Health is wealth is an old proverb, but till today it is applicable to all
human beings. Nature keeps in her green bag the secret of a healthy
life on this earth, perhaps in the luxuriant green cover, the
biodiversity (Sinha and Sinha, 2001). Medicinal plants have been considered as
an important therapeutic aid for alleviating ailments of humankind. Search for
eternal health and longevity and to seek remedies to relieve pain and
discomfort prompted the early man to explore his immediate natural
surroundings to develop a variety of therapeutic agents using natural resources.
Although there are no apparent morphological characteristics in the medicinal
plants growing with them, yet they possess some special qualities or virtues
that make them medicinally important (Kirtikar and Basu, 2001).

The applications of plants as medicines date back to prehistoric period.
The widespread use of herbal remedies and healthcare preparations, as those
described in ancient texts such as the Vedas and the Bible, and obtained from
commonly used traditional herbs and medicinal plants, has been traced to the
occurrence of natural products with medicinal properties (Lucy and Edgar,
1999). The medicinal plants are extensively utilized throughout the world in
two distinct areas of health management; traditional system of medicine and
modern system of medicine. The traditional system of medicine mainly
functions through two distinct streams, local or folk or tribal stream and,
codified and organized system of medicines like Ayurveda, Siddha, Unani etc.
(Singla et al. 2012). Plants like Rawolfia serpentina, Papaver somniferum and
Cinchona officinalis have long been used to treat disease of body and mind.
Some knowledge of ancient Indian medicine and medicinal herbs has been
handed down through generations and has survived among the ethnic
communities of India (Bodding, 1925).

Over the centuries, the use of medicinal herbs has become an important
part of daily life, despite the progress in modern medical and pharmaceuticals
research. The Rigveda (3700 BC) mentions the use of medicinal plants. It is
estimated that 40% of the world populations depends directly on plant based
medicine for their health care (Gupta et al. 2004; Sandhu and Heinrich, 2005). In India, medicinal plants offer low cost and safe health care solutions. There are several attempts were made to explore indigenous knowledge on use of common medicinal plants for the treatment of diseases related to various systems of human beings (Prasad and Tyagi, 2015).

**Traditional use of medicinal plants**

Traditional medicine is the sum total of the knowledge, skills and practices based on the theories, beliefs and experiences indigenous to different cultures used in the maintenance of health, prevention of diseases and improvement of physical and mental illness. In practice, traditional medicine refers to the following components: Acupuncture (China), Ayurveda (India), Unani (Arabic countries), traditional birth attendant’s medicine, mental healer’s medicine, herbal medicine and various forms of indigenous medicine (Fig. 1.1). Complementary or alternative medicine refers to a broad set of healthcare practices that are not part of a country’s own tradition and are not integrated into the dominant healthcare system (Iwu et al. 1999; Idu et al. 2007; Mann et al. 2008; Ammara et al. 2009; Ampofo et al. 2012).

![Fig. 1.1: Plant species used under different medicinal systems (NMPB, 2008)](image)

Traditional medicine has maintained its popularity in all regions of the developing world, and its use is rapidly spreading in industrialized countries. Knowledge of plants and of healing has been closely linked from the time of human being’s earliest social and cultural groupings. Knowledge of the
medicinal plants used in the drugs of traditional systems of medicine (TSM) has been of great significance, especially as a lead for the discovery of new single-molecule medicines for modern system of medicine. Thus, medicinal plants are used in crude or purified form in the preparation of drugs in different systems.

In countries like India, China and others with well-founded traditional systems of medicine, plant-based formulations occupy an important place in health management. However, the recent broadening of the horizons of drug discovery, due to advances in instrumentation and Bioinformatics, has opened up new avenues for use of this knowledge in drug development research (Wink et al. 1999). Structural novelty and new modes of action are common features of plant drugs. This has been shown by anticancer agents like vinblastine, vincristine and paclitaxel, cardiovascular agents like forskolin, anti-HIV agents like calanoid and antihyperlipidemic agents like guggulsterones (Cragg and Newman, 2013).

