INTRODUCTION
Throughout the ages humans have relied on nature for basic needs for the production of food, shelter, clothing, means of transportation, fertilizers, flavors, fragrances, and medicines (Newman et al., 2000). The great ancient Chinese, Indian, and North African civilizations provided written evidence of man’s utilization of plants for the treatment of a wide range of diseases. In South Africa, western and traditional systems of medicine exist together, the first dating back only 300 years with the influx of European settlers and the latter possibly to palaeolithic times (Van Wyk et al., 1997). Evidence accruing from observation of animals demonstrated that even chimpanzees use a number of plant species for their medicinal value (Huffman and Wrangham, 1993).

It has been estimated that 60% of the World’s population rely on traditional medicines for their health care needs. In 1976 the World Health Assembly drew attention to the reserve constituted by those practicing traditional medicine. A year later it urged member states to utilize their traditional systems of medicine, and in 1978 highlighted the importance of medicinal plants in the health care systems of many developing countries. In 1978 at the historic International Conference of Primary Health Care at Alma Ata, the World Health Assembly recommended that governments give high priority to the incorporation of Traditional Medicinal Practitioners (TMPs) and Birth Attendants into the health care team and proven traditional remedies into the national drug policies and regulations. Despite the dramatic advances and advantages of conventional medicine, it is clear that a role has been identified for herbal medicine. In the last 50 years or so, humans have relied on plants to treat all manner of illnesses, from minor problems such as coughs and colds to life-threatening diseases such as tuberculosis and malaria. Herbal medicine is presently experiencing a dramatic renaissance in Western countries, partly because of renewed interest in this field, gaining popularity worldwide as alternative and complementary therapies. The medicines for internal use prepared in the traditional manner involve simple methods such as hot- or cold-water extraction, expression of juice after crushing, powdering of dried material, formulation of powder into pastes via such a vehicle as water, oil or honey, and even fermentation after adding a sugar source. The range of products that could be obtained from medicinal plants is given in Fig. 1.
Medicinal Plants: Indian Wealth and Heritage

India is a varietal emporium of medicinal plants and is one of the richest countries in the world as regards to genetic resources of medicinal plants. All known types of agroclimatic, ecologic, and edaphic conditions are met within India. 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). A survey conducted by the All India Coordinated Research Project on Ethnobiology (AICRPE) during the last decade recorded over 8000 species of wild plants used by the tribals and other traditional communities in India for treating various health problems (Laloo et al., 2006). 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" (Nandkarni, 1976) also gives a large number of
medicinal plants for the treatment of various diseases. In rural areas, 75 percent of the
population is dependent on herbal medicines for healthcare. In the last few decades,
herbal medicine has been found to have some impressive credentials. In India, over
2600 plant species have been considered useful in the traditional system of medicine
like Ayurveda, Unani, Siddha and Home remedies (Khandelwal, 1988). Number of
herbal drugs and their compositions are recommended for combating human ailments
in the ancient texts as well as in modern medicine (Sastri, 1962).

**Indian System of Medicine**

Ayurveda, meaning the “science of life,” is said to be the oldest and most
complete medical system in the world and dates back to 5000 B.C. There is no
denying the benefits of Ayurvedic treatments that several Indians and others across
the globe have experienced. The diagnostic and treatment procedures used are unique
and are still valid today as are its foundational principles of panchamahabhutha (five
basic elements of nature), tridosha (three humours) and prakrithi (individual
constitution) (Venkatasubramanian, 2007). Ayurveda has vast literature in Sanskrit
and various Indian languages, covering various aspects of diseases, therapeutics, and
pharmacy (Dev, 1999). The original source of Ayurveda is the Vedas and the texts
known as the Samhitas, which are treatises on health care and describe medical
procedures, including surgery and a form of massage of vital energy points (Ebadi,
2007). The earliest references to such plants are found in the Rig Veda and the
Atharva Veda, dating back to the second millennium B.C. The Charaka Samhita, (900
B.C.) is the first recorded treatise fully devoted to the concepts and practice of
Ayurveda; its primary focus was therapeutics (Chandra, 1986; Sharma, 1981). This
text sets out all the fundamental principles of Ayurveda but concentrates most of its
attention on digestion (described as internal fire, or agni). Another early classic, the
Susruta Samhita, focuses on surgical techniques (Majumdar, 1971; Krishnamurthy,
1991). The Astanga Hridayam, written in about 500 A.D., sets out most of the
detailed principles of Ayurveda, including the dosha and subdosha (Garde, 1954;
Sharma, 1979). The Madhava Nidana, (800-900 A.D.) was the next important
milestone; it 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,
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fire, air and space) in different proportions. The material could be living as well as non-living things. Depending on the predominant combination of the elements, nature can be categorized into three doshas, namely vata, pitta and kapha:

- Vata, linked to the wind, the force that controls movement and the functioning of the nervous system in the body
- Pitta, the force of heat and energy, linked with the sun, that controls digestion and all biochemical processes in the body
- Kapha, the force of water and tides, influenced by the moon, the stabilizing influence that controls fluid metabolism in the body

When balanced these three forces ensure that the body is healthy, but when they are "abnormal" or unbalanced, disease follows (Thomas, 1997). India has a rich cultural heritage of traditional medicines which chiefly comprised the two widely flourishing systems of treatments i.e. Ayurvedic and Unani systems since ancient times. Ayurveda is considered not just as an ethnomedicine but also as a complete medical system that takes in to consideration physical, psychological, philosophical, ethical and spiritual well being of mankind. It lays great importance on living in harmony with the Universe and harmony of nature and science. This universal and holistic approach makes it a unique and distinct medical system. This system emphasizes the importance of maintenance of proper life style for maintaining positive health (Ravishankar and Shukla, 2007). Nature has bestowed upon us a very rich botanical wealth and a large number of diverse types of plants grow wild in different parts of our country. In India, the use of different parts of several medicinal plants to cure specific ailments has been in vogue from ancient times (Bhattacharjee, 1998). India is one of the 12-mega biodiversity centers having about 10% of the world’s biodiversity wealth, which is distributed across 16 agro-climatic zones (Shiva 1996).

