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In-vitro Evaluations of Quality Control Parameters of Different Brands of Metronidazole Tablets Marketed in Al-Bayda City, Libya

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Abstract

This study was an attempt to evaluate the quality of some of the chosen metronidazole products for marketing in Libyan community pharmacies. Various quality control measures for pharmaceutical products can ensure their optimal therapeutic action, as well as their purity and bioavailability. Tests were performed in vitro on the commonly used quality control parameters, such as weight variation, hardness, friability, content uniformity, disintegration time, and dissolution test. According to this analysis, the weight variation ranges from 664 to 990 mg, the hardness of metronidazole tablets was 14.88 to 29.87 kg/cm^2, the friability of all the brands was below 1%, and the disintegration time was between 4:32 min and 8:31 min. Content uniformity was between 93% and 108%, and all brands showed a satisfactory dissolution profile as they released more than 85% of the drug in 60 minutes. The results showed that all the brands passed the weight variation, friability, disintegration test, content uniformity, and dissolution test and met the compendial criteria of USP. Eight brands failed the hardness test.

Keywords: Quality Control, Metronidazole, Tablets, Weight variation, Hardness, Friability, Content uniformity, Disintegration time, and Dissolution test.

INTRODUCTION

Metronidazole chemically is a nitroimidazole anti-infective medication used to treat a variety of parasitic illnesses, including trichomoniasis, giardiasis, and amoebiasis (Aleanizy et al., 2017). Metronidazole is pro-drug. Anaerobic bacteria and sensitive protozoal organisms are able to selectively absorb unionized metronidazole due to their organisms to decrease metronidazole intracellularly to its in active state. After, this lowered metronidazole covalently binds to DNA, causing the helical helix to be broken, preventing the production of bacterial nucleic acids and subsequent bacterial cell demise. Oxygen's presence stops the decrease of metronidazole, thereby diminishing its cytotoxic effects. Right now, the affordable medication metronidazole has good penetration. It has comparatively few adverse effects, is available in the formulary in the majority of hospitals to pre-vent anaerobic infections following colon surgery, to treat an abscess in the wound, and for therapy for colitis linked to antibiotics induced by Clostridium difficile. Metronidazole is accessible as orally, intravenously, vaginally and rectally introductions, in spite of the fact that the foremost clinically utilized is the verbal introduction. Its verbal dose shapes of 250 or 500 mg are quickly retained and disseminated nearly to the whole body (Kassim et al., 2016 Hernández Ceruelos et al., 2019; Noor et al., 2017).

In the medical field, the dose type that is most frequently prescribed is a tablet. The pharmacies provide a variety of brands of metronidazole tablets that are deemed pharmaceutically equivalent if they reach the same compendia guidelines as purity, strength, and quality and have the same quantity of active ingredient in the same dosage form nevertheless there may be variances in shape, packing, excipients, and branding specifications (Jacobs & Seifried, 2007). Pharmaceutical dosage forms' effectiveness is typically influenced by their formulation and manufacturing method; hence dosage form quality may differ (Chowdary KPR, 2001). To evaluate the

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physicochemical characteristics of drug's formulations, many tests are utilized as weight variation, friability, hardness and drug content, while disintegration and dissolution tests are used to investigate the drug release pattern from tablet dosage forms (Noor et al., 2017). The aim of this study is to evaluate and com-pare between eight different metronidazole tablet brands available in the Libyan market by applying official and unofficial compendia methods following the USP.

MATERIALS AND METHODS

Materials

Metronidazole tablets (500mg) of eight different brands were purchased from various private pharmacies in Al-Bayda City, Libya, and were randomly coded as MT (1), MT (2), MT (3), MT (4), MT (5), MT (6), MT (7), and MT (8). The identity and specifications of the various brands collected in the study are given in Table 1. Metronidazole Reference Standard (Sigma-Aldrich, USA), hydrochloric acid (Riedel-de Haën, Germany), reagents, and chemicals utilized were of analytical grade, and double distilled water was used in this study. Standard procedures were used in all the analysis.