**Exploration of medicinal plants**

Plants are a great source of therapeutic molecules. In the early 20th century, taxonomic surveys established the identity of plants, followed by ethnomedical surveys documenting the use of plants as medicine and other uses. The identification of active principles of medicinal plants leads to the use, misuse and abuse of substances of vegetal origin. The use may be curative (eg. vincristine and vinblastine, reserpine, ephedrine, aspirin, morphine, digoxin) or narcotic abuse (cocaine, morphine and cannabis), and misuse has made several plants endangered species, eg. *Podophyllum hexandrum*, *Taxus baccata*, *Coptis teeta*, *Picrorhiza kurroa* and *Nardostachys jatamansi* (Ramawat, 2009). This over exploitation has resulted in depletion in germplasm resources, particularly in third world countries, and urgently warrants the development of alternative biotechnological methods for micropropagation, the study of seed and reproductive biology, and last but not least, social awareness. It is estimated that approximately 1500 plant species in India are threatened, including 124
endangered species. About 250,000 species of higher plants are yet to be investigated for pharmacological activity. Plants can be a source of effective remedies for Alzheimer’s, Parkinson’s, epilepsy, migraine, arthritis and schizophrenia (Kinghorn et al. 2011).

Increased demand for natural drugs has led to the domestication of several plants such as *Catharanthus roseus* and *Taxus baccata*, and several others (*Psoralea corylifolia*, *Carthamus tinctorius*) are being evaluated for agronomic traits. Plant chemicals have evolved in nature in response to needs and challenges of the plant environment. Nature has been carrying out its own combinatorial chemistry for over three billion years (Zhang et al. 2005). The total number of natural products produced by plants has been estimated at over 500,000. Ethnobotanical and traditional usage of medicinal plants serves as a source of information for the isolation of active compounds eg. as direct therapeutic agents (D-tubocurarine from *Chondrodendron tomentosum*), as the starting drug for semi-synthesis (diosgenin from *Dioscorea floribunda*), the model drug for new synthetic drugs (coca from *Erythroxylum coca*), for the synthesis of local anaesthetics and lastly, as taxonomic markers for identification (David et al. 2015). Drug discovery from plants requires the combined efforts of botanists, pharmacognosists, phytochemists and other scientists to screen the products. Improvements in isolation techniques to meet the demand for pharmacology, the generation of large numbers of samples from correctly identified plants from the tropics for high-throughput screening, elaborate arrangements for preclinical (pharmacology, toxicology, pharmacokinetics and drug delivery) and lastly, for clinical trials are required for drug development (Fig. 1.2) (Rajesh et al. 2013).

![Fig. 1.2: Steps involved in drug development](image)
Bioactive molecules of medicinal plants: Secondary metabolites

The secondary metabolites (SMs) are chemicals produced by plants which are not directly involved in normal growth, development and reproduction but usually has an important ecological function (Karuppusamy, 2009). Each plant family, genus and species produces a characteristic mix of these chemicals and they can sometimes be used as taxonomic characters in classifying plants.

The content of SMs varies hugely among plant species; some may contain as little as 1% or up to a one third of their dry weight. Generally, tropical and sub-tropical plant species contain much greater amounts of extractives than the ones in the temperate regions. Furthermore, the concentration of SMs in all parts of a plant is not uniform and different amounts may be present in leaves, flowers, fruits, bark, heartwood, roots, branch bases and wound tissues. Variations in the content of SMs have also been found among species between plant of a given species and between different seasons (John and Daniel, 2001; John, 2004).

The functions of secondary metabolites are varied. For example, some secondary metabolites are toxins, used to deter predation, and others are pheromones used to attract insects for pollination. Phytoalexins protect against bacterial and fungal attacks. Allelochemicals inhibit rival plants that are competing for soil and light. However, it was the potential use of plant SMs in health care and personal care products, and as lead compounds for the development of novel drugs, that led to a huge interest in their isolation and characterization from major plant species over the past few decades. At present, the array of compounds reported is daunting, and the total number of identified SMs exceeds 100,000 with wide ranging chemical, physical and biological activities (Winks, 1999).

