. 2012;13:7; 2 Somogyi-Végh, A. et al. BMC Pharmacol Toxicol. 2019;20:36.

Clinically significant drug-drug interactions in hemodialyzed patients

SZABÓ, A.[1], HARIS, Á.[2], CSEH, I.[1]
[1]Central Pharmacy Department, Szent Margit Hospital; [2]1st Department of Medicine and Nephrology, Péterfy Hospital, Budapest

Background: Drug interactions mean interference between drugs, or drugs and environmental factors. Due to such interactions pharmacokinetics may be altered, which modify the expected effects of the medications. Contraindication types of drug-drug interactions (DDI) have outstanding clinical significance, as may cause severe clinical consequences, therefore need special attention when prescribing complex therapy for patients.
Aims: In Szent Margit Hospital Taraba István Hemodialysis (HD) Unit we investigated contraindications of medication therapy in 101 HD patients. Mean age was 69±12 years, 54% of them were male.
Methods: By using DDI Medscape interaction checker we found 10 interactions per patient as an average, and among them 2 were contraindications. We summarize the most important groups of contraindications, indicate the mechanisms of elevated risks, the number of cases at risk, and present some examples.
Results: DDI caused elevated risk of high serum potassium 15 patients, e.g. by administering LMWH and ACEI together. Risk of Stevens-Johnson syndrome might be elevated due to allopurinol and ACEI, or ASA and ACEI interactions (20 cases). Conjugates of some drugs, as calcium-carbonate and ASA, or omeprazole and clopidogrel taken in the same time may lead to antagonism (26 cases). Drug toxicity can be caused by coadministration of digoxin and pantoprazole, also by carbamazepine and alprazolam (22 cases). In patients with reduced liver or renal function coadministering amlodipine and simvastatin increases the risk of rhabdomyolysis by 60% (2 patients). Residual renal function may decrease if taking regularly NSAID and ACEI together (32 patients). Very often patients need to take more than one medications influencing the coagulation system to prevent clotting in HD system and due to thrombotic diseases or atrial fibrillation (contraindication with increased bleeding risk was experienced 44 cases).
Conclusion: Recognition of frequent contraindication DDI has outmost importance. Several investigations have proven that almost one third of hospitalizations are caused by potentially preventable side effects of medications or incorrect drug therapy. Advanced age per se is a risk factor for DDI. In HD patients the minimal residual renal function, high number of comorbidities and the large number of prescribed drugs increase the risk of DDI, which monitorization and elimination are significant tasks of the clinical pharmacologist.

Survey of fifth-year pharmacy students' views on the current state of clinical pharmacy, on their future plans and workplace expectations at Semmelweis University

SZILVAY, A.
University Pharmacy Department of Pharmacy Administration, Semmelweis University

Background: In recent years, pharmacists have been paying increasing attention to pharmaceutical care in community pharmacies and clinical pharmacy services in hospitals. The latter position, which is becoming widespread in Hungary and in the practice of Semmelweis University, provides an opportunity

to assess, identify, and solve problems in the patients' medication. University pharmacy education also has to adapt to the new tasks, failing which, a discrepancy may develop between the students' perception of the profession and the actual situation, the competences taught and applied in practice.
Aims: The aim of our study was to find out the fifth-year students' perceptions and opinions about hospital-clinical pharmacist work, to assess students' workplace expectations, future plans (with a hospital-clinical pharmacist focus) and explore differences between students' image and reality.
Methods: During the research, Semmelweis University's fifth-year pharmacy students completed a questionnaire developed by our Institute in October 2019. The 20 questions in the questionnaire covered three topics: hospital-clinical pharmacy concepts, workplace expectations and future plans.
Results: 88 students completed the questionnaire. Students considered professional development as a hospital-clinical pharmacist (4.00 points on a 5-point scale), the main profile of the work is drug supply and drug therapy supervision (3.79; 3.84), however, they think that physicians do not treat pharmacists as equal partners (2.13) and students do not feel prepared to work in this field (2.09). The most important of the workplace conditions is a good relationship with colleagues (4.66), an appropriate salary (4.64), an opportunity for development (4.58) and professional appreciation (4.52). 54% of students want to work abroad for a while and about 30% would like to work in a hospital. The most popular area of work is unit-dose dispensing (4.4) and working as a clinical pharmacist in a hospital ward (4.6), as opposed to ordering and dispensing medicine ("speci"; 2.6) or working in the community pharmacy unit ("kispatika"; 2.9).
Conclusion: Our results will help us better understand the prospects of future graduates, which can help facilitate their integration into the hospital-clinical setting and provide a good basis for mapping the impact of fifth-year education on this.

