Introduction

Man’s existence on this earth has been made possible only because of the vital role played by the plant kingdom in sustaining his life. The three important necessities of life, i.e. food, clothing and shelter and also a host of other useful products are supplied to a great extent by the plant kingdom. The nature has provided a complete store-house of remedies to cure all ailments of mankind. Since the dawn of cultivation, in addition of food crops, man cultivated herbs for his medicinal needs. Plants are the only economic source of a number of well established and important drugs, in addition, they are the source of some chemical intermediates needed for the production of a number of drugs. At rough estimate, 25 percent modern drugs are directly or indirectly derived from plant products. Before independence, the production of plant based drugs in India was confined mainly to cinchona and opium alkaloids in three state owned factories, the other products were mainly galenicals (i.e. extracted from plants) and tinctures. In the last three decades bulk production of plant drugs has become an important aspect of the Indian pharmaceutical industry. India has, since independence, moved on to export of crude drugs through total extracts to production of bulk drugs and steroid intermediates.

Undoubtedly the plant kingdom still holds many species of plants containing substances of medicinal value which have yet to be discovered; large numbers of plants are constantly being screened for their possible pharmacological value (particularly for their anti-inflammatory, analgesic, antipyretic, sedative, diuretics, antitussive, antihypertensive, antirheumatic, wound healing, antibacterial and cytotoxic properties). Another development which has increased interest in medicinal plants is the amount of research on, as for example, Chinese materia medica. A fascinating area of research, which has not proved unrewarding, is the examination of plants used for
medicinal, narcotic and other purposes by primitive tribes. With the westernization of so
many such peoples there is a great need to register local knowledge before it is
completely lost. Also, with the extermination of plant species progressing at an alarming
rate in certain areas even before the plant has been recorded, much less studied
chemically, the need arises for increased efforts directed towards the conservation of gene
pools of locally used medicinal plants.

As a result of modern isolation and pharmacological testing procedures, new plant
drugs usually find their way into medicine as purified substances rather than in the form
of older galanical preparations. For the drugs it is important that the pharmacist, rather
than be fully conversant with the macroscopical and histological characters of the dried
plant, is able to carry out the chromatographic and other procedures necessary for the
identification and determination of purity of the preparation supplied. The use of single
pure compounds, including synthetic drugs, is not without its limitations and in recent
years there has been a considerable revival of interest in the herbal, Homoeopathic and
Ayurvedic systems of medicine, all of which rely heavily on plant sources.

Many of the botanical, chemical and physical technique employed in Pharmacognosy,
are also applicable to the analysis of other commodities (e.g. foods, spices, gums,
narcotics, fabrics, cosmetics and perfumes) and are, therefore, also used by public
analysts, forensic scientists and quality control chemists associated with other industries.

Whilst Pharmacognosy has been generally pursued for utilitarian ends and may thus
be called an applied science. It has played an important role in the development of the
pure sciences, e.g. in descriptive botany, plant taxonomy and phytochemistry. Chemical plant taxonomy, genetical studies involving secondary metabolites, the artificial and tissue culture of plants, the effects of chemical on plant metabolites and the induction of abnormal synthesis in plants are now attracting the attention of more and more botanists, chemists and pharmacognosists.

The plants which have been selected for use, often over thousands of years, constitutes the most obvious choice for examination in the current search for new therapeutically effective drugs. At present the World Health Organization is taking an official interest in indigenous systems of medicines, particularly plant remedies. The World Health Organisation (WHO) defined traditional medicine recently as comprising “therapeutic practices that have been in existence, often for hundreds of years, before the development and spread of modern scientific medicine and are still in use today. These practices vary widely, in keeping with the social and cultural heritage of different countries” (WHO, 1991). Attempts have been made by scientists to justify or rationalize, on a scientific basis, many aspects of the practice of traditional medicine.