It is the medicinal plants that are rich in secondary plant products, and it is because of these compounds that these are termed ‘medicinal’ or ‘officinal’ plants (Newman and Cragg, 2012). These secondary metabolites exert a
profound physiological effect on mammalian systems; thus they are known as the active principle of plants. With the discovery of the physiological effect of a particular plant, efforts are being made to know the exact chemical nature of these drugs (called active principle) and subsequently, to obtain these compounds by chemical synthesis.

Plants synthesize a bewildering variety of secondary metabolites - phytochemicals but most are derivatives of a few biochemical motifs and some major groups are explained below.

**Nitrogen-containing alkaloids and sulphur-containing compounds:** Alkaloids contain a ring with nitrogen; with over 10,000 known structures, but they are only found in 20% of the angiosperms. Alkaloids are generally present in higher concentrations in bark, seeds, roots and leaves than in wood. All alkaloids contain nitrogen heterocycles and are mainly present in plants as salts of carboxylic acids. Alkaloids have a wide variety of chemical structures and are classified according to the type of ring *viz.* pyrrolidine (hygrines, stachydrine), piperidine (arecoline, lobeline), purines (caffeine, theophylline) *etc.* and their biosynthetic origin. Alkaloids amines often affect neuroreceptors, or modulate other steps in the signal transduction *eg.* ion channels and enzymes (Winks and Schimmer, 1999). This is because alkaloids are derived from the same amino acid precursors as neurotransmitters and their structures often mimic those of neurotransmitters. Furthermore, alkaloids may affect the function of ion channels by inhibiting neurotransmitter-degrading enzymes (such as acetylcholinesterase) or by modulating enzymes involved in signal transduction (such as adenyl cyclase, protein kinase) (Winks, 1999). Alkaloids are well known for potent pharmacological activities, such as analgesics (morphine, papavarine), antimalarial (quinine) antispasmodics, and for treatment of hypertension (reserpine), mental disorders and tumours (vincristine).
The major sources of sulphur-containing plant compounds are derived from the cruciferous crops such as cabbages, and allium crops such as garlic (A. sativum), onions (A. cepa). Epidemiological studies with both cruciferous crops and allium crops suggest that they provide health benefits, particularly with regard to a reduction in risk of cancer. Experimental approaches with animal and cell models suggest that the sulphur-containing compounds of these crops may be the major bioactive agent. Additionally, these compounds may also protect against atherolosclerosis and other inflammatory diseases (Crozier et al. 2006).

**Phenolics:** These contain phenol rings. The anthocyanins that give grapes their purple color, the isoflavones, the phytoestrogens from soy and the tannins that give tea its astringency are phenolics. These organic compounds are characterized by the presence of a hydroxyl (-OH) group, attached to a benzene ring or to other complex aromatic ring structures. Phenols with more than one hydroxyl group per aromatic ring are known as polyhydric phenols (eg. catechol and hydroquinone). Phenolic compounds range from simple phenol (found in essential oil of Pinus sylvestris) to polyphenols such as anthocyanin pigments and tannins. Tannins are mainly found in bud and foliage tissues, but bark and heartwood often contain the highest levels. The tannins have been reported to possess essential pharmacological properties such as wound healing, antioxidant, antimicrobial, antifungal, antiviral, antitumor, antifeedant, anthelminthic, anti-inflammatory, cytotoxic etc. (Harborne, 1991).

Another important type of polyphenolic compounds is water-soluble pigments, flavonoids that have useful antioxidant properties. Of the 8000 known phenolic compounds, around 4000 are flavonoids (Harborne, 1991). Flavonoids commonly occur in foliage, bark, sapwood and heartwood in trees. The other properties reported for flavonoids include anti-inflammatory, antihistaminic, antiviral and antidiabetic. For example, quercetin (found in bark of Quercus spp.) has been reported to block the sorbitol pathway, which is linked to certain problems associated with diabetes.
Some phenolics occur as glycosides and lignans *etc.* and display a wide range of biological activities including fungal growth inhibition, fish toxicity, insect antifeedant and juvenile hormone functions (Gottlieb and Yoshida, 1989).

