1. INTRODUCTION:

Traditions are dynamic entities of unchanging knowledge. Traditional medicine is in an evolutionary process as communities and individuals continue to discover new techniques that can transform practices (Patwardhan et al., 2004). Since ancient times, natural products notably those from plant origin, have consistently been an important source of therapeutic agents. According to a WHO (2002) estimate, about 80% of the world population relies on traditional systems of medicines for primary health care, where plants form the dominant component over other natural resources; specifically developing countries like India (70%), Uganda (60%), Tanzania (60%), and Ethiopia (90%) extensively use traditional and alternative medicines for health care. Plants and plant-based products are an integrated part of most of the traditional and alternative systems of medicines world-wide. In developed countries like Belgium (31%), USA (42%), Australia (48%), France (49%), Canada (70%), a significant percentage of the population has used traditional and alternative remedies at least once for health care. Renewed interest of developing as well as developed countries in the natural resources with the perspectives of safety, efficacy and quality will help not only to preserve this traditional heritage but also to rationalize the use of natural products in the health care.

The current accepted modern medicine has gradually been developed over the years by scientific and observational efforts of scientists. However, the basis of its development remains rooted in traditional medicine and therapies. The future of natural products drug discovery will be more holistic, personalized and involve wise use of ancient and modern therapeutic skills in a complementary manner so that maximum benefits can be accrued to the patients and the community. Traditional medicine has some strength that western medicine is lacking, particularly in the holistic view of the patient's situation (Wexler-Morrison, 1988).

The increased interest in drugs of plant origin is due to several reasons, namely, conventional medicine can be inefficient in effects, abusive and/or incorrect use of synthetic drugs results in side effects and other problems,
further a large percentage of the world’s population does not have access to conventional pharmacological treatment. According to some estimation, around 35,000–70,000 plant species are being used worldwide in health care systems. India has about 45,000 plant species; medicinal properties have been assigned to several thousands. About 2000 are found in the literature; indigenous systems commonly employ about 500–700 species.

A considerable amount of research on pharmacognosy, chemistry, pharmacology and clinical therapeutics have been carried out on Ayurvedic medicinal plants (Dahanukar et al., 2000; Patwardhan et al., 2004). Many rasayana drugs form an integral group which has been reported to possess strong antioxidant (Rege et al., 1999), adaptogenic (Brahma and Debnath, 2003) and hepatoprotective activity (Govindarajan et al., 2005). Numerous drugs have entered the international pharmacopoeia through ethnobotany and traditional medicine and various molecules like rauwolfia alkaloids, piperidines, phyllanthins and psoralens have come out of ayurvedic experiential base (Patwardhan, 2000). There are many similarities in traditional systems of medicine as well as ethno medicines being connected to each other as ‘great traditions and little traditions’. Indian healthcare consists of medical pluralism and Ayurveda still remains dominant compared to modern medicine, particularly for treatment of a variety of chronic disease conditions (Wexler-Morrison, 1988).

There is growing evidence to show that medicinal plants contain synergistic and/or side effects neutralizing combinations. The plants in their crude form show interesting combination of activities and there is a huge potential of medicinal plants not only as a source of new drugs but also their use in the form of botanicals both in developing countries and in industrialized world (Anwarul and Atta-ur-Rahman, 2005).

Herbal drug development includes various steps, starting from correct identification, pharmacognostic and chemical quality standardization, safety and preclinical pharmacology, clinical pharmacology and randomized, controlled clinical trials (Jain, 1994).
Addressing standardization is vital and needs broader consideration. The concept of active markers in the process of standardization needs a flexible approach in favour of the complex nature of this material. The basis of traditional medicine is in its use for a number of years and therefore its clinical existence comes as a presumption. However, for bringing more objectivity and also to confirm traditional claims, systematic clinical trials are necessary. In ayurvedic medicine research, clinical experiences, observations or available data becomes a starting point. In conventional drug research, it comes at the end. Thus, the drug discovery based on ayurveda follows a 'reverse pharmacology' path. Traditional knowledge-driven drug development can follow a reverse pharmacology path and reduce time and cost of development (Vaidya et al., 2001). Therefore many plant species mentioned in the ancient texts of Ayurveda and other Indian systems of medicines should be explored with the modern scientific approaches for better leads in the health care. A majority of the present day diseases are reported to be due to the shift in the balance of the pro-oxidant and the antioxidant homeostatic phenomenon in the body. Pro-oxidant conditions dominate either due to the increased generation of the free radicals caused by excessive oxidative stress of the present day life, or due to the poor scavenging/quenching in the body caused by depletion of the dietary antioxidants (Dringen, 2000; Schulz et al., 2000). Over about 100 disorders have been reported as reactive oxygen species mediated. Some specific examples of ROS mediated diseases include Alzheimer's disease, Parkinson's disease, atherosclerosis, cancer, and ischemic reperfusion injury in different tissues including heart, liver, brain, kidney and gastrointestinal tract (Govindarajan et al., 2005). The physical factors, like restraint stress, electromagnetic field exposure, (Bonhomme et al., 1998; Flipo et al., 1998; Bagchi et al., 1999), environmental factors, like ozone, carbon monoxide, nitrogen dioxide, sulphur, lead, asbestos (Campbell and Hilsenroth, 1976; Menzel, 1979; Sevanian et al., 1979) and chemicals factors like alcohol, CCl₄, DDT, pyrogallol, alloxan (Norman et al., 1992; Sakurai, 1994; Koner et al., 1998; Ereal et al., 2000) are known to produce oxidative damage.
Oxidative stress is one of the major causes of liver disease. In all types of liver damage there is consistent evidence of enhanced production of free radicals and/or significant decrease of antioxidant defense. As a consequence, a large number of studies have focused on the pathogenic significance of oxidative and nitrosative stress in liver injury as well as on therapeutic intervention with antioxidant and metabolic scavengers (Jones and Czaja, 1998).

