CHAPTER-I

INTRODUCTION
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1.1 Medicinal plants

Plants have been used from ancient times to attempt cures for diseases and to relieve physical suffering. These primitive attempts at medicine were based on speculation and superstition. Most savage people have believed that disease was due to the presence of evil spirits in the body and could be driven out only by the use of substances that rendered the body a disagreeable habitat. The knowledge regarding these ailments was usually restricted to the medicine men of the tribe. As civilization progressed the early physician were guided in great part by these observations and beliefs.

Drug plants were always of special interest. As early as 5,000 B.C many drugs were in use in China. There are Sanskrit writings in existence which tell about the methods of gathering and preparing drugs. The Assyrians Babylonians and ancient Hebrews were all familiar with their use. In Egypt there are records dating to 1600 B.C naming many of the medicinal plants used by physicians of that period. The Greeks were familiar with them by the works of Aristotle, Hippocrates, Pythagoras and Theophrastus. The supernatural element continued to remain prominent in those times. Only few individuals were able to distinguish between valuable and harmful plants, due to some special powers. Hippocrates (460-377 B.C) discussed the illness and treatment of several diseases in a chronological manner and earned his reputation as the “Father of medicine”. By 77 B.C. Dioscorides wrote his great treatise “De Materia Medica” dealing with the nature and properties of all the medicinal substances known at that time. Pliny and Galen also described and wrote about drug plants. Following the Dark Ages, there came the period of the herbalists and encyclopaedists. It was about this time that the curious Doctrines of signatures came into being. This superstitious doctrine suggested that all
plants possessed some sign, indicated to the use for which they were intended. Thus a plant with heart-shaped leaves should be used for heart ailments, the liver shaped leaf for liver troubles etc. Many of the common names of plants are their origin to this superstition. Names such as heartease, dogtooth violet, Solomon’s seal and liverwort are such examples.

Pharmacology and pharmacognosy owe their beginnings to the earlier beliefs and knowledge about medicinal plants. The interest in medicinal plants was especially pronounced among the early botanists who were often physicians. Medicinal plants have always occupied a vital position in human health care. Herbal drugs are preferred over allopathic drugs on account of their efficiency, easy availability and are also said to be free from side effect. It is revealing to that about 80% modern drugs are derived from plants. The history of medicine in India can be traced to remote past. The earliest mention of the medicinal use of plants is found in the Rig Veda, perhaps the oldest repository of human knowledge, having been written between 4500 and 1600 B.C. In, Ayurveda the properties of various drugs have been given in detail. Susruta Samhita, which was written not later than 1000 B.C. contains a comprehensive chapter on therapeutics and Charaka Samhita, written about the same period, gives a remarkable description of the ‘Materia Medica’ as it was known to ancient Hindus (Hill and Sharma, 1996).

Systematic investigation of drugs used in indigenous medicines in India on modern scientific lines, was started more than fifty years ago. A number of important medicinal plants prescribed by Vaidyas and Hakim have been investigated. The constituents have been examined, pharmacological action of the active principles worked out by animal experimentation, and preparations made from the drugs have been tested on patients in hospitals. Antibiotic drugs have revolutionize the treatment of bacterial and
rickettsial diseases and antibiotics control even some viral diseases, which considered incurable a few years back, are now cured by their use.

There is currently a large and ever expanding global population base that prefers the use of natural products in treating and preventing medical problem. This has influenced many pharmaceutical companies to produce new formulations extracted from plants or herb.

1.2 Status of medicinal plants in the world

That branch of medical science dealing with the drug plants themselves is known as Pharmacology. It is concerned with the history, commerce, collection, selection, identification and preservation of crude drugs and raw materials. Worldwide there are several thousand plants that are being used for medical purposes. Many of these are restricted in use by native people who have long resided in any given area. A plant's medicinal value is due to the presence of some chemical substance or substances that produce a physiological action on the body. Most important are the alkaloids, compounds of carbon, hydrogen, oxygen and nitrogen. Glycosides, steroids, fatty oils, resins, mucilage, tannins and gums are all utilized.

1.2.1 Drug Classification

Generally it is found that the active principles are present in the storage organs of the plants, especially in roots and seeds, and less in leaves bark, wood or other parts.

