 DOI: https://doi.org/10.82351/wajp.vol37no2.490

Quality Assessment of Azithromycin Tablets and Capsules in Ibadan, Nigeria

Mariam V. Lawal[1], Olufunke D. Akin-Ajani[2] and Oluwatoyin A. Odeku[2]

[1]Department of Pharmacy, University College Hospital, Ibadan, Nigeria.
[2]Department of Pharmaceutics and Pharmaceutical Technology, University of Ibadan, Nigeria.

Corresponding author: Oluwatoyin A. Odeku
Email: pejuodeku@yahoo.com; o.odeku@ui.edu.ng
Telephone: +234 8057320466

ABSTRACT

Background: Azithromycin is a widely used macrolide antibiotic. The high prevalence of generic brands in Nigeria raises concerns about quality, efficacy, and the risk of antimicrobial resistance. Post-marketing surveillance (PMS) is essential to ensure therapeutic safety and compliance with pharmacopeial standards.

Objective: To assess the quality of various generic brands of azithromycin oral dosage forms marketed in Ibadan, Nigeria, in comparison to the innovator brand.

Methods: Thirteen generic azithromycin brands (500 mg tablets (T_A-T_J) and 250 mg capsules (C_A-C_D)) and the innovator product were obtained from pharmacies and vendors. These were assessed for organoleptic properties, weight variation, friability, hardness, and release profile. Azithromycin was assayed using HPLC, while microbiological potency was assessed against six bacterial species.

Results: The innovator and eight generic brands satisfied all quality criteria. All brands passed the weight uniformity test and complied with monograph specifications for tablet hardness and disintegration times. Brands T_B and T_D exhibited high friability. T_D also failed the 30-minute specification for 80 % drug release. Assay revealed substandard azithromycin content in T_I 86.52 %, T_J 83.71 %, and C_B 88.45 %. Most generics had microbiological potency comparable to the innovator, with C_D exhibiting the highest overall activity. C_B, T_I, and T_J were inactive at low concentration (6.25 ug/ml) against some bacterial species.

Conclusion: Eight generic azithromycin brands met quality requirements and performed comparably to the innovator brand, while five generics, C_B, T_B, T_D, T_I, and T_J, failed some quality specifications. Routine PMS is critical in maintaining therapeutic efficacy, preventing antimicrobial resistance, and safeguarding public health in Nigeria.

Keywords: Azithromycin, Post-marketing surveillance, Tablets, Capsules

 DOI: https://doi.org/10.82351/wajp.vol37no2.490

Évaluation de la qualité des comprimés et gélules d'azithromycine à Ibadan, au Nigéria

Mariam V. Lawal[1], Olufunke D. Akin-Ajani[2] and Oluwatoyin A. Odeku[2]

[1]Département de pharmacie, Centre hospitalier universitaire d'Ibadan, Nigéria.
[2]Département de pharmacie galénique et de la technologie pharmaceutique, Université d'Ibadan, Nigéria.

Auteur correspondant : Oluwatoyin A. Odeku
Courriel : pejuodeku@yahoo.com ; o.odoku@ui.edu.ng
Téléphone : +234 8057320466

RÉSUMÉ

Contexte : L'azithromycine est un antibiotique de la classe des macrolides largement utilisé. La forte prévalence des marques génériques au Nigéria suscite des inquiétudes quant à la qualité, l'efficacité et le risque de résistance aux antimicrobiens. La surveillance post-commercialisation (SPC) est essentielle pour garantir la sécurité thérapeutique et la conformité aux normes de la pharmacopée.

Objectif : Évaluer la qualité de diverses marques génériques de formes pharmaceutiques orales d'azithromycine commercialisées à Ibadan, au Nigéria, par rapport au produit princeps (innovateur).

Méthodes : Treize marques génériques d'azithromycine (comprimés de 500 mg (T_A-T_J) et gélules de 250 mg (C_A-C_D) et le médicament de référence/produit innovateur/produit princeps ont été obtenus auprès de pharmacies et de vendeurs. Ces produits ont été évalués pour leurs propriétés organoleptiques, la variation de poids, la friabilité, la dureté et le profil de libération. La teneur en azithromycine a été dosée par HPLC et son activité microbiologique a été évaluée sur six espèces bactériennes.

