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FORMULATION AND EVALUATION OF MOUTH DISSOLVING TABLETS OF CARVEDILOL

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ABSTRACT

The aim of the present research work was to enhance the solubility of Carvedilol by solid dispersion method and to formulate a mouth dissolving tablet. Drugs are more frequently taken by oral administration. The solubility of Carvedilol enhanced with different ratios of PVP by the solvent evaporation method .In-vitro release profile of solid dispersion obtained in SGF without enzymes and Ph 6.8 phosphate buffer indicate that 100% drug release found within 20 min. These solid dispersion were directly compressed into tablets using Crospovidone, sodium starch glycol ate, croscarmellose sodium and polyacrylic potassium in different concentrations as a super disintegrants. The prepared tablets containing the solid dispersion of Carvedilol having sufficient strength of 2.5-4 kg/cm2. The disintegrated in the oral cavity with in 21 sec. contain Crospovidone (5%) as super disintegrant.

KEYWORDS: Carvedilol, PVP, Super Disintegrants, Mouth Dissolving Tablet.

INTRODUCTION

An ideal dosage regimen in the drug therapy of any disease is the one, which immediately attains the desire therapeutics concentration of drug in plasma (or at the site of action) and maintains it constant for the entire duration of treatment. Drugs are more frequently taken by oral administration. It is considered most natural, uncomplicated, convenient, safe means of administering drugs, greater flexibility in dosage form design, ease of production and low cost.

Tablets: Tablets may be defined as solid pharmaceutical dosage forms containing medicament with or without suitable excipients and prepared either by compression or molding.

Tablet Manufacturing Methods: Tablets are manufactured by wet granulation, Dry granulation or direct compression method.

1. Wet Granulation: Wet granulation is the process in which a liquid is added to a powder in a vessel equipped with any type of agitation that will produce agglomeration or granules. These granules after drying are compressed to form tablets.

2. Dry Granulation: In this technique, there is no use of liquids. The process involves the formation of Slugs. Then the slugs are screened or milled to produce granules. The granules formed are then compressed to form tablets.

3. Direct Compression: The term direct compression is used to define the process by which tablets are compressed directly from powder blends of active ingredient and suitable excipients, which will flow uniformly in the die cavity and forms a firm compact.

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. Sometimes 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, raiment, porous tablet, or dispersible tablet, Rapidly Disintegrating tablet, or mouth disintegrating tablet.

Benefits of Mouth Dissolve 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 An increased bioavailability, particularly in cases of insoluble and hydrophobic drugs, due to rapid disintegration and dissolution of these tablets.
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 Tablet: 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

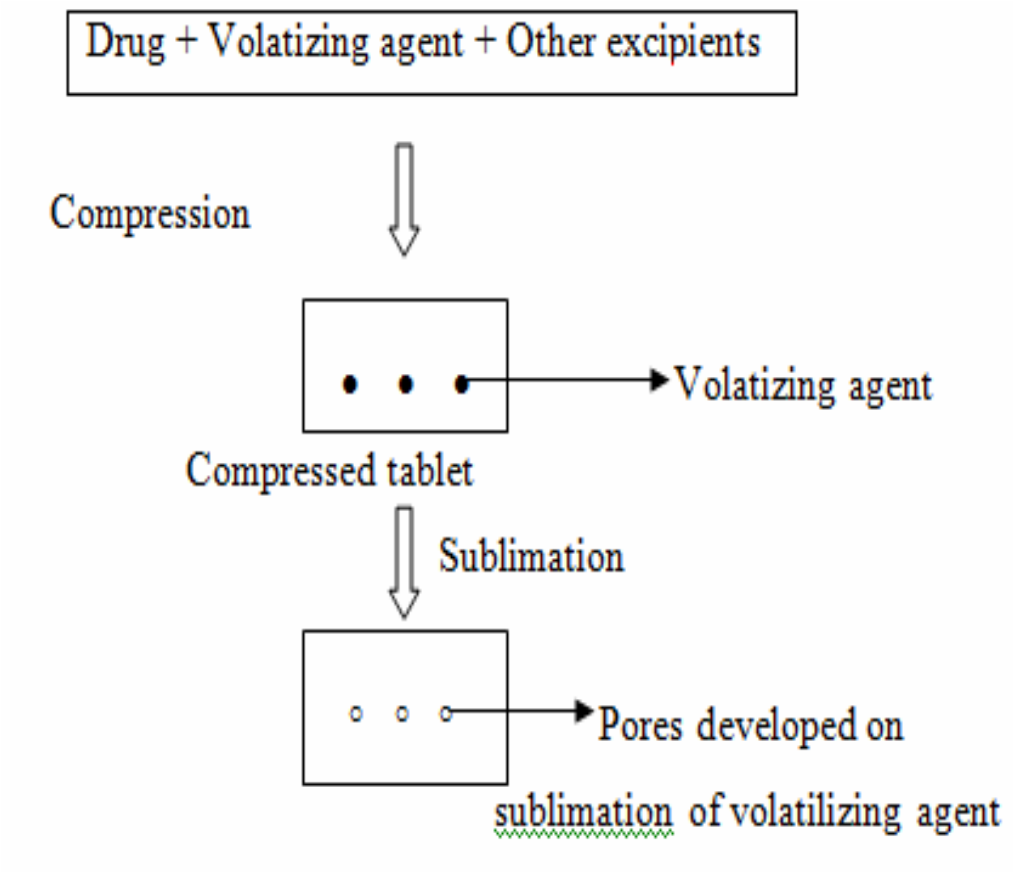
fundamentals, to formulate mouth-dissolving tablet. Some of the techniques are described below.

