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Research Article

FORMULATION DEVELOPMENT AND EVALUATION OF TADALAFIL ORAL JELLY COMPARATIVE WITH MARKETED PRODUCT

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ABSTRACT

The present study aimed to develop immediate release tadalafil oral jellies for the treatment of erectile dysfunction. The jellies were prepared by using carbopol 940 with different concentration as a gelling agent with water miscible base. The result of physico-chemical parameter such as pH, appearance and viscosity shown all formulation were within standard limit and compare to F5 formulation is considered as best in their characteristics. In vitro dissolution study results of all formulations shows immediate release and it varied according to the concentration of carbopol 940. The percentage release of drug from F1 to F6 formulation increased from 64.75% to 95.4%. The observed result complies with marketed product this f5 is considered as a best formulation. The result of drug content F1to F6 shows 70.25 to 98.80%. In F5 formulation shows maximum drug content 98.80% and marketed product 99.60%. When increasing the concentration of polymer the alteration between the polymer and drug will be increased thus increasing concentration of drug in dosage form. Similarity factor (f2) values of all the (F1toF6) formulation were 50.64, 56.72, 61.80, 70.93, 93.58 and 86.30 respectively compared with marketed product. The results were fitted with release kinetics and it shows all the formulation follows first order release with fickian mechanism. Stability study was performed for the best formulation F5 and the result indicates that the prepared jelly was stable during its storage. Thus, it was concluded among the all formulation F5 having better release characteristics due to the optimum concentration of carbopol 940 as a water miscible base and it could be beneficial to improve the bioavailability of tadalafil.

Keywords: Tadalafil, Oral jelly, Carbopol 940, Erectile dysfunction, Similarity factor.

INTRODUCTION

Erectile dysfunction (ED) is the most common sexual problem in men[1]. ED is defined as a difficulty in initiating or maintaining penile erection adequate for sexual activity. ED has a weighty effect on intimate relationships, quality of life, and overall self-esteem for men. In addition, ED may also be an early indication of undetected cardiovascular disease. Currently Erectile dysfunction (ED) is treated with PDE5 inhibitors, lodenafil, sildenafil, tadalafil, udenafil vardenafil, avanafil and trazodone. Tadalafil is used to treat erectile dysfunction in men and it is a selective inhibitor of cyclicguanosine monophosphate (cGMP) and specific phosphodiesterase type5 (PDE 5)[2].

The recommended tadalafil starting dose for men is 10 mg, taken as needed before sexual activity (but not more than once daily).The dose may be increased to 20 mg or decreased to 5 mg, per its efficacy and the man's personal tolerance of the drug. To avoid the inconvenience of a man having to program and plan using tadalafil around the time of his anticipated sexual activity. Gelling agent used normally are tragacanth, sodium alginate, pectin, starch, gelatin, cellulose derivative like hydroxy propyl methyl cellulose (HPMC), methyl

cellulose (MC), carbomer, polyvinyl pyrrolidone.[3] Carbopol 940, which are very high molecular weight polymers of acrylic acid, have been used mainly in liquid or semi-solid pharmaceutical formulations, such as gels, suspensions and emulsions, as a thickening and viscosity agent, in order to modify the flow characteristics .[4]

MATERIALS

The gift sample of Tadalafil from M/s, Sai mirra inno pharma pvt ltd., Chennai, and Carbopal 940, Triethanolamine-- Alpha chemical pvt ltd, Chennai

METHODS

FORMULATION OF JELLY

Tadalafil should be added to the Propylene glycol solution until the drug gets dissolved and cool it at room temperature. Carbopal 940 sieved at 100 # mesh and triethanolamine added and kept it for 30 mins and looks like jelly. Sucrulose dissolved in DM water and mixed to the jelly. Finally colouring and flavouring agents were added. This formulation was carried out with different formulation F1 –F6 whose quantity is given in the tabular column (Table 1).

EVALUATION OF PREPARED ORAL JELLY

APPEARANCE

The prepared jelly was inspected visually for clarity, color and presence of any particulate materials. The test is important regarding patient compliance and acceptance[5].

