PRE-CONGRESS LECTURES: SERIALIZATION

Assessment of the Hungarian serialisation status after one year – what is behind us and what is still to come

ANTAL FELLER
Hungaroharma Ltd.

As a result of the closed distribution channels, the strict regulatory environment and cooperation between the participants no counterfeit medicines have entered distribution via pharmacies (retail and institutional) in Hungary. In the interest of being able to comply with the EU Directive that entered into force on 9 February 2019, and for the above statement to remain true in the future too, all pharmaceutical production and distribution participants have complied with the prescriptions of the Directive. The founders established the HUMVO Magyarországi Gyógyszer-azonosítási Nonprofit Zártkörűen Működő Részvénytársaság [HUMVO Hungarian Pharmaceutical Identification Nonprofit Closed Stock Company], HUMVO set up the HUMVS system, the pharmaceuticals manufacturers have applied unique identifiers to their prescription products and have created tamper evident packaging, have uploaded / are uploading the product identifiers to the European database, the end users have joined the system, and are continuously performing identification and reporting. All this has represented a very serious financial burden for all market participants. After a year, within the stabilisation period, we can now say that we have caught up, and within the EU we are in fourth or fifth place in terms of operation (proportion of those joining the system, absolute number of controls and reports, and the most important indicator, the ratio of false alarms). What is still to come? The system is operational, and we are now in the fine-tuning phase:

- We have to set up an alarm mechanism that, after the expiry of the stabilisation period, takes us to the point of certainty in suspicious cases (the product is certainly not a counterfeit, i.e. it may be released / it is very probably a counterfeit product, i.e. it may not be released);
- Hungarian legislation gave exemption from joining the system for certain products and end users until 9 February 2021 – it is necessary to decide what to do after this deadline expires...

And all this must be implemented so that drug safety is not violated in Hungary, and so that there is no reduction in confidence in the supply of medicines, in other words all patients are able to obtain safe therapy at the appropriate time and place using the medicinal product prescribed for them.

Implementation of EU Falsified Medicines Directive in the Hungarian hospitals

ANDRÁS FITTLER[1], KATALIN RICHTER[2]
[1]*Department of Pharmaceutics, University of Pécs, Pécs;*
[2]*Hospital of Szent Borbála, Tatabánya*

The EU falsified Medicines Directive 2011/62/EU delegated regulation came into force and has been applied in Hungary since 9th of February 2019. Implementation of the directive in community pharmacies was in the focus of attention, however it was somewhat unclear how decommissioning would be managed within hospitals and how hospital pharmacists will deal with the upcoming tasks. Based on interviews with practicing hospital pharmacists, literature review and our representative online questionnaire amongst Hungarian hospital pharmacies the supply chain from the retailer to the pharmacy, and the drug commissioning and distribution process within the hospital to wards are discussed in the presentation. Furthermore, due to the relative lack of in-depth assessments of cost implications for hospital pharmacies, we describe the financial burden of FMD on Hungarian hospitals based on human resource requirements, infrastructural and IT developments and authentication procedures. The FMD has notable short and long term impact on hospital pharmacies. Identification and dissemination of good practices in serialization during the stabilization period, and the discussion of potential forthcoming opportunities (e.g. stock management, automation solutions) will likely support hospital pharmacy practice.

The greatest challenges for the pharmaceutical industry: serialization

LÍVIA ILKU,
Gedeon Richter Plc.

According to European law; pharmaceutical products must comply with the requirements of serialization according to Directive 2011/62/EU (FMD) of the European Parliament and of the Council of 8th June, 2011 amending Directive 2001/83/EC of the Community code relating to medicinal products for human use, in regards to the prevention of the en-

DOI: 10.33892/aph.2020.90.41-84

try into the legal supply chain of falsified medicinal products and its related Commission Delegated Regulation (EU) 2016/161 (Delegated Regulation). Products released after 9th of February, 2019 must comply with the above regulations and with the relevant specific regulations in the market where the product is intended to be sold. The aim is to establish appropriate processes that increase transparency and facilitate an audit trail, while at the same time being in full compliance with GDP and FMD requirements. One of the greatest challenges for the pharmaceutical industry over the past year has been understanding the rules of serialisation and make them operational. Prior to February 9, 2019, we focused on the corporate level to understand the requirements, as Marketing Authorization Holder to structure the data, create the system and upload the information to repositories. As manufacturer ensure that new safety features are placed on the boxes and as Wholesaler perform verifications, decommissions and undo-decommissions in the National Medicines Verification System ("NMVS"). Pharmaceutical companies, including Richter, supported the project with enormous financial and human resources. After February 9, 2019, the system was launched, the main task was maintaining the process. We are currently in a stabilization period, meaning that alerts issued by the system, although generating a task for the supply chain, can be dispensed to the patient for most of the alerts. At the same time, several authorities have indicated that they will to close the stabilization period as soon as possible and, accordingly, they have set expectations for the alert process. Alert handling is of paramount importance because, at the end of the stabilization period, counterfeiting-related alert preparations cannot be dispensed to patients. This can lead to patient care problems. So the issue of proper alert management and closure of the stabilization period is a key concern for all participants in the supply chain. The task of regulation must therefore be addressed with a view toward ensuring the safe and secure supply chain of medicines to patients.

Obligations and experiences of the national competent authority after the first year of the pharmaceutical serialization

ÁDÁM PANKER
National Institute of Pharmacy and Nutrition

The pharmaceutical serialization is a relatively new approach to help secure pharmaceutical products around the world but it is already expected to cover approximately 80% of the global drug supply. It was not surprising that the European Union also decided to apply this strategy because as the European Parliament and the Council stated in the Directive 2011/62/EU, "there is an alarming increase of medicinal products detected in the Union which were falsified in relation to their identity, history or source", and "such falsified medicinal products do not reach patients only through illegal means, but via the legal supply chain as well". The pharmaceutical serialization was expected to stop this unfavourable phenomenon but in some member states like Hungary where the supply chain was safe traditionally, it is debated if initial costs exceed benefits. Although the European Commission declared that all stakeholders must be ready to meet their obligations on 9th February 2019, it was predictable that for such complex and varied supply system like the European the available time will be not enough to complete all these tasks. This resulted in an awkward situation for national competent authorities, whose responsibility was to supervise the functioning of the new end-to-end verification system and sanction any violations without causing any drug shortages at the same time. Because of the above, OGYÉI proclaimed a stabilization period and tried to play an active role as facilitator to help all stakeholders to comply. Over the past year, many problems had to be solved which were sometimes unpredictable. Many batches generated false alerts making hard to filter out potentially real falsification cases and it revealed the need for an alert handling protocol. By now, also the authority and the industry gathered enough experience to make the next step in ending the stabilization period.

ORAL PRESENTATION

Pharmaceutical activities of the former Hungarian order province of hospitaller order of St John of God

AMBRUS, T.
Department of Applied Pharmacy, University of Veterinary and Pharmaceutical Sciences / Masaryk University, Brno, Czech Republic

Background: The Hospitaller Order of St John of God was founded by Juan Ciudad in 1537 in Granada, Spain. Their first place of working in the Central European region was Feldsberg/Valtice, where a convent was established in 1605. On the territory of the Hungarian Kingdom the order members settled in the second half of 17th century. The Hungarian Order Province was established in 1856 and its existence suspended after 2nd Word War. Up to 1918, the Province included 13 convents, each of them operated a hospital and pharmacy.
Aims: To characterize the main attributes of everyday operation of the pharmacies run by the Order, with special attention to their location, equipment, assortment and personnel.
Methods: Methods of historical research were applied to reconstruct the past pharmaceutical activities of the Order. As main sources were used archival documents and other historical sources published in the studied period (journals, statistical publications, order schematisms, etc.).
Results: Historical sources from the studied period make possible the reconstruction of several partial attributes of pharmacy operation. Based on the study of authentic archival documents were obtained valuable data on the furniture and equipment of the pharmacies, logistics and economic aspects of their operation, contacts of the pharmacies with other specialized workplaces, like hospitals, pharmaceutical manufacturers, wholesalers or educational institutions.
Conclusion: The Hospitaller Order of St John of God played an important role in the development of modern healthcare and pharmacy culture and forming of the network of healthcare facilities. Historical research oriented to the study of Order's pharmaceutical activities gives specific information related to the healthcare services provided by religious orders, and could also contribute to generalization of the knowledge of historical development of pharmacy network.

Formulation and stability testing of inhalable powder preparation containing an antibiotic agent

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

Background: Pulmonary drug delivery can be divided into three main categories (pressured metered-dose inhalers, nebulizers and dry powder inhalers /DPIs/). Recently, the development of DPI products observed due to the production of traditional, carrier-based and carrier-free DPI systems. It should be emphasized that the harmony of the DPI formulation, the DPI device, and the patient are essential to achieve successful inhalation performance. Because most DPI devices are capsule-based, after the phase of particle engineering the investigation of DPI capsules has become more important to have the final dosage form [1, 2].
Aims: Our recent work introduced a novel combined formulation method, where the surface modification of the inhaled lactose and particle engineering of the drug were used before the blending. Therefore, the effect of magnesium stearate and sodium stearate on the final formulation was investigated. The effect of different DPI capsule types (gelatine, gelatine-PEG, HPMC) on the stability of novel combined formulated DPI samples was tested.
Methods: Ciprofloxacin (CIP) was the applied model drug. The developed novel formulation was filled in different capsules and stored (6 months) according to ICH guidelines. As a physical examination, particle size distribution, morphology and structure were studied. The in vitro aerosolization properties were investigated with the Andersen Cascade Impactor.
Results: The same formulation was filled in different capsules showed almost consistent lung deposition results before storage, but after 1, 3 and 6 months, the formulation stored in the HPMC capsule clearly had the best aerodynamic values, which correlated with the results of physical examinations. It can be established that the properties of the capsule shells influence the aerosolization results due to the change in the residual water content of the capsules, in the size and shape of the punctured area, and the different morphology of the DPI powder.
Conclusion: The development of dry powder inhalation capsules by manufacturers and the testing of

DPI powders in different capsules open a new way to increase the effectiveness of DPI products.
Acknowledgment: EFOP-3.6.2-16-2017-00006 LIVE LONGER project is acknowledged.

References: 1 Wauthoz, N. et al., Int. J. Pharm., 2018;553:47-56; 2 Ambrus, R. et al., Eur. J. Pharm. Sci. 2018;123:20-27

Heritable and environmental factors in schizophrenia and depression

BAGDY, G.
Department of Pharmacodynamics, Semmelweis University, Budapest

Common disorders are called also complex disorders that are characterized by heritable and environmental factors. The ratio of heritable and environmental factors is, however, highly variable. This is true also for psychiatric disorders. Ratio of heritable factors is high (> 80%) in schizophrenia and bipolar disorder (formerly bipolar depression), and low (ca. 30-40%) in major depression (unipolar depression). Heritable factors were calculated in twin studies earlier, but genomics took it over with the development of genotyping technology in genome wide association studies (GWASs), where the ratio of millions of genetic variants are compared in case (disorder) and control (healthy) populations without any information about environmental factors. Highly significant effects of several variants have been described in schizophrenia and bipolar disorder in GWAS studies providing evidence for the significance of heritable factors. Furthermore, there is a relatively broad overlap in the presense of these variants in these two disorders. In major depression, however, the number of reproducible hits is very low. In conclusion, genomic studies suggest that there are similarities in the biological background of schizophrenia and bipolar disorder, while ethiopathology of major depression is different.

Chromone derivatives as modulators of oxidative stress: in vitro biological evaluation and oxidative transformation

BAK, I.[1], CSÉPÁNYI, E.[1], KISS, A.[2], LEKLI, I.[3]
[1]Department of Bioanalytical Chemistry; [2]Department of Organic Chemistry; [3]Department of Pharmacology, University of Debrecen, Debrecen

Background: Oxidative stress (OS) is a phenomenon, which is related to the formation of free radicals and reactive oxygen species in excess. One of the major consequences of OS is the damage of biological macromolecules leading to the development and/or progression of numerous illnesses. Nowadays, there is an increase in the application of natural products for the prevention of different disorders, or adjuvant substances next to pharmacological treatment. Phytochemicals include different chromone derivatives, which possess a wide spectrum of biological activity.
Aims: In the present study we investigated the antioxidant activity, cytotoxicity and oxidative transformation of ten chromone derivatives.
Methods: We determined the radical scavenging activity (ABTS, DPPH, Galvinoxyl), the oxygen radical absorption capacity (ORAC) and the ferric reducing antioxidant power (FRAP) of the tested molecules. The cytotoxicity and their effects against H_2O_2 induced cell death were studied on H9c2 cell cultures by MTT assay. Finally, we investigated the oxidative transformation of the molecules. The oxidation was carried out by Fenton-reaction and the potential metabolites were detected by LC-MS/MS.
Results: The molecules have negligible effect against Galvinoxyl and DPPH radicals, while compound 2243 and 1675 showed significant activity against ABTS. In case of FRAP assay 2243 and 1675 also possessed significant effect, however, molecule No. 1617 exhibited the highest FRAP value. Furthermore, compound 2243 has low ORAC value, while 1675 and 1617 were the most active compounds during the ORAC assay. Based on the MTT assay neither of the molecules showed cytotoxicity. Moreover, those molecules, which showed significant activity in the antioxidant assays (1617, 1675, 2243), significantly improved the cell viability, when the cells were treated with H_2O_2 compared with the positive control.
Conclusion: In conclusion, based on the results the (2E)-3-(4-oxo-4H-chromen-3-yl)prop-2-enoic acid (1617), 4-oxo-4H-chromen-3-carboxilyc acid (1675) and 3-[5-(chloromethyl)-1,3,4-oxadiazol-2-yl]-4H-chromen-4-on (2243) possess significant antioxidant activity, non-cytotoxic at the applied concentration and stable metabolically, hence, it is worth to investigate further in OS related diseases models.

Acknowledgement: This study was supported by the GINOP-2.3.2-15-2016-00043 (IRONHEART), the Higher Education Institutional Excellence Program NKFIH-1150-6/2019 and EFOP-3.6.1-16-2016-00022 „Debrecen Venture Catapult" projects.

Novel investigation methods and innovative 3D printing possibilities in the pharmaceutical technology

BÁCSKAY, I.
Department of Pharmaceutical Technology, University of Debrecen, Debrecen

Background: Nowadays, 3D printing is one of the major top 10 innovative research fields in the pharmaceutical sciences. Rapid prototyping and additive

manufacturing are also the synonimes of this technique. Briefly, it is a layer by layer printing process using special digital code. The first step is the design which could be computer aided design or 2D method where the structures of layers are planned. The second step is the conversion of these design for STL file, which is mainly the basis of 3D printing. In the third step, the raw materials are prepared as granules, extruded filament or binding solutions. Finally, as the last step the product is printed layer by layer, then solidification and the removing of supplementary components are made. 3D printing techniques have many benefits, because complex, personalized products are manufactured by automated, low-cost operation. 3D printing is widely used in the field of arts, architecture, industry, nevertheless it has a great impact on the preparation of medical, pharmaceutical products.

Aims: The presentation objective is to give a short summary about the methods which have high application possibility in the pharmacy and pharmaceutical industry.

Methods: In this review, inkjet printing, stereolithography, fused filament fabrication method, hot melt extrusion technology are summarized.

Results: In the pharmaceutical industry, Spritam was the first FDA approved medicine in 2015, it was produced by ZipDose technology. Thin powder layer was bound, it was repated until the appropriate tablet format was reached.

Conclusion: The main pharmaceutical significance of 3D printing is the rapid, individualized, personalized medication, however qualification and authorisation of the printed products have to be regulated.

References: 1 Alhnan, M. AT. et al., Pharmaceut Res 2016;33:1817-1832; 2 Liska, R, et al., J. Coat Tech Res 2007;4:505-510

Challenges for the next quarter century. Quality in hospital pharmacy – hospital pharmaceutical quality development framework

BECSKEHÁZI-TAR, A.[1], KOVÁCS, ZS.[2], MOLNÁR, B.[3], RICHTER, K.[4], SZABÓ, A.[5]

[1]Central Clinical Pharmacy, University of Debrecen, Debrecen; [2]Hospital Pharmacy, Borsod-Abaúj-Zemplén County Hospital, Miskolc; [3]Central Clinical Pharmacy, University of Pécs, Pécs; [4]Hospital Pharmacy, Szent Borbála Hospital, Tatabánya; [5]Hospital Pharmacy, Szent Imre Hospital, Budapest

In the last quarter of the 20th century, the supply of medicines has been steadily improving, and the reliability of supply has increased. In the recent past, development has come to a halt and shortcomings are beginning to emerge again. Pharmacy must be prepared for the challenges of the next quarter of this century.

What are the most important factors in changing the economy and society and how should pharmacists prepare for it?

Negative trends, dangers are as follows:
- *economic crises*
- *climate crisis*
- *increase in energy and logistics costs*
- *an aging society*
- *decrease in active money earners*
- *more expensive research*
- *mental illnesses, abuses*
- *outbreaks of epidemics*

Positive trends, opportunities:
- *Industry 4.0*
- *Society 5.0*
- *digital world, artificial intelligence, big data*
- *development of education*

All members of the pharmaceutical profession must be prepared for the changes. Together with economic and state actors, pharmaceutical and professional organizations are developing programs for change. In addition to securing financial resources, the task is to reduce losses and make better use of opportunities and opportunities. Applying positive trends to practice will be key to development.

The quality requirements of the hospital pharmacy fit tight to the function of the health care provider institution. The quality of the medication determines basically the efficiency of the therapy. Hospital pharmacists must closely cooperate with other health care personnel. In the international practice there are preconceived standards for the cooperation between hospital pharmacists and associate professions. Therefore, we can access both to the European (EAHP) and American (ASHP) hospital pharmaceutical standards.

Our aim was to create the quality management frame of the hospital pharmacy after summarizing the standards concerning Hungarian hospital pharmacy.

We have processed the standards of Hungarian health care system regarding to pharmacy. We have also processed the ASHP (American Society of Health-System Pharmacists) Guidelines: Minimal Standards for Pharmacies in Hospitals, and the standards of the European Association of Hospital Pharmacists (EAHP).

We have formulated the quality management requirements of hospital pharmacy. The Hungarian Society of Hospital Pharmacists have published it in a book form.

The publication is necessary for hospital pharmacists. It is practical to provide a training for all hospi-

tal pharmacists in order to introduce them the standards.

Reference: Becskeházi-Tar A, et al.: Minőség a kórházi gyógyszerészetben; Klinikai Gyógyszerészeti Minőségfejlesztési Keretrendszer; Galenus Kiadó Budapest, 2019. ISBN 978-963-7157-56-1

The implementing and evaluating of Medication Management standards in cases Joint Commission Accreditation and Hungarian Health Care Standards (MEES)

BECSKEHÁZY-TAR, J.
SGS Hungary Ltd. Certification and Business Enhancement Division, Budapest

Background: As hospital pharmacists have expanded their role from simple drug dispensing to patient-oriented clinical practice, they have augmented their professionalism (the attitude sand belief as professional and quality) as hospital pharmacists. This it has been important to make them commit to hospital quality standardization and evaluation programmes based on several international or national standard frameworks. Introducing and evaluating standards is a big challenge for pharmacists because: – they do not have sufficient experience in audit, – no professional network of evaluators yet, – there are several standards that contradict the Hungarian rules – for example the use of own medications. The management of personal medical treatmentsof patients hospitalised in health facilities follows regulatory requirements. Failure to respect these requirements may resultin iatrogenesis, with sometimes severe consequences for thepatients.

Aims: My goal is to present my own audit experience gained over the past 12 years in implementing and evaluating of Medication Management standards in cases Joint Comission Accreditation and Hungarian Health Care Standards (MEES). I have a special focus: The detection of critical errors and opportunities for improvement in cases of patients' own medications.

Methods: Audit has been realised in order toassess how the medical staff follow standard criterias, risk-matrix and protocols on medical data sheets and personal awareness.

Results: Of the 379 audit reports submitted about patients taking their own medications from home while in the hospital, more than 25% of the reports mention a medication considered to be a "high-alert" medication. High-alert medications are medications that have an increased risk of causing significant patient harm when they are used in error. The reports also showed that nearly 8% of the reported events resulted in a transfer of the patient to a higher level of care, with 67% of these cases involving patients taking their own controlled substances (narcotic/pain meds) from home.

Conclusion: Let's give space for common answers – interactive quiz: Why Do Patients Bring Their Own Medications? What Do Clinical Pharmacist Need to Know to for Patients safety? How do prepare for an audit? What role do risk assessments and problem-solving techniques play in evaluation? What competencies are needed in the audit team? How to multiplicate auditor knowledge?

New perspectives of skin penetration investigational methods for dermal preparations

BERKÓ, S., ZSIKÓ, S., CSÁNYI, E.
Institute of Pharmaceutical Technology and Regulatory Affairs, University of Szeged, Szeged

Background: Dermal drug therapy has increasing importance nowadays in drug development. Modelling of penetration into the skin is a complex challenge. Human skin tests give the most relevant information however, because of the high cost, it is advisable to choose simpler methods in the early stages of development of dermal preparations. Not only the device, the membrane and acceptor solution, but also the properties of the carrier system itself influence how the particular system can be most effectively tested.

Aims: The aim of this work was to summarize the novel knowledge about the main in vitro methods available to study the skin penetration and present various experimental models used to investigate drug penetration into the skin effectively.

Methods: There are many types of equipment on which in vitro release tests (IVRT) and in vitro permeation tests (IVPT) of drug carrier systems can be performed. Two types of vertical Franz diffusion cell (Hanson Microette TM Topical & Transdermal Diffusion Cell System and LOGAN Automated Dry heat sampling system) with different membranes (synthetic and biological) and the Skin-PAMPA method have been compared.

Results: The reproducibility, sensitivity and specificity of the method are essential for reliable in vitro testing. Based on our results, we can select the optimal in vitro test for modelling the penetration into human skin, and in vivo results can be predicted.

Conclusion: In this work, the most well-known and state-of-the-art methods for studying drug penetration through the skin have been presented, which can provide significant support during the development phase of the dermal preparations.

How to plan a smart patient safety sytem?

