International Journal of PharmTech Research
CODEN (USA): IJPRIF ISSN : 0974-4304
Vol.2, No.1, pp 84-88 Jan-Mar 2010

Formulation and Evaluation of Orodispersible tablets of Alfuzosin

S.A. Raju[1]., M.V. Rampure*[1],S.B. Shirsand[1]., P.V. Swamy[1]., D.Nagendrakumar[2]., B. Basawaraj[1] and D. Raghunandan[1]

1.Department of Pharmaceutics, H.K.E. Society's College of Pharmacy, Sedam Road, Gulbarga-585 105,India.

2. S.V.E.T. College of Pharmacy, Humnabad, Dist: Bidar,India.

E-mail: mrampure@gmail.com

Abstract: In the present work, orodispersible tablets of alfuzosin were prepared by sublimation method with a view to enhance patient compliance. In this method, camphor was used as subliming agent along with varying concentrations of croscarmellose sodium, crospovidone and sodium starch glycolate 2-10% w/w. The prepared batches of tablets were evaluated for hardness, friability, drug content uniformity, wetting time, water-absorption ratio and *in-vitro* dispersion time. Based on in-*vitro* dispersion time (approximately 5 seconds). Three promising formulations (one from each superdisintegrants) were tested for *in-vitro* drug release pattern (in pH 6.8 phosphate buffer), short term stability (at 40°C/75% Relative humidity for three months) and drug-excipient interaction (IR spectroscopy). Among the promising formulations, the formulation SCP_3 containing 10% w/w crospovidone and 30% w/w camphor as subliming agent emerged as the overall best formulation ($t_{50\%}$1.44 minutes) based on drug release characteristic (in pH 6.8 phosphate buffer) compared to controlled formulation ($t_{50\%}$15 minutes). Short-term stability studies on the promising formulation indicated that there are no significant changes in drug content and *in vitro* dispersion time ($p<0.05$).
Keywords: Orodispersible tablet, Alfuzosin, sublimation croscarmellose sodium, crospovidone, sodium starch glycolate, camphor

Introduction and Experimental

Dysphagia is a common problem encountered in all age groups in concern to solid dosage forms, which results in high incidence of non-compliance and ineffective therapy[1]. Recent advances in novel drug delivery systems (NDDS) aim to enhance safety and efficacy of drug molecule by formulating a convenient dosage form for administration and to achieve better patient compliance i.e., one, which will rapidly disintegrate in the mouth without need of water (fast dissolving tablet). Advantages of this drug delivery system include administration without water, accuracy of dosage, easy portability, alternative to liquid dosage forms, ideal for pediatric and geriatric patients and rapid onset of action[1-4]. Alfuzosin is an alpha-adrenoceptor blocker used in the management of hypertension and it also relieves symptoms of urinary obstructions in benign prostatic hyperplasia[5]. The concept of formulating orodispersible tablets containing alfuzosin offers a suitable and practical approach in serving desired objective of rapid disintegration and dissolution characteristics with increased bioavailability.

Materials and Methods

Alfuzosin was obtained from Dr Reddy's Labs, Hyderabad, India and croscarmellose sodium (CCS) crospovidone (CP), sodium starch glycolate (SSG), directly compressible mannitol (Pearlitol SD200) were gift samples from Ranbaxy, Mumbai. Sodium stearyl fumarate (SSF) and aspartame were generous gifts from Strides Arco Labs, Bangalore and camphor used was of analytical grade.

Preparation of Orodispersible Tablets by Sublimation Method[6]:

In sublimation method, camphor was used as subliming agent along with varying concentrations of croscarmellose sodium, crospovidone and sodium starch glycolate (2-10%w/w). The ingredients were

passed through sieve No. 44 and thoroughly mixed in a tumbling cylindrical mixer for 10 minutes at 15 rpm, then aerosil was added to blend to impart hardness to the tablet and then lubricant and glidant SSF and talc (# 200 mesh) were added and mixed for further 5 min. The blend thus obtained was directly compressed into tablets of 150 mg. using 8mm round flat punches on 10 station rotary tablet machine. A batch of 60 tablets was prepared for all the designed formulations. The compressed tablets were then subjected to sublimation at 60±1ºC for 6 hours in hot air oven. The tablets were evaluated for *in-vitro* dispersion time in pH 6.8 phosphate buffer and formulae used for preparation of tablets are shown table no.1.

Evaluation of formulated tablets

Tablet Hardness[7]

The hardness of the tablet was determined using Monsanto Hardness Tester a tablet hardness of 2-4 kg/cm^2 is considered adequate. An average of three determinations.

