International Current Pharmaceutical Journal

ORIGINAL RESEARCH ARTICLE OPEN ACCESS

Formulation and evaluation of fast dissolving tablet of albendazole

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ABSTRACT

Albendazole is broad spectrum anthelmintic use against many helminths. It is used for treatment of Threadworm, Hookworm, and Tapeworm. It has low bioavailability due to its first pass metabolism. In the present work, fast dissolving tablet of Albendazole was design with a view to and provide a quick onset of action. The main objective of the study was to formulate fast dissolving tablets of Albendazole to achieve a better dissolution rate and further improving the bioavailability of the drug. Fast dissolving tablets prepared by direct compression and using super disintegrants in different concentration and evaluated for the pre-compression parameters. The prepared tablets were evaluated for post compressional evaluation. Among all, the formulation F3 containing 5%w/w superdisintegrant Crospovidone and 20%w/w Microcrystalline Cellulose was considered to be best formulation, which release up to 99.097% in 40 min.

Key Words: Albendazole, superdisintegrants, *in vitro* disintegration time, *in vitro* dissolution test.

INTRODUCTION

Recent advance in novel drug delivery system aims to enhance the safety and efficacy of the drug molecule by formulating a dosage form being for the administration (Kuchekar *et al.*, 2003). Difficulty in swallowing is experienced by patient such as pediatric, geriatric, bedridden, disabled and mentally ill (Seager *et al.*, 1998). Fast dissolving tablets are solid dosage form containing medical substances which disintegrate rapidly, usually within few seconds when placed upon tongue requiring no additional water to facilate swallowing (Shu *et al.*, 2002; Bradoo *et al.*, 2001). Albendazole (ABZ), methyl [5-(propylthio)-1-H-benzimidazol-2yl] carbamate, is a benzimidazol derivative with a broad spectrum of activity against human and animal helminth parasites (Cook *et al.*, 1990). ABZ is effective in the treatment of echinococcosis, hydrated cysts and neurocysticercosis (Wen *et al.*, 1993).

Direct compression is one of the techniques requires the incorporation of a superdisintegrants into the formulation the use or highly. The basic approach used in development of FDT was the use of superdisintegrants like cross linked Croscarmellose Sodium, Polyvinyl Pyrrolidone K30, Microcrystalline Cellulose, Crospovidone etc. which provide instantaneous disintegration of tablet after placed on tongue, thereby releasing the drug in saliva.

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MATERIAL AND METHODS

Albendazole was obtained as a gift sample from Brasica Pvt. Ltd. Boisar (India). Crospovidone, Microcrystalline cellulose and Croscarmellose sodium were gift sample from Curex Pharma, Jalgaon. Polyvinyl Pyrrolidone K30 was obtained as gift sample from Emcure Pharma, Pune and Mannitol, Aspartame were gift samples from Merck Ltd, Mumbai, India. All chemicals and reagents used were of analytical grade.

Preparation of fast dissolving tablets

Fast dissolving tablets of Albendazole were prepared using direct compression method incorporating superdisintegrants Microcrystalline cellulose (MCC), Crospovidone (CP), Croscarmellose Sodium (CCS), Polyvinyl Pyrrolidone K30

Table 1: Formulation of albendazole fast dissolving tablets.

Ingredients	Formulations									
	F 1	F 2	F 3	F 4	F 5	F 6	F 7	F 8	F 9	F 10
Albendazole (mg)	200	200	200	200	200	200	200	200	200	200
Microcrystalline cellulose*	-	-	20	20	-	20	15	15	-	15
Crospovidone*	5	-	5	-	5	5	5	-	5	5
Croscarmellose sodium*	-	5	-	5	5	5	-	4	4	4
Polyvinyl Pyrrolidone K30*	3	3	3	3	3	3	3	3	3	3
Aspartame*	2	2	2	2	2	2	2	2	2	2
Magnesium Stearate*	1	1	1	1	1	1	1	1	1	1
Mannitol q.s.(mg)	500	500	500	500	500	500	500	500	500	500

*Amounts of ingredients are in percentage (%)

(PVPK30). The Albendazole equivalent to 200mg, Mannitol and Microcrystalline Cellulose were mixed thoroughly in glass mortar using a pestle. Superdisintegrants were incorporated in the powder mixture according to each formulation in the tablets and finally Aspartame, and Magnesium stearate was added. The whole mixture was passed through Sieve No. 60 twice. Tablets were prepared using 12mm round flat-faced punch of the rotary tablet machine [Jaguar (JMD4-8)]. Compression force was constant for all formulations are showed in Table 1.

