

Invited commentary

Phytomedicines for healthcare

A. Subramoniam

Tropical Botanic Garden and Research Institute, Pacha-Palode (P. O), Thiruvananthapuram - 695 562, Kerala, India

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Plants provide food, raw materials for medicine and various other requirements for the very existence of life from the origin of human beings. Even the current conventional medicine is using a lot of plant derived chemicals as therapeutic agents. It should be noted that in the present day also, the majority of the global population utilizes medicinal plants for their healthcare. Therefore, there is a compelling need for detailed scientific validation of all traditional medicinal plant drugs to establish their efficacy and safety in light of modern science.

Although it is generally believed that plant drugs are not toxic, it is known that many plant products cause toxicities such as neurotoxicity, reproductive toxicity, liver toxicity, *etc.* A well known example is the presence of hepatotoxic pyrrolizidine alkaloids in certain traditional medicinal plants. Many plants from the Boraginaceae, Compositae and Leguminosae families contain well over 100 hepatotoxic pyrrolizidine alkaloids. Therefore, detailed toxicity studies are required for herbal drugs which are not tested for toxicity previously.

There are thousands of plants used in traditional medicine by different cultural groups throughout the world. A large number of these traditional medicinal plants remain to be studied. There is a need for detailed studies on each plant and to prepare monographs on them. The gap areas are to be identified for follow up studies. Substantial number of monographs on the medicinal plants was prepared by China, Germany, WHO, *etc.* However, this is insufficient to a large extent. Every country has to work on its medicinal flora to a fuller extent for optimal utilization of the plants for the development of new healthcare products and for the improvement of existing herbal medicines. This involves huge amount of work.

Ecotypes and genotypes variations are one of the major hindrances in the development of phytomedicines (refined Ayurvedic type of drugs with safety and efficacy comparable to conventional medicine). This can be overcome, to a large extent, by developing agrotechnology (suitable cultivation conditions) for deserving medicinal plants, keeping in view with the medicinal quality of the

plant; biotechnological intervention is required in some cases, such as rare and endangered plants, to get required biomass for drug development as per demand.

Success of phytomedicine or herbal drug development is linked to the production of good quality plants as per requirement. Since many of the medicinal plants are weed-like plants, they can be grown easily in villages without much financial input. Many of the plants produce more medicinally valuable phytochemicals in relatively adverse conditions. They may not require much fertilizers and watering. Agrotechnology or suitable cultivation conditions have to be developed for the plants to improve their medicinal value (content of active principles). Pharmacological and phytochemical assays are to be used to assess the medicinal quality while developing suitable agrotechnology.

The concept of creation of almost self sufficient and sustainable biovillage with the efficient utilization of bioresources and clean energy is an excellent one for human development in a sustainable and healthy manner. Cultivation of appropriate medicinal plants at the village level and family level and supplying them (at the district or state level with a co-operative net-working) to concerned Ayurvedic and other pharmaceutical companies, engaged in plant drug production as well as for exporting (for foreign exchange earnings) can form an important part of such biovillages. In the case of rare and endangered plants which are not amenable to common cultivation conditions, appropriate facilities should be set up in the villages with trained man power for biotechnological intervention. This will enable sustainable production of good quality plant materials for drug development.

Even today, we continue to use traditional medicines without an expiry date determined based on experimental evidence. Controlled clinical trials were not carried out to most of the traditional medicines to establish their safety and efficacy. There are no chemical profiles such as HPTLC/HPLC for most of the medicines to set as standards. Without defined standards for authenticity of the medicine, uniform quality (efficacy and safety) of the medicine cannot be assured. The quality control mechanism is very weak. So it is natural that, these medicines are not approved by the drug controllers of the Western countries where the conventional medicine is rooted. There is a need to determine safety and efficacy as in the case of conventional medicine; the yard-stick for safety and efficacy should be same for all medicines. This needs systematic scientific studies and extensive research plan for each medicine, starting from the source plant materials to the mechanism of actions of the plant phytochemicals present in the medicine in their combined state. Although the marker compounds and the major active compounds

