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ERGOT
The Genus *Claviceps*

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PREFACE TO THE SERIES

There is increasing interest in industry, academia and the health sciences in medicinal and aromatic plants. In passing from plant production to the eventual product used by the public, many sciences are involved. This series brings together information which is currently scattered through an ever increasing number of journals. Each volume gives an in-depth look at one plant genus, about which an area specialist has assembled information ranging from the production of the plant to market trends and quality control.

Many industries are involved such as forestry, agriculture, chemical, food, flavour, beverage, pharmaceutical, cosmetic and fragrance. The plant raw materials are roots, rhizomes, bulbs, leaves, stems, barks, wood, flowers, fruits and seeds. These yield gums, resins, essential (volatile) oils, fixed oils, waxes, juices, extracts and spices for medicinal and aromatic purposes. All these commodities are traded world-wide. A dealer’s market report for an item may say “Drought in the country of origin has forced up prices”.

Natural products do not mean safe products and account of this has to be taken by the above industries, which are subject to regulation. For example, a number of plants which are approved for use in medicine must not be used in cosmetic products.

The assessment of safe to use starts with the harvested plant material which has to comply with an official monograph. This may require absence of, or prescribed limits of, radioactive material, heavy metals, aflatoxin, pesticide residue, as well as the required level of active principle. This analytical control is costly and tends to exclude small batches of plant material. Large scale contracted mechanised cultivation with designated seed or plantlets is now preferable.

Today, plant selection is not only for the yield of active principle, but for the plant’s ability to overcome disease, climatic stress and the hazards caused by mankind. Such methods as in vitro fertilisation, meristem cultures and somatic embryogenesis are used. The transfer of sections of DNA is giving rise to controversy in the case of some end-uses of the plant material.

Some suppliers of plant raw material are now able to certify that they are supplying organically-farmed medicinal plants, herbs and spices. The Economic Union directive (CVO/EU No. 2092/91) details the specifications for the obligatory quality controls to be carried out at all stages of production and processing of organic products.

Fascinating plant folklore and ethnopharmacology leads to medicinal potential. Examples are the muscle relaxants based on the arrow poison, curare, from species of Chondrodendron, and the antimalarials derived from species of Cinchona and Artemisia. The methods of detection of pharmacological activity have become increasingly reliable and specific, frequently involving enzymes in bioassays and avoiding the use of laboratory animals. By using bioassay linked fractionation of crude plant juices or extracts, compounds can be specifically
targeted which, for example, inhibit blood platelet aggregation, or have antitumour, or antiviral, or any other required activity. With the assistance of robotic devices, all the members of a genus may be readily screened. However, the plant material must be fully authenticated by a specialist.

The medicinal traditions of ancient civilisations such as those of China and India have a large armamentaria of plants in their pharmacopoeias which are used throughout South East Asia. A similar situation exists in Africa and South America. Thus, a very high percentage of the World's population relies on medicinal and aromatic plants for their medicine. Western medicine is also responding. Already in Germany all medical practitioners have to pass an examination in phytotherapy before being allowed to practise. It is noticeable that throughout Europe and the USA, medical, pharmacy and health related schools are increasingly offering training in phytotherapy.

Multinational pharmaceutical companies have become less enamoured of the single compound magic bullet cure. The high costs of such ventures and the endless competition from me too compounds from rival companies often discourage the attempt. Independent phytomedicine companies have been very strong in Germany. However, by the end of 1995, eleven (almost all) had been acquired by the multina-tional pharmaceutical firms, acknowledging the lay public’s growing demand for phytomedicines in the Western World.

The business of dietary supplements in the Western World has expanded from the Health Store to the pharmacy. Alternative medicine includes plant based products. Appropriate measures to ensure the quality, safety and efficacy of these either already exist or are being answered by greater legislative control by such bodies as the Food and Drug Administration of the USA and the recently created European Agency for the Evaluation of Medicinal Products, based in London.

In the USA, the Dietary Supplement and Health Education Act of 1994 recognised the class of phytotherapeutic agents derived from medicinal and aromatic plants. Furthermore, under public pressure, the US Congress set up an Office of Alternative Medicine and this office in 1994 assisted the filing of several Investigational New Drug (IND) applications, required for clinical trials of some Chinese herbal preparations. The significance of these applications was that each Chinese preparation involved several plants and yet was handled as a single IND. A demonstration of the contribution to efficacy, of each ingredient of each plant, was not required. This was a major step forward towards more sensible regulations in regard to phytomedicines.

My thanks are due to the staff of Harwood Academic Publishers who have made this series possible and especially to the volume editors and their chapter contributors for the authoritative information.

Roland Hardman
Ergot (*Claviceps purpurea*) is best known as a disease of rye and some other grasses. However, it is probably the most widely cultivated fungus and it has become an important field crop.

The main reason for its importance is ergot alkaloids, which are extensively used in medicine. No other class of compounds exhibits such a wide spectrum of structural diversity, biological activity and therapeutic uses as ergot derivatives. Currently, ergot alkaloids cover a wide spectrum of therapeutic uses as the drugs of high potency in the treatment of uterine atonia, postpartum bleeding, migraine, orthostatic circulatory disturbances, senile cerebral insufficiency, hypertension, hyperprolactinemia, acromegaly and parkinsonism.

Ergot—once dreaded pest and cause of epidemic intoxications has now become a profitable crop for farmers. However, the danger of intoxication and crop damage still persists. The fungus was already well known in the middle ages, causing outbreaks of ergotism or “epidemic gangrene” called for example, St Anthony’s fire.

Ergot alkaloids are traditionally obtained by extraction of ergot sclerotia artificially cultivated on cereals. The parasitic cultures are not able to produce some, e.g., clavine alkaloids necessary for most semisynthetic drugs. Crop fluctuations and market demands lead to the development of submerged cultivation in production plants. Present trends in ergot cultivation are the development of saprophytic cultivation processes and improvement of field production by, for example, introduction of new hosts and ergot strains. Even though there is a constant effort to prepare ergot alkaloids synthetically their bioproduction is still much more competitive. In the contemporary economical crisis of agriculture, especially in Europe, the ergot is a good and profitable alternative crop for farmers. Thanks to the new advanced technologies it experiences a real renaissance.

Various strains of *Claviceps* served as models for study of the fungal metabolism, biogenesis, physiological and genetic aspects of ergot alkaloids production. This interest continues because of good perspectives of submerged and field production of ergot alkaloids.

The volume on the *Claviceps* genus should provide readers with both biotechnological aspects of ergot alkaloid production, genetic and physiological data but also with newly emerging dangers of toxicology and environmental risks of ergot infection and contamination of food and forage. Chemistry and pharmacology of ergot alkaloids will demonstrate both their use as classical drugs and their newly discovered pharmacological applications.

Vladimír Křen
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