- Drugs obtained from roots and other underground Parts: e.g. Aconite, Gentian, Goldenseal, Ginseng, Licorice, Serpentine, Valerian etc.
- Drugs obtained from Barks: Curare, Quinine, elm etc.
- Drugs obtained from stems and woods: Ephedrine, Quassia.
- Drugs obtained from Leaves: Aloe, Belladonna, Cocaine, Aspirin, Digitalis, Henbane, Senna, and Stramonium.
Fig-1.1: Break up of medicinal plant by their parts utilized
(All India Ethno biological Survey, Ministry of Environment and Forests, Govt. of India, 2000).
• Drugs obtained from flowers: Chamomile, Santomin, etc.
• Drugs obtained from fruits and seeds: Bel, chaulmoogra oil, Nux vomica, Opium, Wormseed (Hill and Sharma, 1996).

1.2.2 Ethnic Knowledge

A traditional health care practice of indigenous people pertaining to human health is termed as Ethno medicine. It is the mother of all other systems of medicine such as Ayurveda, Siddha, Unani, Nature cure and even modern medicine. Rural and urban poor people in India rely on herbal remedies since these are within their reach. In fact in remote areas this is the only source of health care available.

It is possible today to bring out new products or find out new use of existing products based on traditional knowledge utilizing the technological developments in the field of biotechnology. This is proved beyond doubt particularly in the field of medicines, agriculture etc. The bio-prospecting helps the scientists in the modern pharmaceutical research laboratories to get the know-how to develop new products or new use of existing products. Similarly traditional designs of the articles are reproduced by the modern industries for its application in the consumer products. Traditional knowledge is generally associated with biological resources and is invariably an intangible component of such a biological resource.

Historically, the communities survived on their traditional knowledge base. The products they manufactured formed part of their livelihood. Even today many local and indigenous communities in the Asian countries meet their basic needs from the products they manufacture and sell based on their traditional knowledge. Maintenance of their health even now is based on traditional medicines derived from plants and other natural products. World Health Organization (W.H.O) has also given emphasis on utilization of herbal medicines due to their benefits, as cost effectiveness and minimum side effects.
Table-1.1: Modern drugs developed from traditionally known drugs

<table>
<thead>
<tr>
<th>Modern Drug</th>
<th>Traditional Medicinal use</th>
<th>Plant</th>
</tr>
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<tbody>
<tr>
<td>Aspirin</td>
<td>Reduces pain and inflammation.</td>
<td><em>Fillipendula ulmaria</em></td>
</tr>
<tr>
<td>Codeine</td>
<td>Eases pain, suppresses cough</td>
<td><em>Papaver somniferum</em></td>
</tr>
<tr>
<td>Quinine</td>
<td>Combats malaria</td>
<td><em>Cinchona pubescens</em></td>
</tr>
<tr>
<td>Diosgenin</td>
<td>Contraceptive</td>
<td><em>Dioscorea floribunda</em></td>
</tr>
<tr>
<td>Digetoxin</td>
<td>Dropsy, relieves heart congestion</td>
<td><em>Digitalis purpurea</em></td>
</tr>
<tr>
<td>Ephedrine</td>
<td>Reduces nasal congestion</td>
<td><em>Ephedra sinica</em></td>
</tr>
<tr>
<td>Ipecac</td>
<td>Controls vomiting</td>
<td><em>Psychotria ipecacuanha</em></td>
</tr>
<tr>
<td>Pilocarpine</td>
<td>Reduces pressure in the eyes</td>
<td><em>Pilocarpus jaborandi</em></td>
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<tr>
<td>Reserpine</td>
<td>Sedative, mental illness</td>
<td><em>Rauvolfia serpentina</em>.</td>
</tr>
<tr>
<td>Theophyllin</td>
<td>Opens bronchial passage</td>
<td><em>Catharanthus roseus</em></td>
</tr>
<tr>
<td>Scopalamine</td>
<td>Eases motion sickness</td>
<td><em>Datura stramonium</em></td>
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</table>
1.3 Status of Medicinal Plants in India