Author for correspondence: Dr. A. Subramoniam
Professor and Former Director, Tropical Botanic Garden and Research Institute, Pacha-Palode (P. O), Thiruvananthapuram-695562, Kerala, India
Residence: Vininivas, T.C. 14/80, Anyara (P.O.), Near KIMS Hospital, Thiruvananthapuram-695029, Kerala, India
E-mail: asubramoniam@yahoo.com
Tel.: +91-09496093609
Fax: 91-472-28696

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are known in some of the very commonly used medicinal plants, all the active principles in a given traditional medicine and their interaction to exert specific actions in the living body are not fully understood. Further, traditional doctors advocate specific dietary conditions (restricted dietary items to be consumed) while undergoing treatments with a specific medicine for a disease. The importance of this and other practices followed in traditional medicine and the interaction of dietary chemicals with those of medicine and the consequent changes in the pharmacodynamic aspects of the medicine, therapeutic value of the medicine, *etc.*, remain to be studied in light of modern science.

In traditional medicines, a large number of polyherbal formulations are used in the treatment of liver diseases, diabetes, old age related degenerative diseases, *etc.* Now, it is increasingly recognized that combination therapy is better to treat complex diseases involving several drug targets. With the traditional knowledge in the preparation of polyherbal formulations to treat various diseases, new rational polyherbal formulations have to be developed using extracts, active fractions and /or active principles. The required ingredients and their specific ratios have to be established by pharmacological and toxicological studies. The effects of various permutations and combinations of the ingredients have to be studied. This involves enormous amount of work in each case.

Traditional medicines including those used in traditional systems of medicine such as Ayurveda, and Sidha and other local health traditions, originated from time immemorial with the knowledge and belief existed in those times. These medicines should be studied in light of current knowledge in biology and medicine. This includes systems biology and reverse-pharmacological approaches. Systems biology is an interdisciplinary field of biological study that focuses on complex interactions within various biological systems, using an integrated holistic approach. Reverse pharmacology is also relatively a new concept wherein pharmacological experiments and clinical trials are carried out first on the basis of the evidence that the medicine has been used since thousands of years as in Ayurveda. Then the drug is characterized; mechanisms of actions are identified; safety is established; drug is formulated; and drug comes in market. Thus, it is the 'clinics to lab and then back to clinics' approach. All this involves a lot of inter disciplinary studies.

Another important research area is nutraceuticals and food supplements for health benefits and control or cure of specific diseases. The edible plant parts possessing nutritional as well as pharmacological actions are known as nutraceuticals; the pharmacologically active compounds isolated from edible plant materials are also nutraceuticals. There are nutraceuticals which can prevent diseases such as cancer, cardiovascular problems, liver diseases, neurological diseases and infectious diseases; body's immunity against infections can be augmented with food supplements containing appropriate nutraceuticals. Food supplements and dietary formulations are prepared with nutraceuticals, for health improvement and control or cure of diseases. Medicines have to be used at the optimum levels for desired health benefits; similarly nutraceuticals should be consumed at the optimum levels. Animal experiments and clinical trials are required, among other things, to determine the optimum levels. For example, resveratrol, a nutraceutical present in grapes, peanuts,

etc. have many beneficial biological effects, dependent on the dose used. Animal experiments have shown that this compound has a protective effect at low doses against cardiovascular injury, gastric lesions, ischemic stroke, Alzheimer's disease and osteoporosis, but an adverse effect or no beneficial effect was observed in these cases at high doses. Epidemiologic and clinical trials are needed to assess the nature of the dose-response of nutraceuticals such as resveratrol in humans. Globally nutraceuticals have great demands.

Pharmacogenomics is applicable to phytomedicines also. Pharmacogenomics is the study of how genes affect a person's response to drugs. It combines pharmacology and genomics (the study of genes and their functions) to develop effective and safe medications and doses that will be tailored to a person's genetic makeup. The field of pharmacogenomics is still in its infancy, but new approaches are under study in clinical trials. In the future, pharmacogenomics will allow the development of tailored herbal drugs/ phytomedicines to treat a wide range of health problems. There are tremendous hopes for research in this area.

