Chapter: 1

General Introduction

Man has been dependant, cent per cent, on plant and animal resources for survival from the very beginning, by way of meeting various requirements such as food, shelter, clothing, plus items of medicinal and cultural use. Even today, hundreds of millions of people, mostly in the developing countries, derive a significant part of their sustenance and subsistence needs, including income from plant and animal products (Iqbal 1993; Walter 2001). Among these medicinal plants (much more than the products of animal origin) play a pivotal role, not only as traditional herbal medicines used for health care, but also as trade commodities which meet the demand of often distant markets. Plants continue to be a major source of medicine even today, as they have been throughout human history, but more so in recent times with increased global
interest in “naturals” over their synthetic counterparts. Some medicinal plants, such as the opium poppy, have long been recognized and widely used, while others, such as the Mayapple (Podophyllum species) and yew (Taxus) have gained worldwide recognition as the original sources for the anti-tumor and anti-cancer compounds, such as podophyllotoxin, taxol, respectively are relatively new additions to mainstream medicine. In addition to providing the basis for between 30 and 40 per cent of today’s conventional drugs, the medicinal and curative properties of various plants are also employed in herbal supplements, botanicals, nutraceuticals and teas. Drug discovery, ethnobotany, and traditional and indigenous medicines have long been basic to medicinal plant research.

Herbs are staging a comeback and herbal ‘renaissance’ is happening all over the globe. The herbal products today symbolise safety in contrast to the synthetics that are regarded as unsafe for the humans and environment. Although herbs had been priced for their medicinal, flavouring and aromatic qualities for centuries, the synthetic products of the modern age had surpassed their importance, for a while. However, the blind dependence on synthetics is over and people are returning to the naturals with hope of safety and security. As per the WHO estimates, even today, over three-quarters of the world population relies mainly on plants and plant extracts for health care.

1.1 Medicinal plants in India

India is amongst the world’s 14 mega biodiversity centers with the presence of over 45000 different plant species. India’s diversity is unmatched due to the presence of 16 different agro-climatic zones, 10 vegetation zones, 25 biotic provinces and 426 biomes (habitats of specific species). Of these, about 15000-20000 plants have some known medicinal value, and of which, only 7000-7500 species are used for their medicinal value by traditional communities (Joy et al., 2001). In India, drugs of herbal origin have been used in traditional systems of medicines, such as Unani and Ayurveda since ancient times. The Ayurveda system of medicine uses about 700 species, Unani 700, Siddha 600, Amchi 600 and modern medicine around 30 species. The drugs are derived either from whole plant or from different plant parts (organs), like leaves, stem, bark, root, flower, seed, etc. Some drugs are prepared from excretory plant products such as gums, resins and latex. Even the Allopathic system of medicine has adopted a number of plant-derived drugs which form an important segment of the modern pharmacopoeia. Some
important chemical intermediates needed in the manufacturing of modern drugs are also obtained from plants (e.g. diosgenin, solasodine, β-ionone). The plant-derived drugs not only offer a stable and growing market worldwide, but the plants continue to be an important source for new drugs and nutraceuticals.

In recent years, due to growing recognition of natural products and processes in sustaining human and environmental health, the economic as well as environmental importance of the medicinal plant resources have enhanced tremendously. In the global context for this sector tremendous opportunities exist for India, a country unrivalled in terms of diversity of medical systems and practices, in addition to being a major storehouse of biological diversity, with 2 of the 14 mega biodiversity areas of the world located within its borders (Joy et al., 2001).

India is of course already, an active participant in the global medicinal plant market, having been for some time the world’s largest supplier of raw materials (though an insignificant supplier of finished products) (Patnaik, 1994).

1.2 Medicinal plants and phytomedicines

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 the plants. The use of medicines from plants in the form of local medicine dates back to 4000-5000 B.C. While the medicinal values of these plants are due to the presence of small amounts of active compounds/principles which produce physiological actions in the human and animal body (Zaidi, 1998).

