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Bioactive Natural Products from Plant Sources

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Editorial

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INTRODUCTION

Botany today has moved far ahead of the days when most of the work in this branch of science was centered on reporting new species from various geographical regions. It was dominated by taxonomists, who held the expertise for identification of various plant species based on their morphological and other characters. Another notable aspect was that of plant physiology. However no heavy emphasis was given on bioprospecting of the vast plant biodiversity. Though almost all ancient cultures had their own system of plant-based-therapy, no strong connection of these traditional medicinal practices was there with the modern scientific research practice until few years back.

Now there seems to be a paradigm shift, and more and more researchers of the present time are getting interested in discovery of novel bioactive compounds from the plants. Notable plant diversity exists in almost all parts of the world, and the number of species untapped remains much higher than the few which have been investigated systematically with respect to the bioactive compounds possessed by them. Plants can be viewed as a biological factory capable of producing a large number of metabolites. The structural diversity and complexity of these myriad plant-derived metabolites is highly impressive and overwhelming. These phytochemicals are very much likely to represent altogether novel classes of metabolites, as compared to those synthesized by animals and microorganisms. This vast structural diversity is a strong invitation for the natural product chemists to solve the structure and replicate the same in a synthesis lab. Similarly the variety and variability with respect to the biological activity is worthy of meticulous attention by those working on medicinal / therapeutic potential of the plant products.

There are several successful examples of plant-derived metabolites being effectively used in modern medicine, e.g. quinine and artemisinin as antimalarials; vinblastine, vincristine, and paclitaxel as anticancer agents, etc. Phytochemicals like lycopene (derived mainly from tomatoes ^[1], curcumin (from turmeric), gallic acid, quercetin ^[2], catechin, reserpine, etc., have been reported to possess one or more biologically relevant effect(s). There are many reports describing antimicrobial effects of lycopene, quercetin, and curcumin. Catechin has been a well-known inhibitor of quorum-sensing in bacteria. Reserpine is known to inhibit the bacterial efflux-pumps.

One of the major focus areas of the current times is to find novel antimicrobial substances from plant sources. Most of the currently used antibiotics have come from microorganisms, particularly from the *Actinomycetes* among bacteria, and from the species of fungi like *Penicillium* and *Cephalosporium*. However, the rapid acquisition of drug-resistance among the pathogenic microbes has necessitated the development of new antimicrobials, which may have a structure and mode of action different than those already in use. It is assumed that it should take some time for the pathogenic microbes to develop resistance against these structurally-different type of molecules. Plants do not have well-developed immune system like animals, and they can also not move away from their respective place when attacked by phytopathogenic microbes. This had made the plants to evolve towards synthesis of a large variety of antimicrobial secondary metabolites, which they can use for their protection from plant-pathogenic

bacteria, fungi or viruses. Many of these antimicrobial secondary metabolites can also be effective against human-pathogenic species.

The possibility of discovery and development of novel antimicrobial compounds from plant sources seems to be attractive, however there are several challenging issues to be considered while working with natural products (whether they are of plant origin or otherwise). I have discussed some of these issues in my article in the *AASCIT Communications* [3]. While working in the field of bioactive natural products, one will usually go through the stages like: extract preparation from the selected plant material, screening the extracts for the desired biological effect(s), characterization of the potent extracts, which may then be followed by *in vivo* experiments. It should be noted that always it is not possible to isolate and identify a single chemical entity as the active compound from a crude extract. This is for the reason that many of the plant compounds present in a given extract work in synergy, and may exert little or no effect when tested in purified form. This makes the scenario bit complicated, as till now the pharmaceutical field has largely focused on use of a single pure substance as the active ingredient of a given formulation.

In context of the synergistic action, poly-herbal formulations become important. These formulations can contain one or more standardized crude extracts. Much work remains to be done in the area of standardization of the crude plant extracts. This issue is complicated by the fact that plant preparations can experience considerable batch-to-batch variation owing to multiple factors such as the time of collection of the plant specimen, extraction protocol employed, storage conditions, etc. During storage if proper protection from light and air is not provided, then many of the plant compounds (particularly phenolic compounds) may undergo oxidation. Similarly hygroscopic preparations need to be protected from moisture. One way for standardization of a crude extract is to generate its chromatographic profile (TLC and/or HPLC), which can serve as a reference for that particular extract formulation.

Another aspect requiring attention is development of rapid extraction methods which should not degrade the heat-labile phytoconstituents. Novel methods like Microwave Assisted Extraction (MAE), sonic extraction, supercritical fluid extraction, etc. are emerging as attractive alternatives to the traditional methods [4]. These methods offer advantages like lesser solvent consumption, rapid extraction in short time, preservation of the heat-labile plant metabolites during extraction, etc. Among them MAE has been of particular significance owing to its simplicity and low cost. We have been employing MAE since the year 2007 for preparation of plant extracts, and we have reported many extracts thus prepared to possess one or other type of biological effect e.g. antioxidant, antibacterial, antifungal, anti-quorum sensing [5], anti-biofilm [6], beta-lactamase inhibitory property, etc. MAE can be performed either in *open vessel* or *closed vessel* mode, latter being more suitable for the thermolabile components. A combination of Soxhlet and MAE -*Soxhwave*- can also be tried to combine the benefit of high extraction efficiency obtained in Soxhlet method with the rapidness of MAE. It may be noted that *efficacy* is always not having a direct correlation with the *extraction yield*.

Though the possibility of wide-spread therapeutic use of plant products for human-welfare seems to be a feasible option, a long way is there to go. Issues like authentic identification of correct species, proper choice of solvent and extraction method, standardization of the crude preparations, minimizing batch-to-batch variation, designing effective and reliable bioassays to identify the desired biological activity in the test extracts, isolation and identification of active ingredients from the crude extracts, etc. need to be solved. Separate regulations need to be established for approval of polyherbal formulations for pharmaceutical use. Issue of adulteration too, is there to be dealt with. To harness the benefit of the vast metabolic diversity of the plant kingdom for the betterment of human health, a multidisciplinary approach is necessary, wherein experts from multiple fields (such as plant taxonomy, natural product chemistry, pharmacognosy, toxicology, pharmacology, microbiology, etc.) need to come on a common platform and work synergistically. A link needs to be established between the folklore practices of traditional plant-based medicine (as described in *Ayurved*), and the modern medicine. Modern tools and techniques should be used to authenticate and validate the plant formulations prescribed in various tribal cultures or ancient medicinal writings. Mining the ancient wisdom with new tools will pave the way for a healthier future of mankind.

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