The Indian subcontinent is a vast repository of medicinal plants that are used in traditional medical treatments (Ballabh and Chaurasia, 2007). Many westerners have long regarded the Indian systems of medicine as a rich source of knowledge. In India, around 20,000 medicinal plants have been recorded (Dev, 1997) however traditional communities are using only 7,000 - 7,500 plants for curing different diseases (Kamboj, 2000). Even today, majority of the medicines are prepared from the plant and animal products, minerals and metals etc. Major pharmaceutical industries
depend on the plant products for the preparation of Ayurvedic medicines. Plants, especially used in Ayurveda can provide biologically active molecules and lead structures for the development of modified derivatives with enhanced activity and/or reduced toxicity. The small fraction of flowering plants that have so far been investigated have yielded about 120 therapeutic agents of known structure from about 90 species of plants. Some of the useful plant drugs include vinblastine, vincristine, taxol, podophyllotoxin, camptothecin, digitoxigenin, gitoxigenin, digoxigenin, tubocurarine, morphine, codeine, aspirin, atropine, pilocarpine, capscicine, allicin, curcumin, artemesinin and ephedrine (Kumar et al., 1997). In some cases, the crude extract of medicinal plants may be used as medicaments. On the other hand, the isolation and identification of the active principles and elucidation of the mechanism of action of a drug is of paramount importance. Hence, work in both mixture of traditional medicine and single active compounds are very important. With a view to strengthen the medicinal plants sector all over the country as well as to conserve the wild stock, the NMPB (National Medicinal Plants Board) was set up by the Government of India in 2000. The prime objective of setting up the board was to establish an agency which would be responsible for coordination of all matters with respect to the medicinal plants sector, including drawing up policies and strategies for in situ conservation, cultivation, harvesting, marketing, processing, drug development, etc. (Kala and Sajwan, 2007). In India, several steps have been taken to improve the quality of Ayurvedic medicines. Good manufacturing practice (GMP) guidelines have been introduced so as to ensure quality control. Medicinal plant boards have been constituted at state and central level to inspire people particularly the farmers for adopting cultivation of medicinal plants. Herbal gardens have been developed to make common man conversant with the rich heritage of Indian 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 Institute (CDRI) are playing pivotal role in laying down standards for Ayurvedic system of medicine (Singh, 2007).

Medicinal Plants

Although one can be gifted genetically with a powerful immune system nutrients help to ensure optimal development of one’s immune system. Plants constitute the base of the food chain and provide the most valuable source of natural
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nutrients. Additionally, constituents of medicinal importance are also present in plants (Anonymous, 2000). Plants used for medicinal purposes contribute significantly to the development of major medical drugs that are used today. Most of our common medicines have compounds extracted from plants as their primary active ingredients and many have also provided blueprints for synthetic or partially synthetic drugs (Simpson and Ogorzaly, 2001).

A major part of using plants as medicines involves the use of plant extracts or their active principles. Medicinal plants and plant-derived medicines are widely used in different traditions all over the world and they are becoming increasingly popular in modern scientific communities as natural alternatives to synthetic chemicals (Van Wyk and Wink, 2004). Many plants synthesize substances that are useful to the maintenance of health in humans and other animals. These include aromatic substances, most of which are phenols or their oxygen-substituted derivatives such as tannins. In many cases, substances such as alkaloids serve as plant defence mechanisms against predation by microorganisms, insects and herbivores. In general many herbs and spices are used for food seasoning which also underlies useful medicinal properties (Lai, 2004).

A single plant can be viewed from a purely scientific perspective as a biosynthetic facility manufacturing a large number of molecules from simple nutrients, water, carbon dioxide and solar energy. The resulting chemistry is quite complex and includes all the final molecules in the biosynthetic pathway, together with their precursors. Molecules that are produced when an alternative pathway has been activated and are not required in primary metabolic processes are known as secondary metabolites, and some are believed to have evolved to form part of the plant's defense mechanism. Many of these secondary metabolites have biological activities that can be assayed in the laboratory, providing a scientific rationale for the use of the particular plant. In some cases isolated active compounds are subsequently channelled into drug development regimes and eventually commercialised. In this regard, it has been estimated that about a quarter of all modern drugs were originally derived from plant sources with relatively complex or advanced characteristics.

Well-known examples of plant-derived medicines include quinine (from Chincona species), morphine and codeine (from Opium species), colchicines (from Colchicum autumnale), atropine (from the Solanaceae family), reserpine (from Rauwolfia serpentine), salicin (from Salix alba) and digoxin (from Digitalis...
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Important advances in anti-cancer drugs such as taxol (from *Taxus brevifolia*) and vincristine (from *Catharanthus roseus*) have been developed from plants (Dewick, 2002; Simpson and Ogorzaly, 2001; Van Wyk and Wink, 2004).

The vast knowledge of herbal remedies in traditional cultures is believed to have developed through trial and error over many centuries, with the most important cures being carefully passed on via the verbal route from one generation to the next (Van Wyk and Wink, 2004). One of the spin-offs derived from such a plethora of traditional knowledge, is that many new and important remedies are still being discovered.

**Herbal medicine and reasons for use of medicinal plants**

Nature has been a source of medicinal agents for thousands of years and an impressive number of modern drugs have been derived from natural sources, many of these isolations were based on the uses of the agents in traditional medicine (Cragg and Newman, 2001). Herbal Medicine is defined as a branch of science in which plant based formulations are used to alleviate diseases. It is also known as botanical medicine or phytomedicine. Lately phytotherapy has been introduced as more accurate synonym of herbal or botanical medicine. In the early twentieth century herbal medicine was prime healthcare system as antibiotics or analgesics were not as yet discovered. With the advent of allopathic system of medicine, herbal medicine gradually lost its popularity among people, which is based on the fast therapeutic actions of synthetic drugs (Singh, 2007). Recently there has been a shift in universal trend from synthetic to herbal medicine, which can be said “Return to Nature”. Medicinal plants have been known for millennia and are highly esteemed all over the world as a rich source of therapeutic agents for the prevention of diseases and ailments. The search for eternal health and longevity and for remedies to relieve pain and discomfort drove early man to explore his immediate natural surroundings and led to the use of many plants, animal products, minerals etc and the development of a variety of therapeutic agents (Nair and Chanda, 2007). Historically, all medicinal preparations are derived from plants, whether in the simple form of raw plant materials or in the refined form of crude extracts, mixtures, etc (Krishnaraju et al., 2005). In the early development of modern medicine, biologically active compounds from higher plants have played a vital role in providing medicines to combat pain and diseases. For example, in *The British Pharmacopoeia* (1932), over 70% of organic monographs are on plant-derived products. However, with the advent of synthetic...
medicines, and subsequently of antibiotics, the role of plant derived therapeutic agents significantly declined (mostly) in the economically developed nations. Thus, in the British Pharmacopoeia (1980), the share of plant-based monographs fell to approximately 20%. In terms of new chemical entities introduced as medicinal agents over the past several decades, the share of plant-based drugs has been no more than 2%. The recent resurgence of interest in plant remedies has been spurred on by several factors reasons (WHO 2002; WHO 2005; Calixto, 2000; Kong et al., 2003):

