

Looking backward to find the path forward

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This month I have the pleasure of having a co-author, Rosari Kingston. Ms. Kingston is the former chair of the Professional Association of Medical Herbalists in Ireland — the Irish Institute of Medical Herbalists. Over the past two decades, Ms. Kingston has sought to develop research for practicing herbalists, so as to provide information about their clinical practice. She is currently carrying out research in the continuity of the Irish herbal tradition through the centuries.

As I did not provide an editorial in last month's Pharmacognosy Research, in the current issue I will cast my eye over interesting articles from both the present issue and the previous one. In both issues, I was struck by the very obvious fact of how many countries have utilized their indigenous botanicals for many generations. You may say that they had no alternative, and this is quite true! This has prompted me to consider and examine the parallels between Irish and British 'herbal cures' and traditional remedies from other regions of the world. Another seemingly obvious fact is that it is only relatively recently, when scientific techniques and technologies became available that we have realized that the use to which the herbs were put in the past were entirely valid and appropriate, and in fact in many instances, had a very sound scientific basis.

I have focused particularly on herbs used to treat inflammatory diseases as well as on plants that exert blood glucose lowering effects.

In the last issue of Pharmacognosy Research, Stephen *et al.* demonstrated the corroboration between traditional use and sound science. *Clerodendron splendens*, a native Ghanaian shrub, has been used for generations to heal skin infections

and injuries, and this group, by using *in vitro* and *in vivo* test models, has shown that the methanolic extracts of these shrubs are active against gram positive and gram negative bacteria, including some fairly resistant strains. In addition, the extract exhibits antifungal activity and also acts as a free radical sink.^[1]

In Ireland and Britain a common traditional remedy used for the alleviation of skin ailments is chickweed, a member of the carnation family, genus *Stellaria media*; the herb is associated with accelerating the wound healing process and its emollient properties soothe the itching and irritation. Its chief constituents include mucilage, triterpene saponins, hentiacontanol, coumarins, phytosterols, tocopherols, gamma-linoleic acid, minerals, flavonoids (mainly apigenin C-glycosides and rutin), organic acids (carboxylic acids), and vitamin C. The plant is an ubiquitous weed and is not restricted to Ireland; it is found in most temperate regions and even stretches as far as the north Arctic regions.

Most cultures have also identified natural analgesics that are applied externally or taken internally to alleviate pain and discomfort. In last month's issue Mustaffa *et al.* at the center for Drug Research, at the University of Sains Malaysia, have investigated the analgesic activity of the methanolic extracts from the leaves of an evergreen plant called *Cinnomomum iners*, belonging to the *Lauraceae* family. This plant has been used traditionally in various Asian countries for the treatment of digestive ailments, fevers, and headache. Its bioactive constituents include saponins, terpene, eugenol, and cinnamic aldehyde. By using Gas chromatography-Mass spectrometry (GC-MS), the authors have identified two interesting bioactive compounds in *C. iners*: beta-caryophyllene and stigmasterol.^[2] Beta-caryophyllene is a bicyclic sesquiterpene that is found in several essential oils, including oil of cloves, rosemary, and hemp oil. Ghelardini *et al.* have found in a study published in 2001, that beta-caryophyllene has local anesthetic effects.^[3] In 2008, a study conducted by Gertsch *et al.* has demonstrated that beta-caryophyllene can selectively bind to CB₂, a type-2 cannabinoid receptor, and by using mice studies they have shown that the compound exerted an

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anti-inflammatory effect.^[4]

Stigmasterol is another very interesting compound; it is an unsaturated plant sterol found in plant oils and is abundant in soya bean and rape seed oil. Many health benefits have been attributed to this compound including anti-cholesterolemic activity, anticancer activity, as well as anti-inflammatory properties. In 2008, Backhouse *et al.* published an article in the Journal of Ethnopharmacology, entitled 'Analgesic, anti-inflammatory, and antioxidant properties of *Buddleja globosa*, Buddlejaceae'. Buddlejaceae is a plant native to Chile and has been used for generations in the treatment of inflammatory illness. The plant is colloquially known as 'matico' ('Matico' is the name of the Spanish soldier who accidentally discovered the properties of the leaves when wounded in Peru.). The research has focused on establishing the bioactivity of plant extracts, the team demonstrates that the fractions that are rich in stigmasterol and β -sitosterol display anti-inflammatory properties.^[5] A very recent study indicates that stigmasterol inhibits several pro-inflammatory mediators typically involved in osteoarthritis.^[6]

Thus, the findings and conclusions of Mustaffa *et al.*^[2] in the last issue of this journal are well-founded and are strongly corroborated by the findings of many other research groups investigating other plant species.

