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Research Article

Formulation and Evaluation of Chewable Tablets of Mebendazole by Different Techniques

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ABSTRACT

The objective of the study was to develop an effective formulation of mebendazole chewable tablets. Mebendazole is a benzimidazole derivative with broad spectrum anthelemthic activity and excellent tolerability. Orally it is rapidly absorbed and metabolized to hydroxy and hydroxyamino, which may be responsible for its anthelmenthic action. It is widely used in the treatment of worm infestations in both humans and animals. Mebendazole chewable tablets (200 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: Mebendazole, Chewable Tablets, Granulation, Direct Compression

INTRODUCTION

Chewable tablets are designed for use by the children and such persons who may have difficulty in swallowing the tablets.[1] These are intended to be chewed in the mouth prior to swallowing and are not intended to be swallowed intact.[2] Additionally, chewable tablets facilitate more rapid release and hence more rapid absorption of active ingredients and provide quick onset of action.[3] Hence it was decided to formulate mebendazole chewable tablet to improve the compliance in children and to improve the solubility and dissolution.

Mebendazole is benzimidazole derivative that has been widely used in the treatment of worm infestations in both humans and animals. Mebendazole is widely employed in the treatment of intestinal nematode infection. Mebendazole has low water solubility, limiting its oral absorption and resulting in a lower bioavailability.[4] 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 mebendazole 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.[5]

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

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advantages in children with two years of age and above. In the present paper mebendazole 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 mebendazole chewable tablet by different technique and to evaluate these using different parameters.[6]

MATERIALS AND METHODS

Materials

Pure drug sample of mebendazole was procured from sequent scientific Ltd, Bangalore**.** All other ingredients *viz.* Lactose, Starch, Sodium starch glycolate, Isopropyl alcohol. Sodium Saccharine etc. used were of pharmaceutical grade.

Methods

(a.) Nonaqueous Granulation

All the ingredients were separately weighed and sifted using mesh no. 40. Mebendazole, 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 40-500 ^{0}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 513 mg weight each. A minimum of fifty tablets were prepared for each batch.

(b.) Aqueous Granulation

All the ingredients were separately weighed and sifted using mesh no. 40. Mebendazole, 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 40-500C 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 513 mg weight each. A minimum of fifty tablets were prepared for each batch.

(c.) Direct Compression

All the ingredients were separately weighed and sifted using mesh no. 40. Mebendazole, 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 513 mg weight each. A minimum of

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fifty tablets were prepared for each batch. The manufacturing formulas for the tablets used in the above three methods is given in table I.

EVALUATION OF TABLETS

(a.) General appearance[7]

The general appearance of all tablets, its visual identity and overall elegance is essential for consumer acceptance. The formulated chewable tablets were evaluated for size, shape, organoleptic characters such as, colour, odor and taste.

(b.) Dimensions[8]

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 ±5% variation of a standard value. Also the thickness must be controlled to facilitate packaging.

(c.) Weight variation[9]

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:-

Percentage deviation = [(Individual weight-Average weight) /Average weight]×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.

(d.) Bulk density (BD)

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 Mebendazole tablets were calculated and shown in Table III.

(e.) Tapped density (TD)[10]

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 Mebendazole tablets were calculated and shown in Table III.

(f.) Carr's Index[11]

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

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Compressibility index (%) = DT-DB x 100
Where,
DT= Tapped density
DB= Bulk density

(g.) Hausner Ratio
The Hausner Ratio of Mebendazole tablet was determined by the following equation.
Hausner Ratio = Tapped density / Bulk density
Value less than 1.25 indicates good flow, while greater than 1.25 indicates poor flow.

(h.) Hardness test
Hardness is a force required to break a tablet across the diameter. The hardness of a tablet is an indication of its strength. The hardness was measured using Monsanto Hardness tester. The values were expressed in Kg/cm2.

(i.) Friability test
The friability of tablets were determined by using Roche Friabilator. Ten tablets were weighed and placed in friabilator and rotated at 25 rpm for 4 minutes. Then the tablets were taken out, dusted and reweighed. The percentage friability of the tablets were calculated by the formula,
Percentage Friability = [(Initial Weight – Final Weight)/ Initial Weight] × 100

(j.) Disintegration test[12]
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 ^{0}C, preferably in a 1L beaker. For compressed uncoated tablets, the testing fluid was usually water at 37 ^{0}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.

(k.) Content Uniformity test
Weighed accurately quantity of the powder containing about 0.1 g of Mebendazole. 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 308 nm, Calculated the content of Mebendazole taking 742 as the specific absorbance at 308 nm.

