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2. REVIEW OF LITERATURE

2.1. Medicinal Plants

In the existence and survival of man, plants play a vital role. They supply foods and oxygen for breathing. They also provide wood and fibers, used for shelter, housing and diverse purpose. Apart from these, plants are also known for potential therapeutic properties (Lewis and Elvin-Lewis, 1995). The use of the plants as medicines predates written human history. There are written records of over 500 years back on clay tablets of hundreds medicinal plants such as myrrh and opium. Ebers papyrus written by ancient Egyptians in 1500 B.C contains information on over 850 medicinal plants including garlic, juniper, cannabis, castor bean, aloe and mandrake (Sumner and Judith, 2000). India has survived through more than 3000 years using plant based drugs and had several traditional medicinal systems such as Ayurveda and Unani. The rich heritages of indigenous herbal practices of material medica have helped to sustain the health of most rural people of India (Sridevi and Chandana, 2013). Ayurveda meaning “Science of life” which dates back 5000 B.C. is said to be oldest and most complete medical system in the world. Ayurveda covers various aspects of diseases, therapeutics and pharmacy and has a vast literature in Sanskrit and various Indian Languages (Dev, 1999). Vedas is the original source of Ayurveda and the texts known as Samhitas, which describes medical procedures and treatises on health care including surgery and a form of massage of vital energy points (Ebadi, 2007).
Rig Veda and the Athara Veda dating back to the second millennium B.C have the references of such plants. The first recorded treatise” the Charaka Samhita (900 B.C)’ is fully devoted to the concepts and practice of Ayurveda and primarily focused on therapeutics (Charaka Samhita, 1949; Mehta 1979). This text consists of all fundamental principles of Ayurveda but mainly concentrates the attention on digestion (internal fire of Agni). The Susruta Samhita, another early classic focuses on surgical techniques (Singhal 2009; Majumdar, 1971).

In 500 A.D., the Astanga Hridayam set out most of the detailed principles of Ayurveda, including the dosha and subdosha (Garde 1954, Sharma, 1979). The next important milestone, “The Madhava Nidanad (800-900 A.D).’ is the most famous Ayurvedic work on the diagnosis of diseases. As per Ayurveda, every material (Dravya) is a manifestation of five elements (earth, water, fire, air and space) in different proportions. The nature can be categorized into 3 defects, based on the predominant combination of these five elements.

1. Vata –the wind, the force that controls movements and functioning of nervous systems in the body.
2. Pitta- the heat and energy (sun), the force that controls digestion and biochemical processes in the body.
3. Kapha- the water and tides (influenced by moon), the force that controls fluid metabolism in the body.
The balanced forces of vata, pitta and kapha ensure that body is healthy, but when unbalanced or abnormal, disease follows (Thomas, 1997).

2.2. Traditional Systems of Medicine

2.2.1. Asian Medicinal Systems

The most established herbal therapeutic traditional medicine systems are Ayurveda, Unani and Siddha of Indian origin, Kampo of Japan, WU-Hsing of china. Ayurveda is not just an ethanomedicine but also a complete medical system that takes into consideration psychological, philosophical, ethical, physical and spiritual well being of mankind. Ayurveda is a unique medical system with universal and holistic approach and lays great importance on living in harmony with universe and harmony of nature and science. It emphasizes the maintence of proper life style for positive health (Ravishankar and Shukla, 2007). In India the Ayurvedic medical system describes the plants and plant products based medicines and determine the morphological, pharmacological or pharmacognostic character for better understanding the mode of action of their active principles.

2.2.2. European Herbalism

The root of European traditional medicine has been traced back to ancient Mediterranean civilization. In the middle ages, the color and shape of the plant part denoted a cosmic clue to its medical usefulness. Eg. Heart shaped leaf used as heart remedy, yellow plant parts for treating hepatisis. Some of the medicinal plants had
become a part of pharmacopeias of allopathy, naturopathy and homeopathy by 19th century.

2.2.3. Neo-Western Herbalism

In Neo-Western Herbalism, European traditional medicine has matured along with American herbal medicine. In this system, single plant preparation that have been either selected from formulations found in ancient pharmacopeias or derived from medicinal plants valued in other countries including those of indigenous origin, are sold alone or as mixtures in assortment of combinations. Eg. Echinacea one of the most popular plant used in Europe has its origin in North American indigenous medicine. (Soller, 2000; Elvin Lewis, 2001).

2.2.4. Indigenous Herbalism

One of the most diverse and still practiced medicinal systems is indigenous Herbalism. The knowledge may reside exclusively with traditional healers, or may be generally known. Information regarding parameters of efficacy and toxicity vary and plants selected can be quite specific, generic or inadvertently adulterated. It usually follows that the efficacy and safety have a sound therapeutic bases only when a remedy is wide spread in acceptance. (Elvin-Lewis, 2001).

2.2.5. African Traditional Medicine

The oldest and most diverse medicine systems of all are African Traditional Medicine. Africa has a rich biological and cultural diversity with different regional healing practices, thus it is considered to be a cradle of mankind. But unfortunately,
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Systems of medicines are poorly recorded and remain so till date (Gurib Fakim, 2006). African traditional medicine is holistic involving both the body and mind. The healers diagnoses and treat the physiological basis of illness before prescribing medicines to treat symptoms (Gurib-Fakim, 2006).