BERTALAN, Á.
Karolina Hospital, Mosonmagyaróvár

Background: Smart devices are gaining more and more ground in our everyday lives. Robots and virtual assistants are popping up left and right. Until today, however, the Hungarian health care system has been resisting the spread of modern technology, partly due to the peculiarities of the financing system and the passive resistance of professionals.
Aims: By utilizing innovative technologies of the private sector and by taking the special needs of the healthcare institution into account, our goal is to create an IT system that records the data in a central database in a form that can be analyzed by decision support algorithms, and thus support medical decisions according to the expectations of the 21st century. In addition, the medical system should be able to manage and automatically document medication, nursing, and medical activities performed according to protocols.
Method: In a development project financed by a tender, we are carrying out a transformation on our medical system with the help of the participating system administrator, which makes it possible to record the patient documentation data as described above. To plan the transformation of the medical system, we set up a multidisciplinary working group, which included delegates from the IT company, our own IT specialists, clinicians from various professional groups and pharmacists.
Results: After months of consultation, the working group prepared a detailed specification of the database and a feasibility study. The programmers handed over a beta version of the modified program. Testing of the program has been started by members of the planning committee and will be continued by the pilot departments once the identified errors have been corrected. Integration into the daily patient care routine is a time-consuming process, but we plan to extend certain functions to the entire institution within a year.
Conclusion: Based on our experience so far, we have concluded that the construction of such a complex system is only possible with the involvement of dedicated professionals. One of the most important participants in the working group is the mediator, who can translate between healthcare professionals and IT professionals. The reason for failure in most of these attempts is that the developer and the customer do not understand each other..

New medication-related developments in The Hungarian Electronic Prescription System and other eHealth services

BERTALAN, L.[1,2]
[1] National eHealth Infrastructure National Healthcare Services Center; [2] Faculty of Health Sciences, Semmelweis University, mail: bertalan.lorant@aeek.hu

In all countries, where electronic health services such as e-prescriptions have been introduced, patient safety has improved and the standard of medical and pharmaceutical care has increased. ePrescription (eRecept) - launched in Hungary as well - has become the most used eHealth module of the EESZT (National eHealth Infrastructure) by all healthcare providers in the past near 3 years. During the COVID epidemic emergency e-prescription system has been a huge help to patients, relatives and caregivers too. In this period the proportion of electronic issued prescriptions exceeded 90% of all prescriptions written.
The e-prescription system contributes to the better and faster information of healthcare professionals, supports the well-based therapy decisions, helps preventing and eliminating medication errors. Adverse drug reactions (allergies, interactions, polypharmacy etc.) can be more easily identified with the daily use of this service. Less paper administration can increase the time and quality of patient counseling both at the doctor's and in the pharmacies. Medication adherence can also be simply monitored by pharmacist as well. After patient registration - using social security number (SSN/ TAJ) -, written maximum 1 year earlier and/ or by other pharmacy dispensed prescriptions will be also downloadable soon from the central database. These functions and real time data contribute to the implementation of high-quality pharmacotherapy advising services in pharmacies as healthcare institutions, made in accordance with the specific standards and protocols.
The new functions of the Patient Portal (e.g. Legal Representation) and mobile surfaces provide patients and their relatives access to follow their care process, prescriptions, labs, etc., already on their smartphone too. From the beginning of May 2020, serial-produced medical aids mostly sold in pharmacies, can be electronically issued. The full integration of all the medical aids may be completed next year in a separated module. A simple web-based prescriber (so-called miniHIS) has been developed for connected private doctors, who do not consult in institutions.
Measured values of the (smart) medical devices can be uploaded into the personal data repository of the

Patient Portal on a voluntary basis. Good measurement results of the blood pressure, sugar, body weight, etc. recorded here demonstrate therapy fidelity, providing feedback to the patient and professionals. Telemonitoring services can be build on this module, so the software can send alerts to the assigned doctor, pharmacist or family member.
Keeping data protection rules strict, depersonalized pharmacotherapy data uploaded to the central eHealth database will be searchable soon for professional and scientific purposes.

A break in the drug supply chain

BICZÓ, Á.
Pharma Patika Újpest Pharmacy, Budapest

Background: What does medication shortage mean? As a practicing pharmacist, we have a different concept behind than OGYÉI, or even a pharmaceutical manufacturer. Neither will the patient or the customer be more reassured if we provide the official legal explanation for the seemingly simple question, "Why don't I get my medicine?"
Aims: What is the important for us in the community pharmacies, is whether we can provide the patient with a solution? As the last link in the chain, we are also a collision interface, as this presents us a toll on our everyday practice. Sometimes we know the answer, sometimes we have little information about why we can't make the desired order for the patient. What's really going on in the background may be unknown for many colleagues working in community pharmacies…
Methods: Where does the story medicine shortage start? I searched through the supply chain for possible causes, development and resolution of medicine shortages: starting from the authorities and pharmaceutical manufacturers, wholesalers, raw material manufacturers, and finishing at the pharmacy.
Results: Officially reported reasons for shortage in case of registered pharmaceuticals may be shipping, storage problems, active ingredient, raw material issues, manufacturing issues, market considerations, increased market demand, administrative issues, etc. The real reason usually can be described by a complex set of factors. Since officially only registered products are considered for shortage, I dealt with them only during my analysis, guiding them through the market. According to the possibilities of the development of the drug shortage, I found different reasons among the market players. There are specific deficiencies specific per each particular actor.
Conclusion: What reflects the views of all actors involved in supply chain management are shortage of labour, the rise in quality standards, the globally expanding market, which has led to over-demand rather than over-supply.

An overview of health management patterns: preferences, adherence and the electronic prescription attitudes in the community pharmacy

BICZÓ, Á.
Pharma Patika Újpest Pharmacy, Budapest

Background: Health self-management of pharmacy customers has a complex impact on society beyond individual well-being, and our priority is to know and improve the determinants thereof, such as preferences, adherence, and to describe and use attitudes related to the electronic prescription, all of which serve the purpose of compiling a better community pharmacy service package for patients.
Aims: In the cross-sectional, retrospective study, our goal is to assess, on a representative sample of n = 472 people, what the elements of patient health management are, what are their main characteristics, and what conclusion can be drawn for a community pharmacy.
Methods: We created our own Hungarian questionnaire consisting of 20 questions for the survey. We have sought to use language that is understandable to the patient, and to create simple and quick questions that require no more than 10 minutes to complete.
Results: The results describe the profiles, preferences, attitudes of patients of two pharmacies in Budapest and the Department of Ophthalmology, as well as the current status of electronic prescription as an increasingly popular and frequent service. The current study is being developed to a longitudinal one, which provides further insights into the community pharmacy aspects of the above questions.
Conclusion: There are different trends across ages of patients regarding pharmacy loyalty, night service use, and adherence rates. A personalised approach should be applied to meet these client needs.

Drug developments for rare diseases

BIRINYI, P.[1], TINTA, A.[1], ÁRVAI, I.[1], HUBAY, Z.[1], VUKMAN, N.[1], HORVÁTH, A.[2]
[1]*Mikszáth Pharmacy, Budapest;* [2]*Institute of Pharmacognosy, University of Pécs, Pécs*

Background: There are many rare diseases for which no speciality drug is available, but it is known from the literature that therapy is possible. In most cases, the rare disease therapeutic protocol is part of professional guidelines.
Aims: Therefore, we aimed in the Mikszáth Pharma-

cy, as far as our possibilities, based on the clinical evidence develop and produce niche drugs.
Methods: We have been able to count on the help of Hungarian and many foreign medical universities in the development of newly developed medicines. Our pharmacy laboratory has been designed to produce all pharmaceutical forms. Eg: injections, intravesical solutions, tablets, capsules, etc. The new active substances (Bismuth citrat, Zinci acetate) to be introduced were "positive list" after OGYÉI approval, and received TTT code and health insurance support from NEAK. In all cases, our new magistral formulations are tested according to the Pharmacopoeia. We also place great emphasis on checking the biocompatibility (pH, osmolarity) of all ophthalmic and intravesical preparations. In addition, we closely monitor the patients' drug therapy. Together with the treating physicians, we examine the clinical and therapeutic efficacy of our products.
Results: Over the past 12 years, we have developed a niche magisterial drugs against more life-threatening diseases. We currently provide nearly 3,500 patients in Hungary with our newly introduced drugs in the indications below:
– *Wilson's disease – Comprimata zinci acetas*
– *Helicobacter pylori infection – Second line eradication (Capsula bismuthi et metronidazoli)*
– *Nephropathic cystinosis -Oculogutta cysteamini*
– *Fusarium keratitis – Oculogutta argenti nitrici*
– *Acanthamoeba keratitis – Oculogutta polyhexanidi*
– *Stenotrophomonas maltophilia keratitis – Oculogutta/ Oculentum trimethoprimi et sulfamethoxazole*
– *Uveitis – Oculogutta/ Oculentum prednisolone*
– *Central hypogonadismus – Injection alfa-koriogonadotropini (grants specific aid to NEAK)*
– *Chronic bladder pain syndrome – Solutio GAG stratum restitutor cum adapter*
– *Status epilepticus- Solutio midazolam cum MAD nasal*
Conclusions: The magistral formulations developed and produced in the pharmacy laboratory are niche and indispensable for the continuous and safe supply of medicines.

New challenges in the pharmaceutical development

BÓDIS, A.
Gedeon Richter Plc., Budapest

The pharmaceutical companies working on the development of new medicinal products have to face continuously changing challenges. These changes have various reasons. In medicine, the background of many illnesses has been explored and become well understood, and this contributes to the efficiency of the pharmaceutical product development. The share of biological medicinal products – which require special technological apparatus and analytical knowledge – is expending, but even in cases of medicinal products with small molecule active substances, more advanced technological procedures are applied during development and production. New types of excipients appear which can also be used to modify or control the release and even the absorption of active substances. At the same time the regulatory requirements are getting stricter and to comply with these regulations means high cost and time in many cases. There are great expectations of the prices and differentiation of medicinal products by health insurance companies, doctors and even by patients as well. The pharmaceutical product development has to work in this multi-pole system and find the fastest and the most cost effective way to elaborate the preparation and to execute the economical commercial manufacture of new medicinal products which are modern, satisfy patients' need, and have the required quality as well. The pharmaceutical industry needs to investigate the efficiency of technological processes and the feasibility of commercial manufacturing, and meanwhile to pay special attention to the production cost and yield. New measurement techniques are involved in the development and production which help us to acquire deeper knowledge about our processes. The question is whether the pharmaceutical industry and education is prepared for these changes?

Possible service of hospital-based outpatient pharmacies: dispensing of medicines with special patient information requirements

BODÓ, G.[1], BENKŐ, R.[2], MATUZ, M.[2]
[1]*Central Pharmacy, Albert Szent-Györgyi Health Center;*
[2]*Department of Clinical Pharmacy, University of Szeged, Szeged*

Background: Physicians working at the University of Szeged, Albert Szent Györgyi Health Centre („SZAKK") can prescribe medicines to discharged patients and to patients who seek medical care at the hospital's outpatient services. These prescriptions can be redeemed at the hospital's outpatient pharmacies but also in other community pharmacies.
Aims: To analyse the quantity and pattern of drug prescriptions issued by physicians working at the SZAKK.
Methods: The retrieve all prescriptions issued at the SZAKK during 2018 from the informatic system (e-MedSolution® Electronic Patient Workfilesystem) and transfer it to Excel. Drug were classified according to the WHO ATC system (version 2019). Drug prescription was quantified as number of prescribed packages and gross price.
Results: Slightly over than half million (594 thou-

sand) drug packages were prescribed during 2018, corresponding to 900 different active agents. Drug products of the „L" ATC main group (antineoplastic and immunomodulating agents) made up nearly 65% of all costs. Ranking active agents according to gross price, the top ten agents were: teriflunomide; fingolimod; somatropin; tacrolimus (oral); ruxolitinib; natalizumab; glatiramer acetate; alemtuzumab; sunitinib and mycophenolate mofetil. These active agents were marketed min. 5 years ago. Six agents have oral, 4 parenteral administration route.

Conclusion: Pharmacists working at the outpatient dispensing pharmacy of the SZAKK should be sufficiently knowledgeable about these medications and should work closely with the prescriber to optimise drug treatment.

Formulation of innovative ophthalmic preparations

BUDAI-SZŰCS, M., L. KISS, E., CSÁNYI, E.
Institute of Pharmaceutical Technology and Regulatory Affairs, University of Szeged, Szeged

Background: The locally administrated ophthalmic formulations on the market have poor bioavailability thanks to the elimination mechanisms (reflex lacrimation and blinking) and barrier function of the eye. It would therefore be useful to design a new formulation which is able to prolong the residence time reducing the administration frequency; and are able to increase the penetration of the drug into the deeper layers of the eye (when not the eye surface is the site of action).

Aims: The aim of our study was to improve the bioavailability of poorly water soluble ophthalmic steroidal anti-inflammatory drugs (prednisolone and dexamethasone). Two different strategies were applied: 1) increase the residence time on the ocular surface using cyclodextrin modified mucoadhesive polymers; and 2) application of nano lipid carriers in order to increase the penetration of drug through the cornea.

Methods: To analyse the improved residence time and controlled drug release, rheological and mucoadhesive investigations, drug diffusion tests were applied. For the formulation and characterization of the nano systems, preformulation studies, and a 23 full factorial design were used, the advances of the nano formulations were evaluated by penetration and drug diffusion studies.

Results: The application of the mucoadhesive polymers can increase the residence time of the formulation on the eye surface, which is indicated by the mucoadhesive measurements. The combination of the mucoadhesive polymer with cyclodextrin can increase the solubility of the steroid drug, and the cyclodextrin immobilization can control the drug release. The application of nano lipid carriers enable to dissolve the lipophilic drug, which resulted 2-fold drug amount in the dissolution medium, and could help its penetration into the hydrophilic stroma in the cornea, which can serve as a depo for the further deeper penetration steroidal drug.

Conclusion: Both of the applied strategies can effective in ophthalmic formulations. In the first case, the improved residence time and the immobilization of the drug-cyclodextrin complex can the key factor of the effective controlled drug release. In the case of the second strategy, the improved drug solubility, the penetration enhancing effect of the nanocarriers can place these formulations into the innovative ophthalmic preparations.

Potential applications of BGP-15 in clinical cardiology -review of available preclinical data

CSANÁDI, Z.[1], JUHÁSZ, B.[2], BÁCSKAY I.[3], SZILVÁSSY Z.[2]
[1]*Institute of Cardiology;*
[2]*Department of Pharmacology and Pharmacotherap;*
[3]*Department of Pharmaceutical Technology, University of Debrecen, Debrecen*

BGP-15 in heart failure and atrial fibrillation.

Growing incidence of heart failure (HF), especially the form with preserved ejection fraction (HFpef) defined as the presence of HF symptoms and elevated level of biomarkers with left ventricular ejection fraction (LVEF)>50% has recently been demonstrated. There is no specific therapy available for this entity. Atrial fibrillation (AF) is another global health problem with rapidly increasing incidence. Significant relationship between AF and HF and frequent coincidence of both with type 2 diabetes mellitus has also been established. The critical role of fibrosis in these pathologies has been suggested by imaging and laboratory tests. The drug candidate BGP-15, an insulin-sensitizer and heat-shock protein demonstrated efficacy and safety in patients with type II diabetes and in healthy controls. Further, this small molecule was tested in a rat model of diabetic cardiomyopathy and mouse models of both HF and AF. Significant improvement in diastolic function and attenuation of myocardium fibrosis were demonstrated in these preclinical investigations.

BGP-15 in inappropriate sinus tachycardia.

Inappropriate sinus tachycardia is defined as an elevated resting heart rate in the absence of an underlying cause and/or a rapid increase in the heart rate with minimal exertion. Available treatment with beta-blockers, Ca-channel blockers or the I_f channel-

blocker ivabradine often fail to provide sufficient symptom control and titration of beta-blocker to a sufficient dose might be limited due to significant hypotension. Result of animal studies suggest modest effect of BGP-15 on resting heart rate. Allosteric modulation of beta-receptors in the cell membrane as demonstrated by lipidomic investigations suggest that co-administration of BGP-15 and beta-blockers might be worth study in this difficult patient cohort.

Acknowledgement: GINOP-2.3.2-15-2016-00043, and the research was also financed by the Higher Education Institutional Excellence Programme (NKFIH-1150-6/2019) of the Ministry of Innovation and Technology in Hungary, within the framework of the Therapeutic Purpose Development thematic programme of the University of Debrecen.

Drug-device combination products in view of the new MDR (Medical Device Regulation)

CSEH-PÁLOS, A.
Medicines Authorization Division, National Institute of Pharmacy and Nutrition, Budapest

In recent years there has been an increase in the number of marketing authorisation applications (MAAs) and scientific advice requests where a medicinal product incorporates a medical device for the use of the medicine. The availability of commercialised devices with automated functions is increasing and this may benefit patients with regular and long-term dosing requirements in an outpatient setting, either by self-administration or with the support of a professional or lay caregiver. This reduces the burden on patients and on healthcare systems.

Given the wide diversity of devices supplied with medicinal products, the continuous technological developments and the differences in medical device and medicinal product legislation, the data supplied in the MAA dossiers is often inconsistent and incomplete. Therefore, EMA has decided to publish a guideline on quality aspects of the dossier requirements for drug device combinations (DDCs) to show that the they are appropriately designed and controlled and can be used correctly in the intended clinical situation.

The guideline addresses the new obligations in Regulation (EU) 2017/745 on medical devices, in particular the requirements under Article 117. According to this article the marketing authorisation application (MAA) should include a CE (Conformité Européenne) certificate or declaration of conformity for the device or, in certain cases, an opinion from a notified body on the conformity of the device.

Medical devices supplied as integral to a medicinal product, such as pre-filled syringes, inhalers, and auto-injectors, are more complex than container-closure systems, due to the associated delivery and measuring or metering function. Inappropriate use of these devices may compromise the safety and efficacy of the medicinal product and result in adverse drug reactions or medication errors. Complex DDCs have the highest risk of inappropriate usage.

Evaluation of fitness for the intended purpose (e.g. administration of a medicinal product) needs to take into account the quality aspects of the device in itself and its use with the particular medicinal product, as well as the complexity of the device component, the patient characteristics, the caregiver characteristics where relevant and the clinical situation in which the DDC is to be used.

Flow-through hydrotoxicology equipment for testing chemicals on zebrafish

CSENKI, Z.[1], BOCK, I.[1], GARAI, E.[1], KEREKES, F.[1], VÁSÁRHELYI, E.[1], SIMON, G.[2], IMRE, P.[2], DREVNÓ, AG.[2], URBÁNYI, G.[1]
[1]*Department of Aquaculture, Szent István University, Gödöllő;*
[2]*Sentimento Ltd., Érd*

Background: Zebrafish (Danio rerio) has had the biggest carrier in the field of toxicological tests recently. In addition to its role in licensing various active agents, today, due to the large number of desease models produced, there have already been results obtained on zebrafish used in human medicine. Despite some variations between the methodologies of the treatments applied, in general, the treatment concentrations used should remain as stable as possible throughout the experiment in order to obtain reliable results. However, the implementation of this criteria in aquaous environment is difficult.

Aims: To solve the problem mentioned above, our goal was to develop an equipment suitable for hydrotoxicological tests which is also capable to maintain the treatment concentrations with the least human intervention ensuring reliable results during the experiments.

Methods: Our goal has been achieved by a system created to test pure agents and mixtures on aquatic organisms which is:

- *able to prepare specific concentrations or concentration-range from a previously prepared stock solution based on the given parameters by diluting the stock solution.*
- *Is capable to adjust the amount of solvent used in each test pool to the same concentration.*
- *Is capable to replace the test solution automatically at a set time in a static, semi-static, or flow-through system.*
- *Is able to investigate certain chemical and physical parameters of the test solution and of treating and purifying the effluent.*

– *Minimizes the risk of human contamination.*
– *Can be introduced for tests made in GLP (Good Laboratory Practice) systems.*

Results and conclusions: The flow-through toxicological equipment is suitable for performing zebrafish toxicology tests. The applicability of its final prototype has been verified by analytical and toxicological tests, which have already met the quality criteria of the most commonly used OECD standards in the case of water soluble substances.

New therapeutic possibilities of astaxanthin administration

CSERNOCH, L.
Department of Physiology, University of Debrecen, Debrecen

Astaxanthin (AX) a marine xanthophyll carotenoid is a powerful natural antioxidant which emerged in the spotlight due to its potential anti-cancer, anti-diabetic, anti-inflammatory, immune-stimulating effects. Here the effects of AX in skeletal muscles from young adult (4-5 months old) male C57Bl7 mice fed with AX for 4 weeks (AstaReal A1010, 0.05% w/w added in standard rodent chow) were evaluated. The actions of AX feeding on food intake, energy homeostasis, and the arcuate nucleus of mice expressing were examined. Furthermore, electrophysiological experiments were carried out on isolated canine ventricular myocytes acutely treated with 2.5μM AX.

At the end of the 4 weeks feeding period the body weight gain of the AX group was significantly less when compared to control (0.16±0.33 vs 1.22±0.31g, $p<0.01$) although the mice consumed roughly the same amount of chow. The voltage activation of calcium transients of single isolated *flexor digitorum brevis* (FDB) fibers of AX treated and control animals was identical. The mitochondrial Ca^{2+} uptake in FDB fibers upon repetitive stimulation was found to be less prominent in the AX group. The amplitude of *ex vivo* tetanic force measured on the *extensor digitorum longus* muscles was significantly higher in AX than in control (7.1±0.5 in CTRL vs 8.7±0.5 kN/m^2 in AX, *$p<0.05$). Neurons of AX supplemented mice displayed significantly greater frequency of spontaneous inhibitory postsynaptic currents (sIPSC). Similar, although weaker frequency increase was seen on POMC-positive neurons when AX was applied acutely. 77% of the GABAergic neurons displayed higher frequency of calcium transients, and a subpopulation of GABAergic neurons showed augmented excitability and received excitatory postsynaptic currents (EPSCs) with a greater frequency. In canine ventricular myocytes acute AX administration significantly decreased the APD50 and APD90 durations, as well as Vmax and the mid-plateau potential. Based on our results, AX improves tetanic force in skeletal muscles without affecting the ECC mechanism and exerts a protecting effect on the mitochondria against calcium overload. In neurons from the arcuate nucleus that play a cardinal role in the control of feeding AX increased the maximal AP and IPSC frequency. In cardiac myocytes AX shortened the duration of the APs which could have potential anti-arrhythmic implications.