Characterization of acute stress by gastrointestinal and cardiac electromyography in awake rats

SZŰCS, K.[1], VIGH, D.[1], DUCZA, E.[2], GROSZ, G.[3], SÜLE, M.[3], GÁSPÁR, R.[1]
[1]Department of Pharmacology and Pharmacotherapy; [2]Department of Pharmacodynamics and Biopharmacy, University of Szeged, Szeged; [3]MDE GmBH, Budapest

Background: Stress, anxiety, and various neuropsychiatric disorders are often associated with gastrointestinal (GI) symptoms and heart rate changes. The simultaneous detection of the myoelectrical slow-waves of the GI tract with the changes in heart rate and other parameters may provide more accurate information on patients' acute anxiety and psychological status, but such a method is currently not available in the clinical practice.
Aims: Investigation of acute stress response and stress response reducing drugs with simultaneous detection of GI, cardiac, plasma corticosterone and body temperature changes in wakeful rats.
Methods: The sensor was placed under the abdominal skin of male SPRD rats (300-310g) to record simultaneously the GI tract myoelectric signals, cardiac signals, and body temperature. The primer GI records were analyzed by fast Fourier transformation. The rats were also treated with diazepam (5mg/kg) or haloperidol (1mg/kg) intraperitoneally. The changes in plasma level of corticosterone were determined by ELISA.
Results: Acute stress induced a significant increase in the electromyographic signals of each segments of the GI tract, as well as corticosterone plasma levels, body temperature and heart rate of the animals. Diazepam and haloperidol reduced stress-related parameters, except heart rate, as these agents cause tachycardia. The hypothermic action of diazepam masked the body temperature alterations in the treated rats.
Conclusion: Acute stress can be measured with a single sensor for simultaneous detection of GI- and cardiac myoelectric activity, plasma corticosterone levels and body temperature. During psychopharmacological studies in rats, the change in stress level can be accurately followed by GI electromyography that shows good correlation with the changes in stress hormone levels. The other investigated stress parameters did not fully reflect the changes. Our method may open new perspectives in the diagnosis and treatment of psychosomatic disorders.

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The effectiveness of immunotherapy in non-small cell lung cancer based on real-world data

TAKÁCS, G., CZIBULA, E., MOLDVAY, J.
Korányi National Institute of Pulmonology, Budapest

Background: Nivolumab is a widely used immune checkpoint inhibitor, which is indicated in many solid tumors including metastatic non-small cell lung cancer (NSCLC). The CheckMate-057 clinical trial demonstrated its efficacy compared to conventional chemotherapy in advanced stage non-squamous (adenocarcinoma, ADC) NSCLC. CheckMate-017 trial verified its efficacy in advanced stage squamous cell carcinoma (SCC) NSCLC patients.

It is confirmed that under controlled clinical research conditions, health gain produced by a drug is better than the outcome in the daily therapeutic routine. Health benefit achieved in the daily practice is called the effectiveness of the therapy. Beside efficacy, also effectiveness of a therapy should be considered when quantifying the net benefit of care.

Aims: Our main goal is to obtain real-world evidence about the promising immunotherapy in the therapy of lung cancer. Therefore we measured primary endpoints in a real-world population. We compared progression-free survival (PFS) and overall survival (OS) measured in the CheckMate-017 and CheckMate-057 clinical trials with the same endpoints (OS, PFS) of the patients cured in our hospital.

Methods: With the help of our hospital medical informatical system the anamnesis of 83 patients (50 men, 33 women) receiving nivolumab was reviewed retrospectively. The data were statistically analyzed; PFS, OS and survival curves were determined using SPSS software.

Results: In ADC (43 patients, median age 62 years) the median OS was 9.8 months, the one-year OS rate was 37.2%, the median PFS was 2.9 months, the one-year PFS rate was 11.6%. In SCC (40 patients, median age 63.5 years) the median OS was 13.3 months, the one-year OS rate was 55.0%, the median PFS was 6.2 months, the one-year PFS rate was 30.0%. In the case of ADC, the effectiveness results measured in our institution are poorer, while in SCC are more beneficial, than the efficacy results measured in the clinical trials.

Conclusion: Based on these results, the gap between efficacy demonstrated in clinical trials and effectiveness experienced in real-world studies can be quantified. Effectiveness data registered in our institution can be regarded as a suitable base for the development of outcome-based financial models. With such data analyses we can capture the real value of nivolumab in NSCLC therapy in Hungary and create an outcome-based financing scheme.