Precompression parameters

Angle of Repose

Angle of repose was determined using fixed funnel method. The blend was poured through a funnel that can be raised vertically until a maximum cone height (h) was obtained. Radius of the heap (r) was measured and angle of repose was calculated using formula (Rockville *et al.*, 2007).

$\theta = tan^{-1}\left(\frac{h}{r}\right)$

Where, θ is angle of repose, h is height of pile and r is the radius of the base pile.

Bulk Density

Apparent bulk density *(LBD)* was determined by pouring blend into a graduated cylinder. The bulk volume *(Vo)* and weight of powder *(M)* was determined. The bulk density was calculated using the formula (Rockville *et al.*, 2007; Liberman *et al.*, 1990).

$$LBD = \frac{weig\,ht\ of\ the\ powder\ \ (M)}{volume\ \ of\ the\ packing\ \ (Vo)}$$

Tapped Density

The measuring cylinder containing known mass of blend was tapped for a fixed time. The minimum volume (Vt) occupied in the cylinder and weight of powder blend (M) as measured. The tapped density (TBD) was calculated using the formula (Rockville *et al.*, 2007; Mukesh *et al.*, 2009).

$$TBD = \frac{weig\,ht\ of\ the\ powder\ \ (M)}{tapped\ \ volume\ \ of\ the\ packing\ \ (Vt)}$$

Carr's Compressibility Index

The simplex way of measurement of the free flow of powder is compressibility, an indication of the ease with which a material can be induced to flow is given by compressibility index of the granules was

Table 2: Physical properties of powder blend.

Formulations	Angle of Repose (°) ±SD	Bulk Density (g/ml) ±SD	Tapped Density(g/m) ±SD	Carr's Index (%)±SD	Hausner's Ratio ±SD
F1	27.97±0.34	0.44±0.022	0.66±0.022	14.87±0.60	1.52±0.008
F2	28.62±0.55	0.41±0.018	0.61±0.020	13.72±0.27	1.51±0.003
F3	27.65±0.39	0.42±0.024	0.70±0.024	10.71±0.71	1.13±0.009
F4	26.32±0.78	0.38±0.037	0.67±0.051	15.31±0.99	1.18±0.014
F5	25.71±0.59	0.43±0.025	0.72±0.036	13.81±0.77	1.58±0.011
F6	26.93±0.46	0.41±0.024	0.69±0.032	12.96±0.49	1.54±0.009
F7	27.65±0.43	0.38±0.029	0.62±0.036	10.43±0.23	1.51±0.006
F8	26.99±0.35	0.44±0.019	0.66±0.029	14.60±0.81	1.44±0.011
F9	28.62±0.38	0.42±0.025	0.61±0.051	14.21±0.81	1.55±0.011
F10	24.68±0.59	0.47±0.025	0.71±0.012	13.30±0.81	1.52±0.019

Table 3: Evaluation data of the prepared albendazole fast dissolving tablets.