Quality by Design and Process Analytical Technology in pharmaceutical development

CSÓKA, I.
Institute of Pharmaceutical Technology and Regulatory Affairs, University of Szeged, Szeged

Background: Quality by Design (QbD) is a systematic approach to development that begins with predefined objectives and emphasizes product and process understanding and process control, based on sound science and quality risk management. Process Analytical Technology (PAT) is defined as a system for designing, analyzing, and controlling manufacturing through timely measurements (i.e., during processing) of critical quality and performance attributes of raw and in-process materials and processes with the goal of ensuring final product quality. This paradigm change has the advantage of promoting a better understanding of the material characteristics and process parameters affecting the final quality of the targeted product, also brings a holistic and risk-based structured way of thinking into industrial manufacturing procedures. The so called "R&D QbD" is advised to be introduced into the early development phase of dosage form and manufacturing process design, including modern risk assessment and further quality tools.

Aims: The aim of this summary is to disseminate the knowledge and experiences of the R&D QbD model introduced into different challenging projects, such as designing colloidal carrier systems for nanomedicine use specially in case of peptide-protein drugs.

Methods: The main elements of "R&D QbD": Preformulation Design, Stakeholder Analysis, Initial Risk Assessment, Composition & Process Design, Design of Experiments, Design Space Development, Control Strategy.

Results: The selected experimental examples prove the efficiency of involving the elements of QbD in composition design and preparation of non-biological and biological complex drug formulations.

Conclusion: Application of the methodologies of "QbD" and "PAT" facilitates knowledge and technology transfer from early phase of pharmaceutical development to industrial manufacturing, resulting

quicker market access e.g. in case of non-biological and biological complex drugs for unmet clinical needs.

How can I improve the patient safety as a pharmacist?

CSONTOS, J. D.[1], LÁM, J.[2], HIGYISÁN, I.[1]
[1]*Bajcsy-Zsilinszky Hospital and Clinic Hospital Pharmacy;*
[2]*Semmelweis University Health Services Management Training Centre, Budapest*

Patient safety is a serious global public health issue. That was first discussed during the World Health Assembly in 2002 since then WHO have been developing policies and publishing declarations, guides and brochures in order to draw attention to patient safety. In the past decade projects focusing on patient safety were carried out one after the other in Hungary as well, to empower care givers and institutions in the national health care system. Safe medication is one of the most important aspect of patient safety that can be guaranteed by prevention of medication error. Pharmacists have a key role both in outpatient and inpatient settings. In order to do that, pharmacists need to develop their knowledge and skills. The presentation will cover the methods offered by WHO which have appeared in the Hungarian developments and the ever more popular patient safety programmes.

The health care is a very complex system therefore it involves risks, but it can be made safer by recognising the potential errors, and by developing systems and strategies to learn from mistakes so as to minimize their occurrence and effects. As health-care workers it is important to be mindful of situations that increase the likelihood of error for human beings. For improving patient safety, we have to develop a work culture that encourages the reporting of adverse events and near misses in health care. The aim is to understand the nature of error and how health-care providers can learn from errors to improve medication safety.

Health care is rarely carried out by single individuals. Safe and effective care is dependent not only on the knowledge, skills and behaviours of workers, but also on how those workers cooperate and communicate in the work environment. For example only a part of the prescribing errors that are made reach patients; the others are caught in time by pharmacists and other health-care workers. This fact underscores the importance of teamwork. We understand and use the other tools of patient safety developing and we avoid to reliance on memory we simplify and standardize processes and procedures, use checklists and do not only reliance on vigilance.

Possibilities of social media in the improvement of adherence

DÉR, P.
Kígyó Pharmacy, Mogyoród

Background: The success of a medication lies not only within taking the medicine, but more within the adherence of the patient. Therefore, the patient's lifestyle is not marginal in the outcome of the therapy, the enhancement of the quality of life.

Aims: An outstanding task of the pharmacist is to support the adherent behaviour of the patient.

Methods: I have evaluated the role of online pharmaceutical consultation and the effects of online presence in the analyses of several online surveys. These show unequivocally that the online presence of the pharmacist helps medical professionals to be the primary source of information. Besides, great responsibility lies within providing authentic information.

Results: I have the greatest experience in connection with consultation on Facebook, since 2014. I would like to present its development, and what steps have been made in order to make the process more professional. Today, this consultation is not the task of an individual, but the cooperation of 7 pharmacists. We provide answers to more than 6,500 persons' questions almost every day, within 12 hours. We strive to encourage people to ask questions, our principle is that there is no stupid question.

Conclusion: When answering, comprehensibility, up-to-date knowledge and the possibility of a conversation between questioner and professional are very important. This makes the clearing of vague areas and follow-up possible. The process being written is very helpful in this, as this makes history and anamnesis accessible. All this enhances the patient's trust in the professional, which enables us to deal not only with questions of therapy, but also improve the patient's adherence.

Experiences with the website of the Hungarian Society for the History of Pharmacy

DOBSON, SZ.
Hungarian Society for the History of Pharmacy, Budapest

The Hungarian Society for the History of Pharmacy started a systematic development of its website (www.gyogyszeresztortenet.hu) in 2013, which opened a new era in the history of pharmacy in Hungary. We currently have full pdf copies of about 320 books, 52 doctoral theses and diploma works, more than 2000 articles (an estimated 90% of all papers in the last 60 years), a Lexicon of more than 350 out-

standing Hungarian pharmacists, a Lexicon of more than 1000 old drugs based on the labellings of pharmacy jars, journals, hundreds of photos of old pharmacy equipment, old industry-made preparations and prescriptions, in addition to useful links (such as links to our fellow Societies). everyday newsflow. Since these pdf files have been prepared using optical character recognition, by a built-in Google search engine researcher of our website can search for any information simulteneously in more than 100,000 pages of highly diverse literature sources. Our website even provides information to people searching Google or other search engine in general, having heard nothing about or website before. Consequently, we have been contacted by individuals in and outside Hungary who have found genealogy and other data, and the very efficient identification of any keyword or expression stimulated research and publication activity as well. For example, this electronic researh tool opened way to co-operating with more than a dozen pharmacy student to puzzle out the meaning of acronyms of materia medica on the labels of old pharmacy jars and glassware. This presentation intends to share our experiences in developing and using electronic research in history of pharmacy.

Examination of the effectiveness of medication review done by pharmacists in Hungarian community pharmacies

DOBSZAY, A., SZILVAY, A., SOMOGYI O., MESKÓ, A., ZELKÓ, R., HANKÓ, B.
University Pharmacy Department of Pharmacy Administration, Semmelweis University, Budapest

Background: According to the definition of Pharmaceutical Care Network Europe „Pharmaceutical Care is the pharmacist's contribution to the care of individuals, in order to optimize medicines' usage and improve health outcomes." The main tool to this activity is medication review, which is the evaluation of the patients' medicines. A successful review can reveal Drug-Related Problems (DRP), which are „situations in which in the process of use of medicines cause or may cause the appearance of a negative outcome associated with the medication".
Aims: The aim of our study is the qualitative and quantitative description of DRPs detected by community pharmacists, including interactions, and to confirm the importance of patient education related to medication review.
Methods: Data were collected from patients with polypharmacy by resident community pharmacists within a project from October 2017 to March 2018 practicing medication review. Patients's knowledge of medicines was measured by a self-developed questionnaire survey, while the responses were recorded through patient interviews. The pharmacists categorized the DRPs uniformly (DRP1-DRP6) and determined the root causes as well. The frequencies of the drugs and drug-classes causing interactions were determined and all the interactions were classified by clinical risk as well (UpToDate Lexicomp®)
Results: In the project, 763 patients were enrolled by 78 pharmacists in 78 pharmacies. The average number of products taken by the patients was 9.34, which value did not change significantly. The average knowledge of medicines increased by 3.8% from the initial 67.9%. On average 1.1 DRP per patient were reported, mostly due to interaction risk (41.5%). The overwhelming majority (68.5%) of interactions were between two prescription medicines. The most commonly reported interacting agents were perindoprile, amlodipine, acetylsalicylic acid, metformin and bisoprolol. 20.9% of the interactions carried a serious clinical risk, while 30.7% of them were irrelevant clinically. The most common intervention of the pharmacists was patient education (29.2%).
Conclusion: The results of this research confirm that the application of the mentioned pharmaceutical methodology can improve patients' knowledge of medicines and that pharmacists are able to reveal several DRPs that would remain hidden without the work of the pharmacist. Our results provide a good basis for developing a uniform procedure for medication review in Hungary.

New target in the tocolytic therapy: aquaporin-5 water channel

DUCZA, E.[1], CSÁNYI, A.[1], SZŐKE, É.[2], POHÓCZKY, K.[2], HAJAGOS-TÓTH, J.[3], KOTHENCZ, A.[3], TAHERIGORJI, H.[1], GÁSPÁR, R.[3]
[1]Department of Pharmacodynamics and Biopharmacy, University of Szeged, Szeged; [2]Department of Pharmacology and Pharmacotherapy, University of Pécs, Pécs; [3]Department of Pharmacology and Pharmacotherapy, University of Szeged, Szeged

Background: The aquaporin (AQP) water channels are small hydrophobic integral membrane proteins. Most of them are expressed in the female reproductive tissues and they play important role during pregnancy. We proved in our earlier study, that AQP 1, 2, 3, 5, 8 and 9 are detectable in the late-pregnant rat uterus and the AQP5 expression showed a dramatic downregulation on the last day of pregnancy. Moreover, our results lead us to suppose that the AQP5 expression is regulated by oxytocin and female hormones.
Aims: We hypothesized an osmotic pathway – through AQP5 – might have influence on the changes

in transient receptor potential vanilloid 4 (TRPV4) function and uterus contraction. Our aim was to determine the possible role of AQP5 in this osmotic regulation of TRPV4, thus in pregnant uterine contraction.
Methods: The expression of the TRPV4 and AQP5 were measured by RT-PCR and Western blot techniques for during pregnancy in rat uterus. Their localization in pregnant uterus was determined by immunohistochemical studies. The role of TRPV4 in uterus contraction was investigated in an isolated organ bath system. In vitro uterus contractions were stimulated with potassium chloride and its effect was investigated with the selective TRPV4 agonist (RN1747), antagonist (RN1734) and citral (3,7-dimethyl-2,6-octadienal) which is the active ingredient of lemongrass oil and lemon peel.
Results: The TRPV4 expression continuously increased from day 18 to the last day of pregnancy. We determined an inverse correlation between the AQP5 and TRPV4 mRNA and protein expression. The co-expression of TRPV4 and AQP5 was found in the late pregnant uterus tissue. The TRPV4 antagonist significantly decreased the uterine contraction; in contrast the TRPV4 agonist had no effect but induced the contractions in high dose. Citral treatment induced uterus relaxation on gestational day 22.
Conclusion: We presume the decreased AQP5 expression induces a hypertonic stress, which activates TRPV4 and increases uterine contraction on the day of labor. A potential hormone regulated cooperation exists between the AQP5 and TRPV4 expression. Based on these results, we acquired new information about the mechanism of birth and this link between AQP5 and TRPV4 could be a new target in tocolytic therapy.
Acknowledgement: This work was supported by the National Research, Development and Innovation Office, Hungary (grant FK19-132499).

Dimensions of safe pharmaceutical supply

EL KOULALI, Z.
National Institute of Pharmacy and Nutrition, Budapest

Nowadays medicine is an indispensable tool of healing. A constant, safe and cost-efficient pharmaceutical supply chain is an essential part of a healthcare system operating efficiently at a high standard.
When we talk about pharmaceutical supply, we distinguish between public and institutional pharmaceutical supply. The safety of both can be assessed from different perspectives; from the perspective of the recipient of the service (the patient), the service provider (public/ institutional pharmacy), the financer or the authority, but the goal should always be the same. Right quality, cost-effective medicine should be provided to the right person at the right time.
The area of pharmaceutical supply cannot escape development, innovation and accelerating life. Despite this, it is of great importance that pharmacist-patient meetings continue, and pharmacists find their place among the changing circumstances. It is essential to eliminate contingencies in the area of pharmaceutical supply as well, in order to have as many controlled processes as possible, in which the same input results in the same output. The diversified activities of pharmacies require healthcare providers to operate an internal quality control system. This is complemented by the external quality control system which is operated by the designated public health authority.
The Chief Pharmaceutical Division – as the authority responsible for the supervision of pharmaceutical retail (designated public health authority) – is also an integral part of the system of safe pharmaceutical supply. Because its activity is that of an independent, objective helper, it operates as an external control system. It feeds back the experience of on-site inspections in two directions: to the organization providing the health care service, and also to the legislator. The aim of the two-way feedback is to ensure that the service providers comply with current laws in all cases, and that the legislation is also suitable for regulating the sector.

OGYÉI website security incident – behind the scenes

ERDÉLYI, G.
National Institute of Pharmacy and Nutrition, Budapest

Background: In october 2018 the website of the National Institute of Pharmacy and Nutrition (OGYÉI) has been successfully attacked. As we are the licensing authority for pharmaceuticals in Hungary, the incident received wide media publicity after being announced on our website.
Aims: My aim is to provide information on the institute's IT security goals and the current state. I will talk about the method used by the attackers and the conclusions we've drawn. The presentation will contain all the necessary information on IT security and information security so that no prior knowledge will be needed in the field to understand it.

Survey on antidiabetics and complementary and alternative medicines among NIDDM patients, ratio of adverse drug reaction and the outcome with a voluntarily completed anonymous questionnaire

FAHMY, MM.[1], FEKETE, K.[2], HOMORÓDI, N.[3], FEKETE, I.[2], HORVÁTH, L.[1]
[1]*Department of Pharmaceutical Surveillance and Economics;* [2]*Department of Neurology;* [3]*Institute of Cardiology, University of Debrecen, Debrecen*

Background: Type 2 Diabetes mellitus (T2DM) is a

major public health challenge, both in developed and developing countries. T2DM leads to several complications e.g. macrovascular and microvascular diseases. Pharmacological and non-pharmacological management are used to improve glycaemic control in patients with T2DM. Complementary and alternative medicines (CAM) for the treatment of T2DM are probably based mainly on treatment of its obvious symptoms of pronounced thirst and polyuria. Nature is an outstanding source of antidiabetics and plants may be valuable dietary supplements to improve blood glucose control and prevent long-term complications in T2DM. Co-administration of herbal products with medicines may result in unfavourable interactions.

Aims: Collecting data about the use of CAM among T2DM patients. Besides this, data about the antidiabetics, its adverse drug reactions (ADR), outcome, patients' demographic characters, lifestyle, and other health behaviours were also collected.

Methods: A non-interventional study with self-developed questionnaire was used accepted by the Regional Ethical Committee. It was distributed among adult NIDDM patients who have suffered from cardiovascular consequences. A database was compiled from the anonymous questionnaires filled in voluntarily by the patients. Basic statistics were used to analyse database.

Results: A total number of 101 questionnaires were filled in. Mean age was 65.7 ± 10.9 years. Of the patients 57% were male. Average body weight was 85.5 kg. Eighty-one percent of patients said that they follow certain diabetic diet to control their blood glucose levels. Nine percent of patients reported last measured blood glucose level higher than 10 mmol/L. Concerning last measured HbA1C value, 16% of patients had higher than 6.5%. Eight patients have reported ADR due to metformin. Twelve percent of patients use CAM because they believe in CAM. Two out of them have reported ADR. Mean cost of CAM therapy was 3120 HUF/month.

Conclusion: Our findings confirmed that most of the patients adhere to the recommendations on diet. Unfortunately, high blood glucose level and HbA1C lab findings were reported which suggest ineffective treatment or non-adherent patients. CAM users are minor portion in this population. These facts support the idea that patients' education and motivation is essential. Clinical pharmacists should contribute in these activities and enhance patients' adherence in order to improve patients' quality of life.

The greatest challenge of the 2020s – medicine shortages

FELLER, A.
Hungaropharma Ltd., Budapest

Today one of the greatest challenges of the supply of medicinal products is how to handle medicine shortages. It is not a new phenomenon, and is neither solely Hungarian nor European, but a global problem. In order to elaborate the appropriate responses, we have to come to an agreement in a number of fundamental questions:

- *How to define medicine shortage;*
- *What are the causes of the shortages;*
- *What is the task of the participants;*
- *How is it necessary or possible to restructure the medicine supply / support system to be able to reduce the number of shortages in the long term, and eliminate the causes – is there a solution to this at all?*
- *How can a shortage be handled so that*
  - *Patients receive the appropriate therapy under all circumstances;*
  - *No reduction in confidence in healthcare occurs;*
  - *The solution is cost-effective and safe for all participants;*
  - *The efficient medicine supply framework established in Hungary does not become distorted.*

The lecture aims at finding answers to these questions and also presents the solution proposals coming from certain European Union Member States.

Pharmacokinetics and tissue distribution of PET radiotracer labelled β-cyclodextrin derivatives

FENYVESI, F.[1], HAJDÚ, I.[2], MALANGA, M.[3], FENYVESI, É.[3], SZENTE, L.[3], VÁRADI, J.[1], BÁCSKAY, I.[1], VECSERNYÉS, M.[1], TRENCSÉNYI, G.[2]
[1]Department of Pharmaceutical Technology; [2]Division of Nuclear Medicine, Medical Imaging Department, University of Debrecen, Debrecen; [3]Cyclolab Ltd., Budpest

Background: Hydroxypropyl-β-cyclodextrin (HPBCD) and Random Methyl-β-cyclodextrin (RAMEB) are widely used in drug formulations and recently orphan designation was granted for HPBCD in the treatment of Niemann-Pick disease, type C. HPBCD is considered to safe, but the exact mechanism of action and side effects are not completely understood. Labelled cyclodextrin derivatives are required to reveal the biological activity and in vivo distribution by imaging techniques.

Aims: The aim of our study was to synthetize the 68Ga-labelled NODAGA-HPBCD (68Ga-NODAGA-HPBCD) and 68Ga-labelled NODAGA-RAMEB (68Ga-NODAGA-RAMEB) and test their pharmacokinetic properties and in vivo distribution by positron emission tomography (PET).

Methods: We conjugated HPBCD and RAMEB with NODAGA and labelled with Gallium-68 (68Ga). The radiochemical purity and in vitro stability were determined and found to be suitable for in vivo application. For in vivo dynamic and ex vivo biodistri-

bution studies we used control BALB/c mice, while for the in vivo tumor model we used SCID mice.
Results: 68Ga labelled NODAGA-HPBCD and RAMEB were mainly excreted by the kidney, due to their hydrophilic properties. The accumulation of the radiotracers in abdominal organs was low, and no uptake was found in the brain. Interestingly elevated uptake was observed in the lung and in tumors.
Conclusion: In conclusion 68Ga-NODAGA-HPBCD and 68Ga-NODAGA-RAMEB were successfully produced for the first time and tested in vitro and in vivo. The outcome of our study indicates that the in vivo behaviour of radiolabelled cyclodextrins can be examined by PET techniques, thus these derivatives are suitable for further pharmacokinetic and cancer targeting measurements.

Acknowledgement: This study was supported by FK_17 (FK124634) research grant of the National Research, Development and Innovation Office, Budapest, Hungary and by the János Bolyai Research Scholarsip of the Hungarian Academy of Sciences (BO/00290/16).

History of CERTA Laboratory between its establishment in 1924 and nationalization

GAÁL, E., SZMODITS, L.
Róna Pharmacy, Budapest

Background: Development of the Hungarian pharmaceutical industry started in the middle of 19th century. In the interwar period there worked 57 pharmaceutical factories and manufacturing laboratories in Hungary. Pharmaceutical industry played an important role in the general economics and supplying of pharmacies.
Aims: To characterize the establishment and operation of the CERTA Laboratory in Budapest and contribute to the history of Hungarian pharmaceutical industry.
Methods: Methods of historical research were applied to reconstruct the working and professional activities of CERTA Laboratory. As main sources were used archival documents and other historical sources published in the studied period – pharmaceutical journals, statistical publications, photographs, maps.
Results: The history of CERTA Laboratory has been studied in the period between its establishment in 1924 and nationalization in 1950. CERTA was specialized in manufacturing of injections. Operation of the Laboratory reached its highest level in the 1930s when the professional management members were Mária Quittner and Tamás Löcherer. Several new machines, processes of production and quality control were introduced to the manufacturing process to produce high quality and safe medicinal products.
Conclusion: Some aspects of development of the pharmaceutical industry in Hungary are characterized on a specific example of a smaller manufacturing company – CERTA Laboratory established in the interwar period. Its 26-years existence represents every important development trends of industrialization in pharmacy including founding process, expansion, modernization, decline of production and damage caused by war, renewal of operation, and nationalization.

Development of biological drugs

GÁLOS, Z.
Gedeon Richter Plc., Debrecen

Education of future pharmacists: visions and challenges

GÁSPÁR, R.
Educational Section, Hungarian Society for Pharmaceutical Sciences, Budapest

The education of pharmacist is always a hot topic. Students frequently feel that they must study too much and additionally, a given proportion of the curriculum seems unnecessary or useless. On the other hand, teachers frequently feel that the capacity and the professional interest of the students are constantly decreasing. All these feelings may be rooted in the shortfall of the educational system, the system that is the meeting point for teachers and students. Nobody debates that our world and the generations are changing quickly, but what about our educational system? It is easy to hind behind laws and rules to avoid fundamental changes, but who will response to the real professional needs?
This section is not to praise but to promote the education of future pharmacists. Deans and leaders of pharmacy faculties, student representative, pharmacist top athlete will flash their ideas and visions about the desired future of undergraduate and postgraduate trainings of pharmacists. The lectures will be continued in a round table discussion with the participation of the ministerial commissioner for medical education. The audience will have limited possibility to comment and ask during the round table discussion.

