Before you start some work, always ask yourself three questions - Why am I doing it, what the results might be and Will I be successful. Only when you think deeply and find satisfactory answers to these questions, go ahead.

- Chanakya

Chapter 2

Aim of present Work
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It has been estimated that about 35-40 percent of all new chemical entities (NCE) entering drug development programs possess insufficient aqueous solubility. Some of the BCS class-II drugs have poor bioavailability because they have poor water solubility and poor dissolution. Poorly water-soluble drugs have become a challenge to the formulation scientist to formulate it as a solid dosage form. Solid dispersion and Complexation are the most common strategies to increase the solubility as well as dissolution.

The objective of the present work is to develop and characterize solid oral combination dosage form of Atorvastatin calcium (AT) (10.28mg equivalent to Atorvastatin 10mg), Fenofibrate (FE) (160mg) and Ezetimibe (EZ) (10mg) for better therapeutic strategy and patient compliance.

The specific research aim of the work is:

- Development and validation of analytical method for Simultaneous determination of AT, FE and EZ using HPLC with PDA detector.
- Preformulation study of AT, FE and EZ.
- Drug excipient compatibility study of all three APIs.
- Impurity profiling of API used.
- Development of biorelevant dissolution medium for combination product.
- Saturation solubility study of APIs.
- Solubility enhancement of APIs by complexation method and characterization of final product.
- Solubility enhancement of APIs by solid dispersion method and characterization of final product.
- Application of QBD approach for optimization in solubility enhancement techniques.
- Mathematical treatment to dissolution data obtained.
- Solid state stability study of final combination of AT, FE and EZ, with enhanced solubility.
- Development of combination tablet dosage form and comparative in vitro characterization with market product available.
- In vivo study of optimized formulation in animal model and determination of pharmacokinetic parameters.
- Establishment of IVIVC.
- Development of formulation and evaluation of reduced dosage form

Hypothesis

Most of the drugs are poorly water soluble. Solid dispersion and inclusion complex are the methods to enhance the solubility of drug and therefore their bioavailability is increased by these methods. Today, fixed dose combination of drugs is prescribed by the doctors for patient compliance. These methods are used to enhance the solubility of single drug and not used for combination of drug. An attempt was made to formulate and evaluate the combination of drug complex and compare with individual drug complex.