Green plants synthesize and preserve a variety of biochemical products, many of which are extractable and used as chemical feed stocks or as raw material for various scientific investigations. The plant kingdom synthesizes diverse array of novel molecules, called “phytochemicals”, which are secondary metabolites synthesized by plants. Apart from primary metabolites, plants synthesize further group of compounds called secondary metabolites. These secondary metabolites are, in principle, non-essential to life but they definitely contribute to the overall species fitness and survival. The plants produce a plethora of secondary metabolites and store them in various organs like leaf, root, stem, bark, flowers, fruits, etc. for immediate and future use. These secondary metabolites are classified as steroids, terpenoids, flavonoids,
glycosides, alkaloids etc based on their chemical structure. These various natural compounds present in plants can act almost on all systems of the body and have high therapeutic activity.

Since olden days, plants are used to treat many ailments, and India with approximately 45,000 plant species in its vast plant wealth seems to include several thousand which have been claimed to possess medicinal properties (Grover et al., 2002). It is also well known that certain foods may have the potential to prevent diseases (Tulp et al., 2006; Zhang, 2007). For instance, the Mediterranean diet is helpful to lowering the risks of coronary heart disease, cancer and cognitive impairment (Trichopoulou et al., 2003; Scarmeas et al., 2006; Yang et al., 2007)). Consumption of green tea is beneficial for reducing the process of aging, in addition to preventing cancer and Alzheimer's disease (AD) (Fujiki et al., 2002; Chen and Zhang, 2007; Kuriyama et al., 2006). It is also reported that adherence to vegetables (including cruciferous vegetables, green leafy vegetables, yellow vegetables, allium vegetables, tomatoes and others) and legumes (including soybean, peanut, etc.) is inversely associated with the risk of type 2 diabetes (T2D) in a large Chinese population (Villegas et al., 2008a; 2008b). Plants have been the basis of many traditional medicinal systems throughout the world for thousands of years and continue to provide mankind with new remedies. Many plant based medicines now serve as the basis of novel drug discovery (Samuelsson, 2004). The active principles of many plant species are isolated for direct use as drugs as lead compounds or pharmacological agents (Fabricant and Farnsworth, 2001). Thus medicinal plants are the most important source of life saving drugs from various disorders for the majority of the world’s population.

Many secondary metabolites of plant are commercially important and find use in a number of pharmaceutical compounds. 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. Some of the useful plant drugs include vinblastine, vincristine, taxol, podophyllotoxin, camptothecin, digitoxigenin, gitoxigenin, digoxigenin, tubocurarine, morphine, codeine, aspirin, atropine, pilocarpine, capsicicine, allicin, curcumin, artemesin in and ephedrine, etc. among others. In some cases, the 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, researches in both areas (use of mixture of traditional medicine and single active compounds) are very important. Where the active molecule cannot be synthesized
economically, the product can be obtained through the process of cultivation (and not by way of reckless harvest from the wilds) of relevant plants, as renewable source of important drugs. The scientific study of traditional medicines, derivation of drugs through bioprospecting and systematic conservation of the concerned medicinal plants are thus of vital importance.

In spite of the tremendous advances made in the modern medicinal field there are still a large number of ailments for which suitable drugs are not available. Diabetes Mellitus is one among those and nowadays it is a global problem. Diabetes Mellitus was known to ancient scholars of Ayurveda some 3000 years back. The association of frequent urination with a sweet tasting (and ants attracting) substance in the urine was first time reported in Charaka Samhita, the ancient Ayurvedic classic (Apollo Hospital’s Group, 2002).

1.3 Diabetes mellitus

Diabetes is derived from two Greek Words “dia” which means “through” and “betes” which means “to pass”; “Mellitus” is another Greek word, which means “sweet”. In this disease the patient passes large quantities of urine containing a sweet substance namely glucose. Diabetes is a chronic condition that occurs when the body cannot produce enough or effectively use insulin (IDF, 2011). Insulin is a hormone produced by the pancreas that allows glucose from food to enter the body’s cells where it is converted into energy needed by muscles and tissues to function. As a result, a person with diabetes does not absorb glucose properly, and glucose stays circulating in the blood (hyperglycaemia) damaging tissues over time. This damage leads to life-threatening health complications.