Weight Variation Test[7]

Twenty tablets were selected at random and weighed individually on shimdzu BL-220. The individual weights were compared with the average weight for determination of weight variation.

Friability[7]

Friability of the tablets was determined by using Roche friabilator. Tablets of a known weight (20 tablets) are kept in the drum for a fixed time (100 rotations per minute) and weighed again. Percentage friability was calculated from the loss in weight. The weight loss should not be more than 1%. An average of three determinations.

Tablet Thickness[7]

Tablet thickness was measured using varnier calipers. The thickness was measured by placing tablet between two arms of the varnier calipers. An average of three determinations.

Drug Content Uniformity[8]

For content uniformity test, ten tablets were weighed and powdered a quantity of powder equivalent to 10 mg of alfuzosin was extracted into pH 6.8 phosphate buffer and filtered. The alfuzosin content was determined by measuring the absorbance spectrophotometrically at 248.5 nm after appropriate dilution with pH 6.8 phosphate buffer. The drug content was calculated using the standard calibration curve. The mean percent drug content was calculated as an average of three determinations.

In-vitro Dispersion Time[9]

For determination of *in-vitro* dispersion time, one tablet was placed in a beaker containing 10 ml of pH 6.8 phosphate buffer at 37±0.5ºC and the time required for complete dispersion was determined. An average of three determinations.

Wetting and Water absorption Time[9 & 10]

For determination of wetting time and water absorption ratio, a piece of tissue paper folded twice was placed in a small petri dish (having internal diameter of 5 cm) containing 6 ml of water. A tablet was placed on the paper and the time required for complete wetting was measured. The wetted tablet was then weighed. Water absorption ratio 'R' was determined using the equation, $R=100(Wb-Wa)/Wa$; where, W_a is weight of tablet before water absorption and W_b is weight of tablet after water absorption. An average of three determinations.

In-vitro Dissolution study[11]

In-vitro dissolution of alfuzosin orodispersible tablet was studied in USP XXIII type-II dissolution apparatus (Electrolab, Model-TDT 06N) employing a paddle stirrer at 50 rpm using 900 ml of pH 6.8 phosphate buffer at 37±0.5ºC as dissolution medium. One tablet was used in each test. Aliquots of dissolution medium (5 ml) were withdrawn at specified intervals of time and analyzed for drug content by measuring the absorbance at 248.5 nm. The volume withdrawn at each time interval was replaced with fresh quantity of dissolution medium. Cumulative percent of alfuzosin released was calculated and plotted against time.

Stability Testing

Short-term stability studies on the promising formulation (SCP_3) were carried out by storing the tablets (in amber coloured rubber stoppered vials) at 40º/ 75% Relative humidity over a period 3 months. At interval of one month, the tablets were visually examined for any physical changes, changes in drug content and *in-vitro* dispersion time.

Results and Discussion

Orodispersible tablets of alfuzosin were prepared by sublimation method employing three super-disintegrants viz., CCS, CP and SSG, along with camphor as subliming agent and directly compressible mannitol (Pearlitol SD 200) was used as a diluent to enhance the mouth feel, and aspartame which serves as a sweetening agent and helps in masking slight bitter taste of the drug. A total of nine formulations and a control formulation (without super-disintegrants) were designed. As the material was free flowing (angle of repose value <30º and Carr's index <15) tablets obtained were of uniform weight (due to uniform die fill), with acceptable variation as per IP specifications i.e., below 7.5%. Drug content was found to be in the range of 96-101 %, which is within acceptable limits. Hardness of the tablets was found to be about 2.45 to

3.0 Kg/cm². Friability below 1% was an indication of good mechanical resistance of the tablets (Table 2). Water absorption ratio and wetting time, which are important criteria for understanding the capacity of disintegrants to swell in presence of little amount of water were found to be in the range of 69-77% and 6-49 sec respectively. Based on the *in-vitro* dispersion time (6seconds), three promising formulations viz., SCP_3, SCC_3 and $SSSG_3$ were tested for *in-vitro* drug release pattern (in pH 6.8 phosphate buffer), short term stability (at 40ºC/75% RH for 3 months) and drug interaction (IR spectroscopy). Among the promising formulations, the formulation SCP_3 (containing 10% w/w of CP and 30% w/w of camphor) was found to be promising and displayed an *in-vitro* dispersion time of approximately 6 seconds.

In-vitro dissolution studies on the promising formulations (SCP_3 SCC_3, $SSSG_3$), and control formulation (SC_0) were carried out in pH 6.8 phosphate buffer and the various dissolution parameter values, viz., percent drug dissolved in 5 minutes (D_5), 10 minutes (D_{10}), $t_{50\%}$, $t_{70\%}$ and $t_{90\%}$ are shown in Table 3. Among the promising formulations, SCP_3 has shown 10-fold faster drug release ($t_{50\%}$1.44 minutes) compared to control formulations (15 minutes.) when $t_{50\%}$ values were considered in pH 6.8 phosphate buffer and thus emerged as the overall best formulation.

