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R E S E A R C H A R T I C L E

Formulation Development and Evaluation of Tadalafil Mouth Dissolving Tablet

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A B S T R A C T

Tadalafil has some of the ideal characteristics required for an Mouth dissolving Tablet. There were some challenges faced during this formulation development. The aims of the present research were to mask the bitter taste of Tadalafil and to formulate Mouth dissolving Tablets of taste masked drug. Oral dispersible tablets of Tadalafil were prepared by direct compression method with a view to enhance patient's compliance. Five different super disintegrants viz. cross povidone XL10, sodium starch glycolate, crosscarmellose sodium Disintegration time was effectively reduced by adding disintegrating agents such as crospovidone and croscarmellose sodium. The resultant ODT tablets were then evaluated for particle size and the tablets prepared were evaluated for weight variation, thickness, hardness, friability, drug content, water content, in vitro disintegration time and in vitro drug release Tadalafil In the present work.

Keywords: sodium starch glycolate, crosscarmellose, XL10

A R T I C L E I N F O

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C O N T E N T S

1. Introduction

For most therapeutic agents used to produce systemic effects, the oral route still represents the preferred way of drug administration, owing to its several advantages and high patient. Compliance compared to many other routes [1, 2]. European Pharmacopoeia has used the term orodispersible tablets. Orodispersible tablets are also called as Mouth dissolving Tablet, mouth-dissolving tablets, rapid dissolving tablets, fast-disintegrating tablets, fast-dissolving tablets [3,4]. Tablets and hard gelatin capsules constitute a major portion of drug delivery systems that are currently

available [5,6]. To fulfill these medical needs, pharmaceutical technologists have developed a novel oral dosage form known as oral dispersible tablet [7,8]. Oral dispersible tablets (MDTs) are dosage forms that are placed in mouth, allowed to disperse/dissolve in the saliva without the need of water and provide a quick onset of action [9,10]. Most drugs pass through the barrier by molecular diffusion, or through pores called pore diffusion [11,12]. In pore diffusion the drug release rate is controlled by the crystal size, molecular size, pore size, pore structure and tortuosity of the polymers. In passive transport (Fick's first law) the drug moves from high concentration to the low concentration, while in active transport energy is required for the movement of drug from low to high concentration region through one or more transport mechanisms[11,12]. It requires energy or carrier such as enzyme, protein. Recently, This may be defined as uncoated tablets intended to be placed in the mouth where they disperse readily within 3 min before swallowing [13,14]. The fast disintegrating tablets prepared by direct compression method, in general, are based on the action established by superdisintegrants such as crosscarmellose sodium, crosspovidone and sodium starch glycolate. The effect of functionality differences of the superdisintegrants on tablet disintegration has been studied. Current study focus Formulated MDT tablet and evaluate following test thickness, Hardness, Friability test, Weight variation test, Disintegration time, Content uniformity test[15,16].

2. Materials and Methods

Formulation

Preparation of fast disintegrating tablet of tadalafil

Fast disintegrating tablets of tadalafil were be prepared by direct compression method. The drug, diluents, super disintegrants, and sweetener was screened through 40 # and properly mixed together. Talc and magnesium stearate was screened through 60 # and blended with initial mixture. Powder thus obtained was compressed into tablets on an 8 station single punch rotary tablet compression machine using 9.0 mm SC punches [17].

Formulation of post compression studies

Evaluation of tablets:

The formulated tablets were evaluated for the following physicochemical parameters.

Thickness

The thickness of tablet can vary without any change in weight. This is generally due to the differences of density of granules, pressure applied for compression and the speed of compression. It was measured by vernier caliper. (United State Pharmacopoeia 30- National Formulary 25, 2007, 634) [18]

Hardness

Tablets require certain amount of strength to have a resistance from breakage, while transportation and handling before use. It was measured by Monsanto Hardness Tester. The test was performed on six tablets and the average was calculated [19].

Friability test: The friability of the tablet was determined using Friabilator. It is expressed in percentage (%).Twenty tablets were initially weighed (W1) and transferred into the Friabilator. The Friabilator was operated at 25 rpm for 4 minutes in which tablets are subjected to combined effect of shock and abrasion in a plastic chamber dropping the tablets at a height of 6 inch in each revolution. The tablets were de dusted and weighed again (W2). The % Friability was then calculated by %.

% friability = (W1 - W2 / W1) × 100

Where,

W1 = weight of tablets before test

W2 = weight of tablets after test

Weight variation test

Twenty tablets were selected randomly and weighed individually. Average weight of tablets were calculated and compared with that of the individual tablets. For the tablet to be accepted, the weight of not more than two tablets deviates from the average weight by no more than 7.5%[20].

Disintegration time

The disintegration time was performed using an USP disintegration test apparatus with distilled water at 37±0.5 °C. The disintegration time was taken to be the time when no granules of any tablets were left on the mesh of the apparatus. The time reported to obtain complete disintegration of six tablets were recorded. The mean disintegration time and standard deviations were calculated [21].

Wetting time

Wetting time is closely related to the inner structure of the tablets and to the hydrophilicity of the excipient. The water penetration rate into the powder bed is proportional to the pore radius and is affected by the hydrophilicity of the powders.

It is obvious that pores size becomes smaller and wetting time increases with an increase in compression force or a decrease in porosity. A linear relationship exists between wetting time and disintegration time. Thus wetting is the important step for is integration process to take place. A piece of tissue paper folded double was placed in a petri dish (internal diameter is 6.5 cm) containing 6ml of water. The tablet was placed on the paper, and the time for complete wetting of the tablet was measured in seconds. The method was slightly modified by maintaining water at 37^0C [22].

Wetting-time corresponds to the time taken for the tablet to disintegrate when kept motionless on the tongue.

Content uniformity test

Twenty tablets from each batch were powdered and weighed accurately. The drug content was determined using the standard calibration curve. The mean percent drug content was calculated as an average of three determinations. Weighed quantity of powder samples were diluted suitably and analyzed for cumulative drug release using HPLC [23,24].

Evaluation of Postcompression Studies

Preliminary trials of fast disintegrating tablets of tadalafil: Table 5.4 shows composition of preliminary trial batches of fast disintegrating tablets of tadalafil. All prepared batches checked for various evaluation parameters.

3. Results and Discussion

The mouth dissolving tablets of tadalafil were prepared by employing disintegrant at various concentrations by direct compression method. These properties were studied by determining average weight, thickness, drug content, hardness, friability, and disintegration time of the prepared tablets. The average percentage of deviation of 20 tablets of each formula is less than 3%, hence all the formulations passes the test for uniformity of weight as per official requirements. The thickness of the prepared tadalafil tablets was ranged from 3.47 ± 0.52 mm to 3.54 ± 0.16 mm. Good uniformity in drug content is found among the different batches of tablets as all the values are within 97.20 – 99.80% of the labeled claim. In general, increase in the concentration of diluent contributes to higher hardness values. The hardness is, however, not an absolute indicator of strength. Hardness of the prepared tablets fell in the range of 2.5 ± 0.2 to 3.0 ± 0.26 kg/cm^2. The friability of the prepared tablets fell into the range of 0.52 ± 0.02 to 0.97 ± 0.03. The European pharmacopoeia states that loss up to 1% is acceptable. The disintegration time of the all formulations found in the range from 20 ± 2.3 to 40 ± 1.4 respectively. Therefore, these results were considered satisfactory. There was no marked difference in the friability observed with the tablets prepared using different disintegrant concentrations. These findings were in good agreement with the results of thickness measurement, supporting the idea that the used disintegrant does not alter the binding properties. All the tablet formulations showed acceptable pharmaco technical properties and complied with the specifications for weight variation, drug content, hardness and friability. The results were shown in Table 1and Figure 1 to 3.