There are three main types of diabetes, (Harris and Zimmet, 1997), Type 1 diabetes- Insulin Dependent Diabetes Mellitus (IDDM), Type 2 diabetes – Non Insulin Dependent Diabetes Mellitus (NIDDM) and Gestational Diabetes Mellitus (GDM). In spite of all advances in therapeutics, diabetes still remains a major cause of morbidity and mortality in the world. The estimated number of adults living with diabetes has soared to 366 million, representing 8.3% of the global adult population. This number is projected to increase to 552 million people by 2030, or 9.9% of adults, which equates to approximately three more people with diabetes every 10 seconds (IDF Atlas 2011). India accounts for the largest number of people (50.8 million) suffering from diabetes in the world. India continues to be the “diabetes capital” of the world,
and by 2030, nearly 9 per cent of the country’s population is likely to be affected from the disease (IDF Atlas 2011).

Currently available therapeutic options for non-insulin-dependent diabetes mellitus, such as dietary modification, oral hypoglycaemics, and insulin, have limitations of their own. Allopathic drugs like insulin, sulphonylureas, biguanides, etc. have definitely helped in controlling the blood sugar levels and improving the quality of life but none of them have been unequivocally successful in maintaining normal glucose levels and avoiding late stage complications of diabetes.

1.4 Plants as a potential source of antidiabetic drugs

The most common conventional treatment for diabetes is insulin which has prominent side effects. Neither insulin nor other modern pharmaceuticals have been shown to modify the course of diabetic complications. Here lies the significance of drugs of herbal origin. Many natural products and herbal medicines have been recommended for the treatment of diabetes. Plants are being used heavily to treat diabetes mellitus, an effort that resulted in having more than 700 recipes containing more than 400 plants reputed for their antidiabetic activity (Bailey and Day, 1989; Ajgaonkar, 1979; Rahman and Zaman, 1989; Ivorra et al., 1989; Day, 1990; Karunanayake and Tennekoon, 1993). The comprehensive review on antidiabetic medicinal plants compiled by Rahman and Zaman (1989) provides information regarding nearly 343 plants reputed for their blood glucose lowering activity. According to the review compiled by Mohamed et al., (2006), the families of plants with the most potent hypoglycaemic effects include: Leguminosae (11 species), Lamiaceae (8 species), Liliaceae (8 species), Cucurbitaceae (7 species), Asteraceae (6 species), Moraceae (6 species), Rosaceae (6 species), Euphorbiaceae (5 species) and Araliaceae (5 species). Babu et al., (2006) has created DiaMedBase, a diabetes literature database of medicinal plants that includes 742 records, consisting about 309 genera and 389 species of plants, described to possess medicinal properties against diabetes.

India is facing an explosive increase in the incidence of diabetes mellitus and, therefore, there is an urgent need to find cost effective, if possible, indigenous and safe drugs for diabetes. An ideal antidiabetic drug will be one which lowers raised blood glucose to normal level without causing hypoglycaemia in any state of nutrition. In addition, modern therapies are far too costly to be used by the majority of diabetes sufferers from relatively poorer nations.
Keeping this in mind the present investigation aims to scientifically screen study and evaluate one of the plants, *Costus pictus* D. Don, as a potential source of an effective, affordable, easily available herbal medicine for diabetes mellitus.