In both developed and developing countries, herbal medicines are in great demand. They are used as a source of primary health care owing to their attributes having wide biological and medicinal activities, lesser costs and high safety margin. For thousands of years, human beings have used plants for treatment of diverse ailments (Sofowara, 1982; Hill, 1989). According to world’s health organization, since most of the populations cannot afford the products of Western pharmaceutical industries, for their psychological and physical health requirements rely on traditional medicines. And also the western products are together with side effects and lack health care facilities (Rabe and Van Stoden, 2000; Salie et al., 1996; Griggs et al., 2001).

Asian continent is bestowed by nature with very rich botanical wealth and large number of diverse wild type of plants which grow in different parts of our country. From ancient times, in India the different parts of several medicinal plants are used to cure specific ailments (Bhattacharjee, 1998).

India owing one of the 12-mega biodiversity centers and has about 10% of the world’s biodiversity wealth, which is distributed across 16 agro-climatic zones, 10 vegetative zones and 15 biotic procinces (Zeeshan et al, 2009). Recently, around 20,000 medicinal plant species have been recorded in India (Dev, 1997). But for curing different
diseases only about 800 plant species were used by more than 500 traditional communities (Kamboj, 2000).

The NMPB (National medicinal plants board) was set up by the government of India in 2000, with a view to strengthen the medicinal plant sector all over the country as well as to conserve the wild stock. The main objective of NMPB was to establish an agency which would be responsible for co-ordination of all matters related to medicinal plants sector, including drawing up policies and strategies for insitu conservation, cultivation, harvesting, marketing, processing, drug development etc. (Kala and Sajwan, 2007). In order to improve the quality of Ayurvedic medicines, several steps have been taken in India. To ensure quality control, good manufacturing practice guidelines have been introduced. To inspire people particularly the farmers for adopting cultivation of medicinal plants, Medicinal plant boards have been constituted at state and central level. And to make common man conversant with the rich heritage of Indian system of medicine, herbal gardens have been developed. To lay down standards for Ayurvedic system of medicine, various institutes like National Institute of Pharmaceutical Education and Research (NIPER), National Botanical Research Institute (NBRI), Central Institute of Medicinal and Aromatic Plants (CIMAP) and Central Research Drug Institutes (CDRI) are playing vital role (Singh, 2007). In the field of new drug research and development, natural products are having an important role, but it was not until 19th century that man began to isolate active principles from medicinal plants. The landmark discovery was made by French scientists Caventou and Pelletier in the year 1890, with the isolation of
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Quinine from Cinchona bark (Delepine, 1951). A series of natural products were isolated from higher plants, prior to World War II, which became clinical agents and a number of them are still in use today (Kong et al, 2003).

For centuries, Natural products have served as a major source of drugs and about half of the pharmaceuticals are derived from natural products. Most of the drugs like Quinine, theophylline, penicillin G, Morphine, Paclitaxel, Digoxin, Vincristine, Doxorubicin, Cyclosporin and Vitamin A all share two important characteristics: They all are natural products and they are corner stones of modern pharmaceutical care. (Ebadi, 2007). In fact, most of the major anticancer drugs like bleomycin, doxorubicin, daunorubicin, vincristine, vinblastine, mitomycin, streptozocin and more recently paclitaxel, irontecan a camptothecin derivative and etoposide and tenoposide (podophyllotoxin derivatives) are derived from plants or micro-organisms. (Ebadi, 2007).

Extract of plants forms the basis for all Indian systems of medicine, as they were used for the treatment of various diseases and are of great significance to therapeutic treatment. However, when compared to modern system of medicine, this area is not much developed, mainly because of lack of scientific documentation in the field (Kalimuthu et al, 2010).

Knowledge of medicinal properties of herbal medicines is growing, thus are an essential and growing part of the international pharmacopeia. Furthermore, the results of research and testing will make them an increasingly safe alternative or a preferred option to allopathic medicine.
The current widespread belief that “green medicine” is safe and more dependable when compared to costly synthetic drugs which have adverse side effects, today there is an increasing demand and renewed interest in plant derived traditional medicines (Parekh and Chanda, 2006). Phytochemical constituents of a plant with its pharmacological activity are of growing interest (Gupta, 1994; Vaidy, 1994). Scientists have even worked to correlate the botanical properties of phytochemical with pharmacological activity (Rawat et al, 1997). In future it is expected to correlate botanical and phytochemical properties to specific pharmacological activities by more co-ordinated multidimensional research (Dahanukar et al., 2000). Thus the biological activities of traditional medicinal plant are helpful to the rural communities and informal settlements.

To isolate the active compounds from the species that show high biological activity, currently several studies are being undertaken like bioassay guided fractionation during screening. Further studies can be carried out with the availability of primary information like standardization of extracts, identification and isolation of active principles and pharmacological studies of isolated compounds. Therefore, to develop drugs for diseases, these scientific investigations are necessary.

2.3. Pharmacognostic studies

Pharmacognosy is the study of drugs in their crude condition. It is one of the branches of pharmacology, which involves the study of remedial agents or material medica. The pharmacology includes:

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- Pharmacy: preparation of drugs for the use by the medical practitioners.

- Pharmacodynamics: physiological action of drugs on living organisms.
  
  (Smith, 1905).

The word pharmacognosy is derived from the Greek “Pharmacon”, a drug and “Gignosco”, to acquire knowledge. Pharmacognosy means study of naturally occurring biological substances derived from medicinal plants. Thus it includes the knowledge of drugs with reference to botany and chemistry (Smith, 1905).

According to American society of Pharmacognosy “It is the study of physical, chemical, biochemical and biological properties of drugs, drug substances or potential drugs or drug substances of natural origin as well as the search for new drugs from natural sources”. But as practiced today, Pharmacognosy involves the broad study of natural products which may be derived from various sources including plants, bacteria, fungi and marine organisms. It deals with the study of both botanical dietary supplements including herbal remedies and single compound drug which may proceed as approved medicines after proper development by Food and Drug Administration (FDA) (Cardellina, 2002; Tyler, 1999).