- The effectiveness of plant medicines
- Source of direct therapeutic agents
- Affordable by the people
- Raw material base for the elaboration of more complex semi-synthetic chemical compounds
- Models for new synthetic compounds
- Taxonomic markers for the discovery of new compounds
- The production, consumption and international trade in medicinal plants and phytomedicines are growing and expected to grow in future quite significantly
- Renewable source
- The preference of consumers for natural therapies, a greater interest in alternative medicines and a commonly held belief that herbal products are superior to manufactured products
- A dissatisfaction with the results from synthetic drugs and the belief that herbal medicines may be effective in the treatment of certain diseases where conventional therapies and medicines have proven to be inadequate
- The high cost and side effects of most modern drugs
- Improvements in the quality, efficacy, and safety of herbal medicines with the development of science and technology
- Patients belief that their physicians have not properly identified the problem; hence they feel that herbal remedies are another option
- A movement towards self-medication, investigation of the chemical and biological activities of plants during the past two centuries have yielded compounds for the development of modern synthetic organic chemistry as a major route for discovery of novel and more effective therapeutic agents.
The Recent Development of Natural Drugs

A total of 122 biologically active compounds have been identified, derived only from 94 species of plants. A conservative estimate of the number of flowering plants occurring on the planet is 2,50,000. Of these, only about 6% have been screened for biological activity and 15 percent have been evaluated phytochemically. Consistent findings should be carried out to discover a probable abundance of medicinal extracts in these plants (Turker and Usta, 2008). Furthermore, an increasing reliance on the use of medicinal plants in the industrialized societies has been traced to the extraction and development of several drugs and chemotherapeutics from these plants as well as from traditionally used rural herbal remedies (UNESCO, 1998). The Pharmaceutical Research and Development Committee report of Ministry of Chemicals, Government of India also underscores the importance of traditional knowledge (Mashelkar, 1999). The increasing use of traditional therapies demands more scientifically sound evidence for the principles behind such therapies and for effectiveness of medicines. Recent advance in the analytical and biological sciences, along with innovations in genomics and proteomics can play an important role in validation of these therapies. Western scientific community views traditional medicines cautiously and stresses the concerns related to research, development and quality (Patwardhan et al., 2003; Fabricant and Farnsworth, 2001). A large proportion of such medicinal compounds have been discovered with the aid of ethno-botanical knowledge of their traditional uses. The rich knowledge base of countries like India and China in medicinal plants and health care has led to the keen interest by pharmaceutical companies to use this knowledge as a resource for research and development programs in the pursuit of discovering novel drugs (Krishnaraju et al., 2005). Data analysis has shown that more and more people are consulting the herbal medicine practitioners. World Health Organization has also identified the importance of herbal medicines. According to a study from U.S., 60-70% patients living in rural areas are dependent on herbal medicine for their day to day diseases. Several authors have reported favorable results with herbal drugs (mostly in the form of extracts) either in animal or in human studies (Padma, 2005).

Standardization of Phytomedicine

Herbs are natural products and their chemical composition varies depending on several factors, such as botanical species, used chemotypes, the anatomical part of the plant used (seed, flower, root, leaf, fruit rind, etc.), also storage, sun, humidity,
type of ground, time of harvest, geographic area etc. This variability can result in significant differences in pharmacological activity involving both pharmacodynamics and pharmacokinetics issues (Park, 2008). It is very important that a system of standardization is established for every plant medicine in the market because the scope for variation in different batches of medicine is enormous (Ekka et al., 2008). Herbal medicines are very different from well-defined synthetic drugs. For example, the availability and quality of the raw materials are frequently problematic; the active principles are frequently unknown; and standardization, stability and quality control are feasible but not easy. Strict guidelines have to be followed for the successful production of a quality herbal drug. The medicinal plants should be authentic and free from harmful materials like pesticides, heavy metals, microbial and radioactive contamination. The source and quality of raw materials, good agricultural practices and manufacturing processes are certainly essential steps for the quality control of herbal medicines and play a pivotal role in guaranteeing the quality and stability of herbal preparations. The herbal extract should be checked for biological activity in experimental animal models. The bioactive extract should be standardized on the basis of active compound. The bioactive extract should undergo limited safety studies (De Smet, 1997; Blumenthal et al., 1998; EMEA 2002; WHO 2004; Ahmad et al., 2006; Samy and Gopalakrishnakone, 2007).

