Chapter 2

Research Envisaged
Background of the research

A bioavailability enhancer in any pharmaceutical composition designated for rapid release and absorption of drugs into a bloodstream and increasing its availability at the site of action. Historically a group of spices that has been documented very frequently as essential part of about 70% of Ayurvedic prescriptions is *Trikatu*. Based on clues from Ayurvedic literature, an approach of increasing the bioavailability of drugs including poorly bioavailable drugs had been conceptualized at RRL Jammu. *Trikatu* comprises of three acrids viz. long pepper, black pepper and dry ginger in equal proportions (Majeed et al., 1998; Johri and Zutshi, 1992). A single major alkaloidal constituent from peppers (piperine) was found to be responsible for bioavailability enhancing effect. Influence of piperine was extensively studied on anti-TB drugs. It was determined that in combination with piperine the dose of rifampicin can be reduced by about 50% while retaining the therapeutic efficacy of this anti-TB drug at par with the standard dose (Zutshi, et al., 1985). Several studies have reported enhancement of blood levels of drugs like vasicine, sparteine (Atal et al., 1981), phenytoin, sulphadiazine (Bano et al., 1987), propranolol, theophylline (Bano et al., 1991), pefloxacin (Dama et al., 2008) and oxytetracycline (Singh et al., 2005) when coadministered with *Trikatu* or its ingredient. Based on these findings several other reputed plants were evaluated for bioavailability/bioefficacy enhancing activity. Polar and non-polar extracts of parts of a few plants viz., *Zingiber officinale* and *Carum carvi* increased significantly (25-300%), the bioavailability of a number of classes of drugs, for example, antibiotics, antifungals, anti-virals, anticancer, cardiovascular, CNS, anti-inflammatory/anti-arthritic, anti-TB/antileprosy, anti-histaminic, corticosteroids, immunospressants. Such extracts either in presence or absence of piperine have been found to be highly selective in their bioavailability/bioefficacy enhancing action (Qazi et al., 2009).

Research envisaged

The present research work is directed to identification and characterization of active fractions from the plant, which includes their isolation, purification and characterization, which enhance bioavailability of drugs. It also relates to the chemical characterization of the active extracts.
Selection of plants
A background for the selection of various plants or plant products was gained from the review of literature. Based on the information reported in the literature following plants have been selected:

(a) *Camellia sinensis* (L.) Kuntze leaves
(b) *Nigella sativa* Linn. seeds
(c) *Piper longum* Linn. fruits

Their extracts, fractions and isolated compounds were evaluated for increasing the bioavailability of a model drug Amoxicillin (BCS Class III) and characterized chemically using chromatographic and spectroscopic techniques.

Aim
The present research has been designed to provide bioavailability enhancers and their characterization. Extracts/fractions of selected plants that increase transport of therapeutically important drugs (BCS Class III) across the biological membranes are aimed in the current project.

Objectives
To achieve above stated aim following objectives have been designed:

1. Study the effect of concomitantly infused selected plant extracts on the permeability profile of model drug through everted rat sac model.
2. Characterization of the effective plant extracts using chromatographic and spectroscopic methods- CC, GC-MS, MS, NMR, FTIR.
3. *In-vivo* evaluation of the bioavailability enhancing effect of most effective extract on a model drug using UPLC-MS/MS for estimation of drug in plasma.

Plan of work

1. Acquisition and authentication of plant materials.
2. Preparation of plant extracts.
4. Isolation of compounds using column chromatography.
5. Characterization of compounds using MS, NMR, FTIR.
6. Characterization of fatty acid composition of hexane extract using GC-MS.
7. *In-vivo* evaluation of bioenhancing effect of most effective extracts.
References