At present the major task of pharmacognostics is the standardization of medicinal plants. The medicinal plants find their application for their economic and nutritional uses (viz therapeutic) and also these herbal medicines are set with problems like misleading botanical identification, adulteration, diversified attribute including lexicographic errors,
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misinterpretation of ethnobotanical nomenclature, variability in application of common standardization procedures.

The study of plant drugs from the pharmacognostical point would include study of habitat of plant, general character of the plant from which drug is derived, its place in botanical systems, the organ or organs of plant used their gross and minute structure in whole and powdered condition and chemistry of constituents which are used in therapeutics (Smith, 1905).

The basis for manufacturing wide range of medicinal preparations needed by people is “Crude Drug”. Thus for procuring therapeutically potent medicine prepared from genuine drug material, the development of pharmacognostical research has become indispensable. The pharmacognosists have a serious responsibility to take the initiative to correctly locate the plant mentioned in old treatises and pharmacopeias and make them available to scientists in other disciplines to put to test the use for which they are acclaimed (Kamble et al., 2010).

Pharmacognosy is the scientific study of crude drugs originated from natural sources like plant, animals, minerals and metals. However, it is estimated that 90% of the crude drug are originated from plant sources (Joy et al., 1998). Thus pharmacognosy is largely related to medicinal plants. These plants have inherited active substances for treating various ailments (Okigbo et al., 2008). So evaluation of plant material and their derived products has always been an important part for professional expertise of pharmacognostics (Brain and Turner, 1975). The main reason for evaluation of crude
drug is to find (i) biochemical variation in the drugs (ii) Detoriation due to treatment and storage and (iii) substitution and adulteration due to carelessness, ignorance or fraud (Mritunjay et al., 2013).

Rajeshwari et al., (2011) have carried out the pharmacognostic study of leaf extract of *Indogofera barberi* (Fabaceae) to establish the pharmacognostical standards. The pharmacognostical standard of *Cordia Rothii Roem* and *Schult* was established by Hajabhai et al., (2012) using the reported methods of standard text.

Niyati et al., (2012) developed detailed pharmacognostical and physicochemical parameters as recommended by WHO and Pharmacopoeias and also developed the high performance thin layer chromatography (HPLC) method for the quantitative analysis of roots of *Gmelina arborea Roxb* using β-sitosterol as a chemical marker.

Many researchers in the different part of the world have carried out the Pharmacognostic and phytochemical studies on different medicinal plants such as *Elephantopus scaber* L., *Pothos scandens* L., *Averrhoa Carambola* L., *Syzygium cumini* Linn, *Averrhoa carambola* L., *Corchorus fascicularis* Lam, *Mimosa pudica* (Lajvanti), *Ocimum americanum*, (Thomas et al., 2008; Mohan et al., 2010; Lalitharani et al., 2010; Modi et al., 2010; Milind and Anupam, 2010; Rajput et al., 2011; Sai koteshwar et al., 2011) in order to establish the pharmacognostical standard of the herbal drugs to be used as therapeutics.
2.4. Phytochemicals

Phytochemicals are the plant derived chemicals and have the capability of disease prevention, thus beneficial to human health. (Chung et al., 1998). Phytochemicals produced by the plants are of two types: Primary metabolites and Secondary metabolites. Since ancient times and now secondary metabolites are an important source of drug and almost 50% of the practical drugs used are derived from natural sources (Wang et al., 2008). Secondary metabolites like alkaloids, tannins, phenols, flavonoids, saponins, antraquinones, cardiac glycosides and cyanogenic glycosides etc., are of pivotal importance. A survey of current pharmaceutical use revealed that, of the total prescription drugs dispensed, 25% are plant derived (Farnsworth and Morris, 1976; Ogundipe et al., 1998). Plant compounds are highly varied in structure; many are aromatic substances, most of which are phenols or their oxygen-substituted derivatives.

2.4.1. Polyphenols

Phenolic compounds or polyphenols constitute one of the major and widely distributed groups of secondary metabolites in the plant kingdom and currently more than 8000 phenolic structures were found (Paixao et al., 2007). Polyphenols being one of the secondary metabolites of plants arise biogenetically from two main synthetic pathways – the shikimate pathway and acetate pathway (Ross and Kasum, 2002). Natural polyphenols can range from simple molecules such as phenolic acids to highly polymerized compounds, such as tannins. Primarily they occur in conjugated form, with one or more sugar residues linked to hydroxyl groups, or direct linkages of the sugar unit
to an aromatic carbon atom also exist. Interest for polyphenolic compounds is initiated due to the interest in antioxidant and free radical scavenging abilities, which are associated with some phenols. It is also suggested that polyphenols have the ability to possess antiulcer (Saito et al., 1998), anticarcinogenic (Liu and Castonguay, 1991), and antimutagenic activities (Liviero et al., 1994). All of those functions of polyphenols can be contributed to its strong antioxidant power in quenching free radicals (Naczk and Shahidi, 2004).

2.4.2. Polyphenols in plants

Polyphenolic compounds present as secondary metabolites are ubiquitous in all plant organs in response to stress conditions such as infection, wounding and UV radiation (Naczk and Shahidi, 2004). Phenolics present in plant include simple phenols, phenolic acid (both benzoic and cinnamic acid derivatives), coumarins, flavonoids, stilbenes, hydrolysable and condensed tannins, lignans and lignins (Naczk and Shahidi, 2004).