A plant may be accepted to be of medicinal value only when its medicinal properties or applications are in use by some systems of medicine. In the Indian context, a medicinal plant is one, which may be used by Ayurveda, Unani, Siddha, Tibetan, Homeopathy, Allopathy or the numerous ecosystems based medical traditions. Further, in spite of the emergence of many drugs from the synthetic field, the problems of senescence and so called ‘civilization’ disease e.g. Immuno deficiency syndromes, arthritis, mental disorders, cancer, cardiovascular diseases, cannot be tackled and side effects of allopathic drugs, chemotherapy etc. have sacred people all over the world, which are very expensive too, therefore, there is a greater demand for natural medicines and ‘health-food’ today than ever before in the world. India is ranked sixth among the 12 mega biodiversity countries of the world. Over 47,000 species of plants have been recovered by the Botanical Survey of India, (2003). With only 2.4% of the land area, India already accounts for 7% to 8% of the recorded species of the world. This number is based on the survey of 65-70% of the total geographical area of the country. India is equally rich in traditional and indigenous knowledge, both coded and informal. Hence India can be source of a variety of drugs.

The huge plant resource of India has been distributed into nine floristic regions, Eastern Himalayas, Western Himalayas, West Indian Deserts, Gangetic plain, Assam, Central India, Malabar, The Deccan and Andaman. According to the climatic conditions, four climatic zones (Wet Zone, Intermediate Zone, Dry Zone and Arid Zone) and four types of vegetations or forests; Tropical forests, Montane sub tropical forests, Temperate forests and Alpine vegetation are found in India.

According to an All India Ethnobiological survey carried out by the Ministry of Environment & Forests, Government of India, there are over 8000 species of plants being
used by the people of India. Fig. 1.2 represents the plant in various Indian systems of medicine.

Of the 386 families and 2200 genera in which medicinal plants are recorded, the families Asteraceae, Euphorbiaceae, Lamiaceae, Fabaceae, Rubiaceae, Poaceae, Acanthaceae, Rosaceae and Apiaceae share the larger proportion of medicinal plant species with the highest number of species (419) falling under Asteraceae (Fig. 1.3).

At present, 90% collection of medicinal plants are from the wild and since 70% of plants collections involve destructive harvesting many plants are endangered or vulnerable or threatened. Currently medicinal plants are collected without paying attention to the stage of maturity. They are stored haphazardly for long period of time under unsuitable conditions. This results in deterioration in quality. Hence there is urgency for conservation of medicinal plants.

1.3.1 Potential of Medicinal Plants

It is estimated that about 4.3 lakh plant species are spread over on earth and out of which 40% is available in India (The World Conservation Unions, IUCN, 2003). Recently, the World Health Organization (WHO) has compiled a list of 20,000 medicinal plants used in different parts of the globe. However, only about 10,000 plants are used for phytotherapy in Indian systems of medicine. Amongst these, over hundred botanicals are reported to have consistently in larger demand and are utilized in major drug markets in the world. The potential for earning foreign exchange by India from the export of medicinal and aeronautic plant is estimated to be over US$6,000 million/annum.

Now-a-days herbal medicines find market as neutraceuticals, which are nutritional or medically enhanced food with high health benefits. The current market for these neutraceuticals is estimated at about $270 million in the developed countries, which may increase many folds in due course.
Fig-1.2: Plants being used by various systems of medicines

(All India Ethno biological Survey, Ministry of Environment and Forests, Govt. of India, 2000).

Fig-1.3: Distribution of Medicinal Plants by Important Angiospermic Families.

(Report of the Task Force on Conservation and Sustainable use of Medicinal Plants, Govt. of India, 2000).
1.2

Number of Species

System of Medicines

1.3

Number of Genera

Asteraceae
Euphorbiaceae
Lamiancesae
Fabaceae
Rubiaceae
Poaceae
Acanthaceae
Rosaceae
Apieceae

419
214
214
214
208
168
141
129
118
Our per capita annual consumption of drugs of Rs.125 is the lowest in the world mainly because medicinal plants constitute the principal health care resources for the majority of population. WHO estimated that 80% of the population of developing countries relies on traditional medicines, mostly plant drugs, for their primary health care needs. Also, modern pharmacopoeia still contains at least 25% drugs derived from plants and many other, which are synthetic analogues, built on prototype compounds, isolated from plants. Global resurgence in the use of plant based drugs is an opportunity for India to attain self-reliance and boost the export of herbal drugs.