Medicinal plants as a source of important drug

Different type of isolation methods have been used to obtain pharmacologically active compounds which can be used as drug for different diseases. The methods which includes isolation from plants and other natural sources, combinatorial chemistry, synthetic chemistry, and molecular modeling (Geysen et al., 2003; Ley Baxendale, 2002 and Lombardino and Lowe, 2004). According to survey in 2001-02, approximately one quarter of the best-selling drugs in the world were either natural products or derived from natural products (Butler, 2004). It has also been reported that approximately 48% of new chemical entities (NCEs) between 1981 and 2002 were natural products or natural product-derived natural products (Newman et al., 2003) Further more, natural products also provide a starting point for laboratory syntheses with diverse structures and often with multiple stereo centers that can be challenging synthetically (Koehn and Carter, 2005; Clardy and Walsh, 2004; Peterson and Overman, 2004; Nicolaou and Snyder, 2004). Natural products shows many structural features in common (e.g., aromatic rings, chiral centers, degree of molecule
saturation, complex ring systems, and number ratio of heteroatoms) which have been shown to be very important to drug discovery efforts (Feher and Schmidt, 2003; Piggott and Karuso, 2004; Clardy and Walsh, 2004; Koehn and Carter, 2005; Lee and Schneider, 2001). Many synthetic and medicinal chemists are working in the creation of natural product and natural-product like libraries that resembles the structural features of natural products with the compound-generating potential of combinatorial chemistry (Eldridge et al., 2002; Burke et al., 2004; Hall et al., 2001a; Ganesan, 2004; Pan, 2004). Some natural products that are isolated from medicinal plants can serve not only as new drugs themselves but can also be made useful by further necessary modification by medicinal and synthetic chemists. The developments of high-throughput screening technique may show to the point and more selective activity directed towards these targets, when use the reported compounds from medicinal plants. Compounds isolated from traditionally used medicinal plants also shown to act on newly validated molecular targets, one example is indirubin, which targeted and inhibit cyclin dependent kinases (Eisenbrand et al., 2004; Hoessel et al., 1999) and another example is kamebakaurin, which has been shown to target and inhibit NF-κB (Lee et al., 2002; Hwang et al., 2001).

Phytochemistry

Phytochemistry is a branch of science that deals with the chemicals obtained with desirable activities (Kartishwaran, 2010). Several plants species endowed with this phytochemicals have been documented to serve as a potent against antimicrobial agent against several pathogenic microorganisms (Anonymous, 1976; Ray and Majamudar, 1976; Fransworth, 1988; Rastogi and Mehrotra, 1991, 1993; Asolkar et al., 1992; Cox, 1994; Perry and Metzer, 1998; Khan et al., 2002). Plants have been a major source of therapeutic agents since time immemorial and traditional herbal system of medicine, like Ayurveda resulted in revival of ancient traditional medicine. Therefore indispensable scientific authentication of these medicinal values of plants will pave the way for future herbal drugs.

Many plants, whole and parts and their products have been used in folklore medicine since ancient time for curing human ailments. Hence it is urgent need of hour to study the various pharmaceutical applications of medicinal plants and harvest the important medicinal potential of these in various human pathologists. Medicinal plants constitute the main source of new pharmaceuticals and healthcare products (Ivanova et al., 2005). The use of medicinal plants in industrialised societies has been
traced to extraction and development of several drugs from these plants as well as from traditionally used folk medicine (Shrikumar and Ravi, 2007). Extraction and characterization of several active phytocompounds from the green factories have given birth to some high activity profile drugs (Mandal et al., 2007). The use of traditional medicine is widespread in India (Jeyachandran and Mahesh, 2007). It is believed that crude drug extracts from medicinal plants are biologically active than isolated compound and its synergistic effect (Jana and Shekhwat, 2010). Phytochemical screening of plants has revealed the presence of numerous chemicals including alkaloids, tannins, flavanoids, steroids, glycosides and saponins etc. Several studies have described the antioxidant properties of medicinal plants, foods and beverages which are rich in phenolic compounds (Brown and Rice-Evan, 1998; Krings and Berger, 2001). Natural antioxidant mainly come from plants in the form of phenolic compounds such as flavonoids, phenolic content show good antioxidant activity that is there is a direct correlation between total phenol content and antioxidant activity (Brighente et al., 2007; Salazar et al., 2008).

Alkaloids

Alkaloids are naturally occurring chemical compounds containing basic nitrogen atoms. The name derives from the word alkaline and was used to describe any nitrogen-containing base. Alkaloids are produced by a large variety of organisms, including bacteria, fungi, plants, and animals and are part of the group of natural products (also called secondary metabolites). Many alkaloids can be purified from crude extracts by acid-base extraction. Many alkaloids are toxic to other organisms. They often have pharmacological effects and are used as medications and recreational drugs. Examples are atropine, the local anesthetic and stimulant cocaine, the stimulant caffeine, nicotine, the analgesic morphine, or the antimalarial drug quinine. Some alkaloids have a bitter taste.

Figure 2: Chemical structure of the alkaloid Atropine
Alkaloids are usually classified by their common molecular precursors, based on the metabolic pathway used to construct the molecule. When not much was known about the biosynthesis of alkaloids, they were grouped under the names of known compounds, even some non-nitrogenous ones (since those molecules' structures appear in the finished product; the opium alkaloids are sometimes called "phenanthrenes", for example), or by the plants or animals they were isolated from. When more is learned about a certain alkaloid, the grouping is changed to reflect the new knowledge, usually taking the name of a biologically-important amine that stands out in the synthesis process.

- Pyridine group: piperine, coniine, trigonelline, arecaidine, guvacine, pilocarpine, cytisine, nicotine, sparteine, pelletierine.
- Pyrrolidine group: hygrine, cuscohygrine, nicotine
- Tropane group: atropine, cocaine, eegonine, scopolamine, catuabine
- Quinoline group: quinine, quindine, dihydroquinine, dihydroquinidine, strychnine, brucine, veratrine, cevadine
- Isoquinoline group: The opium alkaloids (morphine, codeine, thebaine, Isopapadimethoxy-aniline, papaverine, narcotine, sanguinarine, narceine, hydrastine, berberine), emetine, berbamine, oxyacanthine
- Phenethylamine group: mescaline, ephedrine, dopamine, amphetamine
- Indole group:
  - Tryptamines: DMT, N-methyltryptamine, psilocybin, serotonin
  - Ergolines: the ergot alkaloids (ergine, ergotamine, lysergic acid, LSD etc.)
  - Beta-carbolines: harmine, harmaline, yohimbine, reserpine
- Rauwolfia alkaloids: Reserpine
- Purine group:
  - Xanthines: caffeine, theobromine, theophylline
- Terpenoid group:
  - Aconite alkaloids: aconitine
  - Steroids: solanine, samandaris (quaternary ammonium compounds): muscarine, choline, neurine
- Vinca alkaloids: vinblastine, vincristine. They are antineoplastic and binds free tubulin dimers thereby disrupting balance between microtuble polymerization and depolymerization resulting in arrest of cells in metaphase.
- Miscellaneous: capsaicin, cynarin, phytolaccine, phytolaccotoxin
Flavonoids

Flavonoids are a group of polyphenolic phytochemicals that include flavones, isoflavones, (iso)flavanones, flavonols, catechins, anthocyanidins and chalcones. Over 4,000 flavonoids have been identified and they occur in relatively high concentrations in fruits, vegetables, nuts and grains, beverages (tea, coffee, beer, wine and fruit drinks) and in various herbs and spices (Sanderson et al., 2004).

