A Review on the Recent Advances in Pharmacological Studies on Medicinal Plants: Animal Studies are Done but Clinical Studies Needs Completing

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ABSTRACT
There is a growing focus on the importance of medicinal plants and traditional health systems in solving the health care problems of the world. Use of plants as a source of medicine has come to new developing world from ancient practices. In this study, the most recent studies published in experimental advances in medicinal plants during January 2010 to April 2011 have been reviewed to indicate the extent of advances using ASCI database. Most of studies addressed antioxidant effects of medicinal plants followed by antimicrobial, anti-diabetic anti-inflammatory, hepatoprotective, antifungal and anticancer properties. Fabaceae was found to be the most abundantly studied family with a total of eleven studied plants, followed by Lamiaceae, Combretaceae, Euphorbiaceae, Leguminosae, Malvaceae, Asteraceae, Apocynaceae, Cucurbitaceae, Rubiaceae, Zingiberaceae, Apiaceae, Compositeae, Anarcardiaeae, Acanthaceae, Asclepiadaceae and Rutaceae. In spite of the fact that tremendous efforts were done by the researchers by providing an alternate with minimum side effects, easy accessibility and excellent compatibility, future clinical trials and standardization are still desired as an important steps in drug discovery.

Key words: Medicinal plants, current research, use of medicinal plants, importance of medicinal plants, antimicrobial activities

INTRODUCTION
Use of medicinal plants comes from ancient especially in the Africa, Asia and Latin America where the majority of the world’s people live. It is not surprising to estimate that about 90% of people have tried medicinal plants at least once in their life. Information relating to medicinal plants and traditional medicine can be found in documents and databases aimed at readers in a wide range of disciplines including botany, ecology, chemistry, medicine, veterinary science, etc. However, there are few publications reporting current work or reviewing and analyzing recent advances. Access to relevant information by the public decision makers and local communities is still very limited.

Some of medicinal plants have been registered for medical use in some countries and in some cases poor people are dependent on medicinal plants for management of their diseases. Every day, a new study is published in the world journals to confirm pharmacological effects of medicinal
plants that have been used traditionally. Therefore, collection of all data about pharmacological effects of medicinal plants from all search sources if we do not say it is impossible, it is at least unpractical. Just to get an idea, if one search for the key words of medicinal plants and pharmacology together in a general search engine like google, about 1,180,000 records would be found. This indicates the extent of studies conducting in this field. In the present study, Asian Science Citation Index (ASCI) that covers 2622 journals was selected as the basis of search and time of study was limited only to January 2010-April 2011 (Table 1). Therefore, we aimed to collect only parts of studies in pharmacological effects of medicinal plants from the world but we sure, results deserve adequate attention to reach a conclusion in better designing future studies in this field to discover and introduce effective new drugs to world.

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Fabaceae was found to be the most abundantly studied family with a total of eleven studied plants. Almost all plant parts like roots, leaves, flowers, pods and seeds were used for various purposes. Acacia concinna, Albizia lebbeck, Caesalpinia sappan and Cassia spectabilis have been reported for their antimicrobial properties (Krishnan et al., 2010; Menghani et al., 2011; Butkhup and Samapto, 2011). Different plant parts extract of Cassia occidentalis and Peltophorum pterocarpum have shown potential antioxidant activity (Arya and Yadav, 2011; Jain et al., 2011a). Pongamia pinnata, Senna spectabilis and Tephrosia calophylla are reported for their anti-hyperlipidemic, anti-diabetic, anticonvulsant and hepatoprotective activity, respectively (Kumar et al., 2010; Bum et al., 2010; Adinarayana et al., 2011).

Second important family with eight studied plants was Lamiaceae. Plant parts like leaves, aerial parts and whole plant have been employed for various medicinal purposes. Plants of this family are mostly used due to their potential antioxidant (Rosmarinus officinalis and Origanum vulgare), antifungal (Rosmarinus officinalis and Thymus vulgaris) and anti-inflammatory activity (Salvia syriaca and Scutellaria baicalensis). Aerial parts of Salvia verticillata have shown
potential anti-diabetic activity (Eidi et al., 2011a). Significant antioxidant, antifungal, anti-inflammatory and anti-diabetic activities of these plants show the medicinal importance of this family.