These polyphenols are widely present in various kinds of food, including cereals and legumes (barley, corn, nuts, oats, rice, sorghum, wheat, beans and pulses), oilseeds (rapeseed, canola, flaxseed and olive seeds), fruits and vegetables and beverages (fruits juices, tea, coffee, beer and wine (Naczk and Shahidi, 2004). They are not only exhibit health related functions as an excellent source of antioxidant but also play an important role in maintaining quality of fruits and vegetables with enzyme composition (Naczk and Shahidi, 2004).
2.5. Pharmacological Activity of Medicinal Plants:

2.5.1. Antimicrobial Potential of Medicinal plants

Mostly the pharmacological activity of the medicinal plants is due to the presence of secondary metabolites, which are of great significance to therapeutic treatment. Thus these natural products provide clues to synthesize new structural types of antimicrobial chemicals that are relatively safe to man.

The phytochemicals and plant extracts with known antimicrobial properties, are of great significance to therapeutic treatments (Nagesh and Shanthamma, 2009). The basis for all Indian systems of Medicine is the use of plant extract for the treatment of various diseases. However, due to the lack of scientific documentation in this field, this area is not much developed when compared to modern system of medicine (Kalimuthu et al., 2010).

Large numbers of researchers have studied the effect of plant extract on bacteria (Reddy et al, 2001; Edro urul, 2002; Ateb and urul, 2003). Agarry et al., (2005) studied on the potent antimicrobial activities of the gel and leaf of Aloe vera against a wide range of bacteria. Bearberry and Cranberry juice have been used to treat urinary infections while plant species such as lemon balm, garlic and tea tree are described as broad spectrum antimicrobial agents (Rios and Recio, 2005).

Mathabe et al., (2006) reported that methanol, ethanol, acetone and hot water extracts from different plant parts (leaves, roots, bark and stem rhizome), of Indigofera daleoides, Punica granatum, Syzygium cordatum, Gymnosporia senegalensis, Ozoroa
insignis, Elephantorrhiza elephantina, Elephantorrhiza burkei, Ximenia caffra, Schotia brachypetala and Spirostachys africana showed remarkable antibacterial activity against Vibro cholera, Escherichia coli and Staphylococcus aureus, Shigella species and Salmonella typhi.

Many species of Acacia caesia are found to have diverse phytochemical compounds having medicinal properties (Lee et al., 2000). The antibacterial activity of methanol extract and its petroleum ether, chloroform and ethyl acetate fractions from the root bark of Akanda (Calotropis gigantea) were investigated by Ashraful et al., (2008).

Antibacterial activities of aqueous and methanol extracts of some medicinal plants reported by Girish and Satish, (2008) against some human pathogenic bacteria showed that the methanol extracts had wider range of activity on these organisms than the aqueous extracts, which indicates that the methanol extracts of all selected plants may contain the active components.

Senthilkumar and Reetha, (2009) investigated that the methanol extract of Aegle marmelos and Cassia auriculata extract have showed higher antibacterial activity to a group of bacterial pathogens. Mandal et al., (2005) have showed the potent antimicrobial activity of two acylated bisglycoside saponins isolated from the funicles of Acacia auriculiforms against various pathogenic organisms.

Polyphenols from four medicinal plants of Burkina faso, Combretum micranthum, khaya senegalensis, Pterocarpus erinaceus and Sida acuta, were screened for their
antioxidant and antimicrobial activities against pathogenic bacteria (Damintoti et al., 2005).

The antibacterial effect of 10 different plant polyphenols were evaluated against several food-borne pathogenic bacteria. (Toshitsugu et al., 2004). Nikitina et al., (2007) showed antibacterial activity of polyphenolic compounds isolated from plants of Geraniaceae and Rosaceae families.

The comparative antimicrobial activities of the gel and leaf of Aloe vera were tested against pathogens (Agarry et al., 2005). Paiva et al., (2010) reviewed that the antimicrobial activity of secondary metabolites and lectins are usually associated to defense mechanism of plants.

Cladonia verticillaris lichen lectin (ClaveLL) showed antibacterial activity against Gram-positive (Bacillus subtilis, Staphylococcus aureus, and Enterococcus faecalis) and Gram-negative (Escherichia coli and Klebsiella pneumoniae) assayed strains, with greater inhibitory effect on growth of E. coli (MIC of 7.18 µg/ml). The lowest minimum bactericidal concentration (MBC of 57.4µg/ml) was detected against Enterococcus faecalis (Dalila De Brito et al., 2014).

2.5.2. Antioxidant potential of medicinal plants

In living systems, oxidation is a basic part of the normal metabolic process, in which Reactive oxygen species (ROS) (hydrogen peroxide and hypochlorous acid) and many free radicals (hydroxyl radical (OH) and superoxide anion) are generated (Finkel and Holbrook, 2000; Halliwell, 2000; Pietta, 2000; Vijayabaskaran et al., 2010). Rapid
production of free radicals may cause alteration in the structure and function of cell constituents and membranes and can results in human neurologic and other disorders such as cancer, diabetes, inflammatory disease, asthma, cardiovascular, neurodegenerative diseases, and premature aging (Mclarty, 1997; Young and Wood, 2001; Yang et al., 2001; Sun et al., 2002; Bimal et al., 2011). Therefore, the prevention in the production of free radicals and ROS, it requires the presence of antioxidants or the free radical scavenging molecules in the body.