IR spectroscopic studies indicated that the drug is compatible with all the excipients. The IR spectrum of SCP_3 showed all the characteristic peaks of alfuzosin, thus confirming that no interaction of drug occurred with the components of the formulation. Short-term stability studies of the above formulation indicated that there are no significant changes in drug content and *in vitro* dispersion time at the end of 3 months ($p<0.05$).

Table 1: Composition of different batch's of orodispersible tablets of alfuzosin

Ingredients (mg/ tablet)	Formulation Code*									
	SC_0	**SCP_1**	**SCP_2**	**SCP_3**	**SCC_1**	**SCC_2**	**SCC_3**	**$SSSG_1$**	**$SSSG_2$**	**$SSSG_3$**
Alfuzosin	10	10	10	10	10	10	10	10	10	10
Camphor	30	15	30	45	15	30	45	15	30	45
Crospovidone	------	3	7.5	15	-------	------	------	-------	------	-------
Croscarmellose sodium	-------	-------	------	-------	3	7.5	15	------	------	-------
Sodiumstarch glycolate	-------	--------	------	------	-----	-----	------	3	7.5	15
Aspartame	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5
Aerosil	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0
Flavour (Trusil banana)	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Sodiumstearyl fumarate	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75
Talc	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0
Pearlitol SD- 200	97.25	109.25	89.75	67.25	109.25	89.75	67.25	109.25	89.75	67.25

* A batch of 60 tablets was prepared for each formulation and formulations SCP_3, SCC_3 and $SSSG_3$ were used for further studies.

Table 2: Evaluation of orodispersible tablet formulations

Formulation	Hardness* (Kg/cm²)± SD	Friability (%)	Thickness* (mm)±SD	Percent drug content*± SD	*In vitro* dispersion time* (s)±SD	Wetting time*(s)±SD	Water absorption ratio (%)
SC_0	2.88±0.10	0.49	2.50±0.136	101.33±0.57	156.83±1.60	159±2.50	69.2±0.214
SCP_1	2.64±0.36	0.83	2.41±0.16	99.03±0.77	27.08±2.17	26.47 ±1.76	77.3±0.654
SCP_2	2.55±0.29	0.69	2.48±0.215	96.66±0.48	14.04±0.53	18.51±0.82	76.4±0.586
SCP_3	2.45±0.36	0.75	2.40±0.133	98.66±0.23	5.31±0.25	6.79±0.32	76.4±0.204
SCC_1	2.86 ± 0.15	0.73	2.58±0.205	97.33±0.61	47.04 ±0.68	49.03 ± 0.78	74.3 ± 0.224
SCC_2	2.50 ± 0.07	0.84	2.25±0.121	98.36±0.81	38.72± 0.42	39.80 ± 0.27	71.6 ± 0.287
SCC_3	3.00±0.05	0.61	2.35±0.057	100.13±0.65	26.50 ± 0.14	27.19 ± 1.23	75.6 ± 0.324
$SSSG_1$	3.00 ± 1.20	0.63	2.58±0.110	99.00±0.37	36.01 ± 2.0	38 ± 0.30	69.6 ± 0.313
$SSSG_2$	2.80 ± 2.01	0.56	2.46±0.085	98.36±0.67	30.50 ± 2.45	31 ± 0.20	72.1 ± 0.354
$SSSG_3$	2.65 ± 0.65	0.59	2.42±0.085	97.96±0.12	39 ± 1.60	42 ± 0.32	77.0 ± 0.246

- Average of three determinations.

Table 3: *In vitro* dissolution parameters in pH 1.2

Formulation	D_5 (%)	D_{10} (%)	DE_{10min} (%)	$t_{50\%}$ (min)	$t_{70\%}$ (min)	$T_{90\%}$ (min)
SC_0	20.85	44.12	49.55	>15	>15	>15
SCP_3	78.35	99.96	72.55	1.44	3.67	9.47
SCC_3	69.55	85.20	64.05	1.55	5.84	11.59
$SSSG_3$	66.85	79.07	61.03	1.64	7.56	13.02

SCP_3, SCC_3 and $SSSG_3$ are rapidly disintegrating oral tablet formulations, SC_0 is control formulation, D_5 is percent drug released in 5 minutes, D_{10} is percent drug released in 10 minutes, DE_{10}min is drug elimination in 10 minutes $t_{50\%}$ is time for 50% drug dissolution, $t_{70\%}$ is time for 70% drug dissolution and $t_{90\%}$ is time for 90% drug dissolution. Formulation SCP_3 was selected as the best and used in further studies.

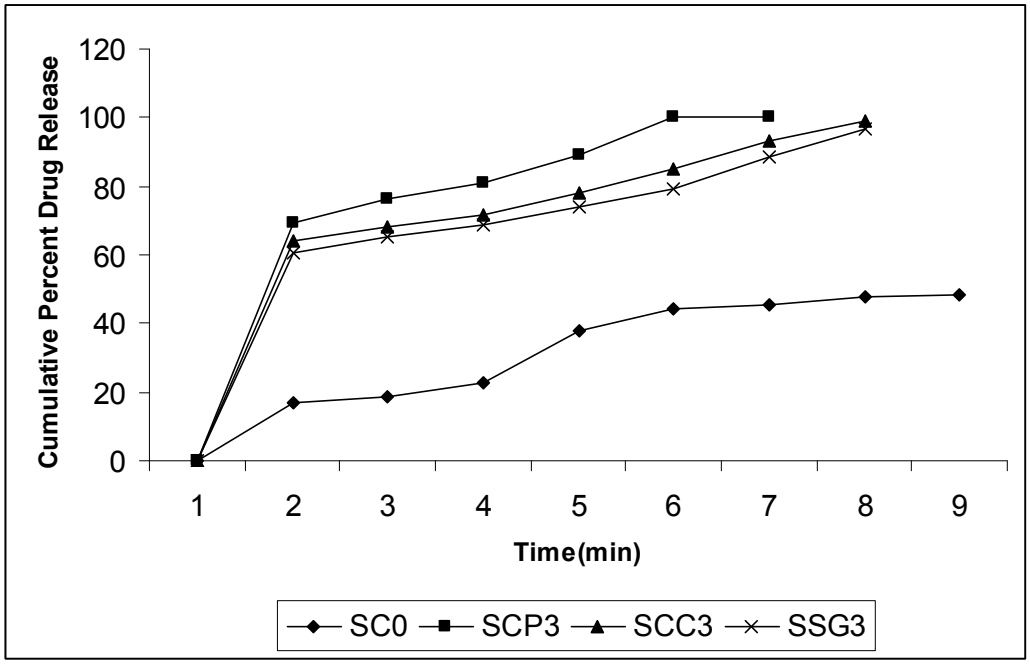

Figure 1: Cumulative percent drug release versus time profile of promising formulations.
In vitro cumulative percent drug release vs time profile of promising alfuzosin formulations SC_0 (♦), SCP_3 (▪), SCC_3 (▲) and SSG_3 (×) in pH 6.8 phosphate buffer.

References

1. Seager H. Drug delivery products and the Zydis fast dissolving dosage forms. J Pharm Pharmacol. 1998; 50:575-82.
2. Chang RK, Guo X, Burnside BA and Cough RA. Fast dissolving tablets. Pharm Tech 2000; 24(6): 52-58.
3. Dobetti L. Fast melting tablets: Development and Technologies. Pharm Tech. 2001 (Suppl): 44-50.
4. Kuchekar BS, Arumugam V. Fast dissolving tablets. Indian J Pharm Edu. 2001; 35: 150-52.
5. Sweetman SC, editor Martindale: The Complete Drug Reference, 33rd edn., Pharmaceutical Press, London; 2002: p. 833.
6. Patel DM, Patel MM. Optimization of fast dissolving etoricoxib tablets prepared by sublimation technique. Indian J Pharm Sci; 2008.70: 71-76.
7. Banker GS and Anderson NR, Tablets. In: Lachman L., Lieberman HA, Kanig JL, editors. The theory and practice of industrial pharmacy, 3rd edn. New Delhi: Varghese Publishing House; 1987. p. 293-99.
8. Indian Pharmacopoeia: Controller of Publications, Ministry of Health and Family Welfare, Govt of India, New Delhi; 1996. p. 735.
9. Chaudhari PD, Chaudhari SP, Kolhe SR, Dave KV, More DM. Formulation and Evaluation Of Fast Dissoliving Tablets of Famotidine. Indian Drugs 2005: 42(10): 641-49.
10. Bi Yx, Sunada H, Yonezawa Y, Danjo K. Evaluation of Rapidly Disintergranting Tablets by Direct Compression Method. Drug Dev Ind Pharm. 1999; 25(5): 571-81.
11. Bhagwati ST, Hiremath SN, Sreenivas SA. Comparative Evaluation of Disintegrants by Formulating Cefixime Dispersible Tablets. Indian J Pharm Educ 2005; 39(4): 194-97.

*****