Plants of Combretaceae family have been reported for their potential use as antibacterial, antioxidant, anti-inflammatory and anti-diabetic activities. Fruits, leaves, galls and aerial parts have been analyzed for their potential use as therapeutic properties. Various plant extracts of Terminalia catappa, Combretum acutum, Combretum sericeum and Guiera senegalensis have shown significant antioxidant activity (Annegowda et al., 2010a, b; Coulidiati et al., 2011; Sombie et al., 2011). Leaves and fruits of Terminalia muelleri and Terminalia bellerica have been reported for antibacterial and anti-diabetic activities, respectively (Anam et al., 2010b; Latha and Daisy, 2010).

Six plants of Euphorbiaceae family have shown their potential medicative effects. Mainly leaves, fruits and flowers of these plants have been screened for their potential therapeutic potentials. Plants have shown their significant remedial effects for a wide range of diseases. Significant anticancer activity of Acalypha hispida and Euphorbia hirta has been proven in various studies (Onocha et al., 2011; Bangou et al., 2011). Alchornea cordifolia, Euphorbia hirta, Emblica officinalis and Cnidococius aconitifolius have been reported in different studies for potential antibacterial, anti-diabetic, anti-inflammatory and hepatoprotective activities, respectively (Gatsing et al., 2010; Widharna et al., 2010; Deshmukh et al., 2010; Oyagbemi and Odetola, 2010).

Plant parts like leaves, beans and even whole plant of Leguminosae family have been explored for their potential curative effects. Acacia nilotica plant is reported for its antimycobacterial, antibacterial and antifungal due to its various pharmacologically active substances (Mariita et al., 2011). Ethanolic extract of Indigofera tinctoria leaves have shown significant antibacterial, antioxidant and cytotoxicity activity (Renukadevi and Suhani Sultana, 2011). Pallophorum ferrugineum have been reported for its profound antioxidant activity in different studies (Chanda et al., 2011; Kharunnuur et al., 2010). Cassia fistula and Parkia clapperloniana have been reported for their significant Anti-inflammatory and Hepatoprotective activities, respectively (Gobianand et al., 2010; Patrick-Iwuanyanwu et al., 2010).

Proven anti-diabetic, antioxidant and anti-inflammatory activity of plants belonging to Malvaceae family makes it an important family with respect to the potential therapeutic activities of these plants. Significant antioxidant activities of Cienfuegosia digitata, Hibiscus sabdariffa, Sida acuta Burn and Sida alba have been reported in different studies (Konate et al., 2010; Anokwuru et al., 2011). Abelmoschus manihot and Hibiscus rosasinensis are known for their profound Anti-inflammatory and Anti-diabetic potentials (Jain and Bari, 2010; Mandade and Sreenivas, 2011).

Plant of Asteraceae family have shown significant therapeutic activities against important diseases like diabetes and cancer. Silybum marianum and Artemisia sieberi have been reported for their significant anticancerous and Anti-diabetic activities (Abdelmeguid et al., 2010; Irshaid et al., 2010). Artemisia monosperma and Tithonia rotundifolia two other plants of Asteraceae have been reported for significant antioxidant properties (Al-Saheer, 2011; Chanda et al., 2011).

Stem roots and in some cases whole plant of species associated with Asclepiadaceae family have been examined for their possible medicinal uses. Studied plants of this family have shown antimalarial, antibacterial, antioxidant and hypolipidemic activity. Various extracts of Leptadenia hastata, Calotropis procera and Gymnema sylvestre have shown significant Anti-androgenic, Hepatoprotective and Antihyperlipidemic activities (Bayala et al., 2011; Chavda et al., 2010; Rachh et al., 2010).
Total of four studies were found exploring the therapeutic potential of four medicinal plant of Cucurbitaceae family. Seed, fruit, leaf and aerial parts of these plants possess significant therapeutic activities. *Benincasa hispida* seeds have been reported for their potential antioxidant, Anti-inflammatory, Antioxidant and Analgesic activities (Gill et al., 2010, 2011b). Methanolic extract of *Cucurbita maxima* aerial parts have shown significant anti-diabetic activities (Saha et al., 2011).

