

## Role of Medicinal Plants in Modern Medicine

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**ABSTRACT** The use of plants, plant extracts or pure chemicals isolated from natural products to treat disease is a therapeutic modality, which has stood the test of time even if much of the science behind such therapy is still in its infancy. Indeed today many pharmacological classes of drugs include a natural product prototype. Morphine, digoxin, quinine, atropine, reserpine, physostigmine, pilocarpine, vincristine, vinblastine, artemisinin and taxol are a few examples of what medicinal plants have given us in the past. Some active principles have limited application in modern medicine but are invaluable as pharmacological "tools" for evaluating the mode of action of other drugs or investigation of basic physiological function. Some examples are atropine, muscarine, nicotine, cocaine, reserpine, yohimbine and himbacine. The modern medicine is now beginning to accept the use of botanicals once they are scientifically validated. *Ispaghula*, *Garlic*, *Ginkgo*, *St. John's Wort*, *Saw palmetto* are a few examples of botanicals which are gaining popularity amongst modern physicians. The number of plants that still have not been studied for content of biologically active compounds is vast. Only 3-5% of terrestrial plants have been reasonably well investigated and hence there is huge potential on research on medicinal plants. Teamwork amongst ethnobotanists, Ethnopharmacologists and Phytochemists is essential for the fruitful outcome on medicinal plants research.

(Medicinal plants, ethnopharmacology, modern medicine)

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### HISTORICAL ASPECTS

According to the world health organization (WHO), about three-quarters of the world population relies upon traditional remedies (mainly herbs) for the health care of its people. In fact, herbs/plants are the oldest friends of mankind. They not only provided food and shelter but also served the humanity to cure different ailments. The herbal medicine also sometime called as, traditional or natural medicine existed in one way or another in different cultures/civilizations, such as Egyptians, Western, Chinese, Kampo (Japan) and Greco-Arab or Unani/Tibb (south Asia).

Historians from all around the world have produced evidence to show that apparently all primitive peoples used herbs-often in a sophisticated way. Quinine from *Cinchona* bark was used to treat the symptoms of malaria long before the disease was identified and the raw ingredients of a common or garden aspirin tablet have been a popular painkiller for far longer than we have had access to tablet-making machinery.

By the middle of the nineteenth century at least 80 per cent of all medicines were derived from herbs. Then came the revolution inspired by the development of the pharmaceutical industry and synthetic drugs dominated, though herbal medicine has never been out of scene. Even today if you walk into any pharmacy in the West, you will find at least 25 % plant-derived drugs. Indeed today many pharmacological classes of drugs include a natural product prototype. Morphine, digoxin, quinine, quinidine, atropine, reserpine, physostigmine, pilocarpine, vincristine, vinblastine, taxol and artemisinin are a few examples of what medicinal plants have given us in the past. Most of these plant-derived drugs were originally discovered through the study of traditional cures and folk knowledge of indigenous people, some of these could not be substituted despite the enormous advancement in synthetic chemistry.

Morphine isolated from *Papaver somniferum* is one of the early molecules entered into modern medicine as a narcotic analgesic drug. Only the cancer patients suffering from terminal pain can appreciate the value of morphine, which remains

drug of choice today despite its abuse potential. Indeed, the isolation of morphine from crude opium by Serturmer in 1806 stimulated so much wide-spread research on the vegetable drugs that Megendie was able to publish a medical formulary in 1821 which contained only pure chemical agents, hence laid the foundation for the use of pure chemicals as the alternative to the botanicals.

One of the important areas in which compounds from plant sources have contributed successfully is cardiovascular research [1]. Digitalis and the cardiac glycoside derived from the foxglove (*Digitalis purpurea*) are perhaps the classic example. They represent a widely used group of clinically effective compounds which produce positive inotropic effect on the failing heart as well as having value in the treatment of atrial fibrillation. As a group they are unrivalled to date by any synthetic or semi-synthetic substitutes even though they are among the most toxic group of clinically useful drugs and have unique mode of action with selective cardiotoxic activity, without accompanying tachycardia [2].

A second discovery of cardiovascular activity in natural products led to the isolation of reserpine over five decades ago [1]. Reserpine, obtained from the roots of the Indian plant *Rauwolfia serpentina*, was brought to the attention of the modern Western world in 1949 by Vakil who described its use in hypertension; in rapid succession between 1952 and 1958, reserpine was isolated from *Rauwolfia*, its structure determined and its total synthesis achieved [3]. The indiscriminate use of reserpine as an antihypertensive agent and tranquilizer led to reports of depression and Parkinsonism effects. These findings stimulated further investigation and evidence was found that reserpine depleted not only brain serotonin but also nor-epinephrine and dopamine [4]. This was a major stimulus for continued research on transmitter amine defects in depression and Parkinson's disease. This in part laid the foundation for the development of many of the modern psychoactive drugs and stimulated a significant interaction between researchers and drug industry.

