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Research Article

Comparative *In-Vitro* Antihelmintic Activity of Prepared, Branded and Generic Albendazole Samples in *Pheretima Posthuma*

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Abstract

Albendazole is a benzimidazole derivative with great tolerability and broad-spectrum anthelmenthic action. Albendazole tablets (400 mg) were made using 3 different methods: Non-aqueous granulation, aqueous granulation, and direct compression. The prepared tablets were then tested for various evaluation parameters, including average weight, hardness, tapped density, Carr's index, friability, and dissolution. The specifications were determined to be satisfied by every parameter. When compared to other batches and commercially available products, the investigation on the dissolution profile showed that product A3 (made using the direct compression method) had a quicker dissolving rate. The range of the assay values was between 90% and 110%. The main challenge in treating helminthes illness is the development of resistance in helminths to traditional anthelmintics. To clarify the prospective formulation, the anthelmintic activity of produced tablets was compared with that of the brand and generic allopathic dosage forms. For the *in vitro* comparative investigations on the anthelmintic activity against Indian worms (*Pheretima posthuma*), albendazole tablets were used in this work. For the activity, several concentrations of these formulations (10 mg/ml, 20 mg/ml, 30 mg/ml, 40 mg/ml) were utilised, with 0.5% of NaCl serving as the reference standard. To address the paralysis and death of earthworms, the results were expressed in terms of time in minutes.

Keywords: Benzimidazole derivative; Broad-spectrum anthelmenthic; Brand and generic allopathic dosage

Introduction

The principal degenerative diseases that impact a sizeable portion of the world's population include helminthes infections, sometimes known as helminthiasis. In developing countries, they pose a severe threat to public health because they increase the risk of pneumonia, eosinophilia, anaemia, and malnutrition. The parasitic helminths are typically found in the digestive tract of humans, while their larvae can also be found in tissue. In terms of morbidity and economic and social hardship, helminthiasis-related disorders are typically chronic and devastating, and they probably impact more humans and animals than any other class of parasites. Helminthiasis and parasitic worm infections can affect humans. Anthelminthic medications can eliminate worms in the GIT locally or eradicate adult helminths or developing versions that assault organs and tissues systemically [1].

Numerous formulations are given for their anthelmintic action in the allopathic medical system. These formulations' anthelmintic activity has not been quantitatively evaluated in order to recognise their impact. A benzimidazole derivative with high tolerance and broad range anthelmenthic action, albendazole [2]. Its anthelmenthic effect may be due to its oral fast absorption and metabolism to sulfoxide and sulfone. Ascarisis, hookworm, and enterobiasis cure rates with a single dosage of albendazole are equivalent to those following a 3-day mebendazole course. Its chemical name is carbamate of methyl [5-(propylsulphanyl)-1H-benzimidazol-2-yl].

For *in vitro* comparative investigations on the anthelmintic activity against *Pheritima posthuma*, several concentrations of albendazole (10 mg/ml, 20 mg/ml, 30 mg/ml, and 40 mg/ml) were utilised as a reference standard, and normal saline (0.9% NaCl) was used as the control treatment. The data were expressed in terms of time in minutes to reflect the earthworms' paralysis and time of death. The results of the investigation suggest that an anthelmintic impact exists [3,4].

Materials and Methods

Materials

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

Manufacturing procedure

Non-aqueous granulation: Each component was measured and sifted through mesh no. 40 individually. Albendazole, lactose monohydrate, and sucrose were combined for 10 minutes in a plastic bag. Isopropyl alcohol was used to dissolve starch to prepare PVPK 30 binder solution. The granulated aforesaid dry mixture was then dried in the tray dryer at a temperature of 40ºC to 50ºC until the moisture content was NMT-2%. Mesh number 30 was used to filter Mannitol (Perlitol 200) from the dried granules. The mesh number 60 was used to filter out pineapple flavour. Finally, all of these were combined with the dry granules for 10 minutes of blending. Magnesium stearate, Talc, and Aerosil were used to lubricate the aforementioned mixture for 2 minutes [5]. The flow characteristics of the powder mixes were assessed, and they were determined to be satisfactory. Using an 11.5 mm round flat punch, the assessed blend was crushed into tablets with a 400 mg weight each [6,7]. For each batch, a minimum of 250 tablets were created.

Aqueous granulation: Using mesh size 40, each component was individually weighed and sifted. Albendazole, lactose monohydrate, and sucrose were combined for 10 minutes in a plastic bag. Purified water was used to make the sucrose binder solution, and it was agitated with a glass rod until it was fully dissolved. The granulated aforesaid dry mixture was then dried in the tray dryer at a temperature of 40˚C to 50˚C until the moisture content reached NMT-2%. The granules were put through mesh number 30 after drying. Then, pineapple flavour was transferred through mesh number 60 after Mannitol (pearlitol200) was passed *via* mesh number 30. After adding all of them, the dry granules were mixed for 10 minutes. The aforesaid mixture was then lubricated for 2 minutes using magnesium stearate, talc, and aerosil. The powder mixture's flow characteristics were assessed, and they were determined to be favourable. The analysed mixture was compressed into tablets using a round; flat 11.5 mm punch to produce 400 mg tablets each tablet. For each batch, a minimum of 250 tablets were created [6].

