# Natural product taking its own place!!!

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As researchers we are well aware that plants provide an abundance of compounds, many of which have been shown to be effective in the treatment of ailments for hundreds of years. In the recent past, much work has been undertaken to investigate active compounds in plants traditionally used in herbal medicine, venoms and toxins of animal origin and micro organisms. Researchers have developed *in vivo* and *in vitro* models to study bioactivity and have used instrumental means to determine their structure and metabolites. Natural products versus synthetic pharmaceuticals are expanding their market share world wide, even in Western countries like France and Germany.[1] Many 'natural medicine' practitioners claim that by using natural whole extracts the active ingredient is accompanied by other 'synergistic compounds', including related analogues, which influence (enhance or moderate) their therapeutic effect making the action of the active ingredient safer and, thereby, diminishing unpleasant side effects (many of these claims are scientifically unproven). Patients often favor plant (or naturally derived) medications for the treatment of long term chronic diseases, for their perceived long standing efficacy and good safety record (occasionally a mistaken belief, a point that I will return to later). Therefore there is a clear need for chemical characterization of plant-derived materials, scientific rigor, clinical trails and stringent quality control measures. Often, naturally derived and isolated compounds are used by pharmaceutical companies as lead compounds (drug targets) in the development of new synthetic drugs. In 1991, Kinghorn and Balandrin estimated that over half of the world's best selling drugs owed their origin to natural products, including enalapril and capropril: ACE inhibitors; the β2-agonist salbutamol; the immunosuppressant ciclosporin, and the non-steroidal anti-inflammatory agents - diclofenac and naproxen.[2]

The diversity of bioactivities and the potential for exploiting plant extracts/formulations derived from natural sources is reflected in this issue of Pharmacology Research. Mohanty and Cock have examined the antibacterial properties of extracts from the evergreen *Syzygium jambos*, and demonstrated that the leaf extracts were effective at inhibiting the growth of certain strains of gram positive and gram negative bacteria. Hessanzadeh *et al,* demonstrate that the essential oils from the leaves of several species of *Cupressus lusitnmica*, found in North America amongst other regions, possess both antibacterial and antifungal activity against *Bacillus cereus* and *Aspergillus niger* respectively. Both the aforementioned plants have been used as traditional remedies for generations. Of late there has been much interest on the extraction of natural antimicrobial compounds from plants; apart from the traditional uses of such extracts as topical antiseptics and such, there has been a huge interest in the potential use of these compounds as antiseptic agents in food.[3,4] Annually there are as many as 76 million cases of food-borne illness in the US, which result in about 5,000 deaths, many associated with microbial food-borne contaminants including *Listeria monocytogenes*, *Salmonella*, *Staphylococcus aureus* and *Toxoplasma gondii*.[5] There is also a genuine desire on behalf of the public to minimize the consumption of foods loaded with chemical preservatives; together with strong objectives at the use of antibiotic agents in foods of animal origin. However, one of the main stumbling blocks to the incorporation of natural preservatives and antimicrobials into foods is that they can compromise the flavors of the food even at very low concentrations.

Several articles in this bimonthly issue have focused on identifying potential plant extract alternatives for pharmaceutical preparations. As stated previously, there is a strong appetite for such products amongst the general population. Ranjith *et al,* have discovered that a dried formulation of the leaves or solvent extracts of a plant native to India called *Solanum tribatum* can act as a natural antihistamine. In fact the authors illustrate that unlike commercially available antihistamines, which mainly alleviate the symptoms of allergy, the aqueous and alcoholic extracts of this plant act by interfering with the preliminary biochemical mechanism of response induced by the allergen. Health concerns have arisen

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over several of the synthetic antihistamines for example methapyrilene hydrochloride (MP) has been shown to be a potent hepatocarcinogen in rats,[6] while topically applied diphenhydramine has been implicated in cases of toxic encephalopathy to name but two known adverse reactions.[7] Though the aforementioned are classified as first generation antihistamines they continue to enjoy widespread use in poorer and developing countries**.** In the 1980's a new so-called second-generation of antihistamines were put on the market - these were the non-sedating and specific histamine $H_1$-receptor antagonists. However, since their introduction, terfenadine and astemizole were found to increase significantly the risk of ventricular tachyarrhythmias.[8]