1.5 Description of the proposed plant

The genus *Costus* belongs to the family *Costaceae*, which has been separated from family *Zingiberaceae* on the basis of the presence of spirally arranged leaves, and the rhizomes being free from aromatic essential oils. More than 100 species of the genus are distributed in the tropics all over the world. *Costus pictus* D. Don (Spiral ginger) commonly known as ‘insulin plant’ was introduced in India very recently during 2002-03, from Mexico by missionaries and it is normally grown in home gardens as an ornamental plant, especially in Kerala (Merina, 2004). The major attraction of this plant is its stem with spiral leaves and light, airy and tissue paper like flowers. Red coloured stem enhances the beauty of the glossy linear leaves and strongly spiraling canes. The leaves have sour taste. The flowers are produced in a terminal cone, yellow in colour with an orange red tip and last for 3-4 days. Usually the plant grows up to 2-3 m with 1.5-2.0 m spread. The flowers are displayed in a dramatic form high above the leaves (Fig. 1.1). While the flowers do not produce aroma, they do produce a beautiful effect sitting atop the tall spiraling stems. Propagation is carried out through stem cuttings and rhizomes. It grows very fast and healthy growth is reported in wet soil.

![Fig. 1.1 Costus pictus plant](image)

The species is similar to *Costus speciosus* (Koening) Sm., which is commonly known as *Channakkoora* in Kerala and *Kew* in Hindi. The leaves of this species are less fleshy and have an acrid taste. The rhizomes are cooked and eaten. Local people eat the leaves for curing diabetes. The roots are used as tonic and are also anthelmintic (Roy and Pal, 1991). Silva *et al.*, (1998)
had isolated new furostanol glycosides from *Costus spicatus*. *Costus pictus* (Spiral ginger) has come to be commonly known as ‘Insulin plant’ and is grown in home gardens as an ornamental especially in the central part of Kerala (Merina, 2004). Its value is on account of medicinal (hypoglycaemic) properties. The preliminary toxicity and hypoglycaemic activity of the extract of this plant have been studied recently (Merina, 2005; Merina *et al*., 2005a, 2005b).

According to Merina (2004) the oral feeding of *Costus pictus* crude preparation, up to a dose of 1g kg⁻¹ body weight, did not produce any acute toxic effects in mice. Three months oral feeding of the extract up to a dose of 200 mg/ kg body weight did not produce any change neither in hematological and biochemical parameters nor in the histology of internal organs.

The R&D section of Arjuna Natural Extracts Ltd., Kerala has, for the first time, studied scientifically the antihyperglycaemic activity of *Costus pictus*. The hypoglycaemic properties were well established both in streptozotocin and alloxan induced diabetes in animals (Merina, 2004; Merina, 2005). The physical and chemical properties of the same have also been subjected to study (Merina, 2006). According to Merina, (2006) the oxalic acid is the major acid present in the leaves of *Costus pictus* which imparts the sour taste.
1.6 The outline of proposed work

The most pronounced effect, the antidiabetic property of *Costus pictus*, has not been proved clinically in human experiments. Nevertheless people have started to consume the leaves as a remedy for diabetes (Sabu, 2006). Since this is a recently introduced plant, investigations have to be made to confirm the morphological, molecular, biochemical, phytochemical and pharmacological characteristics of the plant to exploit it beneficially. Detailed research on the chemistry and pharmacology of products of this plant are also essential and this may eventually lead to the discovery of the “magic” medicine that can be used in the treatment of diabetes. The present study is, therefore, proposed with the following objectives.

1. To verify the survival capacity of the plant (3 clones/accessions collected from different parts of Kerala) in different agroclimatic zones of India by cultivating them in Sitapur, U.P, and in Nainital, Uttarakhand. If the plant grows well under these contrasting conditions, it will be a good indication and suggestive of the fact that it can perhaps be cultivated widely in India, which is dreadfully affected with diabetes mellitus.

2. Propagation protocols of this plant will be standardized using stem cuttings.

3. Isolation of DNA for molecular analyses to find out the genetic diversity, if any, of the herb that is collected from different regions of Kerala.

4. Extraction, separation, isolation and purification of major phytochemicals present in the rhizome, stem and leaves followed by fractionation and screening for the presence of active compounds.

5. Evaluation of hypoglycaemic activity of the plant and isolated compounds followed by standard assays.