Formulations	Thickness (mm)±SD	Hardness (kg/cm²)±SD	Weight Variation (mg)±SD	% Friability ± SD	Disintegration time (Sec) Mean±SD	Wetting time (Sec) Mean±SD	Water absorption ratio Mean±SD	Content uniformity Mean(%)±SD
F1	4.71±0.040	3.33±0.12	301.54±0.33	0.52±0.18	48.16±0.61	40.22±0.25	91.68±0.56	99.27±0.63
F2	4.55±0.039	3.41±0.31	300.65±0.32	0.60±0.14	57.11±0.42	38.90±0.11	89.27±0.78	96.99±0.55
F3	4.56±0.055	3.42±0.25	301.48±0.64	0.52±0.19	40.51±0.23	34.45±0.20	109.34±0.81	99.81±0.35
F4	4.87±0.045	3.36±0.13	302.41±0.23	0.58±0.11	54.20±0.55	36.15±0.24	90.65±0.45	98.85±0.20
F5	5.01±0.049	3.49±0.23	300.60±0.21	0.59±0.16	57.86±0.82	38.75±0.35	88.36±0.78	97.81±0.44
F6	4.83±0.042	3.42±0.37	301.41±0.33	0.49±0.14	56.52±0.41	36.65±0.53	95.28±0.91	98.92±0.87
F7	4.87±0.052	3.41±0.34	300.30±0.12	0.54±0.10	48.52±0.84	35.90±0.47	90.91±0.78	96.97±0.38
F8	4.53±0.050	3.50±0.06	302.55±0.28	0.61±0.20	51.69±0.76	34.98±0.58	83.69±0.54	98.64±0.29
F9	4.44±0.044	3.39 ±0.10	301.50±0.36	0.60±0.18	55.60±0.63	39.11±0.22	90.65±0.89	99.69±0.63
F10	4.87±0.042	3.37±0.10	300.22±0.65	0.67±0.24	49.92±0.69	37.50±0.45	89.90±0.79	98.78±0.84

*Results are presented as Mean±SD

determined by Carr's compressibility index (C) which is calculated by using the following formula (Rockville *et al.*, 2007).

$$C = [(TBD - \frac{LBD}{TBD})] \times 100$$

Hausner Ratio

Hausner ratio is an indirect index of ease of powder flow. It is calculated by the following formula (Rockville *et al.*, 2007).

$$Hausner\ ratio = \frac{Tapped\ \ density\ \ (TBD)}{Bulk\ \ density\ \ (LBD)}$$

Where *TBD* is tapped density and *LBD* is bulk density. Lower hausner ratio (< 1.25) indicate better flow properties than higher ones (>1.25).

Post compression parameters

All the batches of tablets were evaluated for various parameters like weight variation, friability, hardness, drug content, disintegration and dissolution and results reported in Table 3.

Uniformity of weight

This test is performed to maintain the uniformity of weight of each tablet which should be in the prescribed range, this is done by sampling and weighing 20 tablets at random and average weight is calculated. Not more than two of the individual weights deviate from the average weight by more than the percentage show in the Table 3 and none deviate by more than twice the percentage The mean and standard deviation were determined (Thahera *et al.*, 2012).

Thickness

The thickness and diameter of the tablets was determined using a Micrometer screw gauge. Five tablets from each type of formulation were used and average values were calculated. It is expressed in mm (Liberman *et al.*, 1990).

Hardness Test

The hardness of the tablet was determined using Monsanto Hardness Tester (Rockville *et al.*, 2007).

Friability Test

Six tablets from each batch were examined for friability using Roche Fribilator (Tropical Equipment Pvt. Ltd. Mumbai, India) and the equipment was run for 4min at 25 revolutions per minute. The tablets were taken out, dedusted and reweighted and % friability was calculated (Rockville *et al.*, 2007).

$$Percent\ friability = \frac{Initial\ \ weig\,ht - Final\ \ weig\,ht}{Initial\ \ weig\,ht} \times 100$$

Water Absorption Ratio

A piece of tissue paper folded twice was kept in a Petri dish (internal diameter 5.5cm) containing 6ml of purified water. The tablet was placed on the tissue paper and allowed to wet completely. The wetted tablet was removed and reweighted. Water absorption ratio, R was determined according to the following equation (Bandari *et al.*, 2008).

$$R = \frac{wa - wb}{wawb} \times 100$$

Where Wb and Wa are the weight before and after water absorption, respectively.