The export potential of raw medicinal plants and pharmaceutical products is steadily increasing from Rs. 2718 lakh in 1997- 88 to Rs. 44630 lakh in 1998- 99. This implies that demand for the medicinal plants is increasing greatly and it has great future for our country. In 2000 the International market of medicinal plants was estimated to be over US$60 billion per year, which is growing at the rate of 7%. India in the same year showed its export data related to herbal material and medicines to the tune of Rs.6446.3 crores only which is projected to be raised to Rs3000 crores by 2005. China and India are two great producers of medicinal plants having more than 40% of global biodiversity. There is thus an enormous scope for India also to emerge as a major player in the global herbal product based medicines. By the end of 2015 the export potential can boost, between15, 000 -20,000crores (World Bank, 2003; All India Ethno-biology Survey, Govt.of India, 2009).

1.3.2 Urgency to conserve medicinal plants

About 90% of medicinal plants used by industries are collected from the wild. While over 800 species are used in production by industry, less than 20 species of plants are under commercial cultivation. Over 70% of the plant collections involve destructive harvesting because of the use of parts like roots, bark, wood, stem and the whole plant in
case of herbs. This poses a definite threat to the genetic stocks and to the diversity of medicinal plants. Recently some rapid assessment of the threat status of medicinal plants using IUCN designed CAMP methodology revealed that about 112 species in southern India, 74 species in Northern and Central India and 42 species in the high altitude of Himalayas are threatened in the wild. The urgency and seriousness of the problem has rightly deserved and drawn worldwide attention. The Govt. of India has banned export of medicinal plant species and is giving attention to conservation, popularization and systemic cultivation of this wealth of nature through various schemes. For conservation of diversity, Department of Biotechnology (DBT) has set up three gene banks, viz. a) Central Institute of Medicinal and Aromatic Plants (CIMAP), Lucknow. b) National Bureau of Plant Institute (TBGRI), Thiruvananthapuram. The Ministry of Environmental and Forests, Government of India has also adopted very tough policies to confine exploitation of medicinal and aromatic plants from wild sources. Also, National Medical Plant Board (NMPB), Department of AYUSH, Ministry of Health and Family Welfare, New Delhi, is coordinating all matters relating to development and sustainable uses of the medicinal resources in India.

In order to fully convert the potential of our medicinal plants into economic wealth, a very active R & D programme is essential. We should cover all aspects relating to the species from collection to utilization. For convenience we can categories medicinal species into those on which sufficient leads are available and those on which much work is required to be done. For conservation of medicinal plants research investigations concentrate on evolving and optimizing the most appropriate technologies for conservation, especially for endangered or endemic species (e.g. *Rauvolfia serpentina*, *Gloriosa superba* etc.) and molecular methods for characterization. Detailed studies on life cycle and breeding behaviour, taxonomy, seed biology. Population and habitat
viability studies. Optimizing appropriate methods for postharvest handling, processing and storage. Investigation on shelf life of raw materials and finished products. Biotechnology showed promising results in the field of propagation, secondary metabolite production, and development of new plant varieties through tissue culture techniques.

1.4 Plants Drugs for Cardiovascular Diseases

In the area of cardiovascular drugs, plants are still the basis of treatment. In the world some of the plants accepted by most pharmacopoeias, include *Digitalis sp*, *Convallaria majalis*, *Adonis vernalis*, *Helleborus viridis* and *Crataegus oxycantha* which primarily act on the heart and *Hydrastis sp*, *Veratrum sp*, *Ammi visnaga* and *Viscum album* which act more specifically on blood vessels. Phytoconstituents which are commercially available to cardiotonic pharmaceuticals are Digoxin, Digitoxin and Lanotosides from *Digitalis species*, K-Strophanthidin from *Strophanthus* seeds, Quabain from *Acokanthera schimperi*, Thevetin from *Thevetia nerrifolia*, Convallatoxin from *Convallaria majalis*, Scillaren from *Urgenia scilla* and Colenol drug ‘Forskolin’ from *Coleus forskohlii*. Many more Indian plants are likely to give such leads in the future. Yellow Oleander (*Thevetia*) has been known to be rich in cardiotonic steroidal glycosides (peruvoside, therererrin, and nerrifolin), enzymatic conversion can yield digitoxigenine and digitoxose (Dwivedi, 1997). There are plants on which there is information to be helpful in cardiovascular ailments, others have shown considerable potential.

