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Quality Assessment of Seven Brands of Albendazole Tablets Marketed in Yemen

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ABSTRACT

Objective: To assess certain quality control parameters for seven brands of albendazole tablets obtained from different retail pharmacies.

Methods: The physicochemical properties and active ingredientsofseven randomly selectedbrands of albendazole tablets were assessed weight uniformity, hardness, friability, disintegration and dissolution

Results: All seven albendazole brands met the British Pharmacopeia (BP) quality control standards of weight uniformity, friability and the active ingredient content. Five brands met the BP disintegration criterion,whereas only two brands complied with the BP quality control parameters of the dissolution specifications.

Conclusions: Out of the seven brands of albendazole (400 mg) tablets, only two fulfillthe BP quality control standards and show physicochemicalquivalence. This emphasizes the need for regular assessment of marketed drugs to assure equivalenceof these drugs to their innovators.

Keywords: Quality, Albendazole, disintegration, dissolution ,Tablets, Yemen

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1. Introduction

One of the major health problems is parasitic infection, particularly in the third world countries. Moreover, it has been recognized that there is evidence of emerging resistance to all major animal anthelmintics. One of the most effective wide-spectrum anthelmintic agents is Albendazole (1).

Selection of pharmaceutical products from several generic drug products having the same active ingredients is a matter of concern for healthcare practitioners. The first step to assure therapeutic equivalence of any drug product involves assuring the chemical and biopharmaceutical equivalence of such drug (2).In developing countries, assurance of quality and interchangeability of multisource drug products poses a challenge (3). Clinical response variability and batch inconsistency among generic drugs have been reported (4). For instance, such discrepancy has been demonstrated among metformin and metronidazole tablets (4).

Most oral dosage forms rely heavily on in vitro dissolution studies to predict their in-vivo bioavailability (6, 7). Drug dissolution testing not only plays an essential role in the monitoring of batch-to-batch consistency but also acts as a surrogate parameter for in vivo bioavailability (8). As in other developing countries, few drug quality control studies have been conducted so far in Yemen (9-13). studies reported that such drugs are often obtained irrespective of the quality standards. Moreover, drug quality standardization during purchasing is not implemented by non-governmental organizations in such countries (14).

The present study aimed to assess certain quality control parameters of seven brands of albendazole tablets obtained from different regions of Yemen. The findings of the present study can be used as a source of information to drug manufacturers and drug regulatory authorities in the country.

2. Methods

2.1. Study design

This was a comparative in-vitro study to assess a number of quality control parameters of albendazole tablet brands locally distributed in the Yemeni market, including weight variation, hardness, friability as well as disintegration and dissolution times of such brands.

2.2. Sample collection and identification

Albendazole tablets (400 mg) of seven commercial brands were conveniently purchased from pharmacies in the Yemeni market. Six brands were in the form of uncoated compressed tablets, while the seventh brand was in the form of coated tablets. All the obtained tablets were coded with the letters A to G (Table 1). These were stored according to manufacturers' instructions prior to investigations, and codes were removed after performing the investigations. Study samples were collected in the period from 20 February to 20 March (2013) from four Yemeni governorates; namely, Sana'a, Ibb, Marib, and Hodeidah.

2.3. Quality assessment procedures

Different analytical quality control tests for the development and manufacture of pharmaceutical formulations (15) were used for the assessment of albendazole tablet brands in the present study. These tests included:

2.3.1. Weight variation test

Ten tablets of each brand were weighed using an analytical weighing balance (OHUAS Adventurer®, New Jersey, USA; Model: AR2140). The average

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weight and the percentage weight variation from the mean value were obtained for each brand. Appropriate tablet hardness and friability is attributed to weight controlling within a tight range, where the percentage weight variation was ensured not to exceed 5% (16). The average weight variations for all brands of albendazole tablets were calculated mathematically using the following equations (17):

Highest weight variation = (Highest weight – Average weight/Average weight) × 100

Lowest weight variation = (Lowest weight – Average weight/Average weight) × 100

Table 1. Identity and specification of albendazole brands included in the present study*

Country of origin	Code	Batch number	Manufacturing date	Expirydate
France	A	314567	01-02-2012	01-02-2017
India	B	11al02	01-10-2011	01-09-2014
India	C	Kw2748	01-10-2012	01-09-2015
Yemen	D	106t	01-02-2013	01-02-2016
India	E	180212	01-09-2012	01-10-2015
Cyprus	F	37909	01-09-2008	01-09-2013
South Korea	G	7903p	01-10-2009	01-10-2014

* The strength of all brands was 400 mg.

2.3.2. Hardness test

The hardness of 10 tablets selected randomly from each brand was determined using a tablet breaking-strength tester (Germany, PHARMA TEST: PTB). The hardness for each tablet was recorded, and the mean hardness was calculated according to well-established equations (18).