Plants of Rubiaceae family are well reported for their potential therapeutic activities (Karou et al., 2011). Leaves and roots of *Nauclea latifolia* have been reported for significant antimicrobial, antidepressant, myorelaxant and anxiolytic activities (Okie et al., 2011; Taiwe et al., 2010). Stem and leaves of *Uncaria calophylla* and *Uncaria longiflora* have shown potential antioxidant activities (Ahmad et al., 2011). Significant anticancer and antimicrobial activities of *Myrmecodia pendens* and *Nauclea latifolia* are reported in different studies (Soeksmanto et al., 2010; Okie et al., 2011).

Plants of Zingiberaceae family were explored for their antimicrobial, antioxidant, vasorelaxant and antifungal activities. *Alpinia galangal* and *Curcuma longa* have shown strong inhibitory effect on different microbes (Butkhp and Samappito, 2011; Singh et al., 2011). *Kaempferia parviflora* and *Zingiber officinale* have been reported for their profound antioxidant and antifungal effects respectively (Butkhp and Samappito, 2011; Tagoe et al., 2011).

Seeds, leaves, roots and other aerial parts of plants from Apioaceae family have shown strong antibacterial, antimicrobial and antioxidant activity. Ethanolic extract of *Smyrnium cordifolium* aerial parts have shown significant antimicrobial and antioxidant activities (Khanahmadi et al., 2010). Different reports have proven the antibacterial, anticancer, antioxidant activities of *Anethum graveolens*, *Astrodaucus orientalis* and *Cuminum cyminum*, respectively (Jana and Shekhawat, 2010; Razavi et al., 2011; Sultana et al., 2010).

Plants belonging to Compositae family have been screened for a range of therapeutic activities. *Vernonia ambigua* and *Aspilia africana* have been reported for their potential anti-malarial and antifertility activities (Builders et al., 2011; Oyesola et al., 2010). Leaf extract of *Gynura procumbens* and *Gochnata polymorpha* have shown significant antioxidant and antispasmodic activities, respectively (Puangprongpitag et al., 2010; Schlemper et al., 2011).

Plant of Anarcadaceae were found to be effective for a range of important diseases like cancer, diabetes, oxidative stress and infections. Bark extract of *Lannea acida* is reported to have significant antibacterial activity (Quattara et al., 2011). Different reports have shown significant anticancer, antioxidant and hypoglycemic activities of *Sclerochrysa birrea, Mangifera indica* and *Semecarpus anacardium*, respectively (Bangou et al., 2011; Vaghaisiya et al., 2011; Jaya et al., 2010).

Various parts of Acanthaceae plants have been investigated for hepatoprotective, anti-inflammatory and antioxidant activities. Anti-Inflammatory, Analgesic, antioxidant and hepatoprotective activities of *Justicia gendarussa* stem and aerial parts have been reported in various studies (Jothimanivannan et al., 2010; Krishna et al., 2010). Al-Attar (2011) reported the hepatoprotective, gastroprotective and antiulcerogenic activities of *Avicennia alba* leaves extract.

Leaves, stems and roots of Asciapiaceae plants were analyzed for their potential therapeutic effects. Chavda et al. (2010) concluded that *Calotropis procera* root bark have significant antioxidant and hepatoprotective and potentials. Anti-androgenic and antihyperlipidemic activities of *Leptadenia hastata* and *Gymnema sylvestre* are well proven, respectively (Bayala et al., 2011; Rachh et al., 2010).
Plants of Rutaceae family have been studied and promising anticonvulsant, antimalarial and antispasmodic activities are reported. Gansane et al. (2010) proved the bark of *Zanthoxylum zanthoxyloides* have significant antimalarial activities. Leaves of *Zanthoxylum capense* and *Ruta chalepensis* have been reported for their significant anticonvulsant and antispasmodic activities, respectively (Amabeoku and Kinyua, 2010; Moazedi et al., 2010).