The development of a semi-solid formulation containing cinnamon essential oil as a hand-sanitizer preparation

TAKÁCSI-NAGY, A., SZÉKELY, A., PÁL, SZ.
Institute of Pharmaceutical Technology and Biopharmacy, University of Pécs, Pécs

Background: Pharmacy practice includes traditional and extemporaneous products that are well-tolerated by patients, for which shelf-life time cannot be accurately provided. In such cases, the product may not meet the desired requirements even within the expiry date. This problem not only gives rise to uncertainty among patients and pharmacists but is also of quality concern [1,2]. Moreover, by carrying out certain examinations, even in the small-scale production, an appropriately stable pharmaceutical composition can be prepared.

Aims: The aim of this study is focused on the reproduction of a routinely used individual preparation, its physicochemical, accelerated and real-time stability testing to predict the rate of change at a proposed storage temperature.

Methods: Five variations of the chosen ointment were freshly prepared and subjected to accelerated stability testing at 40°C; 75±5% relative humidity and 25°C; 60±5% relative humidity. The preparations were monitored, and few units of the reference material were taken at 1, 3 and 6 month intervals. During the stability testing process the following experiments and tests were conducted according to the Hungarian and European Pharmacopoeias: Dropping point and freezing point measurements, extensometric test, microscopic examination, pH measurements of the aqueous phase, rheometric, dissolution and diffusion tests.

Results: The study revealed that the choice of an optimal method of preparation results in a more stable pharmaceutical product than the original preparation. Even similar production methods resulted in ointments with significantly different physicochemical parameters. Based on the study, we can recommend a good manufacturing practice, expiry date, packaging material and storage conditions regarding the chosen formulation.

Conclusion: These results confirmed that the physical and chemical stability of the ointments were achieved with the appropriate choice of the preparing conditions.

References: 1 WHO Expert Committee on Specifications for Pharmaceutical Preparations – WHO Technical Report Series, No. 863 – Thirty-fourth Report; 2 Falconer, J.R. & Steadman, K.J. Aust Prescr 2017;40,5-8.

Dr. (Hermányi) Sztankay Aba from Debrecen as a pharmacist he became a private university teacher

TATÁR, GA.[1], SZABÓ, A.[2,3], BÁCSKAY, I.[2], JÓZSA, L.[2], FEHÉR, P.[2]
[1]Hungaropharma Inc. (retired); [2]Department of Pharmaceutical Technology, University of Debrecen; [3]Bethlen Pharmacy, Debrecen

Family roots: The Sztankay family comes from Croatia and their original name was Ztanechich. The family can be traced back to János Ztanechich, who was the secretary of the Transylvanian prince

István Báthori. Nobility was given to the family by the Transylvanian prince Zsigmond Báthori on May 26, 1596. During the religious upheavals, a member of the family converted to the Lutheran faith and therefore he fled to Gömör County. A pharmacist and landowner from Selmecbánya, Ferenc Sztankay (April 19, 1835 – May 29, 1910) was descended from this family branch. He married Abraham Rosalia on October 18, 1864 in Verespatak. Eleven children were born from the marriage, but most of them did not reach adulthood. The family moved from Verespatak to Selmecbánya in 1873, where Ferenc first became the owner of a pharmacy and then a landowner, thus ensuring his family welfare. Three children were born in Verespatak: Gyula Aba (March 27, 1868 – January 21, 1936) – the protagonist of our story – humanities scientist, pharmacist and university private teacher, Béla Farkas (1869 – 1955) graduated engineer, director of the Royal Industrial School, first in Gölniczbánya and then in Debrecen, and Margit (1870 -?). Sztankay Aba married Sára Zsilkay in 1895. From their marriage three daughters were born: Klára (1895-1920); Sára, who died of pneumonia in 1936, and Dóra, who married Major General Lajos Burget and left the country in 1947. One daughter was born from their marriage, Dorothea (Thea) (June 2, 1926 – November 29, 2016), she moved to the United States where she married and had two children.

The most outstanding successes of his work:

I. *He was only 16 years old when he published his dissertations on the history of pharmacy in the weekly "Aesculap", with which he also helped the development of the terminologie of pharmacy.*
II. *From 1886 onwards, his writings were published in Hungarian and German, among which it is worth mentioning e.g. the "Handbook of Urine Tests, for practicing pharmacists, physicians and those dealing with similar chemical tests", or "Commentary in Section II of the Hungarian Pharmacopoeia" or "the correctness of the information provided in the appendix of the Hungarian Pharmacopoeia on the content of Tokaj wine extract".*
III. *In the laboratory of the pharmacy "Salvator" in Bát, he produced an intestinal disinfectant and anti-diarrhoea drugs called "Tanninum albuminatum keratinatum", which was known to the public as his fancy name "Hontin". As he could not find a domestic manufacturer, he was forced to sell it to an Austrian company, through which the product spread throughout Europe. (For posterity, he continued to live under the name "Albumen tannicim" – PhHg VII.)*
IV. *In the Hungarian Pharmacopoeia II, a preparation containing theobromine, called "Diureticum", was official. Because theobromine is poorly soluble in water, Sztankay experimented with a more beneficial compound that resulted in "Theobromino natriosalycilicum" and then "Anisotheobromine".*
V. *In 1900, Professor Vámossy discovered the laxative effect of phenolphthalein. In his long experiments, Sztankay found that the drug is more soluble in water in its amorphous state and thus more effective than in crystalline form. Stankay formed amorphous phenolphthalein using NaOH. He named this compound "Eulaxans". The product containing phenolphthalein with Na_2CO_3 was named "Perrectal", suggesting that it is an excellent laxative when administered rectally and can be used even in animals.*