Table :(1). The evaluated brands of metronidazole tablets

Brand code	Strength in (mg)	Name of company	Country of origin	Expiry date	Batch number
MT (1)	500	Amriya pharmaceuticals	Egypt	22/06/2027	8015146A
MT (2)	500	Julphar	United Arab Emirates	08/2025	0343
MT (3)	500	Tabuk pharmaceuticals	Saudi Arabia	11/2024	1KV760
MT (4)	500	Sanofi	Egypt	09/2025	CEG102
MT (5)	500	Laboratories Galenica	Maroc	11/2024	J2621
MT (6)	500	Sanofi-aventis	Spain	08/2024	1R1V7
MT (7)	500	Hikma pharmaceuticals	Jordan	4/2025	0242A
MT (8)	500	Industria farmaceutica nova-argentia	Italy	12/2024	200003

Methods

Weight variation test:

From each brand, twenty tablets were taken. The weights individually were evaluated by using an electronic digital balance (Sartorius, Germany). The average weight and the per-centage deviations from the average weight were calculated (Bayoumi et al., 2019).

Hardness test:

The tablet hardness was measured using the TBH 220 D tablet hardness tester (Erweka GmbH, Germany). So as to evaluate the average hardness of each brand, 10-tablets were selected at random (Bayoumi et al., 2019).

Friability test:

The friability of twenty tablets of each brand was evaluated using a friability tester, an Erweka TAR

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220 (Erweka GmbH, Germany). Weighed and placed tablets in a friability compartment, which was operated for 4 min (25 rpm).

Disintegration test:

The disintegration time is evaluated when six tablets of each brand are placed in the six tubes of a tablet disintegration tester (Hanson Research, USA) and immersed in distilled water at 37 °C. The time taken for all six tablets to disintegrate into particles and pass into the disintegration medium is noted as disintegration time (Noor et al., 2017). For each brand, the mean disintegration time was evaluated.

Preparing the metronidazole standard curve:

An amount of metronidazole reference standard powder (50 mg) was dissolved in 100 ml of 0.1 N HCL to produce a stock standard solution (500 µg/ml). To estimate the wavelength of maximum absorbance (λmax) of the drug, 5 ml of stock standard solution was transferred to a volumetric flask and filled to 100 ml with 0.1 N HCL, and UV-Vis spectrophotometer (Thermo Fisher Scientific, USA) was used to scan from 200 to 400 nm. A range of solutions that had various metronidazole concentrations (2.5–40 µg/ml) were produced using the stock standard solution (500 µg/ml). These solutions were then analyzed spectrophotometrically at the λmax of the drug using a GENESYS 10S UV-Vis spectrophotometer. The measured absorbance of each sample was plotted against the respective concentration to construct a calibration curve for metronidazole in 0.1N HCL (Bayoumi et al., 2019).

Drug Content Test:

The drug content for each brand is determined by using 10-tablets selected randomly, and each tablet is individually evaluated using the following procedure:

One tablet and approximately 100 ml of 0.1N hydrochloric acid were put in a volumetric flask (250 ml) and shaken for half an hour, the volume completes with 0.1N hydrochloric acid, mixing, and filtration. A 0.2 mg/ml solution of metronidazole was prepared by diluting 1 ml of the filtrate with 0.1 N hydrochloric acid in a 10 ml volumetric flask. Pipetting 1 ml of this solution into a 10-ml volumetric flask, diluting it with 0.1N hydrochloric acid to volume, and mixing.

Measurements of the absorbance of this sample solution and those of a similarly prepared solution of metronidazole reference standard, with a known concentration of about 20 µg/ml, were made in 1-cm- matched cells at the drug's λmax using a GENESYS 10S UV-Vis spectrophotometer (Thermo Fisher Scientific, USA) with a blank (0.1N hydrochloric acid).

The following formula is used to calculate the amount of metronidazole (mg) in each tablet:

$$(TC/D)\ (Au/As) \quad \ldots\ldots\ldots \quad (1)$$

in which:

The amount of metronidazole labeled on the tablet (mg) is T, the metronidazole reference standard concentration in the standard solution (µg/mL) is C. The metronidazole concentration in the sample solution (µg/mL) is D, based on the amount per tablet that is listed and how much has been diluted , and the absorbances of the sample solution and the standard solution are AU and AS, respectively (Aleanizy et al., 2017).

