Review of Literature
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Civilized societies have bequeathed myths and compendiums of healing herbs and the herbal remedies from people of preliterate societies continue to surprise us with their extensive green pharmacy (Balick, 1996; Cox, 1994). The herbal healing lore was passed from generation to generation by word of mouth. Biodiversity of natural resources like plants, animals, microbes, minerals and marine sources has served not only the primary human needs but also health care since time immemorial (Patwardhan et al., 2004).

Even in ancient cultures, people methodically and scientifically collected information on herbs and developed well-defined herbal pharmacopoeias. Perhaps one of the earliest pharmacopoeias is the De Materia Medica (79 A.D) by the Greco-Roman military physician Dioscorides in the 1st century A.D (Ackerknecht, 1973). Later, in the second century of the present era, Galen (131, 201 A.D.) shaped pharmaceutical practice for centuries to come (Christopher, 2002). Indeed, well into the 20th century much of the pharmacopoeia of scientific medicine was derived from the herbal lore of native people.

The entire Middle East has a rich history of herbal healing. There are texts surviving from the ancient cultures of Mesopotamia, Egypt and India that describe and illustrate the use of many medicinal plant products. The Ebers Papyrus, the most important of the preserved Egyptian manuscripts, was written around 1500 B.C. and includes much earlier information. It contains 876 prescriptions made up of more than 500 different substances, including many herbs (Ackerknecht, 1973). In 2735 B.C., the Chinese emperor Shen Nong wrote an authoritative treatise on herbs that is still in use today. Traditional Chinese medicine was brought to Japan via Korea and Chinese-influenced Korean medicine was adapted by the Japanese during the reign of Emperor Ingyo (411-453 A.D).

The Indian subcontinent, with the history of one of the oldest civilizations, harbors many traditional health care systems. One of the ancient classics, “Charak Samhita” (Chandra and Sharma, 1986) is the oldest text available on the complete treatment of diseases which specifies the use of hundreds of herbs in the complete treatment of diseases. The Ayurveda, whose history goes back to 500 B.C., is one of the ancient health care systems, which is a potential source of indigenous drugs. A large number of such herbs are mentioned in “Bhavprakash” (Vaishya, 1835) as well as ”Aryavaidhya Kalanidhi” (Krishnamurthi, 1986),
“Indian Materia Medica” (Nadkarni, 1976) also gives a large number of medicinal plants for the treatment of various diseases.

Fossil records date human use of plants as medicines at least to the Middle Paleolithic age around 60,000 years ago which was evidenced by a burial site of a Neanderthal man uncovered in 1960 (Solecki, 1975).

According to a WHO estimate, about 80% of the world population relies on traditional systems of medicines for primary health care, where plant form the dominant component over other natural resources (Duraipandiyan et al., 2006). Today, the renewed interest in traditional pharmacopoeias reveals that researchers are concerned not only with determining the scientific rationale for the goal of herbal drug research, but also for development of single and multi-component bioactive natural products that may lead to development of new pharmaceuticals which addresses unmet therapeutic needs. The demand for plant-based medicine is not only enormous, but keeps increasing worldwide (Srivastava, 2000).

The traditional systems of medicine in the world for treatment of chronic diseases and heavy metal poisoning related to herbal traditional medicines were studied by Umashanker and Shruti (2011). The benefit of using herbal medicines as Antipyretic, Antiulcer, Antidiabetic and Anti-cancer activity was suggested by evaluating the action among traditional medicinal plants.

Some indigenous Pakistani medicinal plants were studied by Ikram et al., (1987). One of the plants under their study was *Gmelina asiatica*. They reported that the roots of this plant exhibited prominent oral antipyretic activity.

