PLENARY LECTURES

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Pharmaceutical technological innovations serving therapeutical safety and efficacy

Background: There is a growing interest toward the development of innovative pharmaceutical dosage forms that provide new opportunities for improving the safety and efficacy of drug therapy. The innovatively structured and functioning formulation based on advanced excipients may serve as a drug delivery system capable of increasing efficacy and / or reducing side effects through innovative technological solutions. The active ingredient is an essential component of pharmaceutical formulations, but the dosage form is the one which carries and liberates its contents as drug substance targeted to the site of action. Various polymeric excipients and manufacturing processes can be used for formulations and their structures allow to modulate drug release mechanisms and to optimize the pharmacokinetic profiles.
Aims: The objective of the review is to present the new results of the development of pharmaceutical technology related to marketed medicinal products, as well as to the latest literature and own research and developmental data.
Methods: Aspects of presentation and evaluation: patient compliance and therapeutic adherence, conditions and special warning of use, pharmacokinetic profile, appropriate bioavailability, desired onset and duration of action, improved dosage regimen, manufacturability and quality.
Results: Many novel formulations have gained therapeutic and diagnostic significance. Depending on the mode of application, they may be incorporated into solid (capsules, tablets, sachets), semi-solid (gels, creams, pastes) or liquid (solutions, suspensions, or parenteral) dosage forms. Nanoparticles (e.g., nanocrystals, vesicles, conjugates) are useful not only for solubilization but also for reducing side effects through targeted drug delivery. The microparticles increase applicability and, as independent drug delivery units, result in predictable and predictable blood levels. Digital pharmaceutical technology represents a new development trend, combining formulation and information technology solutions for tracking as well as to enable treatment management, collaboration and therapeutic adherence.
Conclusions: It has become clear that the right dosage form is an important prerequisite for the success of therapy, and that patient-centricity, personalized and precision medicine requires a paradigm shift in the field of pharmaceutical technology.

References: 1 Stegemann, S., et al. Eur J Pharm Sci 2011;44(4):447-454; 2 Lengyel M. et al. Sci Pharm 2019;87:1-31.

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Utilization of real world data to evaluate and optimize drug therapy

With the rapid growth of data-driven healthcare and digital medicine real world data (RWD) are increasingly used to improve drug therapy and clinical research. The utilization of RWD offers both physicians and practicing pharmacists the opportunity to improve drug therapy and engage in drug development. Thereby healthcare patient care can deliver "data driven" in both research and routine care.
We aimed to explore the potential of domestic RWD through some practical issues related to medication and therapeutic outcomes.
The data required for our studies were obtained from the available health care databases in Hungary (PULVITA, NHIFH or NEAK, IQVIA) and from the clinical database of Clinical Center of University of Pécs. The period analyzed, depending on the individual issues, was between 2000 and 2018. The collected data covered the entire process and history of individual patient care.

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We aimed to address four major questions. First we investigated high-risk drug combinations. Based on data of prescription collection of four years, it could be stated that the problem we are facing is far from negligible, as incidence of the riskiest drug pairs (ca 40) is approximately 1.8 million per year. Our second investigation focused on adverse drug reactions. We wanted to find out whether the Hungarian hospital database can be used for such purposes besides the known sources of ADRs. It was found that the number of cases that could be determined by more than a hundred ICD codes was high, which proved the novel applicability of RWD. The presented third study of medications of schizophrenic patients was based on the use of active substances and outcomes. It especially focused on rehospitalization events, based on hospital and outpatient care data between 2010-2016. The fourth study shows aimed to determine relationships between the nutritional status of patients and their clinical data, to evaulate whether malnutrition can affect the output of healing. The observed data-patterns confirmed, that consequential effect of malnutrition can concern up to 20-50% of patients (depending on the disease).

Our studies demonstrate that RWD analysis can be useful for improving therapy, despite its many limitations. Comprehensive understanding of RWD collection and analysis is needed to achieve its full potential. This way, drug development can become continuous and involve both practicing physicians and pharmacists.

ISTVÁN GREINER, RESEARCH DIRECTOR
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New chemical entity R&D at a CEE midpharma company (From here to eternity)

As the cost of new chemical and/or biological entity R&D is continuously increasing, reaching 1.5-2.5 billion USD, its feasibility in case of a midpharma company is getting to be more and more questionable. At the same time it is even more challenging in the CEE environment where both the financial and the human resources are much more limited than in the developed countries. Notwithstanding the aforesaid four years ago a compound invented and co-developed in Hungary has got marketing authorization in the US, the biggest market of pharma products on the world. The success is ongoing, now its sales reached nearly half billion last year and can jump up to 1 billion USD peak sales according some analysts. During my lecture a short story of cariprazine R&D and in connection with it the related challenges we are facing here will be presented. While I have no crystal ball to show the future only my ideas and thoughts will be shared with the participants about the possible way out from this labyrinth and reach success on this very difficult field of innovation.

