1.1 Nature as source of drug compounds

Man has used Nature for his benefits and to cure him from the various day to
day ailments since time immemorial. The medicines prepared from various sources
include aromatics, oils, ointments from plants, milk, cereals, stems of herbs and
metallic ores. Man has suffered a lot right from his emergence on this planet due to
various forms of diseases. Mother Nature had provided for man’s well being by
placing the cures for diseases in close proximity to their causes. The prehistoric man
first turned to nature in search of remedies and nature did not disappoint him. Man
hunted animals, fished, gathered with fruits and leaves, and grubbed up the edible
roots of wild plants. He may or may not have reached instinctly in his rejection of
poisonous plants. He must have experimented with and come to know the many plants
within the limit of his nomadic wanderings. Most of the plants were innocuous and
bland: some nourished him; a handful was particularly pleasant to taste and some
equally unpleasant. In a lengthy process of trial and error, by which early man in
different communities slowly built up a corpus of knowledge about plants. By trial
and error, he discovered that some could relieve pain, some proved fatal, and a few
had a strange unearthly effect on his mind and body. Thus, the relationship between
man and plants has been very intimate throughout the development of civilization.
From the very ancient time, Ayurvedic medicine was in practice in India. According to ancient saint in India, “Ayurveda is the truth of life”. After a careful and in-depth study of all the living and non-living things, scientists believe that the Creator of the Universe is the Omnipotent God. The great sages who had the foresight to see the past, present and future have confirmed that the generation of this world is God. When this visible world was not existent; the seed of the creation was laid in the Hiray Grabh. God decided to create the world to enable the people to balance their karmas and Due to their skills and interest in the healing qualities of plants, the drug-hunters gained an honoured place in the society as medicine men. The earliest medicine men became associated with the whole structure of religious belief in a community. Many were priests who acted as instruments of the gods, receiving their powers of healing from them. Like the use of Rauwolfia serpentina in Ayurvedic system to cure blood pressure, the awareness of the scientific community towards the untapped resources in the world of traditional medicines gave the required impetus (The Europress Millenium Encyclopedia, 2000).

Despite the rise of combinatorial chemistry as an integral part of lead discovery process, the natural products still play a major role as starting material for drug discovery (http://en.wikipedia.org/wiki/Natural_product_drug_discovery#cite_note-1#cite_note-1). David Newman and Gordon Cragg have made a remarkable contribution to the evaluation of the significance of natural products in drug discovery via their analysis of the sources of approved drugs. The latest update of the report was published 2007 (http://en.wikipedia.org/wiki/Natural_product_drug_discovery#cite_note-
covering years 1981-2006. According to their report, of the 974 small molecules, 63% were natural derived or nature-inspired (semisynthetic derivatives of natural products, compounds synthesised by use of natural product pharmacophore or compounds otherwise designed to mimic the natural ligand/substrate of the target). For certain therapy areas, such as antimicrobials, anticancer, antihypertensive and anti-inflammatory drugs, the numbers were even higher, approximately 75% of all approved small molecule new chemical entities were derived from nature. Natural products have been especially successful as lead structures for antibacterial therapies (http://en.wikipedia.org/wiki/Natural_product_drug_discovery#cite_note-1#cite_note-2). A potential explanation beyond the success of natural products as drugs is the classification of natural compounds as so-called privileged structures. This is because chemical agents produced by living organisms (particularly the secondary metabolites) have evolved over millennia under the evolutionary pressure, and are therefore more likely to have a specific biological activity than “randomly” assembled, man-made synthetic chemicals. Despite the enormous potential, only a minor fraction of globe’s living species has ever been tested for any bioactivity. For instance, approximately only 10% of all existing plant species has been assayed, and in the case of microbes the value is even lower (http://en.wikipedia.org/wiki/Natural_product_drug_discovery#cite_note-1#cite_note-3).

In the recent past, there has been a global trend towards revival of interest in the medicinal plants. It is because, the herbal medicines are believed to be comparatively safer than that most of the modern drugs. Moreover, they are economical and environmentally better suited for local conditions. It was only in the beginning of the twentieth century that there was a sudden surge of interest in the use
of the ancient remedies to cure diseases which are thought to be incurable (http://www.newcrops.uq.edu.au/listing/species_pages_B/Basella_alba.htm)

A modern drug hunter in search of new remedies from old sources – folk medicines – can lead to an effective drug. One of the most successful examples is the discovery of reserpine, one of the first tranquilizers, which had long been used by folk practitioners in India from Snake-root (Rauwolfia serpentina) to treat insomnia and insanity. It was reported in Siam (now Thailand), elderly natives got a new lease on life by eating the root of the Kwao vine, a jungle creeper of the bean family. Chemical studies showed that the root contained a strong estrogen – a substance akin to certain female hormones – which, in case of elderly women at least, could indeed be expected to have some rejuvenating effect. Some of the important drugs which are obtained from plant sources are emetine (antiamoebic) from Ipeca cuanha, morphine (analgesic) from Papaver somniferum, quinine (anti malarial) from cinchona, vinblastine and vincristine (anti tumour, anti leukemia) from Catharanthus (Vinca species), artemisinin (most promising anti malarial) from Artemisia annua, camphothecin (a potent anti tumour drug) from Campotheca acuminata, taxol (drug against breast cancer) from Taxus brevifolia, hypericin (anti viral agent) from Hypericum perforatum, gossipol (male contraceptive) from Gossypium species, yuchchukene (anti fertility agent) from Murraya paniculata, forskolin (a novel hypotensive and anti spasmodic drug) from Coleus forskoli; and so on.

