3rd World Congress on

NATURAL PRODUCTS CHEMISTRY AND RESEARCH

&

12th WORLD PHARMA CONGRESS

October 16-18, 2017 Budapest, Hungary

Keynote Forum

Day 1

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Yukihiro Shoyama

Nagasaki International University, Japan

Licorice constituents activate the *in vitro* fertilization

Licorice is one of the most important natural products from time immemorial and until now since it has various pharmacological activities depending on five hundred or more constituents. Among them glycyrrhizin is the most popular active compound having many pharmacological activities and developed as a medicine for liver diseases and allergy in Japan. Therefore, we first prepared monoclonal antibodies against glycyrrhizin with a major flavonoid, liquiritin and set up the ELISA system for qualitative and/or quantitative analysis, and developed a new immunostaining system, eastern blotting. Under the survey of active components in licorice using immuno-chemical assay system developed, we found that the licorice extract can accelerate the *in vitro* fertilization of mice. The ethyl acetate fraction from the crude extract indicated most active resulting in the isolation and identification of two active components, hormononetin and isoliquiritigenin. We confirmed that the addition of them in the medium promoted the *in vitro* fertilization resulting in birth, and that the active components were incorporated into the sperm activating the sperm movement. The active mechanism will be also discussed in this congress.

Biography

Yukihiro Shoyama worked in MGH in Boston as a Post-doc in 1975. During 1978 to 1991, he worked as an Associate Professor and as a Full Professor during 1991 to 2007 in Kyushu University. During these periods he was the Director of Pharmacognosy Department, the Director of Herbal Garden, and held Deanship (2004-2006). He moved to Faculty of Pharmaceutical Sciences, Nagasaki International University as a Full Professor from 2007. He was the President of Japanese Society of Pharmacognosy (2007-2008) and Vice Chairperson of Specialty Committee of Traditional Chinese Medicine, Pharmaceutical Chemistry of World Federation of Chinese Medicine Societies (2012-2020). His research interests are marijuana studies like structure elucidation of biosynthetic enzyme protein by x-ray analysis, monoclonal antibodies against over 40 natural bioactive products, biotechnology of medicinal plants and bioactive natural products like saffron resulting in approximately 400 original papers and over 200 review articles.

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Takashi Takahashi

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Synthesis of natural products and their derivatives using automated synthesizer and flow reactor

Automated synthesis and flow chemistry have attracted a great deal of attention in recent years because these processes improve both the reproducibility and reliability of synthesis. Development of automated synthetic procedures and storage of relevant digital data allow anyone to reproduce the same results anytime and anywhere using the same apparatus and reagents. As a result, synthetic chemists can spend more time on advanced and challenging problems. Automated synthesis and flow chemistry often enhance the safety profile of the synthetic processes. Flow chemistry is effective for the hazardous reactions using toxic reagents or high pressure gases. Here in, we report the automated synthesis of taxol, enediyne, lewisx and ketopiperazine analogues and the flow synthesis of peptides and aliphatic aldehydes.

Biography

Takashi Takahashi is a professor of Medicinal Chemistry at Yokohama University of Pharmacy, Japan. He has his expertise in Natural Products and Medicinal Chemistry of drug development.

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Minjun Chen

US Food and Drug Administration, USA

The development of liver toxicity knowledge base to support the assessment of drug-induced liver injury risk in humans

Drug-Induced Liver Injury (DILI) is a frequent cause of Adverse Drug Reaction (ADR) resulting in clinical trial failure, warnings and withdrawals of numerous medications. Despite the research community's best efforts, current testing strategies aimed at identifying hepatotoxic drugs prior to human trials are not sufficiently powered to predict the complex mechanisms leading to DILI. Tremendous efforts were conducted to fulfill this knowledge gap. In the FDA's National Center for Toxicological Research, we developed the Liver Toxicity Knowledge Base (LTKB), aiming to improve our understanding and the prediction of DILI risk in humans via integrative analysis of diverse drug-elicited data. In this practice, we discovered that several drug properties and toxicological properties, such as daily dose, lipophilicity and the capability to form Reactive Metabolites (RM), are strongly associated with serious DILI potential in humans. Here, we will introduce the rule-of-two model (i.e. daily dose≥100 mg/day and logP≥3) and DILI score model (i.e. a scoring model derived from daily dose, logP and formation of RM) developed by the NCTR research team. We will discuss the applications of these models in the context of regulatory processes with the discussion of independent validations reported in literature. Our studies suggest that these predictive models (e.g. RO2, DILI score) could help better assess the human DILI risk in drug development process.