The role of health technology assessment to optimize the societal level benefit of the treatment of the biological agents in immune mediated inflammatory diseases

GULÁCSI, L.
University Research and Innovation Center, Óbuda University, Budapest

Background: Health economics, including health outcome evaluation is playing an important role to

improve and optimize the health gain in patient and societal level.
Aims: There are number of challenges to face in improving health of the public.
Methods: The life expectancy of the population and the (well) treated patients are rising. The increasing prevalence of various chronic diseases and health states, due to improvements in treatment has led to an increase in the number of patients requiring treatment. Growing number of incurable and unpreventable diseases, such as rare diseases, blood disorders (chronic lymphocytic leukemia for instance) are becoming ‚treatment related' chronic diseases (similar to rheumatoid arthritis, hypertension or diabetes). Growing number of patients suffering in chronic diseases and the rising number of multiple co-morbidities, due to the increased life expectancy, creates escalating long-term financial commitments/ burden on the societies, families and individuals.
Results: More resources and more sophisticated resource allocation decision making is needed to achieve efficiency gain and to maintain Universal Health Coverage. Health Technology Assessment (HTA) is a tool for informing decision-making on value for money of publicly reimbursed health technologies and their conscious introduction and use. This is one possible avenue to increase efficiency of health systems. In most of the European countries all medical services claiming public funds are subject to HTA.
Conclusion: Another important challenge is to achieve better equity and access in Europe and elsewhere. Biological drugs for instance are recognized as important treatment options in European clinical guidelines in rheumatology, gastroenterology, dermatology and hematology. Despite this, the impact of biological therapies is often diminished in clinical practice by (huge) inequalities in patient access. Significant health benefits would result from better reimbursement and improving adherence to existing treatments, these are among the key sources today in improving health of the public.

The National eHealth Infrastructure (EESZT) from a policy perspective: challenge and opportunity

HANKÓ, Z.
Hungarian Chamber of Pharmacists, Budapest

The e-Prescription system, the first service of EESZT was initiated on 1 November 2017. It required pharmacies to be the first of the healthcare providers to completely join the EESZT. The relationship between the EESZT and the pharmacies has been the focus of attention ever since.
In addition to the common expectations (e.g. continuous, safe and fast operation, data protection) towards the EESZT from different parties (politics, EESZT system developers, IT service providers, pharmacies, healthcare providers and patients), pharmacies have also required the followings since the beginning: uniform master list and database, secure NEAK settlement, prescription writing in accordance with the provisions, and user-friendly operation.
In the upcoming period, emphasis will be placed on the development of other EESZT functions, but it is also important that medicine- and pharmacy-related developments continue. Such development could be the EESZT support of periodic safety update validation and a record of patients' past medications. These are important features from a treatment adherence perspective. The EESZT can help to harmonize medications for inpatient and outpatient care, as well as to achieve health and economic objectives. Trade and utilization analyses can also support the management of pharmacies. Today, pharmacies provide the same data to multiple locations, but here is a chance for simplification.
To materialize all these opportunities, close cooperation is needed with all parties in the system. Attention must be paid to ensure that developments are carried out in a targeted manner and not according to particular interests.

Hungarian dream and American reality in child healthcare

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

Last fall, I had the opportunity to spend three months at Cincinnati Children's Hospital Medical Center in Cincinnati, Ohio. The hospital is the second largest and the third best (Honor Roll) Children's Hospital in the US, covering the entire vertical of child healthcare. Every year, more than 1.3 million children are provided with 670 beds and 400 home-care facilities, with more than 15,500 employees. During the study visit, I had opportunity to know widely to the healing work, patient education and disease prevention work as well in the hospital.
Of course, neither the size of our children's hospitals, the structure of childcare, nor the financial resources availability are comparable to those in the US. However, there are some welcome similarities, many practices to consider that possibly could be implemented at home. There are serious and less serious deficiencies in today's Hungarian child healthcare.
As a clinical pharmacist, I went through many of the hospital's units and departments and looked at the work there. I often watch with envy of the patient and drug safety infrastructure, human resources, IT system, well-organized and coordinated work, and the work of multidisciplinary teams in healing.

It has been a pleasure for me to see that working together and appreciating common values stemming from a sense of vocation, together with the recognition of it, makes healing work successful and satisfies the children and their parents and the staff who work with them.
I have a "dream" to me as well, that must surely be a dream for all of us, and we are no further from the realization of our dream than Martin Luther King when he gave his famous speech in 1963. I have a dream that one day, maybe in the time of our children, or maybe only of our grandchildren, the Hungarian healthcare will reach what I saw and experienced in Cincinnati.

Psychosis spectrum disorders – a contemporary approach to the treatment of schizoprenia and bipolar disorder

HEROLD, R.
Department of Psychiatry and Psychotherapy, University of Pécs, Pécs

Background: Previously schizophrenia and bipolar disorder was considered as distinct disorders, however according to the contemporary view of psychotic disorders they can be rather described along a spectrum.
Aims: Contrary to the former categorical approach, biomarker research on various psychotic disorders shifts thinking toward a dimensional approach.
Methods: The various psychotic disorders overlap in many aspects and share common biomarkers.
Results: According to our present knowledge, psychosis spectrum disorders are considered to be neurodevelopmental disorders, in which the interaction of biological-genetic and environmental factors plays an important role. Recent results also highlight the synergistic effects of various environmental factors. As a result, the staging approach in treating psychotic illnesses is increasingly emphasized.
Conclusion: According to this approach, psychotic disorders progress in stages with increasing severity, and efforts must be made to provide the best evidence-based treatment appropriate to the given stage.

Contained & safe handling of hazardous bulk solids

HILDEBRANDT, M.
HECHT Technologie GmbH, Germany

In this presentation we will introduce you to the wide Containment-topic. You will learn about the definition of containment, the key-issues and initial steps of planning a Containment project. Further topics will be the threshold-classification of solids and other bulk materials and how you choose the right equipment for these solids. We will provide an overview about different basic thresholds and how they are calculated as well as a critical view on safety data sheets. Furthermore, you will be taught about important steps of process planning during a containment project and where potential risks occur. To show you the risks, you will see a typical pharmaceutical example process. To qualify machines and to validate processes we will discuss the Smepac-test. SMEPAC means: Standardized Measurement of Equipment Particulate Airborne Concentration. It is designed to give you an orientation and a method to validate suitability of the equipment for the intendent use with dangerous products. One of the most underrated topics is the "human factor". We will discuss some interesting insights about planning ergonomic and easy to use equipment. Finally, we will talk about the cleaning process as well as different cleaning methods like WIP and CIP.

Dead end or inadequate regulatory environment? – The current issues of the legal framework governing the distribution of herbal products

HORÁNYI, T.
Béres Pharmaceuticals Ltd., Budapest

Background: Nowadays it requires extreme effort if a company intends to place herbal medicinal products (including traditional herbal medicinal products) on the Hungarian or European market. Although the inventory of herbal substances having known or assumed to be known efficacy proved by published clinical studies contains numerous substances for various therapeutic areas, the real challenge is (even for the largest pharmaceutical companies) to find herbal active substances (herbal drugs or herbal drug preparations as defined in the European Pharmacopoeia) of adequate quality manufactured and documented according to the EU Good Manufacturing Practice (EU GMP) requirements.
Aim: The aim of the presentation is to review the advantages and burdens of the possible legal categories available for herbal products. Furthermore, to provide practical advices for healthcare professionals and consumers on the selection of efficacious herbal products with satisfactory quality and safety.
Methods: The legal frameworks for authorisation/notification and distribution of herbal medicinal products and herbal food supplements are compared with special focus on the quality requirements of the herbal substances. The consequences of the revealed differences are analysed in order to evaluate the current and future prospects of herbal remedies.

Results: The burden to put herbal medicinal products on the market is so high that new herbal (traditional herbal) medicines are hardly available while the number of herbal food supplements increasing continuously. Additionally, the compositional and quality aspects of the herbal food supplements are not adequately controlled by the current European legislation allowing the marketing of products with questionable value.
Conclusion: It seems that the current pharmaceutical legislation is not appropriate or perhaps not intended to provide solution for fulfilling the growing consumer demand on herbal products. In contrast the shortcomings of the food-supplement legislation ensure excellent possibility for those who have recognised the real or presumed business opportunities in the application of herbal substances without actually facing the threefold requirements of quality, safety and efficacy.

Advanced pharmaceutical care for interstitial cystitis

HORVÁTH, A.[1], BIRINYI, P.[2]
[1]Institute of Pharmacognosy, University of Pécs, Pécs; [2]Mikszáth Pharmacy, Budapest

Background: Interstitial cystitis (IC) is a barely known disease that causes urinary problems and pain. The number of people affected in Hungary is estimated at 20,000. Currently, 600 patients have been diagnosed. The cause of IC is unknown. It is due to the thinning of the bladder surface mucosa, which is made up glycosaminoglycan (GAG). This process can lead to the development of sterile inflammation. If this condition remains untreated, the disease can lead to cystitis and kidney failure. We believe that pharmacists can take part in recognizing and treating this disease because a lot of patients arrive at the pharmacy with urinary complaints.
Aims: Therefore, our goal is to develop a protocol that will help to recognize the symptoms of the disease and will guide the drug therapy in patients' care.
Methods: During the planning process, we took into account our existing professional guidelines, consulted with the specialist for treatment and conducted our own questionnaires.
Results: For mild symptoms of patient with IC: we can recommend a special IC diet, which has been prepared based on a number of foreign diets and an own questionnaire. For moderate symptoms of patient with IC: in addition to diet, medication is also important. The goal is to alkalize the urine to reduce the irritating effects of the urine. Oral GAG-layer regenerating drugs such as chondroitin sulphate and collagen-containing tablets can also be taken and a small amounts of vitamin C is necessary for proper incorporation of these compounds into the GAG layer. Initial treatment can be supplemented. In case of severe symptoms of patients with IC: the most effective is the combination therapy (oral and topical). In this way, combined treatment and regeneration of the GAG layer is expected. In addition to oral drugs, the use of intravesical solution containing GAG layer components may help in the regeneration process. If no satisfactory result is achieved, it may be supplemented with symptomatic treatment. We may suggest strong analgesics, antidepressants and muscle relaxants.
Conclusion: IC is a severe autoimmune disease with a high prevalence in Hungary and a pharmacist's role in the care of this condition could be decisive. Many patients visit pharmacies with urinary problems. Based on the newly developed algorithm, pharmacists will be able to recognize IC and refer the patient to a specialist, also manage the drug therapy and the proper diet.

Experiences in the treatment of pregnant women with epilepsy in the last decades

HORVÁTH, L.[1], MÉSZÁROS, Z.[2], FEKETE, I.[2], FEKETE, K.[2]
[1]Department of Pharmaceutical Surveillance and Economics;[2]Department of Neurology, University of Debrecen, Debrecen

Background: Epilepsy is a complex issue that has an impact on the patients' quality of life especially among women of childbearing age. Fertility is significantly lower among patients with epilepsy. The underlying pathophysiology is an endocrine disturbance. Hormonal changes particularly during pregnancy may influence the seizure frequency. Controlling and preventing seizures are essential for both mother and foetus. Antiepileptic drugs (AED) might be linked to congenital malformation (CM) mainly in a dose-dependent manner. Treating epilepsy means a life-time treatment, so real-life studies are important.
Aims: Our aims were to analyse patients' history, AED treatment of women with epilepsy and the outcome in terms of pregnancy.
Methods: East-Hungarian Epilepsy Database (from 1992) was created in order to analyse the data of patients through their case histories from out-patient files. Basic statistics were used to analyse database.
Results: There were 112 pregnancies. Number of deliveries, miscarriage and artificial abortion were 88, 17 and 7, respectively. One third of the patients has not taken AED and remainders have received monotherapy and bitherapy. Three pregnant patients have stopped their AED arbitrarily. During organogenesis, the most common AEDs were carbamazepine

and lamotrigine. Newer type AEDs were preferred to prescribe for those who were regularly checked-up. No CM was confirmed. Seizure frequency has not changed during the pregnancy. One stillbirth was registered. One foetus has died at 24 weeks of gestation due to asphyxia in preeclampsia. In a twin pregnancy, placenta detachment has occurred. Only one patient's outcome was related to epilepsy who had four times generalized tonic-clonic seizures during pregnancy, she was non-adherent. Seven patients during their pregnancies did not visit an epileptologist at all or only after completed 26 weeks of gestation. After the delivery, AED dosage has been increased in three cases and decreased in four cases. Since newer type ADEs were marketed, the approach to pregnancy changed even from the point of view of patients.

Conclusion: Frequency of miscarriage was quite a same and artificial abortion less frequent among epileptic patients than in the population. Despite of known teratogen effects of some AEDs, CM were not identified in our database. Our findings highlight the importance of continuous care and established AED treatment in pregnancy. Clinical pharmacists may play a role in patients' care in epilepsy treatment besides the epileptologist.

Development of vaccines and vaccines for pandemic threats (in particular for COVID19)

JANKOVICS, I.
CMC Clinic, Budapest

Vaccines, currently used for prophylactic purposes, prevent more than three million deaths every year from diseases like diphtheria, pertussis, tetanus, poliomyelitis, measles and influenza.

The general six stages of the development of a new vaccine are: i) Exploratory stage; ii) Pre-clinical stage; iii) Clinical development; iv) Regulatory review and approval; v) Manufacturing; vi) Quality control. Clinical development is a three/four-phase process. During Phase I, small groups of people receive the trial vaccine. In Phase II, the clinical study is expanded. In Phase III, the vaccine is given to thousands of people and tested for efficacy and safety. Many vaccines undergo Phase IV formal, ongoing studies after the vaccine is approved and licensed. Phase IV studies, also referred to as postmarketing surveillance studies (PMS). These processes are very similar to drug developments.

However, there are several differences compared to drug development, namely: i) unlike drugs, which are given to patients, vaccines are received by healthy individuals, thus the safety margin should be very high; ii) as vaccines have to be stored under refrigeration, there are always logistical challenges during clinical trials; iii) Adjuvants are incorporated into vaccine formulations to modulate and improve the immune response (antigen/adjuvant formulation are important aspects of clinical development); iv) The immune response primarily measured during early stages of vaccine development (Phase I/II) should evaluate: Humoral/ cell-mediated/ cross-reactive antibodies or immune complexes/ „immune landscape".

A challenge in responding to pandemic diseases is that vaccines may not exist for them. For newly emerging threats without licensed vaccines, such as SARS, MERS, Marburg virus, Nipah virus, SARS CoV-2 and the like, the time required to develop and produce a safe, effective vaccine is unknown and would depend on the nature of the threat and the state of current vaccine research for that threat. In almost all cases, several months would be needed to respond with the first doses of vaccines.

Unfortunately, six month later than WHO declared the public health emergency of international concern (27/01/2020) there are five important questions, essential for vaccine development that remain open for scientists, namely: 1) Why do people respond so differently to infection? 2)Has the virus developed any worrying mutations? 3)How well will a vaccine work? 4)Can we develop immunity and if so, how long does it last? 5)What is the origin of the virus?

Until a safe, effective vaccine was ready, other public health and medical measures (social distancing, quarantine, and aspecific medications) would need to be employed to try to limit disease spread.

Pharmaceutical technological aspect of magistral formulations in Hungary. Storage conditions, incompatibilities and expiry dates of often Used magistral preparations

JÓJÁRT-LACZKOVICH, O., RÓNASZÉKI, A., HAJAGOS, G., AIGNER, Z.
Institute of Pharmaceutical Technology and Regulatory Affairs, University of Szeged, Szeged

Background: In Hungary magistral preparation work is a determinative and traditional part of pharmaceutical activity. The reformation of Formulae Normales is a topicality of today. It often occurs that incompatible compositions or industrial preparation containing magistral compositions are produced in Hungarian pharmacies. In unique magistral production the uncertainty of expiry dates is often experienced.

Aims: Our aim was to choose a frequently applied active pharmaceutical ingredient (API) in magistral compositions which causes incompatibility prob-

lems and to work out an investigation method to determine and explain the changes. Further aims were to make stability investigations with magistral preparations at different storage conditions. With these date we could calculate the exact expiry date of these productions.
Methods: The applied methods were UV-VIS spectroscopy to determine the API content, X-ray powder diffraction, Raman spectroscopy and differential scanning calorimetry to detect the physical and chemical changes of the samples and dissolution and diffusion investigations to model the samples properties in in vitro conditions.
Results: Our results show that investigated APIs causes a lot of incompatibility problems in magistral forms. These changes can be organoleptic detectable and masked also. They can be followed instrumentally well. The stability or instability of these special forms modifies the correct storage conditions. The rethinking and the differentiation of expiry dates is needed also.
Conclusion: The instability of magistral preparations can cause series application problems and inaccuracies in treatment. In this way we have to recognise, clarify and treat appropriately them. Our work's results can help to solve these problems in pharmacies.

Preclinical studies of the nicotinic-acid derivative BGP-15

JUHÁSZ, B.[1], PRIKSZ, D.[1], VARGA, B.[1], BOMBICZ, M.[1], SZILAGYI A.[1], SZEKERES, R.[1], WILISICZ, T.[1], GESZTELYI, R.[1], KISS, R.[1], PAPP, Z.[2], TÓTH, A.[2], BALLA, G.[3], BALLA, J.[3], CSANÁDI, Z.[4], SZILVÁSSY, Z.[1]
[1]Department of Pharmacology and Pharmacotherapy; [2]Division of Cardiology, Department of Cardiology, Faculty of General Medicine, University of Debrecen; [3]HAS-UD Vascular Biology and Myocardial Pathophysiology Research Group, Hungarian Academy of Sciences; [4]Institute of Cardiology, University of Debrecen, Debrecen

Background: Increasing evidence suggests that small molecule BGP-15 improves muscle function, and reduce arrhythmias in disease models; however, its exact cardiovascular effects and mechanism of action are still not clear.
Aims: Our aim was to evaluate the effects of BGP-15 in different animal models. Mechanistic and molecular biology studies were aimed to particularly describe its actions on the cardiac function and signal-transduction pathway.
Methods: Rabbits suffering atherosclerotic cardiomyopathy, Zucker Diabetic Fatty (ZDF) rats, and Goto-Kakizaki rats were used as models for the preclinical experiments. Echocardiography was performed on the animals to assess acute, mid-term and chronic effects of BGP-15. Moreover, thoracotomy was also performed, then the vascular status of rats was evaluated using an isolated aortic ring method. Furthermore, endothelium-dependent vasorelaxation was investigated on isolated aortic rings. Western blot and ELISA methods were carried out to evaluate the expression and activity of mitochondrial proteins, cardiac enzymes.
Results: BGP-15 significantly improved diastolic dysfunction both in rabbits, ZDF, and Goto-Kakizaki rats. Vascular status was unaffected, but fibrosis improved after the treatments. The drug restored mitochondrial function in ZDF rats and increased survival rate. BGP-15 restored diastolic parameters and improved Tei-index compared to untreated Goto-Kakizaki rats. Vascular status was unaffected by BGP-15. Expression of vasodilator-stimulated phosphoprotein (VASP) and phospholamban (PLB) increased in BGP-15-treated rats, in comparison to the diabetic rats.
Conclusions: GP-15 significantly improves cardiac function in different disease models by exerting multiple actions. Determination of the molecular target of the drug candidate merits further investigations.

Acknowledgement: GINOP-2.3.2-15-2016-00043, and the research was also financed by the Higher Education Institutional Excellence Programme (NKFIH-1150-6/2019) of the Ministry of Innovation and Technology in Hungary, within the framework of the Therapeutic Purpose Development thematic programme of the University of Debrecen.

Novel drug candidates for neuropathic pain: small molecule somatostatin 4 receptor agonists.

KÁNTÁS, B.[1], SZŐKE, É.[1], HORVÁTH, Á.[1], BÁNHEGYI, P.[2], HUNYADY, Á.[1], BORBÉLY, É.[1], KÉRI, G.[2], SZOLCSÁNYI, J.[1], PINTÉR, E.[1], HELYES, Z.[1]
[1]Department of Pharmacology and Pharmacotherapy & Szentágothai Research Centre, University of Pécs, Pécs; [2]Avicor Ltd., Budapest

Background: Treatment of neuropathic pain is an unment medical need. Somatostatin released from capsaicin-sensitive peptidergic nociceptors at the periphery and GABAergic interneurons in the brain has analgesic and anti-inflammatory effects mediated by its sst4 receptor without involvement of endocrin functions [1]. Native somatostatin cannot be drug candidate due to its short elimination half-life and various endocrin effects. Sst4 receptor is highly expressed in pain-related brain regions and so can be a new target for drug development [2].
Aims: We investigated the effects of our novel small molecule sst4 receptor agonists in mouse models of neuropathic pain and acute neurogenic inflammation.
Methods: Sst4 receptor activation by our pyrrolo-py-

rimidine compounds was determined by the gamma-GTP-binding assay on sst4-expressing CHO cells. The effects of the two most potent and efficacious agonists were tested on partial sciatic nerve ligation-induced traumatic mononeuropathic hyperalgesia and resiniferatoxin (RTX)-induced thermal allodynia and mechanical hyperalgesia.

Results: Our novel compounds proved to be effective in G-protein assays and exert 60-70% maximal antihyperalgesic effects in the neuropathy model after a single oral administration of 500 μg/kg doses. In addition, one of the agonists is also effective analgesics in RTX-induced neurogenic inflammation model.

Conclusion: Our orally administered sst4 agonists are promising analgesic drug candidates for treating neuropathic pain.

Support: National Brain Research Program 20017-1.2.1-NKP-2017-00002, GINOP-2.3.2-15-2016-00050, GINOP-2.3.2-15-2016-00048 and EFOP-3.6.2-16-2017-00008, Gedeon Richter's Talentum Foundation, János Bolyai fellowship, ÚNKP-19-3 New National Excellence Program of the Ministry for Innovation and Technology.

References: 1 Szolcsanyi et al. Br. J. Pharmacol. 1998;123:936–942; 2 Sándor et al. Eur J Pharmacol. 2006;539:71–75.

