

FORMULATION DEVELOPMENT AND EVALUATION OF CHEWABLE TABLET OF ALBENDAZOLE BY DIFFERENT TECHNIQUES

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ABSTRACT

Albendazole is a benzimidazole derivative with broad spectrum anthelmthic activity and excellent tolerability. Orally it is rapidly absorbed and metabolized to sulfoxide and sulfone, which may be responsible for its anthelmthic action. Single dose administration of albendazole has produced cure rates in ascariasis, hookworm and enterobiasis which are comparable to three day treatment with mebendazole. Albendazole chewable tablets (400 mg) were prepared by three methods viz. non aqueous granulation, aqueous granulation and direct compression and were named as NAG, AG and DC respectively. Tablet prepared by these three methods were evaluated by different parameters such as average weight, hardness, carr's index, tapped density, friability, disintegration, content uniformity test, *in vitro* dissolution etc. All the parameters were found within the specifications. The study on the dissolution profile revealed that product 'DC' had faster dissolution rate while compared to remaining batches and marketed product. Assay values were within the limits of 90% to 110%.

Keywords: Albendazole, Aqueous granulation, Non aqueous granulation, Direct compression, Chewable tablets.

INTRODUCTION

Albendazole is a benzimidazole derivative with broad spectrum anthelmthic activity and excellent tolerability. Orally it is rapidly absorbed and metabolized to sulfoxide and sulfone, which may be responsible for its anthelmthic action. Single dose administration of albendazole has produced cure rates in ascariasis, hookworm and enterobiasis; which are comparable to three day treatment with mebendazole. It is described chemically as methyl [5-(propylsulphanyl)-1H-benzimidazol-2-yl] carbamate. [1]

Administration of drugs through oral route is the most common and the easiest way to administer a drug. But it is a challenge in children who have not yet learned to swallow tablets. Hence it was decided to formulate albendazole chewable tablet to improve the compliance in children. Chewable tablets are the tablets which are required to be broken and chewed in between the teeth before ingestion. These tablets are given to the children who have difficulty in swallowing and to the adults who dislike swallowing. [2] The advantages of chewable tablets include palatability, stability, precise dosing, portability and ease of delivery. The available literature suggests that chewable tablets provides a safe, well-tolerated alternative to traditional pediatric drug formulations and offer significant advantages in children with two years of age and above. [3] In the present paper Albendazole chewable tablets were prepared by three different methods and all the three batches were evaluated. The main objective of the present study was to formulate and evaluate Albendazole chewable tablet by different technique and to evaluate these using different parameters.

MATERIALS AND METHODS

Materials

Pure drug sample of Albendazole was procured from Arandy Laboratories Ltd. All other ingredients viz. Lactose, Starch, Sodium starch glycolate, Isopropyl alcohol. Sodium Saccharine etc. used were of pharmaceutical grade.

Method

Nonaqueous Granulation

All the ingredients were separately weighed and sifted using mesh no. 40. Albendazole, Lactose monohydrate, Starch and Sodium Starch Glycolate was mixed in a poly bag for ten minutes. For the preparation of binder dispersion, isopropyl alcohol was taken in a beaker, stirred with glass rod to disperse starch until no lumps were observed. Then the above dry mixture was granulated with binder

solution and dried in the tray drier at the temperature of 40-50°C until the moisture reduce down to NMT-2%. The dried granules were passed through mesh no. 30, Mannitol (Perlitol200) through mesh no. 30. Sodium Saccharine, Carmofine color and pineapple flavor were passed through mesh no. 100. All these were finally added to the dried granules and blended for ten minutes. The above blend was lubricated with Magnesium stearate, Talc, Aerosil for two minutes. The powder blends was evaluated for the flow properties and were found to be good. The evaluated blend was compressed into tablets to get tablets of 785 mg weight each. A minimum of fifty tablets were prepared for each batch.