**Terpenoids** (Terpenes): Terpenoids are built up from terpene building blocks. Terpenes are the largest group of natural products from plants with over 20,000 known structures, comprising essential oils, flavours, fragrances and lipid-soluble plant pigments. These hydrophobic compounds are usually stored in plants in resin ducts, oil cells or glandular trichomes (Winks and Schimmer, 1999). Terpenes are derived from 5-carbon isoprene units \([\text{CH}_2=\text{C}(\text{CH}_3)-\text{CH}]=\text{CH}_2\]\), such as C5 hemiterpenes, C10 monoterpenes, C15 sesquiterpenes, C20 diterpenes, C25 sesterpenes, C30 triterpenes, C40 tetraterpenes and C50 polyterpenes. While lower terpenoids are found in volatile emissions and essential oils, higher terpenes are mainly present in plant’s lipid soluble pigments. The fragrance of rose and lavender is due to monoterpenes. The carotenoids produce the reds, yellows and oranges of pumpkin, corn and tomatoes.

Sterols and steroids are modified triterpenes, and are found in woods of a number of gymnosperms and angiosperms including *Larix, Pinus, Fagus* and *Quercus* spp. Phytosterols are different from animal sterols in that they have an extra methyl or ethyl substituent in the side chain.

Terpenes are widely used in the food, pharmaceutical and perfume sectors, as well as in a wide range of pharmacological applications. Menthol, a monoterpane (10 carbons) isolated from various mints, is a topical pain reliever and antipuretic (relieves itching). Most terpenes disturb fluidity of membranes and efflux of ions, while some may cause cell death (cytotoxic, antimicrobial). Saponins are haemolytic, while others can inhibit the vital enzyme Na+/K+ ATPase in the pests to deter herbivory. Steroids, such as cortisone, are most often used as anti-inflammatory agents, but many have other uses such as in birth control pills. Ruminants are known to avoid high terpene diets because
they kill microbial populations in their gut that are needed to digest cellulosic materials.

**Glycosides:** These consist of a glucose moiety attached to an aglycone. The sugars found in glycosides may be monosaccharide such as glucose, rhamnose and fucose, or more rarely deoxy sugars such as the cymarose found in cardiac glycosides. The aglycone is a molecule that is bioactive in its free form but inert until the glycoside bond is broken by water or enzymes. Some pharmacologically important glycosides are salicin, populin, digoxin, diosgenin, sennosides *etc.*

**The values of medicinal plants in global market**

Recent estimates suggest that over 9,000 plants have known medicinal applications in various cultures and countries, and this is without having conducted comprehensive research amongst several indigenous and other communities (Ramesh and Janagam, 2011). Medicinal plants are used at the household level by women taking care of their families at the village level by medicine men or tribal shamans and by the practitioners of classical traditional systems of medicine such as Ayurveda, Chinese medicine or the Japanese kampo system (Pushpangadan, 1995).

According to the world Health Organization, over 80% of the world’s population or 4.3 billion people rely upon such traditional plant based systems of medicine to provide them with primary health care (WHO, 2011). Allopathic medicine too owes a tremendous debt to medicinal plants; one in four prescriptions filled in a country like the U.S are either a synthesized form or derived from plant materials. According to the International Trade Centre, as far back as 1967, the total value of imports of starting materials of plant origin for the pharmaceuticals and cosmetics industry was one of the order of USD 53.9 million. India was the largest supplier by far, with 10,055 tons of plants and 14 tons of vegetables alkaloids and their derivatives (Girendra *et al.* 2014). The participation of various companies in the market also attests to its new strength and importance (Fig. 1.3).
By 1990, some 223 major companies worldwide were reportedly screening plants for new leads; the figure had been zero in 1980. In response to the overwhelming interest in alternative therapies, many of the prestigious allopathic medicinal institutions have also recognized their importance: an example is the National Institute of Health which created the Office of Alternative Medicine in 1991 to provide the public with information on alternative treatments and to assess those therapies which have been proven successful. According to one account, in 2010 significant amounts of at least 74 species of medicinal plants were being commercially traded in the global market. In addition, there are many related botanical products sold as health foods, food supplements, herbal teas, and for various other purposes related to health and personal care. The extent to which herbal preparations are prescribed within conventional medicine varies greatly between countries, for instance being much higher in Germany than in the UK or USA. During the last 3 years, approximately 40,000 tons of plants drug materials were imported into Germany, annually (Gonsalves, 2010).