Instead of "I saw it on the internet, it must be true" – Patient education in the Cancer Center of Semmelweis University

KLEINER, D.[1], HANKÓ, B.[1], DANK, M.[2]
[1]*University Pharmacy Department of Pharmacy Administration;*
[2]*Cancer Centre, Semmelweis University, Budapest*

Background: Although greater and greater efforts were made to cure or at least treat long-term cancer, the society's reaction is very critical. It seems, that education programs can reduce the negative attitude of patients. For this, we have introduced weekly presentations in 2017.05.11 in the Cancer Centre of Semmelweis University, in conjunction with oncoteams. In the questionnaires we measured the reactions, but we have not checked how understandable is it. As the institute had to move because of the renovation of the building, we had a short break in the presentations, but started again in 2019.07.25 with few developments. In the past, a main pretence was a published document about the presentation, so an e-book has been published.

Aims: Our aim was to measure the reactions to the restarted presentations, with regard to the changes.

Methods: Simple survey was used, without harm of personal rights. The questionnaires have been made on the same day of the presentations from 25 July 2019 to 24 October 2019 Statistical analysis was made with Microsoft Office Excel 2016 (Redmond, WA).

Results: In this three-month period, the survey was filled by 53 people [mean age ± SD = 58 ± 13 (years)]. Most of the participants had cancerous disease and waiting for oncoteam (49%) or they were their relatives (43%). The remaining participants were waiting for treatment or consultation. We asked how beneficial the presentation was (answer type: fully useful/partially useful/partially useful, but mainly not beneficial/not useful). Most participants thought, it was fully useful (87%), while 13% thought it was partially useful. We asked, if it was understandable. Only one person thought it was just partially understandable, but mainly clear, all other thought, it was fully understandable. We asked what other topics the participants are interested in. Most of them (62%) highlighted the new biological treatments that may need a new presentation in the future.

Conclusion: All in all, our patient education program seems useful as no negative answer was in the survey. It is maybe the consequence of the plain language what most participants could understand and realize the significance of their role in the therapy.

Development of dermal semisolid dosage forms based on Quality by Design approach

KOVÁCS, A., CSÓKA, I., CSÁNYI, E.
Institute of Pharmaceutical Technology and Regulatory Affairs, University of Szeged, Szeged

Background: Background: Semisolid dosage forms for dermal use receive more and more attention in the pharmaceutical and cosmetic fields. Semisolid systems are the most usual formulations for the delivery of drugs through the skin. Topically applied anesthetics are employed in order to eliminate the pain caused by needle insertion and injection, thus improving patient compliance. Due to fast market growth, a larger emphasis has been placed on proper planning of product development and on using modern tools such as the Quality by Design (QbD) concept. In such a way, the duration and costs of the development process can be reduced, while the requirements of the stakeholders, namely the patient, the industry and the regulatory authorities can be met more precisely.

Aims: The aim of our present work was to evaluate the applicability of Quality by Design (QbD) methodology in the development of semisolid dosage forms for dermal use.

Methods: The QbD concept involves identifying the quality target product profile (QTTP), the critical material attributes (CMAs) and the critical process parameters (CPPs) into the critical quality attributes (CQAs) of a drug product at the beginning of the development. The CQAs influencing the quality and efficacy of the final drug formulation were then defined in order to select the control points and proper

methods for measurements. The quality management tools (e.g. Ishikawa diagram, risk estimate matrix, Pareto analysis, etc.), Design of Experiments (DoE) techniques and the Design space are useful tools for QbD implementation. LeanQbD Software and StatSoft. Inc. Statistica for Windows were applied to identify the risks in the case of this study.
Results: The model systems were a Nanostructured Lipid Carrier (NLC) and a semisolid film-forming system preparation. The most critical CMAs and CPPs were chosen to be the independent variables and the CQAs were chosen to be the dependent variables in a 23 factorial design process. Based on our experiments, an optimal formulation can be obtained.
Conclusion: The risk assessment method is a helpful tool for the optimal product development process, allowing us to define the optimal semisolid formulation. Furthermore, the predefined aims (QTPP/CQA) is a powerful tool to guide the formulation and process design and to keep the product development effort focused and efficient.

Considering real-world data in regulatory decision making paves the way for innovation in clinical trials: the potential for using synthetic control arms in generating evidence

KOVÁCS, S.[1], ZEMPLÉNYI, A.[2], ERDŐSI, D.[1], VINCZE, G.[1], BOTZ, L.[3]
[1]Health Technology Assessment Centre; [2]Division of Pharmacoeconomics Department of Pharmaceutics; [3]Faculty of Pharmacy, University of Pécs, Pécs

Background: Randomized controlled trials (RCTs) have been the gold standard for measuring effectiveness of health technologies. Randomization provides a method for limiting systematic bias related to patient selection and treatment assignment. Although RCTs reduce the risk of bias compared to single arm trials, they tend to require large sample sizes, take longer to complete enrollment and actually patients have typically a lower propensity to enroll because of their fear of being put on a placebo arm. Recently, availability of data collected from electronic health records (EHR), prior clinical trials, lab tests, wearable devices and insurance claims has increased the interest in using real-world data (RWD) as a "synthetic" or "external" control arm in generating evidence.
Aims: The aim of this study was to describe the current regulatory environment of real-world data and derived real-world evidence (RWE) regarding their applicability and acceptance in healthcare decision making especially in comparative effectiveness studies.
Methods: Presented here is information summarized and interpreted from recently published guidelines of regulators, white papers and peer reviewed articles were found via a targeted literature review performed by our center. Here we present the basic definitions approved by regulators and the process and constraints applied during the development of fit for regulatory purpose RWE.
Results: The currently adopted definition of RWE reflects the fact that evidence generation is broader than passively-collected observational data and retrospective analytical approaches. Conceptually it allows prospective collection of wide variety of data and the use of study designs that are embedded in clinical practice but retain randomization. The applicability of RWE, which is suitable for specific regulatory purposes, depends on the study design to assess the effects of the treatment on the outcomes of interest, on the understanding of the context in which the treatments are used and on the transparency required during its development.
Conclusion: Although RWD are generally accepted as an adjunct to RCTs, more work must be done to clarify which types of RWD and derived RWE are robust enough to provide information on effectiveness, risk–benefit assessment and cost-effectiveness. For that purpose regulators have to clearly define key performance indicators of quality and conformity to support wide applicability of real-world evidence.

Encapsulation of human interferon-alpha (IFN- α) into core-shell nanoparticles

KRISTÓ, K.[1], MÁRKI, Á.[2], KELEMEN, A.[3], DÉKÁNY, I.[4], CSÓKA, I.[1]
[1]Institute of Pharmaceutical Technology and Regulatory Affairs; [2]Department of Pharmacodynamics and Biopharmacy; [3]Department of Applied Informatics; [4]Department of Physical Chemistry and Materials Science, University of Szeged, Szeged

Background: Nowadays, the administration route of IFN-α is frequent injection of the dissolved protein, because it is a very sensitive material. The frequent injections have disadvantages such as low patient compliance because of the pain they cause. One of the solutions can be the application of oral delivery of the IFN-α [1]. Patient compliance can also be increased with application of sustained release injection, for which the administration frequency is considerably lower. In a previous study bovine serum albumin (BSA) based core–shell NPs were developed as carrier systems for drug transportation [2].
Aims: The aim of our work is to achieve sustained IFN-α release after injection and test it in animal trials.
Methods: First step of the core-shell nanoparticle (NP) preparation was the precipitation of human serum albumin enriched in recombinant human

interferon-α (HSA-IFN-α) (Trigon Biotechnology Rt.) from its buffered solution with Na_2SO_4 solution. The resulting particles were separated by centrifuging. The second main step was the preparation of the polymer layers: poly(sodium-4-styrenesulphonate (PSS) and chitosan (Chit) (Sigma-Aldrich). The precipitated HSA-IFN-α was redispersed in the polyelectrolyte solutions followed by continuous stirring. Finally, the HSA-IFN-α core-shell NPs were lyophilized. The obtained HSA-IFN-α core-shell NPs were characterised with thermal analysis, zeta potential and dynamic light scattering measurement, X-ray diffraction, transmission electron microscopy, IFN-α activity test, dissolution study and in vivo study with rabbits.

Results: The new particle is formed by salt-precipitation of IFN-α containing HSA to 10nm sized particles and building up three polyelectrolyte layers on the particle surface in L-b-L strategy. The particle size is in the nano-size range, and that the outer surface is negatively charged were demonstrated. Encapsulation the precipitated protein renders it fully amorphous. IFN-α activity was not decreased. Both in vitro and in vivo release kinetics experiments have proven slow active agent dissolution from the formulation.

Conclusion: In this work a novel method of core-shell nanoparticle preparation for protein drugs or protein-bound active compounds was presented, which provides a relatively easy and inexpensive way of the formulation of sustained release products.

References: 1 Caldorera-Moore, M., et al. J. Drug Target. 2019;5-6:582-589; 2 Varga, N., et al. Coll. Surf. B: Biointerf. 2014;123:616–622.

Challenges and pharmacist aspects of health-economic assessment of computer provided order entry systems.

LANGER, A.[1], CSANÁDI, M.[2], BELLA, R.[1], ZEMPLÉNYI, A.[3], BOTZ, L.[1]

[1]*Department of Pharmaceutics and Central Clinical Pharmacy, University of Pécs, Pécs;* [2]*Syreon Research Institute, Budapest;* [3]*Health Technology Assessment Center, University of Pécs, Pécs*

Background: Mediaction errors (ME) and the consequent preventable adverse drug events (pADE) are a major burden to inpatient care. They not only cause patient harm but as a result of this prolonged length of stay (LOS) and increased healthcare cost. Computerized physician order entry (also known as computer provided order entry) with or without a clinical decision support tool (CDS) have been shown to increase patient safety. Due to the increasing burden on healthcare financing it is important to seek cost-effective solutions.

Aims: Our aim was to collect studies examining CPOE systems in inpatient care with cost or other resource utilization related outcomes, and to evaluate these studies from a methodological perspective, with special regard to full economic evaluations.

Methods: We conducted a systematic search of Scopus, PubMed and Web of Science database. Search terms were determined according to PICO. Non-english papers and studies providing no original data were excluded.

Results: Following a screening of 1693 abstracts, 67 full text articles were analyzed of which 27 met the inclusion criteria. We have identified 18 partial and 8 full economic evaluation. In this study we analyzed the full economic evaluations. The clinical outcomes are dominated by pADE, although LOS (1 case), QALY (1 case) are also apparent. The input parameters on the contrary are quite different. Each study has demonstrated cost-reducing and patient safety enhancing effect but differences are present in methods (perspective, discounting, duration, inflation, sensitivity, definition of ADE). Also most of the articles doesn't provide details about the level of CDS and if clinical pharmacist services were involved in the intervention.

Conclusion: Differences in methods and quality in health-economic analyses concerning CPOE are raising questions about the comparability of these studies. Currently in Hungary there's a good opportunity to analyze and compare CPOE systems due to the appearance of multiple Automated Drug Dispensing (ADD) systems in the country. Our results may help these studies from methodological perspective. In the following we will assess the type of CPOE, level of CDS and pharmacist interventions regarding Hungarian ADD systems.

In what is similar and in what is different? – Cariprazine, a new atypical antipsychotic

LASZLOVSZKY, I.

Medical Division, Gedeon Richter Plc., Budapest

Background: Dopamine D2 receptor partial agonists are representing a new generation of atypical antipsychotics. Cariprazine is one of the representatives of this group, which has received centralized market authorization from the European Medicines Agency in 2017 for the treatment of adult patients with schizophrenia including those with predominant negative symptoms of schizophrenia. Cariprazine is a dopamine D3 preferring D3/D2 receptor partial agonist with similar dopamine receptor subtype selectivity as the neurotransmitter dopamine.

Aims: Its short-term efficacy was proven in three phase 2/3 studies. The investigated doses were in the range of 1.5 to 9mg/day. Long term efficacy of cariprazine was proved in prevention of relapse after

26-96 weeks' treatment showing high separation from placebo both in the number of relapses and in time to relapse. In a head to head comparative study cariprazine showed significant improvement in the symptoms as well as in the everyday functions of predominant negative symptom patients of schizophrenia compared to the antipsychotic risperidone.
Methods: Cariprazine treatment generally was well tolerated by the patients and has a good safety profile. It doesn't cause prolactin elevation, QT prolongation, there is no remarkable and significant weight gain and there is no significant change in the metabolic parameters. Due to its pharmacokinetic properties once a day treatment with cariprazine is adequate and it doesn't cause significant food effect.
Results: Further phase-3 clinical studies proved the efficacy of cariprazine in acute treatment of manic or mixed episodes associated with bipolar I disorder, as well as in bipolar depression. For the adjunctive treatment of major depressive disorder, phase 3 studies are in progress.

Basic pharmacological characterization of EV-34, a new H_2S-releasing ibuprofen derivative

LEKLI, I.[1], GYÖNGYÖSI, A.[1], VERNER, V.[1], BAKAI-BERECZKI, I.[2], KISS-SZIKSZAI, A.[3], ZILINYI, R.[1], BAK, I.[4], BORBÁS, A.[2], HERCZEGH, P.[2]
[1]Department of Pharmacology; [2]Department of Pharmaceutical Chemistry; [3]Department of Organic Chemistry; [4]Department of Bioanalytical Chemistry, University of Debrecen, Debrecen

Background: The cardioprotective effect of H_2S is being suggested by a handful number of manuscripts. Furthermore, H_2S plays a role in relaxation of vascular smooth muscle, protects against oxidative stress and modulates inflammation.
Aims: The goal of the present work is the synthesis and basic pharmacological characterization of a newly designed H_2S-releasing ibuprofen derivative.
Methods: After synthesis of EV-34 oxidative stability assays were performed (Fenton, porfirin assay). Furthermore, stability of the molecule was studied in rat serum. With the help of a hydrogen sulfide sensor H_2S-releasing ability of the molecule was studied in media originated from H9c2 cell culture. MTT assay was carried out to monitor the possible cytotoxic effect of the molecule. Cyclooxygenase (COX) inhibitory property of EV-34 was also evaluated. Finally, carrageenan assay was carried out to compare the anti-inflammatory effect of EV-34 to ibuprofen.
Results: Our experiments revealed that the molecule is stable under oxidative condition; however, in rat serum it undergoes biodegradation. In cell culture medium H_2S is being released from EV-34. No cytotoxic effect was observed at concentrations of 10, 100, 500μM. The COX-1 and COX-2 inhibitory effects of the molecule are comparable to those of ibuprofen. Furthermore, based on the carrageenan assay EV-34 exhibits an anti-inflammatory effect similar to that of equimolar amount of ibuprofen (100mg/bwkg).
Conclusion: Taken together our results suggest that the newly synthetized EV-34 is a nontoxic chemically stable compound, which release H_2S in biological systems. In addition, EV-34 has COX inhibitory and anti-inflammatory properties.

This study was supported by the GINOP-2.3.2-15-2016-00043 (IRONHEART), the Higher Education Institutional Excellence Program NKFIH-1150-6/2019 and EFOP-3.6.1-16-2016-00022 „Debrecen Venture Catapult" projects.

Quality Assurance Systems in Pharmaceutical Industry in the viewpoint of audits/inspections

LUKÁCS, F.
Directorate for Inspection, Drug Inspectorate. National Institute of Pharmacy and Nutrition, Budapest

Dealing with the growing number of inspections/audits
– new countries starting to perform inspections (Russia)
Implications of MRA between US and EU (Is it possible to reduce the number of inspections?)
Possible optimization approaches
Tackling data integrity challenges and genotoxic impurity
Experiences of inspections

Machine vision as a multi-purpose PAT tool for continuous pharmaceutical manufacturing

MADARÁSZ, L., MÉSZÁROS, L., KÖTE, Á., GALATA, D., DOMOKOS, A., CSORBA, K., MAROSI, G., NAGY, ZK.
Department of Organic Chemistry and Technology, Budapest University of Technology and Economics, Budapest

Background: Current manufacturing processes inherit several problems from process development, many of which can be prevented by shifting to continuous manufacturing processes. Some benefits of this shift include improved consistency (resulting in lowered scrap or recall costs), as well as better quality control- and manufacturing efficiency. With the installation of process monitoring tools, Process Analytical Technology (PAT) allows for real-time quality control. In addition, large amounts of data acquired during production can be used to further

enhance process understanding and efficiency. A process monitoring tool used extensively in many areas of the industry is computer vision, which could also prove useful in the pharmaceutical industry as well.

Aims: The aim of this work was to utilize computer vision for the in-line monitoring of different continuous pharmaceutical manufacturing processes (e.g. crystallization, tablet manufacturing). The real-time acquired data then can be used for quality control, process understanding or even process control.

Methods: A software was developed by the authors for rapid, real-time image analysis. A custom reactor was used for the continuous crystallization of Acetylsalicylic Acid, which allowed for real-time image analysis-based particle size analysis. Samples collected from the process were dried and analyzed via a Parsum IPP-70-S for reference particle size measurement. Tablets with different tableting compression forces were prepared for image analysis-based determination of tablet hardness.

Results: The developed image analysis software was successfully used to monitor the particle size distribution change during continuous crystallization, as well as to determine the steady state of the process. Tablet hardness was also successfully estimated from images via image analysis.

Conclusion: These solutions, when adopted by the pharmaceutical industry, can lead to well controlled technologies where the quality of the product is understood to a much deeper extent, and thus it can be assured that the patient will receive a treatment of the desired quality

The rough road to the first successful Hungarian gene therapy in Bethesda Children's Hospital of the Hungarian Reformed Church

MAGYAR, B., HANTOS, M., GERGELY, A., MIKOS, B.

Bethesda Children's Hospital of the Hungarian Reformed Church, Budapest

Background: Spinal Muscular Atrophy (SMA) is a fatal neurodegenerative disease which demands multidisciplinary care. SMA belongs to the class of orphan diseases, the occurance of the disease is 1:6000 among newborns, which means 12-15 new patients per year in Hungary. Before 2017 treatment did not exist for the disease. The first medicine – called Spinraza with active agent nusinersen – has been granted a marketing authorization in May 2017. In Hungary this therapy is funded to those children who are entitled to individual permission by the health insurance department. This treatment is available in two SMA centers: II. Children's Clinic of Semmelweis University and in Bethesda Children's Hospital of the Hungarian Reformed Church. The second milestone in the treatment was reached in 2019, when gene therapy called Zolgensma has been granted a marketing authorization by Food and Drug Administration (FDA) in the USA. The drug is not registered yet in Europe due to the few experience and the short time.

Aims: A child diagnosed with SMA was treated with Zolgensma in October 2019 first in Hungary, in Bethesda Children's Hospital of the Hungarian Reformed Church. The path leading to the treatment was not easy at all. I intend to present the professional background, the related challenges and the solutions.

Methods: I present the case study retrospectively about the treatment's circumstances that was used for the first time in Hungary and the fourth time in Europe. I expound the disease, the medicine in terms of effect mechanism, the process of getting the permission, the logistics and also the financial issues. I introduce the team who worked on this project and the cooperation within the hospital and with other institutes. This treatment required the development of a supportive therapy, which was implemented in collaboration with the pharmacists and the parents.

Results: After a month of careful organization, the therapy can be considered a scientific and professional success. After the therapy, the child is monitored.

Conclusion: Gene technology as a drug therapy can be seen as a paradigm shift in medicine that could open new paths for healing in the future. During the preparation of the treatment, the role of the multidisciplinary team in healing was confirmed.

Clinical decision making and pharmacist prescribing

MÉSZÁROS, Á.

University Pharmacy Department of Pharmacy Administration, Semmelweis University, Budapest

Background: Today's healthcare works within the framework of Evidence-Based Medicine, where scientific knowledge improves exponentially. Clinical decision making, therapeutic choices are made by teams, where one of the most important team members is the pharmacist. The pharmacist plays an essential role in health prevention as well as medication therapy management. Nowadays, in several countries, pharmacists have to face new challenges such as the complex activity of prescribing, this process started in England in 1999 within the framework of non-medical prescribing.

Aims: The presentation provides an overview of the actual experiences.
Methods: Expert's reports s and a literature review were performed between 2009-2018, in Medline with the following keywords: [non-medical or pharmacist] and prescribing with a limit to full text articles.
Results: Prescribing has three main aspects, prescribing as a discrete clinical activity, prescribing as a health professional activity, and prescribing as a policy process. It is a complex (with appropriate ethical and professional framework) evidence-based process, where one shall take patient preferences into account as well.
Non-medical prescribing, in the form of supplementary prescribing was suggested first for nurses by the first Crown Report (Review of Prescribing and Administration of Medicines (the Crown Report) Department of Health London 1989), the regulation came into power in 1992; supplementary prescribing meant that district nurses could prescribe limited number of drugs for certain conditions. This practice was developed further and was advised to be extended to pharmacist and optometrists in 1999 by the second Crown report (Crown J: Review of Prescribing, Supply and Administration of Medicines. Department of Health London 1999.) Supplementary prescribing for Pharmacist was made possible by the Department of Health in 2002. As this practice was successful nurses and pharmacist were enabled to become independent prescribers in 2009 (Medicines and Healthcare products Regulatory Agency 2009). Nurse and pharmacist prescribers today in the UK have the same prescribing rights as medical doctors.
Today the Health and Care Professions Council (HCPC) is the professional body who set the standards to carry out prescribing.
Conclusion: Clinical practice and various studies, such as Weeks et al, Courtenay et al 2017, Reid et al 2017 provide evidences that independent pharmacist prescribing is well functioning and is a safe activity both from the view of patient safety and health–service-provision safety; patients are aware, and they are very much accepting Pharmacist Prescribing as part of the GP practices.

References: 1 Weeks et al. Cochrane Systematic Review – Intervention Version published: 22 November 2016 https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD011227.pub2/full; 2 Courtnay et al: BMJ Open 2017;7:e013515; 3 Reid et al 2017: Res Social Administr Pharmacy, 2017;14(1):62-68.

