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Therapeutic Potential of Medicinal Plants: A Review

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ABSTRACT: Plants have been well documented for their medicinal uses for thousands of years and traditional medicines are still a major part of habitual treatments of different maladies in different parts of the world. In recent years, there has been growing interest in alternative therapies and the therapeutic use of natural products, especially those derived from plants. Plants are considered as one of the main sources of biologically active materials. Phytochemical screening of medicinal plants has contributed a great deal for the discovery of new drugs. A number of medicinal plants have been subjected to detailed chemical investigations and this has led to the isolation of pure bioactive molecules which have been pharmacologically evaluated. As a result, new drugs have been discovered, along with new applications.

Keywords: Medicinal Plants; Therapeutic Potential; Traditional Knowledge; Pharmaceutical; Natural Products.

INTRODUCTION: The therapeutic use of herbs is as old as human civilization and has evolved along with it. Local practitioners have used indigenous plants and herbs for centuries all over the world to treat a variety of ailments and these have exhibited clear pharmacological activities. Historically, herbal drugs were used as tinctures, poultices, powders and teas followed by formulations, and lastly as pure compounds. Across the cultures, knowledge about use of medicinal plants exists in the form of local folklore available with families, tribes and cultures, handed down from generation to generation. Medicinal plants or their extracts have been used by humans since time immemorial for different ailments and have provided valuable drugs such as analgesics (morphine), antitussives (codeine), antihypertensives (reserpine), cardiotonics (digoxin), antineoplastics (vinblastine and taxol) and antimalarials (quinine and artemisinin). Medicinal plant drug discovery continues to provide new and important leads against various pharmacological targets including cancer, malaria, cardiovascular diseases and neurological disorders (Ramawat et al., 2009).

Plants have proven to be a novel source for bioactive natural products. They have evolved and adapted over millions of years to withstand bacteria, insects, fungi and weather to produce unique, structurally diverse secondary metabolites. Their ethnopharmacological properties have been used as a primary source of medicines for early drug discovery (McRae et al., 2007; Fellows and Scofield, 1995). According to the World Health Organization (WHO), 80% of people still rely on plant-based traditional medicines for primary health care (Farnsworth et al., 1985) and 80% of the plant derived drugs were related to their original ethnopharmacological purpose (Fabricant and Farnsworth, 2001). Natural products have been used since ancient times and in folklore for the treatment of many diseases and illnesses (Dias et al., 2012). They have been the source of most of the active ingredients of medicines. This is widely accepted to be true when applied to drug discovery in 'olden times' before the advent of high-throughput screening and the post-genomic era (Sneader, 1996).

In spite of the recent domination of the synthetic chemistry as a method to discover and produce drugs, the potential of bioactive plants or their extracts to provide new and novel products for disease treatment and prevention is still enormous (Raskin et al., 2002). The persistence of killer diseases like diabetes and arthritis, coupled with the harmful side effects of synthetic drugs, prompted a shift in interest from allopathy to natural/alternative systems of medicine. Compared with chemical synthesis, plant derived natural products represent an attractive source of bio-

logically active agents since they are natural and available at affordable prices (Ghosh et al., 2008). Also plants derived agents may have different mechanisms than conventional drugs, and could be of clinical importance in health care improvement (Eloff, 1998).