Risk assessment in preparation of magistral medicines

TISZAI, D., PAPP, Á., BECSKEHÁZI-TAR, A., BUCHHOLCZ, G.
Central Clinical Pharmacy, University of Debrecen, Debrecen

Background: The Committee of Ministers Resolution CM/ResAp (2011)1 on quality and safety assurance requirements for medicinal products prepared in pharmacies for the special needs of patients. It serves to assess the potential risk factors for the new medicinal products which is prepared in pharmacies. This resolution is a recommendation and does not give a specified method for a fully objective risk analysis; we have begun to develop a new, more comprehensive risk analysis system.
Aims: To develop a more detailed methodology which can help to identify, analyze, and evaluate potential risks in preparing, quality and stability of products prepared in pharmacies and determine how to minimize chemical exposure for the pharmacy staff's health, and how to ensure the safety medication of patients.
Methods: Risk analysis based on a developed table with objective choices. Using points system, the percentage of objectively qualified risk that value can be evaluated in textual form, thus the nature of the risk can be determined.
Results: The developed mathematical-based method quantifies the risk, and the value expressed as a percentage which gives the degree of risk. The pharmacist considering the risk and decide to prepare a high-risk preparation, or minimize the risk by applying appropriate precautions.
Conclusions: There are different sources of risk including the events, causes and consequences during the preparations of magistral medicines. The elaborate set of criteria seeks to fully identify potential risk factors. The severity assessment of the risk gives information to minimize the risk.

Personalized intranasal device development

TO QUOC, T., UJHELYI, Z., BÁCSKAY, I., VECSERNYÉS, M.
Department of Pharmaceutical Technology, University of Debrecen, Debrecen

Background: Air pollution is a global health threat and causes millions of human deaths annually. The late onset of respiratory diseases in children and adults due to prenatal or perinatal exposure to air pollutants is emerging as a critical concern in human health. Globally, seven million deaths were attributable to the joint effects of household and ambient air pollution. Subjects with chronic respiratory diseases such as chronic obstructive pulmonary disease (COPD) and asthma are especially vulnerable to the detrimental effects of air pollutants. Air pollution can induce the acute exacerbation of COPD and onset of asthma, increase the respiratory morbidity and mortality. The health effects of air pollution depend on the components and sources of pollutants, which varied with countries, seasons, and times.
Aims: The objective of this research was to develop personalized nasal filters by 3D fused deposition modeling technique. The design had been performed by 3D imaging technique and prototypes had been manufactured at the department by FDM 3D printer. As the part of the development our aim was to evaluate the physical properties of the formulated devices as well. According to the research plan the final output of the project is two products; a simple nasal filter for everyday use and a medical device with different application possibilities.
Methods: Main tasks of research are; state-of-the-art literature research. 3D modeling, design and development. Application of pharmaceutical technology rules at the formulation stages. Test, validation and calibration of the developed models and control procedure according to pharmaceutical standards. In vitro biocompatibility measurements.
Results: First class devices are 2 ways multi Cores nasal equipments intended to protect users from harmful allergens in the growingly polluted environment, their designs in theory were meticulous, but still lacking sufficient testing. There are 5 designs until now: Mk1, Mk2, Mk3, Mk4, MkV; each was an improvement from the last, each was inspired from the previous model, but they all carry their merits and their disadvantages. Emergency Nasal Filters are 3D printed functional nasal filters with several possible fuctions that patients can rely on whenever and whatever situation.
Conclusion: We can conlude that 3D printing tehnique is the most suitable procedure for our formulation. Our development, combined with biocompatibility measurements ensure innovative product and safe application as well.