There are plenty of antioxidant substances and the free radical scavenging molecules present in plants (fruits, vegetables, medicinal herbs, etc.) in the form of phenolic compounds (e.g. phenolic acids, flavonoids, quinones, coumarins, lignans, tannins), nitrogen compounds (alkaloids, amines), vitamins, terpenoids (including carotenoids), and some other endogenous metabolites, (Zheng and Wang, 2001; Govindarajan et al., 2005). So to maintain a healthy body, one should always increase the intake of foods rich in antioxidant compounds that lower the risk of chronic health problems associated with the above disease conditions (Halliwell, 1994; Klipstein et al., 2000; Bimal et al., 2011).

For prevention and treatment of free radical-related disorders, naturally occurring antioxidants can be used in foods (Middleton et al., 2000; Kumar and Kumar, 2009) and which can also be replaced by commercially available, synthetic antioxidants such as butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT), which are quite unsafe to use and is restricted due to their carcinogenic effects (Velioglu et al., 1998;
Vinay et al., 2010). Nitric oxide (NO) is a potent pleiotropic inhibitor of physiological processes such as smooth muscle relaxation, neuronal signaling, inhibition of platelet aggregation and regulation of cell mediated toxicity. It plays many roles as an effector molecule in diverse biological systems including neuronal messenger, vasodilatation and antimicrobial and an antitumor activity as it is a diffusible free radical (Shreejayan and Rao, 1997; Hagerman et al., 1998; Balakrishnan et al., 2009).

The most commonly used methods for measuring antioxidant activity are those which involve the generation of free radicals and are then neutralized by antioxidant compounds. DPPH is a well-known radical and a trap ("scavenger") for other radicals. (Husain et al., 1987, Visioli et al., 2000; Parr et al., 2004; Solai et al., 2010).

Deepa et al., (2012) showed that the different solvent extracts of Sansevieria roxburghiana exhibited a good antioxidant effect and strong free radical scavenging effects on free radicals and oxidants (DPPH, NO). The methanolic extract of Polygonum bellardii All. (flowering aerial parts) and its fractions in addition to the isolated compounds showed significant antioxidant potential by DPPH scavenging activity technique (Adel et al, 2012).

Marja et al., (1999) have investigated the antioxidant activity of 92 phenolic extract from edible and non edible plant materials (berries, fruits, vegetables, herbs, cereals, tree materials, plant sprouts and seeds) by autooxidation of methyl linoleate. Avani et al., (2010) reported that Tephrosia purpurea Linn. (Leguminosae) leaves possess the antioxidant substances which may be potentially responsible for the treatment
of jaundice. In vivo antioxidant and hepatoprotective activity of methanolic extracts of *Daucus carota* seeds (DCSE) in experimental rats revealed that the DCSE has contributed to the reduction of oxidative stress and the protection of liver in experimental rats (Kamlesh et al., 2012). Al-Shahrani et al., (2013) have measured antioxidant activity using in vitro assays as paramount in the evaluation of various food products and nutraceuticals for determining antioxidant benefit.

Antioxidant capacity of Sudanese medicinal plants *Helianthus annuus* L. (Asteraceae), *Ricinus communis* L. (Euphorbiaceae), *Nigella sativa* L. (Ranunculaceae), *Sesamum indicum* L. (Pedaliaceae) and *Balanites aegyptiaca* (L.) Del (Zygophyllaceae) seeds fixed oils was studied by Muna et al., (2014).

### 2.5.3. Anti-inflammatory activity of Medicinal plants

Inflammation is a local response of living mammalian tissues to the injury, infection or destruction. It is body defense reactions which eliminate or limit the spread of injurious agents (Mitchell et al., 2002). It is characterized by heat, redness, swelling, and disturbed physiological functions. However, if it remains unchecked may leads to onset of diseases such as vasomotor rhinnorrhoea, rheumatoid arthritis and atherosclerosis (Sujit K Chaudhary, 2001; Henson et al., 1989).

Inflammatory diseases are becoming common in aging society throughout the world. Recent studies indicate that the mediators and cellular effectors of inflammation are important constituents of the local tumors (Tripathi KD, 2008). The non-steroids anti-inflammatory drugs are commonly used for management of inflammatory condition,
which have several adverse effects especially gastric irritation leading to formation of gastric ulcers (Sangita et al., 2012). As a result, there is a need for search of other alternatives drugs. Natural products have contributed significantly towards the development of modern medicine. The major merits of herbal medicines seem to have their efficacy, low incidence of serious adverse effects and low cost. Many references are available in the field of ethanomedicinal plants used as anti-inflammatory drugs. Bagul et al., (2005) have reported anti-inflammatory potential of methanol extract of *Stepenia glabra* of Menispermaceae family. The extract depicted anti-inflammatory activity at the dose of 150 mg/ kg body weight (Bhattacharya et al., 2005). The anti-inflammatory activity of bioactive fractions isolated from seeds of *Trigonella foenum gracium* L., roots of *Glycyrrhiza glabra* L. and fruits of *Coriandrum sativum* L. has been studied by Ammar et al., (1997).

Arogh, a polyherbal ayurvedic formulation, composed of a plant ingredients was tried for its analgesic and anti-inflammatory activities. Some of its constituents like *E. alba* (karthikumar et al., 2007), *Z. officinale* (vendruscolo et al., 2006), *G. glabra* (khaksa et al., 1996), *T. chebula* (Dongmo Bertrand et al., 2006), were claimed to reduce inflammation and pain.

