

Editorial

The 2006 annual meeting of the Phytochemical Society of North America: Special issue of phytochemistry, phytochemistry pioneer awards and the 2006 meeting scientific highlights

This issue of *Phytochemistry* is dedicated to selected contributions from the 2006 Phytochemical Society of North America's Conference held on the campus of The University of Mississippi in Oxford, Mississippi. The special issue currently replaces the 40 plus annual volume of Recent Advances in Phytochemistry, which had been edited by Dr. John Romeo for over the last decade. The meeting was hosted by the National Center for Natural Products Research, the Department of Pharmacognosy at The University of Mississippi, and the United States Department of Agriculture, Agriculture Research Service, Natural Products Utilization Research Unit.

Phytochemistry pioneer awards: S.A. Brown, N.H. Fischer and G.H.N. Towers

The Phytochemical Society of North America (PSNA) honored three of its phytochemistry pioneers for their contributions to the society and seminal natural products research. The awards were presented to Dr. Stewart A. Brown, Dr. Nikolaus H. Fisher, as well as posthumously, to Dr. G.H. Neil Towers. In addition, a special memorial presentation was given in honor of the late Dr. G.H. Neil Towers whose widow Elizabeth was in attendance. The presentation featured a warm recollection of Neil's life and phytochemical research achievements, and whose life touched many scientists (see following write-up about G.H.N. Towers). At the meeting banquet, the Society also recalled fond memories of Bill Ayer, a quite remarkable natural products scientist, PSNA member Emeritus and frequent contributor to *Phytochemistry*; his obituary follows after the Editorial section.

Professor Nikolaus H. Fischer, Professor Emeritus, Department of Pharmacognosy, School of Pharmacy, The University of Mississippi, received an award in recognition of his outstanding contributions to the fields of Chemistry and Phytochemistry. This award was in recognition of his pioneering work with terpenoids and his leader-

ship and guidance provided to the PSNA. Professor Fischer obtained a Ph.D. degree from the University of Tübingen, Germany in 1965, and then spent two years as a postdoctoral research associate at the University of Texas at Austin with Professor Tom J. Mabry. In 1966, the entire Mabry group was actively involved in organizing the 6th annual meeting of the Plant Phenolics Group which would later that year become the PSNA as it is known today. Professor Fischer initially joined the Department of Chemistry at Louisiana State University (LSU) in 1967 to begin building his Natural Products Chemistry group where he remained until 1999. Following his retirement from LSU, he joined the Department of Pharmacognosy in the School of Pharmacy at The University of Mississippi where he retired in 2003.

Professor Fischer has been a key figure in the study of the chemistry and biological activities of terpenoids with an emphasis on sesquiterpene lactones. His specific interests include: isolation, structure determination and chemistry of natural products; biochemical systematics; biosynthesis, synthesis and chemistry of natural products from higher plants; studies of higher plants as a source for pharmaceuticals and agrochemicals; and plant–plant interactions in natural ecosystems; among others. He has been very prolific and has published ca. 210 original research papers, about 15 review articles or book chapters, as well as many books on plant natural products. He continues to serve in an advisory role and on graduate committees.

Dr. Stewart Brown was also honored in a similar manner, and a historical account of his scientific and profession achievements also follows this Editorial.

PSNA annual meeting scientific highlights

The objective of this meeting was to highlight the multitude of disciplines and expertise represented by the members of the society and their scientific interests. These

disciplines and expertise are represented by individuals who may refer to themselves as chemists, biochemists, physiologists, molecular biologists, etc. The scientific program aimed to encompass the broad research interests of the society rather than to focus on a specific specialty area. To this end, symposia were organized representing the following topics: natural product synthesis and biosynthesis (two sessions); natural product isolation, structure elucidation and methods for analysis; discovery and development of natural products for pest management; metabolic engineering of natural products; and herbal products and nutraceuticals. In addition, the program was designed to include presentations by graduate students, post-doctoral researchers, early career scientists, and established scientists. It was our hope that this type of program would help further unify the society by providing an appreciation of the scientific contributions of those individuals outside of their chosen discipline, and to cater to the research interests of the entire PSNA membership.