(l.) *In-vitro* dissolution test[13]
The *in vitro* drug release studies were performed using USP dissolution apparatus Type II (paddle) using 900 ml of 0.1N hydrochloric acid as the dissolution medium. The temperature of the dissolution medium was maintained at 37±0.5oC and the paddle was rotated at 50 rpm. Aliquots were withdrawn at different time intervals of 10, 20 and 30 minutes and replaced by adding equal volume of fresh dissolution medium. The samples were suitably diluted and absorbance of the solutions was determined at the wavelengths of maximum and minimum absorbance at about 308 nm and 350 nm, in a UV- visible spectrophotometer.

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(m.) Drug content[14]

Five tablets were powdered and the blended equivalent to 200 mg of Mebendazole 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 Mebendazole tablets were within the range of 90% to 110% of stated amount of Mebendazole. From the data obtained it was found that 87% 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 Mebendazole tablets was in the following order AG<NG<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.

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

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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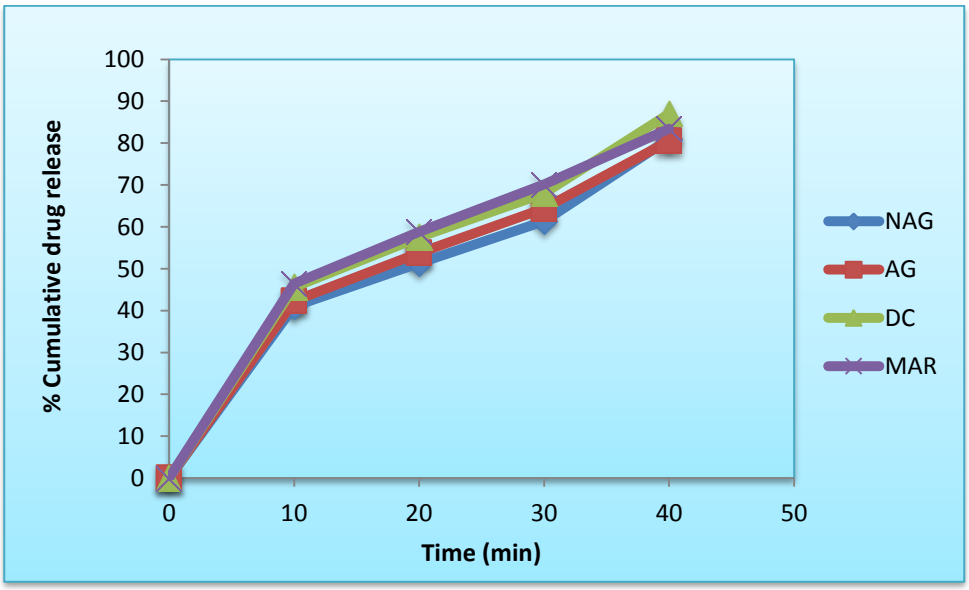

Fig. 1: Comparison of dissolution profiles of three batches of tablets and marketed product

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Table I: Manufacturing formulas for preparation of Tablet

S.No.	Name of the ingredients	Nonaqueous Granulation (mg/tablet)	Aqueous Granulation (mg/tablet)	Direct Compression (mg/tablet)
1.	Mebendazole	200	200	200
2.	Lactose mono.	100	100	100
3.	Starch	50	39.2	78.4
4.	Sodium starch glycolate	25.23	25.23	25.23
5.	Starch	20	39.2	--
6.	Isopropyl alcohol	q.s	--	--
7.	Purified water	--	q.s	--
8.	Mannitol	90	90	90
9.	Sodium saccharide	5	5	5
10.	Carmofine color	0.5	0.5	0.5
11.	Pineapple flavor	3	3	3
12.	Magnesium stearate	5	5	5
13.	Talc	5	5	5
14.	Aerosol	10	10	10

Table II Grading of the powder for their flow properties according to Carr's index

Percent Compressibility	Type of flow
5-15	Excellent
12-16	Good
18-21	Fare passable
23-25	Poor
33-38	Very poor
>40	Extremely poor

Table III.: Comparative evaluation of tablets using different parameter

Parameter	Tablets code			
	NAG	AG	DC	MAR
Weight of tablet (mg)	513±3.0	513±4.5	513±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 ration	1.14	1.14	1.14	---
Hardness (kg/cm2)	5.2±0.25	5.1±0.10	5.5±0.09	---
Friability test (%)	0.65	0.55	0.25	---
Desintegration time (min)	5	4	3.5	---
Dissolution time cumulative % of drug dissolved in 30 min	81	80.5	87	83.42
Drug content (mg)	99.50	99.20	99.70	--
Assay (%)	97	95	99	--

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