DETERMINATION OF pH

The pH values (Table 3) of 1% aqueous solutions of the prepared jellies were checked by using a calibrated digital pH meter (Elico India) at constant temperature. For the purpose 1g of the weighed formulation was dispersed in 100 ml of distilled water and the pH was noted. The standard pH of the jelly was 7.5-8.1[6].

DETERMINATION OF VISCOSITY

Viscosity of the jelly was carried out by using (LV) Brookfield viscometer (Dial type). As the system is non-Newtonian spindle no. 4 was used. Viscosity was measured for the fixed time 2 min at 1.5rpm. Viscosity determination of jelly was done by Brookfield viscometer (Dial type)[7].

IN VITRO DRUG RELEASE STUDIES

Standard Preparation

Weigh accurately 20 mg standard of Tadalafil into a 100 mL volumetric flask. Dissolve in 10 mL Acetonitrile and dilute to volume with Acetonitrile and mix. Transfer 5 mL of this solution into a 100 mL volumetric flask and dilute to volume with dissolution medium and mix[8].

Sample preparation

Each jar containing 5gm of sample in 1000 mL dissolution medium that has been equilibrated to 37°C ± 0.5°C. Take care to exclude air bubbles from the surface of the tablets, start the apparatus immediately. Collect the sample after 45 minutes. Withdraw sample from a zone midway between the surface of the medium and top of the rotating blade and not less than 1 cm from the vessel wall and filter through Whatman No.1filter paper by discarding first 5 mL. Transfer 5 mL of this solution into a 10 mL volumetric flask and dilute to volume with dissolution medium and mix.

Procedure

Measure the absorbance of standard and sample preparations at 285 nm using dissolution medium as blank.

DRUG CONTENT ESTIMATION BY HPLC METHOD

Mobile phase: Buffer: Acetonitrile (70: 30)

[Buffer : Acetate Buffer pH 2.8 - Dissolve 4 g of anhydrous Sodium Acetate in about 840 ml of water, add sufficient Glacial Acetic Acid to adjust the pH to 2.8 (about 155 ml) and dilute to 1000 ml with water.]

Standard preparation: Weigh accurately 20 mg of Tadalafil WRS into a 100 mL volumetric flask. Dissolve and dilute to volume with diluent.

Sample preparation: Weigh accurately5gm of sample (equivalent to about 20 mg of Tadalafil) into a 100 mL volumetric flask. Add 30 mL of diluent and sonicate for 30 minutes. Cool and dilute to volume with diluent. Mix well. Filter through 0.45 µ membrane filter by discarding the first 5 mL.

STABILITY STUDIES AT VARIOUS TEMPERATURES

Stability studies of prepared jelly at different temperature condition were carried out with regards to temperature 4^{o}C, 45^{o}C and at room temperature. The stability studies are carried out for 3 months and the formulations were analyzed for the changes in the physical parameters like appearance, pH, viscosity, sugar crystallization and stiffness at 15 days, 30 days, 60 days and 90 days

Table 1: TADALAFIL ORAL JELLY FORMULATION

Ingredients(Mg)	F1	F2	F3	F4	F5	F6
Tadalafil	20	20	20	20	20	20
Sorbital	2200	2200	2200	2200	2200	2200
Propylene glycol	2715	2712.5	2710	2707.5	2705	2702.5
Carbapol 940	5	7.5	10	12.5	15	17.5
Triethanolamine	30	30	30	30	30	30
Sucrolose	30	30	30	30	30	30
Orange flavor	1ml	1ml	1ml	1ml	1ml	1ml
Sunset yellow	1ml	1ml	1ml	1ml	1ml	1ml
Total in (Gm)	5	5	5	5	5	5

