



Secondary Plant Substances in Agricultural Plant Protection, Human and Veterinary Medicine, Pharmacy, Toxicology and Industrial Applications- with special emphasis on Neem and push- pull techniques

Hans E. Hummel^{1,2}

¹ Ecological Plant Protection, Justus Liebig University Giessen, Karl-Gloeckner-Str. 21 C, 35394
Giessen, Germany

² University of Illinois Urbana-Champaign, Prairie Research Institute, Champaign, Illinois 61820, USA

Before the advent of synthetic chemistry, the agriculturist, physicist, pharmacist, and toxicologist had mainly 2 natural sources for organic substances derived from plants: 1. those from the terrestrial, and 2. those from the (still largely unexplored) marine environment. Stone-age mankind collected what could be found in the woods. Curious individuals discovered, largely by trial and error, what was beneficial and detrimental, and acted accordingly. Truly innovative people like Paracelsus, however, proceeded from qualitative to quantitative considerations, thus anticipating developments that were useful centuries later in medicine, toxicology, and natural product chemistry of our days and age. And along came Berzelius in Sweden, and Liebig and Wöhler in Germany to prepare the ground for modern age organic chemistry, including industrial type agriculture. These advances would have been unthinkable without first having the microanalytical tools of Thenard and Gay-Lussac (Paris) and Liebig (Giessen).

By and large, 3 main application areas were identified for use of secondary plant substances: 1. for agriculture and plant protection, 2. for human and veterinary medicine including pharmacy and toxicology, and 3. industrial applications.

Along with constant refinements of organic and analytical chemistry during the 19th and 20th century, we today are blessed with a toolbox from which we freely can take what we need. Chromatography and spectroscopy are very helpful in identifying and quantifying any of the secondary plant substances in question. Thus, the following subfields of interest can be described as

- feeding preferences of insects, generally invertebrates and vertebrates, on plants
- biochemical as well as hormonal interactions between higher plants, as well as interactions between higher plants and animals, and plants and insects,
- use of plant toxins in pest control
- biochemistry of plant pollination (now an exceedingly important field for species diversity and species conservation).

Each of these subfields is characterized by a wealth of published literature and textbooks. Some are cited below in the references. Pyrethrum (later to become pyrethroids) and carbamates provided the blueprint for synthetic chemists to follow in their search for lead structures, not always to the best of ecology.

Chemically, the CHO compounds are the largest group of natural products, followed by the group of alkaloids with ten thousands of identified members, which are then followed in number, but not necessarily in importance, by other heteroatomic compounds containing S, P, Se, halogens, and trace metals.

In the author's experience, natural products of the *marine* environment occupy an important rank. Most advanced, however, is our knowledge about natural products of the neem (Meliaceae) family of *Azadirachta* and *Melia* spp. We owe praise for major advances to ancient Indian physicians of the last millenia, but also to modern investigators of the last and this century. Specifically, Schmutterer established the worlds renowned laboratory at J. Liebig University of Giessen where scientists and students from many parts of the Developing world were gathering to learn the tricks of the trade for later transportation and exportation to Africa, SE Asia, the Caribbean, and Latin America. Tetranortriterpenoids of neem seeds with antifeedant and insect development modifying properties were investigated at an extremely large scale and are covered in a number of seminal chapters within the textbook of Schmutterer, ed., in the 1st (of 1995) and the second edition of 2002. W. Kraus, E.D. Morgan, M.B. Isman, O. Koul, and B. Siddiqui recently discovered and isolated many new substances from neem and described their properties of an astoundingly wide chemical and also activity spectrum. Thus, the acronym of the neem tree as "village pharmacy of India" bears some justification. It is worth mentioning that Prof. S.V. Ley and his research group in Cambridge, England, succeeded in the exceedingly difficult task of synthesizing the most complicated azadirachtin molecule by means of advanced organic chemistry. Its total synthesis, however, is mainly of academic interest since the end product is by a large margin much more cheaply produced via large scale solvent extraction from natural, imported neem seeds. The author of this abstract successfully used neem extracts (and neem oil) as externally sprayable materials for protection of *Zea mays* in Illinois against the western corn rootworm beetle, *Diabrotica v. virgifera* (Coleoptera: Chrysomelidae), an obnoxious pest species of maize which is resistant against most major synthetic insecticides. Neem extracts also have been used in the Sahel zone against the migratory desert locust *Schistocerca gregaria*, a pest known since biblical times. Schmutterer was the first to recognize the feeding deterrent properties of neem trees which saved them from attack by the voracious locust swarms. Later on, natural product chemists in an international effort identified the feeding deterrent principles, e.g. azadirachtin, marrangin, salannin and nimbin, among many dozen of related structures.

Recently, chemical ecology, a subject area still under vigorous investigation, tries to combine natural product chemistry with ecological considerations and innovative applications in plant protection against insects, among them the maize stem borer in East African countries. Unfortunately, many natural product classes are poorly explored, and the identity of these natural products is completely unknown. Yet insects trying to attack plants have to deal with the presence of these compounds and are therefore constantly exploring new ways of evading the biochemical defense barriers.

Natural plant products are also the basis of the push-pull technology introduced by Khan and Pickett during the last 2 decades and now mainly practiced but not limited to sub-Saharan Africa. Hummel et al. (2012 and 2017), Winter et al. (2014) and Bauer (2017) of the Giessen laboratory may be cited as examples for what is possible with a minimum of effort and technology and what may be accomplished in innovative plant protection within the foreseeable future. Those substances are partly chemically identified but are inexpensively being used in situ without ever isolating them. It is sufficient to interplant them with the crop to be protected and let the volatile and non-volatile natural products work. Most efficient is the *simultaneously practiced* attraction of beneficial insects (by the inherent kairomones) and the repulsion of destructive insects (by allomones). This general principle also works between and among plants via exchange of diffusable root exudates below the soil surface. Further in depth exploration of these mechanisms is mandatory for innovative future pest management.

Medicine in India was unthinkable without neem. Western medicine today still can profit from antibacterial, antifungal, antiviral and antiparasitic properties of neem, not to mention benefits in birth control and wound healing in humans and animals.

In conclusion, there is strong support for the notion of secondary plant substances playing a decisive role as signal compounds, a role that is indispensable for daily life in developing tropical countries, agriculture, plant protection, toxicology, stored products protection, academic teaching, medicine, and industrial applications.

Literature

Some selected relevant literature follows (for brevity, only authors and year of publication are cited):

Bauer J.M. (2017); Harborne, J.B. (1977); Hummel H.E. (1983); Hummel H.E. (1989); Hummel H.E. et al. (1997); Hein D.F. & H.E. Hummel (1998); Hein D. F. (1999), Doctoral Dissertation, Justus Liebig University Gießen; Hummel H.E. et al. (2012); Hummel H.E. et al. (2017); Isman M. (1997); Kalinowski H.O. et al. (1993); Koul O. (2004); McClintock, J.B. & B.J. Baker, eds. (2001); Sondheimer, E. and J.B. Simeone, eds. 1970; Schmutterer, H. ed. (1995 and 2002); Siddiqui B.S. et al. (2009); Winter E. et al. (2014)