The two sessions (I and III) on *Natural Product Synthesis and Biosynthesis* comprised four invited, two Arthur E. Neish Young Investigators, and 10 contributed presentations. The first of the invited speakers was *Norman G. Lewis*, Washington State University, who discussed the factors affecting the formation and accumulation of biologically active plant phenolics, such as lignans, chlorogenic acid, and the extremely complex biopolymer, lignin. *Toni M. Kutchan*, Danforth Research Center, presented an update on the enzymes, genes, and spatial organization in the tetrahydrobenzylisoquinoline alkaloid biosynthesis field, and how these could be utilized to investigate a new class of alkaloids. *David G. I. Kingston*, Virginia Polytechnic Institute and State University, reviewed the discovery of the tubulin-binding conformation of paclitaxel, and then discussed the design and synthesis of bridged paclitaxel analogs that have activities superior to those of paclitaxel. *Mitch A. Avery*, The University of Mississippi, summarized their progress towards the total synthesis of the ethnobotanical antifungal agent, pseudolaric acid B.

Steven G. Ralph, University of British Columbia, and *Reuben J. Peters*, Iowa State University, were the two Arthur E. Neish Young Investigator speakers. Dr. Ralph discussed functional genomic approaches to characterize the role of phenolic metabolism in induced spruce defenses against the stem-boring insect, the white pine weevil. Dr. Peters elaborated on the central role of gibberellic acid phytohormones in plant growth and development, and subsequently presented his results relevant to the enzymatic analysis of gibberellic acid biosynthesis.

Georg G. Gross, University of Ulm, began the contributed presentations by describing how enzyme studies can be used to unravel the biosynthesis of the complex class of hydrolysable tannin natural products. *Mark A. Bernards*, The University of Western Ontario, discussed the analysis of aliphatic carbon flux during wound-induced suberization, as well as the two main metabolic fates of newly formed fatty acids in this process. *Dylan Levac*,

Brock University, disclosed their results relevant to the differential extraction of leaf epidermal enzymes by a carborundum abrasion technique to purify, characterize and clone tabersonine 16-*o*-methyltransferase from *Catharanthus roseus*. *Daniel G. Vassão*, Washington State University, discussed the biosynthesis of the phenolic flavor compounds in basil (chavicol, eugenol), and described the pathway where phenylalanine is transformed through the phenylpropanoid pathway into hydroxycinnamyl alcohol esters, and ultimately allyl/propenyl phenols. *Jack W. Blount*, the Samuel Roberts Noble Foundation, presented results regarding a comparative study of the *Medicago truncatula* glycosyltransferases that are involved in flavonoid and isoflavonoid biosynthesis. *Daneel Ferreira*, The University of Mississippi, gave an overview of the synthetic protocols that are available for the conversion of B- into A-type proanthocyanidins. *Oliver R.A. Corea*, Washington State University/University of Western Ontario, discussed the identification and characterization of arogenate dehydratase(s) in phenylalanine biosynthesis in *Arabidopsis thaliana*. *Mary Magnotta*, Brock University, described the identification of a low vindoline accumulating cultivar of *Catharanthus roseus* via a process of monoterpenoid indole alkaloid and enzymatic profiling. *Syed G.A. Moinuddin*, Washington State University, discussed chemical methods towards defining interunit linkage sequences in the very complex lignin primary structure. *Kye-Won Kim*, Washington State University, concluded the Natural Product Synthesis and Biosynthesis Sessions with a presentation describing studies towards defining the molecular basis of differing enantiospecificities of pinoresinol–lariciresinol reductases in western red cedar using site-directed mutagenesis.

Session II on *Natural Product Isolation, Structure Elucidation, and Methods for Analysis* began with an invited contribution by *William Reynolds*, University of Toronto, in which he focused on overcoming problems in natural product structure elucidation using NMR techniques. The lecture was directed towards potential problems that may either lead to an incorrect assignment or the inability to unambiguously determine a structure. Much of his talk focused on overcoming problems as a result of signal overlap. He also emphasized the importance of simple techniques such as “benzene titration” to overcome such problems. In addition, he discussed the use of HSQC (not HMQC), 1D-TOCSY and HSQC-TOCSY for use in structure elucidation.