Dissolution test:

The dissolution test was performed using Erweka DT600 (Erweka GmbH, Germany) in six replicates for each brand at 75 rpm. 900 ml of 0.1 N HCL were used as dissolution medium and equilibrated to 37°C. 5 ml of the aliquot was withdrawn at intervals of 15, 30, 45, and 60 minutes. Fresh dissolution media were added instead of withdrawn volumes. The sample was filtered, and to prepare the working solution, 1 ml of filtrate was further diluted. At the λmax of the drug using 0.1N

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HCL as the blank, the absorbance of the working solution was measured, and the average drug release percentage for each brand was determined (Ahmed et al., 2020).

RESULTS AND DISCUSSION

Weight variation test:

The results of the weight variation test that was performed on eight brands of metronidazole tablets available in private pharmacies in Al-Bayda City, Libya, are presented in Table 2.A careful assessment of the tablets' weights showed the brands MT (3) and MT (1) had the lowest and highest weights, respectively (664 mg and 990 mg). Nonetheless, the maximum deviation percentage from the average weight value was not more than 3% of brand MT (2), and the minimum percentage deviation was - 4% of brand MT (7). Therefore, all eight brands tested in this study fulfilled the USP pharmacopeial limitations for uniformity of weight, which state that the percentage deviation allowed for tablets weighing more than 324mg is generally ± 5%.

Table: (2). Weight variation measurement of eight brands of metronidazole tablets.

Brand Code	Average weight per tablet (mg) ± SD	% Deviation from average weight (n=20)
MT (1)	990 ± 9.4	-2 to 1
MT (2)	970 ± 11.1	-2 to 3
MT (3)	664 ± 3.2	-1 to 1
MT (4)	699 ± 8.4	-3 to 3
MT (5)	901 ±11.4	-2 to 2
MT (6)	702 ± 5.4	-2 to 1
MT (7)	766 ± 14.3	-4 to 3
MT (8)	698 ± 3.5	-1 to 1

Hardness test:

The hardness of metronidazole tablets was found to be quite high (14.88 to 29.87 kg/cm^2) as compared to the permissible limit; this could be because of the film coat that has been placed on the surface of tablets, increasing its mechanical strength (Majeed et al., 2021). Thus, all the brands failed to meet the manufacturer's requirement for hardness.

Table :(3). Hardness of eight brands of metronidazole tablets.

Brand Code	Average hardness (kg/cm^2) ± SD
MT (1)	25.47 ± 0.8
MT (2)	24.09 ± 2.1
MT (3)	15.88 ± 1.3
MT (4)	21.56 ± 4.6
MT (5)	16.87 ± 1.4
MT (6)	15.02 ± 0.7
MT (7)	29.87 ± 1.8
MT (8)	14.88 ± 1.2

Friability test:

As per the USP criteria, tablets are considered acceptable if their friability is less than 1%. The result of the tablet friability test, as shown in Table 4, shows that the friability of all the brands

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was below 1%. This finding may be related to the tablet's coat, which signifies that all of the brands are mechanically stable (Sudipta Das & Soumitra Das, 2019).

Table:(4). Friability of eight brands of metronidazole tablets

Brand Code	MT (1)	MT (2)	MT (3)	MT (4)	MT (5)	MT (6)	MT (7)	MT (8)
Friability %	0	0	0	0	0	0	0.01	0.4

Disintegration test:

According to the USP specification, the disintegration time for film-coated tablets is 30 minutes (Ahmed et al., 2020). As shown in Table 5, all eight brands complied with the USP tablet disintegration requirements, as the maximum disintegration time was 8:31 min in the case of brand MT (1), while the minimum one in the case of brand MT (6) is 4:32 min.

