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Celebration of Eric E. Conn's Life

(January 6, 1923 – September 2, 2017)

by Norman G. Lewis and Laurence B. Davin, Institute of Biological Chemistry, Washington State University.

An Appreciation

Professor Eric Edward Conn, a highly respected, highly admired U.S. National Academy of Sciences (NAS) member and a true plant science luminary, passed away 2 September 2017. Rarely in modern biochemistry research does one scientist make an enduring and lasting impact on metabolic pathways that stands the test of time, and which guides follow-on research of scientists throughout the world. ***Eric was an exception***.

From pioneering work in plant biochemistry and metabolic pathways, his work is relevant today and has led to numerous exciting follow-on discoveries. Yes, he died in September 2017. However, his love of science and his positive attitude lives on. ***We are all the better for it***.

At the 50th PSNA Meeting in Hawai'i in December 2011. (Photo courtesy of L.B. Davin).

All other uncredited photos in this article are from the Eric E. Conn website: (http://www.ericeconn.com/biography).

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Reflections

All of us fondly remember the productive interactions with Eric over many, many years. These were marked by his wonderful enthusiasm for, and sincere interest in, each and every scientific research program or project brought to his attention.

PSNA had the signal honor to have Eric at both its 50th anniversary meeting in December 2011 on the Island of Hawai'i, and then again in August 2016 at UC Davis for its 55th annual meeting during which a Symposium was dedicated to him. At both venues, Eric displayed the same infectious enthusiasm and interest in research as he had always done. Wonderful to have had this sprightly and enthusiastic "youngster" in his 88th and 93rd years at both meetings!

Let's celebrate his life, his seminal contributions, his impact on all of us, and his wonderful relationships with his family and with UC Davis.

The web PDF version can be downloaded from the website: www.psna-online.org.

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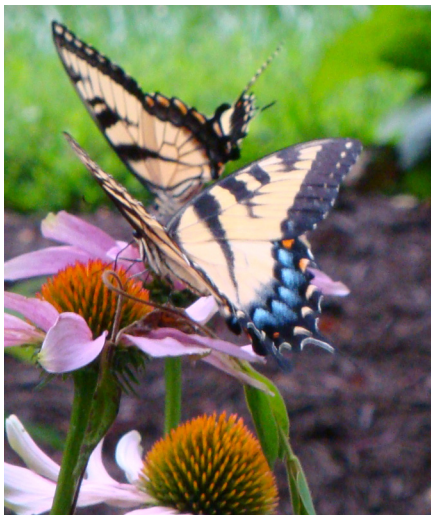

The Phytochemical Society of North America

The Phytochemical Society of North America (PSNA) is a nonprofit scientific organization whose membership is open to anyone with an interest in phytochemistry and the role of plant substances in related fields. Annual membership dues are U.S. $60 for regular members and $30 for student members. Annual meetings featuring symposium topics of current interest and contributed papers by conference participants are held throughout the United States, Canada, and Mexico. PSNA meetings provide participants with exposure to the cutting-edge research of prominent international scientists, but are still small enough to offer informality and intimacy that are conducive to the exchange of ideas. This newsletter is circulated to members to keep them informed of upcoming meetings and developments within the society, and to provide a forum for the exchange of information and ideas. If you would like additional information about the PSNA, or if you have material that you would like included in the newsletter, please contact the PSNA Secretary or visit our website at www.psna-online.org. Annual dues and changes of address should be sent to the PSNA Treasurer. Also check the PSNA website for regular updates.

The PSNA is an all volunteer organization which depends on its membership to run the organization. We appreciate the time and effort these volunteers are putting in to keep the organization up and running. As a member, please consider volunteering to serve on one of these committees. The PSNA can always use more help!

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Eric Conn at the 50th Anniversary PSNA Meeting, December 2011, Hawai'i
(Photo courtesy of L.B. Davin).

55th Annual PSNA Meeting, August 2016, UC Davis.
Eric Conn with Norman Lewis and Laurence Davin
(Photo courtesy of L.B. Davin).

An Incredible Life

This compilation marks the loss of a long personal friend and the loss of a legendary plant scientist. More importantly though it allows for the most pleasant opportunity to celebrate and reflect upon a remarkable life. Here are just a few of the striking reasons which are elaborated upon later.

Eric's lab led to impressive and far-reaching research productivity and breakthroughs.

Eric displayed exemplary dedication and professionalism. This included his tireless commitments to various societies, i.e. the Phytochemical Society of North America (***PSNA***) and the American Society of Plant Biologists (***ASPB***).

Eric was a long standing and highly respected ***Phytochemistry*** Editorial Board member (1961–1999). He also served as Assistant Editor, ***Plant Physiology*** (1968–1972), as Executive Editor of ***Archives of Biochemistry and Biophysics*** (1975–1991), as Executive Editor (or equivalent) of ***Recent Advances in Phytochemistry*** (1984–1989), and in editing the ***Biochemistry of Plants*** in 1981.

Eric's excellent training and guidance (over a long career) of researchers and aspiring researchers alike still resonate all over the world and are as strong as ever today!

The classic textbook, ***Outlines of Biochemistry***, was first published in 1963, when Eric and Paul K. Stumpf (his close friend and colleague at UC Davis), together with Roy Doi and George Bruening, thankfully provided it for the academic/scientific community.

Some Selected Accolades

1981 PSNA Life Membership: This well-deserved recognition was in honor of Eric's remarkable scientific achievements, as well as for his dedication and commitment to the Society in myriad ways (see later).

1988 Election to the U.S. National Academy of Sciences: Both Eric and previous graduate student Tsune Kosuge were individually recognized for their various stellar contributions on 25 April 1988 through their election to the U.S. National Academy of Sciences. This was a bittersweet moment for Eric, as Tsune (then in very poor health) died very shortly after being informed of his NAS election. In his final days, Tsune was delighted to learn that Eric was being recognized that year as well[1] (see later).

1991 ASPB/ASPP Charles Reid Barnes Life Membership Award: This is the oldest award from the American Society of Plant Biologists, ASPB (then the American Society of Plant Physiologists, ASPP) and was established in 1925 at the first ASPP meeting. It is awarded annually for meritorious work in plant biology, and Eric most deservedly

received this prestigious recognition in 1991.

1994 Pergamon Phytochemistry Prize: This coveted prize recognized Eric's tremendous scientific contributions to the field of phytochemistry over more than 4 decades, and in his roles as an excellent scientist, teacher, and colleague. The publishers and the Editorial Board of Phytochemistry particularly noted that "He is a modest and warm human being who has touched the lives of three generations of scientists, including all of us" (http://www.ericeconn.com/Pergamon.pdf).

2007 PSNA Phytochemical Pioneer Award: This Award, quite infrequently made, is reserved for those that have made significant scientific contributions in the field of phytochemistry, as well as being stalwarts of the Society. Eric was a well-deserved recipient in 2003.

2009 ASPB Fellow: Established in 2007, this ASPB Award is made in "recognition of distinguished and long-term contributions to plant biology and service to the Society". There can be no more than 0.2% of the current ASPB membership each year receiving this honor. ***Eric seamlessly met those requirements!***

2011 ASPB Eric E. Conn Young Investigator Award: ASPB honors Eric's contributions in plant biology by recognizing young scientists who will be inspired to follow in Eric's footsteps. ***ASPB will ensure Eric's name lives on in perpetuity.***

Eric Conn's Research Accomplishments: An Appreciation

Here we humbly try to do some justice to the many scientific breakthroughs, albeit so very briefly summarized and with personally selected – and perhaps personally biased – examples. It is not possible to cover everything that Eric and his lab did herein – but hopefully this gives some good insight. It is important to emphasize though that breakthroughs from Eric's lab helped provide the foundation that today we take for granted. Furthermore, the technologies deployed from the beginning of the body of his scientific work to his retirement (at UC Davis) relied initially upon lengthy extractions and isolations of co-factors commercially unavailable, to usage of radio-tracer and stable isotope labeling approaches to probe biochemical pathways, and in developing protocols to isolate and/or detect enzymatic processes of interest.

The younger readers here might find it useful to consider that the contributions made in science by someone of Eric's stature depended also on the technologies available at the time, and the fresh approaches such pioneers took to prevailing dogma (which oft times turned out to be incorrect). Indeed, in those pioneering days, many of the enzymes, co-factors, pathways, and intermediates were generally unknown. Younger readers might also find it instructive that Eric's foundational studies provided knowledge of the enzymes that were ultimately cloned and later studied in depth with the advent of modern molecular biology.

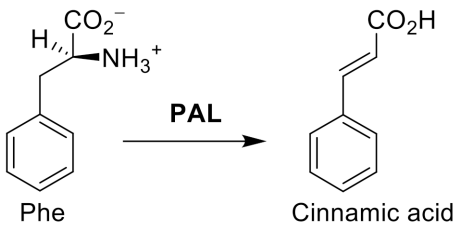
Phenylalanine Ammonia Lyase (PAL) Discovery and Coumarin Biosynthesis: Contributions with Tsune Kosuge and Jane Koukol

Perhaps one of the most highly regarded and highly publicized contributions from the Conn lab is the very early work in determining how metabolism of aromatic amino acid (Phe) occurred to give *trans*-cinnamic acid. This conversion is often described as the "entry point" to the plethora of phenylpropanoid plant natural products which are derived from Phe in land plants. Indeed, this pioneering research ultimately led to discovery of phenylalanine ammonia lyase (PAL), originally named phenylalanine deaminase in the initial papers. This discovery, in turn, was later viewed as one of the key steps in eventually enabling the evolutionarily transition of aquatic plants to a dry land habitat.

The history of this important development more or less began with the study of coumarin biosynthesis in white sweet clover (*Melilotus alba*). It started with Eric's first graduate student, Tsune Kosuge, who had a master's degree in Plant Pathology from Washington State University (WSU). He had applied to UC Davis for PhD training in plant biochemistry in order to complement his plant pathology training. Tsune arrived with an interest in how coumarins were formed and he joined the Conn lab in the 1950s, completing his PhD thesis in 1959. His research, under Eric's superb supervision, resulted in discovery of steps in coumarin biosynthesis that were emerging at the enzyme level.[2] According to Eric, Tsune's work also led to the first detection of an enzyme preparation that converted Phe into cinnamic acid using dialyzed extracts of sweet clover.

