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REVIEW ON FORMULATION AND EVALUATION OF MOUTH DISSOLVING TABLET AZELNIDIPINE BY USING SOLVENT EVAPORATION

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ABSTRACT

The aim of this study was to develop a month dissolving tablets(MDT) by solid dispersion using hydrophilic substances to enhance its dissolution (%) and oral bioavailability in rats. MDT-SD formulations were prepared with various co-polymers using a solvent evaporation method. The physical properties of MDT-SD formulations were confirmed using field emission scanning electron microscopy (FE-SEM), differential scanning calorimetry (DSC), powder X-ray diffraction (PXRD), and attenuated total reflectance Fourier transform infrared (ATR-FT-IR) spectroscopy. The toxicity and oral bioavailability of MDT-SD formulations were evaluated. Formulations were evaluated for Weight variation, hardness, and thickness, friability, wetting time uniformity of dispersion, drug content, disintegration time and in vitro dissolution studies. The drug content of all the formulations was within the acceptable limits of the United States Pharmacopoeia XXVII. Optimized formulation showed good release profile with maximum drug being released at all-time intervals.

KEYWORDS: Mouth Dissolving tablets, Solvent evaporation, solubility, polymer.

INTRODUCTION

A major interest in oral administration is that more and more new drug candidates were reported to have low solubility and poor absorption following an oral dose. Among them, approximately 75 % new compounds belong to the biopharmaceutics classification system (BCS) class and IV drugs. In order to improve the oral bioavailability of poorly water-soluble drugs, many researchers have developed methods to improve the solubility and dissolution of drugs. In particular, poorly water-soluble drugs comprise 40% of the top 200 oral drugs in the US and Europe.For such poor soluble drug candidates, especially most of the BCS class IV drug.

The improvement of the inherent solubility (low water solubility) of drugs is a challenge during the development of drug formulation strategies. Several systems have been used to increase the solubility of drugs, such as solid dispersion, complexation, Nano crystal, self micro (nano) emulsification drug delivery systems, emulsion and co-crystal.Among them, the solid dispersion (SD) system has been widely used to enhance the solubility and dissolution (%) of poorly water-soluble drug in pharmaceutical fields. Several process involves in solid dispersion steam such as melting ,super critical , solvent evaporation, anti solvent process and freeze drying.Many decades formulation of obtain new drug formulation having a High solubility and dissolution.

Mouth Dissolving Tablet

Recently pharmaceutical preparations used for elderly patients have been investigated to improve the treatment compliances and quality of life of patients. Recent advances in Novel Drug Delivery System (NDDS) aims to enhance safety and efficacy of drug molecule by formulating a convenient dosage form for administration and to achieve better patient compliance. One such approach is "Mouth Dissolving Tablet". The concept of Mouth Dissolving Drug Delivery System emerged from the desire to provide patient with conventional mean of taking their medication. Difficulty in swallowing (Dysphasia) is a common problem of all age groups, especially elderly and pediatrics, because of physiological changes associated with these groups of patients.

Other categories that experience problems using conventional oral dosage forms includes are the mentally ill, unco-operative and nauseated patients, those with conditions of motion sickness, sudden episodes of allergic attack or coughing. Some times it may be difficult to swallow conventional products due to unavailability of water. These problems led to the development of novel type of solid oral dosage form called "Mouth Dissolving Tablets". This tablet disintegrates instantaneously when placed on tongue, releasing the drug that dissolves or disperses in the saliva. The dispersible tablets allows dissolution or dispersion in water prior to administration but the Mouth

Dissolving Tablet instead of dissolving or disintegrating in water is expected to dissolve or disintegrate in oral cavity without drinking water. The disintegrated mass then slides down smoothly along the esophagus along with saliva. The growing importance of mouth dissolving tablet was underlined recently when European Pharmacopoeia adopted the term "Or dispersible Tablet" as a tablet that to be placed in the mouth where it disperses rapidly before swallowing.

The main criteria for mouth disintegrating (dissolving) tablet is to disintegrate or dissolve rapidly in oral cavity with saliva in 15 to 60 seconds, without need of water and should have pleasant mouth feel. Mouth dissolving tablets are also known as fast dissolving tablet, melt in mouth tablet, rapiment, porous tablet, orodispersible tablet, Rapidly Disintegrating tablet, or mouth disintegrating tablet.

Benefits of Mouth Dissolved Tablets

1. Administered without water, anywhere, any time.
2. Suitability for geriatric and pediatric patients, who experience difficulties in swallowing and for the other groups that may experience problems using conventional oral dosage form, due to being mentally ill, the developmentally disable and the patients who are un-cooperative, or are on reduced liquid intake plans or are nauseated.
3. Beneficial in cases such as motion sickness, suede episodes of allergic attack or coughing, where an ultra rapid onset of action required.
4. An increased bioavailability, particularly in cases of insoluble and hydrophobic drugs, due to rapid disintegration and dissolution of these tablets.
5. Stability for longer duration of time, since the drug remains in solid dosage form till it is consumed. So, it combines advantage of solid dosage form in terms of stability and liquid dosage form in terms of bioavailability.

Limitations of Mouth Dissolve Tablets

The tablets usually have insufficient mechanical strength. Hence, careful handling is required. The tablets may leave unpleasant taste and/or grittiness in mouth if not formulated properly.

Fundamentals of Mouth Dissolving Tablets.

For rapid dissolution or disintegration of dosage form, water must rapidly penetrate into the tablet matrix to cause quick disintegration and instantaneous dissolution of the tablet. Several techniques are used to achieve these fundamentals, to formulate mouth-dissolving tablet. Some of the techniques are described below.