Direct compression: Using mesh size 40, each component was individually weighed and sifted. Lactose monohydrate, sucrose, and albendazole were all passed through mesh number 30. The necessary amounts of mannitol (pearlitol 200), sodium starch glycolate, and pineapple flavour were mixed for 10 minutes in a poly bag after being passed through a 60 mesh sieve. The aforesaid mixture was then lubricated for 2 minutes with Magnesium stearate, Talc and Aerosil. The powder mixture's flow characteristics were assessed, and they were determined to be favourable [7]. The analysed mixture was compacted using a round, flat 11.5 mm punch into tablets weighing 400 mg each. For each batch, a minimum of 250 tablets were created. The formulae for 3 different methods were given in Table 1.

Table 1: Manufacturing formulae of Albendazole tablets by three methods

Method of manufacturing process	Non-Aqueous granulation A1	Aqueous granulation A2	Direct Compression A3
Ingredient	**mg/Tablet**	**mg/Tablet**	**mg/Tablet**
Intra granular			
Albendazole	200	200	200
Lactose mono.	100	100	100
sucrose	55	50	60
Binder preparation			
Sucrose		10	
Purified water	--	q.s	---
Poly vilnyl pyrolidone	5	--	--
Isopropyl alcohol	q.s	--	---
Extra granular			
Mannitol (perlitol SD200)	28	28	28
Talc	2.5	2.5	2.5
Aerosil	1	1	1
Pineapple flavor	1.5	1.5	1.5
Magnesium stearate	2	2	2

Evaluation of tablets

Weight variation: The average weight of 20 tablets was calculated after random selection. The minimal % variation was then calculated after weighing each pill individually, comparing it to the average weight.

Hardness test: Monsanto's hardness tester was used to assess hardness or tablet crushing strength (Fc), which is the amount of force needed to break a tablet in a diametric compression, 5 pills were tested, and the average result was noted [8].

Tensile strength: The Tensile strength (T) of the tablets was calculated using the following formula

$$T = 2Fc/\pi dt$$

Where,

Fc, d and t denote crushing strength, diameter and thickness of the tablet respectively.

Friability test: The Roche friabilator was used to assess the friability of tablets. In a plastic container that rotates at 25 rpm, this gadget shocks and abrades the tablets simultaneously. The friabilator was filled with a pre-weighed sample of tablets, and it was rotated 100 times. The tablets were reweighed after being dedusted using a delicate muslin towel. The formula, which yields the Friability (f),

$$f = (1\text{-}W_O/W)100$$

Where,

wo=weight of the tablet before the test

w=weight of the tablet after the test.

Disintegration test: A medicine must initially be in solution before it can be absorbed from a solid dosage form following oral administration, and the first crucial step towards this state is often the breaking up of the tablet, a process known as disintegration. The disintegration test calculates the amount of time needed for a batch of tablets to break down into small enough pieces to pass through a 10-mesh screen under a certain set of circumstances. The disintegration tester, which consists of a basket rack holding 6 plastic tubes open at the top and bottom with a 10-mesh screen covering the bottom of the tube, is used to conduct the disintegration test. The basket was submerged in a bath of appropriate liquid maintained at 37°C, ideally in a 1L beaker. The testing fluid for compressed uncoated tablets was typically water at 37°C, however some monographs specify the use of simulated stomach juice.

Drug content: A combination of 5 tablets that contained 200 mg of albendazole was weighed and dissolved in the appropriate amount of water. Filtered and appropriately diluted, the solution was then examined spectrophotometrically at 307 nm for drug content. The prepared sample was examined 3 times [9]. The data is given in Table 2.

Table 2: Comparative evaluation data of Albendazole tablets with marketed tablets

Ṭ9	Tablets code			
	A1	A2	A3	Marketed
Weight of tablet (mg) ± S.D	4000 ± 0.23	398 ± 0.33	400 ± 0.12	398 ± 0.17
Hardness (kg/cm2) ± S.D	5	5.1	6	5.2
Friability test (%)	0.19	0.18	0.16	0.17
Drug content (mg)	99.85	99.75	99.95	99.8
Assay (%)	100	99	99	99
Dissolution time cumulative % of drug dissolved in 60 min	93	85	99	93
Disintegration time (min)	10	9	8	11

Collection of different albendazole samples: Different samples of Albendazole tablets (Branded and Generics) were collected from various pharmacy stores, Vijayawada.