Many natural products and synthetically modified natural product derivatives have been successfully developed for clinical use to treat human diseases in almost all therapeutic areas (Newman and Cragg, 2007). In 1805, morphine became the first pharmacologically active compound to be isolated in pure form from a plant, although its structure was not elucidated until 1923. The 19th century marked the isolation of numerous alkaloids from plants used as drugs, namely, atropine (*Atropa belladonna*), caffeine (*Coffea arabica*), cocaine (*Erythroxylum coca*), ephedrine (*Ephedra* species), morphine and codeine (*Papaver somniferum*), pilocarpine (*Pilocarpus jaborandi*), physostigmine (*Physostigma venenosum*), quinine (*Cinchona cordifolia*), salicin (*Salix* species), theobromine (*Theobroma cacao*), theophylline (*Camellia sinensis*), and (+)-tubocurarine (*Chondodendron tomentosum*). Following these discoveries, bioactive secondary metabolites from plants were later utilized more widely as medicines, both in their original and modified forms (Salim et al., 2008).
Medicinal plants are rich in secondary plant products, and it is because of these compounds that these are termed 'medicinal' or 'officinal' plants. These secondary metabolites exert a profound physiological effect on mammalian systems; thus they are known as the active principle of plants. With the discovery of the physiological effect of a particular plant, efforts are being made to know the exact chemical nature of these drugs (called active principle) and, subsequently, to obtain these compounds by chemical synthesis (Ramawat, 2007)). At present there are 125 clinically useful drugs of known constitution which have been isolated from about 100 species of higher plants. It has been estimated that about 5000 plant species have been studied in detail as possible sources of new drugs (Tantry, 2009). Since less than 10% of the world's biodiversity has been evaluated for potential biological activity, many more useful natural lead compounds await discovery with the challenge being how to access this natural chemical diversity (Cragg and Newman, 2005).

TRADITIONAL HEALTHCARE PRACTICES: Since prehistoric times, the treatment and cure of diseases has been one of the primary concerns of mankind (Tantry, 2009). The traditional medicine is increasingly solicited through the tradipractitioners and herbalists in the treatment of diseases. Traditional preparation comprises medicinal plants, minerals and organic matters etc. Herbal drug constitutes only those traditional medicines that primarily use medicinal plant preparations for therapy (Samy and Gopalakrishnakone, 2007). Phytomedicines are a major component of traditional system of healing in developing countries, which have been an integral part of their history and culture (Arif et al., 2009). Plants have formed the basis of sophisticated traditional medicine practices that have been used for thousands of years by people in China, India, and many other countries. Traditional medicine is the sum total of the knowledge, skills and practices based on the theories, beliefs and experiences indigenous to different cultures used in the maintenance of health, prevention of diseases and improvement of physical and mental illness. The use of traditional medicine is widespread and it is based on centuries-old practices based on beliefs and local traditions before the development and spread of modern scientific medicine. Before the realization that pharmacologically active compounds present in medicinal plants are responsible for their efficacy, the "doctrine of signatures" was often used to identify plants for treating diseases. For example, goldenrod with a yellow hue was used to cure jaundice, red-colored herbs were used to treat blood diseases, liverworts were used for liver diseases, pileworts for hemorrhoids, and toothworts for toothache (Sneader, 2005).

Traditional medicinal practices have formed the basis of most of the early medicines followed by subsequent clinical, pharmacological and chemical studies (Butler, 2004). Probably the most famous and well known example to date would be the synthesis of the anti-inflammatory agent, 'acetylsalicyclic acid' (aspirin) derived from the natural product and 'salicin' isolated from the bark of the willow tree *Salix alba* L. Investigation of *Papaver somniferum* L. (opium poppy) resulted in the isolation of several alkaloids including 'morphine', a commercially important drug, first reported in 1803. It was in the 1870s that crude morphine derived from the plant *P. somniferum*, was boiled in acetic anhydride to yield diacetylmorphine (heroin) and found to be readily converted to codeine (painkiller). Historically, it is documented that the Sumerians and Ancient Greeks used poppy extracts medicinally, whilst the Arabs described opium to be

addictive. *Digitalis purpurea* L. (foxglove) had been traced back to Europe in the 10th century but it was not until the 1700s that the active constituent 'digitoxin', a cardiotonic glycoside was found to enhance cardiac conduction, thereby improving the strength of cardiac contractibility. 'Digitoxin' and its analogues have long been used in the management of congestive heart failure and have possible long term detrimental effects and are being replaced by other medicines in the treatment of "heart deficiency" (Der Marderosian and Beutler, 2002). The anti-malarial drug 'quinine' isolated from the bark of *Cinchona succirubra* Pav. ex Klotsch, had been used for centuries for the treatment of malaria, fever, indigestion, mouth and throat diseases and cancer. Formal use of the bark to treat malaria was established in the mid 1800s when the British began the worldwide cultivation of the plant. 'Pilocarpine' found in *Pilocarpus jaborandi* (Rutaceae) is an L-histidine-derived alkaloid, which has been used as a clinical drug in the treatment of chronic open-angle glaucoma and acute angle-closure glaucoma for over 100 years. In 1994, an oral formulation of pilocarpine was approved by the FDA to treat dry mouth (xerostomia) which is a side effect of radiation therapy for head and neck cancers and also used to stimulate sweat glands to measure the concentrations of sodium and chloride (Aniszewski, 2007).