In this issue, Deep Kaur and Saraf and another group, Bhstia *et al,* have investigated the sun protection factor (SPF) of various essential oils and plant extracts as alternatives to commercially available sun screens or which could be integrated into sun cream formulations. This research has huge commercial potential; many of the commercial formulations contain suspect ingredients which the informed consumer would like to avoid if at all possible. Many topical sunscreen preparations have been shown to contain significant levels of sun filters that can induce endrocine disruption.[9] For example, some ultraviolet (UV) filters can induce pronounced estrogenic, antiestrogenic and antiandrogenic activities.[10]

A persistent theme in this issue is the use of instrumental methods to determine chemical constituents and the use of *in vitro* and *in vivo* models to assess the effects and toxicity of plant-derived materials; this I think forms the basis of modern Pharmacognosy and we have now reached a stage where technology enables this. It is now evident that Pharmacognosy has expanded its meaning from the study of bioactivities and toxicities of plant-derived compounds to encompass the fields of chemistry, biology, ethics, pharmacology, biochemistry and bioinformatics and this journal encompasses and encourages this multi-interdisciplinary approach.

In conclusion, if I may return to a theme that I have previously alluded to and one which is close to my heart: Ensuring quality control, safety and efficacy of medicines/ formulations of plant origin. I was delighted to see an evaluation of the heavy metal content in medicinal plants frequently used in formulations in Ghana in this issue.[11] As previously noted there is a persistence and mistaken assumption amongst consumers and even some practitioners that 'natural' products are safe. Let us think of some of the high profile cases that have emerged in recent years of adverse effects in herbal preparations containing toxic compounds. A slimming preparation containing a plant known for many years to be toxic *Aristolochia fangchi* was put on the market in Europe and subsequently caused kidney damage in some of the women taking the formulation. Among the chemical constituents in *Aristolochia fangchi* were the carcinogenic and mutagenic and nephrotoxic substituted nitrophenanthrene carboxylic acids, which induced kidney failure and cancer amongst users.[12,13] Another recent controversy arose out of a product which was manufactured in the USA and contained Kava. Kava comes from the root of *Piper methysticum*, a native plant of Polynesia, and is used in the treatment of anxiety and insomnia. This formulation became associated with incidents of hepatotoxicity and was banned in several countries as a consequence.[14,15]

I think what we can deduce from incidences like these is that there is now an urgent need to evaluate the chemical composition, pharmacology, bioconversion, safety and efficacy of herbal extracts and formulations (indeed this is a recognized cause and is the impetus for European Union (EU) directives such as The Directive on Traditional Herbal Medicinal Products (Directive 2004/27/EC)[16] so that we may guarantee safety and enjoy the benefits of this bountiful earth. I think this journal will contribute to this objective and to the discovery of new and exciting possibilities.

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## ABOUT THE EDITOR-IN-CHIEF

**Dr. Ambrose Furey** presently serves as director of a research team called Team Elucidate at Cork Institute of Technology, Cork, Ireland. His background involves in-isolation and structural elucidation of natural bioactive compounds from marine and terrestrial plants and micro organisms. He is also involved in determining contaminants present in natural products intended for human consumption. He has been employing various techniques in advanced chromatographic methods and liquid chromatography-multiple tandem mass spectrometry (LC-MS/MS) and Nuclear Magnetic Resonance (where sufficient quantities of sufficient purity are available) together with bioassays to assess the nature of the bioactivity and the potency of the isolated compounds. Dr. Furey is mainly interested in developing rapid quantitative LC-MS/MS methods to ensure the quality control of herbal products on the market. His major concerns and interests resonate and are reflected upon in the articles in this journal; my editorial 'style' will favor the contemplation and contextualization of a selection of the articles in the journal and, from time to time, address issues of particular relevance to the field of Pharmacognosy.