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FORMULATION AND EVALUATION OF MOUTH DISSOLVING FILM OF TADALAFIL

SHRISHAIL M. GHURGHURE[1], MANISHA S. DYAWARKONDA[*1], VARSHA JAKUNE[1], JYOTI KHADTARE[1], SACHIN YANJANE[1]

1. D.S.T.S. Mandal's College of Pharmacy Solapur-413004. Maharashtra, India.

ABSTRACT:

Objective: Mouth dissolving films these are novel dosage forms it comes under fast dissolving drug delivery system. It disintegrates or dissolves within the oral cavity. It does not require water for administration so that it is convenient for medications for the pediatric and geriatric patients which have the difficulty in swallowing. This research work was aimed to enhance the oral bioavailability and provide faster onset of action of Tadalafil by formulating its mouth dissolving film (MDF).

Method: The MDF of Tadalafil was prepared by solvent casting method. Tadalafil it is a BCS class II and it has the oral bioavailability of about 28%. HPMC k-15, Xanthan gum, Sodium alginate (film forming agent), Glycerol (plasticizer), Tween 80 (solubilizing agent), Citric acid (saliva stimulating agent), Sucrose (sweetening agent), vanillin (flavoring agent), Propyl paraben (preservative). The formulation was evaluated for weight variation, thickness, folding endurance, drug content, disintegration time and *in-vitro* dissolution study stability study.

Conclusion: Based on the results F2 was showed enhanced bioavailability and rapid onset of action as compared to other dosage form.

Keywords: Tadalafil, Mouth Dissolving Film, Bioavailability.

INTRODUCTION:

Fast dissolving oral film it is the popular drug delivery system because of its variety of benefits. Fast dissolving drug delivery system was developed in 1970s to overcome the problems related with tablets and capsules for pediatric and geriatric sufferers. These preparations come in contact with saliva and dissolve or disintegrate within a minute, without need of water or chewing. MDFs are prepared by solvent casting method or hot melt-extrusion technology. MDFs are enhancing the bioavailability of the drug and patient compliance. [1, 2]

Mouth dissolving films these are novel dosage forms it comes under fast dissolving drug delivery system. It disintegrates or dissolves within the oral cavity. It does not require water for administration so that it is convenient for medications for the pediatric and geriatric patients which have the difficulty in swallowing. The strip of film is placed sublingually or under buccal cavity so that it avoids the first pass metabolism of the

drug and increases the bioavailability of the drug by enters into the direct blood stream. The penetrability of the buccal mucosa is 4 - 4,000 times larger than the skin, and is less than that of the intestine. Based on the active pharmaceutical ingredient these oral film strips have a shelf life of 2-3 years. [3, 4]

Erectile dysfunction (ED) is treated with PDF5 inhibitors. Tadalafil is used to treat ED in men and it is an impotence agent which was approved by FDA. It is a selective inhibitor of cyclic guanosine monophosphate (cGMP) - specific phosphodiesterase type 5 (PDF5). It is a BCS class II drug it achieves its maximum concentration in plasma after 2-3 hours of administration. [5, 6]

MATERIAL AND METHOD:

Materials:

Tadalafil was purchased and other ingredients were used of analytical grade.

Preparation of calibration curve of Tadalafil:

Aliquot from the standard solution was taken and diluted with DMSO to get concentration of 20µg/ml and it was scanned between 200-400nm which showed the maximum absorbance at 285.6nm. Aliquots of working standard solution were further diluted with DMSO to get concentration of 10,20,30,40, and 50µg/ml. Finally, the prepared standards were measured at 285.6nm in each case against a solvent Dimethyl Sulfoxide as blank. [7 to 10]

Method for the preparation of MDF:

Solvent casting method was used for the preparation of mouth dissolving film. In this method the required quantities of water soluble polymer like HPMC K-15 was dissolved in distilled water in a beaker with continuous stirring on magnetic stirrer at 1000 rpm at room temperature.

Then weighed all other ingredients with drug was dissolved in distilled water in another beaker. After that drug solution was slowly added into the polymer solution. This solution was allowed to continuous stirring for 2 hrs. After continuous stirring of 2 hrs the solution was kept constant for 12-16 hrs to remove all the entrapped air bubbles. Then the solution was poured into the petri dish which was previously lubricated with glycerin. The film was allowed to dry at room temperature. After drying of the film it was removed from the petri dish and cut in squares of 2x2 cm. [11 to 13]

table no. 1: formulation optimization of mdfs of tadalafil.

Sr. no.	Ingredients	F1 (mg)	F2 (mg)	F3 (mg)
01.	Tadalafil	20	20	20
02.	HPMC K-15	150	250	350
03.	Glycerol (ml)	0.4	0.4	0.4
04.	Sodium starch glycolate	10	10	10
05.	Tween 80 (ml)	0.25	0.25	0.25
06.	Citric acid	20	20	20
07.	Sucrose	5	5	5
08.	Vanillin	0.25	0.25	0.25
09.	Propyl paraben	0.05	0.05	0.05
10	Distilled water	q.s.	q.s.	q.s.

EVALUATION OF MDFs OF TADALAFIL: [14 to 17]

1. **Weight Variation of the film:**
   2x2 cm film was cut from different locations in the film. The weight variation was calculated by taking the weight of each film stip.