2.3.3. Friability test

Five albendazole tablets were dusted and weighed together before friability testing using a US Pharmacopoeia (USP)-compatible friabilator Germany (PHARMA TEST: PTB) which was set to run for four minutes at a speed of 25 rounds per minute (rpm). After removing the tablets from the friabilator, they were dusted and re-weighed. Friability was calculated using the following equation (16):

% Friability = (Wi – Wf) / Wi) × 100
Wi= weight of tablet before friability
Wf = weight of tablet after friability

Conventionally, compressed tablet weight loss was generally ensured to be less than 0.5 to 1% (17).

2.3.4. Disintegration time test

Disintegration time of uncoated tablets was determined using a USP disintegration tester (Electrolab, Mumbai, India; Model: ED-2L) in 0.1 N HCl medium at 37±1 °C according to the British Pharmacopoeia (BP) (16). For each albendazole brand, six tablets were selected and placed in separate cylindrical tubes in a basket rack. The time required for each tablet to disintegrate and pass out through the mesh was recorded, and the mean disintegration time for each brand was then calculated (19).

2.3.5. Dissolution time test

Drug release pattern during a specific period was determined by dissolution time testing (20). The drug release pattern for each brand of albendazole was determined using a dissolution tester (Pharma Test, Hainburg, Germany; Model: PT-DT70). The dissolution process was carried out in a medium of 900 ml 0.1 N HCl using a speed of 50 rpm at 37±1 °C. Up to three 5-ml samples were withdrawn every 10 minutes and replaced with the same amount of fresh dissolution medium. The obtained samples were suitably diluted and analyzed for albendazole using high-performance liquid chromatography (HPLC) at 254 nm using Shimadzu HPLC system (Shimadzu, Kyoto Japan), where the percentage of drug release was calculated after measuring the absorbance (17, 20).

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2.3.6. Content uniformity test

Active ingredient uniformity test of the tablets was carried out using HPLC (Shimadzu, Kyoto, Japan). Methanol and buffer in a ratio of 700:300 were used as the mobile phase. The flow rate of the mobile phase was 2ml per minute, and the injection volume of the sample was 20 µl. Albendazole detection wavelength was set at 254 nm. Active ingredient chemical identification and content uniformity tests were carried out according to the BP, 2002 (35).

2.4. Data analysis

Weight uniformity, hardness, friability as well as disintegration and dissolution times of albendazole tablets of each brand were analyzed by calculating the mean ± standard deviation (SD) for each parameter using IBM SPSS Statistics version 21.0for Windows (IBM Corp., Armonk, NY, USA).

3. Results

3.1. Weight variation, crushing strength and friability of albendazole brands

Table (2) shows the physicochemical properties of the seven albendazole tablet brands. The mean weight ranged between 910.9 mg for brand F to 1175.7 mg for brand B, while the mean crushing strength ranged between 8.46 kilogram-force (KgF) for brand F to 23.68 KgF for brand B. On the other hand, the percentage friability was in the range of 0.030.49 % for the tested brands.

3.2. Disintegration time, dissolution time and content uniformity of albendazole brands

Table (3) shows that the mean disintegration time for the tested albendazole tablet brands ranged from 4.25 to 30.00 minutes, while the mean dissolution time ranged from 0.80 to 85.62 minutes. On the other hand, albendazole content uniformity ranged from 95.0 to 105.2 grams.

Table 2. Unofficial quality control parameters for seven brands of albendazole tablets (400 mg) marketed in Yemen

Brand code	Weight uniformity (mg) (mean ± SD)	Crushing strength (KgF) (mean ± SD)	Friability (w/w) (%)
A	1030.1 ± 1.9	13.9 ± 0.8	0.27
B	1175.7 ± 0.5	23.68± 1.6	0.11
C	1170.4 ± 1.2	20.5 ± 3.1	0.41
D	970.0 ± 1.4	10.18 ± 2.2	0.39
E	980.3 ± 1.6	14.04 ± 1.6	0.49
F	910.9 ± 0.8	8.46 ± 0.3	0.36
G	930.1 ± 0.8	14.02 ± 1.9	0.03
Limit	± 5	>5kg/cm^2	<1%

SD, standard deviation

Table 3. Official quality control parameters forseven brands of albendazole tablets (400 mg) marketed in Yemen