In West Nepal around eighteen plant species were used in folklore medicine, which were tested for their antibacterial activity by the disc diffusion method (Panthi and Chaudhary, 2006). The bacteria employed were gram-positive and gram-negative. Extracts of eight plants showed encouraging result against three strains of bacteria (*Escherichia coli*, *Pseudomonas aeruginosa* and *Shigella boydii*), while other showed activity against *Staphylococcus aureus*. This findings support the traditional knowledge of local users.
The biogeographic position of India is unique which makes India rich in all the three levels of biodiversity such as species diversity, genetic diversity and habitat diversity (Krishnaraju et al., 2005).

The hypoglycemic and anti hyperglycemic effect in rhizomes of Polygala senega (Kako et al., 1996) and Gmelina asiatica (Kasivisvanath et al., 2005) were reported to have a significant range with reference to the standard drug.

The study was carried out to investigate the anti-inflammatory activity from Gmelina asiatica (Standard drug Indomethacin) were found to be significant (P<0.001) when compared to control. (Merlin et al., 2009). Antiproliferative activity and induction of apoptosis in estrogen receptor-positive and negative human breast carcinoma cell lines by Gmelina asiatica was carried out to analyze the active constituents present in aerial parts of Gmelina asiatica Linn. (Kattyayani et al., 2010). Gmelina asiatica aerial parts were reported to be a hepatoprotective drug and had significant action against liver disorders by Sowjanya et al., (2013).

Antiulcer drugs and the search for novel molecules have been extended to herbal drugs that offer better protection and decreased relapse. The healing property of Ocimum sanctum, Allophylus serratus, Desmodium gagenticum, Azadirachta indica, Hemidesmus racemosus, Asparagus racemosus and Musa apientum was the knowledge of Ayurveda. This knowledge was experimented to isolate, characterise and standardise the active constituents from herbal sources for antiulcer activity by Dharmani et al., (2005).

Mankind's discovery of antibiotics ushered in a new age of medicine during the 19th century, an age wherein many predicted an end to diseases that had plagued the mankind for centuries with the appearance of penicillin during World War II as the first miracle drug (Wainwright, 1990). From 1940s to almost 1980s many classes of antibiotics discovered have helped the terrors of human health.

Advances in synthetic chemistry for identification of many key chemical molecules offered more opportunities to develop novel compounds. Numerous drugs like sulphonamides, isoniazid, anti-psychotics, anti-histamines and penicillin were developed from thousands of chemicals (Projan et al., 2004). Emergence of modern pharmaceutical
industry is an outcome of all these different activities that developed potent single molecules with highly selective activity for a wide variety of ailments. These successes resulted in reduced interest in natural products drug discovery.

It was not until the 1970s that antibiotic resistance was considered to be a real threat. In the past, medicine and science were able to stay ahead of this natural phenomenon through the discovery of potent new classes of antimicrobials, a process that flourished from 1930-1970 and has since slowed to a virtual standstill, partly because of misplaced confidence that infectious diseases had been conquered, at least in the industrialized world. In just the past few decades, the development of resistant microbes has been greatly accelerated by several concurrent trends like urbanization, pollution, AIDS epidemic, etc., (Levy, 1992). These have worked to increase the number of infections and thus expand both the need for antimicrobials and the opportunities for their misuse.

Recently, infections have become the leading cause of death world-wide which has led to an increase in antibacterial resistance, making it a global growing problem (Westh et al., 2004). More and more bacteria are developing resistance to antibiotics (Zajicek, 1996) conferred by randomly mutated genes. Each year infectious diseases cause 14 million deaths worldwide, with mortality increasing even in the United States at an annual rate of 4.8 percent. In 2000, the World Health Organization (WHO, 2000) estimated that pneumonia, diarrhoeal disease and tuberculosis accounted for more than half the deaths due to infectious disease worldwide. The problem is worsened by antibiotic resistance, as well as the emergence of new pathogens with the potential for rapid global spread (Davis, 1994; Service, 1995).

