Formulation and evaluation of fast dissolving tablet of mebendazole

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Abstract

In this study, the focus was on enhancing the therapeutic effectiveness of Mebendazole, a broad-spectrum anthelmintic with applications against various helminths such as Threadworm, Hookworm, and Tapeworm. Recognizing the limitations of its bioavailability due to first-pass metabolism, the research aimed to design fast-dissolving tablets of Mebendazole to facilitate a rapid onset of action.

The primary objective was the formulation of Mebendazole fast-dissolving tablets, targeting an improved dissolution rate and subsequently enhancing the drug's bioavailability. This was achieved through the utilization of direct compression and the incorporation of different concentrations of super disintegrant, which play a crucial role in breaking down the tablet for faster dissolution. The tablets were subjected to rigorous pre-compression parameter assessments to ensure their quality. By assessing various parameters related to fast dissolving tablet, this research contributes to the development of an effective and patient-friendly mebendazole formulation.

Key Words: Mebendazole, superdisintegrant, in vitro disintegration, dissolution, anthelmintic

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1. Introduction:

In recent times, significant progress has been made in innovative drug delivery systems with the primary goal of improving the safety and effectiveness of drug molecules. This progress involves the development of dosage forms tailored for specific modes of administration. Many patients, such as pediatric, geriatric, bedridden, disabled, and mentally ill individuals, encounter challenges in swallowing conventional tablets. To address this concern, the emergence of fast dissolving tablets has proven to be transformative (1,2)

Fast dissolving tablets are solid dosage forms that incorporate medicinal compounds. These tablets disintegrate rapidly upon contact with the tongue, often within a matter of seconds, eliminating the need for additional water to aid in swallowing. This advancement has the potential to greatly enhance patient compliance and ease of drug administration (3).

Mebendazole, a potent broad-spectrum anthelmintic, has proven efficacy against a range of helminthic infections, including Threadworm, Hookworm, and Tapeworm. However, its therapeutic potential is hindered by limited bioavailability attributed to the challenges of first-pass metabolism. To address this limitation and expedite the onset of action, the present study was undertaken with the objective of formulating fast-dissolving tablets of Mebendazole (4,5)

One of the fundamental techniques in the development of fast-dissolving tablets (FDTs) involves the incorporation of superdisintegrant into the formulation. This is particularly important for enabling rapid tablet disintegration when the tablet is placed on the tongue, leading to the immediate release of the drug into the saliva. Key superdisintegrants employed in this approach include cross-linked Croscarmellose Sodium, Polyvinyl Pyrrolidone K30, Microcrystalline Cellulose, and Crospovidone, among others (6, 7).

As we delve into the world of formulating and evaluating fast dissolving mebendazole tablets, we embark on a scientific odyssey that bridges the gap between traditional pharmaceutical dosage forms and contemporary patient needs. By synergizing pharmaceutical expertise with the demands of modern healthcare, this research holds the potential to reshape therapeutic landscapes, providing a glimpse into a future where medication administration is both efficient and patient-friendly.

2. MATERIAL AND METHODS

Mebendazole, Crospovidone, Microcrystalline cellulose and Croscarmellose sodium were obtained as gift sample and all chemicals and reagents used were of analytical grade.

2.1 Preparation of fast dissolving tablets (8)

Fast dissolving tablets containing Mebendazole were created through the direct compression method, utilizing superdisintegrants like Microcrystalline Cellulose (MCC), Crospovidone (CP), Croscarmellose Sodium (CCS), and Polyvinyl Pyrrolidone K30 (PVPK30). The formulation involved thoroughly mixing the equivalent of 200mg Mebendazole with Mannitol and Microcrystalline Cellulose in a glass mortar using a pestle. The specific superdisintegrants were then added to the powder mixture as per each formulation's requirements, followed by the addition of Aspartame and Magnesium Stearate. The entire mixture underwent double sieving through Sieve No. 60. The tablet preparation was carried out using a 12mm round flat-faced punch on a rotary tablet machine. The compression force applied was consistent across all formulations, and the details are provided in Table 1.

Table 1: Formulation of Mebendazole 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**
Mebendazole (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 (%)

2.2 Pre-compression parameters

2.2.1 Angle of Repose (9)

The angle of repose was evaluated employing the fixed funnel method. The blend was introduced into a funnel that could be vertically elevated until achieving the maximum height of the formed cone (h). The radius of the resultant heap (r) was gauged, and the angle of

repose was computed using the provided formula ($\theta = tan^{-1}$ (h/r) Where, θ is angle of repose, h is height of pile and r is the radius of the base pile.

2.2.2 *Bulk Density (10)*

Apparent bulk density *(LBD)* was determined by pouring blend into a graduated cylinder. The bulk volume *(Vo)* and weight of powder *(M)* was deter- mined. The bulk density was calculated using the formula

$$LBD = \frac{\text{Weight of the powder(M)}}{\text{Volume of the packing(Vo)}}$$

2.2.3 *Tapped Density (11)*

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

$$\text{Tapped density} = \frac{\text{Weight of the powder(M)}}{\text{Tapped volume of the packing(Vt)}}$$

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.

2.2.5 *Hausner Ratio (9)*

Hausner ratio is an indirect index of ease of powder flow. It is calculated by the following formula.