Aqueous Granulation

All the ingredients were separately weighed and sifted using mesh no. 40. Albendazole, Lactose monohydrate, Starch and Sodium starch glycolate were mixed in poly bag for ten minutes. For the Preparation of binder dispersion purified water was taken in a beaker, stirred with glass rod to disperse starch until no lumps were observed. Then the above dry mixture was granulated with binder solution and dried in the tray drier at the temperature of 40-50°C until the moisture reduces down to NMT-2%. The dried granules were passed through mesh no. 30. Then Mannitol (pearlitol200) was passed through mesh no. 30, Sodium saccharine, Carmofine and pineapple flavor were passed through mesh no. 100. All these were then added to the dried granules and blended for ten minutes. Finally the above blend was lubricated with Magnesium stearate, Talc, Aerosil for two minutes. The powder blend was evaluated for the flow properties and was found to be good. The evaluated blend was compressed into tablets to get tablets of 785 mg weight each. A minimum of fifty tablets were prepared for each batch.

Direct Compression

All the ingredients were separately weighed and sifted using mesh no. 40. Albendazole, Lactose monohydrate, Starch and Sodium starch glycolate Mannitol (pearlitol200) were passed through mesh no. 30. Sodium saccharine, Carmofine color and pineapple flavor were passed through 100 mesh and required quantities were blended for ten minutes in poly bag. Finally the above blend was lubricated with Magnesium stearate, Talc and Aerosil for two minutes. The powder blend was evaluated for the flow properties and was found to be good. The evaluated blend was compressed into tablets of 785 mg weight each. A minimum of fifty tablets were prepared for each batch.

The manufacturing formulas for the tablets used in the above three methods is given in table I

Table 1: Manufacturing formulas for preparation of Tablet

Sr. no.	Name of the Ingredients	Non Aqueous Granulation (mg/tablet)	Aqueous Granulation (mg/tablet)	Direct Compression (mg/tablet)
1.	Albendazole	410	410	410
2.	Lactose mono.	120	120	120
3.	Starch	60	43.2	86.4
4.	Sodium starch glycolate	29.34	29.34	29.34
5.	Starch	25	43.2	-----
6.	Isopropyl alcohol	q.s.	-----	-----
7.	Purified water	-----	q.s.	-----
8.	Mannitol	100	100	100
9.	Sodium saccharide	10	10	10
10.	Carmofine color	0.5	0.5	0.5
11.	Pineapple flavor	5	5	5
12.	Magnesium stearate	6	6	6
13.	Talc	6	6	6
14.	Aerosil	12	12	12

Evaluation of Tablets

General appearance ^[4]

The general appearance of tablets, its visual identity and overall elegance is essential for consumer acceptance. The control of general appearance involves measurement of attributes such as a tablet's size, shape, color, presence or absence of odour, taste, surface textures, physical flaws and consistency. Hence the tablets were checked for the presence of cracks, depressions, pinholes, uniformity of color, and the polish of the tablet.

Dimensions ^[4]

The shape and dimensions of compressed tablets were determined by the type of tooling during the compression process. At a constant compressive load, tablet thickness varies with changes in die fill, particle size distribution and packing of the powder mix being compressed and with tablet weight. While with a constant die fill, thickness varies with variation in compressive load. Tablet thickness is consistent from batch to batch or within a batch only if the tablet granulation or powder blends is adequately consistent in particle size and particle size distribution, Consistent length of punch tooling, Tablet press and good working conditions Thickness and diameter of the tablets were measured using digital vernier caliper. The values of thickness were used to adjust the initial stages of compression. Tablet thickness should be controlled within a $\pm 5\%$ variation of a standard value. Also the thickness must be controlled to facilitate packaging.

Weight Uniformity test ^{[5], [6]}

Twenty tablets were weighed individually and all together. Average weight was calculated from the total weight of all tablets. The individual weights were compared with the average weight. The percentage difference in the weight variation should be within the permissible limits. The percent deviation was calculated using the following formula:-

$$\text{Percentage deviation} = \frac{(\text{Individual weight} - \text{Average weight})}{\text{Average weight}} \times 100$$

Any deviation in the weight of tablet leads to either under medication or over medication. So, every tablet in each batch should have a uniform weight. Corrections were made during the compression of tablets to get uniform weight. The USP has provided limits for the average weight of uncoated compressed tablets. These are applicable when the tablet contains 50mg or more of the drug substance or when the latter comprises 50% or more, by weight of the dosage form. Twenty tablets were weighed individually and the average weight was calculated. The individual tablet weights are then compared to the average weight. Not more than two of the tablets must differ from the average weight by not more than the percentages stated. No tablet must differ by more than double the relevant percentage.