Traditional system of medicine whether they are of Indian, Chinese, Tibetan, Thailand or Vietnamese origins, have evolved over several hundreds of years through the transfer of knowledge and usage practices from generation to generation. From the vast array of indigenous system it is thought that investigation and research on medicinal plant might bring remedies to the scientific world from alleviation of human sufferings. Despite remarkable achievement of modern medicine and medical research such ancient systems continue to be major component and effectively be used to control disease. The traditional systems of medicines are

- Ayurvedic medicine,
- Unani medicine,
- Homoeopathic medicine,
- Yoga and naturopathic medicine.

The mention of plant drugs is found in Rigveda and Yajurveda both around 2000 B.C. Ayurveda, Siddha and Unani systems of medicine use 600-700 herbs for medicinal use. Plants are the most exclusive source of drugs for the majority of world’s population. There has also been a global resurgence of interest in plant-based drugs. The major criteria should include evidence of safe, effective use in the country or in the region, assured plant availability from wild or cultivated sources and export potential. India has one of the oldest, richest and most diverse cultural traditions associated with the use of medicinal plants. The various traditional systems use plants as medicine often as whole plants or their extracts. The systems also use multiple herbs in their galenical forms with very elaborate processing for specific disease conditions. Such an approach has been justified by invoking immune-modulation as a possible mechanism of action with multiple plant components in a synergistic fashion for therapeutic efficacy with minimum toxicity. Natural therapy also studies the basic human nature and natural feelings like hunger, thirst, sleep, sex etc., and provides measures for a disciplined, disease free life and will give a holistic approach to the therapy.

**Problem with modern drugs**

- High cost and long time taken in development of new drugs.
- Toxicity particularly with allopathic medicine
- Non-renewable source of basic raw materials. Most synthesis of drug utilizes fossil resources like petrochemicals.
- Environmental pollution by the chemical industry.
- Inadequate, specially in management of chronic diseases.
The criteria for the selection of plants for herbal drug research for various human ailments are as follows:

- Actual uses of the medicinal plants in the country of the region.
- Scientific literatures indicating therapeutic efficacy of the plants in certain diseases.
- Mention of the plants in early texts as having therapeutic effects.
- Use of medicinal plant for therapeutic purpose in country outside region.

Advantages of plant based drugs

- Long history of use and better patient tolerance as well as public acceptance.
- Renewable source.
- Cultivation and processing environmental friendly.
- Local availability, especially in developing countries.
- Several important recent breakthroughs.
- Plants constitutes to be major source of new lead generation.

There are several definitions of “Traditional drugs” but the most comprehensive one is where WHO defined it as “The sum total of the knowledge and practices, whether explicable or not used in diagnosis, prevention and elimination of physical, mental or social imbalance and relying exclusively on practical experience and observations handed from generation to generation whether verbally or by writing”. Different traditional medicines have already been proved their efficacy in the treatment of different complicated diseases. Based on the strong traditional knowledge on the use of plants as therapeutic agents, a rational approach is being developed to use medicinal plants as lead for the discovery of active molecules, with one of the largest reservoirs of bio-resources. The modern concepts of molecular pharmacology have been combined with sophisticated chemistry for the development of drugs from plant
sources. To perform fruitful research on medicinal plants leading to discovery of new drug molecules. The following far-reaching changes will have to be made:

- Attracting the best brains in this field.
- Use of appropriate methods and new technology.
- Development of proper infrastructure.
- Training of Pharmacologists and clinical Pharmacologists in medicinal plant research.
- Renewing interest of Pharmaceutical houses in medicinal plant drug development.

**Herbalism**

Herbalism is becoming more mainstream as up-to-date analysis and research show their value in the treatment and prevention of diseases. Herbal medicines are very helpful in providing excellent lead for synthesizing better drugs for variety of ailments. It is, therefore, important to bring use of such remedies into an existing framework of rational use of medicines. It will be useful to consider regulatory and legislative control needs to be exercised on the use of herbal medicines. Herbal remedies were and will be with us for a long time. Linked to these are issues of quality control, both of the raw material and of the finished product and of standardization of herbal remedies.

