Herbal Medicinal Products — Plant Breeding and Good Agricultural Practice (GAP) for Medicinal and Aromatic Herbs©

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INTRODUCTION

Dietary herbs and fermented legumes are excellent sources of phenolic phytochemicals. These phenolic phytochemicals are important, not only as food preservatives, but are also increasingly interesting for therapeutic and pharmaceutical applications (Shetty, 1997). Understanding the nutritional and therapeutic role of dietary phytochemicals is an important scientific agenda for food science and nutrition now and in the future.

Phenolic phytochemicals are becoming very significant in a time when food is playing a major role in disease prevention in a global population projected to increase to 10 billion by 2050. Disease prevention through the diet is potentially the most effective tool to improve health and reduce the increasing health-care costs for the expanding global population. In line with this perspective and vision one of the major goals of Botanical Operations is to use biotechnological tools to develop improved clonal lines of dietary herbs and improved fermentation processes for dietary legumes to generate consistent, nontoxic and clinically relevant levels of phenolic metabolites for use as nutraceuticals (functional or vitafoods, medicinal foods and supplements) (Shetty, 1997; Shetty and Labbe, 1998). Current targets are to use consistent profiles of phytochemicals from Lamiaceae as antimicrobials for herbal medicinal products (HMP) and functional food in the prevention and treatment of emphysema and urinary tract infection. Phenolics from cranberry have a potential use against urinary tract infections caused by *Escherichia scherichia* var. *coli* (Sobota, 1984). Use of diverse antimicrobial-type plant phenolics could lead to a reduced use of antibiotics and therefore reduce the increase in antibiotic-resistant, disease-causing bacteria.

PLANT BREEDING — (INTEGRATED APPROACH TO DEVELOPMENT OF NUTRACEUTICALS)

Botanical Operations has envisioned a seven step approach to the scientific and commercial development of nutraceuticals. These seven steps are:

1) Development of techniques to obtain genetically consistent botanical lines of specific targeted species so that uniform and consistent phytochemical profiles are generated for studying clinical relevancy and safety based on structure-function properties. Based on this concept we have isolated clonal phytochemical profiles by non-

GMO methods that originated from individual heterozygous seeds. We have now targeted specific HMP's against Alzheimer, arthritis, pre-menstrual syndrome, prostate diseases, urinary tract infections, and diseases related to the central nervous system. We are envisioning strategies for choice of HMP using this method for other health targets like diabetes and cardiovascular problems. We are also looking at choice of HMP based on a historical use in traditional medicine. Use of the consistent profile concept based on the long history of use can effectively integrate these botanicals into modern structure-function direction.

2) Development of techniques for sustainable and organic production of selected botanicals with relevant and consistent clonal profiles. This involves not only the use of natural fertilizers for enhancing nitrogen metabolism but more importantly we are developing natural compounds to elicit maximum quantity and quality of the phytochemical profiles. Further, we are trying to understand the role of circadian rhythms (chronobiology) in regulating phytochemical synthesis for maximum clinical efficacy.
3) Development of techniques for natural fermentation and mobilization of functionally relevant phytochemicals from genetically consistent botanicals. In this approach we are targeting the use of food-grade natural fermentation with a long history of use to mobilize functional phytochemicals. We are looking at critical enzymes in the fermenting microorganism that can maximally release functional phytochemicals.
4) Development of food-grade extraction techniques for phytochemicals and instrumentation methods for phytochemical characterization. In this approach nontoxic, food-grade extraction methods are being pursued. Among them are hot water, ethanol, and liquid carbon dioxide methods.
5) Development of consistent food formulations based on structure-function and processing variables, including phytochemical stability. Here we are also looking at synergies between different botanicals and between botanical and nonbotanical foods to improve a particular health state.
6) Development of rapid bioassays for structure-function evaluation that serves as a basis for clinical studies. All the steps from 1 to 5 are being developed with a link to structure-function bioassays. Therefore the issue of consistency of botanical profiles is followed all through these steps.
7) Development of network for global, multi-site clinical studies. In this regard we are building collaborations in the U.S.A., Europe, Australia, Japan, and India.

QUALITY ASSURANCE — (DEVELOPMENT OF COMMON AGRICULTURAL QUALITY POLICY)

European manufacturers of starting material for the production of pharmaceuticals are increasingly being required to provide GMP (Good Manufacturing Practice)

certificates for their third country export markets. In this context, a Community inspection and certification system is of utmost importance. Moreover, the introduction of a system of Community inspection, for both starting material and medicinal product manufacturers, will provide an easily recognisable "label" for manufacturers exporting from the Community.

Within a not too far future, 5 to 7 years, the implementation of the new legal basis for inspection of starting material at manufacturers for compliance with the appropriate GMP, Good Agricultural Practices (GAP) giving specifications and outlining medicinal plant growing and handling conditions has become imperative. In addition to the export/import interests this also needs to become an intrinsic part of any quality assurance system for plant based health care programmes.

In 1998 the European Herb Growers Association (EUROPAM) submitted a draft document based upon the above mentioned to the European Commission and the EMEA (ad hoc working group on herbal medicinal products). In 1999 the European Commission expressed its interest in including the "Europam GAP Guideline" into the draft: Directive GMP for Starting Material (Anon., 1999).

For the medicinal and aromatic herb producers the implementation of such requirements for plant originated starting materials, to cover all steps from cultivating to manufacture of extracts, is a very demanding task. It will require highly qualified guidance to ensure that all objectives are met, at the same time avoiding excessively complicated procedures. Since the area is still not completely harmonised it is in itself both a task and an objective to negotiate a set of rules which is mutually recognised by all relevant authorities throughout the community.

Meanwhile, the "Europam GAP Subcommittee" has now further drafted two more guidelines: Good Organic Agricultural Practice (GOAP) and Good Harvesting Practices (GHP) for wild crafting. These are constructed according to the same principles as GAP to handle the specific issues of organic cultivation and the harvest of wild plants in nature.

LITERATURE CITED

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