![Figure 3: Chemical structure of the flavonoid Quercetin](image)

The flavonoids have aroused considerable interest recently because of their potential beneficial effects on human health. Flavonoids are known to have widely diverse beneficial biological effects, such as anti-inflammatory antioxidant (Pietta, 2000), antiviral (Jassim and Naji, 2003), and anticancer effects (Adlercreutz, 2002; Frei and Higdon, 2003; Rietveld and Wiseman, 2003). They also modulate the function of sex hormones and their receptors. Certain flavonoids, such as the isoflavone genistein, are estrogenic (Wang et al., 1996; Zand et al., 2000), whereas others, such as chrysin, can interfere with steroid synthesis and metabolism. The antiviral activities of bioflavonoids extracted from medicinal plants have been evaluated (Beladi et al., 1977; Tsuchiya et al., 1985).

Saponins

Saponins are glucosides with foaming characteristics. Saponins consist of a polycyclic aglycones attached to one or more sugar side chains. The aglycone part, which is also called sapogenin, is either steroid (C27) or a triterpene (C30).
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The foaming ability of saponins is caused by the combination of a hydrophobic (fat-soluble) sapogenin and a hydrophilic (water-soluble) sugar part. Saponins have a bitter taste. Some saponins are toxic and are known as sapotoxin. Saponins have been found to have significant bioactivities like anti-inflammatory (Wang et al., 2008; Recio et al., 1995), anti-tumour (Jung et al., 2004), antispasmodic (Trute, 1996), antileishmanicidal (Majester et al., 1991), and anti-proliferative activity (Denby 1994).

**Coumarins**

Coumarins owe their class name to 'coumarou', the vernacular name of the tonka bean (*Dipteryx odorata* Willd., Fabaceae), from which coumarin itself was isolated in 1820 (Bruneton, 1999). Coumarins belong to a group compounds known as the benzopyrones, all of which consist of a benzene ring joined to a pyrone. Coumarin and the other members of the coumarin family are benzo-[@]pyrones, while the other main members of the benzopyrone group – the flavonoids – contain the [@]-pyrone group (Keating and O’Kennedy, 1997; Murray et al., 1982). Coumarins may also be found in nature in combination with sugars, as glycosides. The coumarins can be roughly categorised as follows (Ojala, 2001):

- Simple – these are the hydroxylated, alkoxyalted and alkylated derivatives of the parent compound, coumarin, along with their glycosides.
- Furanocoumarins – these compounds consist of a five-member furan ring attached to the coumarin nucleus, divided to linear and angular types with substitutes at one or both of the remaining benzenoid positions.
- Pyranocoumarins - members of this group are analogous to the furano coumarins, but contain a six-member ring
- Coumarins substituted in the pyrone ring.

Like other phenylpropanoids, coumarins arise from the metabolism of phenylalanine via ω-cinnamic acid, p-coumaric acid (Bruneton, 1999; Matern et al., 1999).

\[
\begin{align*}
\text{Coumarin} & \quad R_1 \quad R_2 \quad R_3 \\
\text{Herniarin} & \quad H \quad H \quad \text{OCH}_3 \\
\text{Methyl-umbelliferone} & \quad \text{CH}_3 \quad H \quad \text{OH} \\
\text{Scopoletin} & \quad H \quad \text{OCH}_3 \quad \text{OH} \\
\text{Umbelliferone} & \quad H \quad \text{OH}
\end{align*}
\]

Figure 5: Chemical Structures of Coumarins.

The coumarins exist in larger quantities in the plants of certain families such as Leguminoseae (bean family), Rutaceae (citrus family) and Umbelliferae (parsley-fennel family). They are also available in fungi and bacteria (Murray, 1982). They have been reported to have many biological activities without evidence of toxicity, including inhibition of lipid peroxidation and neutrophil-dependent anion superoxide generation, anti-inflammatory and immuno suppressor actions (Luchini et al., 2008). In addition, coumarin and two of its mono-hydroxylated derivatives (4-hydroxycoumarin and 7-hydroxy coumarin) inhibit prostaglandin biosynthesis (Lee, 1981).

Anthraxquinones

Anthraquinone-containing extracts from different plant sources have been widely used since ancient times due to their laxative and cathartic properties (Thomson, 1986). Anthraquinones are present in the roots, bark or leaves of numerous plants such as senna, cascara, aloe, frangula and rhubarb. Besides their laxative properties, this class of compounds have shown a wide variety of pharmacological activities such as anti-inflammatory, wound healing, analgesic, antipyretic, anti-tumour (Alves et al., 2004), antifungal (Chrysayi-Tokousbalides et al., 2003; Agarwal et al., 2000), antiviral and in vivo inhibitory effects towards P388 leukemia in mice.
They were reported containing the photoprotease activities. They are also used in industry as textile dyes, food colourants (Nemeikaite-Ceniene, 2002) and bugs repellents.

Tannins

Tannins are astringent, bitter plant polyphenols that either bind and precipitate or shrink proteins. The astringency from the tannins is what causes the dry and puckery feeling in the mouth following the consumption of red wine, strong tea, or an unripened fruit (McGee, 2004). The term tannin refers to the use of tannins in tanning animal hides into leather; however, the term is widely applied to any large polyphenolic compound containing sufficient hydroxyls and other suitable groups (such as carboxyls) to form strong complexes with proteins and other macromolecules. Tannins have molecular weights ranging from 500 to over 3,000 (Hemingway, 1989).