Biography

Minjun Chen is a Principal Investigator working at the Division of Bioinformatics and Biostatics of the FDA's NCTR and serve as the adjunct faculty and mentor for the bioinformatics program joint by University of Arkansas at Little Rock (UALR) and University of Arkansas for Medical Sciences (UAMS). He received the FDA award for outstanding junior investigator (2012) and the NCTR scientific achievement award (2014). Currently, he is the Editor together with Yvonne Will (Pfizer) to create a Springer book titled *Drug-Induced Liver Toxicity.* He also served as the Editorial Board Member for the journals including *Peer J* and *Chinese Herbal Medicine*. He has authored and co-authored more than 70 book chapters or scientific publications in the prestigious journals. His primary research interests encompass drug-induced liver injury, biomarker discovery, bioinformatics, and toxicogenomics..

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Euis H Hakim

Institut Teknologi Bandung, Indonesia

Bioactive natural product exploration of Indonesian moraceous plants

About 30,000 species of plants are distributed in Indonesia and 940 species among these had been used for health care, even though only 120 species of which are involved in Indonesian natural medicines. Over the centuries, the use of medicinal plants has become an important part of daily life despite the progress in modern medical and pharmaceutical research. In connection with our continuing studies on Indonesian tropical plant, a phytochemical investigation of several families of plant has been undertaken in our laboratory, including Lauraceae, Dipterocarpaceae and Moraceae. From Lauracea family of plant, we isolated benzylisoquinoline alkaloid, 2-pyrone and lignan derivatives, while Dipterocarpaceae mostly contains stilbene oligomers. The Moraceae which is known as mulberry family comprising about 40 genera and over 1,000 species spread out in tropical and subtropical regions including Indonesia. *Morus, Artocarpus* and *Ficus* are the most important genera belonging to Moraceae family; these genera economically are valuable because of the quality of its timber and produce edible fruit. The leaves of Morus are very popular for feeding of silk worm (*Bombix mori*). Most of these species are used in traditional medicine in many places and well known as "sohakuhi" in Japan and "sangbaipi" in China. All parts of plant tissues of Morus alba species are reported to be used in folk medicine (leaf for hypertension, root bark for asthma, fruit for anemia and branch for arthritis). Chemical evaluation of *Artocarpus* showed mainly prenylated flavonoid with variety of modified skeleton which involved pyrano-, oxepino- and xanthone- rings. And phenolic compounds isolated from Morus mostly stilbenoid and arylbenzofurane derivatives in addition to flavonoid and Diels-Alder type adducts, have exhibited an interesting biological activity including anti-tumor activity. Development of root culture of M. *macroura* yielded mostly Diels-Alder type adduct compounds such as Chalcomoracin and Kuwanon J, while shoots culture of this species produce a prenylated chalcones namely morachalcone and isobavachalcone which are identified as dienophile founded in Diels-Alder type adduct of Morus. The root culture of M. cathayana afforded O-methylated Diels-Alder adduct compounds which were secreted to the media. Further investigation of enzyme which is responsible for the Diels-alder adducts production of Morus plant showed a promising data for combinatorial biosynthesis study. And recently we tried to explore endophyte microbe of Morus, from which some strains of fungi containing highly potential cytotoxic cytochalasins and few compounds of epiquinophomopsin derivatives were identified.

Biography

Euis H Hakim received a Bachelor's degree in Chemistry from Institut Teknologi Bandung (1980) and she joined the Natural Product research group of Professor Sjamsul Arifin Achmad at ITB. She received Master's degree (1989) and a PhD (1994) from the same university. She got a Research Fellowship at the University of Tokyo (1988), DSIR, New Zealand (1991), University of Western Australia (1992), and Post-doctoral research with Prof. Shigeo Iwasaki, the University of Tokyo (1996) and with Prof. Takeya at Tokyo University of Pharmacy & Life Science (2000). She is promoted to the position of Associate Professor in 2000 and as Full Professor in 2004.