In addition to this problem, antibiotics are sometimes associated with adverse effects on the host including hypersensitivity, immune-suppression and allergic reactions (Ahmad et al., 1998). The alarming incidence of antibiotic resistance forced scientists for developing new and effective therapeutic agents with new principles from botanical medicine with novel modes of action that render them impervious to existing resistance mechanisms (Bhavnani and Ballow, 2000; Essawi and Srour, 2000; Shahidi and Karimi, 2004, Parekh et al., 2005; Nair et al., 2007).
Natural products of higher plants may give a new source of antimicrobial agents with possibly novel mechanisms of action (Hamil et al., 2003; Machado et al., 2003; Motsei et al., 2003; Barbour et al., 2004). Contrary to the synthetic drugs, antimicrobials of plant origin are affordable and are not associated with many side effects and have an enormous therapeutic potential to heal many infectious diseases (Iwu et al., 1999).

The pharmacognostic work on stem of *G. asiatica* were reported to identify and authenticate it from the stem of *G. arborea*, further stated that the stem could be used instead of root as it provides the similar properties. (Kannan et al., 2012). Development of Pharmacognostical Parameters and microscopic features of roots with lignified cork, presence of oil globules, scattered stone cell islets in secondary cortex and pitted wood elements were viewed in *Gmelina arborea*. The phytochemical screening revealed the presence of flavonoids, lignans, sterols, tannins, carbohydrate, coumarins and alkaloids (Niyati et al., 2012).

Pharmacognostic studies and preliminary phytochemical investigations on the bark of (*Persea macrantha* Nees) Lauraceae was carried out by Kulkarni et al., (2011). The microscopic, macroscopic, physicochemical parameters were utilized for quick identification of the drug and particularly useful in the case of powdered materials.

The physicochemical evaluation of leaf of *Gmelina arborea*, fresh leaf and dried powder of the leaves were studied through morphology, microscopy and fluorescence analysis. The detailed microscopy revealed that the presence of anomocytic stomata and covering unicellular and multicellular trichomes. Leaf constant such as stomatal number, stomata index, vein islet number, vein termination number were also determined (Chothani et al., 2012). The entire plant, especially the leaves are recognized as valuable drugs and frequently used by many ancient physicians. The work highlights the exomorphology and histomorphology of leaf, petiole, stem and root with Pharmacognostic study of the whole plant. These observations will enable to standardize the botanical identity of the drug in crude form.

With the development of various analytical methods of high precision, advances in molecular biology and genetic engineering, it is now possible to isolate compounds in extremely small quantities. The study of chemical structure, molecular structure and
therapeutic potentialities and then to alter the molecule to be suitable for production of novel selective new therapeutic agents have become easy due to analytical evaluation of the drug. A number of active constituents have been isolated from plants like *Azadirachta indica* (Randhawa and Parmar, 1993), *Senna alata* (Adedayo et al., 2001), *Terminalia bellerica* (Elizabeth, 2005).

High performance liquid chromatography method for quantification of Apigenin from dried root powder of *Gmelina arborea* Linn was simple, fast and precise by reverse phase High Performance Liquid Chromatographic method developed for the quantitative determination of Apigenin, a flavonoid from dried root powder (Vidya et al., 2007; 2011).

HPTLC standardization of herbal extracts of *Gmelina arborea* using umbelliferone (Shafaq et al., 2006) was studied to justify that the usage of this plant as important ingredients in Dashmula. It is also extensively used in the production of popular Ayurvedic preparations like Chyavanprash and Dashmularishta. The whole plant is used as hypoglycemic, stomachic, laxative, galactagogue, anthelmintic, astringent, diuretic, aphrodisiac drug. Umbelliferone has been reported to have antihyperlipidemic and antidiabetic effects and hence it was selected as a marker compound for standardization.

Pharmacognostic and phytochemical investment *Celosia argentea* L. proved to be a potential drug for curing kidney stone and indigenous medicine for wound healing. (Rajini et al., 2013). Their work is also confirmed through HPTLC by isolating quercetin compound which is responsible for the activity.

