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Quality Evaluation of Ciprofloxacin, Metronidazole, Albendazole Tablets and Amoxicillin Suspension, Marketed in Mwanza, Tanzania: A Cross Sectional Study

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In Tanzania, essential medicines like amoxicillin, ciprofloxacin, metronidazole, and albendazole face potential quality challenges due to the risk of substandard and falsified drugs in the market. This study was carried out in Mwanza town, Tanzania to assess the quality of these drugs in order to address concerns about antimicrobial resistance and public safety. For this purpose, physical parameters, assay, and dissolution tests were conducted on samples of various brands according to the USP and BP monographs. All samples met USP standards for physical parameters and assay. But one brand of amoxicillin suspension failed assay test. Ciprofloxacin met dissolution criteria, but only one albendazole sample complied. About 47.6% of samples failed the quality tests performed. These results provide vital insights into pharmaceutical quality, safety and efficacy in the study area.

Keywords: physical parameters, assay, dissolution

INTRODUCTION

Albendazole is a broad-spectrum anthelmintic drug indicated for the treatment of threadworms, roundworms, whipworms, tapeworms, and hookworms.[1,2] Amoxicillin is an oral semisynthetic, β-lactam antibiotic used to treat bacterial infections caused by susceptible microorganisms.[3] Metronidazole is a nitro-imidazole drug that is effective in treating anaerobic bacteria and protozoan infections.[4] Ciprofloxacin is a first-generation fluoro-quinolone active against both gram-negative and gram-positive bacteria. It's effective against *Enterobacter spp*, *Pseudomonas aeruginosa*, *Neisseria meningitidis*, *Salmonella spp, Shigella dysenteriae*, *Chlamydia trachomatis*, *Campylobacter jejuni,* and many others.[5]

Ciprofloxacin, metronidazole, albendazole tablets and amoxicillin suspension appear in the list of essential medicines in current Tanzanian treatment guidelines. Over two-thirds of medicines in the Tanzanian market are imported

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from abroad.[6] Developing countries have often become dumping sites for substandard and falsified medicines in the world.[7,8] This is because of poverty and lack of stringent regulations together with poor technology in the detection of falsified medicines, few skilled personnel, vast importation of medicines because of low manufacturing capabilities, and ineffective regulatory authorities.[9] The occurrence of poor quality and falsified medicines in the African market still poses a major threat, compromising health care and patient outcome.[7, 10, 11] This was explicated by research conducted on six classes of antimalarials and antibiotics in parts of Sub-Saharan African countries.[12,13] The present study aimed at assessing the quality of commonly used antibiotics and anthelmintic drugs namely ciprofloxacin, metronidazole, amoxicillin, and albendazole marketed in Mwanza town, Tanzania.

MATERIALS AND METHODS

Sample collection

Various brands of ciprofloxacin 500 mg (6), metronidazole 200 mg (6), albendazole 400 mg (4) tablets and amoxicillin suspension (4) were collected from retail pharmacies found in Mwanza city. The town was chosen for the study due to the absence of previous research focused on the presence of substandard and falsified medicines therein. Additionally, the city's proximity to four international borders i.e. Kenya, Uganda, Rwanda, and Burundi underscores its significance for this study. Purposive sampling technique was used to select five community pharmacies out of fifteen community pharmacies found in Mwanza town. The summary of information related to the commercial products (samples) is shown in the Table 1.

Table 1: Product information for commercial products marketed in Mwanza, Tanzania

SN	Commercial products	Country of origin	Manufacturing date	Expiry date	Batch No
1	Metronidazole, MT1	Tanzania	10/2016	09/2018	281016
2	Metronidazole, MT2	India	06/16	05/19	7351799
3	Metronidazole, MT3	India	08/2016	07/19	PM66048
4	Metronidazole, MT4	India	09/16	08/19	487
5	Metronidazole, MT5	India	03/16	02/19	MT TT-01
6	Metronidazole, MT6	India	01/2016	12/2018	C2062
7	Albendazole, AL01	Tanzania	08/2016	07/2020	160031
8	Albendazole, AL02	UK	07/2015	07/2020	353291
9	Albendazole, AL03	India	10/2015	09/2018	C1404
10	Albendazole, AL04	South Korea	09/2015	09/ 2020	S001
11	Ciprofloxacin, CP1	India	-	01/2022	-
12	Ciprofloxacin, CP2	India	-	10/2021	-
13	Ciprofloxacin, CP3	Tanzania	-	01/2022	-
14	Ciprofloxacin, CP4	India	-	12/2021	-