Medicinal plants are considered a repository of numerous types of bioactive compounds possessing varied therapeutic properties. The therapeutic potential of plants has been well explored over a very long time period (Raina et al., 2014). Knowledge of the medicinal plants used in the drugs of traditional systems of medicine (TSM) has been of great significance, especially as a lead for the discovery of new single-molecule medicines for modern system of medicine. To determine the chemical nature of such compounds, isolation of a substance in pure form using various separation techniques, chemical properties and spectral characteristics are a prerequisite for establishing its correct structure. Thus, medicinal plants are used in crude or purified form in the preparation of drugs in different systems. In countries like India, China and others with well-founded traditional systems of medicine, plant-based formulations occupy an important place in health management (Ramawat et al., 2009). Ethnobotanical and traditional usage of medicinal plants serves as a source of information for the isolation of active compounds, e.g. as direct therapeutic agents (D-tubocurarine from *Chondrodendron tomentosum*), as the starting drug for semisynthesis (diosgenin from *Dioscorea floribunda*), the model drug for new synthetic drugs (cocaine from *Erythroxylum coca*), for the synthesis of local anaesthetics and, lastly, as taxonomic markers for identification (Balunas & Kinghorn, 2005; Gurib-Fakim, 2006 and Wagle et al., 2007). Thus the ancient wisdom has been the basis of modern medicine and will remain as one important source of future medicine and therapeutics.

NATURAL PRODUCTS DERIVED FROM MEDICINAL PLANTS: Historically, the majority of new drugs have been generated from natural products (secondary metabolites) and from compounds derived from natural products (Lahlou, 2007). Natural products have long been a thriving source for the discovery of new drugs due to their chemical diversity and ability to act on various biological targets (Bhutani and Gohil, 2010). Most natural products are compounds derived from primary metabolites such as amino acids, carbohydrates and fatty acids and are generally categorized as secondary metabolites. The biosynthesis and breakdown of proteins, fats, nucleic acids and carbohydrates, which are essential to all living organisms, is known as primary metabolism with the compounds involved in the pathways known as *"primary metabolites"*. Secondary metabolites are considered products of primary metabolism and are generally not involved in metabolic activity viz. alkaloids, phenolics, essential oils and terpenes, sterols, flavonoids, lignins, tannins, etc. (Ramawat et al., 2009). The mechanism by which an organism biosynthesizes compounds called *'secondary metabolites'* (natural products) is often found to be unique to an organism or is an expression of the individuality of a species and is referred to as "*secondary metabolism*" (Maplestone et al., 1992). Secondary metabolites are produced either as a result of the organism adapting to its surrounding environment or are produced to act as a possible defense mechanism against predators to assist in the survival of the organism (Colegate, S.M.; Molyneux, 2008). The biosynthesis of secondary metabolites is derived from the fundamental processes of photosynthesis, glycolysis and the Krebs cycle to afford biosynthetic intermediates which, ultimately, results in the formation of secondary metabolites also known as natural products. The most important building blocks employed in the biosynthesis of secondary metabolites are those derived from the intermediates: Acetyl coenzyme A (acetyl-CoA), shikimic acid, mevalonic acid and 1-deoxyxylulose-5-phosphate.

They are involved in countless biosynthetic pathways, involving numerous different mechanisms and reactions (e.g., alkylation, decarboxylation, aldol, Claisen and Schiff base formation (Dewick, 2002). The majority of secondary metabolites are synthesized via two principal biosynthetic pathways: (1) shikimic acid pathway producing a pool of aromatic amino acids, which in turn are converted into diverse compounds such as phenolics (lignins, tannins, quinones) and alkaloids (Mustafa and Verpoorte, 2007), and (2) acetyl-CoA mevalonic acid pathway, leading to a vast array of terpenoids (Eisenreich et al., 2004).