Figure 6: A hydrolysable tannin; Gallic acid

Tannins have shown potential antiviral (Quideau et al., 2004; Cheng, 2002), antibacterial and antiparasitic effects (Kolodziej, 2005). In the past few years tannins have also been studied for their potential effects against cancer through different mechanisms (Susumu et al., 2005; Ling Ling et al., 2000). Tannins, including gallo and ellagic acid (epigallitannins), are inhibitors of HIV replication. 1,3,4-tri-O-galloylquinic acid, 3,5-di-O-galloyl-shikimic acid, 3,4,5-tri-O-galloyl-shikimic acid, punicalin and punicalagin inhibited HIV replication in infected H9 lymphocytes with little cytotoxicity. Two compounds, punicalin and punicacortein C, inhibited purified HIV reverse transcriptase.
<table>
<thead>
<tr>
<th>Chemical Group</th>
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<th>Activity Ethno-pharmacology</th>
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<tr>
<td>Alkaloids</td>
<td>Antibacterial</td>
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<td>Antifungal</td>
<td>- Gastro Intestine Tract infections.</td>
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<td>Analgesic</td>
<td>- Colds, coughs, chest pains, TB, Pneumonia</td>
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<td>Flavonoids</td>
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<td>Anti-inflammatory</td>
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<td>- Tapeworm, Ringworm, Bilharzias, Dysentery</td>
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Microbial infections and their health effects

Microbial infections have caused a big burden of diseases and bacteria are listed in the first position among common microorganisms responsible for opportunistic diseases associated with HIV/AIDS (Rathee et al., 2012). In developing countries, bacterial infections are prevalent due to factors such as poor hygiene, sanitation and overcrowding in the living conditions. Throughout history, infectious diseases have been a major threat to human and animal health and a prominent cause of morbidity and mortality, (WHO, 2003). Increased antibiotic resistance has become a global concern, coupled with the problem of microbial persistence, thus highlighting the need to develop novel microbial drugs that are not only active against drug resistant microbes, but more importantly, kill persistent micro-organisms and shorten the length of treatment. Apart from toxicity, lengthy therapy also creates poor patient compliance (Mariita et al., 2010).

Conventional antibiotics and the problem of microbial resistance

Conventional antibiotics refer to the synthetic chemicals used as bactericides and fungicides. Antibiotics act in various ways such as; inhibition of cell membrane functions, inhibition of protein synthesis, inhibition of nucleic acid synthesis and inhibition of cell wall synthesis (Kalayou et al., 2012). Since their discovery, antimicrobial drugs have proved remarkably effective for the control of bacterial infections. However, it was soon evident that bacterial pathogens were unlikely to surrender unconditionally, because some pathogens rapidly become resistant to many of the first discovered effective drugs (Cowan, 1999). Due to indiscriminate use of antimicrobial drugs, microorganisms have developed resistance to many antibiotics and that has created immense clinical problems in the treatment of infectious diseases (Davis, 1994). In addition, antibiotics are associated with adverse effects on host, which include depletion of beneficial gut and mucosal microorganisms, immunosuppression, hypersensitivity and allergic reactions. The drug resistant bacteria have further complicated the treatment of infectious diseases in immuno compromised, AIDS and cancer patients especially in the case of nosocomial infections (McGaw et al., 2001). There is not only the lost of effectiveness of antibiotics against multidrug resistant microorganisms, but also global problem for the lots of budget for treating infectious diseases (Ahmad and Beg, 2001). The emergence of antimicrobial resistance has its roots in the use of antimicrobials in animals and the subsequent transfer of resistance genes and bacteria among animals, animal products and the
environment. The emergence of multi resistant bacteria to antimicrobial drugs has increased the need for new antibiotics or modifications of older antibiotics (Tollefson and Miller, 2000).

**Plant derived antimicrobials**

The antimicrobial compounds from plants may inhibit bacterial growth by different mechanisms than those presently used antimicrobials and may have a significant clinical value in treatment of resistant microbial strains (Shankar et al., 1980). Extracts isolated from several plants have been reported to have biological activity such as antimicrobial, anti-inflammatory and antioxidant activities (Yusuf et al., 2001). Phenolic compounds are one of the most diverse groups of secondary metabolites found in edible plants. They are found in a wide variety of fruits, vegetables, nuts, seeds, stems and flowers as well as tea, wine, propolis and honey, and represent a common constituent of the human diet. In nature they are involved in plant growth and reproduction, provide resistance from pathogens and predators and protect crops from disease and pre-harvest seed germination (Ross and Puther, 1987).

There are different classes of polyphenols known as tannins, lignins and flavonoids. Flavonoids are the most widely occurring polyphenol and are present in almost every form of human consumed vegetation. Dietary flavonoids have attracted interest because they have a variety of beneficial biological properties, which may play an important role in the maintenance of human health. Flavonoids are potent antioxidants, free radical scavengers and metal chelators. They inhibit lipid peroxidation and exhibit various physiological activities including anti-inflammatory, anti-allergic, anti-carcinogenic, anti-hypertensive, anti-arthritic and antimicrobial activities. Consumption of phenol-rich beverages, fruit and vegetables has commonly been associated with reduction of the risk of cardiovascular diseases in epidemiological studies. Flavonoids have been found to be the most abundant polyphenols. The biosynthesis of flavonoids is stimulated by sunlight (ultraviolet radiation), so higher concentrations of flavonoids can typically be found in the outermost layers of fruits and vegetables (i.e. the skins). Extraction of polyphenols can be performed using a solvent like water, hot water, methanol, methanol/formic acid, methanol/water/acetic or formic acid etc. Therefore, the total polyphenol amounts detected from the same plant and their corresponding antioxidant and antimicrobial activities may vary widely, depending on external conditions applied. It was reported that an antimicrobial action of phenolic compounds was related to inactivation of
cellular enzymes, which depended on the rate of penetration of the substance into the cell or caused by membrane permeability changes (Schultz et al., 1992). Terpenoids and essential oils are also plant derived antimicrobials. Terpenes or terpenoids are active against bacteria, viruses and protozoa. The mechanism of action of terpenes is not fully known but it is speculated to involve membrane disruption by lipophilic compounds (Hamed, 2011). Heterocyclic nitrogen compounds are called alkaloids. The mechanism of action of highly aromatic planar quaternary alkaloids is attributed to their ability to intercalate with DNA of microorganisms (Cowan, 1999). Lectins and polypeptides are often positively charged and contain disulphide bonds. Their mechanism of action may be the formation of ion channels in the microbial membrane or competitive inhibition of adhesion of microbial proteins to host polysaccharide receptors (Sher, 2004).