Historical review of drug packaging

MIHU, L.
Piactér Pharmacy, Budapest

Adherence to dietary supplementations especially Calcium and Vitamin D as osteoporosis adjuvant therapy in comparison with prescribed medicines

MIRANI, S.[1,2], HORVÁTH, L.[1], VECSERNYÉS, M.[2], TÓTH, EB[1]
[1]Department of Pharmaceutical Surveillance and Economics; [2]Department of Pharmaceutical Technology, University of Debrecen, Debrecen

Background: A lack of compliance with the advised treatment regarding to every health situation is a common problem that may lead to worsening the medical condition or resulting in a lack of efficacy result. Recent studies have shown the use of calcium and vitamin D in the prevention and treatment of osteoporosis as dietary supplementation (DS) can play role as a general adjuvant therapeutic measure and a specific complement to the treatment with other active compounds.
Aims: To evaluate the possible factors influencing the patients' compliance through a „dietary intake specific questionnaire". To compare the patients' adherence to certain prescribed medications (Rx) rather than the DSs, also the patients' trust in the effectiveness of DSs and herbal medications. In the population who are consuming vitamins, to investigate their feeling of health improvement after a certain time period consuming it, which can be the patient motivation to continue and being adherent to the DSs.
Methods: A self-developed questionnaire was used. A database was compiled from the anonymous questionnaires filled in voluntarily by the patients. Basic statistics were used to analyse database.
Results: We received 477 responds. Gender ratio was 0.42 (139 [29.1%] male and 334 [70%] female). Good adherence to Rx was reported in 51 patients among male and 96 among female (OR: 1.44; 95% CI: 1.02-1.84, $p<0.0001$). 144 patients (30.2%) trust in vitamins and if necessary consume it, from them 96 patients (20.1%) take vitamin D. Out of 64 patients (13.4%) consuming continuously vitamin D, 39 (8.2%) take the same dose over the year and out of 91 patients (19.1%) taking periodically vitamin D, 30 (6.3%) take the same dose (OR: 3.2; 95% CI: 2.5-3.8, $p<0.0001$). Fifty-three patients (11.1%) take Rx and 50 patients (10.5%) are adherent among patients who take regularly vitamins. Seven patients (1.5%) are adherent to Rx out of 23 (4.8%) among vitamin non-consumers (OR: 38.1, 95% CI: 36.6-39.6; $p<0.0001$). Calcium supplementation (CaS) were used by 88 (18.4%) patients regularly, 30 (6.3%) patients frequently, 131 (27.5%) patients sometimes and 226 (47.4%) patients never. Among regular CaS users, 38 (8%) out of 82 (17.2%) patients adhere to their Rx and 44 (9.2%) out of 226

(47.4%) patients (OR: 3.57, 95% CI: 3.0-4.1; p<0.0001).
Conclusion: Adherence to Rx is significantly higher among male. Those patients who consume regularly vitamin D take the same dose during the year. Regular vitamin consumption and CaS enhance the adherence to Rx.

Actualities of quality assurance

MORVAI, M.
Egis Pharmacutical Plc., Budapest

Luteinizing Hormon-Releasing Hormon (LHRH) receptor based new possible targeted therapy for human uveal melanoma

OLÁH, G., HALMOS, G.
Department of Biopharmacy, University of Debrecen, Debrecen

Background: In the past decades, the average survival of patients has not changed in the case of uveal melanoma (UM). The average survival of metastatic patients with UM is less than one year, and despite the treatment of the primary tumor, metastases develop in more than half of the patients. The drawbacks of bad statistics are the rapid dissemination of the tumor cells but resistance to chemotherapy also plays a major role. Cytotoxic LHRH (luteinizing hormonereleasing hormone) analogs can be effectively used for targeting sexual hormone-dependent malignancies like endometrial, ovarian and prostatic cancers but the application of these analogs in hormone-independent cancers such as human uveal melanoma (UM) is not examined jet.
Aims: The aims of the current study were to investigate the expression of LHRH receptor and ligand in human UM tissues, as a potential novel therapeutic target. We also established a new in vitro model to study the cellular uptake and efficacy of cytotoxic LHRH analog AN-152 (AEZS-108, zoptarelin doxorubicin) in a doxorubicin-resistant UM cell line.
Methods: The expression of LHRH receptor and LHRH ligand was tested in 39 human UM specimens by RT-PCR with specific primer set for full length LHRH receptor. Radio ligand binding characteristics of LHRH receptors were studied in tumor membranes of ten UM specimen. The presence of LHRH receptor protein has been confirmed by immunohistochemistry. We established a new doxorubicin (DOX) resistant UM cell line by stepwise administration of DOX to OCM3 human UM cells. The LHRH receptor expression of DOX sensitive (OCM3) and DOX resistant (OCM-3DOX320) UM cell lines was determined by exon specific RT-PCR and the immunocytochemistry. Cellular uptake and intracellular distribution of DOX and AN-152 were imaged with confocal laser scanning microscopy. Comparative cytotoxic activity of DOX and AN-152 were tested on both cell line by MTT assay.
Results: High percentage (46%) of UM specimens expressed the mRNS of full length type 1 LHRH receptor and 69% of samples were positive to LHRH ligand expression. 70% of the tissue samples showed high ligand binding affinity to LHRH receptors. Immunohistochemistry also confirmed the presence of LHRH receptors. We were able to establish a new DOX resistant UM cell line. Our study demonstrated the expression of LHRH receptor splice variants and protein isoforms in OCM3 and OCM3DOX320 cell lines. The cellular uptake of AN-152 was confirmed by fluorescent microscopy.
Conclusion: Based on the MTT assay AN-152 effectively inhibited cell proliferatin in both cell line in dose dependent manner. Our results demonstrated that LHRH receptors and its isoforms can be potential molecular targets for an effective targeted therapy of UM and its metastases.
20428-3/2018/FEKUTSTRAT, ÚNKP-18-3-IV-DE372, GINOP-2.3.2-15-2016-00043 (IRONHEART)

Clinical studies at the University of Debrecen

PÁLL, D., ZRÍNYI, M., MARODA, L., NYISZTOR M.
Coordination Centre for Drug Development, University of Debrecen, Debrecen

The Coordination Centre for Drug Development was established in 2013 to serve as an independent organisation under the guidance of the Rector and Chancellor. After the Senate approved our bylaws of operation, we launched our unit, setup our website, instituted ways of supporting electronic file processing, and followed a single contract model.
Our primary goal was to speed up administrative processes, improve communication with sponsors and CROs, ultimately increasing the number and intensity of trials. We also defined our ambitions to become leaders in the field as well as collaborating intensively in the international arena.
A new strategy in communication was developed, sharing more information about clinical studies and highlighting the advantages of the University of Debrecen, concerning both human resources and infrastructure. We achieved prime partnerships not only with sponsors and CROs but also with general practitioners as well as patients and relatives.
As a result of efforts, during the last five years we more than doubled the number of contracts and tripled the revenue. Recent focus includes improving the quality of our services. Lately we have developed a web-based quality assurance system for all clinical studies run at University level where we record

studies, analyse data, and provide feedback on progress to principal investigators and the University management in a quarterly report.

Losses suffered by the Hungarian pharmacy due to the borders defined by the Treaty of Trianon

PÉTER, H. M.
Marosvásárhely

We must remember an event took place 100 years ago. The consequences of the border adjustments resulting from Trianon have affected the whole country's pharmaceutical network. Transylvania, Máramaros, Partium and East-Bánság have been attached to Romania, thus Hungary lost 102.813km^2. From these areas 1,662.000 people (according to population census in 1910), 31.78% of the total population have come under Romanian authority. The Hungarian pharmacy in 327 towns have lost 477 pharmacies. Later, in the detached towns more pharmacy owners, employees have migrated, so more pharmacies have ceased. As a replacement, the Romanian authority have given 174 new pharmacy rights, this way in the detached areas 65.5% of the pharmacies got into Romanian hands. In an issue, called Gyógyszerészek zsebnaptára (Pocket calendar of pharmacists), published in Budapest, 1918, the pharmacists from Transylvania are included, their pharmacies are mentioned, so does the town where they operated. In later years, the published almanachs (pocket calendars) have no longer reported these data. This way for a period of time the pharmacists from Transylvania were isolated, they could hardly make contact with each other. Jenő Nagy (1891-1980), young pharmacist in his early thirties from Marosvásárhely undertook the task to organize collecting data, then he edited the data his collegues have sent to him and finally, at his own expense, he published the issue named Gyógyszerészek címtára és zsebnaptára (Pocket calendar and directory of pharmacists) for the year 1921, I. period. He stopped collecting data 15th, December, 1920. Publishing data of pharmacists and pharmacies from Transylvania and Bánság have helped making contact with each other for those pharmacists who stayed in Hungary. A tradition has been created, because after this, similar issues, calendars, directories, year books (almanachs) were published regularly, every year or second year, up until 1937.

GMP audits and inspections; similarities and differences

PETHŐ, G.
Global Quality & Compliance, Xellia Pharmaceuticals Ltd., Budapest

GMP audits and inspections are important events for both parties, regardless of which side you stand. They are assessments of the auditee's/inspectee's systems and can play a critical role in the approval or the image of the companies; ultimately they can have a huge impact on market supply to the patients who need to receive pharmaceutical products of the highest quality. This is our mutual interest and mission.

Both audits and inspections are well-defined processes and certain standards are used but the way they are approached, communicated, executed, and followed-up might vary significantly. These aspects, including how the observations are formulated and reported mainly depend on the inspectors/auditors and where the agency/company is from, as well as on the staff of the company that is inspected/audited. The lecture aims to give insight to audits, inspections and self-inspections with respect to how different they could be and what impact they might ultimately have on the companies' compliance level. It is not attempted, to give a „study book" type picture but rather an experience-based personal (but objective) review of these assessments.

Over-the-Counter pain relief: actualities and the role of the pharmacists in the field of self-healing and self-medication

PETHŐ, ZS.
Department of Rheumatology, University of Debrecen, Debrecen

Background: Pain is more than a feeling of discomfort. Depending on the intensity of pain it can affect the quality of everyday life. It may also lead to mental health conditions like depression and anxiety. The amount of pain can influence the overall health. Pain is the most common symptom in the musculoskeletal diseases. People can experience pain as an acute, chronic, or intermittent condition, or a combination of the three. Specifically, chronic pain is a complex condition embracing physical, social and psychological factors, leading to disability and poor quality of life. It seems to be important to support pain relief in a way that is accessible to all. Pain-relief methods range from at-home treatments and prescriptions to over-the-counter (OTC) medications and invasive procedures like surgery. Each person's pain experience is unique to them. A wide variety of painkillers is offered, analgesics and nonsteroidal anti-inflammatory drugs (NSAIDs) are available. This greatly facilitates the patient or many times the doctor's job as well. The future offers an even wider range of over-the-counter drugs, with the possibility of more frequent combinations and side effects. How do we take advantage of this opportunity? How can we save time by not waiting for a medical examination?

Discussion: Among the principles of pain relief, it is important to follow the steps of pharmacological pain relief and consider invasiveness. It is suggested to seize the opportunities of non-medical and percutaneous methods. Both analgesics and NSAIDs reduce fever and relieve pain caused by muscle aches and stiffness, but only NSAIDs can also reduce inflammation. Paracetamol, metamizole and NSAIDs also work differently. Non-opioid painkillers are the most common type of painkiller. Paracetamol is available over the counter and it is often the first treatment for mild to moderate pain. NSAIDs work by inhibiting the activity of cyclooxygenase enzymes (COX-1 or COX-2). In cells, these enzymes are involved in the synthesis of key mediators (prostaglandins), which are involved in inflammation, and thromboxanes, which are involved in blood clotting. Most NSAIDs are non-selective and inhibit the activity of both COX-1 and COX-2. These NSAIDs, while reducing inflammation, also inhibit platelet aggregation and increase the risk of gastrointestinal ulceration. COX-2 selective inhibitors have less gastrointestinal side effects but promote thrombosis and substantially increase the cardio- and cerebrovascular risk, especially in elderly people.
Conclusion: Pain reduction is a professional and social expectation. A wide range of methods is available, yet it is often not an easy task. Especially in the case of elderly people we should count with multiorgan failure and comorbidities, so the individual medication and the adaptation of the side effects profile is essential. In conclusion, due to the importance of the OTC medications the role of the pharmacists is crucial.

Interactions of flavonoid metabolites with serum albumin and biotransformation enzymes

POÓR, M., MOHOS, V., FLISZÁR-NYÚL, E.
Department of Pharmacology, University of Pécs, Pécs

Background: Flavonoids are contained by several foods, dietary supplements, and medications. Flavonoids have poor oral bioavailability, therefore, mainly their metabolites appear in the blood and in other tissues. During the first-pass metabolism of flavonoids, conjugated metabolites are formed in enterocytes and/or in hepatocytes. As a result of the high intake of flavonoids (e.g., through the consumption of dietary supplements), their significant concentrations appear in the colon. The colon microbiota can also biotransform flavonoids, during which small phenolic fragments are formed. Microbial metabolites may also be absorbed. The pharmacokinetic interactions of flavonoid aglycones have been widely studied; however, only limited information is available regarding their metabolites.
Aims: In these studies, we aimed to investigate the interactions of conjugated and microbial flavonoid metabolites with serum albumin and biotransformation enzymes.
Methods: Flavonoid-albumin interactions were examined with fluorescence spectroscopy and ultrafiltration. The in vitro enzyme inhibition assays regarding cytochrome P450 (CYP) and xanthine oxidase (XO) were performed with CypExpress kits and with the pure enzyme, respectively.
Results: Methyl, sulfate, and glucuronide metabolites of quercetin and chrysin as well as 24 microbial flavonoid metabolites were examined. Quercetin-3'-sulfate and chrysin-7-sulfate formed more stable complexes with albumin and showed higher displacing ability than the parent compounds. Some conjugates significantly inhibited CYP2C19 and CYP3A4 enzymes. Sulfate and methyl metabolites showed similar or even higher inhibitory effects on CYP2C9 enzyme compared to the flavonoid aglycones. XO enzyme was strongly inhibited by the sulfate and methyl conjugates of quercetin. Some microbial metabolites (e.g., pyrogallol, desmethylangolensin, and 2,4-dihydroxyacetophenone) were also able to interact with albumin and/or biotransformation enzymes.
Conclusion: Based on our observations, it is reasonable to hypothesize that flavonoid aglycones and some of their conjugated or microbial metabolites may cause the development of pharmacokinetic interactions. Therefore, the simultaneous administration of high-dose flavonoid-containing dietary supplements with drugs need to be carefully considered.

Mucoadhesive films as innovation products.

REGDON, G. JR.
Institute of Pharmaceutical Technology and Regulatory Affairs, University of Szeged, Szeged

Background: This presentation is based on the literature reviews of the benefits of mucoadhesive drug delivery systems, mechanisms involved in mucoadhesion and different factors affecting mucoadhesive drug delivery systems.
Aims: Although the oral route is the most popular way of administration of medicines for patients, the enzymes of the gastrointestinal tract decompose many active substances and the first-pass effect decreases the serum level of active pharmaceutical ingredients, too. Mucoadhesive films are not only local, they can also cause systemic effects, and even special substances such as small molecule proteins can be used. Oral mucoadhesive films are welcome

in paediatrics, but the films are also appropriate for elderly patients who suffer from swallowing disorders.

Results: The author wishes to illustrate with examples from the literature the direction of the research of bioadhesive films, what difficulties are encountered in formulation, which are the critical factors in the preparation of a pharmaceutical formulation. It is very important to understand the different mechanisms involved in mucoadhesion to formulate an optimal dosage form. The first important factor is the choice of the suitable film-forming polymer, for which a variety of chemically structured polymers may be adequate. Of course, it is almost mandatory to use a plasticizer in the composition to make the films elastic, so the type and amount of the plasticizer is a very important parameter. The author would also like to give an overview of the active substances that can be found in the literature of the research of this pharmaceutical form. The testing methods for film rating will also be presented, with particular regard to adhesion property, tensile strength, other physico-chemical properties and, of course, the dissolution test.

Conclusion: By presenting examples from the literature, the author points out that bioadhesive films as pharmaceutical forms provide a relatively new innovative route to therapy that requires appropriate drug formulation.

References: 1 Gottnek, M. et al.: Gyógyszerészet 2013;57:323-329; 2 Mackie, A.R. et al.: Macromol. Biosci. 2017;17:1600534(1-32)

Unit-dose or ward-based medication management, what does the statistics teach us?

SÁGI-POLICS, É., ROMVÁRI, Z., DORMÁN, K.
Mining Rehabilitation and Night Time Sanatorium, Health Centre of Komló, Komló

Background: Our institute declared patient safety as high priority and since the number of medication errors are a good indicator of that, we introduced a new method to try and reduce them. Damages caused by the health sector are a heavy burden to bear by society. Consequently if we invest in patients' safety that would bring obvious benefits to them, and might even reduce our costs.

Aims: Our goal is to compare the types and rate of medication errors occurring at conventional, ward based medication prepared by nurses versus centralized medication supported by automation and clinical pharmacists in the hope that the latter means significantly fewer errors. Additionally we investigate the specific indexes of given wards during both periods such as drug costs per one nursing day/case/weighting factor to see how the new method affects these numbers. Our overall goal is to prove the great usefulness of the new method looking at different aspects.

Methods: Quantitative research at Mining Rehabilitation and Night Time Sanatorium, Health Centre of Komló; internal medicine, chronic internal medicine and nursing departments; 2017 August and 2020 February. On two given days we inspect all the medicines prepared by the nurses or the hospital pharmacy, comparing the written orders and the drugs dispensed (involving the patient's own drugs), at the second date even comparing the written orders and the ones recorded in the medical software. We excluded parenteral medications from our investigation. The target group involves all the patients above the age of 18 from the three wards mentioned before. We do not investigate interactions or the effects on the patients caused by medication errors. We used different kinds of descriptive statistical methods to evaluate our results.

Results: The ward that provided medications for a 24 hour period operated with a 15% error rate, the other two that prepared medications weekly had a 30-50% error rate when the nurses prepared the medications manually from the written instructions. These both came down to a less than 2% error rate with the newly introduced unit-dose system. Besides this the drug costs dropped at the chronic wards by 18% percent just after the first 6 months of using the new method.

Conclusion: Our research verifies that using the unit dose medication system significantly reduces medication errors and drug costs in the specific indexes. Therefore we are more able to ensure patient safety in our hospital followed by reduced drug costs and optimized medication utilization.

Formulation and evaluation of herbal drug preparation for the prevention and treatment of insulin resistance

SINKA, D., PÁLL, J., SZENDI, N., UJHELYI, Z., FEHÉR, P., VECSERNYÉS, M., BÁCSKAY, I.
Department of Pharmaceutical Technology, University of Debrecen, Debrecen

Background: Insulin resistance is a major global health issue of the 21st century, an estimated 33.9% of the U.S. adult population had prediabetes in 2017. It is seen as the threshold of the type 2 diabetes. Insulin resistance can lead to obesity, heart disease, or polycystic ovary syndrome. The treatment of the condition is based on lifestyle changes, including proper, low-carbohydrate diet, physical activity and weight loss. Botanical extracts have been widely used throughout history as medicinal agents for improving metabolism or treating diabetes. There are

scientific investigations of herbal agents used to treat or reverse insulin resistance. The botanical extracts can assure an effective, commonly available and cheap therapy, with a generally higher patient compliance toward it than synthetic drugs.
Aims: In our work, we developed a product taking advantage of the combined effect of fenugreek and pepper.
Methods: We carried out citotoxicity assays of the botanical extracts, transport tests on CaCo-2 human adenocarcinoma cells, and modified dissolution tests to evaluate the product.
Results: Our research proved the safety and the increased bioavailability of the product.
Conclusion: We successfully developed a herbal drug delivery system with increased bioavailability, stability, and sustained API release.

Using Flux Measurements for Prediction of Bioequivalence of Drug Products of Poorly Soluble Compounds

SINKÓ, B.[1], BORBÁS, E.[2], NAGY, ZK.[2], TSINMAN, K.[1], VÖLGYI, G.[3], TAKÁCS-NOVÁK, K.[3]
[1]Pion Inc., Billerica, USA;[2]Department of Organic Chemistry and Technology, Budapest University of Technology and Economics; [3]Department of Pharmaceutical Chemistry, Semmelweis University, Budapest

Background: For generic formulation development traditional (USP) dissolution tests have been used in the pharmaceutical industry to compare the performance of different drug formulations before conducting bioequivalent studies. Although dissolution tests provide a simple way of testing formulations, the in vivo predictive power of these tests is not always satisfactory.
Aims: The aim of this study was to represent how simultaneous dissolution-absorption studies can provide more complex information on brand and generic formulations.
Methods: μFLUX™, BioFluxTM and MacroFLUX™ instruments (Pion Inc) were utilized to compare the behavior of brand and generic formulations. Examples of itraconazole and telmisartan formulations are presented. Assay parameters were aiming to mimic the in vivo conditions.
Results: The dissolution and flux results of three marketed itraconazole and five marketed telmisartan formulations were compared in fasted and fed state to each other and to the in vivo study results published in the public assessment reports. The differences of itraconazole formulations in in vivo human fraction absorbed data were possible to be captured by the in vitro studies reasonably well, especially considering the significant deviation in dissolution kinetics due to the differences in composition and formulation strategy. Telmisartan formulations provided more similar dissolution behavior that made it possible to correlate in vivo deviations to in vitro flux results.
Conclusion: The in vitro test was found to be successful in predicting dissimilarities among formulations caused by different excipients and formulation strategies and produce the same rank order of formulations in fasted and fed state as in vivo results do. Although the applied in vitro models are not able to simulate all aspects of human absorption, they appear to be a useful tool in formulations comparison and in absorption estimation.