Herbivory, pathogens and competition are the driving forces that induce plant species to develop chemical defense compounds. These plant origin compounds are good models for elucidation of their functional roles in medication and treatment of different afflictions (Wood-Sheldon et al., 1997). For example, the lignin in the roots of *Anthriscus sylvestris* showed an insecticidal activity (Kozawa et al., 1982). Poisonous plants exposed to frequent grazing by animals are commonly rich in alkaloids which have many biological activities including anticancer potential (Kintzios, 2006). However, the growth regulatory properties of some plant metabolites allow them to act as chemotherapeutical agents. Flavonoids from *Scutellaria baicalensis* act on cyclin-dependent kinases to inhibit cancer cell proliferation (Dai & Grant, 2003; Chang et al., 2004).

Natural products continue to provide unique structural diversity in comparison to standard combinatorial chemistry, which presents opportunities for discovering mainly novel low molecular weight lead compounds (Dias et al., 2012). One key feature of natural products is their enormous structural and chemical diversity. In fact, about 40% of the chemical scaffolds found in natural products are absent in today's medicinal chemistry, and therefore complementary to synthetically produced molecules. Most possibly this is one of the reasons for their historical success in drug discovery, with 45% of today's best selling drugs originating from natural products or their derivatives (Lahlou, 2013). A number of medicinal plants have been subjected to detailed chemical investigations for isolation of pure bioactive molecules which have been pharmacologically evaluated. This has led to the discovery of new drugs along with new applications (Table 1). These bioactive molecules are used as therapeutic agents, starting materials and new reagents for molecular biology research (Balunas, 2005; Lam, 2007; Mishra, 2008 and Phillipson, 2007).

The drug discovery process from plants is a laborious and time consuming process. The classical examples of drug discovery like morphine, quinine, digoxin, etc which replaced the extracts of their respective plants were mostly responsible for harbouring the idea that a single active ingredient must have been responsible for the bioactivity (Bhutani and Gohil, 2010). Once the medicinal plant is chosen for a single drug molecule based on a literature survey and known phytochemical relationships, the next step is its collection and botanical identification. The plant material is subjected to drying at ambient temperature in a shady place or in an oven with a controlled airflow and temperature. The dried or stabilised plant material should then be powdered to give a suitable mesh size and subjected to a suitable extraction process as per standard operating procedures. For bioactive studies, three extracts (alcohol, alcohol:water, 1:1 and water) are prepared and subjected to a preliminary screening programme. The extracts are subjected to standard chromatographic techniques of fractionation and isolation of bioactive molecules (Tantry, 2009).

'Arteether', introduced in 2000, as Artemotil is derived from 'Artemisinin' (introduced in 1987 as Artemisin) which was first isolated from the plant *Artemisia annua* and are both approved antimalarial drugs (Newman and Cragg, 2007). 'Grandisine A' and 'Grandisine B' are two indole alkaloids which were isolated from the leaves of the Australian rainforest tree, *Elaeocarpus grandis*. 'Grandisine A' contains a unique tetracyclic skeleton, while 'Grandisine B' possesses an unusual combination of isoquinuclidinone and indolizidine ring systems. Both 'Grandisine A' and 'Grandisine B' exhibit binding affinity for the human δ-opioid receptor and are potential leads for analgesic agents (Carroll et al., 2005). 'Galantamine hydrobromide' is an Amaryllidaceae alkaloid obtained from the plant *Galanthus nivalis* and has been used traditionally in Turkey and Bulgaria for neurological conditions and is used for the treatment of Alzheimer's disease (Howes et al., 2003; Heinrich and Teoh, 2004).

'Apomorphine' is a derivative of 'Morphine' isolated from the poppy (*P. somniferum*) and is a short-acting dopamine D_1 and D_2 receptor agonist, as well as a potent dopamine agonist, used to treat Parkinson's disease (Deleu et al., 2004). 'Tubocaurarine' isolated from the climbing plant, *Chondrodendron tomentosum* (Menispermaceae) is one of the active constituents used as a muscle relaxant in surgical operations, reducing the need for deep anesthesia (Dewick, 2002).