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

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

2.3 Post compression parameters

All the batches of tablets were evaluated for various parameters like weight variation, friability, hardness, drug content, disintegration and dissolution etc.

Table 2: Physical properties of powder blend.

Formulations	Angle of Repose (°) ±SD	Bulk Density (g/ml) ±SD	Tapped Densi-ty(g/m) ±SD	Carr's Index (%)±SD	Hausner's Ratio Mean±SD
F1	26.37±0.22	0.34±0.011	0.63±0.021	15.66±0.55	1.45±0.003
F2	27.42±0.44	0.39±0.012	0.59±0.019	14.62±0.37	1.34±0.002
F3	26.35±0.29	0.32±0.014	0.69±0.014	11.51±0.69	1.21±0.006
F4	25.12±0.38	0.34±0.027	0.66±0.011	16.32±0.89	1.22±0.010
F5	25.56±0.33	0.39±0.021	0.71±0.033	14.71±0.79	1.34±0.012
F6	25.83±0.76	0.39±0.022	0.68±0.032	13.86±0.42	1.53±0.002
F7	26.45±0.43	0.38±0.022	0.61±0.034	11.41±0.25	1.51±0.006
F8	25.67±0.32	0.40±0.011	0.65±0.028	15.65±0.71	1.42±0.09
F9	27.32±0.28	0.41±0.015	0.59±0.041	15.31±0.80	1.54±0.010
F10	23.28±0.19	0.44±0.015	0.69±0.011	14.40±0.80	1.50±0.017

Table 3: Evaluation data of the prepared Mebendazole 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	3.66±0.041	3.34±0.11	299.24±0.35	0.32±0.11	47.26±0.51	41.21±0.22	90.68±0.58	96.27±0.62
F2	3.45±0.038	3.41±0.22	299.22±0.31	0.50±0.12	58.12±0.41	39.80±0.12	88.27±0.75	95.59±0.53
F3	3.36±0.053	3.32±0.45	300.41±0.34	0.51±0.16	41.41±0.23	34.45±0.20	107.34±0.80	98.71±0.25
F4	4.45±0.035	3.43±0.11	301.51±0.24	0.55±0.10	53.21±0.45	35.15±0.23	91.45±0.45	97.75±0.23
F5	4.02±0.044	3.34±0.34	299.30±0.21	0.54±0.14	56.46±0.52	36.75±0.35	89.36±0.79	97.81±0.42
F6	3.73±0.022	3.24±0.33	299.41±0.31	0.45±0.12	57.51±0.40	36.44±0.34	96.28±0.71	97.92±0.85
F7	3.47±0.034	3.21±0.32	299.30±0.11	0.52±0.11	48.52±0.84	36.90±0.47	90.91±0.78	96.57±0.38
F8	3.43±0.040	3.20±0.02	301.55±0.22	0.51±0.22	50.69±0.74	35.48±0.51	84.69±0.53	99.24±0.29
F9	3.34±0.042	3.34 ±0.11	300.20±0.32	0.61±0.13	56.60±0.60	38.11±0.32	91.65±0.84	98.69±0.63
F10	3.63±0.032	3.36±0.11	300.21±0.25	0.65±0.22	50.92±0.59	37.50±0.42	90.90±0.74	97.78±0.84

3.0 Result and Discussion:

Mebendazole fast dissolving tablets were prepared using the direct compression method, incorporating superdisintegrants like Crospovidone, Croscarmellose sodium, and Microcrystalline Cellulose. The flow properties, as indicated by the angle of repose (ranging from 23.28 to 27.42°), demonstrated favorable flow characteristics. The bulk density and tapped density values ranged from 0.32 to 0.44 (g/ml) and 0.59 to 0.71 (g/ml), respectively. The Carr's Index (11.41 to 16.32) and Hausner ratio (1.21 to 1.54) values fell within acceptable limits, indicating good flowability. The friability test showed minimal loss (less than 0.61%), meeting IP specifications.

The tablet thickness ranged from 3.34 to 4.45 mm, suggesting suitability for packaging. Content uniformity ranged from 95.59% to 99.24%, ensuring consistent drug distribution. Tablet hardness ranged between 3.20 to 3.43 kg/cm^2, signifying satisfactory mechanical strength.

Disintegration time, a critical attribute of fast dissolving tablets, was within 1 minute (41.41 to 58.12 seconds), indicating rapid dissolution in the oral cavity. Wetting time ranged from 34.45 to 41.21 seconds, and the water absorption ratio was between 84.69 and 107.34, indicating efficient water uptake.

During storage for 0, 30, 60, and 90 days, tablet hardness increased slightly, but it remained within the acceptable range. Disintegration time also increased slightly under various storage conditions but remained below 1 minute, indicating stability in disintegration properties over time.

4.0 Conclusion:

The formulation and evaluation of a fast dissolving tablet of mebendazole offer a promising approach to improve the drug's solubility and dissolution rate. The study aimed to enhance patient compliance by providing a convenient dosage form that addresses challenges associated with conventional mebendazole tablets. By assessing various parameters related to fast dissolving tablet, this research contributes to the development of an effective and patient-friendly mebendazole formulation. Further clinical studies are warranted to validate the therapeutic effectiveness of the fast dissolving tablet and its potential benefits in the treatment of parasitic infections.(12-47)

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