Herbal medicine also called botanical medicine or phytomedicine refers to the use of any plant’s seeds, roots, leaves or flowers for medicinal purposes. Higher plants have played a dominant role in the introduction of new therapeutic agents. Approximately 60% of the antitumour and anti-infective agents that are commercially available in the late stages of clinical trials today are of natural origin. At present there are at least 130 chemical compounds used as drugs and are extracted from higher plants modified further
synthetically for global use. People primarily in the developing countries like India for primary health care is using plant medicine. They stood for their safety, efficacy, cultural acceptability and least side effects. The chemical constituents present in them are believed to have better compatibility with human body.

Ancient literatures mentioned the usage of herbal medicines for age-related diseases namely memory-loss, osteoporosis, diabetic wounds, immune disorders etc., for which modern medicine or only palliative therapy is available.

**Contribution of medicinal plants to modern drugs**

As the synthetic drugs caused several side effects, the plant based medicines have become popular throughout the world nowadays. The contribution of higher medicinal plants in discovery of new drugs has been enormous in terms of value and activity for treating diseases like cancer, hypertension and several other ailments. Many plant based drugs which were introduced in modern medicine were considered as outstanding contributions to drug discovery. The discovery and introduction of reserpine, an alkaloid obtained from the roots of the Indian plant *Rauwolfia serpentina* as drug for the treatment of hypertension and as a tranquilizer was considered as a revolutionary event. The *Rauwolfia serpentina* is highly valued in Ayurvedic system of medicine, the roots of which are used for the treatment of hypertension, Insomnia and insanity (Sukhdev, 1997). The bisindole alkaloids vinblastin and vicristine obtained from the leaves of *Catharanthus roseus* are potent anticancer agents used for the treatment of Hodgekin’s diseases, lymphosarcoma and leukemia in children. Another anticancer compound obtained from *Podophyllum emodi* and *Podophyllum peltatum* is a podophyllotoxin, a lignan (Jain, 1991).
Although several new chemotherapeutic drugs of both synthetic and natural origin are being discovered from time to time, diseases like cancer, hepatitis B, rheumatoid arthritis, AIDS lack satisfactory solution. Anticancer agents from plants appear to be satisfactory for the control of diseases and prolong the life of a patient. Similarly for liver diseases like hepatitis and liver cirrhosis there is no adequate cure in modern medicine. Undoubtedly plants have provided useful drugs to mankind for their health care needs.

Oxidation is well known to be a major cause of material degradation. Most recently oxygen reactive species, in particular free radicals have been recognized to be involved in several diseases including cancer and atherosclerosis. Aging also may be the result of deleterious free radical reactions which occur throughout cells and tissues (Maxwell, 1995). Several studies have revealed that plants produce potent antioxidants to control oxidative stress caused by sunbeams, oxygen which represent the source of new compounds with antioxidant activity. So, the approach of research on plant medicine has radically changed.

**Standardization and safety assessment of herbal drugs**

WHO currently encourages traditional herbal remedies in national health care programs because such drugs are easily available at low cost, comparatively safe and people have faith in such remedies represent a substantial proportion of the global drug market in the respect internationally recognized guidelines for their quality assessment. The WHO assembly emphasized the need to ensure quality control of medicinal plants products by using modern techniques and applying suitable standards. For pharmaceuticals, quality of medicinal plant material must be as high as that of other medicinal preparations.

However, it is impossible to assay for a specific chemical entity when the bioactive ingredients are not known. In practice assay procedures are not carried out even for those medicinal plant material where there are known active ingredients. For example, much of the ginseng or valerian is bought and sold on the basis of its sensory characters rather like tea. For medicinal purposes ginseng should be assayed for its ginsenoside content and
valerian for its valepotriates. Further problem is possessed by those preparations, which contain complex heterogeneous mixtures. Vegetable drugs are inevitable inconsistent because their composition and hence the standardization may be influenced by several factors such as age, origin, harvesting period, method of drying and so on. The purpose of standardizing traditional remedies is to ensure therapeutic efficacy.