Comprehensive, patients' adherence development program in Hungarian community pharmacies The first results of the pilot period

SOMOGYI, O.
University Pharmacy Department of Pharmacy Administration, Semmelweis University, Budapest

Background: The aim of the adherence development projects is to make a patient a real partner in the therapy following the advices of doctors and pharmacists.
Aims: "My Medicines 5xM" pilot program was started in October 2018 as the introductory phase of a comprehensive, adherence development program in the Hungarian community pharmacies. One of the main objectives was to attention to the importance of correct use of medicines.
Methods: A printed leaflet for patients was compiled to focus on the correct, general application rules. It included a short questionnaire in which patients evaluated the usefulness of the text. The leaflets were delivered to 208 pharmacies and a self-developed pharmaceutical guideline was available to them, printed and online (detailed version). In March 2019, feedback was collected from pharmacies and participating professionals.
Results: The patients' questionnaires were collected from 80 pharmacies with 1082 participants. The leaflet helped 91 percent of patients to ask their questions more freely in the pharmacies. After reading, 90 percent of respondents are more aware of information about their medicines. 510 patients changed their incorrect medicines application habits. The text also included new information for 52 percent of participants (e.g. drug-food interactions in 92 cases).
In the electronic, feedback questionnaire survey participated 205 pharmacies. Based on this, 136 pharmacies found the leaflet useful and 40 pharmacies found it very useful. According to the most pharma-

cies (84 responses), the pilot program helped them mostly to increase the therapeutic support of their already known patients, but several pharmacies managed to create a more "patient-friendly" atmosphere (53 pharmacies). The communication section of the pharmaceutical guideline was utilized by the most pharmacies, but tables summarizing interactions were also frequently used.
Pharmacists and assistants responded to the online, feedback questionnaire survey (76 persons). The importance of the program was rated as mean score 4.3 on a five-point scale. The leaflet was considered very necessary by 39 respondents (mean score 4.25). The guideline was found important by 34 professionals, but not very important. The workshops of the program were considered clearly useful.
Conclusion: This program is currently taking place in all Hungarian community pharmacies. In addition, the improved, general pharmaceutical methodology (guideline), other therapy specific guidelines and leaflets have been published.

Role of clinical pharmacists in the risk assessment of healthcare associated infections (hai) in a surgical unit

SÜLI, E.[1], SZABÓ, M.[1], BODÓ, G.[1], LÁZÁR, G.[2]
[1]*Central Pharmacy, Albert Szent-györgyi Health Center, University of Szeged,*
[2]*Department of Surgery, Albert Szent-györgyi Health Center, University of Szeged, Szeged*

Background: The nosocomial infection rate in patients in a facility is an indicator of quality and safety of care. The development of risk assessment process to monitor this rate is an essential first step to identify local problems and priorities, and evaluate the effectiveness of infection control activity. Risk assessment by itself, is an effective process to decrease the frequency of hospital-acquired infections.
Aims: The ultimate aim is the reduction of nosocomial infections, antibiotics and proton pump inhibitors (PPI) overuse. Doctors, clinical pharmacists and hospital hygiene service must work cooperatively to reduce the risk of infection.
Methods: The annexes 2. and 3. of the decree have been adapted to eMedsol computer system. The risk assessment forms are completed by clinical pharmacists. The completed data sheets are displayed in the eMedsol system as a part of the patient's examinations, e.g.: blood tests. The data sheets have to be filled out again as a new risk factor appears, e.g. after operation, catheter placement or intensive care. The risk assessment forms were filled over an 8-week period, from 9 September to 8 November 2019 at the Department of Vascular Surgery.
Results: We have completed the risk assessment for 109 patients. 51 patients were in high and 38 patients were at medium risk for nosocomial infections. 48 patients were in medium and 41 patients were at high risk for multiresistant microbial infections. Most of the patients were elderly (> 65 years old), and have more comorbidities, such as diabetes or obesity. Furthermore, in their anamnesis they had hospitalization within the past year, which contributes to the high risk of nosocomial infections.
Conclusion: Overuse of antibiotics and PPI could be responsible for the high risk of multiresistant microbial infections. In both cases, inappropriate and prolonged use of devices, such as CVCs, urinary catheters, which are also monitored by the questionnaires, may cause high risk. We also aimed to include more surgical departments into our risk assessment, and together with our clinical pharmacist colleagues implement it to several clinics. These questionnaires help us to reduce antibiotics and PPI overuse.

References: 1 EU Council Recommendation (2009 C 151/01) of patient safety, including the prevention and control of healthcare-associated infections, Brussels 2009; 2 HUN 20/2009. (VI.18.) EüM decree, Budapest 2009.

József Antall and the history of pharmacy

SZABÓ, A.
Bethlen Pharmacy, Debrecen

He started to teach in 1955, as a Hungarian literature and history teacher. He graduated from Eötvös Loránd University, Faculty of Humanities. However, because of his political actions, he was permanently banned from teaching, that's how he became a librarian. In the autumn of 1963 he was a scientific colleague in the reorganized Semmelweis Medicinal History Musem, from 1964 he was a senior fellow, over time deputy director, from 1974 appointed director, from 1985 director-general. An unexpected publication request made him well known in scientific circules. He recognized in these times how important it is to know medical history and how unprocessed it was. He determined, that medical and pharmaceutical history is basically a „musem science", because all the relevant data and material can only be found in museums. Enormous tasks awaited him, as a historian. He already has pointed it out in the basic draft, that the Musem and the Library needed to be united. He took on a prominent role in organizing Semmelweis Medicinal History Museum, Library and Archives. He made this institution internationally acknowledged. He noted the needs of Health Care System, elaborated guidelines according to it and the Ministry of Education have approved it under the number 67144/67. This new insti-

tution has become the center of Hungarian medical and pharmaceutical history. The relevance of the institution has truly shown, when József Antall achived that professional history has become a subject in the faculty of medicine and pharmacy in the mid-1980s.

He won the election as the president of MDF party in 1990, thus he could found the government. In spite of his serious illnes, he was the prime minister until 12th december, 1993. As a religious man, he lived his life according to his faith. Just like any other Hungarian politician in the era of enlightment, he had a stiff character, he was well-prepared, classy, he politicised, when he needed to, but he created something everlasting in the area of scientific life.

Synthesis, chemical and biological application of steviol- and isosteviol-based diterpenoids, obtained from *Stevia rebaudiana L.*

SZAKONYI, ZS.
Institute of Pharmaceutical Chemistry, University of Szeged, Szeged

Background: In the recent decade stevia glycosides (isolated from Paraguayan shrub *Stevia rebaudiana L.*), have been proved important natural compounds in the market of artificial sweeteners because of the easy cultivation, the high diterpene glycoside content of the plant, and easy isolation of its glycoside content. Because of the huge volume isolation of glycosides, the aglycon steviol and its isomer isosteviol have come into prominence nowadays as promissing starting material for the synthesis of bioactive compounds.

Aims: The aim of the present lecture is to give a short review on the chemical and biological applications of this promising diterpenoid type compounds according to the literature and our recent results in this field.

Methods: Stevia glycosides have complex diterpenoid glycoside molecules comprised of an aglycone, steviol with the ent-kaurane skeleton and three or four molecules of glucose or other monosaccharides. Hydrolyzed under alkaline or acidic condition, they generate ent-kaurane diterpenoid steviol or ent-beyerane diterpenoid isosteviol. Except for direct applications, they are widely used to provide ent-kaurane or ent-beyerane core structures for further medicinal chemistry study.

Results: Since of its industrial volume preparation, steviol have been proved excellent starting material for the synthesis of ent-kaurane diterpenoids with wide range of biological activity such as cytotoxic and apopthosis, or glutathione S-transferase inducing activity. Some, at C4 position $COOH \rightarrow NH_2$ substituted derivatives possess inhibitory effects against *Hepatitis B virus*. In the recent years several reviews have deeply discussed syntheses of steviol based polyols, or even more complex structures. Isosteviol derivatives prepared with wide range of chemical modification also have proven interest molecules with remarkable pharmacological activities. Some poliol type isosteviol derivatives bear antiproliferative activities, evaluated against human gastric carcinoma MGC-803, HepG-2 and breast carcinoma MDA-MB-231 cell lines. Similarly, excellent antiproliferative activity was observed on the wide range of human cancer cell lines by some structural modifications done at the C-19 of beyerane-skeleton of isosteviol. Some, at C4 modified isosteviol analogues showed suppressing activity against the *Hepatitis B virus* too.

Conclusion: In summary it can be concluded that steviol and isosteviol are excellent starting materials for the development of pharmacologically active diterpenoids, as new drug candidates.

Presentation of our Pharmacy History Collection – past and heritage provide future!

SZALAY, A.[1], SZALAY, L.[1], SZALAY-SZABÓ, AK.[2]
[1]Pátria Pharmacy, Tiszafüred; [2]Betania Pharmacy, Karcag

Background: Nowadays modern expressions like marketing, customers' habits, customers' joy and experience can be also detected regarding pharmacy, new segments in pharmaceutical sciences.

Who knows, whether only new and fascinating trends can be atrractive to the New Age People, or we can trust in classical, well-known and traditional things, as well?

During this 21st century the progress of new technologies, including medical and pharmaceutical sciences is enormous and revolutionary; although past and history seem also essential to remain in focus.

Luckily, in the territory of the former Hungarian Kingdom many traces of old pharmacies and pharmaceutical history can be detected, and those communities are really proud of such mementos, memories.

The most precious ones are considered as real museums with all the connecting prestige: they are pharmacy museums.

There are also collections, and in some cases museum pharmacies can be seen „in everyday work", equipped with precious old pharmacy-furnitures.

At the beginning of the 1990s, in our hometown, Karcag a collection of old medicine and pharmacy history was established and owned by the Town Council; although its operation seemed to be difficult and loaded with many problems. Visitors often encountered difficulties when they wanted to see the reliques.

Aims: Our aim was to establish a pharmacy history collection – as part of our pharmacy; which can be visited parallel with the opening hours of the pharmacy and to enhance the prestige of pharmacy and pharmaceutical sciences int he local community.
We aimed to target those patients and customers who might tend to be susceptible regarding history and pharmacy.
Methods: Beside the establishment of this collection, we do not consider it as „finished" work; we are waiting for further new pharmacy reliques offered in the future.
Results: In 2019, our family-owned pharmacy named „Betania" could have been given place for a pharmacy history collection, where old pharmacy furnitures donated by Karcag Town Council and old family reliques, books can be seen. We are proud of the fact that our Family can be considered as pharmacist dinasty, as from the 18th century there were known pharmacist members among our ancestors.
The room serving as place for the collection used to be the former „officina" of the Betania Pharmacy, and these special values can be seen continously through a special, glazed door.
In case visitors want to look around more precisely among the items of he collection, visit can be organized by us.
Conclusions: Up to our very fresh" experiences, the local community seems to be amazed and interested in historical things; some of our patients have already donated few items for the private collection.
Among our aims, we would like to organize minisymposiums dealing with health sciences, and schools are also warmly welcomed in the future.

We hope, the young generations might get inspiration to choose pharmacy and pharmacist profession.

We would like to inspire our Colleagues – in case proper circumstances are given – to establish such collections for the joy of the local communities.

Targeted delivery of essential oils for pharmaceutical applications

SZÉCHENYI, A.[1], VÖRÖS-HORVÁTH, B.[1], NAGY, S.[1], DAS, S.[2], KŐSZEGI, T.[2], HORVÁTH, G.[3], BALÁZS, VL.[3], VARGA, A.[4], KOCSIS, B.[4], PÁL S.[1]
[1]Institute of Pharmaceutical Technology and Biopharmacy; [2]Department of Laboratory Medicine; [3]Department of Pharmacognosy; [4]Department of Medical Microbiology and Immunology, University of Pécs, Pécs

Background: The medical use of essential oils (EOs) is well known from the traditional medicine, but modern pharmaceutical applications of EOs are made difficult because of the unfavourable physical-chemical properties of EOs, such as hydrophobicity and low water solubility. The traditional method to enhance solubility of EOs is application of their solution, usually ethanolic, or to enhance their solubility with the application of surfactants. Nanotechnology has several successful methods to enhance solubility of poorly water-soluble drugs that has been rarely used to increase the solubility of EOs or to provide targeted delivery of active ingredient from EO to treatment site.
Aims: We aimed to find alternative pharmaceutical applications of essential oils, define the specific targets, and design the delivery form for EO to specific treatment target. We have found several applications where EOs have a proven pharmaceutical activity, like treatment of nail infections, in mouth care or to test general antimicrobial activity of EO. We have chosen to formulate Pickering nanoemulsions with EOs and compare their effectiveness with conventional formulations.
Methods: We have classified EOs regarding their physical-chemical properties. The properties of Pickering emulsions have been defined based on the specific target, mainly considered the size of the emulsion droplets, surface properties of stabilising nanoparticles. For each of the applications, we have optimised the production method for Pickering emulsions to reach the desired properties. The nano formulated EOs have been tested for their effectiveness in antimicrobial tests and in vitro model tests. The toxicological concern regarding nanoformulation has been considered, and several tests have been made to examine the toxical effect of nanoformulation.
Results: We have published our results in several scientific papers, some of the results will be presented in the conference lecture.
Conclusion: We have found that targeted drug delivery can be achieved with nanotechnological formulation. In our research, we have found that Pickering emulsions formulated for a specific target, is more effective than conventional formulations. It has been found that applied nanoparticles have no toxic effect; the toxic concentration of nanoparticles is magnitudes higher then they have been applied in formulations of Pickering emulsions.

Imapct of patient education programs among adolescents

SZILÁGYI-GYERMÁN, A.
Zsálya Pharmacy, Ebes

Background: Adverse effects of medical treatment resulted in 142,000 deaths in 2013 up from 94,000 deaths in 1990 globally. (1) The development of side effects can be a consequence of incorrect medication.

We believe that with a proper patient education, we could prevent several side effects in some cases. At the age of 14, people are allowed to buy their own medicines, meanwhile they possibly don't understand the patient information package leaflet.
Aims: Our aim was to evaluate the 14-18 y.o. children's health status, the level of knowledge about the safe use of medications; the impact of demand within the framework of the national educational system of health-education and wheter the pharmaceutical care provided by pharmacists can be possibly in support for this age.
Methods: We prepared a survey and evaluated 1021 responses with Microsoft Office Excel 2013 program. Within a pilot study an interactive classroom presentation was hold. Shortly after a second questionnaire was distributed to evaluate the impact of information they perceived. Based on results, we established a scholarship among pharmacy students to educate children in schools.
Results: 24% of students take regular medication. 84% of them were ever used medicines as self-medication, 21% never been in a pharmacy, 45% never heard about pharmaceutical care. 10% use webshops to buy OTC medicines and/or dietary supplements. The pilot and following presentations was proved to be successful by feedback: 100% of respondents heard new, useful information, 80% of would take part in similar lecture, 60% prefer to contact a pharmacist for advice for the future.
Conclusion: The proper use of medications has a great impact in aspects of pharmacovigilance. Better knowledge of health and medication-related question among young people achieved by the increase of confidence towards pharmacists in pharmaceutical care would enhance the next generation in safer drug use and health-conscious life to live.

Development of health literacy-promoting communication in Hungarian community pharmacies, investigated in general patients and in a group of patients with type 2 diabetes mellitus

SZILVAY, A., SOMOGYI, O., POLONKAI, K., MESKÓ, A., ZELKÓ, R., HANKÓ, B.
University Pharmacy, Department of Pharmacy Administration, Semmelweis University, Budapest

Background: Health literacy is „the degree to which individuals have the capacity to obtain, process and understand basic health information and services needed to make appropriate health decision." More than half of the Hungarian population has low levels of health literacy. Community pharmacists have a key role in providing patients with adequate and reliable information about their illness and medicines, but it is crucial that the information is consistent with the level of their health literacy.
Aims: The aim of our research was to develop a communication model system in Hungarian community pharmacies that supports health literacy, including a drug dispensing process to the patients that improves their health literacy, and to examine the applicability of the developed methodology in pharmacy practice.
Methods: The research was conducted by pharmacists and pharmacy assistants. The study involved a general patient group and a special group of patients with Type 2 Diabetes (T2D). At the beginning of the project, we conducted self-developed questionnaire surveys of patients' and staff's opinion about the health literacy-friendly practice in their pharmacies, then the employees received a special pharmacy communication training (three-step postgraduate training). Three months later, we repeated the questionnaire with staff, the same T2D patients and other general patients. We conducted a descriptive and deep statistical analysis of the questionnaires.
Results: The study included 333 professionals from 69 pharmacies, 890 (at the beginning) and 847 (at the end) participants from the general patient group and 815 participants from the T2D group. In the general patient group, the mean result of the first questionnaire was 64.19%, which increased to 72.78% by the end of the project ($p<0.001$). In the T2D group, the mean result of the first questionnaire was 57.87%, the mean result of the second questionnaire was 74.73% ($p<0.001$). For professionals, the mean result of the initial questionnaire was 74.68% which increased significantly to 85.20% ($p<0.001$).
Conclusion: All in all, it can be stated that the targeted communication training of the pharmacy staff and the new communication practice in the pharmacies have a positive effect on all patients, whether they are patients with special needs (T2D) or general patients. Based on these results, there is a particular need for the widespread implementation of these developments in Hungary.

Post-splenectomy vaccine prophylaxis in the Department of Surgery

TAKÁCS, A.[1], HIGYISÁN, I.[1], JUHÁSZ, M.[2]
[1]Hospital Pharmacy; [2]Department of Surgery, Vascular Surgery and Thoracic Surgery, Bajcsy-Zsilinszky Hospital, Budapest

Background: Infections caused by Streptococcus pneumoniae (pneumococcus) continue to be a serious problem in both the paediatric and adult populations, causing not only high morbidity but also high mortality rates. The most common and there-

fore probably, the most important adult pneumococcal disease is pneumonia. Patients with splenectomy due to splenic rupture have an increased risk of serious infections caused by pneumococcal disease. Therefore, pneumococcal vaccination is recommended for all patients with anatomical or functional asplenia, which should be given to the patient 2 weeks prior to the planned surgery or 7 to 10 days after the accidental splenectomy. Two types of vaccine are available for active immunization, Prevenar 13 suspension for injection and Pneumovax 23 solution for injection.

Aims: Our aim was to arrange the proper vaccination of patients who have undergone surgery in the Bajcsy Hospital, Department of Surgery. Occasionally, they did not follow the guidelines and the patient was not adequately vaccinated.

Methods: Within the framework of clinical pharmacy, I supervised the prophylactic antibiotic treatment for splenectomized patients, participated in the procurement of vaccines, and made policy choices.

Results: Between January 2, 2019 and July 31, 2019 I have followed the vaccination of 5 surgical patients against pneumococci. Patients received prophylactic antibiotic therapy (2x250 mg Amoxicillin or 2x250 mg Clarithromycin) prior to vaccination. Their final report showed exactly when they received the vaccine. If they have not been vaccinated, when will pneumococcal vaccines be given, all of which will provide the general practitioner assistance and information.

Conclusion: As a clinical pharmacist I have overseen splenectomized patients in order to prevent pneumococcal disease, from antibiotic prophylaxis to vaccination to the new guidelines, thus helping the work of the department and increasing patient safety.

Persistence of biologic treatmens in patients with inflammatory bowel disease

TAKÁCS, H.
University Pharmacy Department of Pharmacy Administration, Semmelweis University, Budapest

Background: Biological drugs are known to be effective for treating inflammatory bowel disease (IBD). However, therapy discontinuation still appears frequently reported by many studies for various reasons. High cost of medication, sideeffects and loss of response can be identified as reasons. for quitting therapy.

Aims: To evaluate the persistence of biologic treatments in patients with IBD and to compare the results with reports from other countries.

Methods: In this single center, retrospective study using administrative claims database of the Hungarian National Health Insurance Fund, patients receiving adalimumab, infliximab, vedolizumab or ustekinumab therapy between 2017 and 2019 were included. Demographic characteristics, therapy discontinuation and switch were analyzed.

Results: Overall, 133 people with IBD were prescribed biological therapy during the two-year timespan, 57 infliximab, 62 adalimumab, 9 vedolizumab and 5 ustekinumab. Biological treatment was switched in 21 cases and only 11 people discontinued the medication completely, all of them were from the Anti-TNF Inhibitor group. 3 out of 11 stopped using infliximab and 8 out of 11 discontinued adalimumab therapy.

Conclusion: 8% (11 of 133) of the patients discontinued the biological therapy for various reasons (2 remissions, 2 bowel resection, 2 no response, 2 patient complience, 1 cancer, 1 adverse drug reaction, 1 unkown). This rate is very low compared to published data. In this cohort, demographical features had no association with persistence of therapy.

From logP to μFLUX. Physico-chemical profiling: past, present and future

TAKÁCS-NOVÁK, K.[1], VÖLGYI, G.[1], SINKÓ, B.[2]
[1]*Department of Pharmaceutical Chemistry, Semmelweis University, Budapest;* [2]*Pion Inc., Billerica, USA*

Pharmacokinetics of drugs is determined by their physico-chemical properties. For today physico-chemical profiling (PCP) became essential tool in drug design and a well-defined field of science. Since the pioneer work of C. Hasch, titled "The logP value and their use" javítandó: "The partition coefficents and their uses" (1971) the logP gained general usage as the measure of lipophilicity in medicinal chemistry and in QSAR. Beside lipophilicity the pKa and the steric parameters were also applied. There was a strong need for the development of new experimental methods including their standardization, validation and also to increase their capacity with miniaturization and robotics. Automated instruments for pKa and logP measurements were marketed. The exclusive role of logP changed in '90-ies due to the appearance of very low solubility APIs. The attention has been focused more and more to the solubility issue. The standardization of the methods which can provide precise reproducible solubility data meant and still means a challenge in PCP. The HT plate methods having high capacity, low material need but producing less precise results are suitable in early discovery phase while GLP conform methods should

be used later in the development phase. The measurements of extremely low solubility (<ng/ml), surfactants, polymorphs, co-crystals and micronized or nanonized compounds are in the front of the present PCP research. The last big change in PCP was the introduction of permeability as first kinetic parameter. The goal of all in vitro permeability methods (cell-cultured based, Franz-cell or PAMPA) is to achieve better IVIV correlation. The measurement in biomimetic media became general and dynamic methods being able to mimic better the living organism have also been developed. The high quality PCP data makes possible to improve the precision of prediction methods, particularly in case of solubility this will be the task of the near future. New perspectives were opened by the invention of μFLUX technique enables the study of dissolution and permeability together. The interest has turned to reveal the effect of additives on solubility and flux of APIs and thus to help the selection of the right excipients for the formulation. With this PCP has entered to the generic development. In the talk we present some results of our lab which significantly contributed to the above process.

