Chapter 1

Introduction
1.0 INTRODUCTION

India has an ancient heritage of traditional medicine. Materia medica of India provides lot of information on the folklore practices and traditional aspects of therapeutically important natural products. Indian traditional medicine is based on various systems including Ayurveda, Siddha, and Unani. Scientific investigations into the ancient claims of these traditional systems have earlier led to the identification of novel bioavailability enhancers such as piperine (Patel and Modi, 1994; Majeed et. al., 1999) and cow urine distillate (Khanuja, et. al., 2002). Shilajit is also one such panacea of oriental medicine which has been used since ages as a rejuvenator and adaptogen. It has been said that there is hardly any curable disease which cannot be controlled or cured with the aid of shilajit. Although this is a tall order, scientific studies over the last 20-25 years have shown that it is indeed a panacea of traditional medicine, effective in a number of ailments.

Shilajit is a naturally occurring organic exudate from steep rocks of different formations found in the Himalayan regions ranging from Arunachal Pradesh in the East to Jammu and Kashmir in the West. It has traditionally been used in indigenous systems of medicine for treating various ailments, for improving virility and as a rejuvenator.

Shilajit has been reported to contain a number of components including resins, fatty acids, sterols, triterpenes, aromatic carboxylic acids, 3,4-benzocoumarins and \( \alpha \)-aminoacids (Ghosal et al., 1976). The biological effects of shilajit have been ascribed to two distinct classes of compounds (Ghosal et al., 1989):

(i) The low molecular weight bioactive organic compounds such as oxygenated dibenzo-\( \alpha \)-pyrones, and

(ii) The medium molecular weight fulvic acids and humic acids.

While the benzopyrones act as the active principles, fulvic and humic acids act as carrier molecules for in-vivo transportation of these bioactive substances. The
chemical structures of these two acids suggest that these have structures exhibiting a hydrophilic exterior and a hydrophobic interior similar to the cavity in β-cyclodextrins. The interior of this complex is thus capable of forming inclusion complexes with non-polar solutes and drug molecules with low bioavailability. These drug molecules can be entrapped in the hydrophobic interior so as to increase their solubility and dissolution rate, thereby enhancing their bioavailability.

Such entrapment is also capable of enhancing the stability of the drug molecules. In fact, it has been reported that the bioactive principles of shilajit owe their stability in the natural habitat due to their entrapment in the voids (micropores) of the fulvic acids of shilajit humus (Ghosal et al., 1991). The antioxidant and rejuvenating properties of shilajit could also be due to the trapping of free radicals and toxins from the body by fulvic and humic acids.

It was thought worthwhile to explore and evaluate the drug complexing, dissolution and solubility enhancing and surface active properties of fulvic and humic acids extracted from shilajit and also see if such an association/interaction between the drug and fulvic and humic acids can lead to an increase in the drug bioavailability and a better pharmacodynamic profile.

There are a number of drugs in the allopathic system of medicine which have problems of low aqueous solubility and/or low intestinal permeability which often limits their bioavailability. The Biopharmaceutical Classification System (BCS) has provided a scientific basis for classifying drugs into four classes based on their solubility and intestinal permeability as high permeability/high solubility (class I), high permeability/low solubility (class II), low permeability/high solubility (class III) and low permeability/low solubility (class IV) (Amidon et al., 1995; Blume and Schug, 1999). Drugs belonging to the Classes II, III and IV usually present a significant challenge to the pharmaceutical industry to formulate them into highly bioavailable and therapeutically useful compositions. Although a number of approaches have been used in the past to overcome the problems of low solubility and/or low permeability, the use of these approaches have often been limited by
several practical factors such as toxicity, irritancy, non-selectivity, poor drug stability, excessive size due to the need for large amount of excipients in relation to the dose, technical manufacturing problems and the high cost of goods. Thus, there exist a definite need for identifying newer and novel approaches to overcome the problems of solubility and permeability of problematic drug candidates so as to augment their bioavailability.

The use of fulvic acids and humic acids extracted from shilajit as complexing agents for such problematic drugs can be a potential approach for increasing the bioavailability of such drugs. Although some preliminary research in this area has shown that fulvic acids indeed act as carrier molecules for such drugs, more work is required before the full potential of this novel carrier can be exploited.