In addition, in 1959, the distinguished Canadian plant scientist Arthur (Art) C. Neish (and his family) came on a study leave from the Prairie Regional Lab (PRL) in Saskatoon to UC Davis. The purpose was to examine how tyrosine (Tyr) was de-aminated in grasses, as well as that of Phe deamination in numerous species. By then, Art Neish and co-workers, such as Stewart (Stew) Brown, had demonstrated that radio-labelled Phe and/or Tyr could be incorporated into the plant lignins. Neish hypothesized around that time[3] that *trans*-cinnamic acid was formed sequentially from Phe in a trans-amination reaction to yield the corresponding *alpha*-keto acid, which would then undergo reduction (with DPNH or TPNH co-factors, now called NADH or NADPH) to yield phenyl lactic acid. The latter could then undergo dehydration to afford *trans*-cinnamic acid.

This proposed DPNH or TPNH dependent pathway seemed, however, at odds with Eric's and Tsune's observation that their dialyzed plant extracts were capable of converting Phe directly into *trans*-cinnamic acid without any obvious co-factor requirement. Moreover, by then a bacterial aspartase had been reported able to deaminate aspartate into fumarate and NH_3 without co-factor addition. Eric and Tsune hypothesized the same type of enzyme might be involved in Phe deamination.



Phenylalanine ammonia lyase (PAL) discovery[4]

Art Neish had brought to UC Davis the needed radio-labeled compounds for investigation of this important problem. Art took on the task of looking for the deamination enzyme(s) for Tyr in grasses, while Eric and Jane Koukol (a post doc from the Vennesland group) simultaneously began to further investigate enzymatic activity in barley (*Hordeum vulgare*) that converted Phe into cinnamic acid. These latter studies led to the discovery and 28-fold purification of an aspartase-like enzyme, trivially named as phenylalanine deaminase, and now called PAL.[4] This seminal paper became the most highly cited contribution from Eric's lab in the Web of Science's Science Citation Index through 2018.

The discovery of what was to be TAL was also made, albeit originally named tyrase. It was purified approximately 40-fold from barley stems and shown able to convert Tyr directly into *p*-coumaric acid and NH_3. Tyrase (TAL) was detected in many other plant sources (sorghum, rice, wheat, oat, corn and sugar cane) and its discovery was reported in the first article of the first issue of Phytochemistry,[5] following the Koukol and Conn contribution in J. Biol. Chem.[4]

Thus, these researchers were in agreement of a single enzymatic deamination step in both cases, with formation of the corresponding cinnamic or *p*-coumaric acids and NH_3. Later, both enzymes were to be named PAL and TAL, respectively. The studies on PAL were then essentially completed as regards Conn lab contributions, although a couple of collaborative studies involving Eric, other scientists, and PAL were reported in 1980. PAL studies were followed up by others shortly thereafter in a race to clone its encoding gene. While reports of putative PAL gene cloning came in 1983/1984,[6,7] PAL proper was first cloned by Edwards et al. in 1985.[8]

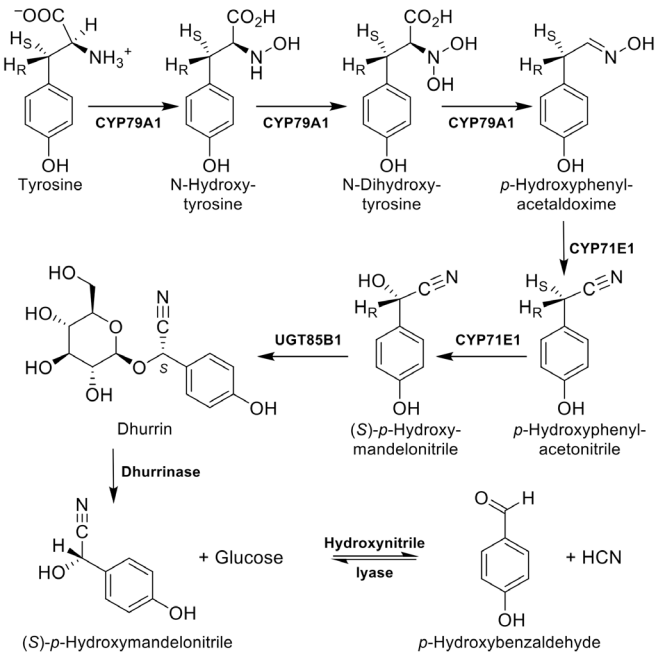
Arogenate and Phe/Tyr

The Conn lab became interested in how Phe and Tyr were being formed *in planta* in the 1980's. This interest stemmed from Roy Jensen's seminal reports of a precursor to Tyr in blue-green algae, that was initially called pre-tyrosine[9] but later renamed as arogenate, Agn.[10] The Agn (pre-tyrosine) route was found to be widespread in blue-green algae[11] and coryneform bacteria,[12] as well as being an intermediate to both Phe and Tyr[13] in *Pseudomonas aeruginosa.* While microorganisms could utilize other routes to Phe/Tyr via transamination of phenylpyruvate and 4-hydroxyphenylpyruvate, *Euglena gracilis*[14] was the first species identified with an apparently strict use of the Agn pathway to both Phe/Tyr.

In vascular plants, Agn had been reported earlier as a Tyr biosynthetic intermediate via the action of arogenate dehydrogenase (ADH) in whole cell extracts of mung bean, although prephenate dehydrogenase (PDH) activity was also detected.[15]

The Conn lab began to explore the role of Agn, and described sorghum (*Sorghum bicolor)* ADH with strict specificity for Agn,[16] in agreement with similar reports of ADH in tobacco.[17]

For Phe biosynthesis in plants, prephenate aminotransferase activity and the apparent absence of phenylpyruvate aminotransferase activity additionally implicated the Agn route.[15,18,19] Arogenate dehydratase (ADT) activity was finally detected in tobacco suspension cultures and spinach chloroplasts,[20] and later in etiolated seedlings of *S. bicolor* in the partial purification of ADT.[21]

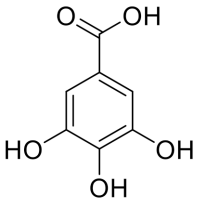


Arogenate (Agn) pathway to Phe and Tyr

Interestingly, our lab has extensively studied Agn and ADT, and the first genes encoding ADT (6-membered gene family) were reported by us in 2007.[22] Eric was pleased to learn in 2016 that we were NASA supported to conduct an International Space Station (ISS) "multi-omics" study – scheduled for May 2018 – using *Arabidopsis* wild type and various (lignin reduced) *ADT* mutants. It may be satisfying to his memory that we generated single double, triple, and quadruple homozygous *ADT* mutants that have differentially reduced lignin contents,[23] some of which will be grown and investigated on ISS.

Gallic Acid Biosynthesis and Sabbatical at Cambridge

Another interest of Eric's came with a sabbatical to the Low Temperature Research Station in Cambridge in 1959/1960. The station at that time housed two highly respected plant scientist researchers and pioneers, Edgar Charles Bate-Smith and Tony Swain. Eric teamed up with the latter to explore the interesting question as to how gallic acid (a principal component of so-called hydrolysable tannins) was produced. In a publication resulting from that work,[24] some important discoveries were made.



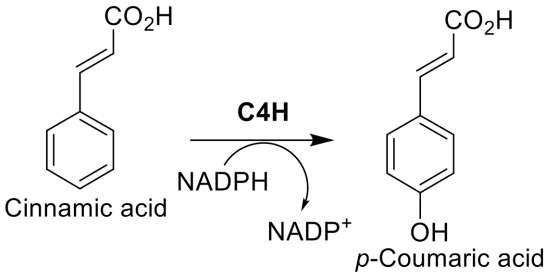
Gallic acid

Using radiolabeled ^{14}C glucose, acetate, and Phe as possible precursors to gallic acid (administered to excised leaves of *Geranium pyrenaicum*), it was established that ^{14}C-Glc was the best precursor. This suggested that a pathway through shikimate was the most likely. However, the results of these experiments could not completely rule out that Phe might also be a precursor, albeit a poorer one. This question of two possible pathways remained topical for many years. Eventually, it was found by other researchers that the primary pathway operative was indeed shikimate derived, via the action of shikimate dehydrogenase.

Cinnamate 4-Hydroxylase (C4H) Discovery and Characterization

With the discoveries of PAL and TAL completed in 1961, the question of how deamination reactions occurred at the enzyme level to give *trans*-cinnamic and *p*-coumaric acids, respectively, was solved. The next target for the Conn lab was to resolve how hydroxylation of cinnamate to afford *p*-coumarate occurred in plants. By 1967, the first report of a membrane-bound enzyme (requiring NADPH as co-factor) was reported from pea seedlings and named cinnamate 4-hydroxylase (C4H).[25] This conversion was later established to display cytochrome P450 behavior.[26] When radiolabeled [4-^{3}H]-cinnamic acid was used as substrate, the tritiated *p*-coumaric acid product obtained had its ^{3}H previously at C-4 now at the *meta* or 3-position (through the so-called "NIH" migration or shift).[27]

As for PAL, the study of C4H was not pursued much more in the Conn lab. There were though an additional four reports in 1974, 1975, 1977 and 1988 as interesting follow-on studies. One of these focused on C4H localization in ER enriched preparations from sorghum seedlings.[28] Mikio Shimada, a co-author on that study, went on to become the "lieutenant" of Takayoshi Higuchi's lab operation in Kyoto University.



Cinnamate-4 hydroxylase (C4H) discovery[25]

Cyanogenesis

Perhaps the largest contributions from the Conn lab scientifically – and certainly numerically – were on cyanogenesis. Almost half of the publications from Eric's lab addressed this topic directly or indirectly. Moreover, Eric, his students, post-doctorals, and other visiting researchers frequently gave presentations at PSNA (and elsewhere) on this subject – for example, Birger Møller. The latter researcher later focused much of his scientific career in Europe on (among other things) the molecular biology of cyanogenesis. Others involved substantially at PSNA in this area were Jonathan Poulton, a good friend and collaborator of Eric, the late Helen Stafford (mainly through her interests in metabolite channeling and enzyme complexes), and David Seigler amongst others.

