CHAPTER-I GENERAL INTRODUCTION

1.1. NATURAL PRODUCTS DRUG DISCOVERY

Throughout the ages, nature has provided human with sources of the essentials of life including food, medicines and raw materials for the manufacture of clothing and shelters. Man began to explore the resources of every type on the earth for their potentialities to cure ailments and interpreted their effects wisely in terms of knowledge in different branches of science prevailing at that time.

Human’s eternal quest for happiness will continue till he draws his final breath. This quest has made him tread many paths, known and unknown. Disease has been an integral part of man from the beginning of his existence. The subject of drugs is also as old as disease and the search for remedies to combat it is perhaps equally old. The human being is more afflicted by diseases and he was very early sought to alleviate his suffering from injury or disease taking advantage of plants growing around him. The plants “The sleeping giant of drug development” represent today, the prime source of medicament all over the world.

The history of drugs is intimately linked with plants from the earliest times and even today plant products have extensive use in the ethno-medicine and traditional systems of medicine. Interesting medicinal plants has increased enormously over the last three decades. The untapped wealth of plant kingdom has become the target for the search of new drugs and lead molecules by multinational drug companies and research institutes. Prominent investigations of
traditional remedies are largely of botanical origin, on which a worldwide majority of the population still relies for its source of medicine.

Nature is unrivalled in its ability to craft small organic molecules, jam packed with structural complexity and biological potency. Since time immemorial with extracts of plants and animals have been recognized to possess biologically important properties.

In the early 1800’s an emerging fascination with such molecules give rise to the field of organic chemistry, so name for its emphasis on the chemistry of living things. Later discrete organic compounds discovered, were known as ‘natural products’ or ‘secondary metabolities’. In particular, higher plants have been the source of medicinal agents since the earliest times and today they continue to play dominant role in the primary health care of about 80% of the world’s population¹. It is not surprising to find that in many countries of the world there is a well established system of traditional medicine, whose remedies are still being compiles.

Natural products and medicinal agents are also an essential feature in the health care systems of the remaining 20% of the population residing mainly in developed countries. With more than 50% of all drugs in clinical use having a natural product origin².

The WHO estimates that 3.5 billion people in developing countries rely on the plant-based medicine for their primary health care. There has been a global resurgence of interest in plant based drugs probably due to the following reasons³.
General Introduction

i) High cost (upward of $2000 million) of synthetic drugs.

ii) Non-renewable sources of basic raw materials of synthetic drugs.

iii) Environmental pollution by the chemical industry.

iv) Long history of use and better patient tolerance as well as public acceptance of plant based drugs.

v) Renewable sources of plant drugs.

vi) Cultivation and processing of drugs.

vii) Plants contribute to be a major source of new lead molecules.

Though herbal medicines are effective in the treatment of various ailments, very often these drugs deserve detailed studies in the light of modern science.

It is estimated that about 7500 plants are used in local health traditions. Among these most of them were cultivated in rural and tribal villages of India. Out of these, the real medicinal value of over 4,000 plants is either little known or unknown to the main stream population. A detailed investigation and documentation of plants used in local health traditions, Pharmacological evaluation of these plants and their taxonomical relatives can lead to the development of invaluable plant drugs for many dreadful diseases.
1.2 BIOACTIVITY OF PLANTS

The traditional use of medicinal plants played a vital role in sustaining disease for free human existence on this planet and can be traced back over five millennia to written documents of the early civilization in China and India.

Although we have drugs of mineral and animal origin from nature and synthetic substances, plants are the almost exclusive source of drugs for the majority of world’s population. Inspite of overwhelming influence of modern medicine and tremendous advances were made in the population of synthetic drugs, traditional medicament refer to now a days as herbal drugs in different places in literature, have retained their place in effective therapy, low cost and comparative freedom from serious toxic effect make these medicaments not only popular but also an accepted mode of treating disease even in developed countries. The isolation of alkaloids such as Morphine, Strychnine, Quinine etc., marked a new era in the use of medicinal plants. Inspite of extensive research in plant products the potential of higher plants has sources of new drugs is still largely explored. Among the estimated 250000-500000 plant species only a small percentage has been investigated phytochemically and the fractions submitted to biological or pharmacological screening is even smaller in many cases the isolated plant constituents do not explain the rationale of using these plants in traditional medicine for particular ailments. Chemical reinvestigation pharmacological screening of extracts may focus on this aspect. In any case,
freedom from toxic effects is must for any herbal medicines, which are commercially available in the market.

The process for the isolation of pharmacologically active pure constituent is a very long and tedious. It requires a multidisciplinary collaboration of botanists, phytochemists and pharmacologists. This approach involves the following steps.¹

1. Collection of plant material with proper botanical identification
2. Pharmacognostic standardization of identified plant material.
3. Drying of plant material and extraction with appropriate solvent
4. Pharmacological screening.

Nearly all ‘wonder drugs’ in use today are derived from natural products. About 120 plant derived drugs commonly used in many countries. 74% were discovered as a result of chemical studies directed by the isolation of the active constituents of plants, which are used in traditional medicine⁴. Well known examples of wonder drugs include the Cardiac glycosides from *Digitalis purpurea*, Anti-hypertensive agent and Tranquilizer : Reserpine from *Rauwolfia serpentine*, Anti-malarial agent : Quinine from Cinchona species, Analgesics: Codeine and Morphine from *Papaver somniferum*. Secondary metabolites isolated from medicinal plants were also served as precursors or models for the preparation of effective agents through semisynthesis are lead-based total synthesis. Examples include in anticancer agents, Etoposide a semisynthetic
derivative of phodophyllotoxin isolated from *podophyllum species*\(^5\) and anticholinergic drugs modeled on the belladona alkaloids isolated from *Atropa belladonna*.

The pioneering studies of the active constituents of *Catharanthus roseus*\(^6\) and discovery of Antileukemic agents, Vincristine and Vinblastine provided convincing evidence that plants could be sources of novel, potential cancer chemotherapeutic agents. It has discovered Taxol from *Taxus brevifolia* now approved for the treatment of ovarian, breast cancer and Camptothecin which has been converted through semi synthesis to several analogues that are currently showing in advanced clinical trails. The role played by plants in providing novel agents having potential in treatment and prevention of many diseases, such as cancer, AIDS and malaria has been reviewed.
1.3 REFERENCES:


