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RESEARCH ARTICLE

PHARMACEUTICS

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 with out 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 polacrilin potassium in different concentrations as a superdisintgrants. The prepared tablets containing the solid dispersion of Carvedilol having sufficient strength of 2.5-4 kg/cm^2. The disintegranted in the oral cavity with in 21 sec. contain crospovidone (5%) as super disintegrant.

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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 with out 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. 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 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 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 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

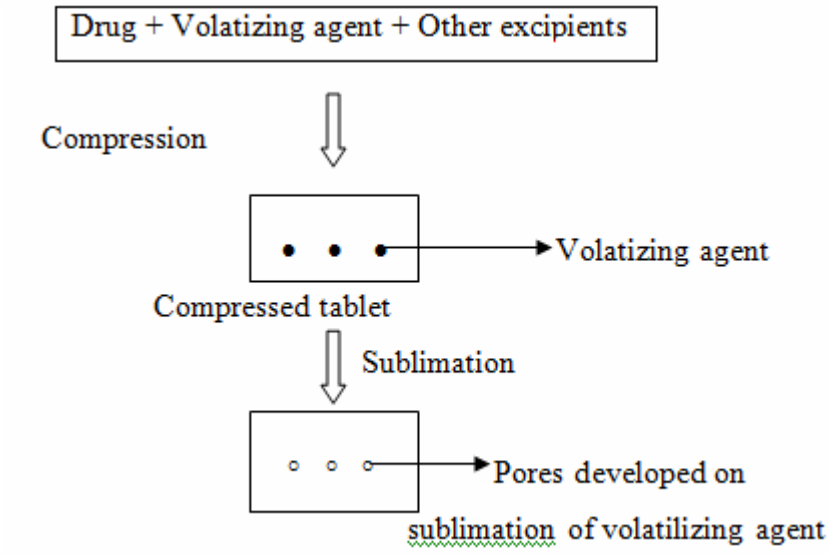

Table no. 1
Material used

Sr. No.	Materials	Manufactures / Suppliers
1	Carvedilol	Matrix Laboratories Limited
2	Polyvinylpyrolidone (PVP)	BASF
3	Mannitol	Roquette
4	Microcrystalline Cellulose(MCC)	FMC Biopolymer
5	Crospovidone	Signet
6	Croscarmellose Sodium	FMC Biopolymer
7	Sodium Starch Glycolate	DMV International
8	Polacrilin Potassium	
9	Talc	Signet
10	Aerosil	Degussa
11	Magnesium Stearate	Ferro
12	Mint Powder Flavor	Firmenich
13	Poloxamer-188	BASF
14	Poloxamer-407	BASF
15	Polyethylene Glycol-6000	Vashudha Chemicals
16	Gelucire 44/14	Gattefosse
17	Potassium dihydrogan O phosphate	Merck
18	Sodium hydroxide	Merck
19	Sodium Chloride	Merck
20	Hydrochloric acid	Merck
21	Methanol	Merck
22	Di-Chloro Methane	Merck

Table No.2
Equipments used.

Sr. no	Equipment /instrument	Manufacture
1	Balance	Sartorius
2	Hot Air Oven	Osworld Labs.
3	Magnetic Stirrer With Hot Plate	Remi
4	pH meter	Thermo
5	Rotatory Evaporator	Remi
6	12 Station Single rotary Compression Machine.	Cadmach
7	Shaker	Orbitec
8	Water Purifier and Dispenser	Barnstead
9	Disintegration Tester (USP)	Electro lab
10	Friability tester	Electro lab
11	Vernier calipers (digital)	Mititoyo
12	Hardness tester 8M	Dr. Schleunger
13	Cleaning machine	Euro Clean Ltd
14	Dissolution Tester (USP)	Electro lab
15	UV-Visible spectrophotometer	Perkin Elmer Lambda-40
16	FT-IR	Perkin Elmer Spectrum one
17	Thermometer	colorcon
18	Melting Point Tester	Electro lab

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

Drug Excipients Compatibility Study

Protocol for Drug-Excipients Compatibility

(a) Drug: Excipients Ratio-API alone, API: Diluent and Binder (Solubility enhancer):- 1:10, API: Lubricant and others:-1:1, API: Super disintegrant:-1:5

(b) Pack details- Glass vials with rubber stopper and aluminum seal.

(c) Storage condition-40ºc/755RH, 60ºc, Control sample at 2-8°c.

(d) 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.
(e) Test to be performed-Description, IR of initial sample.

Preparation of mouth dissolving carvedilol tablets- by direct compression method using superdisintegrants.Carvedilol Mouth Dissolving Tablets were prepared by direct compression method using various Superdisintegrants. The various disintegratants used like Croscarmellose Sodium, Crospovidone, Sodium Starch Glycolate 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.F) The resulting lubricated material was compressed into tablet with 10.5mm flat-face Punches using 12 Station Single rotary Compression Machine.

Summary and Conclusion

The Present study was undertaken with an aim to formulate and evaluate mouth-dissolving tablets of Carvedilol using direct compression method with the addition of super disintegrating agents. Solubility enhancement of Carvedilol was performed by Solvent evaporation method with the use of PVP.The Carvedilol PVP 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 with out enzymes and pH 6.8 phosphate buffer.

Table no. 3
Formulation Trial

FORMULATION TRIAL												
Ingredients	**F-1**	**F-2**	**F-3**	**F-4**	**F-5**	**F-6**	**F-7**	**F-8**	**F-9**	**F-10**	**F-11**	**F-12**
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 Glycolate	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**

Table No.4
Relationship between % compressibility and flow ability

% Compressibility	Flow ability
5 – 12	Excellent
12 – 16	Good
18 – 21	Fair Passable
23 – 35	Poor
33 – 38	Very Poor
< 40	Very Very Poor

Table No.5
Weight Variation Specification as per IP

Average Weight Of Tablet	% Deviation
80 mg or less	±10
More than 80 mg but less than 250 mg	±7.5
250 mg or more	±5

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