Chromatographic Studies on the tannins of *Aerva lanata* (Linn.) Juss. Ex Schultes. Yamunadevi et al., (2012) were developed by HPTLC profiling. The methanol extract of stem, leaves, root, flower and seeds were analysed. In general, higher degree of tannins diversity has been observed in vegetative parts when compared to the reproductive parts.

Biological evaluation is an important field to discover plant potency against microbes and their efficacy of reducing power, Ion scavenging and metal chelating activities. The goal of herbal drug research and development program is to discover single entity and multicomponent bioactive natural products that may serve to lead for the development of new pharmaceuticals which address unmet therapeutic needs. A study was conducted on the
phytoconstituents and antioxidant potential of ethanol, methanol and aqueous crude extracts of 14 plant parts in ten different plant species was evaluated. (Shaik et al., 2014).

Scientific analysis of plant components follows a logical pathway. Plants are collected either randomly or by following leads supplied by local healers. Random collection is to collect readily available plant, prepare extracts and test each extract for one or more types of pharmacological activity. This, broad screening method is a reasonable approach that eventually should produce useful drugs. Evaluation of anti-inflammatory potential of the multidrug herbo-mineral formulation in male wistar rats against rheumatoid arthritis is proved after formulation of several plant drugs. (Patel et al., 2013).

Evaluation of antimicrobial activity of Cleome viscosa and Gmelina asiatica was studied by Sudhakar et al., (2006) and the ethanolic extracts of the roots of Gmelina asiatica were tested for antimicrobial activity. The plant exhibited a broad spectrum of antimicrobial activity, particularly significant against Escherichia coli, Proteus vulgaris and Pseudomonas aeruginosa. The antimicrobial activity of Gmelina asiatica vegetative parts proved to be a potential drug against pathogenic bacterial strains than tested fungal forms. (Girija et al., 2012).

Initial screening of plants for possible antimicrobial activities typically begins by using crude aqueous or alcohol extraction method and can be followed by various organic extraction methods. Since nearly all of the identified components from plants which are active against microorganisms, are aromatic or saturated organic compounds, they are often obtained through initial ethanol or methanol extraction (Vileges et al., 1997). The research on the medicinal plants should be extended with the identification of the active principles in the plants. Scientific examination of the remedies could lead to standardization and quality control of the products to ensure their safety. It is after such evaluations that they can be approved for use in the primary health care. Such research activities could also lead to the development of new drugs.

Methanolic extracts of Plumbago zeylanica (Root), Acorus calamus (Rhizome), Hemidesmus indicus (Stem) and Holarrhena antidysenterica (Bark), used in Ayurvedic medicines for number of ailments, were evaluated for their antioxidant activity by Ferric thiocyanate (FTC) assay and compared with Thiobarbituric acid (TBA) method. The findings
indicated promising antioxidant activity of crude extracts of the plants and needs further exploration for their effective use in both modern and traditional system of medicines (Zahin et al., 2008).

Plants with antioxidant activities have been reported to possess free radical scavenging activity. Free radicals are known as major contributors to several clinical disorders such as diabetes mellitus, cancer, liver diseases, renal failure and degenerative diseases as a result of deficient natural antioxidant defense mechanism. These results indicate that the extracts with high total phenolic and flavonoid contents presented high radical scavenging activities, which could be related to the inherent nature of phenolic and flavonoid compounds, thus contributing to their electron transfer/ hydrogen donating ability. High correlation between radical scavenging and phenolic content has been reported in cereal (Peterson et al., 2001), fruits (Gao et al., 2000; Jimenez-Escrig et al., 2001), beverages (Fogliano et al., 1999) and culinary herbs (Zheng and Wang, 2001). In vitro antioxidant activity of methanolic and aqueous extracts of root, stem and leaf of *Gmelina asiatica* showed that the root and leaf are more efficient antioxidant than stem. (Girija et al., 2011).