Recently many reports have been published highlighting the harmful effects of oxidative stress (Abdelhalim and Moussa, 2010; Saalu, 2010; Marjani, 2010; Abdollahi et al., 2004, 2005; Rezaie et al., 2007). In this review almost 32% of total studied plants have shown potential antioxidant activity showing the high interest of scientists towards finding the new antioxidant agents. Many studies have reported the alarming increased prevalence of pathogenic bacteria and development of resistance to antibiotics (Rattanasena and Somboonwatthanakul, 2010; Ghorashi et al., 2010; Rafeey et al., 2010; Mahmood and Hamid, 2010). Second most almost 14% of total reported plants have been explored for antimicrobial studies and 13% of plants have shown specifically antibacterial activity indicating that this microbial problem is also among scientists priorities. Haque et al. (2011) concluded that use of medicinal plants could help to prevent or maintain diabetes. Antidiabetic activity was the third (10%) most reported therapeutic potential of total reviewed medicinal plants which justifies the conducted research. Karim et al. (2011) has provided a list of nineteen herbs that are proved to be effective against diabetes. Recently different studies have reported the prevalence of fungal diseases (Nweze, 2010; Reddy et al., 2010), six percent of reviewed plants in this study have shown potential antifungal activity. Nine and six percent of plants have shown anti-inflammatory and hepatoprotective activity, respectively. It is well known that phytochemicals have potential used as anticancer agents (Haque et al., 2010) and four percent of plants have shown significant anticancer activity showing the scientists interest in combat against cancer.

According to Hasani-Ranjbar et al. (2010a), there is no review on the use of herbal medicines in the management of drug-induced hyperprolactinemia in human and they reviewed all existing data on the efficacy of herbal medicines in the management of drug-induced hyperprolactinemia in human.

In another systematic review, Hasani-Ranjbar et al. (2010b, c) focuses on the efficacy and safety of Teucrium species that are effective in the management of different conditions in human and animal. In this review they found some animal and one human study showed hypoglycemic effects of Teucrium. In one animal study, Teucrium decreased serum cholesterol and triglyceride in hyper-lipidemic rats. Some studies indicated anti-oxidant, anti-spasmic, anti-nociceptive and anti-inflammatory properties of Teucrium. According to histopathological and biochemical evidences, high doses or long-term administration of Teucrium may induce progressive impairment of neuromuscular coordination and reversible or irreversible hepatic damage. Teucrium has antidiabetic effect by enhancing secretion of insulin from the pancreas. The flavonoids and sterols are responsible for the anti-inflammatory activity of this plant. Isolation and characterization of Teucrium constituents is suggested to reach suitable drugs.

In a review focuses on the efficacy and safety of effective herbal medicines in the management of hyperlipidemia in human Hasani-Ranjbar et al. (2010c) searched out in world known databases with the search term Hyperlipidemia and herbal medicine or medicine traditional. They reviewed fifty three relevant clinical trials for efficacy of plants. This study showed significant decrease in total cholesterol and LDL cholesterol after treatment with Daming capsule (DMC), chunhyul-dan,
Glycyrrhiza glabra, garlic powder (Alllicor), black tea, green tea, soy drink enriched with plant sterols, licorice, Satureja khuzestanica, Monascus purpureus, Went rice, Fenugreek, Commiphora mukul (guggul), Achillea wilhelmsii C. Koch, Ningzh Capsule (NZC), cherry, Compositae Salvieae Dopping Pill (CSDP), shanzha xiaozi capsule, Ba-wei-wan (hachimijogen), rhubarb stalk, Silybum marianum, Rheum Ribes and Jingmingdan granule (primrose oil). Conflicting data exist for red yeast rice, garlic and guggul. No significant adverse effect or mortality were observed except in studies with DMC, guggul and Terminalia bellerica, Terminalia chebula, Emblica officinalis, ginger and garlic powder (Allium sativum). They finally concluded that out of fifty three, 22 natural products were found effective in the treatment of hyperlipidemia that deserve further works to isolate and characterization of their constituents to reach novel therapeutic and more effective agents.

