Chapter 1
Chapter 1 General Introduction

Ayurveda originated in India long back in the pre-vedic period. The Rigveda and Atharvaveda (5000 BC), the earliest Indian documents have references on health and diseases. During the Vedic period the Susruta samhita and the charaka samhita were influential works on traditional medicine. The fundamental and applied principles of “Ayurveda” science”, got organized and enunciated around 1500 BC. Ayurveda traces its origins to the Vedas, Atharvaveda in particular, is connected to Hindu religion. Ayurvedic system of medicine was based on nature and its product. The Indian subcontinent is enriched by a variety of flora-both aromatic and medicinal plants. This is due to the wide diversity of climatic conditions in India ranging from desert to swamplands. Numerous types of herbs have been well recognized and catalogued by botanists from the high ranges of the Himalayan tract up to the sea-shore of Kanyakumari. This extensive flora has been greatly utilized as a source of many drugs in the Indian traditional system of medicine. Over the following centuries, Ayurvedic practitioners developed a number of medicinal preparations and surgical procedures for the treatment of various ailments and diseases. Ayurvedic medicinal preparations consist mainly of plant materials in the form of powders, semi-solid preparations, decoctions, elixirs and distillates. Many of them also contain inorganic chemical substances, minerals and animal products. Alcoholic extracts and alcoholic solutions of the ingredients, tinctures and elixirs are also frequently used in ayurvedic medicine. Besides this, natural medicines have become the part of our daily diet like turmeric, cardamom, garlic, onion, ginger, tulsi, cloves, etc. Fruit, vegetable, pulses, wheat and rice grains which we consume daily provide us with essential nutrients like vitamins, carbohydrates, proteins, and different minerals required for smooth functioning of our body, the idea here is that prevention is better than cure and to the much extent this is true. As a herbal remedy or natural remedy we can easily remember use of ‘turmeric’ to treat body inflammations, burns and further use for skin beautification, ‘Hing’ is well known for digestive disorders, ‘honey’ is very popular as a home remedy for various ailments, the list of herbal or
better call home remedy is very long. Further extension and use of medicinal plants and the
pure isolates from them form the basis of drugs from nature.
Dependence on herbs as medicines in the treatment of disease is common among a large
proportion of population of the rural populace because of its availability and affordability. Due
to the increasing awareness of the importance of traditional medicine in human and animal
healthcare, researches into the efficacy of some of the herbs used in the treatment of some
illness would be worthwhile (Sanny et al., 2009).
Demand for medicinal plant is increasing in both developing and developed countries due to
growing recognition of natural products, being nontoxic, having less side effects, easily
available at affordable prices and sometime the only source of health care available to the
poor. WHO supports the use of effective and safe remedies and accepts traditional medicine
as a valuable resource for primary healthcare (Manila, 1993).
In the modern times with the fast emergence of western modern medicine and synthetic
chemo-therapeutics, the importance of plants and herbs started declining as more and more
attention was paid to the development of synthetic drugs. But today the medicinal plants are
no more the forgotten healers because in last few decades the medicinal plants have shown a
notable resurgence of interest once again, the reason is the increasing awareness about the
limitations of the synthetic chemotherapeutic agents and serious side effects on the face of
high safety margin of herbal drugs. Now herbal medicine and natural products are in big
demand all over the world.
Indeed, well into the 21st century much of the pharmacopeia of scientific medicine was
derived from the herbal lore of native peoples. Many drugs commonly used today are of
herbal origin. Indeed, about 25% of the prescription drugs dispensed in the United States
contain at least one active ingredient derived from plant material. The use of medicinal
plants is gaining momentum worldwide. In fact, the all the nations are looking for the
remedies from the herbs because of the increasing toxicity and allergic manifestations from
the synthetic drugs and also the excessive cost of development and production due to the
involvement of complex research techniques and time taken for their development. India is
one of the largest producers of medicinal herbs in the world. Most medicinal plants of commercial importance grow in India, due to its vast agro climatic zones. In many cases, their theory and application are quite different from those of conventional medicine. Long historical use of many practices of traditional medicine, including experience passed on from generation to generation, has demonstrated the safety and efficacy of traditional medicine. However, scientific research is needed to provide additional evidence of its safety and efficacy.

No wonder, India has become one of the major suppliers of standardized herbal extracts and phytochemicals in the world. With the rapidly escalating demand for herbal products and medicine, the medicinal plants based industry is poised to emerge as a major player in the pharmaceutical sector. For the benefit of all those engaged in cultivating, harvesting, processing and preparing the final product, here is an urgent need to compile and collect all available scientific knowledge on medicinal plants in a standardized format.