SN	Commercial products	Country of origin	Manufacturing date	Expiry date	Batch No
15	Ciprofloxacin, CP5	South Korea	-	12/2021	-
16	Ciprofloxacin, CP6	Cyprus	-	11/2021	-
17	Amoxicillin, Z1	Kenya	-	07/2022	-
18	Amoxicillin, Z2	UK	-	10/2021	-
19	Amoxicillin, Z3	Kenya	-	04/2022	-
20	Amoxicillin, Z4	Bangladesh	-	03/2022	-
21	Amoxicillin, Z5	India	-	11/2021	-

SN – serial number, UK – United Kingdom, - Not recorded

Chemical, reagents and apparatus

Purified HPLC grade water and sodium hydroxide (Loba Chemie PVT Ltd, Mumbai, India), KH_2PO_4 and HPLC grade methanol (Sigma-Aldrich, St. Louis, MO, United States) were used in the experiments. Purified water was prepared on an Aquatron® distiller [Stuart Aquatron, Brockenhurst Way, United Kingdom] in the laboratory.

Instrumentation

Spectrophotometric measurements of albendazole samples were performed using a JENWAY model 6850 UV-VIS Spectrophotometer (Vernon Hills, Chicago, IL, USA) and data were processed using prism software version 5.42. A Shimadzu High performance liquid chromatograph (Shimadzu, Kyoto, Japan) coupled with a photo diode array detector, auto sampler, vacuum degasser system was used for the experiments. Chromatographic separation of metronidazole, ciprofloxacin and amoxicillin samples was achieved using a Knauer C8 column of dimensions 4.6 × 150 mm, 5µm (Knauer, Berlin, Germany).

A Compact S220 pH meter (Mettler Toledo, Greifensee, Switzerland) was used for measuring the pH of a reconstituted amoxicillin suspension. Dissolution was performed using a DT 800 Erweka® dissolution apparatus 1 ((Erweka, Langen, Germany) to provide critical *in vitro* drug release information of both albendazole and ciprofloxacin tablets. Friability was determined using (Copley 10S) Copley® friabilator tester while hardness, thickness, and diameter were measured using integrated hardness tester (Pharma Test, Hainburg, Germany). A VWR sonicator (VWR International, Radnor, PA, USA) was applied in degassing of mobile phases.

Physical tests

Three bottles of amoxicillin suspension, twenty tablets each of ciprofloxacin, albendazole, and metronidazole brands were unpacked and inspected for appearance. Twenty ciprofloxacin, metronidazole and albendazole tablets of each brand were weighed using a calibrated analytical balance. The average weight and standard deviation were calculated for weight variation.

Disintegration test

Six tablets of metronidazole were introduced into each tube of the disintegration test apparatus filled with distilled water at 37°C ± 2°C. The apparatus and timer were simultaneously initiated and the time taken for full disintegration were recorded. Disintegration test for the albendazole and ciprofloxacin were not performed because

dissolution test provides much better drug release data.

Dissolution test

Six tablets each of ciprofloxacin, metronidazole, and albendazole were introduced into individual vessels containing 900 ml dissolution medium as per USP specifications. The temperature was maintained at 37 °C, and rotation rates were adjusted in accordance with the specific method requirements. Aliquots of 5 ml were withdrawn from the solution at 20, 40, and 60-minute intervals, for the purpose of analyzing the dissolved drug concentration. After each withdrawal, the same volume was replenished to the vessel. Subsequently, the samples were filtered and diluted using the dissolution medium. Absorbance measurements were conducted at the specified wavelengths. The acceptance criteria stipulated that no less than 80% of the active ingredient should dissolve within the initial 30 minutes.

pH Measurements

The pH of amoxicillin suspensions was measured by using a calibrated pH meter with the electrode immersed into well-mixed samples of the suspension. The pH readings displayed on the meter were recorded.