Table:(5). Disintegration time of eight brands of metronidazole tablets

Brand Code	Average Disintegration time (min) ± SD
MT (1)	8.31 ± 0.03
MT (2)	5.06 ± 0.25
MT (3)	8.27 ± 0.26
MT (4)	8.07 ± 0.27
MT (5)	6.13 ± 0.30
MT (6)	4.32 ± 0.23
MT (7)	8.13 ± 0.13
MT (8)	4.17 ± 0.31

Standard curve of metronidazole:

The UV/vis spectrophotometer scanning of metronidazole solution gave the λmax of the drug to be 286nm. The calibration curve, as shown in Figure 1, was obtained by plotting the absorbance vs. the various concentrations of metronidazole solutions, producing a linear graph with a high regression coefficient. ($R^2 = 0.9982$).

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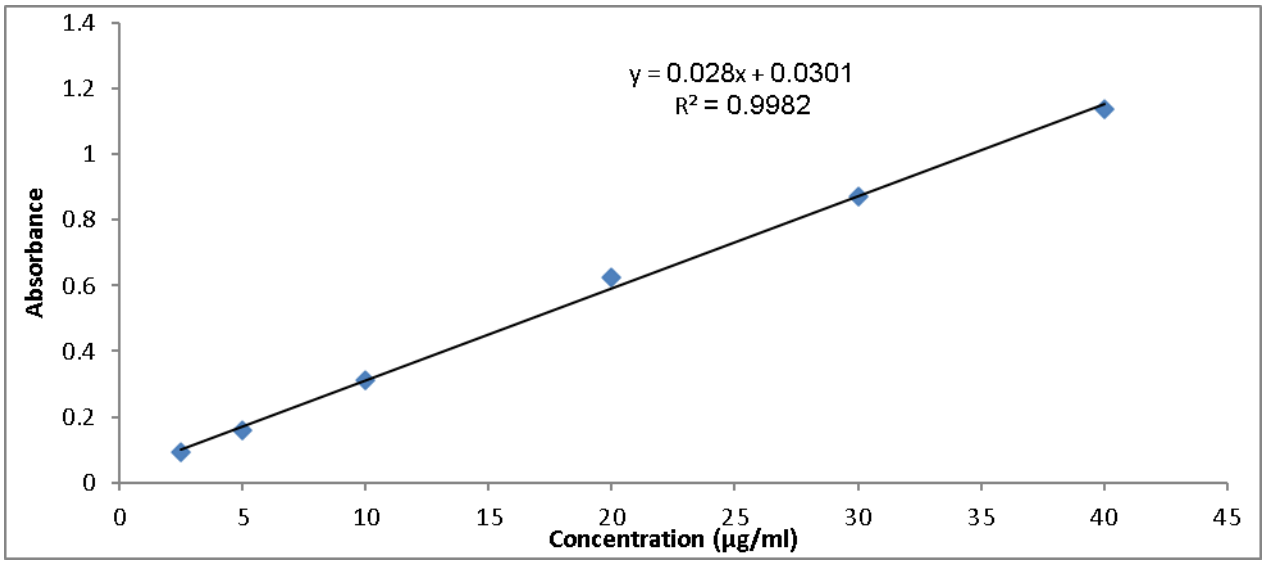

Figure:(1). The metronidazole spectrophotometry calibration curve in 0.1N HCl was determined via a GENESYS 10S UV-Vis spectrophotometer.

Content uniformity test:

The following formula was used for calculating each tablet's % drugs content:

$$\% \text{ of drug content in each tablet} = \frac{\text{Amount of drug present in a single tablet (mg)}}{\text{Strengeth (mg)}} \text{x100} \quad \text{..... (2)}$$

According to USP guidelines, the quantity of metronidazole in tablets cannot exceed more than 110% or less than 90% of the amount that is listed on the label (Ahmed et al., 2020). The results of content uniformity tests are represented in Table 6. Brand MT (8) had 108% of the quantity listed on the label, the highest amount of metronidazole. Conversely, brands MT (4) and MT (5) had the lowest amount of metronidazole, ranging up to 93% of the quantity listed on the label. Consequently, all the brands had drug percentages within the acceptable range of USP specifications.