As the adverse effects of reserpine continued to be revealed through clinical research, interest in the product gradually diminished, particularly when safer antihypertensive drugs were made available, though reserpine is still used in clinical medicine, particularly in low-income population. There is a

revival of interest in its use based on some recent clinical trials, which showed that lower doses of reserpine (0.05-0.1 mg) combined with low doses of thiazide diuretic and hydralazine provides highly effective blood pressure lowering regimen along with renal protective effect; free from conventional side effects and is perhaps the most cost-effective antihypertensive treatment available today [5, 6].

This development of reserpine clearly illustrates the fundamental scientific principle that drugs, in addition to being therapeutic, become tools for further understanding of disease and hence design of new drugs. Other compounds, which are considered invaluable pharmacological "tools" for evaluating the mode of action of other drugs or investigation of basic physiological function, include muscarine and nicotine (pioneer selective agonists for muscarinic and nicotinic receptors respectively), cocaine (catecholamine uptake inhibitor) yohimbine (selective  $\alpha_2$  blocker) and himbacine, a prototype of cardio-selective antimuscarinic agents [1, 7].

#### REVIVAL OF INTEREST IN PHYTOMEDICINE

Despite the increasing interest of public in phytomedicine, very few drugs from higher plants have attained any prominence in conventional medical practice in the last couple of decades. The most notable example is Taxal, a diterpenoid originally obtained from the bark of the Pacific yew tree (*Taxus brevifolia* Nutt.). However, even this effective anticancer agent is now produced by semi-synthesis from a precursor occurring in the needles of the common yew (*Taxus baccata* L.), a rapidly renewable source [8]. Instead, major progress in the last decade has been in the field of phytomedicine, also referred to as botanicals or herbal medicine. In Germany and many European countries, these products are classified as drugs; in USA they are sold as dietary supplements.

Certainly one can see clear evidence of revival of interest in phytomedicine at a global level, the revival which has been so dramatic that sales of herbal products in the world worth staggering over 100 billions dollars a year. There are several specific reasons for this revival in the fortunes of herbalism.

First, there is a massive 'back-to-nature' movement in the Western World - inspired at least in part by the fact that a growing number of people are aware of and frightened of the side-effects associated with chemical drugs.

Second, there are many medical disorders, such as, arthritis, diabetes, hypertension, asthma etc., for which there is no complete cure despite remarkable advancement in science and treatment in orthodox medicine requires the life-long use of expensive drugs mainly for the symptomatic relief.

Third, there is a widespread feeling abroad that the individual should retain responsibility, for his/her own health. It is easier to retain responsibility if you are not taking pills, which have been prescribed for you by someone else.

Fourth, those who promote and sell herbal remedies have managed somehow to convince their potential customers that herbal remedies are entirely safe, which may not necessarily be true.

Fifth, there is recognition of traditional medical systems, particularly of Asian origin, and the identification of medicinal plants from indigenous pharmacopoeias that have shown to have significant healing power, either in the natural state or as the source of new pharmaceuticals.

Whatever the reasons may be for the rise in popularity of herbal medicine, the fact remains that there are today millions of people who use herbal products regularly and the number is growing every day. Compared to the other Alternate practices, such as acupuncture, homeopathy, hypnotherapy, chiropractic, yoga, etc., Herbal Medicine is the most widely used system and closest to the Modern Medicine, in terms of application to a wide variety of diseases and the way it treats disease. It has maximum contribution in modern medicine [1, 9].

In fact, the modern medicine is now beginning to accept the use of botanicals once they are scientifically validated. *Ispaghula*, *Garlic*, *Gingko*, *Gensing*, *St. John's Wort* and *Saw palmetto* are a few examples of botanicals which are gaining popularity amongst modern physicians. Similarly, scientific studies on medicinal plants and the impact factor of the journals publishing such research are growing

with rapid pace. For example, the impact factors of *Fitoterapia* and *Journal of Ethnopharmacolog*, *Phytotherapy Research* and *Phytomedicine* have been increased to double in the last couple of years. One can imagine the popularity of herbal medicine in the west from the fact that an *American Journal of Chinese Medicine* exists in the literature. Thus there is a huge potential of medicinal plants in healthcare of not only in developing countries but also in the industrialized world and the acceptance of botanicals in modern medicine is likely to be increased in the years to come. Teamwork amongst ethnobotanists, Ethnopharmacologists and Phytochemists is essential for the fruitful outcome on medicinal plants research and the role of the phytochemists will obviously shift slightly towards the standardization of botanicals.

East is already well known for its adherence to herbal medicine and China and India are two leading countries in this regard. Even in the western world, popularity of the phytomedicine is increasing at a rapid pace. Germany is the most advanced country in the West in the use of herbal products and shares about 50 % of the total European market of herbal drugs and over 70 % of German Physicians prescribe herbs [10]. German physicians now use *St. Johns Wort* more commonly in mild to moderate depression than a popular modern drug, fluotoxine. In USA a large Center of Complimentary and Alternate Medicine has been established recently at the NIH, with heavy funding [11].

