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FORMULATION AND EVALUATION OF ALBENDAZOLE CHEWABLE TABLET

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Abstract

Albendazole is a broad spectrum anthelmintic used against many helminths and is used for treatment of Threadworm, Hookworm and tapeworm. It has low bioavailability due to its first pass metabolism. Non Aqueous Granulation, Aqueous Granulation and Direct compression are the methods of preparation of Albendazole tablet. Tablet prepared by these three methods is evaluated for Average weight, Hardness, Cars index, Tapped density, Friability, Disintegration and dissolution.

Introduction

Albendazole benzimidazole derivative is a broad spectrum antibiotic. It is rapidly absorbed and metabolized to sulfoxide and sulfone, which may be responsible for anthelmintic action.Recent advances in novel drug delivery system aims to enhance the safety and efficacy of the drug by formulating a dosage form for the administration of the body. Difficulty in swallowing is experienced by patient such as pediatric, geriatric, bedridden, disabled and mentally ill. Fast chewable tablets are solid dosage form containing medical substances which disintegrate rapidly, usually within few seconds when placed upon tongue requiring no additional water to facilitate swallowing. Albendazole is quite hydrophobic and exhibits poor aqueous solubility. The powder exhibits poor flowability and compressibility. Considering the high drug dose, these API characteristics are relevant while formulating chewable tablets. Albendazole is tasteless or the taste is unknown, so a taste masking strategy is not required. Given the poor flowability of Albendazole, the chewable tablet cannot be prepared by roller compaction, so wet granulation is the method of choice. To successfully formulate chewable tablet of desired attribute, a judicious selection of Excipients is warranted. There is no consensus among Pharmacopoeias with respect to specifications for chewable tablets. The monograph for Albendazole chewable tablet is not included in any Pharmacopoeia except the International Pharmacopoeia.

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Mechanism of action

Albendazole is a member of the benzimidazole group of paraciticidal agents that disrupts parasite energy metabolism. It specifically causes degenerative alterations in worm cells by binding to colchicines-sensitive sites of β- tubulin, a constituent cell protein, thus inhibiting its assembly into microtubulin. The specific action of Albendazole against parasitic cells rather than mammalian cells is attributed to its preferential binding to parasitic β- tubulin [1].It leads to impaired glucose uptake by the adult and larval forms of the parasites, and eventually depletes glycogen storage. As a consequence, the production of adenosine triphosphate decreases because of insufficient glucose and leads to the death of parasites[2].

At higher concentrations, Albendazole also disrupts parasitic metabolic pathways by inhibiting metabolic enzymes involved in Krebs cycle, such as malate dehydrogenase and fumarate reductase.Albendazole also prevents the formation of the spindle-fiber needed for alignment of chromatin during cell division, which inturn inhibits cell division, egg production and development, and hatching of existing eggs. Lack of spindle formation also leads to reduced intracellular transport and cell motility[3]. Compared to other agents in the benzimidazole group, such as mebendazole, Albendazole has a higher activity in a single and dose of 400 mg against ascariasis, hookworm infection, trichostongylosis and enterobiasis and trichuriasis[4].

Side effects

Abnormal liver function and headache are the most common side effects of Albendazole treatment. In nearly 16 percent of patients receiving Albendazole, specifically for hydatid disease. The liver enzymes level increases to two to four times the normal level. This goes back to normal once treatment ends. Additional side effects reported include nausea, vomiting, dizziness, vertigo, fever, abdominal pain, temporary hair loss and increased cranial pressure. Some of the side effects are attributed to sudden destruction of parasitic larvae, which causes inflammation. Less common side effects are hypersensitivity in the form of rashes or hives, acute liver or renal failure, drop in the levels of white blood cells, reduced platelet counts, aplastic anaemia, and irreversible bone marrow suppression [5].

Absorption, distribution, metabolism and excretion

Albendazole is poorly absorbed from the gastrointestinal tract due to its low aqueous solubility. Oral absorption of Albendazole in humans is less than 1-5%. As Albendazole undergoes rapid first pass metabolism, its concentration are negligible or undetachable in plasma [6]. The sulphoxide is

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generally considered to be the active metabolite responsible for Albendazole's therapeutic activity. Absorption and metabolism are rapid, as demonstrated by the peak level of radioactivity after oral administration of C- Albendazole and of the intact drug (as sulphoxide) being reached within 2 to 3 hours.

A fatty meal enhances absorption, and a five fold increase in average plasma concentration of Albendazole sulphoxide was achieved when it was co-administered with a fatty meal in comparison to its fasted state. The improved absorption was attributed to increased dissolution of the water insoluble drug in the fatty matrix. [7].

Preparation of Albendazole chewable tablets

Preparation of Albendazole chewable tablet constitute 400 mg Albendazole that was prepared by wet granulation method. The quantity of Albendazole and Excipients were sifted through #30 mesh and all other ingredients were sifted through #40 mesh. Albendazole, maize starch, lactose monohydrate, microcrystalline cellulose (MCC) and sodium lauryl sulphate (SLS) were loaded into rapid mixer to get a dry mix. Povidone K-30 and sunset yellow supra were dissolved in purified water to get a binder. The above dry mix were granulated with binder solution and dried in the rapid dryer at 60˚C. The dried granules were passed through #30 mesh. Then the granules were mixed with croscarmellose sodium (CCS), sodium starch glycolate (SSG), sodium saccharin, orange flavour and peppermint flavour in a granulator for 10 minutes. After that the granules were lubricated with magnesium stearate and aerosil for 2 minutes. The lubricated blend was compressed into tablets by using 19.2×8.9mm punch oval shape and breakline on one surface to get a tablet of the 1000mg weight on 8 station single rotary tablet machine[8].