Development of magistral preparation containing omeprazole

TÖMÖRI, M., PAPP, Á., TISZAI, D., NAGY, T.M., BUCHHOLCZ, G.
Central Clinical Pharmacy, University of Debrecen, Debrecen

Background: Many drugs frequently used in neonatology are not available in suitable dosage forms, in such cases compounded medicines have to be prepared. In addition, it is often the case the absence of an active pharmaceutical ingredient (API), therefore authorized medicines have to be used, as a source of it. For the accurate dosage and reproducibility, the divided or diluted omeprazole content pellets are not adequate formulations, thus a different technological solution is needed.
Aims: The objectives of the project was the development of omeprazole containing dosage forms for pediatrics, refer to the relevant international guidance and to other guidelines.
Methods: Prepare and compare the suspensions from Losec® and Ludea® capsules. Pellets were dispersed in an 8.4 % sodium bicarbonate solution. The compounded suspensions were prepared differently by stirring, grinding and shaking methods, and stored at 2-8 °C. The aspects of the examinations were the resuspendability, pH, dose uniformity and microbiological purity.
Results: Based on the results, we selected the most appropriate formulation and preparation method for shelf life.
Conclusions: Further develop to the experience of the literature, a safe and cost effective omeprazole suspension can be prepared. This dosage form can reduce the lack of available medicines in the field of pediatrics.

Variability in response to antidepressant therapy: a pharmacogenetic approach

TÖRÖK, D.[1], GONDA, X.[1,2], BAKSA, D.[1], ESZLÁRI, N.[1], BAGDY, G.[1], JUHÁSZ, G.[1], PETSCHNER, P.[1]
[1]Department of Pharmacodynamics, Semmelweis University; [2]HAS-SU Neuropsychopharmacology and Neurochemistry Research Group, Hungarian Academy of Sciences, Budapest

Background: The process of the first pass metabolism is accomplished by several number of enzymes. In numerous pharmacogenetic researches the Cytochrome P450 System, consisting of approximately

60 genes, which encode hepatic heme-proteins was investigated. Since, these enzymes play key role in the drug metabolism, the different variants can cause changes in their function that can lead to altered metabolism rate by affecting pharmacokinetic and pharmacodynamic properties. The metabolism rate can be categorized as poor (PM), intermediate (IM), extensive (EM) and ultrarapid (UM).
Aims: The aim was to obtain a comprehensive knowledge about the latest studies investigated this topic.
Methods: I have reviewed some of the latest articles observing the relation between responses to antidepressant treatment and variants in CYP450 family and extracted the most relevant result.
Results: The most studied genes and their variants that have impact on the therapeutic response are CYP2B6, CYP2D6 and CYP2C19 related to the metabolism of paroxetine, escitalopram, citalopram, mirtazapine, desvenlafaxine and sertraline. Paroxetine and mirtazapine showed decreased efficacy in case of the increased function (EM status) of the CYP2D6 enzyme and since the metabolism of sertraline is also mediated by CYP2B6 and CYP2D6, polymorphisms of these genes may also affect the drug plasma concentration during therapy. The altered metabolism of desvenlafaxine caused by polymorphism of CYP2D6 showed lower risk than the other observed antidepressant. Escitalopram and citalopram were more effective in patients with IM status of CYP2D6 and CYP2C19 enzymes and slower CYP2C19 metabolizers (PM status) experienced side effects.
Conclusion: The individual drug therapy could be a great step in the development of the antidepressant therapies, allowing increased therapeutic efficacy and decreased risk of side-effects. To obtain this, the investigation of the responses to antidepressant therapy related to the pharmacogenetic background of an individual is indispensable.

Preformulation studies of ciprofloxacin-loaded polymer-based electrospun nanofibers

UHLJAR, L.É.[1], ALSHWEIAT, A.[1], KAN, S.Y.[2], ESMAIL, A.[2], RADACSI, N.[2], AMBRUS, R.[1]
[1]Institute of Pharmaceutical Technology and Regulatory Affairs, University of Szeged, Szeged; [2]Institute for Materials and Processes, The University of Edinburgh, Edinburgh

Background: Polymer-based electrospun nanofibers are considered as a novel nanocarriers which have numerous advantages such as wide variety of polymers and active pharmaceutical ingredient (API), large surface area and adjustable diameter. Nanofibers mostly prepared by electrospinning process. Incorporation into nanofibers can improve the physico-chemical properties of the API important pharmaceutical technological aspect. Ciprofloxacin (CIP) is a worldwide used fluoroquinolone antibiotic for local and systemic therapy. CIP is a BCS Class II drug indicated by its solubility and permeability.
Aims: Therefore, the aim of the study was to produce and investigate various polyvinyl-pyrrolidone (PVP) based 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 therefore increased.
Methods: Nanofibers in different combination of ingredients (1:0, 1:1, 1:2, 1:3 PVP:CIP) and also nanofibers produced by different flow rate (0,5; 1; 1,5; 2; 3; 4 ml/h) was made. To compare and characterize the samples the micrometric (SEM) and the structural (DSC, XRPD) properties were investigated. The fiber-diameter and in vitro dissolution profiles were also examined.
Results: Conceivably, the nanofiber sample contained 1:1 PVP:CIP and prepared by 2 ml/h flow rate had the best properties. The dissolution rate of ciprofloxacin could increase by formulation of amorphous solid dispersion.
Conclusion: According to this electrospun nanofibers would increase the dissolution of ciprofloxacin. The development of a new pharmaceutical dosage-form with better physico-chemical properties is possible to start after further investigations.