Bulk density (BD) ^[8]

Bulk density (BD) was measured by slowly pouring a powder sample into a 100 ml graduated cylinder at a 45 degree angle. Care

was taken not to shake the sample. BD was calculated by dividing the sample weight with its volume. The bulk density of different Albendazole tablets were calculated and shown in Table II.

Tapped density (TD) ^[8]

To measure tapped density (TD), a powdered sample was poured into a 100 ml graduate cylinder at a 45 degree angle. The sample was mechanically tapped 1500 times. TD was calculated by dividing the sample weight by its final volume. The Tapped density of different Albendazole tablets were calculated and shown in Table II.

Carr's Index ^[8]

The compressibility of Albendazole tablet was determined by the Carr's Index

$$\text{Carr's Index (\%)} = \frac{\{(\text{Tapped density} - \text{Bulk density}) \times 100\}}{\text{Bulk density}}$$

Hausner Ratio ^[8]

The Hausner Ratio of Albendazole tablet was determined by the following equation

$$\text{Hausner Ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

Value less than 1.25 indicates good flow, while greater than 1.25 indicates poor flow.

Hardness test ^{[5], [6]}

Hardness is a force required to break a tablet across the diameter. The hardness of a tablet is an indication of its strength. The tablet should be stable to mechanical stress during handling and transportation. The hardness was tested using Monsanto tester. For determination of hardness factor, the average of the six determinations was determined and reported. The force was measured in kilograms per centimeter square.

Friability test ^{[5], [6]}

Friability is the loss of weight of tablet in the container or package, due to removal of fine particles from the surface. To ensure the ability of tablets to withstand the shocks during processing, handling, transportation, and shipment. Permitted friability limit is 1.0%. Roche friabilator was used to measure the friability of the tablets. Ten tablets were weighed collectively and placed in the chamber of the friabilator. In the friabilator the tablets were exposed to rolling, resulting free fall of tablets (6 inches) within the chamber of the friabilator. It was rotated at a rate of 25 rpm. After 100 rotations (4 min.) the tablets were taken out from the friabilator and intact tablets were again weighed collectively. The percent friability was determined using the following formula:

$$\text{Friability (\%)} = \frac{(W_1 - W_2)}{W_1} \times 100$$

Where, W₁ = Weight of the tablet before test, W₂ = Weight of the tablets after test

Disintegration test ^[6]

For a drug to be absorbed from a solid dosage form after oral administration, it must first be in solution, and the first important step toward this condition is usually the break-up of the tablet; a process known as disintegration. The disintegration test is a measure of the time required under a given set of conditions for a group of tablets to disintegrate into particles which will pass through a 10 mesh screen. The disintegration test is carried out using the disintegration tester which consists of a basket rack holding 6 plastic tubes, open at the top and bottom, the bottom of the tube is covered by a 10-mesh screen. The basket was immersed in a bath of suitable liquid held at 37°C, preferably in a 1L beaker. For compressed uncoated tablets, the testing fluid was usually water at 37°C but some monographs direct that simulated gastric fluid be used. If one or two tablets fail to disintegrate, the test was repeated using 12 tablets. For most uncoated tablets, the BP (British Pharmacopoeia) requires that the tablets disintegrate in 15 minutes (although it varies for some uncoated tablets). The individual drug monographs specify the time disintegration must occur to meet the Pharmacopoeial standards.

Content Uniformity test ^[6]

Weighed accurately quantity of the powder containing about 0.1 g of Albendazole. Add about 150 ml of 0.1 M Methanolic Hydrochloride acid, Shaked for 15 min and dilute to 250 ml with 0.1 M Methanolic Hydrochloride acid, Mixed and Filtered and diluted 5.0 ml of the filtrate to 250.0 ml with 0.1M Sodium hydrochloride measured the absorbance of the resulting solution at the γ max of 309 nm, Calculated the content of albendazole taking 742 as the specific absorbance at 309 nm.