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Xiao-Ling Shen

Guangzhou University of Chinese Medicine, China

Cajanonic acid A from *Cajanus cajan* regulates lipid metabolism *in vitro* and *in vivo*

Prevention of obesity and related lipid metabolic disorder is an important strategy in treatment and prevention of metabolic diseases such as diabetes, hyperlipidemia and hypertension. Cajanolic Acid A (CAA) is a stilbene isolated from the leaves of *Cajanus cajan* (L.) Mills. exhibiting PTP1B inhibitory activity in our previous screening. Activity of CAA on lipogenesis and lipolysis was also investigated. In our study, CAA inhibited the differentiation of 3T3-L1 preadipocyte into mature adipocyte, at the same time it inhibited TG accumulation within mature 3T3-L1 adiocyte and reduced the release of glycerol and Free Fatty Acids (FFA) by the cell. Further study revealed that CAA inhibits adipocyte differentiation and TG synthesis via down regulation of PPARγ and C/EBPα which are key transcriptional factors in adipocyte differentiation, and other adipogenic genes (*ACC, FAS, LPL*, etc.), and inhibits mature adipocyte to release glycerol and FFA by down-regulating genes related to lipolysis (*HSL* and *ATGL*), and up-regulating genes (*ACOX & CPT-1*) crucial to fatty acid oxidation. Ability of CAA to regulate lipid metabolism was confirmed in Zucker fatty rats, treatment with CAA achieved dose-dependent reduction in serum levels of TC and inhibition in increase of serum TG. In T2DM SD rats with hyperlipidemia, CAA not only inhibited the increase in blood glucose, but also significantly reduced the serum levels of TG, TC and LDL-C, and showed protective effect on organ damage brought by hyperglycemia and hyperlipidemia. In summary, CAA improved lipid metabolism both *in vitro* and *in vivo*, showing potential in treatment of hyperlipidemia.

Biography

Xiao-Ling Shen PhD is a Professor at the Laboratory of Herbal Drug Discovery, Tropical Medicine Institute, Guangzhou University of Chinese Medicine. Her research focus is Chinese herbal medicines with anti-obese, anti-diabetic or anti-tumor efficacy.

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Peyman Salehi

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Synthesis of novel norsufentanil analogues via a four-component Ugi reaction and *in vivo*, docking, and QSAR studies of their analgesic activity

Novel pseudo peptide tethered norsufentanil derivatives were synthesized by the four-component Ugi reaction. Norsufentanil was reacted with succinic anhydride to produce the corresponding carboxylic acid. The resulting carboxylic acid has undergone a multicomponent reaction with different aldehydes, amines, and isocyanides to produce a library of the desired compounds (Scheme 1). In all cases, amide bond rotation was observed in the NMR spectra. *In vivo* analgesic activity of the synthesized compounds was evaluated by a tail flick test. Very encouraging results were obtained for a number of the synthesized products. Some of the synthesized compounds such as 5a, 5b, 5h, 5j and 5r were found to be more potent than sufentanil, sufentanil citrate, and norsufentanil. Binding modes between the compounds and mu and delta opioid receptors were studied by molecular docking method. The relationship between the molecular structural features and the analgesic activity was investigated by a Quantitative Structure-Activity Relationship (QSAR) model. The results of the molecular modeling studies and the *in vivo* analgesic activity suggested that the majority of the synthesized compounds were more potent than sufentanil and norsufentanil.

Biography

Peyman Salehi received his BSc in Chemistry in 1987 from Ferdowsi University, Mashhad, Iran. Then he moved to Shiraz University where he received his MSc in 1990 and PhD in 1995 in Organic Chemistry. He started his academic work at Razi University, Kermanshah as an Assistant Professor in 1995. After five years, he moved to Shahid Beheshti University as an Associate Professor. Since 2005, he works as a Professor in the Department of Phytochemistry. He has published more than 160 papers in peer reviewed international journals.

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