Assay

Sample solutions of the respective ciprofloxacin, metronidazole, albendazole tablets and amoxicillin suspension were prepared in suitable solvents as per USP monographs. The resulting solutions were analyzed by using HPLC or UV-spectrophotometry (albendazole).

Data analysis

Statistical analysis was performed using one way Analysis of Variance (ANOVA) and the results are expressed as the mean, standard deviation and percentage.

RESULTS AND DISCUSSION

A summary of the results obtained is presented in Table 2. With respect to appearance, all samples were undamaged, smooth, and in a uniform colour. Furthermore, all samples complied with BP specification on the weight variation (Table 2).

The acceptable content range for the active pharmaceutical ingredient (API) content in metronidazole tablets, ciprofloxacin tablets, albendazole tablets, and amoxicillin suspension, as per the USP specifications is 90% - 110% of the label claim. All samples except one amoxicillin brand suspension complied with assay specifications, as indicated in Table 2.

Regarding metronidazole tablets, while they passed essential tests such as assay and weight variation, the disintegration test results unveiled a disparity. Only three brands met the required standards, while three others did not comply, as evidenced in Table 2. These findings imply that mechanical properties and disintegration behavior may vary across different brands of metronidazole tablets, potentially impacting their performance and patient experience. Remarkably, these results align closely with studies conducted in Zaria, Nigeria[14] and another in Bangladesh.[15]

Table 2: Quality control results for the brands tested

BRAND CODE	pH	DISNTEGR-ATION (MIN)	WEIGHT VARIATION	DISSOLUTION	ASSAY
LIMITS	**5.0- 7.0**	**NMT 15 MIN**	**VARIED**	**≥80% Q (30 MIN) ≥85% Q (60 MIN)***	**90 – 110% LC**
CP1	-	-	Complies	Complies	98.9% ± 1.4 (Complies)
CP2	-	-	Complies	Complies	103.6% ± 0.7 (Complies)
CP3	-	-	Complies	-	93.9% ± 0.4 (Complies)
CP4	-	-	Complies	Complies	95.5% ± 0.5 (Complies)
CP5	-	-	Complies	Complies	101.4% ± 0.2 (Complies)
CP6	-	-	Complies	Complies	95.7% ± 0.5 (Complies)
AL01	-	-	Complies	Does not comply	92.1% ± 1.11 (Complies)
AL02	-	-	Complies	Complies	98.4% ± 1.23 (Complies)
AL03	-	-	Complies	Does not comply	97.2% ± 1.21 (Complies)
AL04	-	-	Complies	Does not comply	91.3% ± 1.09 (Complies)
MT1	-	**17 (Does not comply)**	Complies	Complies	98.3% ± 0.82 (Complies)
MT2	-	3 (Complies)	Complies	Complies	92.8% ± 1.47 (Complies)
MT3	-	**16 (Does not comply)**	Complies	Complies	99% ± 1.42 (Complies)
MT4	-	8 (Complies)	Complies	Complies	99.8% ± 0.74 (Complies)
MT5	-	7 (Complies)	Complies	Complies	100% ± 0.12 (Complies)
MT6	-	**16 (Does not comply)**	Complies	Complies	104.2% ± 0.67 (Complies)
Z1	5.7	-	-	-	104.3% ± 2.28 (Complies)
Z2	5.4	-	-	-	114.11% ± 2.08 (Complies)
Z3	6.1	-	-	-	107.7% ± 0.07 (Complies)
Z4	5.0	-	-	-	113.7% ± 0.19 (Complies)
Z5	5.2	-	-	-	**70% ± 2.25 (Does not comply)**

*Applies to metronidazole tablets only, - Test not performed, CP - ciprofloxacin, AL - Albendazole, MT-Metronidazole, Z - Amoxicillin suspension

The assessment of amoxicillin suspension quality indicated that all brands passed the pH test, as highlighted in Table 2. However, the API content for four brands met requirements with one specific brand of amoxicillin suspension failing in assay. Notably, these results are corroborated by a similar study conducted in the Ashanti Region, Ghana [16].