Santosh kumar et al., (2013) suggested that aqueous extract of *Emblica officinalis* at a dose of 200mg/Kg/ day, has significant anti-inflammatory activity in carrageenan induced hind paw edema in rats.
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Eve et al., (2008) have tested the ability of a characterized extract of *Polygonum cuspidatum* (PCE) to inhibit mouse ear inflammation in response to topical application of 12-O-tetradecanoylphorbol-13 acetate (TPA). Suresh et al., (2012) designed a study to investigate the beneficial outcome of plant *Trigonella foenum graecum* (Fenugreek). They also tested ethanol extract of *T. foenum* against Freund’s complete adjuvant induced arthritis in rats.

Vikas and Vijay, (2011) showed that the petroleum ether, chloroform and ethanol extracts of *Ficus carica* Linn. leaves significantly reduced carrageenan induced paw edema and cotton pellet granuloma in rats.

Gupta et al., (2011) investigated the effect of ethyl acetate extract of *Sarcostemma acidum* for invitro anti-inflammatory activity by human blood cell membrane stabilization method.

The essential oil of *Strobianthus ixiocephala* demonstrated a dose dependant anti-inflammatory activity in carrageenan induced rat paw edema. It has also revealed good activity in cotton pellet granuloma and adjuvant induced arthritis model in rats (Ramesh and vinod, 2003). Mahesh et al., (2007) suggested that the herbal product (DRF/AY/4012) is a promising anti-inflammatory agent of plant origin in the treatment of inflammatory disorders and conditions.

Emodin, an anthraquinone isolated from Chinese herb *Radix et Rhiza Rhei* has been reported to have anti-inflammatory activities on callogen induced arthritis (CIA) (Xiaofeng et al., 2013). Anti-inflammatory activity of the plant *Mollugo pentaphylla*
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(ethanolic extract) was studied by using sub acute model like cotton pellet induced granuloma technique (Mishra et al., 2010).

The anti-inflammatory potential of three medicinal plants, *Xanthium strumarium*, *Achyranthes aspera* and *Duchesnea indica* were evaluated, using both in vitro and in vivo assays (Khuda et al., 2014).

2.5.4. Hepatoprotection potential of Medicinal plants

Till date there is no effective medicine for hepatic diseases which are primarily caused by xenobiotics and hepatitis viruses. Consequently, control of liver diseases has become a major goal of modern medicine. The corticosteroids and immunosuppressants are the drugs offered by modern medicine for the treatment of liver diseases which provide only symptomatic relief mostly without influencing the disease process and their use is associated with the risk of relapse and danger of side effects (Ram and Goel, 1999). In traditional systems of medicine, like Ayurveda, medicinal plants and their formulations are used to cure liver diseases. Some of the plants and herbal preparations have been evaluated for their protective actions against hepatotoxins. Some of the polyherbal preparations were proved to be antihepatotoxic in action as evidenced by clinical trials.

Lin et al., (1997) studied the hepatoprotective effect of various fractions of *Scutellaria rivularis* against CC14, D-galactosamine and acetaminophen induced toxicity in rats. CHC13 fraction and EtOAc fractions exhibited the greatest hepatoprotective effects on CC14-induced liver injuries, the CHC13 fraction and n-hexane fraction were
most effective against D-galactosamine intoxication, and the CHCl₃ fraction represented
the most liver protective effect on acetaminophen induced hepatotoxicity.

Emodin isolated from the stem of Ventilago leiocarpa exhibited hepaprotective
effects on CC₁₄ and D-galactosamine-induced liver damage. Emodin significantly
reduced the activities of SGOT and SGPT. Histopathological examination of the liver
also showed the protective efficacy of emodin (Lin CC et al., 1996).

The protective and curative effect of aqueous-methanolic extract of Artemisia
absinthium was evaluated on acetaminophen and CC₁₄ induced hepatic injury. Pre-
treatment of rats with the plant extract (500 mg/kg) prevented the acetaminophen as well
as CC₁₄ induced rise in serum transaminases. Post-treatment with three successive doses
of the extract (500 mg/kg) restricted the hepatic damage induced by acetaminophen, but
CC₁₄ induced hepatotoxicity was not altered (Gilani and Janbaz, 1995).

Biochemical studies conducted by Khalid and Anwar, (1995) on the
hepatoprotective activity of the aqueous-methanolic extract of A.maritima against
acetaminophen and CC₁₄ induced liver damage in mice justifies the traditional use of this
plant against liver diseases. In their investigation pre-treatment of rats with the plant
extract (500 mg/kg) prevented the hepatotoxin-induced rise in serum transaminases. Lin
et al., (1995) have evaluated the protective efficacy of Curcuma xanthorrhiza on
acetaminophen and CCl₄-induced hepatic dysfunction in mice. Their study revealed that
the medicinal herb extract has reduced the acute elevation of serum transaminases
induced by the two hepatotoxins. *Curcuma xanthorrhiza* also alleviated the degree of liver damage after the intraperitoneal administration of the hepatotoxins.

Treatment with the water extract of *Ganoderma lucidum*, *Ganoderma formosanum* and *Ganoderma neo-japonicum* caused significant decrease in CC1₄ induced toxicity in rat liver and showed free radical scavenging activity. Among these three the *G. formosanum* has showed greatest antihepatotoxic and free radical scavenging activity (Lin et al., 1995). Sane et al., (1995) compared the hepatoprotective activity of *Phyllanthus amarus and Phyllanthus debilis* (whole plants) in the treatment of liver damage in rats exposed to CC1₄. All the biochemical alterations in plasma and liver of rats due to CC1₄ intoxication were restored by treatment with the medicinal herbs (0.66 g/kg). However, *Phyllanthus debilis* has been found to be a better hepatoprotectant than *Phyllanthus amarus*. Seru et al., (2013) have studied the invivo hepatoprotective activity of methanolic extract of *Dendrobium ovatum* L. Kraenzl whole plant against CCl₄ induced hepatotoxicity.

