CHAPTER – III

PLAN OF WORK

3.1 Rational of The Study

The drugs are available in in the market majorly in two forms namely Solids or Liquids. The solid dosage forms include Beads, Capsules, Pellets, Spherules, Tablets, etc. The solid dosage forms are popular because they require less storage and transportation space and are cost-effective. They are also more stable than liquid dosage forms.[1]

They are often coated for various reasons, including masking of unwanted sensory properties, protecting against environmental factors and bodily fluids, increasing mechanical strength, improving appearance, enhancing flow, and achieving customized drug release.[2]

The coating agents are usually dissolved or dispersed in a suitable solvent and then sprayed over a substrate. The mixture is dried until a smooth layer is formed. Fluidized bed coaters are generally used for particulate systems, while perforated pan coaters are used for single-unit systems. Solid dosage forms are currently coated using either aqueous or non-aqueous coatings. An aqueous coating can achieve a smooth and lustrous surface. However, the aqueous coating may cause hydrolysis of some drugs and increase microbial burden, leading to decreased drug stability. Aqueous coating also requires more time for drying and consumes more energy.[3,4]

For non-aqueous coating of dosage forms using organic solvents, there are concerns about environmental pollution, solvent recycling costs, and operator safety issues. Organic solvents are expensive. In 1970, the U.S. Environmental Protection Agency (EPA) enforced the Clean Air Act to reduce atmospheric solvent emissions.[5] In 1976, the Occupational Safety and Health Administration (OSHA) restricted the use of organic solvents to prevent exposure of industrial workers.[6,7]

In order to avoid the issues that come with using solvents, an alternative technique called Hot Melt Coating (HMC) was attempted. HMC is a solvent-free method where the molten material is poured or sprayed onto the surface of the substrate. The Beads, Capsules, Microcapsules, Minitablets, Pellets, and Tablets can be coated using the Pan Coating or Fluidized Bed Coating methods. Generally, natural waxes are used as materials for the HMC technique, as they are more cost-effective compared to the polymers used in solvent-based coating. Waxes offer great flexibility in terms of

solubility and safety. The literature survey shows that HMC has a wide range of applications in Drug Delivery Systems.[8]

PART A: TENOFOVIR DISPROXIL FUMARATE

Tenofovir is an acyclic phosphonate nucleotide analog and the base form of the prodrug Tenofovir Disoproxil Fumarate (TDF). It is used in combination with other Antiretroviral drugs for treating adult patients infected with Human Immunodeficiency Virus (HIV) and Hepatitis. The recommended dosage regimen for TDF is once daily due to its long biological half-life. The bitter taste of TDF reduces patient compliance among all age groups including pediatric and adult patients.[9, 10]

The objective of the present investigation was to assess the taste-masking ability of the hot melt coating technique using Tenofovir Disoproxil Fumarate (TDF) as a model drug.

PART B: SITAGLIPTIN PHOSPHATE MONOHYDRATE

Sitagliptin is a novel antidiabetic agent used to treat type 2 diabetes. It works by inhibiting Dipeptidyl Peptidase-4 (DPP-4), which leads to increased levels of Glucagon-like Peptide-1 (GLP-1) and Glucose-dependent Insulinotropic Polypeptide (GIP).[11-14]

It is a white or off-white crystalline hygroscopic solid with a specific odor.[12,14] The formation of hydrates is crucial in the pharmaceutical industry due to the prevalence of water vapor, as hydrates tend to be more stable.[15] Consequently, the presence of solvates and hydrates significantly impacts the physicochemical properties of the crystals.[16]

Sitagliptin Phosphate Monohydrate (SPM) is commonly used in the pharmaceutical industry. However, little is known about other crystalline forms, such as the anhydrous and base form. This includes the effect of the dehydration process and the production of the base form on the physical and chemical stability of this pharmaceutical hydrate.[15,16]

It is primarily absorbed through the intestine with 89% oral bioavailability. It has a plasma half-life of 11-12 hours and 38% protein binding after oral administration.[17-19] The peak plasma concentration is achieved within 2 hours. Sitagliptin Phosphate is

rapidly absorbed from the gastrointestinal tract. It is administered in doses of 25mg, 50mg, or 100mg once a day, as it is extensively excreted through urine.[16]

Based on the literature review, Sitagliptin is sensitive to water and moisture. It is usually advised to store it in a cool, dry place, away from moisture and light, to maintain its potency and stability. Exposure to water or high humidity can lead to degradation of the drug, which may impact its effectiveness and shelf life. Therefore, some specific storage conditions are recommended for Sitagliptin:

1. Store in a tightly closed container, protected from moisture.
2. Store at room temperature (20°C - 25°C or 68°F - 77°F).
3. Keep away from light and moisture.
4. Do not store in a humid environment.

It is important to note that Sitagliptin is a hygroscopic drug, meaning it tends to absorb moisture from the air. Therefore, it is important to handle the drug carefully and store it in a way that minimizes exposure to moisture. It is important to follow proper handling and storage procedures to maintain the drug's potency and stability. This may include using a desiccant or other moisture-control measures to maintain a dry environment.[20,21]

Numerous solutions have been reported to enhance the stability of drugs in dosage forms like Coating, Microencapsulation, Complexation, etc. The aqueous and solvent-based coatings have multiple demerits and therefore an attempt has been made to improve the stability of Sitagliptin using Hot Melt Coating (HMC). HMC is an easy, economical, flexible, and rapid method to achieve the objective.

3.2 Plan of The Research Work

Part A:

1. Literature Survey
2. Selection of Hot Melt Coating (HMC) agents
3. Analysis of Drug properties
4. Design of Experiments
    a. Preparation of Hot Melt Coated Tenofovir Disoproxil Fumarate (TDF) Pellets and suitability of use of simple equipment such as coating pan.
    b. Preparation of Tablets using Hot Melt Coated TDF Pellets

5. In-vitro Dissolution Study
6. Evaluation of Taste masking using in-vitro method and taste panel method
7. Stability Studies

Part B:

1. Literature survey
2. Selection of Hot Melt Coating (HMC) agents
3. Analysis of Drug properties
4. Design of Experiments (Compression and Coating)
5. Evaluation of Core and Hot Melt Coated Tablets
6. In-vitro Dissolution- testing of Hot Melt Coated Tablets.
7. Comparison with marketed formulation
8. Stability Studies