The global demand for herbal medicine is not only large, but growing (Gunjan et al. 2015). The market for Ayurvedic medicines is estimated to be expanding at 20% annually in India (Subrat, 2002), while the quantity of medicinal plants obtained from just one province of China (Yunnan) has grown by 10 times in the last 10 years (Pei, 2002). Factors contributing to the growth in demand for traditional medicine include the increasing human population
and the frequently inadequate provision of Western (allopathic) medicine in developing countries. Herbal medicine is becoming ever more fashionable in richer countries, a market sector which has grown at 10-20% annually in Europe and North America over recent years (Ten and Laird, 1999). Despite the small number of source species, drugs derived from plants are of immense importance in terms of numbers of patients treated.

The value of medicinal plants to human livelihoods is essentially infinite. A study of the 25 best-selling pharmaceutical drugs in 1997 found that 11 of them (42%) were either biologicals, natural products or entities derived from natural products, with a total value of USD 17.5 billion. The total sales value of drugs (such as Taxol) derived from just one plant species (Taxus baccata) was USD 2.3 billion in 2000 (Fig. 1.4) (Laird and Ten, 2012).

![Diagram showing the world market for herbal medicine in 2012](image)

**Fig. 1.4: World market for herbal medicine in 2012**

As per World Bank reports trade in medicinal plants, botanical drug products and raw material is growing at an annual growth rate between 5 to 15% (Mathur, 2015).

In India the value of botanicals related trade is about USD 10 billion per annum with annual export of USD 1.1 billion while China annual herbal drugs production is worth USD 48 billion with export of USD 3.6 billion. Presently the United States is the largest market for Indian botanical products accounting for about 50% of the total exports. Japan, Hong Kong, Korea and Singapore are the major importer of the herbal drugs making 66% share of China botanical drug export (Sangita Kumar *et al.* 2011).
India and its medicinal wealth

The Botanical Survey of India records over 15,000 plant species occurring in the country, of which at least 7,500 species have been used for medicinal purposes. Attempts to document the plant wealth of India have continued since the landmark publication by Watt (2006). Around 1,700 species have been documented for their biological properties and drug action (FRLHT, 1996) and data is available for approximately 1,200 species, especially those most frequently used in traditional Indian systems of medicine, resulting in a reasonable knowledge base (Gunjan et al. 2015).

India has an over 3,000 year-old medicinal heritage based on herbs. India is well known as an Emporium of medicinal plants. Knowledge of medicinal use of plants in India is amassed over millennia by tribal. For thousands of years Indian plants have been attracting attention of foreign countries. People from countries like China, Cambodia, Indonesia and Baghdad used to come to ancient universities of India like Takshashila (700 BC) and Nalanda (500 BC) to learn health science of India. It is documented that the Indian people have a tremendous passion for medicinal plants and use them for a wide range of health related applications from common cold to memory improvement and treatment of poisonous snake bites to a cure for muscular dystrophy and the enhancement of body’s general immunity. There are estimated to be around 25,000 effective plant based formulations available in the indigenous medical text used in folk medicine and known to rural communities all over India. There are more than 15,000 species of higher plants occur in India of which 9,000 are economically important. Of these about 7,500 are of medicinal value; 3,900 are of food value; 700 are culturally important; 525 used for fiber; 400 for fodder; 300 for pesticide and insecticides; 300 for gum, resin and dyes and 100 provide incense and perfume (Anonymous, 1994). Out of the above, over 9,500 wild plant species are used by tribal societies of India for their varied requirements (GOI, 1995).
**In silico approach in biomedical research**

Pharmacology over the past 100 years has had a rich tradition of scientists with the ability to form qualitative or semi-quantitative relations between molecular structure and activity in cerebro. To test these hypotheses they have consistently used traditional pharmacology tools such as *in vivo* and *in vitro* models. Increasingly over the last decade however it has been realized that computational (*in silico*) methods have been developed and applied to pharmacology hypothesis development and testing. These *in silico* methods include databases, pharmacophores, homology models, quantitative structure-activity relationships and other molecular modeling approaches, machine learning, data mining, network analysis tools and data analysis tools that use a computer. *In silico* methods are primarily used alongside the generation of *in vitro* data both to create the model and to test it. Such models have seen frequent use in the discovery and optimization of novel molecules with affinity to a target, the clarification of absorption, distribution, metabolism, excretion and toxicity properties as well as physicochemical characterization (Ekins *et al.* 2007) (Fig. 1.5).