Brand code	**Disintegration time** (min) (mean ± SD)	**Dissolution time** (after 30 min) (mean ± SD)	**Active ingredient uniformity** (mg) (mean ± SD)
A	5.83 ±0.133	77.83 ± 0.023	105.2±2.449
B	30.00± 0.419	8.38 ± 0.009	95.0 ±1.659
C	10.00± 0.313	0.80 ± 0.003	103.7±2.414
D	30.00± 0.724	57.18 ±0.020	99.4±1.414
E	4.25± 0.558	49.33 ±0.030	100.0 ±4.765
F	5.52± 0.755	17.50 ±0.020	99.5±5.224
G	8.00± 0.425	85.62 ±0.018	95.7±1.760
Limits	< 15	>70%	93-107%

SD, standard deviation

4. Discussion

Up to the best of our knowledge, this study is the first quality control study of the anthelmintic albendazole tablet brands distributed in Yemen. Among the seven tested products of albendazole, only two brands (29%) met the BP quality specification. However, five brands (71%) failed to fulfill the quality control standards. These findings are similar to those of previous studies in Rwanda and Bangladesh, which revealed that the existence of substandard formulations at purchase time is due

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to manufacturers' errors (9, 21, 22). On the contrary, these findings are not in line with previous studies from Yemen, Rwanda and Tanzania, which did not find substandard formulations at purchase time (12, 23).

The quality of manufactured drugs might be affected by several factors such as storage conditions, humidity, packaging materials, transportation, formulation constituents and the nature of the active ingredient that is considered as the most important factor. When the strength is greater than 250 mg, the tablet weight variation meets the requirements if not more than two of the individual weights deviate from the average weight by more than ±5% and none of them deviates by ±10% according to the specifications outlined in the BP. The present study showed that all brands of albendazole tablets have acceptable uniformity of weight because none of the brands has a percentage deviation in weight greater than 5% as specified by the BP.

Tablet hardness gives an insight as to the tablet tooling used by various manufacturers; a force of about 5 kg/cm is the minimum requirement for satisfactory hardness of tablets (24, 25). Generally, all the studied brands passed the hardness and friability specifications of tablet dosage forms. In fact, the difference in tablet sizes, such as weight, diameter and thickness, may have negative psychological impact on the clinicians and on their patients since such a difference might rise up doubt about the equivalence of brands (26). Regarding the unofficial tests all albendazole brands fulfilled crushing strength/hardness specifications. The utmost hardness of 23.65 kg/cm2 was achieved by B product

Adequate hardness and friability of a tablet are necessary for consumer satisfaction (27). The USP states that a tablet friability value should be less than 1% (36).The present study showed that the friability values for all albendazole brands were acceptable, ranging between 0.03% w/w and 0.49% w/w. Tablets with the highest crushing strengths showed a low friability value similar to those for ciprofloxacin brands conducted elsewhere (28).

Tablet disintegration in the gastrointestinal tract is an essential step for drug absorption and bioavailability, and subsequently therapeutic efficacy of medicines (29). In the present study, the brands B and D showed the longest disintegration time of 30.0 minutes. However, the brand E showed the least disintegration time of 4.25 minutes, which might be attributed to the presence of a large amount of disintegrants. According to the USP, the disintegration time of uncoated tablets is up to 15 minutes. Accordingly, the brands B and D exceeded the allowed time, while other brands were within the acceptable limits. It is noteworthy that the batches with longer disintegration times correlate with higher hardness and lower friability values. On the other hand, the brand B had the highest crushing strength and is, therefore, expected to have a longer disintegration time. This finding is in contrary with the fact that tablets with high hardness and compression force values had short disintegration times (30). However, the finding of this study is similar to other studies showing that an increase in the tablet compression pressure leads to a longer disintegration time (31, 32).

Tablet dissolution is a necessary criterion for drug bioavailability. Therefore, tablet dissolution test is considered a critical quality control parameter to ascertain batch-to-batch equivalence as well as product uniformity (33, 34). It is noteworthy that the USP specifies the dissolution time to be not more than 30 minutes (35). All tablets should release the active gradient into the dissolution medium in an amount not less than 60% of the labeled albendazole. On the other hand, the BP state that not less than 70% of a drug should be released at 30 minutes (35). The findings of the present

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study showed that all brands except A and G released less than the accepted amount of their content within the time allowed. It has been described that albendazole tablets should contain not less than 93.0% and not more than 107% of the stated amount (36). The finding of the present study revealed that all albendazole brands met the standard criteria of the (36) for active ingredients. BP specifies that the potency of albendazole tablets should be between 95.0% and 105.0%, i.e., 100.0% ±5.0%.

5. Conclusions

Only two of the seven selected albendazole brands marketed in Yemen meet the BP quality standards. The two brands are physically and chemically equivalent to each other, so they can be used interchangeably during practice. This study highlights the problems associated with multi-component dosage drugssuch as albendazole, where the efficacy of such drugs relies on the precise amount of the active ingredients in the tablet and their release rate.

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Competing interests

The authors declare that they have no competing interests associated with this article.

Ethical approval

Not required.

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