2. **Thickness of the film:**
   The thickness of the film was measured by Vernier Callipers at three different spots of the film and the average thickness was calculated.
3. **Folding Endurance:**
   This test is expressed as the number of folds required for breaking of the film. It is the important test to check the ability of the film sample to withstand folding. It indicates the brittleness of the film. A small strip of 2x2 cm was subjected to this test by folding the film at the same place till it broken or cracks were observed.

4. **Drug Content:**
   The drug content of the each film was determined by using phosphate buffer (pH 6.8). The film was dissolved in 10 ml of PBS (pH 6.8). The solution was filtered by using Whatman filter paper. The filtrate was diluted by PBS (pH 6.8) and the drug content was determined at 285.6 nm by using UV-visible spectroscopy.
5. **Disintegration test:**
   The disintegration test of MDFs was carried out by using 10 ml of distilled water was placed in a 10 cm diameter petri dish. Each MDF was kept at the center of the petri dish and the time required for the disintegration of MDF was noted.
6. ***In – vitro* Dissolution test:**
   The dissolution study of MDF was determined by using Electrolab Dissolution Apparatus. The paddle type dissolution testing apparatus was used. The dissolution media 900 ml of PBS pH 6.8 was used and stirred at 50 rpm at 37° C ±0.5 °C. Aliquot of 5 ml of sample was withdrawn at specific time intervals and filtered through Whatman filter paper and same amount of media was added in the apparatus. The filtrate was analyzed by UV spectroscopy at 285.6 nm.

RESULTS AND DISCUSSION:

1. **Calibration curve of Tadalafil:** [18]
   Six different concentration of Tadalafil were prepared and analyzed. The absorbance of Tadalafil shows appropriate wavelength at 285.6 nm. which is similar to standard peaks.

table 2: linearity of tadalafil

Sr. no.	Concentration µg/ml	Absorbance
1.	10	0.215
2.	20	0.508
3.	30	0.874
4.	40	1.253
5.	50	1.545
6.	60	1.876

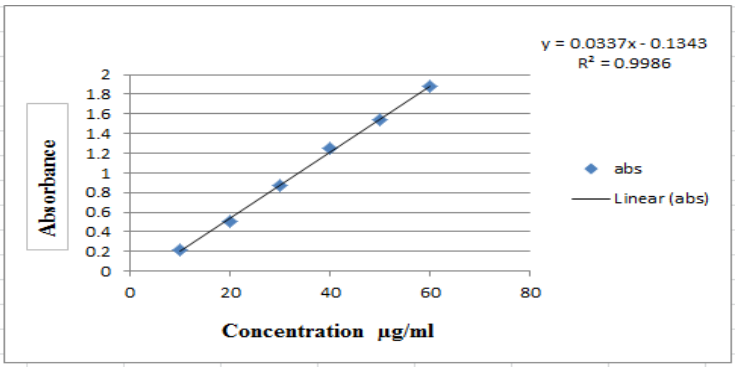

fig 1: calibration curve of tadalafil

table no. 3 evaluation parameters of mdfs of tadalafil

Formulation code	Weight variation (mg)	Thickness (mm)	Folding endurance (times)	Drug content (%)	Disintegration Time (sec)
F1	205.52	0.075	142	86.36%	30
F2	305.57	0.085	150	94.85%	18
F3	405.44	0.09	168	82.89%	37

table no. 4: *in-vitro* drug release of mdfs of tadalafil

Sr. no.	Time (min)	% Drug release of MDFs		
		F1	F2	F3
01.	5	58.66	60.82	54.78
02.	10	65.27	71.59	63.98
03.	15	74.52	78.18	71.72
04.	20	79.00	83.22	78.48
05.	25	83.29	89.35	82.56
06.	30	87.34	92.68	85.12

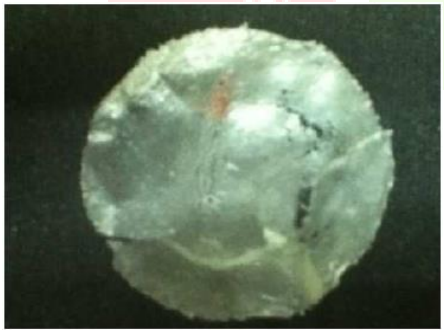

fig. 2: mdfs of tadalafil (f1)

fig. 3: mdfs of tadalafil (f2)

fig. 4: mdfs of tadalafil (f3)

CONCLUSION:

Tadalafil is used to treat ED in men and it is an impotence agent which was approved by FDA. It is a selective inhibitor of cyclic guanosine monophosphate (cGMP) - specific phosphodiesterase type 5 (PDF5). It is a BCS class II drug it achieves its maximum concentration in plasma after 2-3 hours of administration. The oral bioavailability it's about 28%. So that the mouth dissolving film of Tadalafil was prepared to improve the bioavailability and efficacy of the drug. [18]

The calibration curve of the Tadalafil was prepared. The prepared film shows the goof film characteristic features such as thickness, folding endurance, drug content, disintegration time and *in-vitro* drug release study. The prepared film was found to be uniform, flexible and 92.68% drug was released from F2 batch within 30 mins. [19]

From the present research work it was concluded that mouth dissolving oral film formulation cab be a potential novel drug dosage form for pediatric and geriatric and also for other population. Hence MDFs of Tadalafil was found to be suitable for better therapeutic effect in the treatment of erectile dysfunction in men. [20]

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