INTRODUCTION

Health is defined as 'a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity' (as per the World Health Organization). A person who enjoys all the three conditions is a healthy person. The factors such as heredity, diet, exercise, environment and society etc. are the important determinants of health. Physical health indicates perfect functioning of the body. Biologically, physical health indicates optimum functioning of every cell of every organ in perfect harmony with rest of the organs of the body. Mental health is related to active responsiveness to different stimuli with sense. It is a state of balance between the individual and the surrounding world, a state of harmony between oneself and others, a coexistence between the realities of the self and that of other people and of the environment. Social health refers to harmony and integration within the individual, between each individual and other members of society, and between the individuals and world in which they live.

A disease is any change from the state of health. It is a condition of the body in which, some part of the body or organ of the body has its function disrupted or deranged. It is also referred to as homeostatic imbalance. This can occur due to malnutrition, hypo, and hyperfunction of the endocrine glands, degeneration of certain organs, development of tumors, congenital abnormalities and the infection. The infection is the invasion of pathogenic microbes followed by their multiplication and toxin formation, leading to the
disease in the body. The pathogenic organisms can be viruses, bacteria, protozoa, fungi worms etc. (Dandiya, et. al., 1999)

The subject of 'Drugs' is as old as disease. Illness has been man’s heritage from the beginning of his existence, and the search for remedies to combat it is perhaps equally old. The world’s oldest known therapeutic writings come from India and China. The earliest Indian records are Vedas. There are medical descriptions in Rigveda (3000 B.C.). It was Charaka a renowned ancient Indian physician and later Sushruta and Vagbhata described various medicinal preparations and included in ‘Ayurveda’, the science of life. Initially, these consisted of non poisonous herbal drugs and minerals. Charaka described about 241 vegetable drugs and classified them according to their effects into 50 groups. (Satoskar, et. al., 2001)

The great herbal or Chinese Material Medica ‘Pan Tsao’ was probably written in 2735 B.C. and contained many plants, metallic preparations and a few animal products including toad’s eyelids, elephant’s and tiger’s bones, horns etc. The earliest sources of western medicines come from Egypt and the two kingdoms of Assyria and Babylonia. The ‘Papyri’ was the first written account of medical experiences from Egypt. The papyrus was prepared in 1500 B.C. and mentions about 700 herbal remedies including opium. A Babylonian clay tablet discovered in 700 B.C. mentions about 300 drugs. Modern medicine is considered to date from Hippocrates, a Greek physician (450 B.C.), who for the first time introduced the concept of disease as a pathogenic process and
tried to organise the science of medicine on the basis of observation, analysis and deduction. Hippocratic practice did not include extensive use of drugs, probably because he did not believe in the shotgun or magical remedies, but instead recommended judicious use of simple and efficacious drugs.

Paracelsus (1493-1541) said that the 'purpose of chemistry is not to make gold but to cure diseases' (Gandhi, et. al., 1999). This can be considered as one of the major turning points in the history of drugs. Till the beginning of the 19th century, the treatment of diseases included such obnoxious remedies as flesh, excreta and blood of various animals along with a few metal and plant preparations. James Gregory (1753-1821) was responsible for popularizing heroic symptomatic treatment consisting of bloodletting, large doses of emetics and drastic purgatives. Such treatment without any rational basis was called *Allopathy* (meaning the other suffering), a term which is still wrongly applied to denote the system of modern scientific medicine, as opposed to *Homeopathy* (meaning similar suffering).

Crude drugs are naturally obtained from the plants, animals and mineral sources. These are not only used for the treatment of various diseases but also in cosmetics, textile and food industries. During the first half of the nineteenth century Apothecaries stocked the crude drugs for the preparation of herbal tea mixtures, all kinds of tinctures, extracts and juices which in turn were employed in preparing medicinal drops, syrups, infusions, ointments and liniments. The second half of the nineteenth century brought with it a number
of important discoveries in the newly developing fields of chemistry and witnessed the rapid progress of this science (Vinod, 2002). Medicinal plants became one of its major objects of interest and in time, phytochemists succeeded in isolating the pure active constituents which replaced the crude drugs. With the development of semisynthetic and synthetic medicines, they became predominant.

In eighteenth century, the importance of medicinal plants was ignored and thought that man-made synthetic drugs can replace them, which in today's scenario no longer tenable. The medicinal plants, which were rapidly falling into disuse a century ago, are regaining their rightful place in medicine. Researchers are exploiting not only the classical plants but also related species all over the world that may contain similar types of constituents.