Today, the modern specific and sensitive screening methods can detect bioactive molecules present in as low as 1 μg/ ml concentration. The difficulty in purification and the identification are now eliminated with the use of advanced HPLC, high resolution 2DNMR and spectroscopic methods. Drug discovery from natural product is very tedious process involving identification of plant material, preliminary screening of the crude extracts, isolation of various secondary metabolites, elucidation of their structures and finally evaluation of their biological activity (in vitro and in vivo). If the molecule is really interesting with its strong pharmacological properties then further preclinical studies are conducted on the molecules such as toxicity studies, stability and solubility studies, pharmacokinetic studies and mechanism studies where the plausible mode of action are predicted. After undergoing these studies if it is found that molecule is more active than the presently used drug then processes are developed for its economical and easy isolation from the source so that it can be easily available for therapeutic use. Molecule may or may not go for clinical trials, all depends on the bioavailability. In most of the cases natural product as a drug are limited to the active extract (containing mixture of compounds) like most of the ayurvedic herbal
formulations due to their poor bioavailability and high input costs. The last ordeal is clinical trials where the candidate molecule is tested for its safety and efficacy on several group of human volunteers. Counting pre-clinical and clinical trials time, it takes almost a decade for new candidate drug to get approval for launch in market. So development of a new drug from natural source is a time and money consuming process, similar with that of a synthetic molecule. Natural product chemist may also develop feasible synthetic schemes to produce the lead active molecule having poor bioavailability. The plant-derived compounds have a long history of clinical use, better patient tolerance and acceptance. The high throughput screening of natural sources will greatly facilitate the discovery and development of new drugs. It could be concluded that natural products discovered so far have played a vital role in improving the human health and have been the drugs of choice despite facing a tough competition from their synthetic counterparts, due to their safe and long lasting effects. As we know the medicinal plants used in the formulation are known by vernacular or local names, which sometimes are not helpful in the proper identification of the herbs. Different local names are used for a herb in various regions and at times different herbs are known by same name. The situation is further aggravated by a near absence of standard method for evaluating the botanical authenticity and the quality of the material used in traditional system of medicine. *Aerva lanata* is a glaring example, belonging to family Amaranthaceae.

### 1.1 Introduction

Natural products play a significant role in maintaining human health by improving the quality of human life and have served human as well as valuable components of medicines, cosmetics, dyes and beverages. Demand for medicinal plant is increasing in both developing and developed countries due to growing recognition of natural products, being nontoxic, having no side effects, easily available at affordable prices and sometime the only source of health care available to the poor. The World Health Organization (WHO) estimates that 80% of the populations living in the developing countries rely exclusively on traditional medicine for their primary health care needs. A world wide survey has reported that diabetes mellitus
affects nearly 10% of the population. It has been predicted that the prevalence of diabetes in adults will increase from 135 million in 1995 to 350 million in 2030 as given by International Diabetes Federation (Menaka et al., 2010). Currently available synthetic antidiabetic agents produce serious side effects like hypoglycemic coma and hepatorenal disturbances (Sunil et al., 2009). Patients are therefore using herbal medicines which have fewer side effects and have the potential to impart therapeutic effect in complicated disorders like diabetes and its complication (Pandita et al., 2010). Following the WHO’s recommendation for research on the beneficial uses of medicinal plants in the treatment of diabetes mellitus, investigations on hypoglycemic agents derived from medicinal plants have also gained momentum.

Cancer is a major public health burden in both developed and developing countries. Plant derived agents are being used for the treatment of cancer. Cancer is expected to claim 9 million deaths worldwide by the year 2015. A major problem in the use of chemo preventing agent in cancer treatment is the potential toxicity of these drug to normal cells. Although there has been increasing sophistication of current therapeutic strategies, 40% of patients are still likely to die from the disease. Novel potent anticancer compounds are needed to address this growing issue of cancer. Despite skeptical connotations, traditional medicine has aroused renewed interest as worldwide efforts continue the search for novel compounds that exhibit potent and selective anticancer properties. Plant derived natural products such as flavonoids, terpenes, alkaloids etc have received considerable attention in recent years due to their diverse pharmacological properties including cytotoxic and cancer chemopreventive effects (Madhuri and Pandey, 2009).