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Application of machine learning in the identification of oral medicines: a new tool to combat against falsified medicines and increase medication safety

VAJDA, P.[1], FELDMANN, Á.[2], KISANDER, Z.[3], VIDA, RG.[1], BOTZ, L.[1], FITTLER A.[1]
[1]Department of Pharmaceutics and Central Clinical Pharmacy; [2]Department of Behavioural Sciences; [3]Department of Automation, University of Pécs, Pécs

Background: There has been a tremendous focus on falsified medicines in the recent years with more and more regulations have entering into force globally, and in Europe as well. Although, the chance of falsified medicines entering into the regulated drug supply chain is considered to be low in developed countries, unregulated illicit internet sale of medications is an international issue. Illicit internet pharmacies are flourishing and we have limited tools to combat against them and illegally purchased medi-

cines pose a significant medication safety and patient safety risk. The traditional analytical methods have their limitations (time consuming, costly and large sample need). Our previous literature reviews and market searches proved, that currently there is not any mobile software with image recognition that meets this emerging public health need.
Aims: Our aim is to develop a Software as a Service (SaaS) cloud native solution that is able to identify efficiently oral dosage forms.
Methods: During our work we specified a protocol to photograph medicines. We have taken 50.000 photos of 100 medications as follows: 75 photos were taken from the front of the secondary packaging (medicine box), 75 photos from the back. 50 photos were taken of the front of the primary packaging (blister), 50 photos of the back. Further, a total of 250 photos were taken of the drug (tablet, capsule, etc.) itself. We used the Tensorflow Machine Learning library to implement our algorithm. The core of the algorithm is a pre-trained visual convolutional neural network, that was fine-tuned to be able to recognize and classify different type of medicines and medicine boxes. During recognition, the network outputs the most probable medicine candidates with their probability-like measure. Visualization of the performance of an algorithm is evaluated on a confusion matrix and Type I and Type II errors
Results: In our experiments the trained neural network achieved ~90% top-1 accuracy (most probable candidate) on a single image. The results show, that the color and the shape factor have the largest contribution to the confusion between the top-k candidates. In most cases, this accuracy can be improved with aggregating multiple different images of the medicine.
Conclusion: Future application of such methodology can be used in forensics, for public use, to prevent medication error and recognizing drug interactions.

Formulation and studies of the sunscreen's biocosmetics

VARGA, E.[1], JURCA, T.[2], PALLAGI, A.[3], SIPOS, E.[4]
[1]Department of Pharmacy, University of Medicine, Pharmacy, Science and Technology from Târgu Mureș, Târgu Mureș; [2]Department of Chemistry; [3]Department of Pharmaceutical Botany, University of Medicine and Pharmacy from Oradea, Oradea; [4]Department of Drug Industry and Pharmaceutical Management, University of Medicine, Pharmacy, Science and Technolgy from Târgu Mureș, Târgu Mureș, Romania

Background: The benefits of biocosmetics are based on natural ingredients that help maintain the skin's natural state. Some preparation has sunscreen effect when its component or combination of components provides adequate protection against sun rays.
Aims: The aim of this experimental work is the formulation and studies of the cosmetic preparations obtained with extracts of four medicinal plants selected from the spontaneous flora of Transylvania: *Vaccinium myrtillus* (fructus), *Hippophae rhamnoides* (fructus), *Rubus caesius* (fructus), *Calendula officinalis* (flos).
Methods: The lyophilized plant extracts were embedded individually, and in one case blueberry with marigold together, in a Carbopol-based gel and in a o/w cream. The total polyphenol and the total flavonoid content were determined by spectrophotometric method from plants ethanolic extracts and from lyophilisated products. Also with spectrophotometric method were determined the antioxidant capacity by ABTS and DPPH method. The consistency of the gels and creams were determined by rotary viscometer, extensometric and penetrometric methods. The amount of polyphenol dissolved in the gels was determined by in vitro dissolution method.
Results: The total polyphenol and the total flavonoid content from plant ethanolic extracts and lyophilized products were with the same or higher (243mg/100g lyophilised product from Rubi caesii fructus) values with data from literature. The highest concentration of polyphenols and flavonoids were determined from the blackberry extracts. The combination of the two extracts – blackberry and marigold – proved to be effective in vitro dissolution studies, in the meantime the highest polyphenol content was measured from these gels, too. The creams have a pseudoplastic flow (average of creams viscosity: 25Pas and gels viscosity: 15Pas) and the extensometric and penetrometric measurements showed a higher consistency against the gels.
Conclusion: We can conclude that the physicochemical properties, dissolution and the sunscreen character of the creams and gels with antioxidant properties related with the polyphenol content, it was more advantageous in combination of blackberry and marigold lyophillized extracts in gels than gels obtained individually from by one extract.