Collection of earthworms: Adult Indian Earthworms (8 cm long) were collected from rose plant garden, Madhuranagar, Vijayawada.

Procedure: The anthelmintic technique was performed on the adult Indian earthworm *Pheritima posthuma*. Prior to adding them to Petri dishes, 3 samples of each kind of albendazole generic, brand-name, and prepared were diluted with sterile saline to reach concentrations of 10 mg/ml, 20 mg/ml, 30 mg/ml, and 40 mg/ml. Different albendazole samples were diluted in normal saline to produce concentrations of 10 mg/ml, 20 mg/ml, 30 mg/ml, and 40 mg/ml. Simple saline solution (0.9% NaCl) served as control [10]. These various dilutions were consequently added to the Petri dishes. For the experiment 6 groups of earthworms (n=6) were chosen. Each Petri dish had an arrangement of nearly equal sized 8 cm long earthworms [11].

Results and Discussion

Comparative evaluation of tablets

With the batches of tablets that had been manufactured, all assessment tests were successful. The strength of the tablets was evaluated using a Monsanto hardness tester. All the tablets had good hardness. For all of the batches of tablets, the friability test was conducted. The friability of all the prepared tablets was less than 0.2%, which was adequate. The assay result of albendazole tablets fell between the range of 90% and 110% of the prescribed dosage. According to the findings, with the direct compression albendazole tablets, 99% of the medication was released after 30 minutes. Since it was determined from the evaluation data that tablets made using the direct compression method (A3) produced good results, these tablets were chosen for additional research.

Comparison of anthelminthic activity of Albendazole tablets, generic and branded drugs

The mortality and paralysing periods of the *in vitro* anthelmintic activity were recorded. One-way ANOVA was used to statistically analyse the data. The data were presented as mean SD using Graph Pad Prism. The results showed that at a concentration of 10 mg/ml, albendazole G3 showed the best activity for death time (53.00 min ± 3.000 min), whereas albendazole B2 showed the greatest activity for death time (38.67 ± 1.528). At a dosage of 20 mg/ml, albendazole G1 displayed the best activity for death time (45.00 ± 4.357), whereas albendazole B2 had the greatest activity for death time (28.67 ± 1.155). The quickest death times for the 30 mg/ml concentration were recorded by albendazole G1 (37.33 ± 3.215) and albendazole B2 (27.00 ± 1.000), respectively.

Tables 3-5 display the paralysis and death times of several albendazole samples and the standard. The study found that both brand-name and generic albendazole have significant efficacy at higher doses (40 mg/ml). The B2 sample of the different samples had improved effect at a higher dosage (40 mg/ml) when compared to the G1 albendazole. Figures 1-3 represent the antihelminthic activity on pheretimaposthumafor generic, branded and prepared formulations respectively on 4 different concentrations. The mortality times of brand-name and generic albendazole at various concentrations are shown in Figures 4 and 5.

Table 3: *In vitro* anthelminthic effect of different generics of albendazole and prepared albendazole tablets against *Pheritima posthuma*

Treatment	Generic	Concentration	Paralysis Time (min)	Death Time (min)
Sample 1	G1	10 Mg/ml	45.6 7 ± 6.028	53.00 ± 3.606
		20 Mg/ml	38.00 ± 5.000	45.00 ± 4.357
		30 Mg/ml	29.33 ± 2.517	37.33 ± 3.215
		40 Mg/ml	22.33 ± 0.5774	32.00 ± 2.000
Sample 2	G2	10 Mg/ml	47.33 ± 4.041	53.67 ± 4.041
		20 Mg/ml	40.00 ± 2.646	46.00 ± 3.606
		30 Mg/ml	34.33 ± 2.887	40.00 ± 1.000
		40 Mg/ml	29.67 ± 1.528	37.67 ± 2.082
Sample 3	G3	10 Mg/ml	47.00 ± 3.606	53.00 ± 3.000
		20 Mg/ml	40.67 ± 1.528	47.67 ± 3.055
		30 Mg/ml	33.33 ± 1.528	41.67 ± 2.517
		40 Mg/ml	30.00 ± 2.000	38.67 ± 3.786

Table 4: *In vitro* anthelminthic effect of different brands of albendazole and prepared albendazole tablets against *Pheritima posthuma*