Anthelmintics are drugs that are used to treat infections with parasitic worms. This includes both flat worms, e.g., flukes and tapeworms and round worms, i.e., nematodes. Parasitic worms also infect livestock and crops, affecting food production with a resultant economic impact. It is in the context that the people consume several plants or plant derived preparations to cure helminthic infections (Satyavathi, 1990). The quality control of crude drugs and herbal formulations is of paramount importance in justifying their acceptability in
modern system of medicine. But one of the major problems faced by the herbal drug industry is non availability of rigid quality control profile for herbal material and their formulations. An innovative research effort to define the advantage of traditional system of medicine with respect to their safety and efficacy could result in a better utilization of these complementary systems of medicine. WHO has shown great interest in documenting the ethno medical data on medicinal plants. Research to find out scientific evidence for claims by tribal healers on Indian herbs has been intensified. Once these local ethnomedical preparations are scientifically evaluated and disseminated properly, people will be better informed regarding efficacious drug treatment and improved health status (Manandhar, 1987). About 90 % of medicinal plants used by related industries are collected from the wild. While over 800 species are used in industries, less than 20 species of plants are under commercial cultivation. In India there are about 386 families and 2200 genera are recorded as medicinal plants. Of these, the families Asteraceae, Euphorbiaceae, Laminaceae, Fabaceae, Rubiaceae, Acanthaceae, Rosaceae and Apiaceae comprise the largest proportion of medicinal plant species. But the scientific report on the use of Amaranthaceae family in the field of medicine is scarcely available.

1.2 Objectives of the study

1. Procurement of *Aerva lanata* Linn Juss form northern and southern regions of India and selection of the southern species on the basis of HPTLC studies.

2. Proper identification and to determine the physicochemical parameters.

3. To confirm the presence of phytoconstituents in the extracts.

4. To isolate the chemical constituents from MEAL (S) by column chromatography based on phytochemical and HPTLC studies.

5. Characterization and interpretation of isolated compounds.

6. To confirm the efficacy of MEAL and AEAL of the aerial parts of *Aerva lanata* Linn Juss using Pharmacological screening.
1.3 Plan of study

1. Procurement and authentication of plant material.

2. Determination of physicochemical parameters (Mukerjee, 2008).
   a) Moisture content (loss on drying)
   b) Ash values
      i. Total ash
      ii. Acid insoluble ash
      iii. Water soluble ash
   c) Determination of extractive values of *Aerva lanata*.

3. Preparation of the extracts of the drug by successive extraction.

4. Qualitative phytochemical screening (Harborne, 1973).

5. Thin-layer chromatography (TLC) studies (Wagner and Bladt, 1984).

6. HPTLC analysis of methanol extract of *Aerva lanata* Linn collected from southern region coded as MEAL (S) and methanol extract of *Aerva lanata* collected from northern region coded as MEAL (N) (Handa and Kaul, 1997).

7. Isolation of chemical constituents from the methanol extracts of *Aerva lanata* Linn Juss MEAL (S) by column chromatography followed by characterization of isolated compounds by UV, IR, NMR and Mass spectroscopy.

8. Pharmacological activities of MEAL (S) and AEAL (S).
   a) Comparative evaluation of antihyperglycemic and antihyperlipidemic activity in streptozotocin induced diabetic rats
      i. Acute toxicity studies
         Acute oral toxicity study of MEAL and AEAL was conducted according to the guidelines set by Organisation for Economic Co-operation and Development (OECD) guidelines (Bala et al., 2010).
      ii. Weekly (0, 7 and 14th day) body weight, fasting blood glucose, cholesterol and TG level (Salahuddin *et al.*, 2010).
iii. Plasma biochemical parameters such as SGOT, SGPT, creatinine, ALP, BUN and total bilirubin (Reitman and Frankel, 1957).

iv. Total protein by Biuret method (Reinhold, 1953).

v. Catalase, superoxide dismutase (SOD), lipid peroxidation (TBARS), glutathione peroxidase (GPX), reduced Glutathione (GSH) (Kakkar et al., 1984).

vi. Hepatic glucose-6-phosphatase, fructose 1, 6 – bisphosphotase, hexokinase (Brandstrup et al., 1957).

vii. Liver glycogen estimation (Seifter et al., 1950).

viii. The brain, eyes, heart, liver, kidneys and pancreas from all rats were examined for gross pathological findings.

b) Comparative evaluation of anticancer activity against Dalton’s Ascitic Lymphoma in Swiss albino mice (Christina et al., 2004)

i. Acute toxicity studies

ii. Body weight

iii. Percentage increase in life span


v. Evaluation of haematological parameters like RBC, WBC, Hb, platelets and packed cell volume.

vi. The effect of serum enzyme and lipid profile like total cholesterol, TG, AST, ALT, ALP.

vii. The thigh region and liver from all the rats were examined for gross pathological findings.

c) Comparative evaluation of invitro anthelmintic activity

The evaluation was performed on adult Indian earth worm Pheritima posthuma (Ajaiyeoba et al., 2001).
Fig. 1 *Aerva lanata* Linn Juss

Fig. 2 Aerial parts of *Aerva lanata* Linn Juss
References