Cyanogenesis occurs in several thousand plant species where their cyanogenic glycosides, lipids or cyanohydrins accumulate in various tissues. On grinding or macerating (disrupting) such tissues, they come in contact with hydrolytic enzymes (or chemical conditions) that result in release of hydrogen cyanide (HCN). Some examples of cyanogenic plants are flaxseed, sorghum, lima beans, cassava (*Manihot esculenta*, Kranz), *Acacia* species, and *Prunus* species. For the latter, cyanogenic compounds accumulate in, for examples, (bitter) almonds and kernels and seeds of apricot, cherry, peach and plum.

Ingestion of cassava roots not prepared correctly as a foodstuff can be fatal due to cyanide poisoning. Indeed, in spite of its widespread use as a food in the developing world, every year there are avoidable deaths due to cassava being improperly prepared to remove the cyanide liberated. Cassava is also the source of a hard grainy white starch substance, called Tapioca, extracted from cassava root. Growing up with school dinners (lunchtime) in the 1950s and 1960s in Scotland, Norman was very familiar with the oft ridiculed tapioca pudding – often being described by British school children as frog spawn!

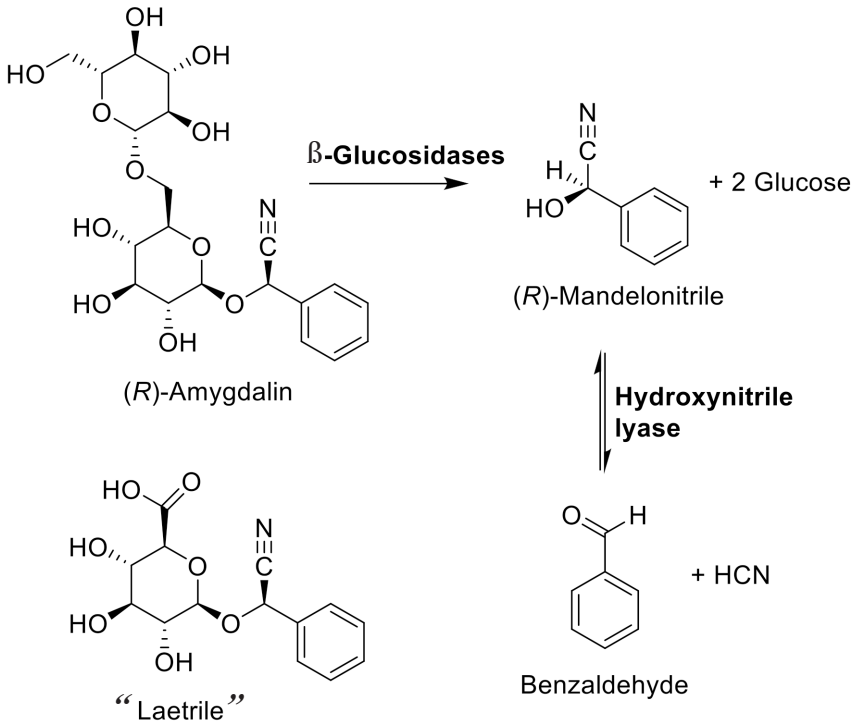
Eric studied many aspects related to cyanogenic compounds beginning in the 1960s.

Laetrile and amygladin: Quackery exposed

Well into Eric's studies on cyanogenesis biosynthesis (discussed below), there were many (quackery) claims in the early 1970s of treating cancer successfully with laetrile, a semi-synthetic hydrolysis product of amygdalin, the cyanogenic compound found in *Prunus* species (see https://en.wikipedia.org/wiki/Amygdalin for an historical perspective). The late actor Steve McQueen (http://www.nytimes.com/2005/11/15/health/mcqueens-legacy-of-laetrile.html) died of cancer in 1980 at the age of 50, and apparently was given laetrile as part of an alternative "chemotherapeutic" regimen. Laetrile was also claimed to be without toxicity by its proponents.

Around the time of McQueen's death, Eric had collaborated with various MDs and which resulted in 2 research papers.[29,30] These publications addressed acute and chronic toxicity of laetrile and amygdalin in both dogs (laetrile) and rats (amygdalin). Among other funding sources, their studies were supported by the American Cancer Society.

The first study with dogs[30] resulted in 6 of the 10 dogs dying through acute cyanide toxicity, 3 others being neurologically impaired (difficulty walking or in a coma), and 1 dog that recovered from the experimental regimen. In that paper, the authors noted that laetrile supporters had stated that "Laetrile is even less toxic than sugar".



Amygdalin and laetrile and HCN release

The study of chronic toxicity in rats[29] was also devastating. Eric and his co-authors concluded that: *"we are able to conclude from our studies that Laetrile remains a hazardous drug, lacking not only therapeutic benefit in patients fearing cancer or having cancer, but possessing harmful effects related to cyanide poisoning. We can predict from our studies that if amygdalin is taken chronically, it will produce neurologic damage in humans similar to that seen in persons suffering from tropical ataxic neuropathy, a disorder attributed to chronic cyanide exposure"*.

We are all fortunate to have scientists like Eric and his colleagues in bringing the truth to the quackery about laetrile and amygdalin. Yet even today some still hold belief that laetrile is an important anti-cancer compound.

Cyanogenesis biosynthesis studies

Eric's comprehensive studies spanned more than 30 years, and largely involved biosynthetic precursor experiments, purification or partial purification of enzymes identified and their characterization, resolving questions on enzyme stereospecificity and compartmentalization, and chemotaxonomy.

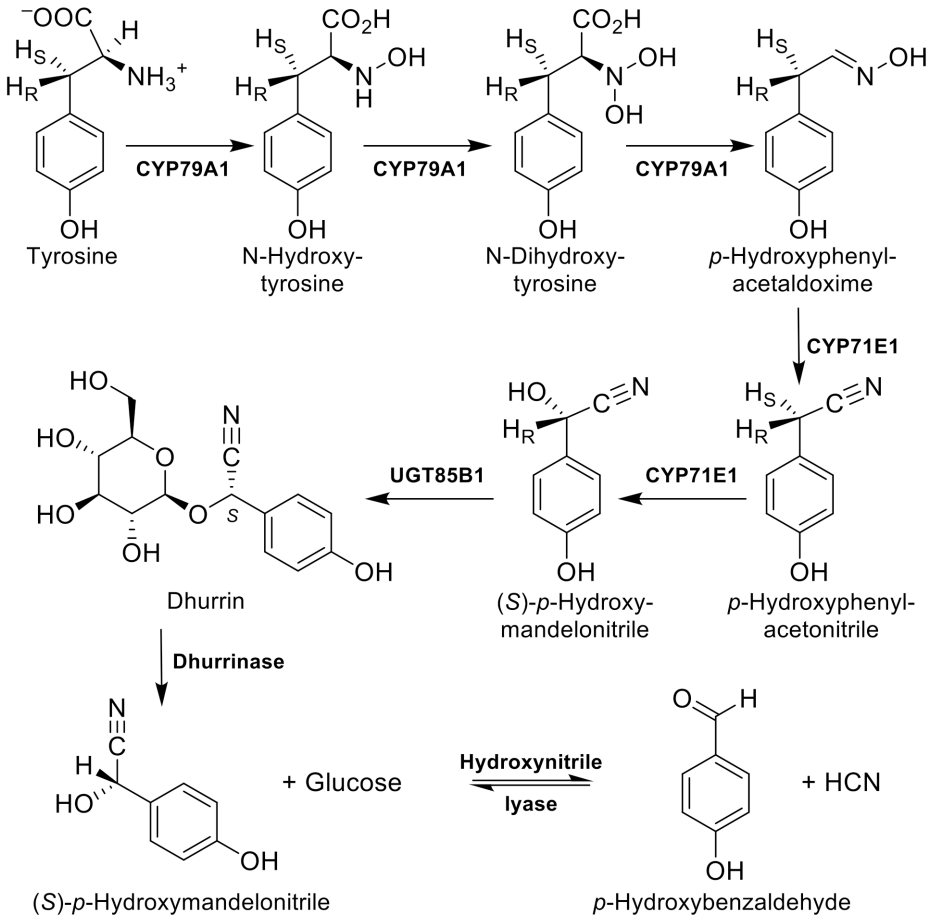
In terms of biosynthetic pathways, the cyanogenic glucosides, dhurrin, taxiphyllin, linamarin and lotaustralin, were the principal targets for investigation. Key questions at the onset of each of these studies were in identifying the precursors to these structurally diverse cyanogenic glucosides, in establishing the source of the N in these compounds, as well as how the HCN was liberated. Then followed investigations on enzymology and compartmentation (of metabolites and enzymes).

Sorghum cyanogenic glucoside dhurrin biosynthesis and HCN release

Eric's first foray into cyanogenesis[31] demonstrated that homogenized etiolated seedling preparations of sorghum (*S. vulgare*) were able to convert its cyanogenic glucoside dhurrin into molar equivalents of HCN and *p*-hydroxybenzaldehyde. One of the corresponding enzymes involved, initially named oxynitrilase, was purified 175-fold from the same source.[32] It catalyzed the conversion of the cyanohydrin of *p*-hydroxybenzaldehyde (*p*-hydroxy mandelonitrile, the deglycosylated derivative of dhurrin) into HCN and *p*-hydroxybenzaldehyde. Later renamed as hydroxynitrile lyase (HNL), it was purified to apparent homogeneity from sorghum with one of the purification steps using the now not too often used – but highly valuable – technique of analytical centrifugation.[33]

Two dhurrinases (dhurrinase 1 from coleoptiles and hypocotyls, and dhurrinase 2 from the leaves) were subsequently isolated and characterized from *S. bicolor*.[34] These investigations thus established how the HCN generating system functioned on tissue disruption.