Many medicinal plants are well known in India from the time immemorial. In India, the sacred Vedas dating back between 3500 B.C. and 800 B.C. give many references of medicinal plants. One of the remotest works in traditional herbal medicine is “Vrikshayurveda”, compiled by Par Sara even before the beginning of Christian era, formed the basis of medical studies in ancient India. The Rig Veda
dating between 3500 B.C. and 1800 B.C., seems to be the earliest record available on medicinal plants and here, healing properties of some herbs are mentioned in the form of sonnets, which were often recited in religious rituals. More detailed accounts are in “Atharvaveda” whose compilation occurred sometimes around 800 B.C. Later came the “Ayurveda”, the practice of which was recorded in Sanskrit by legendary figures of Indian Medicine – Charaka, Sushruta, Nagarjuna, Atreya, etc. Ayurveda was mostly dealing with human philosophy of health including utilization of medicinal plants for restoring normal physical fitness. The further advancement of this process was materialization of “Sushruta Samhita” and “Charak Samhita” (appeared between 400 A.D. to 500 A.D.) which incorporates comprehensive chapters on the therapeutic use of various plant species. Charak Samhita mentions – “The goat-herds, cowherds, shepherds, and the tribals are acquainted with identification of medicinal herbs.” Sushruta Samhita recalls – “Know the men, cowherds, hermits, huntsmen, forest dwellers who cull the fruits and roots of forests; know them they have the knowledge of medicinal herbs.” Thus, both Charak and Sushruta recognized the importance of the laymen and primitive tribal people in the discovery of the medicinal plants. Another notable book was written by Nagarjuna, which was extension of Sushruta’s work. After the Vedas, there is no concrete information on the development of this science in India for about 1000 years.

In India, even the legendary Purans – Brahma Puran and Vayu Puran of the pre-vedic periods mentions about medicinal plants, of which “Sanjiwana” (now identified as Selaginella broyopteris) was called a resurrection plant used to restore life after death.
1.2 Natural Products in Pharmaceuticals

In a study of the pharmaceuticals on the market from 1981-2002, only 43% of the drugs were purely synthetic, while the remaining 57% were derived from a natural source (Figure 1.1). The data shown in Figure 1.1 categorizes natural sources in the following way: biological – a peptide or protein isolated from an organism or cell line; natural product; natural product derivative – derived from a natural product usually with some semi-synthetic modifications; synthetic drug; synthetic drug with a natural product pharmacophore; vaccine (Newman et al., 2003).

![Figure 1.1 Pharmaceuticals containing natural products (1981-2002); (taken from ref. Newman et al., 2003).](image)

The ancient Ayurvedic medical system was basically dependent upon the plants. In those early days, the Ayurvedic practitioner used to prepare medicinal preparation from various plants in the forest. But it was not available in the readily edible form and was time taking and lengthy procedure. Then came the allopathic medicine which was also based on various plants extracts (medicines like digitalis and reserpine) only difference from the Ayurvedic medicines being that the medicinal
preparations were in a readily edible (capsules or tablets form) or parenterally admininisterable form. Some of the excellent drugs like morphine, digitoxin, quinine, thebaine etc are contribution of plant kingdom.

1.3 Plant-derived bioactive material

The vast majority of traditionally used crude drugs have been plant-derived extracts. This has resulted in an inherited pool of information of the healing potential of plant species, thus making them important source of starting material for drug discovery. A different set of metabolites is usually produced in the different anatomical parts of the plant (e.g. root, leaves and flower), and botanical knowledge is crucial also for the correct taxonomical determination of the identified bioactive plants.

In a developing country like India, the utilization of natural products and their improved sustainability is a distinct advantage over the developed countries. It is because natural products would remain very important for affordable health care as our national imperative in view of the implementation of the Dunkel Draft (the GATT agreement and the WTO) and patent protection (Stegemann, 2000). Thus, we have to look at our own sources in search of remedies, and the best option available to us is to explore the potential in medicinal plants.

The introduction of chromatographic, analytical, and spectroscopic methods in the twentieth century provide extremely powerful tools to isolate plant compounds (Digitoxin, Sterols, Morphine, etc.) and to determine which compounds in a plant have particular action. These compounds were then synthesized in laboratories to produce what we now regard as orthodox medicines which have better efficacy over traditional (Ayurvedic, Homocopathic, etc.) system of treating diseases which also uses various plant extracts (Marston, 2007)
However, few reports on the isolation and characterization of compounds from the seed of the plant, *Basella rubra* Linn. have been published. Keeping these in mind, the present work reports the most subtle and challenging problems of isolation and characterization of active compounds from the seeds of medicinally important plant *Basella rubra* Linn. and *Basella alba*. 