Thirteen distinct groups of plant-derived natural products with antitumor properties were documented (Kintzios, 2006). Among them, alkaloids (Facchini, 2001), phenylpropanoids (Dixon & Paiva, 1995) and terpenoids (Trapp & Croteau, 2001) are well known for their antitumor potentials.

It is estimated that 60 % of anti-tumour and anti-infectious drugs already on the market or undergoing clinical trials are of natural origin (Hamburger and Hostettmann, 1991). The most widely used breast cancer drug 'Paclitaxel' (Taxol®) is isolated from the bark of *Taxus brevifolia* (Pacific Yew). The bark from about three mature 100 year old trees is required to provide 1 gram of Taxol® given that a course of treatment may need 2 grams of the drug. Taxol® is present in limited quantities from natural sources, its synthesis (though challenging and expensive) has been achieved (Nicolaou et al., 1994). Baccatin III present in much higher quantities and readily available from the needles of *T. brevifolia* and associated derivatives is an example of a structural analogue that can be efficiently transformed into Taxol® (Dewick, 2002). Other examples of antitumor compounds currently in clinical trials include 'Ingenol 3-*O*-angelate' a derivative of the Polyhydroxy diterpenoid ingenol isolated from the sap of *Euphorbia peplus* (known as "*petty spurge*" or "*radium weed*") which is a potential chemotherapeutic agent for skin cancer (Kedei et al., 2004; Ogbourne et al., 2004). 'PG490-88' (14-succinyl triptolide sodium salt), a semisynthetic analogue of triptolide is a diterpene-diepoxide isolated from *Tripterygium wilfordii* which is used for autoimmune and inflammatory diseases in the People's Republic of China (Kiviharju et al., 2002; Fidler et al., 2003). 'Combretastatin A-4 phosphate' a stilbene derivative from the South African Bush Willow, *Combretum caffrum* acts as an anti-angiogenic agent causing vascular shutdowns in tumors (Newman and Cragg, 2005; Holwell et al., 2002).

Despite the advantages and the past successes, many large pharmaceutical companies decreased the use of natural products in drug discovery screening in last few decades. This has been because of the perceived disadvantages of natural products (difficulties in access and supply, complexities of natural product chemistry and inherent slowness of working with natural products, and concerns about intellectual property rights), and the hopes associated with the use of collections of compounds prepared by combinatorial chemistry methods (Harvey, 2008). The process in natural product drug discovery usually required several separation circles and structure elucidation and was thus time consuming. However, Drug discovery from natural products has reclaimed the attention of the Pharma industry and is on the verge of a comeback due to new technological inputs that promise better returns on investment. In addition to their chemical structure diversity and their biodiversity, the development of new technologies has revolutionized the screening of natural products in discovering new drugs. Applying these technologies compensates for the inherent limitations of natural products and offers a unique opportunity to re-establish natural products as a major source for drug discovery. An integrative approach by combining the various discovery tools and the new discipline of integrative biology will surely provide the key for success in natural product drug discovery and development. Natural products can be predicted to remain an essential component in the search and development for new, safe and economical medicaments (Lahlou, 2013).

Table 1: Important Bioactive Molecules from Medicinal Plants and Their Biological Activity.

Drug	Plant	Biological Activity
Achyranthine	*Achyranthes aspera*	Diuretic
Aegelin, Marmelosin	*Aegle marmalos*	Bowel diseases
Ajmalicine	*Rauwolfia canesocence*	Hypotensive
Allicin	*Allium sativum*	Hypolipidemic
Aloin	*Aloe vera*	Demulcent, Skin diseases
Andrographolide	*Andrographis paniculata*	Hepatoprotective
Arboreol	*Gmelina arborea*	Tonic, Stomachic
Artemisinin	*Artemisia annua*	Antimalarial
Asiaticoside	*Centella asiatica*	Memory enhancer