Dhurrin [(*S*)-*p*-hydroxymandelonitrile ß-D-glucopyranoside] formation itself was also of particular interest as to its biosynthetic pathway, as it is a C_6C_2 metabolite and not a C_6C_3 phenylpropanoid. Nevertheless, Eric's lab demonstrated that radiolabeled dhurrin was derived from [U-^{14}C]-shikimic acid, [3-^{14}C]-and [U-^{14}C]-Tyr, as well as [1-^{14}C]-*p*-hydroxymandelonitrile,



Proposed dhurrin biosynthesis and HCN release

when conducting radiotracer experiments with etiolated sorghum seedlings.[35,36] Double-labeling experiments also showed that only the carboxylic acid carbon of Tyr was lost, and the Tyr nitrogen retained.[37] The corresponding dhurrin producing glucosyltransferase was next purified 77-fold, and found only to stereospecifically glycoslylate (*S*)-*p*-hydroxymandelonitrile, and not the (*R*)-form.[38] Thus the origins of both the C_6C_2 skeleton and the N of dhurrin were determined, as well as the general biosynthetic pathway to dhurrin.

Establishing how Tyr was converted into *p*-hydroxymandelonitrile was the next challenge. Enzymatic activity (NADPH dependent) for this conversion (with intermediary *p*-hydroxyphenylacetaldoxime) was demonstrated using *S. bicolor* microsomal preparations.[39] A subsequent hydroxylation step of *p*-hydroxyphenylacetonitrile into *p*-hydroxymandelonitrile in the microsomes was found to occur with retention of configuration.[40] N-hydroxytyrosine was later shown to be the first intermediate in dhurrin biosynthesis, and at the time this was considered to be the first α-N-hydroxyamino acid in a biological system.[41]

The overall microsomal engendered steps from Tyr are thus considered to be cytochrome P450 catalyzed. One CYP450 apparently produces N-hydroxytyrosine first, followed by its N-dihydroxy counterpart, dehydration of which affords the corresponding oxime (*p*-hydroxyphenylacetaldoxime). A second CYP450 sequentially produces *p*-hydroxyphenylacetonitrile and then the corresponding (*S*)-*p*-hydroxymandelonitrile, respectively. Thus, the entire biochemical pathway to dhurrin had been determined.

The Conn lab next focused on where the corresponding metabolites and enzymes in dhurrin biosynthesis were located, and thus how the process of subsequent HCN liberation occurred. Dhurrin was found to accumulate in *S. bicolor* vacuoles,[42,43] and then later to be almost entirely located in the leaf blade epidermal layers, as was the *p*-hydroxymandelonitrile glucosyltransferase.[44] By contrast, the corresponding dhurrinase (dhurrin-ß-glucosidase) and HNL were almost exclusively in mesophyll tissue.[45]

These results thus beautifully explained how disruption of sorghum tissues (compartments) allowed for HCN generation.

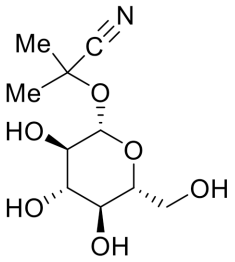
Taxiphyllin (*R*-form of *p*-hydroxymandelonitrile glucoside) biosynthesis in *Triglochin maritima*

In an analogous investigation to that of dhurrin biosynthesis, the pathway to taxiphyllin (*R*-form of *p*-hydroxymandelonitrile glucoside) was investigated using microsomal preparations from *T. maritima* seedlings.[46] This demonstrated that Tyr was converted into (*R*)-*p*-hydroxymandelonitrile, via N-hydroxytyrosine, *p*-hydroxyphenylacetaldoxime, and *p*-hydroxyphenylacetonitrile, respectively.

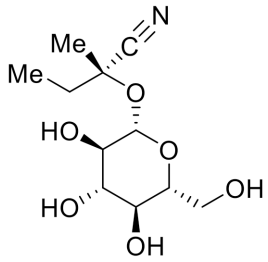
Flax cyanogenic glucosides (linamarin and lotaustralin) biosynthesis and HCN release

Flax (*Linum usitatissimum*) is well known to produce the cyanogenic glucosides, linamarin and lotaustralin, particularly in seed tissue. Both cyanogens are also formed in many other plant species. Linamarin is, for example, the main cyanogen in cassava.

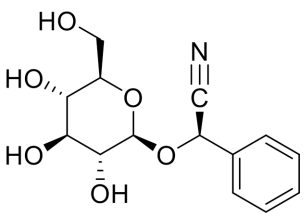
In 1964, Graham Butler and Eric Conn reported[47] initial experiments on investigating their biosynthetic pathways. Using flax seedlings, it was demonstrated that the aglycone moieties of both linamarin and lotaustralin were derived from radiolabeled [U-^{14}C]-L-valine and [U-^{14}C]-L-isoleucine, respectively, thus demonstrating that as for dhurrin, such natural products were amino acid derived. Additional studies demonstrated [U-^{14}C] labeled isobutyraldoxime intermediacy into linamarin,[48] as well as [1-^{14}C]-isobutyronitrile (acetone cyanohydrin) and [1-^{14}C]-α-hydroxyisobutyronitrile.[49] The intermediacy of 2-hydroxyisobutyraldoxime was also another possibility.[50] The corresponding glu-



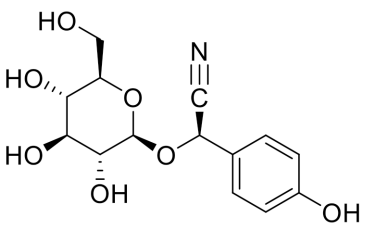
Linamarin



Lotaustralin



Prunasin



Taxiphyllin

cosyltransferase was then partially purified, and exhibited high specificity for acetone and butanone cyanohydrins, as well as UDP-glucose,[51] with subsequent evidence that the same glucosyltransferase catalyzed formation of both laminarin and lotaustralin, based on inhibition experiments.[52] However, the glucosyltransferase could glycosylate both *R*- and *S*-forms of the aglycones *in vitro*.[53] As only the *R*-isomers are formed in flax, the glucosyl transferase only has the *R*-isomers to glycosylate *in vivo*.

Using flax seedling microsomal preparations in the presence of NADPH, it was later demonstrated that these can afford laminarin when incubated with valine. N-Hydroxyvaline and isobutyraldoxime were also converted with the enzymatic activity for these conversions being localized to developing cotyledons.[54] Catalytic formation of both laminarin and lotaustralin by the same enzyme in the microsomal preparation was subsequently reported.[55]

As for the enzymology of HCN release from dhurrin, cyanogenic ß-glucosidases affording the corresponding aglycones were first isolated from flax seeds. These were named linamarase and linustatinase respectively, where the former deglycosylates the cyanogenic monoglucoside linamarin and the latter the diglucoside neolinustatin.[56] The final step generating HCN was catalyzed by the acetone cyanohydrin lyase, purified 136-fold from young flax seedlings.[57]

Linamarin and lotaustralin biosynthesis in other cyanogenic species

The Conn lab also investigated linamarin and lotaustralin in *Lotus*[58,59] and Costa Rican wild lima bean (*Phaseolus lunatus*)[60,61] species. In both *Lotus arabicus* and *L. tenuis*, [^{14}C]-valine and [^{14}C]-isoleucine were incorporated into linamarin and lotaustralin. In the wild lima beans, analyses of mesophyll cells and cell wall extracts indicated that linamarase activity was apoplast localized, whereas the linamarin and HNL were cellular.[60,61]

Peach, cherry laurel and *Ximenia* species prunasin biosynthesis and HCN release

Prunasin differs from dhurrin in lacking a 4-hydroxy group on its aromatic ring. As for the latter, prunasin was also aromatic amino acid derived, as [3-^{14}C]-Phe administered to peach seedlings was incorporated into this cyanogenic glucoside.[62] Follow on studies with cherry laurel (*Prunus laurocerasus*) established that [1-^{14}C]-phenylacetonitrile and α-[1-^{14}C]-hydroxyisobutyronitrile were also intactly incorporated into prunasin;[49] analogous to dhurrin, 2-hydroxyphenylacetaldoxime could possibly be an intermediate to prunasin as well.[50] Corresponding mandelonitrile lyases that hydrolyze benzaldehyde cyanohydrin releasing HCN were later partially purified 4.3 fold and 122-fold from *Prunus lyonii* and *Ximenia americana*,[63] respectively.

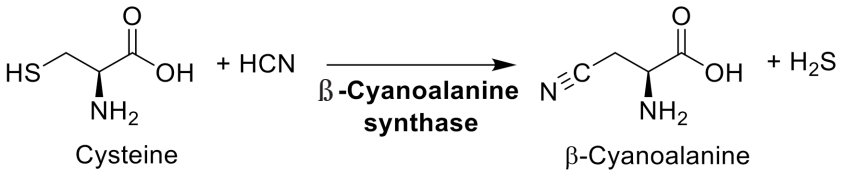
ß-Cyanoalanine and ß-cyanoalanine synthase in *Lotus tenuis*

ß-cyanoalanine is a rare example of a nitrile containing amino acid, that also caught the attention of Eric as an interesting scientific biosynthetic question. Using mitochondria enriched preparations from *L. tenuis* seedlings,[64] it was established that that this preparation was able to catalyze formation of ß-cyanoalanine in the presence of cysteine and cyanide. This enzyme was also purified *circa* 1700-fold from blue lupine (*Lupinus angustifolia*) etiolated seedlings, and was highly specific for L-cysteine.[65] Subsequent studies investigated the stereochemistry of this enzymatic reaction where it was found that it occurred with retention of configuration when the -SH group was replaced by a -CN functionality.[66] ß-cyanoalanine synthase was later localized in mesophyll and epidermal protoplasts from sorghum, maize, and pea,[67] as well as in the mitochondrial enriched preparation from mesophyll protoplasts from barley (*Hordeum vulgare*) leaves.[68]

Acacia and *Eucalyptus* chemotaxonomy studies

Eric's lab has had a long, productive interest in cyanogenic glycosides in *Acacia* and *Eucalyptus* species, but mainly from the perspective of phytochemical identification and chemotaxonomy comparisons. One species of *Acacia* is named in honor of Eric, *Acacia conniana*.[69] Additionally (see below, ***Eric and Louise Conn's Philanthropy and UC Davis***), there is an *Acacia* grove at the UC Davis Arboretum housing 50 *Acacia* species in honor of the Conns.