The only centre established in the country by the Indian Council for Medical Research for the purpose of formulation, standardization and maintaining quality of such drugs inducted in clinical trials in these areas is the Indian Council of Medical Research for advanced research at the Regional Laboratory, Jammu. The centre has prepared protocols for correct identification, botanical authentication right from the source of collection of plant material its drying, powdering, extraction, in process quality control preparation of formulation, standardization of the finished product, stability studies, packing, labeling and for the preparation of such drugs for clinical trials in various hospital in different parts of the country.

The following are the parameters to be considered in standardization of herbal drugs as well as finished product:

1. Morphological Evaluation
2. Microscopic Evaluation
3. Biological Evaluation
4. Physical Evaluation, such as,
   - Viscosity
   - Moisture content
   - Melting point
   - Solubility
   - Optical rotation
   - Refractive index
   - Ash value
   - Extractive Values
   - Volatile oil content
   - Foreign organic matter
The purity of crude drug is ascertained by quantitative estimation of active chemical constituent present. The spectroscopic analysis using the specific absorption of the constituents in UV-vis, fluorimetry, IR, NMR, Mass spectra are the examples of physical assay method. Some modern techniques like TLC, HPLC, GC, HPTLC are becoming popular now a days for
- Identification of raw materials.
- Finger printing of materials
- Isolation of active constituents
- Detection of adulterants
- Quantification of active constituents

The type of standardization ensures the use of correct herbs and quality. In standardisation of evaluation of herbal drugs, assessment of biological efficacy is found to be most assuming method. In this method requirements are a suitable animal model for testing and control, methodology for experiment. The herbal remedies started to regain their significance in therapy in the 20th century. The synthetic drugs are slowly sidelined by the phytomedicine (plant drugs) due to side effects and increasing cases of microbial drug resistance as well as the prevailing diseases that are not completely curable by the synthetic drugs. In this context the Government of various countries are now looking forward to regulate the trade of herbal remedies. To protect the people from adulterated and spurious herbal product, authentication and standardization of herbal drugs are almost essential.

It is only in recent Years the importance of standardization of herbals is realised and efforts are being made to satisfy the regulatory requirments. Herbs serv not only as
medicine but also as nutrient foods. Many are rich in nutrients like proteins, carbohydrates including fibre, fat and minerals besides vitamins. For the development of new antiprotozoal drugs, the plants like Triclisia patents, tilicora trinadra, Atlantia monophylla, Artemesia annua and Celastrus paniculata have provided leads for amoebicidal drugs, Holarrhena antidysenterica is worth investigation and cephaelis ipecacuanha with higher yeild of emetine content needs to be cultivated on large scale. Encouraging results for the development antiulcer drugs have been obtained from plants like Glycyrrhiza glabra, Azadiracta indica, Sideritis mugronensis, Corydalis tubers and dried bannana pulp powder has been recently marketed in India as the pulp of musa species gave concentration dependent increase in postaglandin accumulation in human gastric mucosa.

The interest in medicinal plants in India in the continents of Europe, Soviet union, China and Japan had never really been dismissed and after the world war medicinal plant research institutes were established in almost every country both East and West. Similar attitudes have been taken towards the exploitation of their native plants by the developing countries of Africa and Asia. It is not only the new plants that are‘being examined but also older plants and crude drugs, originally investigated and rejected or considered of little value in the late 19th century are being re-examined using all modern techniques. Because of the definite trend throughout the world for people to use many herbal preparation, the need for proper dissemination of information on safety, efficacy and or potential hazards involved in their use represent a challenge for the pharmaceutical profession and points out to the need for pharmacologically oriented pharmacognosy. This emphasis on pharmacognosy, however will have little meaning , if there is not a proper mixture of Botany, Chemistry and Pharmacology involved. It is true that literature is replete with plants reported to cure different types of illness. This is complemented by the
actual use of several hundreds of plants which are never mentioned in literature. There is undoubtedly a wealth of material. Organizations like the World Health Organization (WHO) and United Nations Children’s Emergency Fund (UNICEF) are much interested in plants to be used for the treatment of childhood ailments. A National Medical Research Council will have its own criteria to be used for supporting research on medicinal plants. The Indian Council of Medical Research, after years of keeping away from supporting research on plants, has recently returned to selectivity support research on the use of medicinal plants.