Francois Magendie (1783-1855) and Claude Bernard (1813-1878) were the pioneers in the introduction of experimental procedures in animals. Various animal experiments have been designed to study the effects of drugs on living organisms, isolated tissues and dispersed cells. These give an insight into where and how a drug acts. The emphasis on critical scientific inquiry has enabled modern scientific medicine to incorporate useful remedies from other, older disciplines including Ayurveda. For the rational treatment of diseases, knowledge of the mode of action of a drug, of its effects on various body systems and of the probable adverse effects is important.
At the end of eighteenth century and the beginning of nineteenth century, methods became available for the isolation of active constituents from the crude drugs. The simultaneous developments in chemistry made it possible to isolate and synthesise chemically pure compounds that would have biological activities. In 1806 Sertumer isolated the first pure active principle morphine from *Papaver somniferum*. The others to follow are emetine from *Cephalis ipecacuanha*, quinine from *Cinchona africanaum*, strychnine from seeds of *Strychnos nux-vomica* and cocaine from *Erythroxylon coca*, taxol from *Taxus brevifolia* etc.

Last 50 years have seen a phenomenal growth in biochemistry, enzymology and molecular biology. These developments have not only charged the face of biomedical research, integrated pharmacology and clinical pharmacology with medicine but have made the discovery of drugs more rational and complex,

Many Indian researchers like Chopra (1954), Kirthikar and Basu (1975), Yoganarasimhan (1996) have done laborious and commendable work in compiling details of Indian medicinal plants. But only for a few plant species detailed chemical analysis and screening the therapeutic efficacy of the plant constituents was worked out. Many medicinal plants occurring in India have yet to be subjected for rigorous chemical, pharmacological and clinical investigations. The investigations of this kind on the evaluation of chemical constituents of medicinal plants will play a significant role in the establishment
of many pharmaceutical industries which are important for stabilizing and enhancing the economy of developing country like India.

In recent years, there has been an awakening all over the world regarding the use of herbal medicament in place of synthetic drugs and antibiotics. There has been a consistent growth in demand for many of these plant based drugs from diverse species. In the development of modern drugs, plants stand in a prime position. Because, they are the complex chemical storehouses which contain many undiscovered biodynamic compounds with unrealized potential for the use in modern medicine.

The tribal and traditional medicines might be considered as solid amalgamation of ancestral knowledge and acquired practical experiences. Even after getting independence, most of the villagers residing in the vicinity of forests still depend upon the herbal medicines for their relief. The acceptability of these drugs is quite high and cheaper when compared to allopathic system of medicines. Further, the natives often observed the positive effect of these drugs. But, mere statements and observations do not satisfy the scientific mind. It has to be evaluated from what source the medicines originated? And what is the active principle present in that plant? Which act upon the disease/symptoms? The way in which they act and the manner in which important organs of the body are affected, has to be proved through clinical experimental evidences.
The present study was aimed to evaluate the hepatoprotective activity effect of some indigenous medicinal plants of Karnataka. Two indigenous trees *Diospyros cordifolia* (Ebenaceae) and *Pterocarpus marsupium* (Papilionaceae) which are being used by the traditional practitioners of Malnad region to cure hepatitis, were selected for pharmacological evaluation. The ethnomedical survey on these plants also enlightened us that the stem bark of these species is also used for wound healing, analgesic, anticonvulsant and CNS depressant activities. So investigation was also conducted to evaluate the wound healing, analgesic, anticonvulsant and CNS depressant activities of these plants in addition to hepatoprotective activity.

*Diospyros cordifolia* Roxb.

*Diospyros cordifolia* Roxb. is a deciduous tree, belonging to the family “Ebenaceae”, and popularly known as Indian ebony and the vernacular name is Balagani (Kannada) (Fig. 1a, b). In Karnataka State, it is sparsely distributed in Nagarahole National Park, Biligiri Rangan Hills, Kollur Reserve Forests and Bhadra Wild Life Sanctuary (Raghavendra Rao, *et al.*, 1981; Keshavamurthy, *et al.*, 1990; Ramaswamy, *et al.*, 2001). The earlier plant explorist Sir Hooker, J. D. (1872-1897) considered this species as the tribe of *Diospyros montana*. Later, Sir Gamble, J. S. (1915-1936) and his successors upgraded this plant as a separate species *Diospyros cordifolia* Roxb. The plant grows upto 10-15 m. Leaves oblong, obtuse at apex, rounded at base. Dicous male flowers 3 in cymes, female flowers usually solitary, calyx- hairy, lobes deeply divided in

Flower-Fruit: March-April.