Acacia species belong to the (pea) Fabaceae family, and plant forms range from shrubs to trees. One of

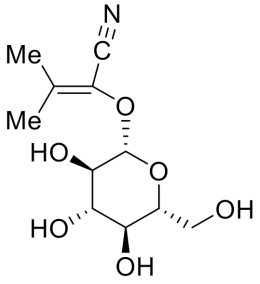


ß-Cyanoalanine and ß-cyanoalanine synthase discovery[64,65]

the best known is mimosa, and various *Acacia* species are also well known for their tannins and uses in tanning leather.

Eric's contributions on *Acacia* cyanogenic glycosides were largely through collaborations with David S. Seigler (Univ. of Illinois at Champagne Urbana), John E. Dunn (UC Davis), and Bruce Maslin (Western Australian Herbarium, South Perth, Australia). Some 11 collaborative papers were published between 1975 and 1988 (10 in *Phytochemistry*, and 1 in Biochemical Systematics and Ecology, respectively).

In the first report in 1975,[70] a cyanogenic glucoside acacipetalin was isolated and identified from *Acacia sieberiana*, with its aglycone found to be isoleucine-derived. The later papers dealt with different *Acacia* species from all over the world (Africa, Australia, Argentina, Costa Rica, North America Mexico, Venezuela, and their cyanogenic glycoside constituents). These and other contributions have helped in revising *Acacia* taxa classifications in recent years.



Acacipetalin

Eric's final research paper (in *Phytochemistry* in 2008),[71] in collaboration with Australian researchers, addressed the frequency and distribution of cyanogenic glycosides in *Eucalyptus* species in Australia, with some 420 species analyzed. Their analysis indicated that 4% of the species contained cyanogenic glycosides. Important chemotaxonomic relationships could thus be deduced, as well for predicting which species might be best for plantations supporting wildlife and in preserving genetic diversity.

Eric's Unflagging Professional Dedication: Phytochemistry, Plant Phenolics Group, Phytochemical Society of Europe (PSE), Plant Phenolics Group of North America (PSNA), Archives of Biochemistry and Biophysics, Plant Physiology, and American Society of Plant Biology (ASPB)

Eric was a tireless supporter of, and leader in, his chosen discipline. From the 1950s onwards, his activities were critical for the expansion of the research efforts in plant biochemistry, plant chemistry, and plant metabolism. First came the period where Tony Swain and Eric worked and spent together, beginning in the late 1950s. This was important not only for the international plant biochemistry/chemistry journal *Phytochemistry* getting off the ground, but also in putting together the Plant Phenolics Group in Europe. By 1957, the Plant Phenolics Group had Tony as founder Secretary and Eric as Chairman.[72]

Tony Swain then met with the legendary publisher mogul Robert Maxwell and Richard Gilbert of Pergamon Press. This resulted in an agreement to begin a new journal *Phytochemistry,* the first issue of which was in 1961. *Phytochemistry* later joined the Elsevier stable. Tony and Jeffrey Harborne were quick to bring stellar scientists, such as Eric, onto the then new and distinguished Editorial Board. Eric remained on the board for about 40 years.

With a rapid level of interest by scientists in the fledgling Plant Phenolics Group in 1957, it rapidly grew in stature and size, eventually becoming the Phytochemical Society of Europe (PSE).

On the other side of the Atlantic, the tireless efforts of Victor Runeckles, Stewart (Stew) Brown, Leonard Jurd, Simon H. Wender, Eric Conn, Tom Mabry, Neil Towers and others also near contemporaneously resulted in formation of the Plant Phenolics Group of North America (PPGNA) in 1961. The society then was amusingly "renamed" by Chris van Sumere as the "Plant Alcoholics Group of North America", this being Norman's recollection of their conversation in the early 1990s!

PPGNA later became the Phytochemical Society of North America (PSNA) in 1966. Chris was also a researcher at the Prairie Regional Laboratory (PRL) in the 1960's, living in a house on the same street where Laurence Davin resided nearly 30 years later while working as


Eric Conn with Jerry McClure at the 1972 PSNA Meeting in Syracuse (Photo courtesy of Connie Nozzolillo).

1984 PSNA Meeting with Eric Conn and Sam Asen (Photo courtesy of Connie Nozzolillo).

a post-doctoral at the then renamed Plant Biotechnology Institute (PBI)!

Note the two photos of Eric at PSNA meetings in 1972 and 1984, respectively.

We can thus collectively thank Eric (and the other pioneers) for their vision, commitment and determination at that time. They put into place—or helped put into place—the key developments from which our fields evolved, including formation of the societies and publication outlets that we so warmly endorse, support, and need.

Some personal reflections: Eric and PSNA

My (Norman's) introduction to Eric Conn and to PSNA can be credited to a long term friend and collaborator, the late G. H. Neil Towers. Norman had known Neil since beginning his PhD (Chemistry) graduate studies at UBC in 1973. They later worked on several projects together until Neil's passing in November 2004.

In 1985, and although Norman was based in greater Montreal at the time, Neil strongly urged him to attend the 25th PSNA Annual Meeting in Pacific Grove (Asilomar Conference Center) in CA. One attractive aspect of the meeting was its focus on the shikimic acid pathway. Another attraction was that PSNA meetings were relatively small (100-300 attendees or so), a welcome change from other conferences numbering in the tens of thousands.

At Asilomar, Norman first met Eric, and his charming wife Louise. Thus began what was to be a long friendship until his passing last year. Norman's memories to this day of the Asilomar PSNA meeting are very fond. From thereon, Norman attended as many of the annual PSNA meetings as he could.

Time's Not Up!

One vivid and slightly amusing memory (at least from Norman's perspective) was with the 27th PSNA Annual Meeting in 1987 held in Tampa, FL, organized by John Romeo. At that meeting, all of the luminaries and stalwarts in the PSNA were in attendance, such as Eric, Neil Towers, Cecilia McIntosh, Helen Stafford, John Romeo, Dave Loomis, Jim Saunders, Mark Berhow, Stew Brown, Connie Nozzolillo and others. At this and all other meetings, Eric always displayed intellectual interest, remarkable tact, pleasant humor, and was a very positive influence in every respect.

Norman's recollection is of one afternoon's session, where the first two talks were given by Dr. Alicja Zobel, a most enthusiastic scientist and speaker. She had very recently married Stew Brown, who by then (in his late 50's or early 60's?) had seemed a confirmed bachelor.

Stew's role that day was as Chairman of the afternoon's session. He was determined to keep it on time. As Norman recalls, the lecture theatre was a bit raised in elevation from where Neil Towers and he sat side by side. Stew first addressed the assembled conferees by declaring his responsibilities as Chairman. Each speaker's allotted time (which if recalled correctly was 15 minutes in total) would include 3 minutes for questions. Stew would rise two minutes before the allocated speaking time (of 12 minutes) and announce to the speaker that 2 minutes were left to speak. To keep the session on time, the 15 minutes would be enforced.

Alicja Zobel began the first talk with essentially a full carousel of 80 slides or so. While Neil and Norman listened attentively, they could see that the carousel's slide show had barely begun. The 10th minute was fast approaching. At that point, Stew announced loudly there were 2 minutes left to speak. Alicja went into what seemed to Norman and Neil as overdrive, and yet the 12th minute arrived with barely a dent in the slides shown.

Stew announced that the speaker was now using the time for questions. The final 3 minutes seemed as a strobe light show, as the pace of slide changing approached warp speed. Fifteen minutes had now elapsed, with a whole slew of slides yet unexposed to the audience.

Cool and unflustered, Alicja halted the presentation apparently midway. She then asked the audience if they had any questions. Only to have the Chairman (and now her beloved hubby) announce "No time for questions"!

Stew went on to introduce the next speaker. This was again Alicja. She was armed with another full carousel of slides. The next fifteen minutes were exactly as before, and again it was "Time's up". Stew began to introduce the next speaker, when

Alicja proudly exclaimed that "The audience want to ask questions".

Stew politely but firmly declined his spouse's request.

So Alicja leaned over the very front of the theatre stage to get as close to the conferees as possible. She again – and now more pointedly – stated that "The audience want to ask questions".

The atmosphere in the lecture hall became highly charged.

Everyone was riveted to their seats!

The newlyweds were apparently in a standoff!

Peace came to reign, when Eric softly purred "I think there's time for some questions".

Questions then followed.

The last thing Norman recalls about the session was Stew loudly muttering from the very back of the stage that: *"I can see the Chairman's NOT in charge"!*

Both Stew and Alicja are accomplished scientists. They have long been great supporters of PSNA and as contributors in many ways. The important point of the recollection here was that Eric tactfully defused what seemed to be (or might have been) a momentary standoff between the newlyweds. The session continued without a hitch following Eric's "intervention".

All of us were to see many examples of Eric's good judgment, coolness, and tact in the years to come.

The next PSNA meeting Norman attended was the following year (1988) in Iowa City (organized by Jonathan Poulton). This was where both Neil and he first met Laurence Davin, who many years later became both Norman's spouse as well as key co-researcher. Laurence fondly remembers meeting Eric there for the first time, where she presented a poster on her work on glucosinolates.

PSNA greatly benefitted from Eric's commitment to the Society. Eric served as Vice-President from 1970-71, then President (1971-1972), before taking on the onerous responsibility of the PSNA's Recent Advances in Phytochemistry where he was Editor-in-Chief from 1984-1989. Eric also ensured that chapters for each volume were on time by withholding reimbursement of travel expenses etc. until the draft manuscript was in hand! This saved him much angst!

Eric and Phytochemistry

As indicated earlier, Eric was on the *Phytochemistry* Editorial Board for a period of nearly 40 years, as well as being a regular contributor to the journal. From Norman's personal perspective as *Phytochemistry* Regional Editor from the nineteen-nineties onwards, Eric was a wonderful Editorial Board member. Eric could always be relied upon for fair, incisive, constructive, and timely reviews.

