3.0 RESEARCH ENVISAGED

The majority of pharmaceutical compounds are poorly water soluble and new bioactive compounds that result from high-throughput screening programs tend to exhibit low solubility in water. Such compounds may exhibit insufficient dissolution throughout the gastrointestinal tract and therefore fail to achieve superior systemic exposure after oral administration. Today, failing bioavailability is one of the main reasons for abandoning innovative oral drug candidates. Circumventing low solubility and unfavorable dissolution equilibrium kinetics are the key issues in the development of an appropriate formulation.

Gliclazide, a second-generation hypoglycemic sulfonylurea and a drug of choice in the treatment of Type 2 diabetes mellitus shows irregular bioavailability due to low aqueous solubility and decreased dissolution rate. Domperidone is an antiemetic and prokinetic with an excellent safety profile but exhibit poor bioavailability. The poor aqueous solubility may be one possible reason for its low bioavailability.

Enhancement of oral bioavailability of gliclazide and domperidone like drugs remains a daunting task. Solid dispersion is one of the many techniques available to enhance drug dissolution and bioavailability of poorly water-soluble drugs. Further, such formulations can be dispensed in the form of fast dissolving tablets which disintegrate and/or dissolve rapidly in saliva; thus may help in improving the bioavailability of such drugs.

Solid dispersion has been used successfully earlier too to increase the solubility of poorly water soluble drugs like prednisone, rofecoxib and diclofenac and the mouth dissolving tablets of classes like neuroleptics, cardiovascular drugs, analgesics and antihistamines have provided an opportunity for a line extension in the market place.

The present project was designed to overcome the solubility problems associated with gliclazide and domperidone. Solid dispersion based solubility enhancement technique employed in the present study was expected to improve the solubility and bioavailability of these drugs.

The development of such dosage form may help in creating new opportunities in academics and industry. The enhanced solubility shall not only improve bioavailability but may also result in reduction of dose and side effects. Moreover, the method(s) employed, seem process friendly which is important criterion for manufacture of dosage forms at large scale.
3.1 PLAN OF WORK

The work was carried out on following lines:

1. Exhaustive literature survey
2. Procurement of Drug(s) and chemicals
3. Preformulation profiling
   - Identification of drug
   - Physicochemical characterization
   - Analytical methodologies
   - Compatibility studies
4. Development of solid dispersion
   - Preparation of solid dispersion using various polymers
   - Characterization of solid dispersion
     - Solubility
     - Powder characteristics by FTIR, DSC & XRD
     - In vitro dissolution studies
5. Development of fast dissolving tablets
   - Preparation of tablet by direct compression methods
   - Characterization of tablet for
     - Hardness
     - Friability
     - Disintegration
     - Dissolution profile
     - Stability studies
6. Compilation /publication and Submission