

Quality of different brands of clarithromycin tablets marketed in Ethiopia; implications for the future

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Background: There are concerns with the availability of substandard antibiotics across Africa, including Ethiopia, exacerbating high levels of antimicrobial resistance (AMR). There are ongoing initiatives across Africa to reduce their availability to reduce AMR, including Pan-African registration, coordination with Interpol, and increasing surveillance. Consequently, the objective of the study was to evaluate the quality of different brands of clarithromycin tablets currently marketed in Ethiopia as a key antibiotic.

Methods: A total of 120 tablets of 12 different brands of clarithromycin 500 mg tablets were purchased from 12 different community pharmacies. Quality control tests, including visual inspection, thickness, diameter, hardness, friability, weight variation, disintegration, dissolution, and assays, were conducted at the Ethiopian Pharmaceutical Company's drug quality control laboratory on the sourced tablets. Tests were performed in accordance with the United States Pharmacopoeia (USP) and the World Health Organization's procedures.

Results: The identification test results confirmed the presence of the active pharmaceutical ingredients. The weight variation tests showed compliance with the USP limits. All clarithromycin brands and tablets met the USP requirements for hardness and disintegration times. The percentage content of all brands and tablets ranged from 95.14% to 100.44%, meeting the USP specifications. The dissolution tests also met required USP limits alongside factor (f1) factor (f2) values, which were within acceptable ranges.

Conclusion: As a result, all tested clarithromycin brands conformed with the required quality standards and were of acceptable quality. Consequently, these different brands of clarithromycin can be used to effectively treat patients and support ongoing national efforts to ensure antibiotic quality and strengthen AMR containment strategies.

Introduction

There are considerable concerns with rising antimicrobial resistance (AMR), especially among low- and middle-income countries (LMICs), with AMR becoming a critical public health issue.¹ The key drivers of AMR among LMICs include the considerable inappropriate prescribing and dispensing of antibiotics, including

those from the World Health Organization's (WHO) Watch and Reserve list with their greater resistance potential.^{2,3} In 2022, the WHO launched its AWaRe book giving guidance on the management of 35 infectious diseases, encouraging the prescribing of Access antibiotics.⁴ There are also ongoing efforts in Ethiopia to increase the appropriate use of antibiotics, which includes

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Table 1. Friability, hardness, weight variation, disintegration time, dissolution, and assay test results for the clarithromycin tablets

Sample code	Friability (%) (n=20)	Hardness (Kpa) (mean ± SD) (n = 10)	Weight variation (%) (mean ± %SD) (n = 20)	Disintegration Time (min) (mean ± %RSD) (n=6)	Dissolution test (%) (mean ± SD) (n=6)	Assay (%) (mean ± %RSD) (n=20)
CL1	0.0085	17.9 ± 1.9	708 ± 2.1	5.29 ± 0.13	100.1 ± 2.2	99.8 ± 0.1
CL2	0.0900	19.4 ± 2.7	1031 ± 4.7	0.72 ± 0.03	100.1 ± 0.4	95.14 ± 0.5
CL3	0.0065	13.5 ± 1.2	683 ± 4.1	9.04 ± 0.1	100.8 ± 0.1	99.83 ± 0.2
CL4	0.0019	12.6 ± 2.3	1025 ± 4.4	0.74 ± 0.03	95.8 ± 3.2	98.58 ± 0.6
CL5	0.0020	12.3 ± 1.1	1041 ± 3.6	0.89 ± 0.03	91.9 ± 1.4	96.09 ± 0.6
CL6	0.0030	17.96 ± 3.7	906 ± 4.6	5.94 ± 0.08	99.6 ± 1.2	100.27 ± 0.4
CL7	0.0030	13.6 ± 2.1	1016 ± 3.8	9.05 ± 0.16	98.5 ± 1.2	98.23 ± 0.6
CL8	0.0030	18.2 ± 1.6	932 ± 4.1	7.03 ± 0.05	98.8 ± 0.2	100.43 ± 0.1
CL9	0.0024	25.92 ± 3.6	1032 ± 4.2	1.89 ± 0.09	97.3 ± 0.3	98.49 ± 0.4
CL10	0.004	16.9 ± 2.1	1035 ± 4.6	1.86 ± 0.1	96.9 ± 0.5	99.12 ± 0.2
CL11	0.005	17.3 ± 2.4	879 ± 4.9	8.66 ± 0.09	94.2 ± 0.4	95.62 ± 0.3
CL12	0.003	17.46 ± 1.2	1033 ± 3.9	1.92 ± 0.42	92.2 ± 0.3	100.44 ± 0.3
Acceptance limit	≤ 1%	≥ 12 Kpa	≤ 5%	< 30 min	≥ 80%	90%–110%

the Ethiopian Food and Drug Authority (EFDA) recently providing a fact sheets discussing ways to reduce AMR.⁵

AMR is further enhanced by the considerable availability and use of falsified and substandard antibiotics among LMICs.^{6,7} Substandard medicines are defined as not meeting agreed quality standards and/or specifications, with falsified medicines fraudulently distorting their identity.^{7,8} Both have appreciable cost, morbidity, and mortality implications alongside adding to AMR.^{7,9}

Asrade Mekonnen et al. (2024) estimated that the prevalence of substandard and falsified medicines in Africa was 22.6%, with antibiotics (44.6%) accounting for most of these.⁸ High rates of substandard antibiotics among African countries may have been enhanced by only a limited number having the capacity to undertake all the necessary regulatory functions.⁷ However, this is changing (Table S1, available as [Supplementary data](#) at JAC-AMR Online).

