2. STATEMENT OF PURPOSE.

2.1 Need of the study.

Quality of any Active Pharmaceutical Ingredient (API) or drug product for patient compliance is directly depending on stability of drug. Instability could lead to chemical degradation and loss of drug potency and the possible formation of new chemical species with potential toxic side effects. The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of physical, chemical and environmental factors such as temperature, humidity and light. Therefore, stability studies provide data to justify and establish the storage condition, shelf-life, retest date for drug substance and drug product.

To aid in the prediction of drug stability, Stress testing or forced degradation and accelerated degradation is performed to elucidate potential degradation products, determine their safety, and develop analytical procedures to quantitate these new chemical species. These forced degradation studies may be predictive of the degradation pathways and intrinsic stability and validate the stability indicating power of the analytical procedure of the drug. The nature of the stress testing will depend on the individual drug substance and the type of drug product involved. In fact, information learned from studying the kinetics of degradation may be used to extrapolate rates of degradation which might apply during normal storage conditions this could be utilized to predict long-term stability under these normal storage conditions.

Moreover, the different excipients of a formulation may interact during exposure to high temperatures or high humidity, reducing the in vitro dissolution, an important quality attribute of a solid oral dosage form. Dissolution Stability is a term that refers to the retention of the dissolution characteristics of a solid oral dosage form, from the time of manufacture to its expiration date. Dissolution stability is considered a critical parameter not only from the standpoint of quality control, but also for the impact on
the bioavailability of the product, because significant changes of the in vitro release profile during storage may affect its bioavailability.

The research attempts are required to evaluate and compare the influence of accelerated-aging conditions on the drug content and in vitro dissolution stability during different duration of storage. Aging conditions could affect the dissolution stability of these formulations in a different manner, playing an important role in drug bioavailability and interchangeability of the products during the shelf life.

2.2 Scope of the study.

The ICH drug stability test guideline Q1A (R2) focus on development of stability-indicating assay methods (SIAMs) for analysis of drugs is increasing in regulatory viewpoint which can confine impact on product’s marketing approaches. The developed SIAMs can identify the changes over time in the physical and chemical properties of the API and formulation, so that the components of analyte, degradation impurities and other components of analyte can be precisely estimated without interference. This will be used for setting purity specifications and for defining the drug which is to be utilized in pre-clinical animal and later human studies.

2.3 Objective of Work.

- The present research work focuses on the development of novel stability-indicating analytical methods using High performance liquid chromatography (HPLC) and High performance thin layer chromatography (HPTLC) for various combined drug products (gemifloxacin mesylate-ambroxol hydrochloride, lamivudine-abacavir sulphate, tenofovir disoproxil fumarate disoproxil fumarate- lamivudine, and cefixime trihydrate-moxifloxacin hydrochloride).

- The objective of the work also includes validation of the developed analytical methods as per ICH requirements to demonstrate the suitability of developed methods to assess the stability of drug products.
Further HPLC method is applied to study the effect of accelerated aging conditions such as thermal degradation, photo-degradation, and also the effect of dissolution rate and release profiles on stability.

2.4 Scheme of work.

Part I.
1. Selection of drugs for project work.
2. Extensive literature survey.
3. Drug profile.
4. Procurement of drugs and drug product.
5. Identification and characterization of drugs.

Part II.
1. Stability-Indicating HPLC method development and validation for analysis of gemifloxacin mesylate and ambroxol hydrochloride from bulk and its combined tablet dosage form.
2. Dissolution stability for significant changes in *in-vitro* release profile of gemifloxacin mesylate and ambroxol hydrochloride from its combined tablet dosage form.
3. Stability-Indicating HPTLC method development and validation for analysis of gemifloxacin mesylate and ambroxol hydrochloride from bulk and its combined tablet dosage form.

Part III.
1. Stability-Indicating HPLC method development and validation for analysis of lamivudine and abacavir sulphate from bulk and its combined tablet dosage form.
2. Dissolution stability for significant changes in *in-vitro* release profile of lamivudine and abacavir sulphate from its combined tablet dosage form.
3. Stability-Indicating HPTLC method development and validation for analysis of lamivudine and abacavir from bulk and its combined tablet dosage form.

**Part IV.**
1. Stability-Indicating HPLC method development and validation for analysis of lamivudine and tenofovir disoproxil fumarate from bulk and its combined tablet dosage form.
2. Dissolution stability for significant changes in *in-vitro* release profile of lamivudine and tenofovir disoproxil fumarate from its combined tablet dosage form.
3. Stability-Indicating HPTLC method development and validation for analysis of lamivudine and tenofovir disoproxil fumarate from bulk and its combined tablet dosage form.

**Part V.**
1. Stability-Indicating HPLC method development and validation for analysis of moxifloxacin hydrochloride and cefixime trihydrate from bulk and its combined tablet dosage form.
2. Dissolution stability for significant changes in *in-vitro* release profile of moxifloxacin hydrochloride and cefixime trihydrate from its combined tablet dosage form.
3. Stability-Indicating HPTLC method development and validation for analysis of moxifloxacin hydrochloride and cefixime trihydrate from bulk and its combined tablet dosage form.

**Part VI.**
1. Collection and interpretation of data.
2. Results and discussion.
3. Thesis writing and submission.