Phytochemistry also recognized Eric's many achievements. In 1994, he was informed that he was chosen to receive the highly prestigious Pergamon *Phytochemistry* Prize and Certificate for his manifold contributions. The photos below show Eric receiving this coveted award later in 1995. There is also a wonderful photo of Eric and the late Ragai Ibrahim at the same meeting!

It does not seem that long ago when, in 2008, Norman handled the processing of Eric's final scientific contribution (to *Phytochemistry*) on cyanogenic glycosides in *Eucalyptus* plant species in Australia with his collaborators there.[71]

Eric with Ragai Ibrahim who passed away on November 19, 2017 (Photo courtesy of Connie Nozzolillo)

Eric receiving the Pergamon Phytochemistry Prize in 1995 during the PSNA meeting held in Sault Ste Marie (Photo courtesy of Connie Nozzolillo)

Eric and the WSU DOE-NSF-USDA Plant Biochemistry Research and Training Center (PBRTC)

With the then great need to produce more plant biochemists (in their myriad forms), Norman submitted a tri-agency proposal in a highly competitive announcement to put in place the WSU DOE-NSF-USDA Plant Biochemistry Research and Training Center (PBRTC). It was selected for funding from 1995 to 2000. Both Eric and Paul Stumpf served on the PBRTC Advisory Committee, and they also gave wonderful talks at the summer course offerings that continued until 2004. In particular, Eric enthralled attendees as to the challenges that they had faced at the beginning of their careers; for example, co-factors had to be isolated as they could not be purchased, such as NADPH and NADP (see segment below "A summary of Eric's own personal reflections") from large quantities of hog liver.

Eric and Archives of Biochemistry and Biophysics (ABB)

Scientific journals, such as Phytochemistry and ABB, fall into the category of specialized (meaning expert-driven) journals. In addition to Eric's Phytochemistry Editorial Board involvement, he tirelessly served as both Editorial Board member of ABB from 1972–1991, as well its Executive Editor from 1975–1991. For many readers perhaps unfamiliar with the roles of a competent, well respected, Editor this was a huge time commitment that was—and remains—greatly appreciated.

American Society of Plant Biologists (ASPB), previously American Society of Plant Physiologists (ASPP)

Eric was also deeply involved with the American Society of Plant Biologists (ASPB), beginning with its forerunner, the American Society of Plant Physiologists (ASPP). There he served in numerous well-received capacities in helping it achieve its tremendous standards and worldwide appeal that it enjoys today. This included him being: Assistant Editor of Plant Physiology from 1968–1972; Editorial Board Member from 1980–1983; President Elect ASPP 1985–1986; and President ASPP 1986–1987.

As important as research is in academia, another is in training the next generation of scientists. In many respects, success of a research lab can be viewed not only from the publications but also in the training and placement of its researchers. The Conn lab was a fertile ground in both endeavors, and many researchers from there went onto very distinguished careers.

A few examples here will suffice: ***Professor Heinz G. Floss*** (now Emeritus), University of Washington, who has left a wonderful legacy in the study of the biosynthesis of many medicinally important natural products, as well as to metabolites such as lysergic acid (LSD). Heinz joined the Conn lab, after studying under the remarkable Meinhart H. Zenk in Germany. Heinz also left a wonderful legacy in his training of members of the now successful current generation of research scientists in academia.

Klaus Hahlbrock, now Emeritus Professor, but previously Max Planck Institute Director. Klaus trained under the guidance of Hans Grisebach, the other plant biochemistry powerhouse in Germany (next to Meinhart's) at the time.

Birger Møller, University of Copenhagen, who has spectacularly pursued many different studies of cyanogenic glucoside research – ranging from biosynthesis, transport, storage, and degradation to applications of synthetic biology.

Many other researchers from the Conn lab have gone onto notable successes in academia – such as ***Adrian J. Cutler, Lee Hadwiger, Basil Nikolau, Jonathan Poulton, James Saunders, David Seigler, Ernie Uribe,*** and ***Eve Wurtele***.

Some Quotes by Eric's Colleagues and Others whose Life He Touched

UC Davis remembers Eric as a Founding Father of Biochemistry and Biophysics at UC Davis (https://biology.ucdavis.edu/news/remembering-eric-conn-founding-father-biochemistry-and-biophysics-uc-davis). Some quotes by current faculty (see link for additional context) and others whose life he impacted include:

Michael Dahmus, UC Davis Distinguished Professor Emeritus and former Chair, Department of Molecular and Cellular Biology. *"Eric was the kind of person you liked to bump into in the hallway, always positive, insightful, inquisitive and just a joy to talk with. He was an exceptional educator and a great role model for young faculty."*

Judy Callis, UC Davis Vice-chair and Professor of Molecular and Cellular Biology, remembered Conn as a mentor who helped co-instruct her

first large biochemistry lecture. *"He was always very fair and patient. He respected students. He gave me advice when needed, but also let me organize my lectures in a way that worked for me. I was very appreciative of his mentorship and guidance when I began teaching!"*

Charles Gasser, UC Davis Professor of Molecular and Cellular Biology, and Eric was Gasser's primary mentor. *"Eric Conn provided advice on almost every aspect of being a professor, from sharing his knowledge on big subjects like how to plan and staff a research program, to small topics like where to find paper clips in the office. His kindness and knowledge were indispensable to me."*

Some other lives impacted:

Bob Stack, Program Manager, Physical Sciences, BES, DOE, previously a UC Davis Biochemistry graduate student, (1976-1981): "Eric had an enormous influence on all the biochemistry graduate students at Davis, even the ones who chose to do their thesis work with other professors. Of course, Eric and "PK" (Paul K. Stumpf) were our unofficial mentors even when we were grad students working in other labs!"

Frank Hagie UC Davis Undergraduate Experience. "I was an undergraduate genetics student at UC Davis in the late 1970's. I took an upper division biochemistry course team taught by Professors Eric Conn and Paul Stumpf. We used their book "Outlines of Biochemistry." Early in the class, I saw them together on campus. I introduced myself and asked whether for their class, I would be better served reading from a more detailed biochemistry textbook. Dr. Conn responded with a smile: ***"No, read and understand our book, listen and take good notes in class, study hard, and the other biochemistry books will be easy."***

He was right.

Frank Hagie, CEO & President of Applied Phytologics (API), Inc. In 1995, I returned to Sacramento, CA and served as the CEO & President of API, Inc., a plant biotechnology company (now Ventria Biosciences, www.ventria.com). In that role, and with this being about 20 years after I took his class, I called Dr. Conn and introduced myself and asked to meet with him about the company. In our first meeting at UC Davis, in his office, I asked him to serve on the company's Scientific Advisory Board. We talked plant biotechnology, and one of the company goals of genetically modifying cereal metabolic pathways to produce lignans in cereal grains. He accepted the position.

When I was leaving his office, he smiled and offered one last comment. ***"Sounds like you understood our book and our class, and it helped you with plant biochemistry"***

He was right again.

Shortly after that initial meeting, Dr. Conn gave me a call and asked me to drop by his office to talk about the lignan project, following his project review. In our meeting, he detailed likely molecular biology changes to cereal grains necessary to modify metabolic pathways to for the first time produce lignans in transgenic cereal grains. At the end of the meeting, he commented as follows. ***"You ought to get in touch with Dr. Norman Lewis from Washington State University for this project."***

Through a very productive collaboration, API and Dr. Lewis' lab generated transgenic rice plants metabolically engineered to product lignans in the transgenic rice grains, a significant advance.

He was right yet again."

Richard Sayre, New Mexico Consortium: "My first personal contact with Eric was as an invited seminar speaker at Davis, when I was with Ohio State University (OSU). I remember the meeting with Eric as one of the most engaging and gracious meetings I had with a senior scientist. We were just starting our work on cyanogenic glycosides in cassava. To meet the "father" of cyanogenic glycosides was one of the highlights of my career.

Several years later, the graduate students in the OSU Plant Biology program invited Eric for the Waller Lecture, which they organized. Over the many years I was involved with the Waller lecture, Eric stood out as one the most impactful lecturers invited. The students universally expressed that their conversations with Eric were among the most engaging and sincere that they had with a guest scientist. Similar thoughts were expressed by others.

During my frequent travels to Africa for the Gates Foundation cassava biofortification programs, I would often encounter African scientists who had trained with Eric and would share stories. Those whom had trained with Eric felt as though they were members of his family. Eric and his wife would often host foreign students in their home for Thanksgiving. Eric's legacies will be many. His science was ground breaking and his many students have gone onto stellar careers.

But, it was his genuine encouragement and support of young scientists that will best serve as an example of Eric's spirit to present and future scientists for many years to come".

Eric and Louise Conn's Philanthropy and UC Davis - From UC Davis Academia to the Arboretum

Throughout his entire life, Eric had enormous appreciation for the progressive academic environment, as well as the positive culture and loyalty, that existed within the UC Davis community. This was important to him, including in support of his own relentless quest for excellence. As Norman can personally attest, Eric's appreciation to UC Davis was reciprocated by both Eric and his wife Louise. One aspect in particular was the UC Davis Arboretum, a favorite walking, cycling, and meeting place on the UC Davis campus for the community and visitors alike. Every time Laurence and Norman were at UC Davis, Eric would urge them to visit the arboretum (which they often did while out running).

Eric, Louise, and the Conn family made various commitments to UC Davis through the Arboretum. This stemmed from Eric's interest in *Acacia* species beginning in about 1960 (http://arboretum75th.ucdavis.edu/75-stories/arboretum-stories-eric-conn). In 2001, they began the Louise and Eric Conn Endowment Fund (see https://give.ucdavis.edu/AARB/122180) to help financially support the Arboretum, and prior to that they had – and continued to – support it as volunteers, researcher, advocates and donors. Indeed, this lovely Arboretum has an *Acacia* grove of more than 50 species in honor of the Conn's, and which includes *Acacia conniana*,[69] that was named in honor of Eric's research on cyanogenesis. By 2012, and following the passing of his beloved Louise, he provided additional (matching funds) to again further support the progression of the Arboretum (http://publicgarden.ucdavis.edu/development/dr-eric-conn-offers-uc-davis-arboretum-first-annual-appeal-matching-challenge).