Sultana et al., (1995) have showed that the presence of the extracts of *Solunum nigrum* and *Cichorium intybus* in the reaction mixture containing calf thymus DNA and free radical generating system protected DNA against oxidative damage to its deoxyribose sugar moiety. The hepatoprotective effect of these crude extracts may be due to their ability to suppress the oxidative degeneration of DNA in the tissue debris as suggested by the investigators.
Chao-Jie Chen et al., (2011) investigated the invitro and invivo hepatoprotective properties of *Cichorium endivia* L. extract (CEE). The CEE significantly blocked the oxidative stress and cytotoxicity induced by tert-butyl hydroperoxide (t-BHP) in HepG2 cells. The methanol extract of plant materials of some plants like *Casuarina equisetifolia*, *Cajanus cajan*, *Glycosmis pentaphylla*, *Bixa orellana*, *Argemone mexicana*, *Physalis minima*, *Caesalpinia bonduc*, belonging to the different family were studied for hepatoprotective activity against swiss albino rats with liver damage induced by carbon tetrachloride (Md. Rajib et al., 2009). Simon et al., (2010) demonstrated the comparative hepatoprotective and antioxidant activity of *Phyllanthus niruri*, *Maytenus emarginata*, *Eclipta alba*, *Aloe vera*, *Solanum indicum* and *Aegle marmelos* against paracetamol induced toxicity.

Oral administration of hydroalcoholic extract of *Alocasia indica* (250 and 500mg/kg) effectively inhibited CCl₄ and paracetamol induced changes in the serum marker enzymes, cholesterol, serum protein and albumin in a dose dependent manner as compared to the normal and standard drug silymarin-treated groups (Wahid et al., 2009). Eman Al-Sayed et al., (2014) investigated hepatoprotective and antioxidant effect of *Bauhinia hookeri* extract against Carbon tetrachloride induced hepatotoxicity in mice.

**2.5.5. Cytotoxicity**

The uses of plants in the treatment of cancer have a long history. Hartwell, (1982) in his review of plants used against cancer, more than 3000 plant species have reportedly been used in the treatment of cancer. In the development of several clinically useful
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Anticancer agents, plant derived compounds have played an important role. These include vinblastin, vincristine, the camptothecin derivatives, topotecan and innotecan, etoposide derived from epipodophyllotoxin and paclitaxel (taxol). Based on selective activity against cancer related molecular targets, several promising new agents are in clinical development including flavopiridol and combretastatin A4 phosphate and some agents which failed in earlier clinical studies are stimulating renewed interest (Crag and Newman, 2005).

The leaves of the cashewplant (*Anacardium occidentale* L.) extract were found to be cytotoxic and to induce apoptosis in Jurkat (acute lymphoblastic leukemia) cells (Nzi Andre et al., 2012). The invitro cytotoxic activity of the aqueous, chloroform and methanol extracts of *Dicronopteris linearis* leaves were investigated against the normal (3T3) and cancer cell lines (MCF-7, Hela, HT-29, HL-60, K562 and MDA-MB-231) using the MTT assay method (Zakaria et al., 2010).

Madhumita et al., (2002) have investigated the action of some phenolic compounds of natural origin in four human tumor cell lines: acute myeloblastic leukemia (HL-60), Chronic myelogenic leukemia (K-562), Breast adenocarcinoma (MCF-7) and Cervical epithelial carcinoma (Hela).

Diet- derived flavonoids particularly Quercetin was evaluated for its effects on Dalton’s lymphoma ascites (DLA) induced solid tumours to identify the target’s action (Kushi et al., 2011).
According to Elumalai et al., (2012) the cytotoxic effects of nimbolide on human breast cancer cells is due to limonoid present in leaves and flowers of the neem tree (*Azadirachta indica*). The molecular mechanisms involved in the apoptotic activity exerted by nimbolide were studied on the estrogen dependent (MCF-7) and estrogen independent (MDA-MB-231) human breast cancer cell lines. The growth inhibitory effect of nimbolide was assessed by MTT assay.

Investigations on the cytotoxic effects of the crude methanol and fractionated extracts (hexane, ethyl acetate) of *C. mangga* against six human cancer cell lines, namely the hormone-dependent breast cell line (MCF-7), nasopharyngeal epidermoid cell line (KB), lung cell line (A549), cervical cell line (Ca Ski), colon cell lines (HCT 116 and HT-29), and one non-cancer human fibroblast cell line (MRC-5) were conducted using an *in-vitro* neutral red cytotoxicity assay (Nurestri et al., 2011). The mangroves, such as *Avicennia* and *Excoecaria Agallocha* (Euphorbiaceae) were evaluated for the antioxidant and anticancer activity using DPPH and MTT Assay (Prajeet et al., 2013). Evaluation of invitro cytotoxic activity of *Crinum latifolium* L. was carried out be Abdul et al., (2014).

### 2.5.6. Pharmacological activity of *Rumex* species.

A perusal of literature has shown the voluminous phytochemical work of the genus polygonaceae. It is evident from the literature that the species belongs to the genus polygonaceae were extensively screened particularly for their biological active groups of *Rumex* species. An attempt is made here to highlight the work briefly.
The genus *Rumex* is found to be distributed worldwide. This genus includes more than 250 species. Most of the species under this genus contain phytoconstituents like, flavonoids, anthraquinones and triterpenoids. Many species are herbs but shrubs also included. Roots are usually taproot but a few are having rhizomes. Very few of them are explored scientifically (*Rumex patientia, Rumex japonicas, Rumex hymenosepalus, Rumex crispus, Rumex dentatus*). 80% methanolic extract of rhizome *Rumex abyssinicus* reported to have diuretic and analgesic activity (Rao et al., 2011).