Another article in the previous issue that deals with the treatment of inflammatory disorders is that of Abotsi *et al.*^[7] The plant of interest in this article is the native African *Ficus exasperata* of the *Moraceae* family and it is frequently used in Ghanaian traditional medicine. The authors have used Freund's adjuvant-induced arthritis model in rats, to determine the anti-inflammatory properties of the ethanolic leaf extracts of the plant and suitable bioassays to determine the antioxidant properties. The authors cite studies that have indicated that free radicals and reactive oxygen species (ROS) play a big role in the pathogenesis of rheumatoid arthritis.^[8] Abotsi *et al.* have found that the extract possesses both anti-arthritic and anti-oxidant properties.^[7] A recent and informative study conducted by Adebayo *et al.* has found that the major constituents of *F. exasperata* include tannins, flavonoid, saponins, Phlobatannins, glycosides, and steroids, with no traces of alkaloids or anthraquinones present in the extracts.^[8] The presence of phenolic compounds are usually associated with beneficial effects in humans, as they can act as antioxidants capable of neutralizing free radicals.

Again drawing Irish parallels, a plant that is used traditionally in Ireland and Britain to combat pain and inflammation is Meadowsweet (*Filipendula*); its use has been traced back as far as the Druids.^[9] The plant is often brewed as a tea.

The main chemical constituents of meadowsweet are essential oil (salicylaldehyde, methylsalicylate, hyperoside), salicylic acid, spireine, gaultherine, spiraeoside, flavonoids (rutin, spiraeoside), vanillin, glycoside, mucilage, tannin, coumarins, and vitamin C. The presence of aspirin-like compounds, which it has in common with willow bark extract, explains its analgesic and anti-inflammatory effects.^[10] However, unlike aspirin, which can aggravate stomach ulcers, the constituents (natural buffering agents, including tannins and mucilages) that are co-extracted into water from meadowsweet, protect the lining of the stomach. This is also true of the willow bark extract.^[11]

A very interesting account in the previous issue is that of Singhai *et al.*, who investigates the targeted delivery of Curcumin (an herb rich in curcuminoids, which are polyphenols), a constituent of turmeric, a spice commonly used in Indian cookery. Curcumin is used in the treatment of colon cancer. *In vitro* and *in vivo* studies to-date have indicated that curcumin may have antitumor effects,^[12,13] antioxidant activity,^[14] and anti-inflammatory properties.^[15]

However Singhai *et al.* acknowledged that the colon was a difficult site to target in terms of the precise delivery of drugs. Their object, therefore, was to investigate a guar gum-based formulation (tablet) that would carry the curcumin at therapeutic levels to the colon and target the release of the drug at the desired location. To this end, the authors evaluated various tablet parameters including hardness, drug uniformity, and *in vitro* drug release characteristics in order to optimize the formulation. The tablets were produced using the wet granulation method, with guar gum and lactose, talc, starch paste, and 2% Sodium Lauryl Sulfate as suitable excipients. The efficacy (bioavailability) was tested using a rat model. The authors demonstrated that guar gum was in fact a highly suitable matrix for the delivery of curcumin to the colon, as the highly branched structure of the guar gum polymer resists enzymatic breakdown in the upper GIT and facilitates targeted release, to allow for both local and systemic action.

Returning to the treatment of inflammatory diseases in last month's issue of Pharmacognosy, research studies by Kumar *et al.* indicates that an aqueous extract of the bark of *Ailanthus excelsa*, commonly found in Asia and North Australia, and known as 'a plant of Heaven' has bronchodilator properties. This plant is known to contain several categories of bioactive phytochemicals including quassinoids, alkaloids, and terpenoids.^[16]

Quassinoids in particular are quite a unique and very interesting group of compounds; they are degraded and highly oxygenated triterpenes. They are found in plants belonging to the *Simaroubaceae* family.^[17] The quassinoids

have been shown to possess a wide array of bioactivities including anti-tumor, anti-malarial, and anti-inflammatory, among others; unfortunately some members of the quassinoids exhibit high toxicity.^[18] Kumar and co-workers have used a number of rat and mouse models to illustrate that extracts from *A. excelsa* could potentially be used to treat and prevent asthma attacks. In fact Kumar *et al.* have not isolated the compound(s) responsible for inducing bronchodilation and have recommended that further research must involve such a study.^[19]

In Ireland some of the common herbs used for the treatment of asthma are the more universal herbs such as Sage, Inula, and Chondrus crispus, which although known commonly as Irish moss grow abundantly along the rocky areas of the Atlantic coast of Europe and North America.

