2.1 RESEARCH WORK: OBJECTIVE

A significant number of active pharmaceutical ingredients (API) being discovered display desirable therapeutic properties, but have undesirable physico-chemical properties (e.g. low solubility) making formulation into an effective drug product challenging. The Biopharmaceutical Classification System (BCS) class II API, which have been reported to account for as many as 40% of new chemical entities, present particular challenges in creating successful drug products. For example, BCS class II compounds do not readily dissolve in the biological media of the digestive tract and thus exhibit poor or variable bioavailability. Consequently, the major obstacle in formulating these compounds into successful commercialized products is the difficulty in enhancing the dissolution rate. Some APIs exhibits polymorphism. The commonly used needle shaped crystals APIs shows poor flowability, compaction behavior and sticking to the punches due to its high cohesivity and adhesivity during compression. A number of strategies and processes have been reported to facilitate the dissolution of these poorly water-soluble drugs.

API are handled and processed predominately as solids and the characterization of the physical structure of particles is today an integrated part of the formulation of solid preparations. The structure of particles can be characterized on different scales, such as the nano-scale. The functional properties of particles will be controlled by their structure and the critical structural property depends on the intended function. Although progress has been made regarding the problem of how to engineer solids in terms of their physical structure, knowledge on how to change the physical structure of a particle in a controlled way and how the structure relates to the intended function is still unsatisfactory.

The engineering of particles with customized properties optimized for dosage form manufacture and advanced drug delivery systems has long been a goal of the pharmaceutical industry. Particles can be designed through modification in the size, morphology, and packing arrangement of the solids. The most common approach in achieving this is through crystallization. The industrial relevance of improved knowledge in this area is obvious, i.e. new knowledge will provide the formulation scientist with a formulation tools that enable the scientist to identify, analyze and control critical properties of particles for their function.

Objective of present research work-

- Development of a unique method for preparation of engineered drug particles alone/or in combination with and without additives by using spherical crystallization technique.
- Evaluation and characterization of the processed drugs as compare to the plain unprocessed drugs to assess the potential benefit of the particle engineering technology like practical yield, surface topography, fourier transformed infrared spectroscopy (FTIR), differential scanning calorimetry (DSC), X-ray powder diffractometry (XRPD), determination of surface area, solubility determination, dissolution studies, flowability and compressibility determination.
- Formulation and development of advanced oral drug delivery system by using developed particle engineered drugs.
- In-vivo animal study to demonstrate the efficiency of developed particle engineered drugs in combination over plain unprocessed drugs.
2.2 PLAN OF WORK

**Literature Survey**
The literature survey will include, referencing of books, official Pharmacopoeias, National and international research papers regarding the particle engineering technologies, its application in advanced oral drug delivery system.

**Selection & Procurements of drug candidate, excipients and chemicals**
(API: Atorvastatin calcium, Fenofibrate & Ezetimibe)

**Characterization of bulk API**
Fourier transformed infrared spectroscopy (FTIR), differential scanning calorimetry (DSC), X-ray powder diffractometry (XRPD), surface topography, determination of surface area, solubility determination, dissolution studies, flowability and compressibility determination.

**Design and development of technology for particle engineering of API**
Spherical crystallization of API with additives

**Characterization of processed particle engineered API**
Practical yield, surface topography, fourier transformed infrared spectroscopy (FTIR), differential scanning calorimetry (DSC), X-ray powder diffractometry (XRPD), determination of surface area, solubility determination, dissolution studies, flowability and compressibility determination.

**Formulation and development of advanced drug delivery system**
Oral drug delivery systems like Orally disintegrating tablets, Gastroretentive Tablets, Rapid release tablets.

**Analytical method development and validation**
Dissolution method development and validation, Assay method development and validation

**In-Vivo animal study**
Institutional Animal Ethics Committee (IAEC) permission, bio-analytical method development, in-vivo animal study evaluation and statistical analysis

**Thesis writing**
Compilation of data
Conclusion of research work
Writing the thesis and submission