![Diagram of Pharmacodynamic (PD) and Pharmacokinetic (PK) Events](image)

**Fig. 1.5: An overview of drug metabolism (Testa and Kramer, 2006)**
Computer-Aided Drug Design (CADD) is a specialized discipline that uses computational methods for the simulation of drug-receptor interactions. CADD methods majorly involve Bioinformatics tools, application and support from information technology, information management, software applications, databases and computational resources for its infrastructure establishment (Antre et al. 2012). In silico drug designing process comprises of 3 major stages (Fig. 1.6).

**Stage 1:** It involves identification of therapeutic target and building a heterogeneous small molecule library to be tested against it. This is followed by the development of a virtual screening protocol initialized by docking of small molecules from the library.

**Stage 2:** These selected hits are checked for specificity by docking at the binding sites of other known drug targets.

**Stage 3:** These selected hits are subjected to detail in silico ADMET profiling studies and those molecules that pass these studies are termed as leads.

![Diagram of in silico drug designing process](image)

*Fig. 1.6: An overview of in silico drug designing process*  (Kumar, 2013)
The foregoing account clearly illustrates the importance of plants in human health care, not only when plant constituents are used directly as therapeutic agents but also when they are used as basic material for the synthesis of drugs or as model for pharmacologically active compounds. It is an undisputed fact that ancient and folklore knowledge coupled with scientific principles can come to the forefront and provide us with powerful remedies to eradicate the diseases. According to one estimate, only 20% of the plant flora have been studied, of these, 15% have been evaluated phytochemically and a reported 6% have been screened for biologic activity (Verpoorte, 2000). This necessitates a continuous exploration and rigorous experimentation of plant products for plant derived drugs in addition to new pharmaceuticals for many of the human ailments. Hence the present research programme has been envisaged.

The study explores the medicinal potentialities of three plants belonging to the genus *Morus* viz. *Morus alba*, *Morus serrata* and *Morus laevigata* which are claimed to possess several medicinal properties in folklore/traditional systems.

**Mulberry**

Mulberry is the most medicinally important plant which belongs to genera *Morus*. It is a monoecious or dioecious plant up to 10-12m high. Mulberry (*Morus*) is believed to have originated at the feet of Himalayan ranges. According to Watt (1873) certain forms of *Morus* were truly wild in India, but according to Vavilov (1926) the primary center of origin of mulberry was the China–Japan gene center, which includes east China, Korea and Japan.
Scientific classification

Kingdom: Plantae
Subkingdom: Tracheobionta
Superdivision: Spermatophyta
Division: Magnoliophyta
Class: Magnoliopsida
Subclass: Hamamelididae
Order: Urticales
Family: Moraceae
Genus: Morus L

This plant is widely distributed in India, China, Japan, North Africa, Arabia, South Europe etc. Mulberry can be grown both in tropics and in the temperate regions. It is also raised in rainfed and irrigated conditions. The optimum temperature ranges from 24 to 29°C, atmospheric humidity from 65 to 80%. In India mulberry is grown on an extensive scale in various parts, namely Punjab, Himachal Pradesh, Uttar Pradesh, Madhya Pradesh, Bihar, Orissa, Assam, Manipur, Karnataka, Andhra Pradesh and Tamil Nadu. It is reported to grow in many Asian and African countries of the World (Zaheer, 1965).

A number of species have been reported within this genus. Initially, Linneaus (1753) divided the genus Morus into seven species: Morus alba L., Morus nigra L., Morus rubra L., Morus tartarica L., Morus indica L., Morus papyrifera and Morus tinctoria.