Asparanin A, Asparanin B, Sarasapogenin	*Asparagus adscendens*	Fertility enhancer
Atropine	*Solanaceae spp.*	Anticholinergic
Bacoside	*Bacopa monneri*	Memory enhancer
Berberine	*Berberis lycium*	Antiemetic
Boeravinones	*Boerrhavia diffusa*	Hepatoprotective
Boswellic acid	*Boswellia seratta*	Antiinflammatory
Caffeine	*Camellia sinensis*	CNS stimulant
Camphor	*Cinnamomum camphora*	Aromatic
Camptothecin	*Camptotheca acuminata*	Anticancer
Capsiacin	*Capsicum annum*	Counter irritant
Cocaine	*Erythroxylum coca*	Analgesic
Codeine	*Papaver somniferum*	Anaesthetic
Colchicine	*Colchicum luteum*	Antiinflammatory
Conessine	*Holarrhena antidysentrica*	Antiamoebic
Curcumin	*Curcuma longa*	Antioxidant
Curcumin	*Curcuma longa*	Antioxidant
Diosogenin	*Dioscorea deltoidea*	Base for steroids
Embelin	*Embelia ribes*	Anthelmintic
Emetine	*Cephaelis ipecacuanha*	Antiamoebic
Ephedrine	*Ephedrae herba*	Hypertensive
Ergotamine	*Claviceps purpurea*	Hemorrhage
Etoposide/Tenopside	*Podophyllum hexandrum*	Anticancer
Forskolin	*Coleus forskolin*	Cardiotonic
Galanthamine	*Leucojum aestivum*	Anticholinesterase
Glycyrrhizin	*Glycyrrhiza glabra*	Antiviral
Gossypol	*Gossypium herbaceum*	Contraceptive
Guggulsterones/Gugallipid	*Commiphora wightti*	Hypocholeromic
Hydroxy citric acid	*Garcinia cambogia*	Antiobesity agent
Hyoscine /Hyoscyamine	*Hyoscyamus niger / H. muticus*	Parasympatholetic
Hypericin	*Hypericum perforatum*	Anti-HIV
Ipecac	*Cephaelis angustifolia*	Emetic
Liquiritigenin, Isoliquiritigenin	*Pterocarpus marsupium*	Anti-diabetic
Lycopene	*Lycopersicon esculentum*	Antioxidant
Methoxsalen	*Ammi majus/Heracleum candicans*	Leucoderma
Monoterpenes, Sesquiterpenes	*Ocimum sanctum*	Respiratory diseases, Immunomodulatory
Morphine/Papaverine	*Papaver somniferum*	Sedative
Polyphenolics, Tannins	*Phyllanthus emblica*	Antioxidant

Protodioscin	*Tribulus terrestris*	Diuretic, Anabolic, Aphrodisiac
Psoralen	*Psoralea corylifolia*	Antileucoderma
Quinine/Quinidine	*Cinchona officinalis*	Antimalarial
Reserpine	*Rauwolfia serpentina*	Hypotensive
Sennoside	*Cassia angustifolia*	Laxative
Shatavarin	*Asparagus racemosus*	Galactogogue, Tonic
Silymarin	*Silybium marianum*	Hepatoprotective
Strychnine	*Strychnose nux-vomica*	Central stimulant
Taxol	*Taxus wallichiana*	Anticancer
Tinosporic acid, Cordifolioside	*Tinospora cordifolia*	Immunomodulatory
Trigonellin	*Trigonella foenum-graecum*	Anti-diabetic
Tubocurarine	*Chondodendron tomentosum*	Muscle relaxant
Tylophorine	*Tylophora indica*	Bronchodilator
Vasacine	*Adhatoda vasica*	Vasodilatory
Vinblastine/ Vincristine	*Cathranthus roseus*	Anticancer
Valepotriates	*Valeraina wallachi*	Sedative
Withanolides	*Withania somnifera*	Immunomodulatory

Source: Tantry, 2009; Bhutani and Gohil, 2010

CONCLUDING REMARKS: Medicinal plants have been a source of wide variety of biologically active compounds for many centuries and used extensively as crude material or as pure compounds for treating various disease conditions. Plant-based Natural products have been recognized for many years as a source of therapeutic agents. These have played a vital role in the discovery of new chemical entities for drug discovery. There is a growing upsurge in demand for herbal and other traditional remedies for curing various ailments among different communities throughout the world. Detailed screening of medicinal plants is required for the discovery and development of novel bioactive agents that would help in reducing human sufferings.

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