In the current issue of this journal I was very interested in studies done by several research groups in finding plant-derived treatments that may be helpful in the fight against Type II Diabetes. Many Western countries regard the ever increasing numbers of individuals presenting with type II diabetes as a 'ticking time bomb'. Experts point to diets abundant in sugar and refined carbohydrates combined with lack of exercise as one of the main causes behind the dramatic increase in this illness among younger age profiles. These experts speculate that the disease, together with the associated co-morbidities, will have a tremendous impact on the quality of life of the sufferers as they age and that this will inflict a huge economic burden on many societies. As Western culture spreads and is embraced worldwide the problems of obesity, Type II diabetes, and associated debilitating illnesses are emerging in countries where heretofore they were not common. Laxmi Verma *et al.* in the current issue have demonstrated that ethanolic extracts of *Cassia occidentalis* Linn. (a common weed that grows in many regions 'from the foothills of the Himalayas to West Bengal' and in Southern India and Sri Lanka) was effective in reducing the fasting blood sugar levels in normal and alloxan-induced diabetic rats. Also in the current issue Mahesh Kumar *et al.* have demonstrated that aqueous and methanolic extracts of the common Indian plant *Salvia splendens* also known as 'scarlet sage' had the capacity to reduce blood sugar levels in streptozotocin (STZ)-induced diabetic rats, when administered orally. A third article in this journal by Karuna and co-workers discusses research that indicates that a leaf powder aqueous suspension of a shrub colloquially known as Madagaskar periwinkle (*Catharanthus roseus*) also demonstrates glucose lowering properties, in normal and STZ-induced diabetic rats.

The use of plant extracts and preparations is very useful, not only for the treatment of diabetes but also presents a huge potential for their integration or incorporation into

foodstuffs (so called nutra-ceuticals) as a prophylactic intervention or 'an advance guard' measure to ameliorate the increasing incidents of diabetes worldwide (together with strong and effective public education campaigns to promote a healthy diet).

There has been much media attention lately on the real and apparent risks of conventional hormone replacement therapy (HRT) in dealing with menopausal symptoms. Reports that HRT can, in certain circumstances, increase the risk of breast cancer, heart disease, and stroke have made many women reluctant to embark on treatment regimes. There is increased demand among this demographic for alternative (safer) treatments. In this month's edition of Pharmacognosy Research, one article that especially caught my eye was on the research conducted by Aswar *et al.* that demonstrates the efficacy of a powder formulation, derived from a shrub native to the hot parts of India, Sri Lanka, Malaya, and West Africa, called *Cissus quadrangularis*, in alleviating the symptoms of menopause.

Finally I was very interested in the study presented in this issue by Annan *et al.*, who examined the concentration of a range of heavy metals in a selection of medicinal botanical formulations commonly used in Ghana. This type of study is very important, as quality control is vital (and often forgotten), in the field of alternative medicine. There is often complacency on the part of the public (and sometimes on the part of producers) with regard to 'herbal' medicines that would not be tolerated in the pharmaceutical or food and beverage industry. Profiling of contaminants and of harmful naturally occurring compounds in plant materials intended for human consumption is paramount in ensuring safety.

Almost all of the articles in Pharmacognosy Research, which are concerned with the scientific investigation of a given herb (its bioactivity or its chemical composition), have in their introductions a statement regarding the herb's 'traditional' use. Many authors cite the fact that the herb has been used for many generations as appropriate treatments for various illnesses. The World Health Organization (WHO) has defined traditional medicine thus: "Traditional medicine is the sum total of knowledge, skills, and practices based on the theories, beliefs, and experiences indigenous to different cultures that are used to maintain health, as well as to prevent, diagnose, improve or treat physical and mental illnesses."^[20]

If we 'read between the lines' we see that the statement from the WHO acknowledges indigenous traditions. I think we, as scientists, owe a debt of gratitude to our forbearers who accumulated and passed down this information that we may now apply our 'tools' and technologies to investigate

and for the most part verify that their knowledge was correct.

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