Beyond the treatment of chronic disorders, everyday care of the health is a cornerstone for the total body health. For example, Liver is the most important organ of metabolism and unfortunately, it is extremely difficult to detect early warning symptoms specific to liver metabolic imbalances. About 20,000 deaths occur every year due to liver diseases (Surendra et al., 2002).

Liver disorders are mainly caused by toxic chemicals, excess consumption of alcohol, infections and autoimmune disorders. Although viruses are the main cause of liver diseases, excessive drug therapy, environmental pollution and alcoholic intoxication are not uncommon (Hikino and Kiso, 1988). Most of the hepatotoxic chemical damages the liver cells mainly by inducing lipid peroxidation and other oxidative damages in the liver (Recknagel and Glende, 1977). Enhanced lipid peroxidation produced during the liver microsomal metabolism of ethanol may result in hepatitis and cirrhosis (Smuckler, 1975).

In spite of the tremendous advances being made in allopathic medicine, no effective hepatoprotective medicine is available. The available therapeutic agents bring about only symptomatic relief without any influence on the curative process, thus, causing the risk of relapses and danger of untoward effects. Modern drugs have very little to offer for alleviation of hepatic ailments whereas most important representatives of phytoconstituents used for liver diseases, include drugs like silymarin, catechin, glycyrrhizin and schizandrin (Hikino and Kiso, 1984). The development of hepatoprotective drugs is a major thrust area in the field of natural product research. The incredible complexity of liver chemistry and its fundamental
role in human physiology is so daunting to researchers that gives a thought that simple plant remedies might have something to offer is astonishing and incredible (Agarwal and Singh, 1999; Shelukar and Dakshinkar, 2000).

Botanical medicines have been used traditionally by herbalists and indigenous healers worldwide for the prevention and treatment of liver disease. There are numerous plants and polyherbal formulations claimed to have hepatoprotective activities. Nearly 150 phytoconstituents from 101 plants have been claimed to possess hepatoprotective activity (Handa et al., 1986; Sharma et al., 1991; Doreswamy and Sharma, 1995). Clinical research has confirmed the efficacy of plants in the treatment of liver disease, while basic scientific research has uncovered the mechanisms by which some plants provide their therapeutic effects. The effectiveness of treatments such as interferon, colchicine, penicillamine, and corticosteroids are inconsistent at best, and the incidence of side effects profound. There is a great need of effective therapeutic agents with a low incidence of side effects. Several botanical medicines potentially constitute such a group but only a handful has been fairly well researched. Liver protective herbal drugs contain a variety of chemical constituents like Phenols, coumarins, lignans, essential oil, monoterpenes, carotinoids, flavonoids, organic acids, lipids, alkaloids and xanthines. Maximum numbers of these drugs possess flavonoids, lignans and volatile oils as the active constituents (Surendra et al., 2002).

_Gmelina arborea_ Roxb, Family: Verbenaceae is an important medicinal plant, which is naturally distributed in the moist deciduous forests of South East Asia. Almost all parts of this tree are used in folk medicine for treating various stomach disorders, fevers and skin problem. In Ayurveda it has been observed that Gamhar fruit is acrid, sour, bitter, cooling, diuretic tonic, aphrodisiac, alternative astringent to the bowels, promote growth of hairs, useful in ‘vata’, thirst, anaemia, leprosy, ulcers and vaginal discharge (Sharma et al., 2001). The root is described as bitter, tonic, stomachic, laxative, and useful in fever, indigestion and anasarca. Roots of _Gmelina_ are used in many well-known Ayurvedic preparations like Dashmula and...
Chyawanprasha. It is an ingredient of the major five roots (*Brihadpanchmoola*) and is therefore much used in a variety of diseases (Tewari, 1995). The plant extracts are reported to exhibit anti-inflammatory and wound healing properties (Shirwaikar et al., 2003) and are also known to inhibit platelet aggregation (Faiza and Darakhshanda, 1998). Chemical constituents of *Gmelina* include lignans (Anjaneyulu et al., 1977), flavonoids (Nair and Subramanian, 1975), iridoid and phenylpropanoid glycosides (Hosny and Rossaza, 1998) and an isoxazole alkaloid (Barik et al., 1992). Since ancient times Dashmoola in form of *arisha* or *asava*, has proved to be a powerful restorative in Ayurvedic therapy. It has been established as a tonic for the treatment of diminished appetite, and energy and in general debility, flatulence, and in nervous and cardiovascular disorders. Roots of this plant were explored for anti malarial and cardiovascular activity but to our knowledge no reports are available till date regarding hepatoprotective and antioxidant activity of this plant. Looking to the multiple uses of *Gmelina arborea* in traditional system of medicine and lacking in the field of pharmacological activities reported for roots, this project was taken up to check and validate the hepatoprotective and antioxidant potentials of the plant and to explore possible mode of action and constituents partly or wholly responsible for the same.