RESULTS

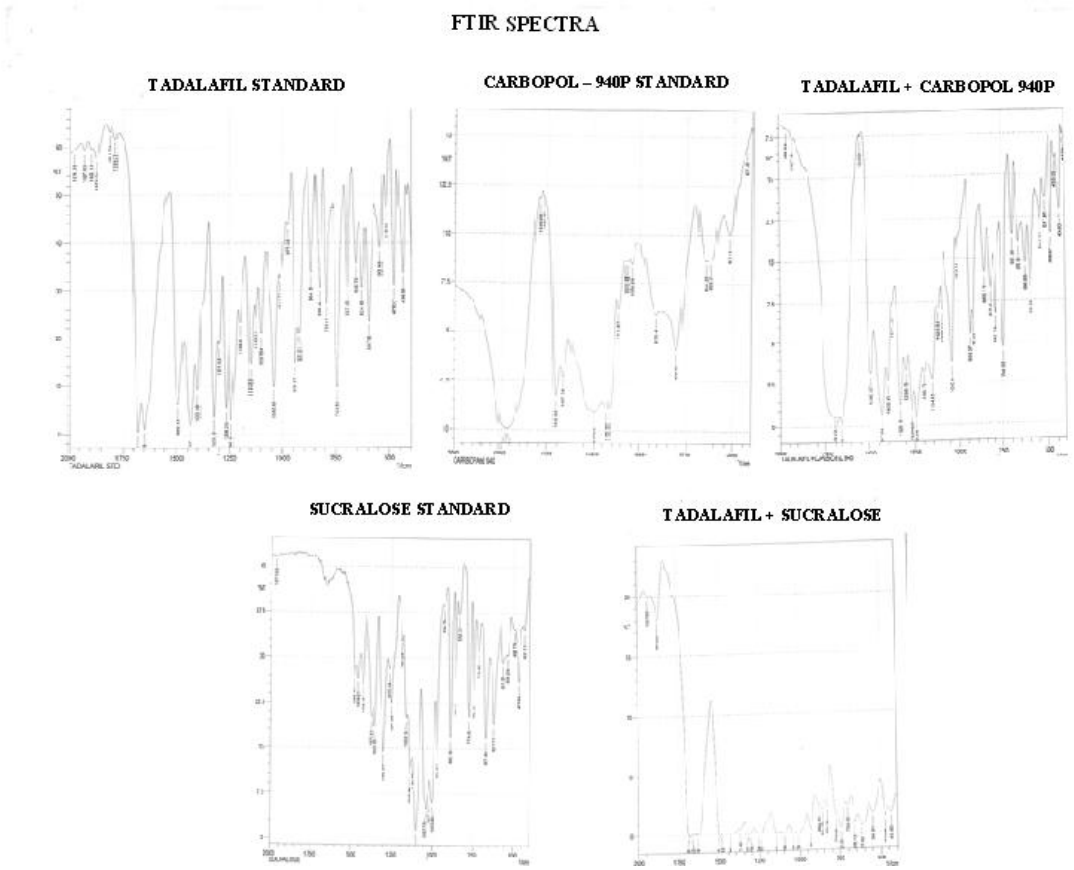

Fig. 1: COMPATABILITY STUDIES [FTIR]

Table 2: DRUG CONTENT ESTIMATION

S. No	Formulation	% Drug Release
		TADALAFIL
1	M P	99.6
2	F1	72.34
3	F2	70.25
4	F3	70.63
5	F4	81.63
6	F5	98.8
7	F6	95.23

Table 3: PHYSICAL PROPERTIES OF THE ORAL JELLY FORMULATIONS

Formulations	Appearance	pH	Taste	Viscosity (dyne sec/cm^2)
F1	Transparent	7.5	Bitter	273600
F2	Transparent	7.6	Bitter	351234
F3	Opaque	7.0	Bitter	542335
F4	Opaque	7.6	Bitter	335435
F5	Opaque	8.1	Bitter	294520
F6	Transparent	7.7	Bitter	482355

SIMILARITY FACTORS

Table 4: COMPARATIVE STUDIES WITH MARKETED PRODUCT

Time in mts	F1	F2	F3	F4	F5	F6	MP
0	0	0	0	0	0	0	0
10	59.5	65.5	70.2	76.1	83.3	77.3	84.9
15	60	68.6	71.6	77.2	85.7	81.9	87.1
20	62.2	69.5	72.5	78.2	89.9	88	95.6
30	63.6	70.2	73.6	79.1	91.1	91	96
45	64.7	71.8	75	81	95.4	93	98.2
f2 value	50.64	56.72	61.80	70.93	93.58	86.30	------