For an antimicrobial to be effective and limit AMR, it must contain the required amount of active pharmaceutical ingredients (API) and meet other official quality requirements.⁸

In view of concerns with the availability of substandard antimicrobials in Ethiopia, coupled with recent initiatives across Africa to reduce the extent of substandard antibiotics (Table S1), we believed it was important to test the quality of current antibiotic tablets in Ethiopia.^{6,10–12} Clarithromycin was chosen for this purpose as it is a macrolide antibiotic, with macrolides widely used and recommended as second-line antibiotics in the WHO AWaRe guidance.^{4,13} Alongside this, there have also been concerns with the quality of clarithromycin among LMICs.¹⁴

Consequently, the objectives of this study were first to assess the quality of clarithromycin tablets currently available in Ethiopia. Secondly, whether the substitution of different brands will affect patient care. Lastly, to provide guidance to improve access to good quality low-cost antibiotics in Ethiopia with high co-payment issues. Recent studies have demonstrated variable issues with different brands of antimicrobials in Ethiopia.^{6,11,15}

However, there are ongoing initiatives to reduce the prevalence of substandard antibiotics (Table S1).

Methods

Study area, antibiotics, and design

The study involving clarithromycin was conducted using community pharmacies in Dessie Town. Dessie Town was chosen because 36 community pharmacies officially operate in the town alongside multiple health-care facilities.¹⁶ This allows most clients to have good access to both prescribed and non-prescribed antibiotics.

A laboratory-based analytical study design was used (Table S2 contains comprehensive details of the methodology).

Sampled product techniques

12 brands of clarithromycin 500 mg tablets were collected from a random selection of 12 community pharmacies in Dessie town using a lottery method (Table S3), with a total of 120 tablets for each brand randomly purchased to ensure enough samples for all quality control parameters. Different quality control test parameters use different sample sizes, and they cannot use the same tablets again. The subsequent testing was conducted in the quality control department of EPHARM.

In vitro quality control testing and inspection

Quality control parameters are those used to evaluate the quality of a product. Testing was conducted in triplicate samples and triplicate analysis ($n=3$).

A visual inspection was conducted to verify the uniformity of the products' shapes and colour, the absence of any physical damage, and the manufacturers' details and expiry date.

Identification, hardness, and friability tests

This test verifies the authenticity of the APIs present in the medicines by confirming their identity through a process of comparison.

The hardness of each tablet was determined by randomly selecting 10 tablets and subjecting them to agreed hardness tests. The friability test

(90%–110%). This indicates that each brand contained the correct amount of API.

Discussion and conclusion

Encouragingly, all tested clarithromycin brands conformed to the required quality standards, indicating that the recent activities in Ethiopia appear to be working to reduce the extent of substandard antibiotics, mirroring the activities in other LMICs.^{3,7,17} This should continue given the range of activities now being planned and instigated by EFDA (Table S1).

The next key area to address is encouraging the routine use of international non-proprietary name (INN) prescribing and dispensing among all key stakeholders (Further details of the rationale, etc., of INN prescribing are included in Table S7.^{18–20}

In conclusion, all tested brands of clarithromycin contained the necessary API. Furthermore, all brands passed the various quality control tests. The similarity of different factors indicated comparable in-vitro release profiles among the tested brands and the comparator, which is encouraging and builds on the appreciable activities of EFDA in recent years.

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Transparency declarations

The authors declare no conflict of interest.

Author contributions

W. T. B. and B. A. M. were involved in the conceptualization, data curation, formal analysis, investigation, methodology, project administration, supervision, validation, visualization, and writing of the original draft. G. K., H. K., J. C. M., and B. G. contributed to the conceptualization, formal analysis, methodology, validation, and writing process. B. A. M. and B. G. also prepared the original draft, revised, and edited the manuscript before submission. All authors have agreed to the journal submission, have approved the final version, and are accountable for all aspects of the work.

Ethics approval and consent to participate

Ethical approval was obtained from the Wollo University's ethical review committee (Ref. No. cmhs2879/20/15). Oral informed consent was obtained before data collection and the study was strictly anonymous.

Data availability

Additional data are available from the Corresponding Author upon reasonable request. However, all available information has been included in the article/Supplementary data.

Supplementary data

Tables S1–S3 are available as Supplementary data at [JAC-AMR Online](https://doi.org/10.1093/jacamr/dlaf033).

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