Table:(6). Percentage of drug content for each tablet of eight brands of metronidazole tablets

Brand	% of drug content in each tablet									
Code	1	2	3	4	5	6	7	8	9	10
MT (1)	98	102	95	97	98	98	100	97	101	97
MT (2)	98	99	98	97	103	97	96	96	96	98
MT (3)	100	96	95	98	101	96	97	101	98	98
MT (4)	97	97	96	99	95	93	97	102	98	91
MT (5)	99	96	100	97	105	98	101	98	100	93
MT (6)	99	98	98	101	99	98	102	94	100	96
MT (7)	102	106	106	103	94	99	100	100	98	98
MT (8)	101	100	100	95	97	103	107	104	100	99

Dissolution test:

The dissolution test results for various brands of metronidazole tablets are shown graphically in Figure 2. The dissolution profiles for eight brands of metronidazole film-coated tablets showed more than 80% release within 15 minutes (with the exception of 27% for Brand MT (8), which showed nearly 82% release after 60 minutes). All brands met with the USP requirement, which states that within 60 minutes, the drug release from film-coated metronidazole tablets must not be less than 85% of the labeled quantity (Noor et al., 2017). Despite being produced by various companies using varying ratios of excipients, all the brands had an acceptable dissolution profile.

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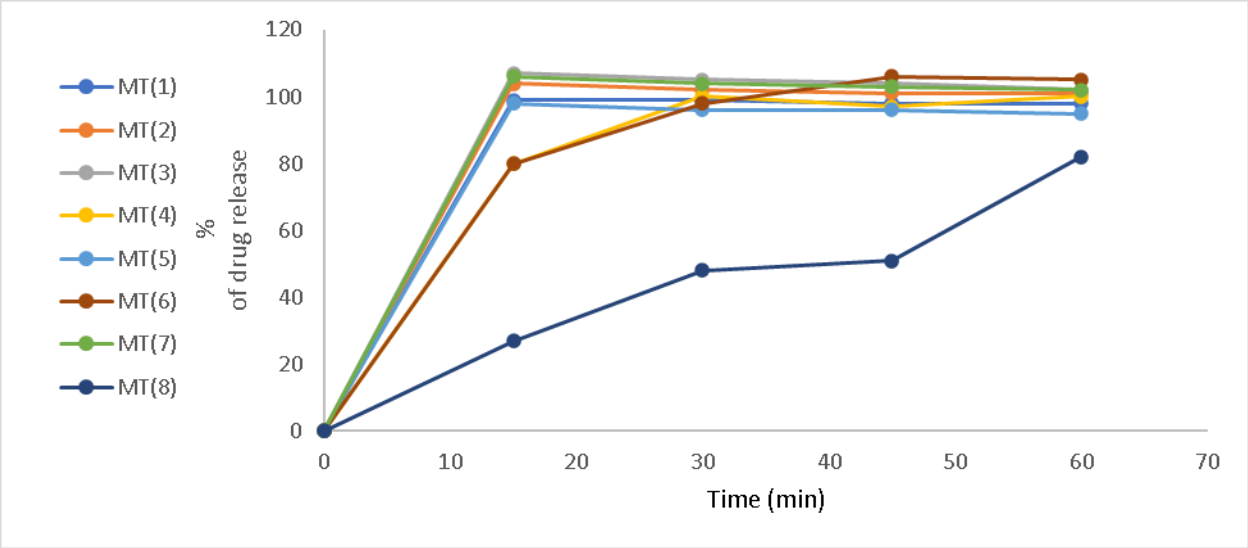

Figure:(2). Dissolution profile of eight brands of metronidazole tablets.

CONCLUSION

The goal of the current study was to measure the quality control parameters of eight brands of metronidazole tablets available in Al-Bayda City, Libya. The results demonstrated that all the metronidazole tablet brands were satisfactory, and they successfully passed all the USP requirements for oral tablet quality control tests (weight variation, content uniformity, disintegration, friability, and dissolution). All eight brands failed the hardness test as their mean crushing strength was found to be outside the range of 4-6 kg/cm^2. These types of studies should be conducted more frequently, which is very helpful for the improvement of the pharmaceutical sector in Libya.

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Author contributions: Contribution is equal between authors.

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