MATERIAL AND METHODS

Techniques for Preparing Mouth Dissolving Tablets: Freeze Drying, Moulding, Sublimation, Spray Drying, Direct compression

Patented Technologies: ZydisTechnology, DurasolveTechnology, Orasolve Technology, Flash Dose Technology, Wow Tab Technology, Flash Tab Technology.

Steps involved in sublimation



Material used: Carvedilol were purchased in Matrix Laboratories Limited, Poly vinyl pyrolidone (PVP), Mannitol, Microcrystalline Cellulose (MCC), Crospovidone were purchased in FMC Biopolymer, Croscarmellose Sodium, Sodium Starch Glycollate, Polacrilin Potassium were purchased in DMV International, Talc, Aerosil, Magnesium Stearate, Mint Powder Flavor, Poloxamer-188, Poloxamer-407, Polyethylene Glycol-6000 were purchased in Vasudha Chemicals, Gelucire 44/14, Potassium di- hydrogan O phosphate,

Sodium hydroxide, Sodium Chloride, Hydrochloric acid, Methanol, Di-Chloro Methane were purchased in Merck chemicals pvt.ltd.

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 Develop formulation. 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

Drug Excipients Compatibility Study Protocol for Drug-Excipients Compatibility

1. Drug: Excipients Ratio-API alone, API: Diluents and Binder (Solubility enhancer):- 1:10, API: Lubricant and others:-1:1, API: Super disintegrant:-1:5
2. Pack details- Glass vials with rubber stopper and aluminum seal.
3. Storage condition-40ºc/755RH, 60ºc, Control sample at 2-8°c.
4. Testing Frequency-2nd week for sample charged at 60ºc, 4th week sample charged at 40ºc/75%RH, and Physical observation shall be done at every week, up to 4 week.
5. Test to be performed-Description, IR of initial sample.

Preparation of mouth dissolving carvedilol tablets: By direct compression method using superdisintegrant. Carvedilol Mouth Dissolving Tablets were prepared by direct compression method using various Superdisintegrant. The various disintegratants used like Croscarmellose Sodium, Crospovidone, Sodium Starch Glycollate and Polacrilin Potassium. A) Mannitol, Microcrystalline cellulose and Piper mint Flavor was Co-sifted through Mesh No.60 .Passed and retained Mannitol and Microcrystalline cellulose keep separately) Carvedilol was geometrically sifted with 60 passed Mannitol and Microcrystalline Cellulose.C) Step 'B' material was co sifted along with retained Mannitol, Microcrystalline Cellulose of each ingredient was taken for each specified formulation (depicted in the Table No 7) through mesh No.40.D) Talc and Aerosil co sifted through mesh No.60 and blended with step 'C' material. E) Magnesium stearate passed through mesh No.60 and lubricate the material of step 'D' with passed Magnesium stearate) The resulting lubricated material was compressed

into tablet with 10.5mm flat-face Punches using 12 Station Single rotary Compression Machine.

Formulation Trial

Ingredients	1 F	2 F	3 F	4 F	5 F	6 F	7 F	8 F	9 F	10 F	11 F	12 F
Carvedilol Solid dispersion with PVP (1:4)	62.5	62.5	62.5	62.5	62.5	62.5	62.5	62.5	62.5	62.5	62.5	62.5
Mannitol	155.9	148.4	140.9	156	148.4	141	155.9	148.4	141	155.9	148	141
Microcrystalline cellulose	63.6	63.6	63.6	63.6	63.6	63.6	63.6	63.6	63.6	63.6	63.6	63.6
Sodium Starch Glycollate	7.5	15	22.5	---	---	---	---	---	---	---	---	---
Croscarmellose Sodium	---	---	---	7.5	15	22.5	----	---	----	---	----	----
Crospovidone	----	----	----	----	----	---	7.5	15	22.5	---	---	---
Polacrilin Potassium	---	----	----	----	---	----	----	----	---	7.5	15	22.5
Flavor	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Talc	3	3	3	3	3	3	3	3	3	3	3	3
Aerosil	3	3	3	3	3	3	3	3	3	3	3	3
Magnesium stearate	3	3	3	3	3	3	3	3	3	3	3	3
Total	300	300	300	300	300	300	300	300	300	300	300	300

Relationship between % compressibility and flow ability.

S.No	% Compressibility	Flow ability
1	5 – 12	Excellent
2	12 – 16	Good
3	18 – 21	Fair Passable
4	23 – 35	Poor
5	33 – 38	Very Poor
6	< 40	Very very poor

Weight Variation Specification as per IP

S.No	Average Weight of Tablet	% Deviation
1	80 mg or less	10
2	More than 80 mg but less than 250 mg	7.5
3	250 mg or more	5

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