The identification of species within this genus from different countries and climatic conditions also remains a matter of intense debate, as several researchers classified mulberry species considering different parameters into account. Brandis (1874) and Hooker (1885) recognized four species of Morus in India: M. alba, M. indica, M. laevigata, and M. serrata. However, according to Kadambi (1949), the most important types of mulberry grown in India for
rearing of silkworm are *M. alba* var. *multicaulis* as bush crops and *M. alba* var. *atropurpurea* as trees. Iyer (1954) reported the presence of the five species, namely *M. alba*, *M. indica*, *M. nigra*, *M. chinensis* and *M. multicaulis*. Gururajan (1960) suggested grouping all cultivated forms of mulberry in India into three species: *M. alba*, *M. bombycis* and *M. latifolia*. Similarly, all the mulberry genotypes under cultivation in China are believed to have originated from four main species. The white mulberry *M. alba*, the Lu mulberry (*M. multicaulis*), the mountain mulberry (*M. bombycis*) and the Guangdong mulberry (*M. atropurpurea*). Thus, it is clear that a comprehensive study using more reliable tools like DNA markers is essential to resolve this complex problem in mulberry.

In India, *Morus* is represented by four species i.e. *M. indica* L., *M. alba* L., *M. laevigata* Wall. and *M. serrata* Roxb. (Tikader and Dandin, 2005) and their distribution map is presented in Fig. 1.7.

![Fig. 1.7: Distribution of Morus species in India](image)
Economic importance of Mulberry

Mulberry is grown extensively for leaves, which are used for raising silkworms (Bombyx mori) in the sericulture industry. Sericulture is an income-generating vocation in rural areas. It suits well for marginal and small-scale farming in view of its low investment profile and family employment opportunities (Lakshmanan et al. 1997). In China, India, Japan, Korea, Pakistan, Bangladesh and in many other Asian countries, Sericulture is one of the major rural industries that provide employment to a large number of people. In India it is practiced in over 50,000 villages providing gainful employment to about 59 lakh people, thus playing a pivotal role in poverty alleviation, employment generation and arrest of rural migration (Ramesh, 1997).

Medicinal value of Mulberry

The medicinal properties attributed to mulberry are extensive. Topically, it is applied for the treatment of wounds (Duke and Wain, 1981). Internally, it is used to relieve insomnia, regulate bleeding during menstruation, treat digestive disturbances, to ease cough and asthmatic breathing, reduce fever and inflammation, as hypolipidemic, anti ageing, antifilariasis, diuretic, and antiulcer agent (Him-Che, 1985; Kimura and Hiromichi, 1986; Ouyang, 2006). Mulberry is known to possess hypoglycemic (Chen et al. 1995; Taniguchi et al. 1998; Lemus et al. 1999; Hansawasdi and Kawabata, 2006), antibacterial (Bown, 1995), astringent (Duke and Ayensu, 1985), diaphoretic (Bown, 1995), antiviral (Nam et al. 2002) and anticancer (Nam et al. 2002) effects among a wide range of pharmacological activities reported for this plant.

Root bark having a bitter acid taste possessed cathartic and anthelmintic properties. Root is one of the constituents of drug named, ‘Glucosidase’ which is used in high blood pressure. Root juice agglutinates the blood and is very useful in killing the worms in digestive system (Shivkumar et al. 1995). The root extract is used to prepare a drug that is effective against inflammation, pyretic conditions (Chatterjee et al. 1983), diabetes, high blood pressure (Shiv
Kumar et al. (1995) and AIDS (Ray, 1989 and 1990). The stem bark is used as purgative and vermifuge (Singh and Ghosh, 1992). On the contrary, interaction study of morin isolated from mulberry with cyclosporine reported that morin maintained the immunosuppression induced by cyclosporine and also decreased the production of nitric oxide from the macrophages (Fang et al. 2005).