INGREDIENTS	QUANTITY TAKEN
Albendazole	400
Lactose monohydrate	269
Starch(intragranular)	274.1
Starch(for paste)	49
Colour Ponceau 4R	0.9
Sodium lauryl sulphate	5
Sucralose	6
Sacharrin sodium	3
Collodal anhydrous silica	5
Magnesium stearate	13

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Croscarmellose sodium	9
Flavour strawberry powder	16
Purified water	q.s

Evaluation of Granules [9,10]

The granules were evaluated for angle of repose, bulk density, tapped density, compressibility index and Hausner's ratio. The angle of repose of the powder or granule was determined by fixed funnel method to assess the flow property of the powder or granules. Bulk density is the ratio between a given mass of the powder or granules and its bulk volume. Tapped density is the ratio between a given mass of powder or granules and the constant or fixed volume of powder or granules after tapping. Bulk and tapped density were determined

using digital bulk density apparatus. The compressibility index and the Hausner ratio are determined by measuring both the bulk volume and tapped volume of a powder.

Formulation	Angle of repose ±SD	Bulk density (g/ml) ± SD	Tapped density (g/ml) ±SD	Carr's Index (%) ±SD	Hausner,s ratio
F1	27.97 ±0.34	0.42 ±0.022	0.65± 0.022	14.87±0.60	1.52± 0.008
F2	27.62 ± 0.55	0.40 ± 0.018	0.60±0.020	13.62±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	25.32 ± 0.78	0.38 ±0.037	0.67± 0.051	15.31±0.79	1.18±0.004
F5	25.71 ±0.59	0.43 ±0.025	0.72± 0.036	13.81±0.72	1.57±0.002
F6	27.89 ±0.37	0.40 ±0.021	0.71±0.035	15.30±0.70	1.55±0.002

IR Spectral Analysis [7]

The drug and polymer must be compatible with one another to produce a product stable, efficacious and safe. Drug and polymer interactions were studied by using FT-IR Spectrophotometer (Shimadzu, Japan). Samples were compressed with potassium bromide and transformed into disk and scanned between 4000-500 cm-1 in a SHIMADZU FT-IR spectrophotometer.

Evaluation of Tablets

General Appearance, Diameter and Thickness [8, 14]

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

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such as, colour, odor and taste. The diameter and thickness of the tablets were measured by using Vernier caliper.

Hardness [9]

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.

Weight variation [10]

Twenty tablets of each formulation were selected at random and weighed individually. The weight of individual tablets was noted. Average weight was calculated and the individual weights were compared with the average weight. The weight of not more than two tablets must not deviate from the average weight by more than 5%.

Friability [11,]

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,

Formulation	Thickness (mm)±SD	Hardness (kg/cm2)±SD	Weight variation (mg)±SD	%Friability ± SD	Disintegration time (sec) Mean±SD
F1	4.71±0.040	3.33±0.12	301.54±0.33	0.52±0.18	48.16±0.61
F2	4.54±0.039	3.41±0.31	300.65±0.32	0.60±0.14	57.11±0.42
F3	4.57±0.055	3.42±0.25	301.41±0.23	0.52±0.19	40.51±0.23
F4	4.87±0.045	3.36±0.13	301.48±0.64	0.58±0.11	54.20±0.55
F5	5.01±0.049	3.49±0.23	300.65±0.21	0.59±0.16	57.86±0.82
F6	4.83±0.042	3.42±0.37	301.41± 0.33	0.44±0.14	56.52±0.41

Content Uniformity Test

Weighed accurately quantity of the powder containing about 0.1g of Albendazole. Add about 150 ml of 0.1M Methanolic Hydrochloride Acid, shaked for 15 minutes and dilute to 250 ml with 0.1M Methanolic Hydrochloride acid, shaked for 15 minutes and dilute to 250 ml with 0.1 M Methanolic Hydrochloride acid, mixed and filtered and diluted 5 ml of the filtrate to 250 ml with 0.1 M sodium hydroxide, measured the absorbance of the resulting solution at Ymax of 309nm.

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FORMULATION	Content Uniformity Mean (%)±SD
F1	99.27±0.64
F2	95.98±0.55
F3	99.81±0.35
F4	98.85±0.20
F5	97.81±0.44
F6	98.92±0.81

InVitro Dissolution test

Dissolution measurements were carried out in a USP dissolution test apparatus. The dissolution profiles of Albendazole chewable tablets were studied in 0.1 N HCL (pH 1.2). The chewable tablets containing 400mg of Albendazole were placed in a rotating basket 50 rpm filled with 900ml of the dissolution medium, thermostated at 37±0.5˚C. At scheduled time intervals, the samples (5ml) were withdrawn and replaced immediately with fresh dissolution medium. The samples were assayed spectrophotometrically at 309nm for the dissolved drug, where samples were automatically filtered before measuring the absorbance against 0.1 N HCL as blank. The amount of Albendazole was calculated from the standard graph.

Result and discussion

Albendazole fast dissolving tablets of were pre-pared 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 parame-ters are showed in Table 2.

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/cm2. 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

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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% . Hardness was increases with time increases but in all cases, hardness was within the limit. Disintegra-tion time: at various storage conditions increases but maximum 40 second which is less than 1min (specifi-cation of IP). Dissolution studies shows there was no significant difference in dissolution data of formula-tions 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.

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