There is World data on plants, helpful in cardiovascular ailments (Annexure-1). In India also there are many medicinal plants which have shown potential in treating cardiovascular ailments, some are known from ancient times, as part of our ethnic knowledge (Annexure2).
1.5 Medicinal plants in Orissa

Orissa, where the present study has been carried out, comes under intermediate zone of vegetation, having 100-200 cm rainfall and possess moist semi evergreen, moist deciduous and dry tropical deciduous type of vegetation. Orissa has the oldest and richest tradition culturally associated with use of medicinal and aromatic plants bestowing with a rich biodiversity of medicinal plants due to its diversified topography and variable climatic conditions. The forest area is extensive, constituting about 42 percent of the total area of the state (Saxena and Dutta, 1975). These are seen mainly in forests and hills, plateaus, plains of most of districts Koraput, Kalahandi, Mayurbhanj, Phulbani, Dhenkanal, Bolangir and Keonjhar etc. The Gandhamardan hill has already been recognized as a valuable source of important life saving medicinal plants as depicted in the Ramayans.

Out of the innumerable type of medicinal plants in Orissa the economic parts and utilization of important plant species are discussed under the trees, shrubs, herbs and climbers which are being maintained at the Horticulture Research Station, OUAT, Bhubaneswar (Anrexure-3).

1.6 Micropropagation

Micropropagation or plant tissue culture is a method of propagating plants in mass, under sterile and controlled conditions. Plant tissue culture can be broadly defined as a collection of methods used to grow large numbers of plants, in vitro (in test tubes), in an aseptic and closely controlled environment. The method involves taking a tissue from various parts of the plant and cultivating new plants in an agar medium which have been fortified with growth hormones and nutrients (Murashige, 1974). While a stem cutting may produce two or three new plants in a conventional manner, it only takes a square centimeter of meristem cells to produce thousands of new plants in tissue culture. This
technique is very effective because almost all plant cells are totipotent - which each cell possesses the genetic information and cellular machinery necessary to generate an entire organism.

Micropropagation has a number of advantages over traditional plant propagation techniques. This method produces nearly disease-free plants, it produces rooted agri-starts ready for growth, rather than seeds or cuttings, it has an extraordinarily high multiplication rate, it is a good way of multiplying plants that produce seeds in small amounts (if at all), and it often produces more robust plants, leading to accelerated growth compared to similar plants produced by conventional methods, thereby shortening the long periods of stratification time required by some medicinal herb seeds (Schippmann et al., 2002).

1.7 Objectives and rationale of the present study for research

Medicinal plants assume important role in fighting against different life threatening diseases. The plant based drugs have been found to be effective in clinical and experimental studies and are found abundantly in India. A rich biodiversity of medicinal plant is also seen in Orissa. Therefore, in Orissa, search for new drugs of plant origin for curing heart ailments can yield great results. Out of the 17 medicinal plants being used for curing heart ailments in Orissa (Annexure-5), four plants have been selected during present investigation, considering their omnipresent response to in vitro culture. These plant based drugs would be cost effective due to its abundance and temperamentally quite suiting to millions of our masses as these plants and their remedies are in use from ancient times. Thus considering the advantages of these plants, the present study deals with the study of micropropagation of plants Emblica officinalis Gaertn., Withania somnifera (L.) Dunal., Ocimum sanctum L. and Boerhaavia diffusa L.
All these plant species have shown some potential in the treatment of cardiovascular diseases.

The primary objectives of the present study concentrate on-

(a) Selection of elite trees of *Emblica officinalis* and collection of plant species of *Ocimum sanctum* and *Boerhaavia diffusa* and seeds of *Withania somnifera* from the wild source. Growing these plant species under greenhouse and experimental field conditions.

(b) Standardization of *in vitro* micropropagation protocol through axillary bud multiplication, organogenesis and somatic embryogenesis for mass propagation of *Ocimum sanctum* L., *Boerhaavia diffusa* L., *Emblica officinalis* Gaertn. and *Withania somnifera* (L.) Dunal. The effects of physical and physiological factors like the age of source plant, composition of culture media, plant growth regulators, light intensity, photoperiod, incubation temperature etc on the rate of propagation will be studied to standardize the propagation protocols.

(c) Acclimatization, hardening and field establishment of the micropropagated plantlets for evaluation of the transplantation success.

(d) Evaluate the standardized micropropagation protocol for production of planting material for commercial plantation and study the role of these plant species in the treatment of cardiovascular ailments.