Scientific data on a good number of medicinal plants investigated has been well documented in the work of Gupta and Tandon (2004). National Formulary could not adopt even a dozen of plant medicines. For this reason, a special effort is needed for development of herbal drugs having therapeutic utility. The work discusses in a broader perspectives several plants reported to have anti-asthma, antiallergic, anti-inflammatory, anti-atherosclerotic, antifertility, antidiabetic and antiviral effects. This work helps to identify the mechanism of action and functional activity of some medicinal plants.

Biochemical modes of action of *Gmelina asiatica* in inflammation was studied by Ismail et al., 1997 in root powder of *Gmelina asiatica*, which was effective in reducing the oedema during the various phases of acute inflammation. The lipid peroxide content of granuloma exudate in liver, glutamyl transpeptidase in the granuloma and serum albumin in granuloma was normalized after administration of root powder. The study also revealed that the serum acid and alkaline phosphatase levels normalized after the treatment.

Peptic ulcer disease is one of the most common gastrointestinal disorders, which causes a high rate of morbidity particularly in the population of non-industrialized countries
Peptic ulcer occurs due to an imbalance between the aggressive (acid, pepsin and *Helicobacter pylori*) and the defensive (gastric mucus and bicarbonate secretion, prostaglandins, innate resistance of the mucosal cells) factors. Number of drugs including proton pump inhibitors, prostaglandins analogs, histamine receptor antagonists and cytoprotective agents are available for the treatment of peptic ulcer but most of these drugs produce several adverse reactions including toxicities and alter biochemical mechanisms of the body upon chronic usage.

Hence, herbal medicines are generally used in such cases when drugs are to be used for chronic periods. Several natural drugs have been reported to possess anti-ulcerogenic activity by virtue of their predominant effect on mucosal defensive factors. Thus medicinal plants play a key role in the human health care because of their efficacy, safety and lesser adverse effects.

Evaluation of gastric anti-ulcer activity in a hydro-ethanolic extract from *Kielmeyera coriacea* was carried out by Fortes *et al.*, (2007). The antiulcer activity of a hydro-ethanolic extract prepared from the stems of *Kielmeyera coriacea* Mart. (Guttiferae) was evaluated in rats employing the ethanol-acid, acute stress and Indomethacin models to induce experimental gastric ulcers. These results suggested that the *Kielmeyera coriacea* hydro-ethanolic extract increased resistance to necrotizing agents, providing a direct, protective effect on the gastric mucosa.

However, the blind dependence on synthetics is coming to an end and people are returning to the naturals with hope of safety and security. As mute witness to this fact, marshmallow root, hyacinth and yarrow have been found carefully tucked around the bones of a Stone Age man in Iraq. These three medicinal herbs continued to be used today. Marshmallow root is a demulcent herb, soothing to inflamed or irritated mucous membranes, such as sore throat or irritated digestive tract. Hyacinth is a diuretic that encourages tissues to give up excess water. Yarrow is a time-honored cold and fever remedy that may once have been used much as aspirin is used today (Zand *et al*., 1994).

The study on *costus afer* and *cleome rutidosperma* leaf extract was screened for the presence of compounds responsible for boosting immune system. The extract significantly increased (p<0.05) white blood cell count and neutrophils at all doses administered when
compared with control. Moreover, the extract significantly reduced (p<0.05) total cholesterol concentration and increase (p>0.05) triglycerides concentration in the serum when compared with controls. (Arhogho et al., 2014).

One of the plants used in treatment of diabetes is *Gmelina arborea*, it is an important medicinal plant in Indian Ayurvedic system of medicine. Its root, fruit, bark and leaves are being used in medicine preparation. (Kulkarni et al., 2014).

Hence the pharmacological study is an important tool to check the toxicity and efficacy of the medicinal herbs. The activity identified by an *in vitro* test provides a basic understanding of a plant's efficacy but it does not necessarily confirm that a plant extract is an effective medicine or a suitable candidate for drug development. Certainly this is a primary concern of ethno-pharmacological research in developing new lead compounds.