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Survey of drug shortages in Hungary

VIDA, R.G.[1], SEBŐK, S.[2], NYAKA, B.[1], KRUCSÓ-HORNYÁK, J.[1], BOTZ, L.[1]
[1]Department of Pharmaceutics and Central Clinical Pharmacy, University of Pécs, Pécs; [2]University Pharmacy Department of Pharmacy Administration, Semmelweis University, Budapest

Background: Drug shortages have become a global public health threat in the recent years and healthcare systems and professionals are struggling to dispense the ordered medications to patients in the hospitals and in the community pharmacies as well.

Aims: As there are limited date regarding drug shortage prevalence and affected therapeutic categories in Hungary, our aim was to assess the characteristics and collect evidence regarding this phenomenon from Hungarian pharmacists.
Methods: With an extensive literature search in 2019 April, we identified 53 surveys. After their review, we developed our Hungarian version with 45 questions categorized in 5 main sections: 1. Pharmacy data and demographics; 2. Prevalence and background; 3. The management of drug shortages; 4. Information sources; 5. Consequences of drug shortages. Data was collected between 15. May and 30. June 2019 with an online survey among pharmacists.
Results: 42 hospital and 49 community pharmacists completed the survey. 70 women and 21 men, mainly between the ages 25-40 years, from various type of pharmacies. 52.4% of the hospital pharmacists and 97.9% of community pharmacists experienced drug shortages more than 10 times in the last 6 months. The top ATC groups were the followings in hospital settings: B – Blood and blood forming organs (52.4%); C – Cardiovascular system (50%); L – Antineoplastic and immunomodulating agents (47.6%); J – Antiinfectives for systemic use (38.1%); N – Nervous system (38.1%) APIs such as immunoglobulins, digoxin, phytomenadione, amoxicillin/clavulanic acid. The main affected therapeutic areas in the community pharmacies were the C – Cardiovascular system (89.6%), N – Nervous system (43.8%) and A – Alimentary tract and metabolism (31.3%) including API bupropion, acarbose, metoclopramide and tramadol. Original and generic drugs, parenteral and oral dosage forms were equally affected at the time of our study. The main reasons highlighted by pharmacists were manufacturing problems, tendering processes, and serialization.
Conclusion: Drug shortages affect the Hungarian pharmacists and patient care as well, with similar tendencies that can be seen globally. We should collect and analyze further data to find possible long-term solutions to manage drug supply problems in various therapeutic areas.

Risk based safety mapping of online pharmaceutical market: A case of ophthalmic preparations

VIDA, R.G.[1], MERCZEL, S.[2], JÁHN, E.[1], FITTLER, A.[1]
[1]*Department of Pharmaceutics and Central Clinical Pharmacy, University of Pécs, Pécs;* [2]*Department of Pharmacy, Somogy County Kaposi Mór Teaching Hospital, Kaposvár*

Background: The growing number of illicit internet pharmacies is a global phenomenon, however the size of the online pharmaceutical market is still unknown and quality of products is of great concern. Descriptive data of this dubious market channel are derived from studies analyzing the online availability of different medications purchased over the internet and their methodology is quite heterogeneous.
Aims: Our aim was to develop a comprehensive and also specific risk evaluation method to select ophthalmic medications with high patient safety risk from the online pharmaceutical market.
Methods: Ten eye drops were selected based upon their sales in every day practice in a community pharmacy in Hungary. As there is no specific risk assessment tool for the risk evaluation of the online pharmaceutical distribution channel, a new tool was developed based upon the two quality and safety standard resolutions in pharmaceutical practice published by the European Directorate for the Quality of Medicines.
Results: We developed 6 criteria for the risk assessment of eye drops: I. General pharmaceutical risks, II. Risk originated from the pharmacological property of the active ingredient, III. Risk associated with application, IV. Risk of microbiological contamination, V. Risk from the limited access to the product, VI. Risk related to potential misuse. The above six criteria were integrated in a comprehensive weighted risk scoring system (maximum 30 points). The probability of purchasing the product from the internet was also assessed based on the number of relevant links in search engine results (0-20 links) and the price of the products (<25 USD; 25-50 USD; >25 USD). The product got 1 point if it was sold on 20 or more websites, and 1 point if the price was less than 25 USD. Based on the above criteria timolol/dorzolamide combination products had the highest overall patient safety risk in the risk assessment matrix with 20 points in the patient safety consequences (severity) and 2 points in the total probability score (likelihood).
Conclusion: Currently, there is no standardized methodology to select specific pharmaceutical products with high patient safety risk for analyzing internet pharmaceutical market and as the test purchase cannot be performed for all of the medicines available, we developed a method that may help in designing and focus similar research and can also be used in case of targeted joint actions against medicine counterfeiting (e.g.: Operation Pangea).