In the case of ciprofloxacin tablets, all brands passed the requisite USP tests, as shown in Table 2. This demonstrates adherence to quality standards with respect to dissolution and weight variation. The consistent compliance across all brands implies favorable quality attributes for ciprofloxacin tablets across the tested products. Interestingly, these results align with a study conducted in Bangladesh [17].

Dissolution tests were performed on ciprofloxacin and albendazole tablets. In accordance with USP guidelines, a release of over 80% within 30 minutes is expected. The findings revealed that all ciprofloxacin samples met this requirement. In the case of albendazole tablets, out of the four samples examined, only one (Zentel®) adhered to the stipulated criteria, as outlined in Table 2 and illustrated in Figure 1.

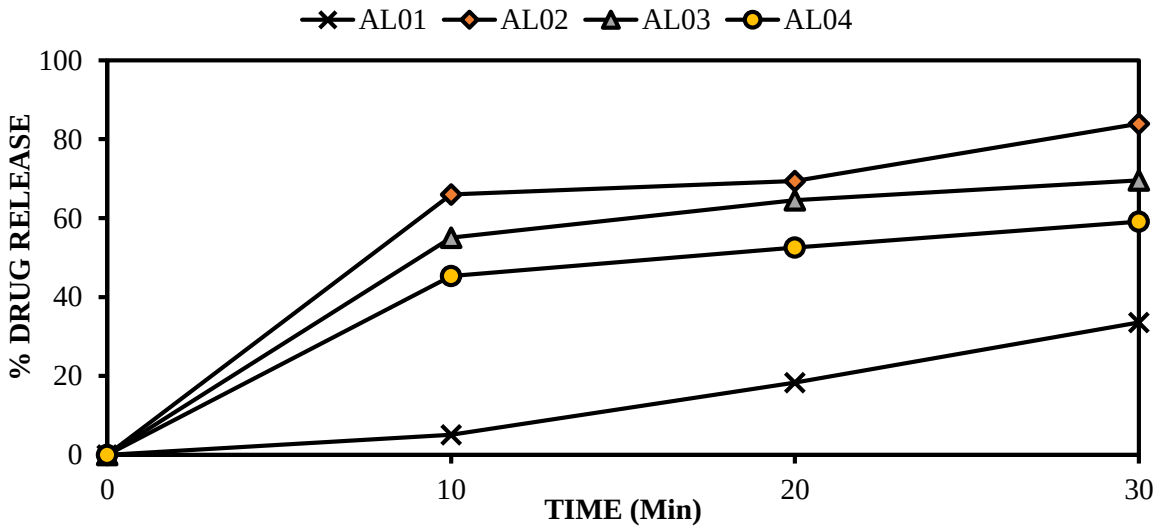

Figure 1: Dissolution profile of albendazole formulations

Among the four brands of albendazole tablets tested as shown in Figure 1 and Table 2, three brands failed the dissolution test. However, these brands did pass other tests such as weight variation, and assay. The failure in the dissolution test suggests potential issues with the drug's release profile, which may affect therapeutic effectiveness. Further investigation is needed to identify the root causes of dissolution failure and to assess the impact on bioavailability. These findings correlate with another study conducted in Mexico by Marcela Hurtado y de la Pen˜a [18] and another study in Ethiopia [19].

CONCLUSION

This study examined the physical properties, weight, assay, and dissolution properties of different pharmaceutical products. The findings revealed that all samples maintained their physical integrity and met the weight requirements. Moreover, the samples complied with assay specifications except for one brand of amoxicillin suspension. In terms of dissolution test, all ciprofloxacin samples met the specified criteria for release, while only one albendazole sample complied. These results offer valuable

information regarding the quality and adherence to standards of the pharmaceutical products tested, ensuring their safety and efficacy. Overall 47.6% of the samples tested are sub-standard as per USP specifications. These findings provide valuable insights into the quality and performance of the tested pharmaceutical products.

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Data availability statement

Data will be made available upon request.

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