The disease is identified first from a national perspective and then plants are selected for being tested in these conditions. Lack of an effective cheap remedy in the allopathic system of medicine and the chronic nature of the disease, the plants have been selected because they are widely available for the use of the plant, either it has been mentioned in literature or it is actually being used, and easy availability of the plants.

The Eastern Mediterranean Regional office of WHO organized an intercountry meeting on “use of medicinal plants at the primary health care level” in Kuwait from 20th to 25th April, 1985. The Minister of Health in Kuwait, H.E. Dr. A.R. Al Awadi, inaugurate the meeting by referring to the rich heritage in the use of medicinal plant and herbal remedies described in Arab medicine and felt that there was no need to use synthetic drugs when simple herbal remedies were available and had been used for centuries to cure common conditions. The Regional Director of the Eastern Mediterranean Region, Dr. Li.Geza, in his message stated that several countries in the Region had been and still were using medicinal plants for health care. He also felt that it was important to ensure
that this heritage should be employed to the full and utilized most effectively for the alleviation of sickness and suffering.

One main objective of the participants, representing seven countries of the Region, was to identify a core list of medicinal plants to be used at the primary health care level. There were representatives from Afghanistan, Egypt, Kuwait, Pakistan, Saudi Arabia, Somalia and Sudan. The representative of the countries all using herbal medicines, identified twelve conditions encountered at the primary health care (PHC) level for which herbal remedies could be used. These conditions are:

- Gastrointestinal diseases
- Respiratory diseases
- Skin diseases
- Helminthic infestation
- Fever
- Pain and inflammation
- Allergy
- Urinary tract infection
- Arthritis conditions
- Eye diseases
- Burns, scalds, wounds, abscesses and swellings
- Snakebites, scorpion stings and insect stings.
Table-1. Model list of plants recommended by WHO

<table>
<thead>
<tr>
<th>Gastrointestinal tract remedies</th>
<th>Anti-emetics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anti-diarrhoeals</strong></td>
<td>Atropa belladonna</td>
</tr>
<tr>
<td>Acacia arabica</td>
<td>Hyoscymus spp.</td>
</tr>
<tr>
<td>Acacia catechu</td>
<td>Mentha spp.</td>
</tr>
<tr>
<td>Berberis aristata</td>
<td>Zingiber officinalis</td>
</tr>
<tr>
<td>Commifera mukul</td>
<td></td>
</tr>
<tr>
<td>Punica granatum</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Laxatives</th>
<th>Remedies for upper respiratory diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aloe ferox</td>
<td>Adhatoda vasica</td>
</tr>
<tr>
<td>Cassia acutifolia</td>
<td>Allium cepa</td>
</tr>
<tr>
<td>Chicorium intybus</td>
<td>Althoea officinalis</td>
</tr>
<tr>
<td>Glycyrrhiza glabra</td>
<td>Ammi vasnaga</td>
</tr>
<tr>
<td>Plantago ovata, p. psyllium</td>
<td>Cassia fistula</td>
</tr>
<tr>
<td>Rhamnus frangula</td>
<td>Cinnamomum zeylanicum</td>
</tr>
<tr>
<td>Ricinus communis</td>
<td>Linum visitatissimum</td>
</tr>
<tr>
<td></td>
<td>Mentha spp.</td>
</tr>
<tr>
<td></td>
<td>Ocimum sanctum</td>
</tr>
<tr>
<td></td>
<td>Prunus domestica</td>
</tr>
<tr>
<td></td>
<td>Psidium guajara</td>
</tr>
<tr>
<td></td>
<td>Urgines maritima</td>
</tr>
<tr>
<td></td>
<td>Zingiber officinalis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Carminatives</th>
<th>Remedies for skin diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cinnamomum zeylanicum</td>
<td>Aloe vera, A.berbadense</td>
</tr>
<tr>
<td>Mentha spp.</td>
<td></td>
</tr>
<tr>
<td>Ocimum sanctum</td>
<td></td>
</tr>
<tr>
<td>Origanuni spp.</td>
<td></td>
</tr>
<tr>
<td>Thymus vulgare</td>
<td></td>
</tr>
<tr>
<td>Umbelliferous fruits</td>
<td></td>
</tr>
<tr>
<td>Anise, carraway Coriander</td>
<td></td>
</tr>
<tr>
<td>Zingiber officinalis</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Spasmolytic</th>
<th>Remedies for arthritic conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyoscyamus spp.</td>
<td>Capsicum minimum</td>
</tr>
<tr>
<td>Atropa belladonna</td>
<td>C. anum</td>
</tr>
<tr>
<td>Datura spp.</td>
<td>Commifera mukul</td>
</tr>
<tr>
<td>Hyoscyamus spp.</td>
<td>Withania somnifera</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stomachics</th>
<th>Remedies of eye diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheum officinalis</td>
<td>Berberis aristata</td>
</tr>
</tbody>
</table>