The role of the pharmacy family Török in establishing the Hungarian pharmaceutical wholesale and industrial drug manufacturing

TATÁR, G.A.
Hungaropharma Ltd. (retired), Debrecen

Background: Due to historic reasons Hungary was unfortunately underdeveloped in most fields of the economy as compared to Western European countries. This also applies to the pharmaceutical wholesale and industrial drug manufacturing.
Aims: The lecture wishes to give an insight into the foundation of the first Hungarian pharmaceutical wholesale and industrial drug manufacturing by the Hungarian pharmacist József Török with an outlook on his beautiful pharmacy built in the 19th century.
Methods: The lecture is based on contemporary documents and periodicals to be found in the Museum of the History of Medicine and the National Archives in Budapest.
Results: The Hungarian family Török with a long-established pharmacy tradition is one of the founders of the Hungarian pharmaceutical wholesale and industrial drug manufacturing. József Török (1824-1899) pharmacist bought the pharmacy of Károly Gömöry (1779-1845) Hungarian pharmacist in 1854. Károly Gömöry (1779-1845) had a new pharmacy built in Pest (Király street) which was completed in 1813. Since Gömöry was fond of arts he entrusted Mihály Pollack (1773-1855) to plan the building of the new pharmacy. The decoration of the officina was prepared by Lőrinc Dunajszky (1784-1833) sculptor. The pharmacy run by József Török turned out to be a successful enterprise. Later he founded a pharmaceutical wholesale. He recognised the significance of advertisement. He advertised the medicine sold by his pharmaceutical wholesale to pharmacists in the Pharmacists' Yearbook and in other pharmaceutical periodicals, to doctors in medical brochures and to the public in local newspapers. He ensured free samples of the medicine to the doctors. Besides his two enterprises – the pharmacy and the wholesale company he expanded his business with the chemical factory "Galenus" which was founded by his son Sándor Török – also a pharmacist – and the Seits family. The first Hungarian pharmaceutical wholesale at 12 Király street operated from 1864 till its nationalisation in 1950 under the name of its founder József Török. After the nationalisation of the wholesale in the communist era it was merged into two other pharmaceutical wholesales under the name "Gyógyért" also located in Király street. "Gyógyért" was transformed after the democratic changes to "Hungaropharma" which has operated since then at 12 Király street.
Conclusion: The wholesale founded by József Török provided continuous supply of medicine to the Hungarian pharmacies until its nationalisation in 1950.

Dietary supplements: important part of the nutrition therapy

TÉLESSY, I.G.
Department of Pharmaceutics, University of Pécs, Pécs

Due to the unhealthy eating a lot of people need supplementation of micronutrients as well as healthy macronutrients. The latter ones are usually supplied with enteral or parenteral feeding however the micronutrients, inclusive vitamins, electrolytes and trace elements are taken as additional diet. Today, additional (concentrated) nutrients normally present in the food usually are not registered as pharmaceuticals but as dietary (food) supplements. The need of various dietary supplements is in general individual since people eat differently and the nutrient intake is different as well. Here I give details about some of the individual nutrients consumed in form of pharmaceutically formulated dosage forms like tablets, capsules solutions etc. in order to improve health condition. Today it is a fashion to take food supplements because of pre-

conceptions initiated by the advertisements however under certain conditions their use is justifiable and constitute nutrition therapy. I demonstrate evidences with regard to representatives of various nutrient groups, like fitonutrients, probiotics, the vitamin D and zinc.

How can herbal products fit into evidence-based medicine?

TÓTH, B.[1], HEGYI, P.[2], HOHMANN, J.[1], CSUPOR, D.[1]

[1]Department of Pharmacognosy, University of Szeged, Szeged; [2]Institue of Translational Medicine, University of Pécs, Pécs

Background: The use of herbal preparations for medicinal purposes is thought to be older than mankind, but it might be challenging for a traditionally used plant to become herbal medicine in accordance to today's regulations. Since the goal of our health care system is to provide the best possible care based on evidence-based medicine, it has become substantial that traditional medicinal plants tended to use as herbal medicines comply with those criteria that are set by either evidence-based medicine or legislation.
Aims: The aims of our work were to reveal the possible bases of the use of herbal medicinal products, and to facilitate the integration of plants and natural products into evidence-based medicine.
Methods: We have assessed European Union herbal monographs and scientific literature to identify those factors that might influence the classification of herbal medicinal products. Moreover, to dispel the misconception that the efficacy of herbal products cannot be proven scientifically, we have established the Hungarian Phytotherapy Study Group. Our Study Group performs the assessment of clinical trials on herbal medicinal products by preparing meta-analyses and systematic reviews to provide the highest evidence on the use of medicinal plants.
Results: Apart from promising in vitro and in vivo animal studies, numerous human clinical trials have been carried out to evaluate the efficacy and safety of plants and natural products. However, by analysing these clinical trials it has become clear that in many cases further and larger trials, performed by independent research groups and employing standard endpoints are needed to properly assess the efficacy and safety of herbal products.
Conclusion: It can be concluded that beside tradition there is a growing body of evidence supporting the use of herbal preparations. Monographs on herbal medicines are mostly based on tradition, but especially in cases of herbs used in Ayurveda, the European tradition is insufficiently documented; thus, it might happen that a plant with proven efficacy cannot be used as medicine. On the other hand, clinical trials of high quality are needed to establish monographs based on well–established use, and by assessing clinical trials, it has become clear that experts on plants are scarcely involved in clinical trials evaluating plants, and therefore the results of these trials are limited. To sum up, herbal products can be implemented into evidence-based medicine, but this process requires multidisciplinary cooperation.

Risk of falls and fractures associated with vitamin D therapies in scope of clinical trials

TÓTH, E.B.[1], MIRANI, S.[1], HORVÁTH, L.[1], TÓTH, Á.[2], VECSERNYÉS, M.[3]

[1]Department of Pharmaceutical Surveillance and Economics, University of Debrecen, Debrecen; [2]Budapest University of Technology and Economics, Budapest; [3]Department of Pharmaceutical Technology, University od Debrecen, Debrecen

Background: Scientific and clinical evidences documented that vitamin D is essential to maintain calcium absorption and consequently the normal funtion of the musculoskeletal system in human. The deficiency is rather endemic due to significant Vitamin D deficiency detected among most of population. Clinical trial data over the past decades clearly support the skeletal benefits of vitamin D supplementation in patients with circulating 25OHD levels of less than 30nmol/L. The role of vitamin D supplementation has been establashed for the indication also in prevention to minimize the risk of falls and fractures in general. However, the use of bolus or high-dose vitamin D supplementation in clinical trials among elderly people shown unexpeced adverse drug reactions and the need for further surveillance in dosing specifications of vitamin D therapies.
Aims: An overall goal is to establish the safety specificiaction of vitamin D supplementation for prevention and also in various medical conditions in order to minimise the risk of falls and fractures in elderly population. Additionally, to identify the risks associated with the most relevant life-style factors and nutritional conditions that may interfere with the success of vitamin D supplementation applied for prevenetion in general.
Methods: The results of clinical trials based on observational studies at clinical facilities and supported by survey in general public focused on alimentary, solar exposition, the use of dietary- and food supplementation but also assessed the edherence to given medications and other life-style factors.
Results: Vitamin D supplementation is indicated below 75 nmol/L, which is almost 90% of population among elderly and approx. 65-70% in general for the mass of population. The risk of fractures is signifi-

cantly higher among patients with low 25OHD levels (OR 2.83; CI: 1.51-5.31, p=0.007). But over 25% of population is not adherent to prescribed OP therapies. Alimenentary and life-style conditions are both needed optimal skeletal health: two-thirds of the subjects are underestimated their daily calcium intake, although only less then 30% of them are aware of the importance of calcium intake. Moreover, the physical activity level is being adequate in case of 28% even among the younger population.
Conclusion: The option of loading plus maintenance dose schedule proven to be efficient in cases of significant Vitamin D deficiency, however with proper nutritional and life-style conditions only in reduction of risk of falls and fractures.

Real-world data to facilitate assessment of health technologies: survival analysis of the treatment for non-small cell lung cancer

TÖRÖK, Z.[1], ZEMPLÉNYI, A.[2], KOVÁCS, S.[1], ERDŐSI, D.[1], VINCZE, G.[1], BOTZ, L.[3]
[1]Health Technology Assessment Centre; [2]Division of Pharmacoeconomics Department of Pharmaceutics; [3]Faculty of Pharmacy, University of Pécs, Pécs

Background: The use of real-world data is becoming increasingly important in order to generate real-world evidence for the assessment of health technologies in terms of clinical effectiveness and cost-effectiveness. However, the wide range of clinical data collected and stored in electronic medical records (EMRs) has not been used sufficiently for such purposes.
Aims: The aim of our analysis is to explore the facilitators and challenges of using EMRs to analyse the effectiveness of chemotherapy in non-small cell lung cancer patients.
Methods: EMR data from patients with advanced NSCLC who were treated at the University of Pécs between 2010 and 2018 were collected. Patients were grouped into two retrospective cohorts based on their first-line treatment: bevacizumab combination and pemetrexed combination. Follow-up was 3 years. A data mart was built with the use of Medsol Analyzer software. Dates of therapy induction and death were collected from structured fields, while data regarding disease progression (RECIST) were collected from unstructured tumour board documents. Kaplan Meier method was used for survival analysis.
Results: A total of 117 and 147 patients were included in the bevacizumab and the pemetrexed group, respectively. Baseline patient characteristics were similar in the two groups. The median overall survival was 525 and 388 (p= 0.0016) days respectively. The main challenge in data preparation was that important information on prognostic factors (e.g. smoking) or complications was not documented in a structured manner and that the date of progression can only be estimated indirectly using tumour board documents. The strength of the data was shown by the large number of parameters (e.g. TNM, ECOG, stadium, metastases, comorbidities) were available or could be generated about baseline characteristics of patients, making it possible to adequately compare the groups and that large volume of information generated at tumour boards enables to follow the therapies and the condition of patients using text mining methods.
Conclusion: EMRs are valuable source of data in the field of oncology, because the patient pathway is well describable due to the nature of the disease and the tumour board documentation provide very detailed and relevant data for analysis. However, data entry has to be improved to provide more structured information on prognostic factors and the progression of the disease. It is proposed to develop a standardized data model for storing the data generated in each Hungarian cancer centres, which could facilitate the use of real data for retrospective studies and for clinical trials (e.g. for external comparators).

Development of oral peptide drug delivery systems

VECSERNYÉS, M.[1], UJHELYI, Z.[1], KÓSA, D.[1], NÉMETH, J.[2], BÁCSKAY, I.[1]
[1]Department of Pharmaceutical Technology; [2]Department of Pharmacology and Pharmacotherapy, University of Debrecen, Debrecen

Background: The therapeutically used peptides are essential in the treatment of many diseases. At present these products are applied only parenterally and there is a great challenge to develop an oral pharmaceutical formulation and delivery system from these peptides. It is also one of the biggest challenge to set up an orally applied insulin drug delivery system. In my presentation, I would like to give an overview of the oral peptide delivery systems.
Aims: In our experiments, melatonin-concetrating hormone (MCH) has been used as a model compound. This hormone significantly affects the food intake and can be useful in the treatment of anorexia.
Methods: MCH was detected with a specific RIA system. Buchi B-395 Enapsulator apparatus was used to formulate alginate microcapsule as carrier system for MCH. First, special calibrations were required in order to ensure reproducible bead shape and size of the microcapsules (these parameters are: nozzle, electrode, vibrating system, frequency gener-

ator). Afterwards the active substance (MCH) was incorporated in microcapsules. The cytotoxicity of components and various penetration enhancing excipients used in the formulation of the delivery system was examined on human adenocarcinoma Caco-2 cell line. In vitro dissolution test was performed for the release of MCH from the beads, followed by a specific RIA examination in order to detect MCH concentration. In addition, the beads swelling properties and the particle size distribution was examined with laser diffraction analysis.

Results: We determined the most important physical properties of the microparticles. The API enclosure and dissolution were also evaluated in vitro. In addition, our in vitro investigations showed on CaCo-2 cell monolayer that all of the excipients of the formulation is safe in the applied concentration. Moreover, we demonstrated that the applied penetration enhancers influence the junctional function (ZO1, Clau1, BCat) of the monolayer. According to the performed Caco-2 transmembrane investigation the abovementioned penetration enhancement had been demonstrated after determination of in vivo MCH absorption from rat blood samples by specific RIA.

Conclusion: Our results indicated that the alginate-penetration enhancing materials containing microcapsules provide a useful opportunity for the development of an oral peptide drug delivery system

---

The use of complementary therapy in biological therapy patients with rheumatologic and dermatological diseases in a university clinical center

VIDA, R.G., SOMOGYI-VÉGH, A., SCHAADT, N., KISS, D., RAJJ, R., MOLNÁR, B., BOTZ, L.
Department of Pharmaceutics and Central Clinical Pharmacy, University of Pécs, Pécs

Background: Biological therapies have revolutionized the treatment of dermatological, rheumatologic and gastroenterological chronic conditions. These chronic inflammatory diseases are usually linked with high rate of complementary and alternative therapy use and we do not know whether these products affect the effectiveness and safety of therapies.

Aims: As there are limited studies regarding biological therapies and complementary therapy use in Hungary, our aim was to assess the frequency and reason for supplement use in patients getting biological therapy.

Methods: 26 dermatological and 37 rheumatologic patients were interviewed through structured personal interviews at the point of dispensing. The personal medication use review was completed with the review of medical records. The questionnaire focused on drug and supplementary product use (dietary supplements, herbal remedies, etc.).

Results: 32 women and 31 men completed our survey and they have been receiving biological therapy for an average of 6.5 years and in case of 33% there was a switch in the therapy. Beside the prescribed medicines (6.6/patient) patients were taking averagely 2.3 (1-8) supplementary products as well and 52.4% used at least 1 dietary supplement or herbal medicine. The main motivations for complementary therapy use included prevention or treatment of side effects (e.g.: liver damage) and to reduce anxiety (magnesium and vitamin B_6). Potential drug-supplement interactions included: Omega-3 fatty acids and clopidogrel, calcium/magnesium salts and glucocorticoids, *Matricaria recutita* and *Ginkgo biloba*.

Conclusion: The increasing effectiveness of biological therapies can be seen in the study population, however there is a limited data regarding factors affecting these therapies, especially when it is the last therapeutic option. Therefore, and because of their costs, it is essential to identify drug-supplement interaction that may compromise biological therapy patient care. With the involvement of hospital and clinical pharmacists in the dispensing of biological therapeutic medications, there is a greater chance of for the optimization of these therapies.

Modulation of nose-to-brain delivery of a P-gp (MDR1) substrate model drug in anesthetized rats

VIDA-ERDŐ, F., BORS, L., BAJZA, Á.
Faculty of Information Technology and Bionics, Pázmány Péter Catholic University, Budapest

Background: During the last decades several new drug formulations were developed to target the CNS from the nasal cavity. The advantages of the intranasal drug administration are the 1) bypass of blood-brain barrier, 2) lower doses needed 3) less systemic side effects, 4) no first pass metabolism 5) rapid absorption and pharmacological effects. However, in these studies less attention was paid to the possible drug-drug interactions in case of multi-drug therapy.

Aims: The aim of the current study was to identify the possible functional role of P-glycoprotein in the drug absorption in nasal cavity and detection of drug-drug interaction by measuring brain and blood concentrations of our test drug.

Methods: In a pilot study quinidine was administered as a nasal solution, and then we moved on with gel formulation. A P-gp substrate model drug, quinidine was tested by IN administration in presence of PSC-833 (specific P-gp inhibitor) given IV or

IN and adrenaline (IN) at low (50ng) or high (20g) dose. The brain and blood levels were monitored using dual-probe microdialysis.
Results: In control animals the brain penetration of quinidine was at the level of detection limit, but in combination therapy with IV PSC-833 the brain levels increased dramatically, similarly to high dose IN adrenalin, where due to vasoconstriction peripheral distribution was blocked.
Conclusion: These results indicate that P-gp has a crucial role in drug absorption and efflux at nasal cavity, while adrenaline is also able to modify the penetration profile of the P-gp substrate model drug at nasal application.

Medication use review (MUR) in community pharmacies – an international pilot program – preliminary report

VIOLA, R., ARGAY, M.L., CZIKRAY, T., FANG, S., GAÁL, A., BODNÁR, E., SOÓS, GY.
Department of Clinical Pharmacy, University of Szeged, Szeged

Background: Medicines Use Review (MUR) is a structured evaluation of patients´ medication use aiming to decrease drug related problems and increase efficiency of drug treatment. MUR service could be provided by different healthcare specialists – GP, nurse and pharmacist, but in many countries MUR service is mostly offered by pharmacists.
Aims: A pilot project is designed to evaluate professional competency of community pharmacists about MUR and impact of MUR service to patient's knowledge about medication use.
Methods: Patient inclusion criteria: patients with polypharmacotherapy (5 and more medicines), adult, but no other age limits. GPs advise patients to turn to community pharmacy where MUR service is available. During the first visit, the patient is registered to the service, personal details and general perception about medications will be documented at pharmacy. During the second visit, the MUR service will be provided with feedback to GP and patient and the third visit will be assigned after about one month. During the third visit, the repeat MUR service will be provided if necessary, but the main focus is oriented to patient´s feedback to their condition and possible problems with still existing with use of medication.
Results: 5 pharmacies participate in the pilot project working with 17 GPs. 66 patients have started MUR service until now, their age on average 68 years, two third of participants are female (49:17). Our study group takes an average of nine daily medications, the highest number was 20. The patients were satisfied with MUR service. GPs' gave controversial feedback, some of them find it useful but others were sceptic about achiving goals. Challanges indicated by pharamacists regarding the service: time constriants and extra efforts required for documentation.
Conclusion: In the future it would be important to increase pharmacist-led MUR service at the community pharmacies because it can contribute to improving the safety of outpatient therapy.

Solubility analysis and real time dissolution monitoring of polymorphs

VÖLGYI, G.[1], TAKÁCS-NOVÁK, K.[1], SINKÓ, B.[2]
[1]*Department of Pharmaceutical Chemistry, Semmelweis University, Budapest;*
[2]*Pion Inc., Billerica, USA*

Background: Polymorphism of drug substances plays an important role in drug research and development. Due to the different crystal structures, the polymorphs may differ in their physico-chemical properties such as stability, solubility or dissolution rate, and therefore can significantly influence the bioavailability of the substance.
Aims: The aqueous solubility and dissolution profile of different polymorphic forms of venlafaxine hydrochloride, oxytetracycline hydrochloride and carvedilol were investigated.
Methods: The pH-dependent aqueous solubility over a wide pH range was measured by validated saturation shake-flask method at 25°C. The solid form present at the solubility equilibrium was identified by X-ray powder diffraction and Raman spectroscopy. The dissolution kinetics was also studied using real time concentration monitoring applying fiber optic UV probes.
Results: In the case of venlafaxine hydrochloride, no difference was found in the equilibrium solubility of the two polymorphic forms in the pH range 7.5-12. In aqueous buffer solutions the polymorphs transformed to a common product. In the case of oxytetracycline hydrochloride, no significant difference of equilibrium solubility values was found in the pH region 4-7.4 between the two polymorphs. The solid phase analysis proved that both forms were converted to an identical dehydrate form. However, in simulated gastric fluid (SGF) at pH 1.2 the metastable Form B showed 1.9 times higher solubility than Form A. The dissolution performance showed also significant difference between them in SGF. In the case of carvedilol, twofold difference was found between the equilibrium solubility of the two polymorphs in the pH range 7-10. It was proved that the crystal structure of the two polymorphs did not change during the measurement. Moreover, the real

time monitoring of dissolution revealed their significantly different kinetics, the faster dissolution and the higher supersaturation concentration of kinetic Form II. In the acidic pH range Form I and Form II precipitated as common salt.
Conclusion: This study illustrates three different possible behaviours of polymorphic substances, and the great importance of the solid state characterization at the beginning and at the end of the solubility and dissolution experiments to provide accurate information on possible transformations.

Standardisation of of quality parameters of plant originated drugs during the production with special respect to the cultivar use

ZÁMBORI-NÉMETH, É.
Department of Medicinal and Aromatic Plants, Szent István University, Budapest

Background: In case of plant originated drugs, the quality requirements of the Ph.Eur. are frequently not satisfied. In order to take appropriate mesures for standardisation, it is necessary to recognise the background which influences the final quality already during the plant life or postharvest proccessing.
Aims: The presentation summarizes the most important factors in determination of drug quality and the possibilities to optimise them with special focus on the role of the intraspecific varieties.
Methods: The results are discussed based on own experimental results on different medicinal plants beside a wide range of scientific references. Numerous examples will be presented.
Results: In numerous plant species different chemotypes can be observed both in natural populations and selected accessions. In Hungary, we have currently 58 registered cultivars which, however belong to 29 species. It means, that for many species there is hardly any choice of varieties. Additionally, several cultivars have primarily been developed for higher yield, resistance or other technological features and active compound content was only a secondary goal. Nevertheless, outranging Hungarian cultivars are known for poppy, marjoram, fennel, fewerfew, among others. The manifestation of the inherited genetic potential, however depends on the ontogenetic phase and on the examined plant organ. Changing environmental conditions contribute directly or indirectly to the instability of the drug quality, too. Genotype-environment interaction seems to be not neglectable either, but unfortunately, this is until now a less investigated subject.
Conclusion: High output cultivars represent the primarily basis for stable plant drugs. However, in many cases the required quality parameter is a complex or a marker compound (e.g. total flavonoid content) which is presents an aggravating factor in breeding. For manifestation of genetic background an assuring a pharmacopoea conform quality, establishment of cultivar specific technologies are also necessary.

Investigation of antimetastatic properties of potential anticancer compounds in vitro

ZUPKÓ, I.
Department of Pharmacodynamics and Biopharmacy, University of Szeged, Szeged

Background: Currently cancer is the second major cause of mortality globally but a transition in the predominant causes of deaths is detected in high-income countries: mortality from cancer became more common than that from cardiovascular disorders.
Aims: Concerning cancer-related mortality, up to 90% of solid tumors is due to consequences of metastasis indicating that antimetastatic pharmacological interventions may have a crucial impact on the overall mortality.
Methods: Metastasis formation is a complex and well-organized procedure including the infiltrating cancer growth through the extracellular matrix, migration and initiation of distant colonies. Identification of innovative antimetastatic compounds requires in vitro methods of relatively high throughput.
Results: The aim of the presentation is to give a summary of the currently available antimetastatic methods including matrix metalloproteinase assay, different types of cell-based migration and invasion assays.
Conclusion: Some preliminary results obtained at our Department will be additionally presented.