Specimen referred –FDD., KUSF-801. (Manjunatha, et. al., 2004)

**Medicinal importance:** The plant is of great medicinal importance and used for liver disorders whooping cough, leprosy, skin eruptions, dysentery, eye infections, abdominal pains, wounds, ulcers, gonorrhea, fever, as emetic and anthelmintic (Nadakarni, 1954; Chopra, 1956). The alcoholic extract of the plant possesses anti-inflammatory, antipyretic, analgesic activity (Kohli et al., 1972) CNS depressant, spasmylytic, produces bradycardia and hypotension (Singh et. al., 1971). The aqueous extract of the stem bark is traditionally used by the tribal people 'Soligas' of Biligiri Rangana Hill range to cure critical jaundiced condition (Krishna, 1996).

**Pterocarpus marsupium** Roxb.

*Pterocarpus marsupium* Roxb. belongs to the family Papilionaceae. It is a deciduous tree (Fig. 1c, d) commonly distributed in the forest of the Western Ghats of India (Gamble, 1928; Saldanha, 1984). It is commonly called as Red Kino tree (English). The vernacular name of this species is Asanahm bijakah (Sanskrit), and Honne Mara (Kannada). Leaves impairipinnate, leaf rachis to 10 cm long, alternate/sub-opposite, leaflets 5-7, elliptic-ovate, to 9 x 6 cm, coriaceous. Inflorescence panicle, terminal, 12-15 cm long, flowers, 1.5 cm long, calyx dark brown and papilionaceous, corolla yellow. Stamens monadelphous. Fruit is a pod, 4cm across, convexly curved.
Figure 1

1 a. A tree of *Diospyros cordifolia* Roxb. growing in Thavareghatta village, Karnataka.

1 b. A close view of the stem bark of *Diospyros cordifolia*.

1 c. A tree of *Pterocarpus marsupium* Roxb. growing in Joldhal forest area of Bhadra Wild Life Sanctuary.

1 d. A close view of the stem bark of *Pterocarpus marsupium*.
Flower - Fruit: January-July.

Specimen referred -FDD-147. (Manjunatha, et. al., 2004)

**Medicinal importance:** The gum obtained from the stem is used as astringent, in diarrhea and for toothache and the leaves are useful in external applications in boils, sores and skin diseases (Chopra, et. al., 1956). The flowers are used in fever, and the gum is locally applied in leucorrhoea and passive haemorrhage (Pullaiah, 1999). The plant is also known for its antihyperglycemic (Manikam, et. al., 1997) and antihyperlipidemic activities (Jahromi, et. al., 1993). The ethnic groups residing in the vicinity of the Joldhal forest ranges of Davanagere District, Karnataka, are using the stem bark of this species in treating wounds, fever, stomachache, diabetes and jaundice (Manjunatha, et. al., 2004).

The therapeutic effect of the various extracts of the stem bark of *Diospyros cordifolia* and *Pterocarpus marsupium* have not been clinically evaluated for hepatoprotective, wound healing, analgesic, anti-convulsant and CNS depressant activities so far. Further, no constituents have been isolated from the stem bark of *Diospyros cordifolia*. Therefore, in view of the high medicinal value of these plants and lack of reports on clinical evaluation, the present investigation has been undertaken.

**The main objectives of the present investigation are as follows:**

1) To conduct preliminary phytochemical examination of the different solvent extractions of the stem bark of *D. cordifolia* and *P. marsupium*.
2) To isolate and characterize the chemical constituents present in the stem bark of *D. cordifolia*.

3) To evaluate the hepatoprotective effect of the crude extracts of *D. cordifolia* & *P. marsupium* and the constituents isolated from petroleum ether and carbon tetrachloride extracts of *D. cordifolia* against toxic hepatitis.

4) To screen the wound healing efficacy of the crude extracts of *D. cordifolia* & *P. marsupium* and the isolated constituents by using different wound models.

5) To study the analgesic activity of the crude extracts of *D. cordifolia* & *P. marsupium* and the isolated constituents by using different experimental models.

6) To evaluate the anti-convulsant activity of the crude extracts and the isolated constituents against maximal electroshock and strychnine induced convulsions in albino rats.

7) To study the sedative effect of the extracts and the isolated constituents on spontaneous motor activity and pentobarbitone sleeping time in mice.

8) To study the histopathological profile of the liver and granulation tissues before and after the administration of the drugs under investigation.