Antimicrobial screening

Extraction (as the term is pharmaceutically used) is the separation of medicinally active portions of plant (and animal) tissues using selective solvents through standard procedures. The products so obtained from plants are relatively complex mixtures of metabolites, in liquid or semisolid state or (after removing the solvent) in dry powder form, and are intended for oral or external use. These include classes of preparations known as decoctions, infusions, fluid extracts, tinctures, pilular (semisolid) extracts or powdered extracts. Extraction methods used pharmaceutically involves the separation of medicinally active portions of plant tissues from the inactive/inert components by using selective solvents. During extraction, solvents diffuse into the solid plant material and solubilize compounds with similar polarity (Ncube et al., 2008).

For the phytochemical screening Eloff (1998) examined a variety of extractants for their ability to solubilise antimicrobials plants and provide a more standardized extraction method. Among the various extractants used in studies published till date Acetone received the highest overall rating. In fact, a review of 48 articles describing antimicrobial properties in the most recent years, only one study used acetone as an extractant. Ethanol and methanol used as initial extractants in approximately 35% of studies (Cowan, 1999). As more active compounds solubilise in methanol (Cowan, 1999) which is the prime choice of solvent for the extraction of active compounds for plants materials. Now- a- days several researchers use various
solvent extractants to isolate the active compounds present in them and find out the antimicrobial activities against several pathogenic resistant microorganisms.

The crucial factor for the ultimate success of an investigation into bioactive plant constituents is thus the selection of plant material (Hostettmann, 1995). In view of the large number of plant species potentially available for study, it is essential to have efficient systems available for the rapid chemical and biological screening of the plant extracts selected for investigation. The following scheme of microbiological methods may help to screen the large number of active principles and finding out the structures for therapeutic use and drug development.

Most of the published procedures till recently are based on the so-called agar-diffusion technique, whereby the antibacterial compound is transferred from the chromatographic layer to an inoculated agar plate through a diffusion process. Zones of inhibition are then visualized by appropriate vital stains. The procedure has several disadvantages and requires the use of suitable microbiological equipment. Considering the problems that arise due to the differential diffusion of compounds from the chromatogram to the agar plate, a simplified procedure through direct bioautographic detection on the chromatographic layer has been published (Lund and Lyon, 1975). Bioautography belongs to microbiological screening methods commonly used for the detection of antimicrobial activity. The screening can be defined as the first procedure, which is applied to an analyzed sample, in order to establish the presence or absence of given analytes (Aerts et al., 1995). Basically speaking, it is a simple measurement providing a “yes/no” response (Muñoz-Olivas, 2004). Bioautography screening methods are based on the biological activities, e.g. antibacterial, antifungal, antitumour, and antiprotozoae of the tested substances. This
detection method can be successfully combined with layer liquid chromatography techniques, such as thin-layer chromatography (TLC), high-performance thin-layer chromatography (HPTLC), over pressured-layer chromatography (OPLC) and planar electrochromatography (PEC). In so-called direct bioautography, i.e. bioautography hyphenated directly with thin-layer chromatography (TLC-DB), both separation and microbial detection are performed on the same TLC plate. Generally, the method measures antibacterial properties of analyzed substances, i.e. changes in bacterial growth. The detection and identification of specific molecules may often be accomplished most conveniently by autographic methods. These procedures, in which nutritionally deficient bacterial cells suspended in solid minimal media show zones of growth in the presence of the required nutrient, possess several advantages over liquid assay methods.

The importance of pharmacological screening of plant extracts for multiple biological activities has been extensively documented. The use of multiple bioassays gives a clearer indication of the effect of the extracts in relation to the disease state (Houghton et al., 2007). According to Gurib-Fakim (2006) medicinal plants contain complex mixtures of compounds that may act individually, additively or in synergy for health improvement. For instance, a medicinal plant containing phenolic compounds may act as antioxidant and as an anti-inflammatory agent. Similarly, Mcgaw et al., (2001) studied the pharmacological activity of different Combretum species and four species demonstrated a significant bioactivity in more than one bioassay. In another study, antibacterial and anti-inflammatory activity of five species in the family Sterculiaceae was reported, as a result a variety of compounds were isolated from the plant species (Reid et al., 2005). Moreover, there is a risk of non-discovery of other potentially useful bioactivity of medicinal plants when only a single biological activity is investigated (Rates, 2001). Furthermore, as helminth and microbial infections have some common symptoms such as diarrhoea, abdominal pains and inflammation, there is a possibility of discovering antimicrobial activity in the investigated plants species.

**Effect of microbial infections on human health**

Although only a small fraction of the thousands of microorganism species are harmful, the impact of these pathogenic microorganisms is of great concern in human medicine. Most microbes are beneficial, playing a crucial role in the ecosystem as decomposers and in the production of antibiotics against human diseases (Black,
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2002). Unfortunately, the living conditions of the majority of people in the third-world and most developing countries are characterized by poor sanitation, low-levels of hygiene and overcrowded environments (Longanga Otshudi et al., 2000; Hotez et al., 2007a). These factors enhance the growth of a wide range of microorganisms, especially the virulent pathogens present within the community (Sleigh and Timburg, 1998). Due to lower immunity caused by these factors, the human skin, mouth, urinary tract, respiratory organs and gastro-intestinal tract becomes more susceptible to infection by these microorganisms (Eisenstein and Schaechter, 1998). Most helminth infections have been attributed to the shift in the host-parasite relationship in favour of the parasite, thereby causing serious health problems (Sleigh and Timburg, 1998)

Bacterial infections

Bacterial infections are caused by a wide range of organisms resulting in mild infections to life threatening diseases. For instance, *Bacillus subtilis* is an aerobic, rod-shaped, motile, and endospore-forming Gram-positive bacterium. It is a soil inhabiting saprophytic organism (Sleigh and Timburg, 1998). Although harmless, it occasionally causes some opportunistic infections such as conjunctivitis (Murray et al., 1998; Buwa and Van Staden, 2006). *Staphylococcus aureus*, a Gram-positive coccus bacterium, is part of the normal flora of human skin and mucous membranes (Murray et al., 1998). This organism is responsible for human staphylococcal skin infections (wounds and impetigo), soft tissues (septic arthritis) and pneumonia (Sleigh and Timburg, 1998). *Escherichia coli*, a Gram-negative rod-shaped bacterium is mostly found inhabiting the human gastrointestinal tract (Ross and Peutherer, 1987). The organism has been implicated in most bacterial infections including urinary tract infection, travellers diarrhoea, bacteraemia and pneumonia (Dupont, 2006). *Klebsiella pneumoniae* is a non-motile, rod-shaped Gram-negative bacterium. The organism is easily observed in culture as it forms large colonies. It is also part of the human intestinal and colon flora, having a prominent polysaccharide capsule that provides resistance against host defence mechanisms (Hugo, 1992). Common human *Klebsiella* infections include community acquired pneumonia, urinary tract infection, lower and upper respiratory tract infections (Einstein, 2000).