A Summary of Eric's Own Personal Reflections

Eric's life journey—so well spent—would not be not complete without glimpses of his early childhood. Eric had—long before our writing this compilation—summarized many key points and events in his life.[73-75] This included his progression to graduate school and the key influences therein, to his wonderful and far-reaching career in academia. In many respects, he was a paragon of virtue and integrity. Here we try to capture some of ***Eric's Early Memories (slightly reworded from the above references and with Norman's personal anecdotes).***

Eric was born in Berthoud, Colorado, on January 6, 1923, the 4th and last child of William and Mary Anna Conn, where his father served as assistant manager of a Farmers' Union grain elevator. His family then moved in the early 1930's to Bellaire, Kansas, for his father's grain elevator business. This was the time of the Great Depression, where they too experienced firsthand the dreadful Dust Bowl years and the corresponding devastating effects on the Great Plains. The Conn family lost most of their assets then, except for their home. During this time, Eric became proficient in playing piano and in developing a lifelong love of trains.

The family next moved to Fort Morgan, Colorado, a small town of around 5,000. There his father ran a gasoline (petrol) filling station, and his mother took in boarders to help make ends meet. This was, in many ways, a time for the family to "start again" in life, as it was for many. While there, Eric learned to play the pipe organ in a local Methodist church. Scholastically, he got off to a great start, graduating as Valedictorian from Fort Morgan High School in 1940. He won an all-tuition scholarship for 4 years to study at the University of Colorado, Boulder.

UC Boulder undergraduate studies

As Eric began undergraduate university life, he lived and worked in the men's dorm, rising early to serve breakfast as a "hasher" to the other male students. At Boulder, he had an interview with a chemistry professor, Dr. Reuben Gustavson ("Dr. Gus"). Dr. Gus convinced Eric to major in Chemistry, and helped him get a military deferment at the beginning of WW2 to let him finish college. He ultimately became a great

influence in his life. Eric graduated with a bachelor's degree in chemistry (*cum laude*) in 1944.

Manhattan Project

Dr. Gus next arranged for Eric to be hired immediately by the Manhattan Project at Oak Ridge, Tennessee. He traveled there by train and worked primarily as an inorganic chemist through the remainder of World War II - first as a civilian, and then with the same work after being drafted into the US Army in 1945 as a private. Eric's first publication (co-authored) was on the half-life of an isotope of nickel produced in the experimental, plutonium-producing uranium pile at Site X-10 in 1946.[76] The Manhattan Project itself was in many ways conceived at the Cosmos Club in Washington, DC, on December 6, 1941 (a day before the Pearl Harbor attack). This occurred through meetings of University of Chicago (UC) Nobel Prize scientist Arthur Compton with top White House science advisers - first through the Plutonium Project and then with the Manhattan Project. (https://books.google.com/books?id=tgjuoe2W4BoC&pg=PT28&lpg=PT28&dq=manhattan+project+and+cosmos+club&source=bl&ots=wJZ1M4SLzP&sig=V0Dp-D9Z7hF0vCj9Fj22iVAKkGo&hl=en&sa=X&ved=0ahUKEwi9m5f7tIXXAhUY02MKHZRKDXgQ6AEISjAI#v=onepage&q=manhattan%20project%20and%20cosmos%20club&f=false).

University of Chicago, Ph.D. degree/post-doc with advisor Birgit Vennesland and opportunities of a lifetime

After WW2, Dr. Gus next became Vice President and Dean of Faculties at the University of Chicago (UC). He encouraged Eric to use the GI Bill to pursue a Ph.D. in their Biochemistry Department. Eric accepted, was enrolled in September 1946, and took the Chicago offer over another from Harvard.

UC was a most exciting place when Eric was there in the early 1950's. He was now in the process of not only gaining a wonderful academic pedigree, but also being greatly influenced by truly exemplary scientists. The distinguished UC Biochemistry Department faculty at that time included his Ph.D. advisor Birgit Vennesland. Her biography, that Eric was greatly involved in compiling, can be accessed at the American Society of Plant Biologists website.[77] UC also had Konrad Bloch (who later was the 1964 Nobel prizewinner in Medicine or Physiology for his cholesterol and fatty acid biosynthesis work), as well as Albert Lehninger (of biochemistry textbook fame), another richly deserving US NAS member. At the same time, UC Chemistry had Frank Westheimer and Henry Taube on its faculty. Taube became the 1983 Nobel prizewinner in Chemistry for his electron transfer reaction work, whereas Westheimer (who later moved to Harvard) collaborated with Vennesland, Conn, and others on the stereospecificity of hydride transfers with NADP (then called TPN). From his own work on the latter topic, Eric believed he had isolated and amassed the world's supply of NADP+/ TPN+ at UC.

Eric at the University of Chicago

The pioneering work with NADP+/ NADPH (TPN+/TPNH) stereospecificity and chirality involved several young luminaries with Vennesland and Westheimer. These included Eric (both as a PhD student and

Eric with Birgit Vennesland

subsequently as a postdoc when she went on sabbatical), Harvey F. Fisher (Professor Emeritus KU Medical Center), the late Frank A. Loewus [later to be a PSNA President, a work colleague and dear friend at Washington State University], and Paul Talalay (US NAS member). The latter's later far reaching work at Johns Hopkins University on cancer prevention through plant-based medicinal intervention became truly game-changing.

Vennesland's laboratory was a sort of Mecca in that it attracted many leading research scientists worldwide. Importantly, she arranged for them to meet with her students (Eric and the others). Eric fondly remembered meeting Hans Krebs (the future 1953 Nobel Prizewinner in Physiology or Medicine), Severo Ochoa and his then young post-doc Arthur Kornberg (the future joint 1959 Nobel Prizewinners), Alexander R. Todd (the future 1957 Nobel Prizewinner in Chemistry), as well as Robert H. Burris (US NAS and Medal of Science recipient) and Rutherford Ness (Bob) Robertson, FRS.

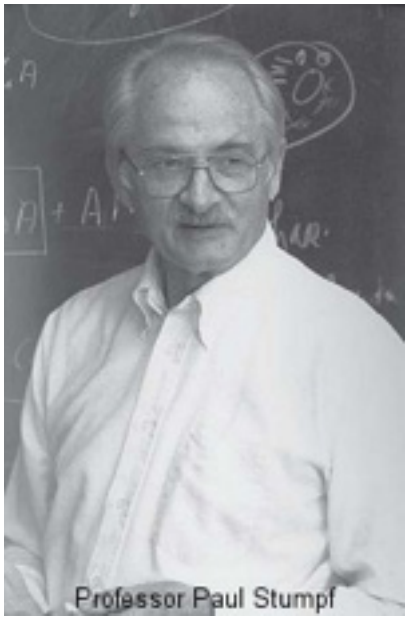
When Norman was at Cambridge (Chemistry Dept.) in the late 1970's, he and others often had morning or afternoon tea with now Nobel Laureate (Lord) Alexander R. Todd, a fellow Scotsman. Lord Todd frequently reminded them that the biggest mistake chemists were making then was to allow molecular biology to get away! In hindsight, how true that observation was then.

During Eric's stay at UC as a postdoctoral appointee (including helping supervise the ongoing research in the Vennesland lab), he taught an introductory biochemistry class as part of an integrated biology sequence of five courses. The late Helen A. Stafford (who in the future also became a PSNA President and Phytochemical Pioneer) joined UC in 1951 to work as a post-doc with Vennesland. She taught botany in that same 5 course sequence. As anyone that regularly attended past PSNA meetings very well knows, Eric (and his family) developed a life-long friendship with Helen. She too deservedly was recognized by ASPB as a *Woman Pioneer in Plant Biology,* and where Eric also played a huge role in compiling this write-up.[78]

By the early 1950s, in addition to his notable graduate student and post-doctoral research successes, Eric had met with and been exposed to a number of truly outstanding scientists of the 20th century and their far-reaching research. By then, he had already met several future Nobel Prize-winners – 1953 (Krebs), 1957 (Todd) and 1959 (Ochoa and Kornberg) – four in all, and with more to follow! This was surely a tremendous experience for the young Eric. How many graduate students and post-doctoral fellows—globally—could "boast" about opportunities for meeting such a number of truly outstanding scientists in their early career years? Such interactions and the exposure to such pioneers, as Norman personally can attest here from his own experiences, can be and are inspirational.

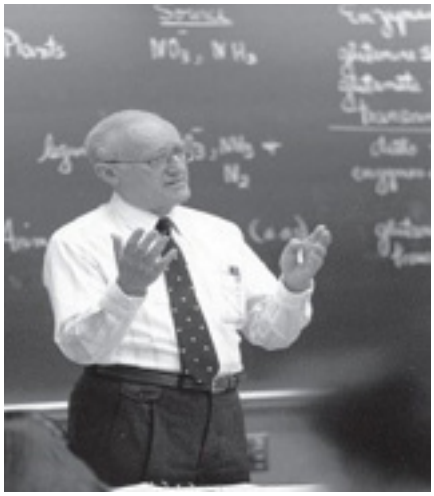
UC Berkeley and UC Davis: The journey from tenure track to Emeritus Professor

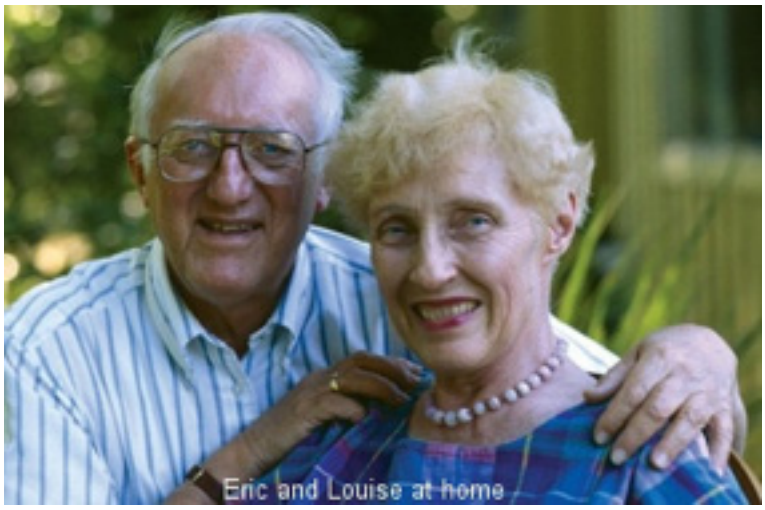
The next phase of Eric's life was now predictably to be firmly rooted in academia. By then, key academic institutions had him on their radar. Interviews for positions at UC Berkeley and Caltech soon followed, with both offered. He accepted the former and joined Dennis Hoagland's famous Department of Soils and Plant Nutrition in a tenure-track position in their College of Agriculture in 1953. However, an exchange in departments of his appointment was suggested by another luminary Paul Stumpf (and future NAS member), who was then chair of the Agricultural Biochemistry Department in the same College. This occurred in 1954, and he joined this small but vibrant department that also had NAS members H. A. Barker and W. Z. Hassid.