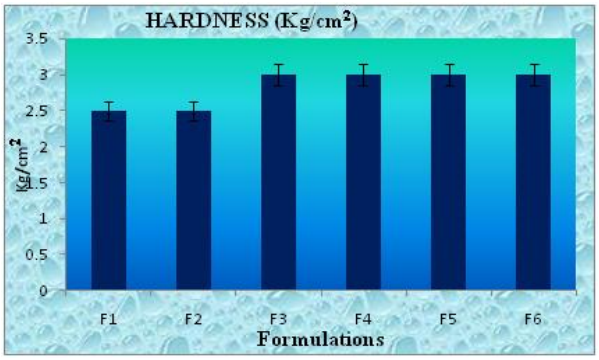

Figure 1: Hardness test

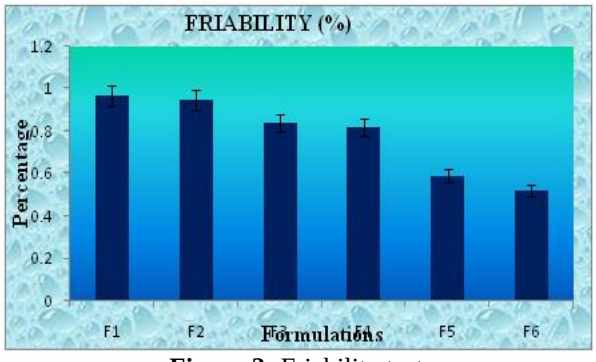

Figure 2: Friability test

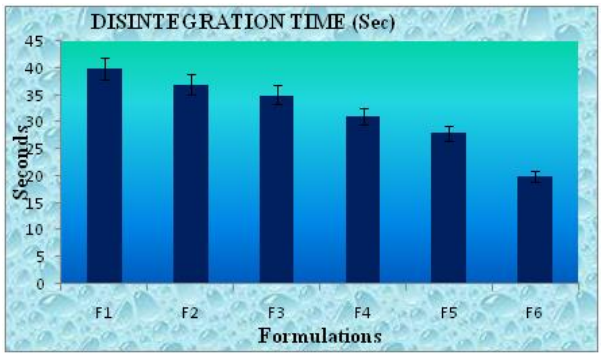

Figure 3: Friability test

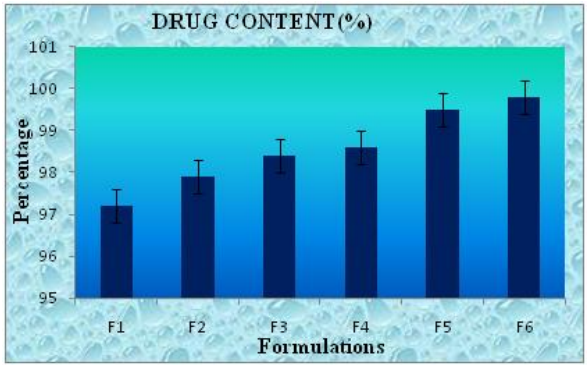

Figure 4: Drug content

Discussion

The mouth dissolving tablets of tadalafil were prepared by employing disintegrant at various concentrations by direct compression method. These properties were studied by determining average weight, thickness, drug content, hardness, friability, and disintegration time of the prepared tablets. The average percentage of deviation of 20 tablets of each formula is less than 3%, hence all the formulations passes the test for uniformity of weight as per official requirements. The thickness of the prepared tadalafil tablets was ranged from 3.47 ± 0.52 mm to 3.54 ± 0.16 mm. Good uniformity in drug content is found among the different batches of tablets as all the values are within 97.20 – 99.80% of the labeled claim. In general, increase in the concentration of diluent contributes to higher hardness values. The hardness is, however, not an absolute indicator of strength. Hardness of the prepared tablets fell in the range of 2.5 ± 0.2 to 3.0 ± 0.26 kg/cm^2. The friability of the prepared tablets fell into the range of 0.52 ± 0.02 to 0.97 ± 0.03. The European pharmacopoeia states that loss up to 1% is acceptable. The disintegration time of the all formulations found in the range from 20 ± 2.3 to 40 ± 1.4 respectively. Therefore, these results were considered satisfactory. There was no marked difference in the friability observed with the tablets prepared using different disintegrant concentrations. These findings were in good agreement with the results of thickness measurement, supporting the idea that the used disintegrant does not alter the binding properties. All the tablet formulations showed acceptable pharmaco technical properties and complied with the specifications for weight variation, drug content, hardness and friability. The results were shown in Table 1and Figure 1 to 3.

Table 1: Comparison of trial batches

S. No.	Ingredients	F1	F2	F3	F4	F5	F6
1	Tadalafil	20	20	20	20	20	20
2	Polacrillin Potassium	20	20	20	20	20	20
3	Sodium Starch Glycolate	40	40	40	40	40	40
4	MCC PH102	80	80	-	-	-	-
5	Mannitol	-	-	80	80	-	-
6	Spray dried Lactose	-	-	-	-	80	80
7	Croscarmellose sodium	50	-	50	-	50	-
8	Crospovidone XL10	-	50	-	50	-	50
9	Sucralose	3	3	3	3	3	3
10	Cherry flavour	2	2	2	2	2	2
11	Banana flavor	2	2	2	2	2	2
12	Magnesium Stearate	3	3	3	3	3	3
Total		**220**	**220**	**220**	**220**	**220**	**220**

Table 2: Results of Postcompression parameters

Test	F1	F2	F3	F4	F5	F6
Average weight (mg)	220.00± 0.48	220.00± 0.31	220.00± 0.13	220.00± 0.34	220.00± 0.27	220.00 ± 0.43
Thickness (mm)	3.50 ± 0.25	3.54 ± 0.35	3.52± 0.46	3.54 ± 0.25	3.49 ± 0.32	3.47± 0.21
Diameter (mm)	9.00 ± 0.33	9.02 ± 0.40	9.01± 0.23	9.02 ± 0.28	9.01 ± 0.43	9.02± 0.11
Hardness (Kg/cm^2)	2.50± 0.43	2.50± 0.36	3.00± 0.22	3.00± 0.45	3.00 ± 0.19	03.00 ± 0.23
Friability (%)	0.97± 0.44	0.95± 0.20	0.84 ± 0.37	0.82± 0.25	0.59 ± 0.37	0.52 ± 0.50
Disintegration Time (Sec)	40.00± 0.43	37.00± 0.26	35.00± 0.18	31.00± 0.38	28.00 ± 0.28	20.00 ± 0.19
Drug Content (%)	97.20± 0.27	97.90± 0.30	98.40 ± 0.42	98.60± 0.15	99.50 ± 0.39	99.80 ± 0.38

4. Conclusion

Tadalafil Mouth dissolving Tablet was prepared by using crospovidone and croscarmellose sodium. Exchange solubility. The evaluation results of all six batches were found to be satisfactory within limit and the disintegration time was quite good than synthetic super disintegrants such as Cross povidone and croscarmellose sodium. The synthetic disintegrating creates hydrodynamic pressure when comes in contacts with saliva and disintegrates the tablets within few seconds by swelling. The conclusion of Tadalafil Mouth dissolving Tablet evaluation of different batches were done evaluated for weight variation, thickness, hardness, friability, drug content, water content, in-vitro disintegration time and in vitro drug release .

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