Off-label solutions to create magistral medicines in our paediatric clinic

VÖRÖS, A., HANTOS, M.
Bethesda Children's Hospital of the Hungarian Reformed Church, Budapest

Background: In the every-day practice of pharmacy,

particularly in paediatrics, we often confront the challenge of the lack of appropriate dosage form of a required agent. We strive to fill this gap in the therapy with magistral preparations. If the positive list of the National Institute of Pharmacy and Nutrition miss the necessary agents, the required dosage form is prepared from pharmaceutical specialties, even if it is off label.

Aim: It is high importance to us to create safe and efficient as well as easily applicable and comfortable therapeutical solutions for our inpatients with different severe conditions.

Methods: We realise the respective innovative ideas in a close collaboration with our specialist physicians. Taking into account the international practice, we strive to find solutions that resemble some medication registered in an other country, possibly in the USA. If this is not possible, we construct the necessary formulae based on our professional knowledge, the medical literature, and guidelines.

Results: Replacing the clysters registered and distributed in Hungary to treat epileptic seizures promised and delivered great success for both children and relatives. We have managed to largely replace the rectally administered solutions with nasally via-MAD applied midazolam for our patients suffering from epilepsy, therewith achieving a more practical treatment of acute seizures.

We also prepare budesonide suspensions to successfully treat the pharyngealis and esophagealis erosions of the affected patients with Crohn's disease.

Children suffering from SMA who received gene therapy – Zolgensma – are administered with prednisolone and famotidine following the US protocol.

Conclusion: In order to provide our patients and physicians with medicines that offer the most optimal therapy, one needs to be open to off-label magistral solutions. Construction of the appropriate medication is within the competence of the pharmacist of high, which can effeciently contribute to the successful medical attendance of our patients

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Application of nanotechnology in formulation of tioconazole and tea tree essential oil for onychomycosis topical treatment

VÖRÖS-HORVÁTH, B.[1], NAGY, S.[1], DAS, S.[2], KŐSZEGI, T.[2], PÁL, S.[1], SZÉCHENYI, A.[1]

[1]*Institute of Pharmaceutical Technology and Biopharmacy;*
[2]*Department of Laboratory Medicine, University of Pécs, Pécs*

Background: The topical therapy of widespread onychomycosis is a long process (10-12 months) and has a low cure rate. The hard keratin act as a barrier to drug diffusion and its hydrophilic structure also reduces the diffusion of high molecular weight and lipophilic drugs. In order to enhance the penetration of drugs, we can use diffusion enhancers or an appropriate formulation. The azole derivatives have a broad antifungal spectrum and it can show synergism with essential oils (EOs). Tioconazole (TO) and tea tree EO (TT) have been chosen for this research. Pickering emulsions (PEs) are stabilized with nanoparticles instead of surfactants, which are used to stabilize conventional emulsions. With appropriate choice of nanoparticles and prudent formulation, a selective and sustained drug delivery system can be prepared.

Aims: Our aim was to prepare silica nanoparticle stabilized PE of TO and TT, which are suitable for onychomycosis topical treatment.

Methods: Because of the lipophilic character of TO, it can be dissolved in TT, and their solution can be used as oil phase for PE preparation. Surface modified Stöber silica nanoparticles (SNPs) were prepared, characterized and used as stabilizing agent of PEs. We have tested the ratio of oil phase to SNP and the size of SNP on the resulting droplet size and stability of PEs, which were determined with DLS measurements. We examined the diffusion properties of PEs through the nail plate and nail matrix model membrane and investigated their antifungal activity against *Candida albicans* and *Trichophyton rubrum*, which species are mainly responsible for fungal nail infections.

Results: The droplet size of emulsion has a correlation with the SNP to oil ratio and with particle size of SNP. The results of diffusion study show, that the droplet size of PEs and particle size of SNPs influence the diffusion properties of PE through the nail plate and nail matrix model membranes. Microbiological examinations show a synergistic effect between TO and TT, furthermore, PE forms show the most effective antifungal activity against *C. albicans* and *T. rubrum* compared with conventional emulsions or ethanolic solution forms.

Conclusion: Our results show, that with PE form selective drug release can be achieved because TO diffuses only through the nail plate where it can act against fungal infection, what makes this drug form applicable in the topical treatment of onychomycosis.