In vitro dissolution test ^[9]

Dissolution measurements were carried out in a USP dissolution test apparatus. The dissolution profiles of Albendazole from chewable

tablets were studied in 0.1 N HCl (pH 1.2). The chewable tablets containing 400 mg of Albendazole were placed in a rotating basket (50 rpm) filled with 900 ml of the dissolution medium, thermo stated at $37 \pm 0.5^\circ\text{C}$. At scheduled time intervals, the samples (5 ml) were withdrawn and replaced immediately with fresh dissolution medium. The samples were assayed spectrophotometrically at 309 nm for the dissolved drug, where samples were automatically filtered before measuring the absorbance against 0.1 N HCl as blank. The amount of Albendazole released was calculated from the standard graph.

Drug content

Five tablets were powdered and the blended equivalent to 400 mg of Albendazole was weighed and dissolved in suitable quantity of water. The solution was filtered, suitably diluted and drug content was analysed spectrophotometrically at 309 nm. Each sample was analyzed in triplicate.

RESULTS AND DISCUSSION

All the prepared batches of tablets were within the range. Using Monsanto hardness tester, the strength of the tablets was tested. All the tablets showed good hardness. Batch 'AG' had minimum hardness (5.1 ± 0.10) while 'DC' had maximum hardness (5.5 ± 0.09). The friability was carried out for all the batches of tablets. The friability was less than 0.2% for all the blends and was satisfactory. Assay value of all prepared batches of Albendazole tablets were within the range of 90% to 110% of stated amount of Albendazole. From the data obtained it was found that 88.8% of drug was released for the trial 'DC' at 30 min while other trials 'NG' & 'AG' had shown 81% & 80.5% drug re-lease at 30 min respectively. The variation in the dissolution rate of Albendazole tablets was in the following order $\text{AG} < \text{NG} < \text{DC}$. The dissolution profile of batches of tablets prepared by direct compression method has shown better results compared to the tablets prepared by other methods as well as marketed product as showed in fig I.

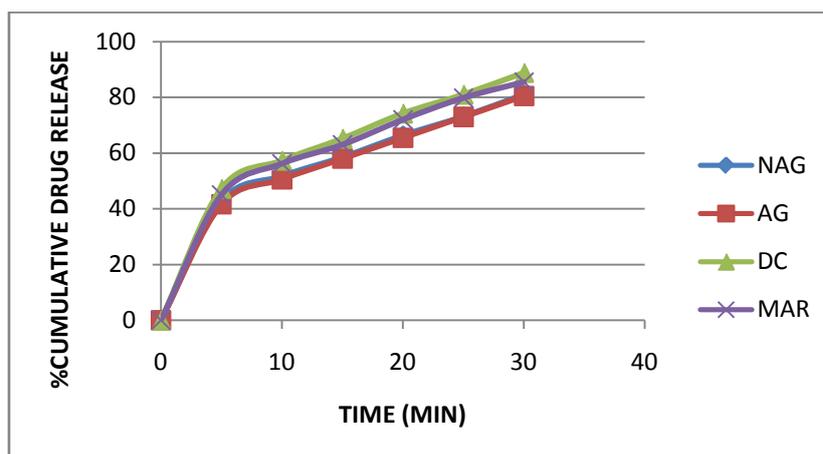


Fig. 1: Comparison of dissolution profiles of three batches of tablets and marketed product

Result of comparative evaluation of tablet using different parameters are shown in Table II

Table 2: Comparative evaluation of tablets using different parameter

Parameters	Tablets code			
	NG	AG	DC	MAR
Weight of tablet (mg)	785 \pm 3.0	785 \pm 4.5	785 \pm 2.5	--
Bulk density	0.48	0.38	0.58	--
Tapped density	0.55	0.44	0.66	--
Carr's Index	12.88	12.89	12.63	--
Hausner ratio	1.14	1.14	1.14	--
Hardness (kg/cm ²)	5.2 \pm 0.25	5.1 \pm 0.10	5.5 \pm 0.09	--
Friability test (%)	0.65	0.55	0.25	--
Disintegration time (min)	5	4	3.5	--
Dissolution time cumulative % of drug dissolved in 30min	81.0	80.5	88.8	85.5
Drug content (mg)	99.50	99.20	99.70	--
Assay (%)	97	95	99	--

CONCLUSION

All the tablets showed satisfactory results with respect to hardness, friability, assay and *in vitro* dissolution studies. The trial 'DC' *i.e.* tablet prepared by direct compression method had the better dissolution rate when compared to trial 'NAQ' and 'AQ' *i.e.* prepared by non aqueous and aqueous methods, respectively.

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