| Anthelmintics                   | Rosa domascena                        |
| Albizia anthelmintica           |                                        |
| Artemesia cina                  |                                        |

| Antipyretics                    |                                        |
| Allium cepa, A. sativum         |                                        |
| Fagonia arbica                  |                                        |
The use of medicinal plants at the primary health care level has several advantages and should be encouraged. In many parts of the World, there are no doctors and no allopathic drugs. Very often, there are doctors but the government budget has run out and there are no medicines to distribute. Sometimes allopathic drugs of indeterminate quality of doubtful origin are smuggled across borders and sold in open markets. Many of these substances have no expiry date. It would be better, in these circumstances, to use herbal medicines chosen with care, supplied with a guarantee of quality, prescribed by practitioners in whom the patients have trust. The use of such medicinal plants should be monitored and changes made in the list of traditional medicines at the peripheral health centres based on the on going experience. The easy availability of these drugs at all times, the relatively low cost of these medicines and less side effects associated with the use of these drugs are some of the factors which may eventually lead to the replacement of some of the modern medicines used at the primary health care level, by medicinal plants.
There are certain issues related to medicines from plants which need to be highlighted. It has been said very often by persons interested in protecting the environment that if environmental pollution continues, our rain forests will be depleted and a resource for developing new medicines from natural flora will be lost for ever. It is hoped that these same environmentalists would support research on some of the resources available (Chaudhury, 1994).

A representative group of experts meeting at a WHO Inter-Regional workshop on the selection and use of Traditional remedies in primary Health Care in Bangkok in December 1985, suggested that the formulary should include the following information:

- Name of plant (genus, species and family)
- Plant part used
- Quality requirement (percentage of active principle, if known)
- Botanical characteristics
  - Macroscopic morphological description, including organoleptic tests.
    - Microscopic description
    - Histological character
    - Powdered sample character
- Purity (foreign matter, adulterant, other contaminants)
- Physico-chemical analysis
  - Qualitative (including microchemical tests)
  - Quantitative (if major active ingredients are known, analytical procedures e.g. thin layer chromatography, nuclear magnetic resonance).
- Bioassays
  - In vitro
  - In vivo
The traditional approach for studying herbal drugs consists of the following ten steps:

- Identification of the plant reportedly in use
- Collection of the plant
- Transport of the plant to the research laboratory.
- Storage
- Preparation of extracts for testing.
- Administration of the extracts to animal models.
- Identification of the active or more active extract.
- Further fractionization of the active extract.
- Identification of the active principle, chemical structure
- Synthesis of the active substance

The present investigation is concerned with the widely distributed indigenous medicinal plant *Eupatorium adenophorum* Spreng. (Asteraceae). From the survey of relevant literature of this plant it is observed that the plant is most well known in traditional medicine practices and many work has been done on aerial parts, flowers but much less work has been performed on the leaves. The study was undertaken to evaluate the Pharmacognostical, Pharmacological and Microbiological aspects of the leaves of *Eupatorium adenophorum* Spreng. (Asteraceae) and presented in this thesis.