#### TRADITIONAL MEDICINE IN THE MUSLIM WORLD

The traditional system of medicine in the Muslim world including Pakistan is referred to as *Unani* or *Greco-Arab* system of medicine (Unani meaning Greek). *Tibb* and *Hikmat*, the two words are also popularly known for the traditional system of medicine in Pakistan and in Arabic speaking countries. Actually these two words are of Arabic origin, *Tibb* means medicine, *Hikmat* meaning the doctrine of medicine. In addition to the exclusive use of herbs in treating the disease, unique herbo-mineral preparations, locally known as "Kushta(s)" are also used in south Asia [12].

The origin of Greek medicine can be traced back to *Aesculapius*, *Galen*, *Hippocrates*, *Dioscorides* and many more who enormously contributed to

the many virtues of herbal medicines. Greek medicine found its votaries among Arabs who developed the traditional medicine manifold; the prominent among them are *Rhazes, Avicenna, Al-Idrisi, Ibn Al-Baitar, Ali Ibn Rabban, Ibn Al-Nafis*, and others. They preserved and gave impetus to the art of learning and practice of traditional medicine. This system of medicine flourished for centuries in Middle East, Southeast and Central Asia. It is for this reason; this system of medicine has been referred to as Greco-Arab medicine. With the spread of Islam from the Arab peninsula to the areas as far as Spain on one side, and on the other side through Iran, Indo-Pakistan, Afghanistan, Central Asian regions, Malaya and up to Indonesia, the Greco-Arab complexion of traditional medical system in the largest context has also been designated to as *Islamic System of Medicine* or the *Eastern or Oriental System of Medicine* to distinguish with the system of medicines in vogue in the west i.e. allopathy and homeopathy (Germany being the home town for homeopathy).

No deliberation on the science of medicine can be complete without a reference to the most famous book of medicine, *al-Qanun fi al-Tibb*, known as "Canon" in the west written by famous Arab physician, scientist and philosopher, Ibn Sina (981-1037 C.E.), known as, Avicenna in the west. This book is an immense encyclopedia of medicine and remained supreme for six centuries because of its systematic approach, formal perfection as well as intrinsic value. British Pharmacology Society (BPS) recently decided to publish regularly in its Bulletin the postage stamps that portray famous physicians. Interestingly, the old famous stamp on herbal medicine issued by Pakistan Post with an image of Ibn Sina, occupied first place in this series [13].

The Greco-Arab system of herbal medicine is based on the philosophy that believed in the individualized treatment considering the genetic variations amongst the individuals, synonymous to different blood groups in different individuals. According to this philosophy, the different treatment options suit to different individuals, which is similar to the concept of Pharmacogenetics in modern medicine? A world-renowned expert on Pharmacogenetics stated at the European meeting of Pharmacologists that if the modern physicians would have considered pharmacogenetic differences at the time of

prescribing, with drawl of some useful drugs from the market could have been easily avoided [14]. Thus the old concept that it is not the "safe medicine", rather the safe physician or the safe use is getting strength. In fact, the concept of side effects and the individualized treatment is perhaps more effectively elaborated in the Greco-Arab system (Tibb), where even herbal products, like ispaghula (which is considered probably the safest by the modern physicians) is not necessarily free from side effects, rather known to rarely cause numbness or impotence (unless combined with honey) if used regularly by the older people in the cold weather.

### ISPAGHULA BRINGS TRADITIONAL AND MODERN MEDICINE CLOSER

There is enormous contribution of traditional practices in the modern medicine however practitioners of the two systems still keep distance. Most physicians of the modern medicine believe that only pure compounds are acceptable in modern medicine without realizing that the modern medicine accepts even the herbal drugs in natural form, once scientifically validated. For example, psyllium husk or ispaghula (seed husk of *Plantago ovata*) is a crude plant material but extensively used by practitioners of modern medicine, as its efficacy in chronic constipation has been proven [15]. Herbalists on the other hand are reluctant to use the pure compounds, even isolated from plants, as they believe that the plant-derived pure compound loses its identity and no more natural or represent the herb in natural form, rather are like any synthetic chemical. They believe that the herbs in natural form contain multiple components and act in synergy or neutralize the side effects. This may be true but needs to be scientifically validated.

We recently found that ispaghula, which has been traditionally, used both in constipation and diarrhoea (two opposite disease states of the gut) has scientific explanation. It was interesting to see that in addition to the known fiber content, it contains both gut stimulatory and inhibitory chemicals, which become more effective in the constipated and hyperactive gut respectively [16]. Studies on possible mechanism revealed that the stimulatory component is partially cholinergic and the inhibitory is mediated through blockade of calcium channels. This is a unique combination, as the relaxant component seen at higher doses, does not allow the stimulatory response to reach beyond certain limit, which would otherwise be harmful.

Interestingly, ispaghula has also been used traditionally in amoebic dysentery and we provided 1<sup>st</sup> evidence that it also contain chemical(s) with antiamoebic activity, concentrated in the organic fraction [17]. In fact, no patented medicine can be claimed to be better than ispaghula in chronic constipation.

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