The leaves are diaphoretic and emollient. Leaves juice keeps skin smooth, healthy and prevent throat infections, irritations and inflammations. In China, mulberry leaves are used as a medicinal herb (Yen et al. 1996) and the mulberry leaf juice is served as traditional drink (Shiv Kumar et al. 1995). The leaf powder has been found to be effective in treatment of obese diabetic patients and hypertensive patients (Suryanarayana, 2002). Recently the health giving properties of mulberry leaf is recognized for its diuretic, blood sugar and blood pressure reducing effects (Iyengar, 2007).

Mulberry fruits are potent source of anthocyanins which play key role in antioxidant activity. The Morus plant is also a rich source of natural isoprenoid substituted phenolic compounds including flavanoids. These compounds have been studied by many investigators with structural, biological and pharmacological interests (Nomura and Hano, 1994).

It is evident that large numbers of biomolecules of medicinal interest are present in mulberry. But extensive work has been carried out mainly targeting Morus alba and thus warranting detailed studies utilizing various other species. Since, the presence and extent of phytochemicals vary not only at the species and varietal level, but within a plant in different parts and are variable under different agronomic conditions and seasons. Such studies therefore would provide information possibly an all together new world of health and therapeutic values.
**Morus alba L. white mulberry**

The white mulberry *Morus alba* (Fig. 1.8), is renowned as the primary food source for silk worms and is widely cultivated in its native China. A medium sized, monoecious, deciduous tree with bark of large stems, brown, rough, height of about 30 and 1.8m in girth indigenous to China and in hilly areas of Himalayas up to an elevation of 3300m. Teeth of leaves uniform, usually blunt, segments of the perianth of female flowers in four numbers, the two outer keeled, style very short, fruit color white, pink and black, bud color brown, oval round in shape. According to sources, white mulberry is the species that has been used exclusively in Chinese medicine since A.D-659. The Chinese Pharmacopoeia (1985) lists the leaves, root bark, branches, and fruits as ingredients in medicinal preparations. The plant is reported to possess Astringent, Anthelmintic, anti-HIV, cough, anti-inflammatory, exudative, high blood pressure, diaphoretic, purgative, emollient, diahorrea, diabetes, atherosclerosis, anti-tumor, hypoglycemic etc.

![Fig. 1.8: Morus alba L. white mulberry](image)

**Morus serrata Roxb.**

It is a large tree 18 – 21m high, with a clean cylindrical bole 3.5m long, found from Trans Indus to Kumaon, principally in the inner regions of Himalayas at an altitude of 1200 – 2700m. Teeth of leaves usually coarse, somewhat unequal and sharp, leaves velvety, coarse, full of minute hair on both
the side, segments of the perianth of female flowers 2-4, usually 3, all similar, style is medium, fruit color white, pink and mucilage fruit. Bud color dark brown, round and bigger in size. The bark of *Morus serrata* contains b Amyrin acetate, betunilic acid, cerylalcohol, querectin and morin (Chemical Abstracts, 1979) (Fig. 1.9).

![Fig. 1.9: Morus serrata Roxb.](image)

*Morus laevigata* wall.

A tree found in outer Himalayas from Kumaon eastwards to Assam. Bark is dark brownish grey in color when young. Teeth of leaves fine, the lateral nerves abruptly curved upwards within the margin, style is very short. Fruit is long greenish, white, dark purple. Bud color brown, elongated, lengthy and elliptical in shape. The milky juice of fruit is used as a plaster for sores and cools the blood. The fruits are rich in citrulline and hydroxyprolines. The seeds are rich source of free amino acids (Ali and Qadri, 1987) (Fig. 1.10).

![Fig. 1.10: Morus laevigata Wall.](image)
Objectives

1. Phytochemical investigation
   a. To extract leaf materials of three species *viz.* *Morus alba, Morus serrata* and *Morus laevigata* by sequential extraction method
   b. Qualitative phytochemical analysis of the extracts
   c. Isolation and characterization of bioactive compounds

2. Pharmacological studies to screen activities *viz.*
   a. *in vitro* antioxidant activities
   b. *in vitro* and *in vivo* anticancer activity
   c. Analgesic and anti-inflammatory activities
   d. Wound healing activity
   e. CNS depressant/stimulant activity
   f. Anthelmintic activity
   g. Antimicrobial activity

3. *In silico* studies on isolated compounds