Professor Paul Stumpf

Although Eric had already met Paul while at the Vennesland lab, this marked the beginning of a wonderful life-long friendship. This was highlighted – at least to the outside world – by their writing the *Outlines of Biochemistry*, and editing the *Biochemistry of Plants*.

By 1958, the University of California system underwent a major expansion at UC Davis, with Eric moving there to join the Biochemistry Department that Paul Stumpf was setting up. The next decade for them saw considerable expansion of their introductory biochemistry course with classes of near 400 students. Eric's contributions as a Professor at UC Davis were highly valued. For course teaching and research, he received the university's highest distinctions. This included: Distinguished Teaching Award of





the Academic Senate, UC Davis in 1973; Faculty Research Lecturer of the Academic Senate, UC Davis in 1977, and UC Davis Prize for Teaching and Scholarly Achievement in1990.

Reflections from the Conn Family, written by Son, Kevin Conn

"Eric loved his family, his university community, and his religious community, the Religious Society of Friends (Quakers). Kindness and intellect were the twin hallmarks of his long life. He passed away at home at the age of 94 with both of his sons at his side.

While in Chicago (as a student), Eric rented a room with the Kachel family where he met the landlady's charming daughter Louise. Louise was primarily working in Paris with the American Friends Service Committee, engaged in humanitarian efforts after World War II, but on occasion she came home to visit her family. Neither of them knew yet that their lives would later join forever.

Louise Kachel re-entered Eric's life and on October 17, 1959, they married. They had two sons, Michael in 1961 and Kevin in 1962. During this busy and productive stage of their lives, Eric focused on both teaching and research. Eric mentored many students from undergraduates to post-docs, treating all of them with care and genuine interest in their success. They loved working in his lab where they could count on the guidance and respect they deserved. Colleagues and students were welcomed with their families into their home for meals, celebration and friendship. Eric and his family kept in touch with many of them up until he died.

Through his wife Louise's influence, Eric came to a deep appreciation for the Religious Society of Friends (Quakers). He always supported his family's involvement and they hosted numerous events for the Davis Friends Meeting. Eric often played the piano for the hymns when he was able. He volunteered as treasurer for several years for the Friends Committee on Legislation of California and contributed to it and the Friends Committee on National Legislation and the American Friends Service Committee, whose views on the dignity of all people and the peaceful resolution of conflict among people and nations resonated with him.

Eric lived a long and full life, never losing interest in making the world a better place. His wife Louise passed away in 2002. He leaves behind his two sons, Michael and Kevin; nephews and nieces including Chuck (Karen) Conn, Paula Conn, Sandra (Bob) Larabee and Kris Wollrich; grand-nephews Price (Del), Daniel (Katie), and Ben; and grand-grand-nephews and niece: Tristen, Leah, Jacob and newborn Noah Eric. Noah Eric was born only a month before Eric passed away, but Eric was pleased to know that he was named after his great-uncle Eric. Eric treated everyone with kindness. Those of us who have been lucky enough to know Eric will always miss him deeply. We will never forget the gentle goodness of this man of such high achievement."

Thank you again Eric for a life well spent!

Eric E. Conn

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PSNA 2018 Conference Program August 4-8, 2018

All oral presentation will be held in the Rogelio Jiménez Auditorium at the Facultad de Ciencias Químicas, UASLP

Speakers: http://congresos.uaslp.mx/57psna/Paginas/Speakers.aspx

The next meeting of the PSNA will be held at the Universidad Autonoma, in San Luis Potosi, Mexico, August 4 – 8, 2018. The meeting will feature the rich phytochemical research of Mexico as well as the great slate of PSNA speakers and presentations. The University has outstanding programs in plant chemistry and biochemistry and is located in historic San Luis Potosi.

"where you can get a glimpse of the past, proudly reincarnated through the finely preserved streets, facades and architecture of our city center"

The PSNA is making a special effort to provide travel awards to encourage the attendanace of students for this meeting. Reserve a spot on your calendar now for this exciting phytochemical-focused meeting. Travel to San Luis Potosi is easy, with direct flights from Mexico City, Houston, and Dallas. Registration, lodging, and abstract information will be posted soon after the new year begins.

We look forward to seeing you in Mexico for 2018!

2018 TENTATIVE CONFERENCE PROGRAM

Saturday, August 4, 2018
Real Plaza Hotel
Conference Registration
Welcome Reception

Sunday, August 5, 2018
Conference Registration, Rogelio Jiménez Auditorium Lobby
Symposiums 1-4
Poster Session with Refreshments, Professional Exams and Council Halls

Monday, August 6, 2018
Plenary Symposiums 5-8
Poster Session with Refreshments, Professional Exams and Council Halls

Tuesday, August 7, 2018
Symposiums 9-11
Presentation PSNA 2019
Traditional "Callejoneada" through historic downtown

Wednesday, August 8, 2018
Symposiums 12 & 13
Tour in Museum Laberinto de las Ciencias y las Artes
Visit to UASLP Botanic Garden
Award Banquet, Edificio Central de la UASLP

LODGING

Meeting attendees are responsible for making their own lodging reservations directly with the hotel. A block of rooms have been reserved at the hotel designate below. Please note that room rates include tax and/or hotel fees. Attendees should identify themselves as with *PSNA 2018* when making reservations. Please verify cancellation policies with each property.
Please book by July 16, 2018 for group rate, based on availability.

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Call for abstracts
http://congresos.uaslp.mx/57psna/Paginas/Call-for-Abstracts.aspx

If you are an undergrad, graduate student or postdoc, you can indicate if you want your submission to be considered for a Travel Award or a Best Presentation/ Poster Award during the submission process. Awards will be presented during the Award Banquet on Wednesday, August 8.

As part of the online submission process, you will be required to upload your abstract as Microsoft Word .doc or .docx.

Registration
http://congresos.uaslp.mx/57psna/Paginas/Registration.aspx

The submission deadline is July 13, 2018.

All fees are in $USD and include receptions, beverage breaks, lunches, banquet and registration materials.

Credit card registration and online abstract submission are now available on the meeting website!

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Call for Applications!

Applications for the Elsevier-PSNA Young Investigator Award for 2018

As we prepare for our 2018 PSNA meeting in San Luis Potosi, Mexico on August 4-8, it is time again to seek applications for the Elsevier-PSNA Young Investigator Award for 2018.

The Elsevier-PSNA Young Investigator Award is selected from applications received of young career scientists for a $10,000 research award and covers travel expenses to the next two PSNA meetings.

We are appealing to our membership to encourage your fellow young scientists to apply for the Elsevier-PSNA Awards. Please forward your nominations to any of the PSNA officers.

We are also looking for nominations for the PSNA Phytochemical Pioneer Awards and PSNA Lifetime Member Awards. The Pioneer Award is selected from nominations by the executive committee for a senior researcher who has had a significant impact on the advancement of phytochemical research over the course of his or her career. The designation Life Member is an award or recognition bestowed by the *Society* on members who have made significant contributions to the activities and advancement of the *Society*. Life Members are entitled to all the privileges of regular members for life, and shall be exempt from payment of dues. The Executive Committee must approve each Life Member.

Any nominations for these awards would be greatly appreciated!!

David Gang
PSNA Awards
Gangd@wsu.edu

Elsevier-PSNA Young Investigator Award for 2018

Application deadline is **April 30, 2018**. Awarded by the PSNA, sponsored by Elsevier

The PSNA's most prestigious award for early-career phytochemists and plant molecular biochemists is the Elsevier Phytochemistry Young Investigator Award, sponsored by the journal Phytochemistry from Elsevier. This biennial award will be awarded again in 2018 to an individual who has exhibited exceptional creativity in and dedication to the field of phytochemistry, plant biochemistry, or plant molecular biology.

The recipient will receive **$10,000 for research** and up to $2,000 for travel and lodging to present a lecture at the 2018 PSNA meeting. The recipient will receive half of the prize money at the 2018 PSNA meeting and half upon submission of **a substantive and original review paper to Phytochemistry** within the next calendar year.

PSNA members are encouraged to nominate candidates and eligible candidates to submit applications to the Chair of the PSNA Awards Committee, **Dr. David Gang, at gangd@wsu.edu.** The deadline for receipt of nominations and applications is April 30, 2018.

Eligibility criteria

Applicants **must be early career scientists** in a research area related to phytochemistry, hold **an independent position**, and be a **current PSNA member**.

Instructions to apply

Applications should include a cover letter, CV, four-page research plan budget, one-page budget justification, and three letters of recommendation

Phytochemical Society of North America
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New Member Application Form

Please fill in the following application and return to the Treasurer with your dues payment. Once your application has been processed, you will receive newsletters and special mailings. You are also eligible for PSNA member discounts on the Recent Advances in Phytochemistry series (See Website).

Payments should be made by one of the following: check drawn on a US checking account, US travelers check, or US money order, International Money Order, Credit Card on the PSNA Website or Paypal payment to psnatreasurer@gmail.com. Please make check or money order payable to the Phytochemical Society of North America.

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