MATERIAL AND METHODS

Techniques for preparing mouth dissolving tablets

- Freeze Drying
- Moulding
- Sublimation
- Direct Compression
- Spray Drying

Patented technology,

- Zydis Technology
- Durasolve technology
- Orasolve technology
- Flash dose technology
- Wow tab technology
- Flash tab technology

Preformulation study

The objective of pre formulation studies are to develop a portfolio of information about the drug substance, so that this information useful to develoformulation.

Organoleptic Characteristics, Solubility, Bulk Density, Tapped Density, % Compressibility, Identification of drug Sample, Drug Excipients Compatibility Study.

Carr's Index [Compressibility Index] And Hausner's Ratio- Carr's index and Hausner's ratio measure the propensity of powder to be compressed and the flow ability of powder. Carr's index and Hausner's ratio can be calculated from the bulk and tapped density.

Carr's index = (Tapped density - Bulk density / Tapped density) X 100

Hausner's ratio = Tapped density / Bulk density

Preparation of solid dispersion

1.Solvent evaporation method

By taking 10 mg drug, polymer and excipients were weighed in the ratio of 1:1, 1:3 and 1:5 and triturated in a mortar pestle for 5 minutes and dissolved in 50 ml of methanol with constant stirring. The solvent was evaporated at 45ºC and dried in a desicator for 12 hrs and passed through sieve No. 60.

2. Preparation of Physical mixtures

Weighing drug , polymer and excipients in the ratio of 1:1, 1:3 and 1:5 and triturated in amortar and pestle for 15 minutes and kept in a dessicator for further use.

3. Solubility study of various type of solid dispersion

The solubility studies were performed by taking 10 mg drug equivalent of solid dispersion from the each batch (SD-A, SD-B and SD-C) were dissolved in water and PBS (pH6.8) and kept in mechanical shaker for 30 min at 30ºc. Sample was taken after 30 min from each volumetric flask and was analyzed spectrophotometerically at 259 nm.

The solubility studies were performed by taking 10 mg drug equivalent of physical mixture from the each batches (PM-A, PM-B and PM-C) and dissolved in water and PBS (pH6.8) kept in mechanical shaker for 30 min at 30ºC. Samples were taken after 30 min from each volumetric flask and absorbance were measured by UV visible spectrophotometer.

Evaluation of Mouth Dissolving Tablets
The Formulated mouth dissolving tablet were evaluated for different parameters like General characteristic, uniformity of weight, hardness, wetting time, Uniformity of dispersion, Disintegration test, Drug release study.

General characteristic
General appearance of tablet, its visual identity size, shape, color of the tablet was evaluated.

Uniformity of Weight
20 tablets of each batch were collected randomly during compression and weight of individual tablets was carried out.

Hardness or Friability
For each formulation the hardness and friability of 6 tablets wear determined using Monsanto hardness tester and the Roche Friabilator.

Content of Active Ingredients
The amount of active ingredient was determined by the method described in the drug content. By crushing the 10 tablets and taking powder equivalent to 8 mg drug. Then this powder dissolved in 100ml 0.1N HCl appropriate dilution of the resulting solution was prepared and absorbances of the resulting solution were taken UV Spectrophotometrically. % drug content has been calculated.

Wetting time
Five circular tissue papers of 10 cm diameter are placed in a Petri dish with a 10 cm diameter. Ten millimeters of water-containing methyl red, a water-soluble dye, is added to Petri dish. A tablet is carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet is noted as a wetting time 10.

Disintegration test
Apparatus for Disintegration of Tablets and Capsules according to Indian pharmacopoeia 1996 used for the determination of disintegration test for dispersible tablets. The beakers containing the 900ml distilled water at 25 ±1˚C and operate the apparatus for three min. and remove the assembly from the liquid. The tablets pass the test if all of them have disintegrated. Dispersible tablets should disintegrate within 3 minutes when examined by the disintegration test according to Indian Pharmacopoeia 1996.

Uniformity of Dispersion
This test is applicable only to Dispersible Tablets. Place 2 tablets in 100 ml of water and stirgently until completely dispersed. A smooth dispersion is obtained which passes through a sieve screen with a nominal mesh aperture of 710 µm (sieve number 22).

Drug release study in simulated salivary fluid pH 6.8 & 0.1 N HCl
The drug release method for mouth dissolving tablets is comparable to the approach to the approach taken for conventional tablets, and is practically identical. The release study carried out in USP Type 2 dissolution apparatus containing 900ml 6.8 pH phosphate buffer and 0.1 N Hcl at 50 rpm and 37oC temperature. The drug release sample 5ml withdrawal by suitable time interval and fresh dissolution medium were added in the each withdrawal. Then appropriate dilution of the samples has been prepared and absorbances of the resulting solution were taken spectrophotometrically.

Stability study
Stability study was conducted by storing the tablets at 40±2º/75±5% Relative humidity for three months. The content, hardness, weight variation and release behavior from dissolving tablets were tested after three month (ICH guidelines).

CONCLUSION
The Present study was undertaken with an aim to formulate and evaluate mouth-dissolving tablets of Azelnidipine by using solvent evaporation method with the addition of super disintegrating agents. Solubility enhancement of Azelnidipine was performed by Solvent evaporation method with the use of polymer. The Azelnidipine Polymer ratio 1:4 was optimized for the solubility enhancement. Soliod dispersion's evaluated for the in-vitro release and found to be 100% release within 20 min in both media SGF without enzymes and pH 6.8 phosphate buffer.

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