Xing-Cong Li, The University of Mississippi, a Neish award recipient, reported on determination of absolute configuration and conformation of several flavanone-(3 → 8'')-flavone type and flavanone-(3 → 8'')-dihydroflavonol type biflavonoids. Detailed analysis of their circular dichroism (CD) and NMR spectra permitted the assignment of their absolute configuration and preferred conformation in solution. Theoretical calculations of electronic CD spectra of these compounds using time-dependant density functional theory (TDDFT) with B3LYP/6-31G* basis

set in Gaussian03 have further confirmed the assigned absolute configurations.

The first of two contributed presentations from Texas A&M University given by “Jay” (*Jayaprakash, G.K.*) discussed unique anticancer limonoids from the seeds of *Citrus aurantium*. The structure elucidation and biological activity work on isolimonoic acid, limonexic acid, deacetylnomilin and deacetyl nomilinic acid glucoside were discussed. The second presentation from this group, by *Amit Vikram*, focused on the simultaneous separation of health promoting bioactive citrus limonoids and their glucosides. He discussed the challenges to quantify both aglycones and glucosides simultaneously with high precision. A simple, rapid and accurate high-performance liquid chromatography (HPLC) method was discussed.

The second invited contribution from session II was presented by *Rachel Mata*, Universidad Nacional Autónoma de México. She discussed natural phytotoxins with calmodulin inhibitory properties, and presented work on her research group’s systematic search for new herbicidal lead structures from natural sources that led to the identification of several phytotoxins with Ca^{2+} /calmodulin (CaM) complex inhibitory properties. These investigations focused on several fungi (*Guanomyces polythrix*, *Malbranchea aurantiaca*, *Phoma herbarum*) and plants (*Hofmeisteria schaffneri*, *Epidendrum rigidum* and *Flourensia cernua*).

Lenong Li, Samuel Roberts Noble Foundation, discussed the crystal structure of a new uridine diphosphate glycosyltransferase from *Medicago truncatula* providing a structural basis for understanding substrate binding, specificity and a possible catalytic mechanism for glycosyltransferases (GTs) in plant. The structural information will facilitate the rational design of GTs to improve the storage and stability of novel engineered bioactive compounds.

This session concluded with a presentation by *Zulfiqar Ali*, of The University of Mississippi, on podocarpaside K, an arabinoside possessing a novel triterpenoid backbone from *Actaea podocarpa*. Podocarpaside K belongs to a new class of triterpenoids, for which the name “runculanane” is proposed.

Session IV on the *Discovery and Development of Natural Products for Pest Management* consisted of a diverse set of presentations on the phytochemical, biochemical and molecular approaches to study plant interactions with insect, fungal and weed pests. This session started with an invited presentation by *Jonathan Gershenzon*, Max Planck Institute for Chemical Ecology, who highlighted the progress made in understanding insect defense mechanisms using the glucosinolate/*Arabidopsis* model system. Integrating these natural defense strategies with preexisting insect resistant crops (Bt-transformants) may lead to the development of new crop varieties with reduced insect damage and may increase the durability of resistance traits.

The contributed presentation by *Raymond Thomas*, The University of Western Ontario, focused on plants defense

against fungi. This study demonstrated that suberin levels in roots of disease-tolerant soybean varieties were higher than in those of susceptible lines. Therefore, root aliphatic suberin levels may be a useful marker in selecting new soybean varieties with higher resistance to the pathogenic fungi *Phytophthora sojae*. *Cecile Bertin*, Cornell University, reported on a new bioherbicide produced by fescue roots, and demonstrated how the allelopathic properties of some fescue varieties may be linked to the root exudation of *m*-tyrosine, a potent phytotoxin.

Stephen O. Duke, USDA-ARS, presented an invited review of the protocols used in the discovery and development of natural products for pest management. These included ethnobotanical, chemical ecological, chemical structure, and other biological activity clues. Successes, such as the discovery of tetranorclerodane insect repellants, the development of a 9,10-anthraquinone derivative as a selective blue-green algicide, the identification of sampan-gine and cyclopentenones as potential agricultural fungicides, and the use of natural products as potential herbicides, were discussed. The rest of the presentation focused on the potential use of genetic engineering to enhance allelopathic traits in crops.