Other examples of medically important bacterial groups, known to cause various infectious diseases in humans, include mycobacterium (tuberculosis), vibrio (cholera), neisseria (gonorrhoea) and spirochaetes (syphilis). In Among infectious
bacterial diseases, especially tuberculosis is increasing due to the high drug resistance and high incidence of HIV/AIDS infection amongst the population (Eldeen et al., 2005; Naidoo, 2008).

**Fungal infections**

Fungal and yeast infections have a major influence on human health causing diseases ranging from mild superficial problems to potentially lethal systemic disorders (infections invading internal organs) (Kobayashi and Medoff, 1998). The number of diseases due to fungal infections is however, lower than bacterial infections. Recently, pathogenic fungal infections have been increasing, mostly due to a compromised immune system as humans have a high degree of innate immunity to most fungi with exception of the dermatophytic type (Murray et al., 1998; Deacon, 2006). Opportunistic fungal pathogens such as *Candida*, *Mucor* and *Aspergillus* are the major causes of morbidity and mortality in humans (Garbino et al., 2001). For instance, *C. albicans* which is part of the normal flora of the upper respiratory, gastrointestinal and female genital tracts is responsible for 90% of fungal infections in immuno-compromised patients globally. Shai et al., (2008) reported high occurrence of candidiasis among South African HIV/AIDS immune compromised patients. In KwaZulu-Natal, a similar trend with associated symptoms such as severe inflammatory diarrhoea and resistance to antifungal chemotherapy was observed (Motsei et al., 2003).

**Treatment of microbial infections**

The development of natural products such as antibiotics created a major breakthrough in the fight against pathogenic microorganisms. The discovery by Alexander Fleming in 1929 of *Penicillium nonatum* (penicillin) inhibition of *Staphylococci* cultures ushered in the antibiotic era and subsequently led to the development of other antibiotics such as streptomycin and tetracycline (Sleigh and Timburg, 1998; Murray et al., 1998). Unfortunately, the emergence of drug resistant bacteria and the elimination of useful bacterial flora leading to host susceptibility to other pathogenic infections are today major problems associated with most antibacterial chemotherapy (Guarnier and Malagelada, 2003).

The number of effective chemotherapies against fungal infections is relatively small when compared to antibacterial drugs. Common antifungal drugs include Amphotericin B, fluconazole and griseofulvin. Amphotericin B is mostly used against fungi causing systemic diseases. It binds to the sterols causing disruption in fungus
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cell membrane and finally leads to death of the organism (Deacon, 2006). Most antifungal chemotherapeutic agents are toxic in high dosage and have limited therapeutic values because of problems with solubility, stability, and absorption by the human body. Furthermore, Candida species are resistant to all antibacterial antibiotics because fungi are eukaryotic microorganisms. Globally, there is a need for new strategies against the increasing microbial infections due to development of resistance to conventional drugs and the adverse effects of most available chemotherapy. Fortunately, plants are described as the best “combinatorial chemists”, and have the potential to provide novel compounds which may turn out to be useful drugs (Saklani and Kutty, 2008).

The scientific investigations and information on the therapeutic potential of these medicinal plants are limited. This lack of scientific knowledge has restricted the use of traditional herbs as remedies to be used in conjunction with or as an alternative to orthodox medical treatment. As of now, only about 20% of the world medicinal plants have been screened for pharmacological and biological activities (Reynold and Lawson, 1978; Ndukwe et al., 2005). Natural products from both plants and microbial sources are used in pharmaceutical preparations either as pure or crude extracts (Parekh and Chanda, 2007). Presently, a lot of attention is focused on higher plants to determine their phytoconstituents with the aim of using them for the prevention and treatment of microbial infections and other diseases of non-microbial etiology as alternatives to synthetic drugs. The ever increasing demand for safer and cheaper herbal recipes in the developed countries has led to the extraction and development of several drugs and chemotherapeutic agents from plants as well as from traditional herbal remedies (Falodun et al., 2006). The scientific literature is full of reports describing plants as the sleeping giant of the pharmaceutical industry (Smith, 1991; Michael, 2002), which when fully exploited will provide novel compounds to fight infectious diseases (Onyeagba et al., 2004; Muhsin and Amina, 2007; El-Mahmood and Ameh, 2007).

Plants are found to be sources of many chemical compounds, most of which account for their various uses by man. The most important of these compounds are alkaloids, terpenoids, steroids phenols, glycosides and tannins (Abayomi, 1993). Characterization of extracts of medicinal plants is necessary, due to its numerous benefits to science and society. The information obtained, makes pharmacological
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studies possible. It also enabled structure-related activity studies to be carried out, leading to the possible synthesis of more potent drug with reduced toxicity.

At present, a majority of botanical drugs under development are derived from ethanobotanical sources and traditional medicinal uses to combat the treatment paused by microorganisms, which became resistance to antimicrobial agents. In this context, the present investigation is aimed to screen the plants belonging to Gujarat state (Table. 1) and to find out the antimicrobial principles present in them. The organisms selected in the study are opportunistic pathogens and can cause serious health problem in the hospitalized patients and in the community as well. The following objectives were selected to fulfill the aim.

1. Bioassay of crude plant extracts for their potential antimicrobial (antibacterial and antifungal) activity.
2. Purification and characterization of active compound/s from effective plant extracts by various chromatographic and spectroscopic methods.