Wetting Time

A piece of tissue paper (12cmX10.75cm) folded twice was placed in a small Petri dish (ID = 9 cm) containing 6ml pH 6.8 phosphate buffer, A tablet was placed on the paper and the time taken for

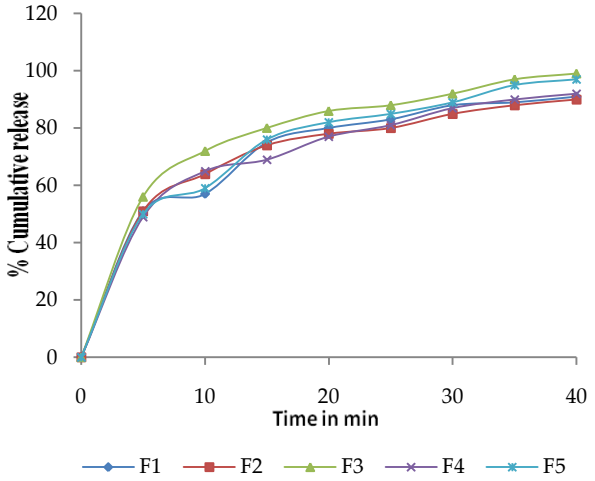

Figure 1: ***In vitro*** **drug release of F1, F2, F3, F4, F5 tablet formulations.**

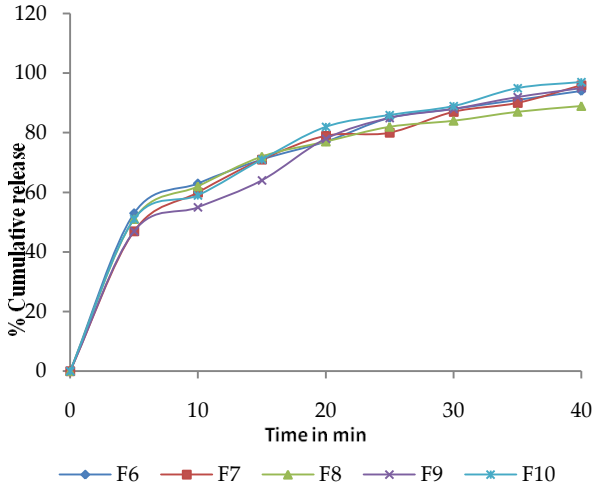

Figure 2: ***In vitro*** **drug release of F6, F7, F8, F9, F10 tablet formulations.**

complete wetting was noted. Three tablets from each formulation were randomly selected and the average wetting time was noted (Jain *et al.*, 2012).

Content Uniformity Test

Twenty tablets of each type of formulation were weighed and crushed in mortar and powder equivalent to 200mg of Albendazole was weighed and dissolved in 100ml of pH 6.8 phosphate buffer. From the stock solution 1ml sample was withdrawn and diluted to 10ml with pH 6.8 phosphate buffer, The absorbance was measured at wavelength 291nm using double beam UV-Visible spectrophotometer (IP, 2007).

Content uniformity was calculated using formula

$$\% \text{ Purity} = 10\ C \frac{\text{Absorbance of unknown (Au)}}{\text{Absorbance of Standard (As)}}$$

Where, C - Concentration

In Vitro Disintegration Time

Initially the disintegration time for fast dissolving tablets was measured using the conventional test for tablets as described in the Pharmacopoeia. Tablets were placed in the disintegration tubes and time required for complete disintegration without leaving any residues on the screen was recorded as disintegration time (EP, 1988).

In Vitro Dissolution Testing

Dissolution study was conducted for all the formulation using USP type-II apparatus (Electrolab, Mumbai, India.). The dissolution test was performed using 900ml of phosphate buffer (PH 6.8) was taken as the dissolution medium at 50 rpm and 37°C±0.5°C. Ten ml of aliquots were periodically withdrawn and the sample volume was replaced with an equal volume of fresh dissolution medium. The samples were analyzed spectrophotometrically at 291nm (Liberman *et al.*, 1990).

Characterization of albendazole tablet

FT-IR studies

Infrared spectrum was taken for the pure Albendazole. FT-IR studies was carried by KBr disk method using computer mediated Fourier transformed infrared spectroscopy (FTIR) (Shimadzu Model – IRAFFINITY-1, Serial No. A21374600405).

RESULTS AND DISCUSSION

Albendazole fast dissolving tablets of were prepared by direct compression method was carried out by using superdisintegrants like Crospovidone, Croscarmellose sodium and Microcrystalline Cellulose in 5%, 4-5% and 15-20% concentration. Angle of repose: range from 24.68 to 28.62° show good flow. Bulk density and tapped density: range from 0.38 to 0.47 (g/ml), and 0.61 to 0.72 (g/ml), respectively. Compressibility index and Hausner ratio range from 10.43 to 15.31 and 1.13 to 1.58 respectively. The results for recompressed parameters are showed in Table 2.