There are many crucial areas in medicine such as liver diseases, arthritis, old age related problems, certain viral infections and cancer where the conventional medicine is devoid of satisfactory treatment. These are among the promising areas of research and development of medicines from the vast highly potential plant resources. Plants are also attractive sources for the development of novel and very effective and safe therapeutic agents against infectious diseases, diabetes, *etc.* Development of valuable phytomedicines and healthcare products from locally available plants will result in multidimensional socio-economical progress.

In view of the ever increasing amount of awesome research work to be carried out in the development of phytomedicines and conventional medicines from plants, a matching increase in the number of good quality, reputed journals is a requirement. In the recent past some new journals have appeared in this and related areas. However, new excellent multidisciplinary journals are in need to cope up with the rapidly increasing research and development activities in this field in the foreseeable future. In this context, the emergence of *Annals of Phytomedicine: An International Journal* is timely. I hope and wish that the journal will grow and flourish like a banyan tree with pillars of support from dedicated researchers and teachers in the area of phytomedicine.

The journals devoted to phytomedicines have an important role in the dissemination of scientific and technological knowledge in this area which facilitates, among other things, research and development in the right direction. The journals should serve as a source of inspiration to the researchers to publish good quality work; the quality of scientific content of research papers should not be sacrificed at any cost. In this context, **Annals of Phytomedicine: An International Journal**, with a commitment to excellence in publishing cutting edge research in all areas of phytomedicine is a welcome arrival. Phytomedicine is truly a multidisciplinary area encompassing several disciplines. It is a challenging job to run such a journal successfully. I am very happy to note that *Annals of Phytomedicine: An International Journal* is already, with certainty, on its way towards accomplishing its mission and reaching greater heights.



Dr. A. Subramoniam

*Professor and Former Director, Tropical Botanic Garden and Research Institute, Pacha-Palode (P. O),
Thiruvananthapuram-695562, Kerala, India*

Residence: Vininivas, T.C. 14/80, Anyara (P.O.), Near KIMS Hospital, Thiruvananthapuram-695029, Kerala, India

Biography

Dr. A. Subramoniam [Former Director, Tropical Botanic Garden and Research Institute (TBGRI), Thiruvananthapuram, India] did his Ph.D. in Biochemistry (Maharaja Sayajirao University of Baroda, 1979) and Post Doctoral Research in USA in Biochemical Pharmacology. He worked in many reputed national and international laboratories and carried out original multidisciplinary research work of very high quality in the broad area of biomedical sciences and plant sciences. He is a recognized Ph.D. guide in Biochemistry, Biotechnology, Pharmacology, Chemistry and Zoology. Several scholars earned Ph.D. under his guidance. He has more than 170 scientific publications which include highly cited original research publications in reputed international journals, chapters in books, review papers in journals. Some of his publications are highly commendable. He has 9 patents in his credit.

At TBGRI, he has established advanced phytopharmacological research. During his period, TBGRI has earned national and international recognition in medicinal plant research for discovering many important leads from plants for the development of valuable medicines. He has received several national awards for his excellent scientific contributions such as Hari Om Ashram Award for Research in Indian medicinal plants; Swaminathan Research Endowment Award for outstanding contribution in the scientific evaluation of medicinal properties of plants for their therapeutic use (awarded by Indian Association of Biomedical Scientists); Jaipur Prize of Indian Pharmacological Society; and Dr. B. Mukerjee Prize (2006) of Indian Pharmacological Society.

He served as President, Southern Regional Indian Pharmacological Society, 2009; Vice President, Indian Association of Biomedical Scientists, 2007-2010; Vice president, Kerala Academy of Sciences (2011-2013). He is currently a Member of Governing Body of Amala Cancer Research Centre, Thrissur, Kerala, India, and a consultant in medicinal plant research.