BALÁZS HANKÓ, DEPUTY STATE SECRETARY FOR HIGHER EDUCATION
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Society and Health Policy Aspects of the XXI. Century Education of Pharmacists

Significant changes in the healthcare system in recent times have also transformed the expectations of pharmacists, mainly in the areas of community and hospital pharmacy and, of course, the pharmaceutical industry. Thus, the regulatory environment of the pharmacy system has been completely changed, which has extended the duties and responsibilities of pharmacists. The pharmaceutical industry, as a priority sector of the national economy, further strengthened. The R & D & I of the pharmaceutical-related health industry is also evolving significantly. Renewed pharmacy education must be able to reflect all these changes in both the graduate and postgraduate fields and within the functional structure of Faculty. It also requires the development of a university infrastructure environment. The main directions of change are as follows:

- *Increasing the proportion of pharmaceutical subjects under the curriculum,*
- *Development of teaching-related infrastructure,*
- *Increase the involvement of practitioners in education and strengthen pharmacy and industrial practice training,*
- *Development of the functional structure of the Faculty of Pharmacy, integrated education in clinics,*
- *Faculty developments must be in line with the national health and pharmaceutical strategic objective,*
- *Expanding domestic and international courses in the Faculties of Pharmacy.*

ZOLTÁN SZILVÁSSY, RECTOR, FULL PROFESSOR
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Innovation trilemma (Higher education and Industry cooperation)

Aim: My work is referred to as an approach to the phenomenon of 'globalisation paradoxone'through potential role of universities with special regards to pharmaceutical industry.

Basic concept and methods: We think that the key element in building an effective pharmainnovation system is a stable cooperation among pharmaceutical companies and a multidisciplinary knowledge centres the latter of which represented by universities and/or academic research institutions. The optimum form of cooperation at least according to our experiences is the creation of industrial clusters of in which the universities serve as knowledge centres with significant capacities of both multilevel education and experimental and clinical research. Moreover, these baseline university medical research capabilities if supplemented with a wide range of natural sciences such as physics, chemistry, biology and informatics and sciences of law end economics within an institution may render the knowledge centre a highly competitive centre of competence.

Results: One and a half decade ago, the University of Debrecen was successful in building an university-industry network in pharmaceutical industry with Richter Gedeon pharmaceutical company as a principal player together with numerous small and SMEs, a system strongly supported by the local government termed Pharmapolis Innovative Cluster of Pharmaceutical Industry. This 'triple helix' innovation structure was then supplemented with participation of financial institutions succeding generation of distinct projects entering the clinical phase. Phase 2/1 results were found to attract either financial partners or capable of eliciting an interest from global players outside the cluster. It is a point of importance that the cluster members are at least in part owned by Hungarian share holders. The major results of the development of the system beyond producing competitive products and/or product candidates derive from creation of manufacturing plants in the city belonging to either directly to pharmaceutical industry or presenting as externals of the particular industrial branch such as manufacturing and distributing radiodiagnostics or offices dealing with regulatory affairs. These results together may answer questions of the major economic trilemma of modern societies as to whether strenghtening of national self-definition, globalisation and/or democratic economy policy is of preference.

Conclusion: We conclude education and university-based innovation of high quality in structured collaboration with national companies yield very good conditions for globalisation.

MÁTYÁS SZENTIVÁNYI, DIRECTOR GENERAL
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How does OGYÉI help the Hungarian pharmaceutical industry?

New era in the pharmaceutical industry is just here. National Competent Authorities like OGYÉI are acting as real authorities and are approving, inspecting, etc. this field. On the other hand, however, OGYÉI is acting as a supporter of the industry and cooperates with the different stakeholders. We provide scientific advises, and try to help the industry in different ways to cope with new regulations. Besides this we do everything we can to keep the stability of the Hungarian pharma market. We work in close collaboration with our stakeholders and we make decisions after consulting with them or we help them to understand new regulations. OGYÉI follows the different laws and regulations and has its own priorities but always wants to make life of the stakeholders easier and wants to ensure that the decisions made are realistic and will result in the processes they are aimed for. OGYÉI is committed to help new innovation and to help those who need support e.g. small and mid-size companies. We always work on updating our financial support program to make financial support happen, too. We are confident that with these actions we will ensure that the Hungarian pharma industry can continue to work as well as its history is determining it.