Suleyman et al., (1991) evaluated the anti inflammatory effect of aqueous extract of roots *Rumex patientia* L. roots. The antioxidant activities, reducing power, DPPH scavenging activities, amount of total phenolic compounds and antimicrobial activities of ether, ethanol and hot water extracts of leaves and seeds of *Rumex crispus* L were studied by Yildrim et al., (2001).

The crude extracts of the leaves of *Dodonaea viscosa* and *Rumex nervosus* as well as the root of *Rumex abyssinicus* were tested for antimicrobial and anti-inflammatory activities (Getie et al., 2003). Effect of methanolic extract of *Rumex hastatus* roots (MRR) and its derived fractions, n-hexane (HRR), ethyl acetate (ERR), chloroform (CRR), butanol (BRR) and aqueous extract (ARR) was studied against carbon tetrachloride (CCl₄) induced hepato and testicular toxicity in rats (Sumaira et al., 2003).

roots of *Rumex patientia* L. (Polygonaceae) (D-1), a traditional Turkish medicine used as a laxative and cholagogue, on drug-metabolizing enzymes, such as cytochrome P4502E1, NADPH cytochrome c reductase, NADH cytochrome b5 reductase and glutathione-S-transferase (GST); and serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were studied in male Wistar albino rat liver.

Elzaawely et al., (2005) have evaluated the total phenolic content and antibacterial activity of ethanol, hexane, chloroform, ethyl acetate and aqueous extracts of aerial parts of *Rumex Japonicus* HOUTT. Anthraquinones isolated from the aerial parts of *Rumex acetosa* (Polygonaceae) and two synthetic derivatives were examined for their cytotoxicities against five cultured human tumor cell lines i.e A549 (non-small cell lung), SK-OV-3 (ovary), SK-MEL-2 (melanoma), XF498 (central nerve system) and HCY15 (colon), using the Sulfrhodamine-B method in vitro and antimutagenic activities by Ames test with *Salmonella typhimurium* TA98 and TA100 and SOS chromotest with *E.coli PQ37*.

Ferrers et al., (2006) studied the phenolic compounds of *Rumex induratus* leaves and determined by HPLC-DAD-MS/MS-ESI. *Rumex induratus* was also investigated for its capacity to act as a scavenger of DPPH and superoxide radicals. Cunado et al., (2007) have study of the meiotic behaviour of the XY bivalent in *Rumex acetosella* and *R. Suffruticosus*.

Jimoh et al., (2008) have evaluated polyphenolic contents and biological activities of *Rumex ecklonianus*. *Rumex dentatus* L. (Polygonaceae) leaf, stem and root extracts are
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evaluated for antibacterial, antifungal, cytotoxic, antitumor and allopathic potential (Nighat Fatima et al., 2009). Gaisler et al., (2010) have studied the survival of seedlings of *Rumex obtusifolius* and *Rumex crispus* on upland grassland in the Jizera Mts. in the north of the Czech Republic.

The antibacterial activity of *Hibiscus sabdariffa* and *Rumex nepalensis* were evaluated against pathogenic strains (Arvind and Alka, 2011). Recent studies of Gescher et al., (2011) indicated that a polyphenol-enriched extract from *Rumex acetosa* L. exerts strong antiviral effects against HSV-1 by influencing adsorption and penetration of the virus into the host cell by oligomerization of viral adhesion proteins.

Md. Rahul et al., (2011) determined the phenolic content, cytotoxic, membrane stabilizing and antimicrobial activities of methanol extract of the seeds of *Rumex maritimus* Linn. El-Bakry et al., (2011) have recorded the differences in growth and chemical composition of invitro grown seedlings of *Rumex vesicarius* L. The methanolic extract of *Rumex nepalensis* were tested for antibacterial efficacy against four bacterial strains and antifungal activity against three fungal strains by well diffusion method (Surjeet kumar et al., 2011).

The methanol extract of ripe *Rumex crispus* L. fruits was evaluated for its antioxidant potential by assays for ferric reducing antioxidant power (FRAP), DPPH- free radical scavenging activity and the influence on lipid peroxidation in liposomes were studied by Maksimovic et al., (2011).
Magdalena Wegiera et al., (2012) have provided evidence for cytotoxicity and induction of apoptosis by investigated *Rumex* species: *Rumex acetosa, Rumex acetasella, Rumex confertus, Rumex crispus, Rumex hydrolapathum* and *Rumex obtusifolius* against 1301, EOL-1 and H-9 cell lines. A comparison between water and ethanol extracts of *Rumex acetosa* for protective effects on gastric ulcers in mice was given by Ji-Yeong et al., (2012).

Quaria and Dildae et al., (2013) evaluated antioxidant and free radical scavenging activities of the methanolic extract of its roots and its sub-fractions in solvents of different polarity employing DPPH free radical scavenging, ABTS, FRAP, Phosphomolybdate, reducing power and lipid peroxidation assays.

The aqueous – methanol leaf extract and fractions of the *Rumex vesicarius* L. was evaluated for the possible presence of spasmogenic and spasmolytic constituents to rationalize its traditional uses in gastrointestinal disorders (Imran Ahmad et al., 2014). However, the phytochemical, pharmacological and pharmacognostic studies of *Rumex vesicarius* L. has not been studied by any researchers. Therefore the present investigation is aimed to deal with the phytochemical screening, isolation of bioactive compound and its pharmacological screening along with pharmacognostic studies.