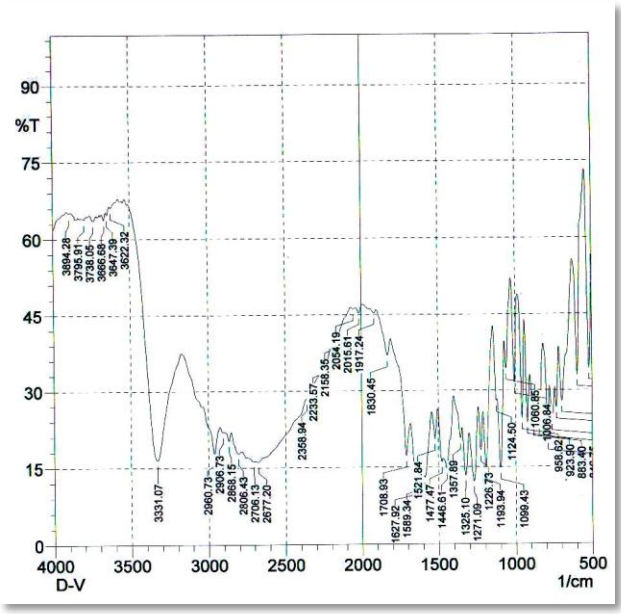

Figure 3: FTIR spectra of albendazole.

Weight variation test range from 300.22mg to 302.55mg as per IP specification. Friability: less than 0.67% the results indicate that the percentage losses were not more than 1.0%. So the tablet complies as per IP specifications. Thickness: range from 4.44 to 5.01 mm; the results indicate that the tablets are suitable for packing. Content uniformity: was found in between 96.97% to 99.81%. Hardness of tablet was found to be between 3.33 to 3.50kg/cm^2. The results indicate that the tablets are mechanically strong and are in limit. Disintegration time: in between 40.51 to 57.86 second the results indicate that disintegration time of tablets is within 1minute. Wetting time: in between 49.45 to 56.11 second and water absorption ratio was found to be 83.69 to 109.34. The post compressed parameters are showed in Table 3. Dissolution Study in 6.8 pH phosphate buffer: formulation of F1, F2, F3, F4, and F5 have a recorded drug release 91.87%, 90.80%, 99.07%, 92.85%, and 97.48% at the end of 40 min the results was showed in Figure 1, formulation F6, F7, F8, F9, and F10 have a recorded drug release 94.88%, 96.43%, 89.80%, 95.97%, and 97.23% at the end of 40 min the result was showed in Figure No. 2. FTIR studies: The FTIR spectra of the pure drug were recorded in between 4000 to 400 cm^{-1}. Characteristics peak and chemical group present in IR spectrum of Albendazole was showed in Figure 3, C-H Stretching of alkane at 2960 cm^{-1}, -COO- Bending of Ketone at 1708 cm^{-1}, N-H Stretching of amine at 3331 cm^{-1}. Storage condition: Tablets were stored at 45°C ± 2°C/75% for a storage period of 0 days, 30 days, 60 days, and 90 days, Hardness was increases with time increases but in all cases, hardness was within the limit. Disintegration time: at various storage conditions increases but maximum 40 second which is less than 1min (specification of IP). Dissolution studies shows there was no significant difference in dissolution data of formulations at initial and after specified storage period.

CONCLUSION

Fast dissolving tablets of Albendazole can be successfully prepared by direct compression techniques using selected superdisintegrants for the better patient compliance and effective therapy. The relative efficiency of these superdisintegrants to improve the disintegration and dissolution rate of tablets was found in order i.e. Crospovidone > Croscarmellose sodium.

ACKNOWLEDGEMENT

The authors are grateful to Brassica Parma Ltd., Boisar for providing gift sample of Albendazole and Curex Pharma, Jalgaon for providing Croscarmellose sodium, Crospovidone and Microcrystalline cellulose.

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