Treatment	Brand	Concentration	Paralysis Time (min)	Death Time (min)
Sample 1	B1	10 Mg/ml	42.33 ± 2.517	49.00 ± 2.646
		20 Mg/ml	35.33 ± 2.082	43.00 ± 1.000
		30 Mg/ml	26.00 ± 1.000	33.00 ± 1.000
		40 Mg/ml	20.67 ± 0.5774	29.00 ± 2.646
Sample 2	B2	10 Mg/ml	33.33 ± 2.517	38.67 ± 1.528
		20 Mg/ml	23.67 ± 2.082	28.67 ± 1.155
		30 Mg/ml	21.67 ± 1.528	27.00 ± 1.000
		40 Mg/ml	19.00 ± 1.732	23.67 ± 2.082
Sample 3	B3	10 Mg/ml	43.33 ± 1.528	51.33 ± 1.155
		20 Mg/ml	34.67 ± 3.215	40.33 ± 3.055
		30 Mg/ml	28.67 ± 2.309	34.67 ± 2.309
		40 Mg/ml	24.33 ± 3.786	31.00 ± 3.000

Table 5: *In vitro* anthelminthic effect of B2 albendazole sample and prepared albendazole tablets (A3) against *Pheritima posthuma*

Treatment	Brand	Concentration	Paralysis time	Death time
Sample 2	B2	10 Mg/ml	33.33 ± 2.517	38.67 ± 1.528
		20 Mg/ml	23.67 ± 2.082	28.67 ± 1.155
		30 Mg/ml	21.67 ± 1.528	27.00 ± 1.000
		40 Mg/ml	19.00 ± 1.732	23.67 ± 2.082

Figure 1: Anthelminthic activity on *Pheretima posthuma* by using generic sample (G1) on 4 different concentrations

Figure 2: Anthelminthic activity on *Pheretima posthuma* in trail 2 using branded sample (B2) in 4 different concentrations

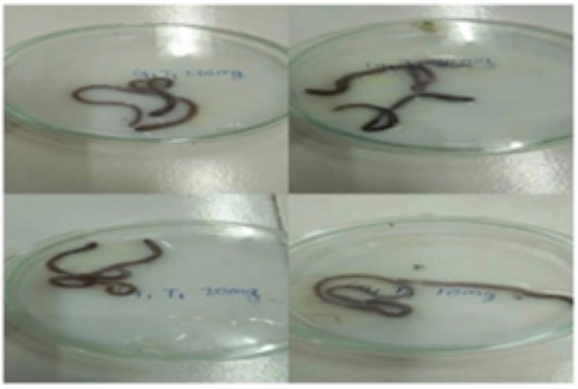

Figure 3: Anthelminthic activity on *Pheretima posthuma* on Albendazole tablets prepared by direct compression method (A3) in 4 different concentrations

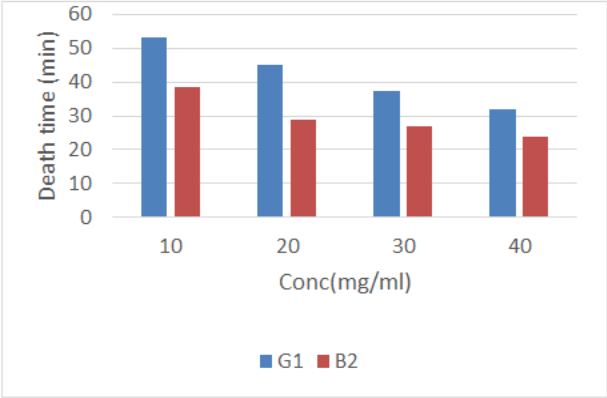

Figure 4: Comparative studies of death time of the effective generic (G1) and the effective brand (B2)

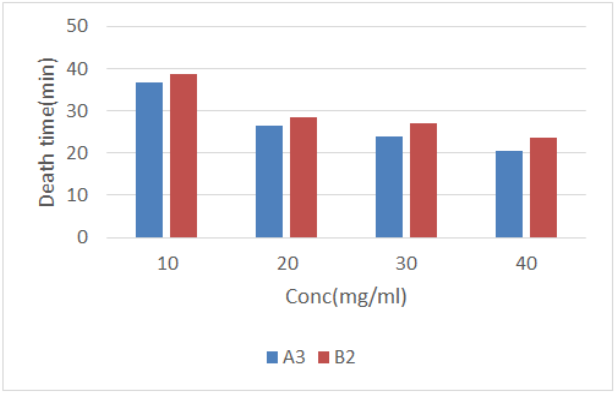

Figure 5: Comparative studies of death times of prepared chewable formulation (A3) and Brand (B2)

Conclusion

When compared to the evaluated brands and generic albendazole samples, B2 demonstrated exceptional efficacy, according to the data from the findings. The prepared albendazole formulation (A3), however, showed shorter paralysis and death times when compared to B2, indicating that A3 is more effective and may quickly kill the worms in a shorter amount of time. The findings of the present investigation show that the formulation of albendazole (A3) prepared by direct compression method has a significant effect on the ability to paralyse earthworms and to induce death in a relatively short period of time.

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Conflict of Interest

Authors have no conflict of interest to declare.

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