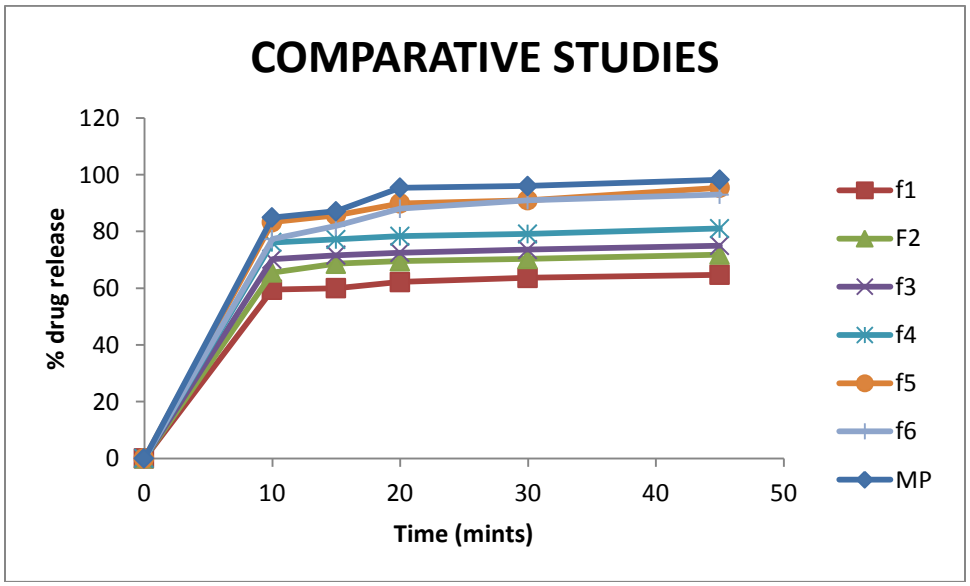

Fig. 2: COMPARATIVE STUDY *INVITRO* DRUG RELEASE PROFILE OF TADALAFIL ORAL JELLY

Table 5: STABILITY STUDIES OF FORMULATION F5

Parameter	Initial	After 1st month	After 2nd month	After 3rd month
Appearance	Transparent, opaque, milky white Semisolid jelly	No change	No change	No change
pH	8.0	7.9	8.0	8.1
Viscosity (dyne sec/cm^2)	294520	294520	294520	294520
Temp ^{0}c	25	25	25	25
Drug content in (%)	98	98	98	98

DISCUSSION

The results of the present study demonstrated that delivery of tadalafil oral jelly could be beneficial to improve the solubility as well as bioavailability of tadalafil. Tadalafil recommend in therapy of erectile dysfunction and available as tablets form. Owing to poor bioavailability of tadalafil may not control the erectile dysfunction effectively. Focusing on this study an attempt was made to develop oral jelly of tadalafil using carbopol 940 with different concentration as a jelling agent. In FTIR spectra there is no disappearance of peak present in drug and physical mixture it shows the compatibility of drug and polymer.

The result of physico-chemical parameter such as pH, appearance and viscosity shown all formulation were within standard limit and compare to other F5 is considered as best in their characteristics. Invitro dissolution study results of all formulations shows immediate release and it varied according to the concentration of carbopol 940.The percentage release of drug increased from 64.75% to 95.4% at higher concentration of polymer. The observed result complies with marketed product this f5 is considered as a best formulation. The result of drug content estimation show concentration of drug was higher in f5 this indicates the influence of polymer. When increasing the concentration of polymer the alteration between the polymer and drug will be increased thus increasing concentration of drug in dosage form. F2valuesof all formulation and marketed product were compared 50.64, 56.72, 61.80, 70.93, 93.58 and 86.30 respectively and these results shows all formulations are suitable for immediate release dosage form. Stability study was performed for the best formulationF5 and the result indicates that the prepared jelly was highly stable during its storage. This indicates that formulation f5 having better release characteristics due to the optimum concentration of carbopol 940 and compared the results of F5 formulation and it was similar that of marketed product and could be beneficial to improve the bioavailability of tadalafil.

CONCLUSION

The study reveals that tadalafil oral jelly released the drug as rapid manner with improved bioavailability. The observed results were found that the concentration of carbopol 940 can influenced the release rate & other physico chemical properties. Thus it can be concluded that tadalafil jellies are beneficial in improving the bioavailability of drug as compared to other oral fast releasing dosage forms.

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