Mohammadrad and Abdollahi (2011) conducted a study to provide a systematic review on the animal or human evidences linking aluminium (Al) toxicity to oxidant/antioxidant imbalance. Embase, Scopus, Pubmed, Web of Science, Google Scholar and SID databases were searched up to 1st October 2010. Over 50 studies including animal and human linking oxidative stress to Al were reviewed. Most of animal and human studies show a significant increase in lipid peroxidation (LPO) by Al. The maximum LPO was reported in the brain. Data about changes of enzymatic antioxidants such as Superoxide Dismutase (SOD), Catalase (CAT), Glutathione Peroxidase (Gpx) post exposure to Al are controversial. Animal studies showed that vitamin E, C, melatonin and pinoline reduce LPO in Al-exposed subjects. Al can affect body oxidant/antioxidant balance in favor of oxidative toxic stress. Among parameters tested in various studies, LPO seems the best indicator of Al toxicity. The role of iron homeostasis in mediation of cytotoxic effects of Al seems important. Since, oxidant/antioxidant imbalance is involved in the pathogenesis of many diseases including inflammatory bowel diseases, diabetes, osteoporosis; it would not be surprising to track roles of Al in many deliberating diseases in future.

Montaz et al. (2010) had undertaken a study to explore the possible biochemical activities of Hyaenanche globosa Lamb and its compounds. In this study they evaluated two different extracts (ethanol and dichloromethane) of four different parts (leaves, root, stem and fruits) of H. globosa for their possible antibacterial, antityrosinase and anticancer (cytotoxicity) properties. Two pure compounds were isolated using column chromatographic techniques. Active extracts and pure compounds were investigated for their antioxidant effect on cultured ‘HeLa cells’. Antioxidant/oxidative properties of the ethanolic extract of the fruits of H. globosa and purified compounds were investigated using Reactive Oxygen Species (ROS), Ferric-Reducing Antioxidant Power (FRAP) and Lipid Peroxidation Thiobarbituric Acid Reactive Substance (TBARS) assays. The ethanolic extract of the leaves and fruits of H. globosa showed the best activity, exhibiting a minimum inhibitory concentration (MIC) of 3.1 mg mL⁻¹ and a minimum bactericidal concentration (MBC) of 1.56 and 6.2 mg mL⁻¹, respectively, against M. smegmatis. The study showed that the ethanolic extract of the fruits of H. globosa (F.E) found the highest percentage of inhibitory activity of monophenolase (60.4% at 200 mug mL⁻¹). In addition, F.E exhibited 50% inhibitory concentration (IC (50)) of 37.7 mug mL⁻¹ on the viability of HeLa cells' using cytotoxicity MTT assay. Subsequently, F.E was fractionated using phase-partitioning with n-hexane, ethyl acetate and n-butanol. The cytotoxicity of these fractions was determined in vitro using different cancer cell lines. The n-hexane fraction exhibited the highest activity of toxicity. Therefore, this fraction was subjected to further separation by chromatographic methods. Two pure compounds known as:
‘Tutin’ and ‘byenanchin’ were isolated and their structures were determined by NMR spectroscopic methods. Unpredictably, none of them showed significant (p<0.01) inhibition on cell viability/proliferation at the concentrations that were used. F.E showed significant anti-tyrosinase, antibacterial and cytotoxicity effects, therefore it can be considered as an effective inhibitor alone or in combination with other plant extracts.

CONCLUSION

In conclusion, the latest published literature (in ASCI Database) on medicinal plants is mainly focused on six families (Fabaceae, Asteraceae, Combretaceae, Euphorbiaceae, Leguminosae and Malvaceae). Most of the plants were explored for their antioxidant, antimicrobial, antibacterial and anti-diabetic activities however, researchers did not overshadow the anti-inflammatory, hepatoprotective, antifungal and anti-cancerous activities of studied plants. In past two years some unexplored plants were also added as an alternate of synthetic drugs because their phytochemical and pharmacological properties were investigated and published for the first time. In short, this study has summarized the latest literature published on medicinal plants. In spite of the fact that tremendous efforts were done by the researchers to help mankind by providing an alternate with minimum side effects, easy accessibility and excellent compatibility, future clinical trials and standardization are still desired as an important steps in pharmacognosy.

REFERENCES


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