Eric Johnson, USDA-ARS, discussed how transgenic expression of the P1-gene elevated the levels of the insecticidal secondary metabolite maysin in newly emerged and mature silks, relative to controls. While the mortality of the corn ear worm larvae feeding on the silks was not affected, their mean weight was significantly lower, suggesting that expressing the P1-gene may be used to increase tolerance to insects.

This session concluded by a contributed presentation by *Audrey Sauldubois*, Université d’Angers/USDA-ARS, who discussed the elucidation of the mode of action of herbicidal β -triketone phytochemicals produced by *Leptospermum scoparium*. This research demonstrated that β -triketone secondary metabolites were potent inhibitors of *p*-hydroxyphenylpyruvate dioxygenase, a key enzyme in plastoquinone synthesis.

Session V on *Metabolic Engineering of Natural Products* highlighted the research progress towards elucidating novel biosynthetic pathways, and the subsequent efforts towards manipulating these pathways. The session consisted of two invited presentations, an invited Neish Young Investigator presentation, and four contributed presentations. *David Gang*, University of Arizona, gave an invited presentation on efforts to use basil and peppermint as models to understand aromatic metabolism and the underlying mechanisms leading to the structural diversity of the resulting metabolites. The second invited speaker *Sanja Roje*, Washington State University, discussed efforts exploring and engineering plant one-carbon and folate metabolism. *Kevin Walker*, Michigan State University, recipient of a Neish Award, presented the efforts towards evaluating the biogenesis and molecular pathways of bioactive plant products with an emphasis to create scaffolds using a biological system for subsequent chemical modifications.

The four contributed presentations provided a wide scope ranging from efforts using model systems to plants with very specialized metabolites. *Jim Brandle*, Agriculture and AgriFood Canada, reported on the identification and characterization of the five steps in the synthesis of the sweet glycosides of *Stevia rebaudiana* using functional genomics. *Chang-Jun Liu*, Brookhaven National Laboratory, discussed efforts towards the genome wide characterization of acyl-CoA dependent acyltransferases (e.g. responsible for isoflavanoid biosynthesis) in *Medicago trunculata* using standard biochemical techniques coupled with structural biology. *Argelia Lorence*, Arkansas State University and Virginia Tech, reported on the enhanced production of specialized metabolites in tobacco hairy root culture over-expressing an AP2-type transcription factor. *David J. Schultz*, University of Louisville/University of Louisville Medical School, discussed the bioactive natural product anacardic acid, and efforts towards characterizing its biosynthetic pathway.

Session VI on *Herbal Products and Nutraceuticals* comprised three invited, one Arthur W. Neish Young Investigator, and two invited contributions. The first invited contribution was delivered by *Mahmoud A. ElSohly*, The University of Mississippi, with an overview of the marijuana project at The University of Mississippi, and elaborating the activities involved in meeting the requirement of their National Institute on Drug Abuse contract, as well as related product development activities. *Ikhlas A. Khan*, The University of Mississippi, discussed the pro-

gram on marker compounds related to botanical medicines in the US, and outlined some approaches to the solution of quality problems with these medicines. *James D. McChesney*, Tapestry Pharmaceuticals Inc./Chromadex Analytics Inc., gave a talk with the provocative title, *Natural Products: Back to the Future or into Extinction*. He discussed the challenges associated with development of natural products as pharmaceuticals with examples from the taxol saga and identified various perceptions that must be addressed to return natural products to the forefront of discovery and development of pharmaceuticals.

The Neish speaker, *Fabricio Medina-Bolivar*, Arkansas Biosciences Institute/Arkansas State University/Nature West Inc., discussed the production of the natural antioxidant, resveratrol, in hairy roots of peanut. *Patrick S. Covello*, National Research Council Plant Biotechnology Institute, Canada, gave a contributed presentation describing their functional genomics approach towards the biosynthesis of artemisinin. *Christina M. Coleman*, The University of Mississippi, concluded the session and the 2006 meeting with a discussion of the bioactive metabolites of cranberry juice pertaining to the prevention of urinary tract infections.

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