Résultats : Le produit princeps et huit marques génériques ont satisfait à tous les critères de qualité. Toutes les marques ont satisfait au test d'uniformité de poids et étaient conformes aux spécifications de la monographie concernant la dureté des comprimés et les temps de désintégration. Les marques T_B et T_D ont présenté une friabilité élevée. La marque T_D n'a pas non plus satisfait au critère de libération de 80 % du principe actif en 30 minutes. L'analyse a révélé une teneur en azithromycine inférieure à la norme dans les marques T_I (86,52 %), T_J (83,71 %) et C_B (88,45 %). La plupart des génériques présentaient une activité microbiologique comparable à celle du produit princeps, la marque C_D affichant l'activité globale la plus élevée. Les marques C_B, T_I, et T_J se sont révélées inactives à faible concentration (6,25µg/ml) contre certaines espèces bactériennes.

Conclusion : Huit marques génériques d'azithromycine ont satisfait aux exigences de qualité et ont présenté des performances comparables à celles du produit princeps, tandis que cinq génériques, C_B, T_B, T_D, T_I, et T_J, n'ont pas satisfait à certaines exigences de qualité. La surveillance post-commercialisation de routine est essentielle pour maintenir l'efficacité thérapeutique, prévenir la résistance aux antimicrobiens et préserver la santé publique au Nigéria.

Mots-clés : Azithromycine, surveillance post-commercialisation, comprimés, gélules

INTRODUCTION

Quality assurance encompasses the totality of systematic measures implemented to ensure that pharmaceutical products meet the required standards for their intended use.[1] Product quality is defined by its fitness for use, denoting compliance with predetermined quality attributes and regulatory specifications.[2] Quality control, in contrast, entails analytical testing of pharmaceutical products at different stages of manufacture, in finished dosage forms, and through post-marketing surveillance (PMS). Such surveillance is particularly vital in low- and middle-income countries, where the circulation of falsified and substandard medicines remains a significant public health challenge.[3,4] In Nigeria, antibiotics and antimalarials are among the most frequently compromised classes, underscoring the need for continuous monitoring to safeguard therapeutic outcomes and public health.

Azithromycin dihydrate (9-Deoxo-9a-aza-9a-methyl-9a-homoerythromycin) is a second-generation, broad-spectrum, semi-synthetic azalide antibiotic of the macrolide class.[5] Azalides, which incorporate nitrogen into a 15-membered lactone ring, were developed to address the poor acid stability of earlier 14-membered macrolides, thereby enhancing pharmacokinetic properties and chemical stability.[6-8] Owing to its efficacy, azithromycin is widely used in the treatment of respiratory tract, enteric, and sexually transmitted infections, and it plays an important role in mass drug administration programs for neglected tropical diseases such as trachoma and yaws.[9]

The extensive use of azithromycin, coupled with the proliferation of generic formulations in Nigeria's pharmaceutical market, highlights the importance of PMS for this antibiotic. Substandard products containing insufficient active pharmaceutical ingredient (API) not only compromise treatment efficacy but also contribute to the emergence of antimicrobial resistance.[10,11] This concern is further amplified by structural vulnerabilities in Nigeria's supply chain, including high generic penetration, variable distribution integrity, and inadequate regulatory enforcement.[12] Ensuring the quality of azithromycin, therefore, represents both a national and global health priority.

Against this background, the present study was undertaken to assess the quality of various brands of azithromycin tablets and capsules available in Ibadan, Oyo State, Nigeria, in comparison with the innovator brand, Zithromax®. Ibadan was selected for the study because it is one of Nigeria's largest metropolitan cities and a major pharmaceutical distribution hub, with a diverse range of locally manufactured and imported azithromycin products available through hospitals, community pharmacies, and medicine vendors[13]. The city's high antibiotic consumption and representative medicine supply chain make it an ideal setting for assessing the quality of azithromycin formulations and generating findings that are relevant to medicine quality surveillance and antimicrobial resistance control in Nigeria.

MATERIALS AND METHODS

Collection of Samples

Samples were collected using stratified random sampling.[14] Azithromycin tablets (500 mg) and capsules (250 mg) were purchased across six local government areas from licensed pharmacy premises and patent medicine vendors within the Ibadan metropolis, South-Western Nigeria. The details of each brand, including country of origin, batch number, and manufacturing and expiry dates, are presented in Table 1.

Table 1: Physical presentation, country of origin and expiry dates of azithromycin dosage forms

Tablet	Presentation	Tablet Outer Colour	Country of Manufacture	Azithromycin Content (mg)	Expiry date
T_A	Film-coated tablets	Peach	Pakistan	500	April 2024
T_B	Film-coated tablets	White	Nigeria	500	May 2024
T_C	Film-coated tablets	Cream/Dull orange	India	500	February 2024
T_D	Film-coated tablets	Yellow	India	500	January 2024
T_E	Film-coated tablets	White	India	500	June 2024
T_F	Conventional tablet	White	Nigeria	500	December 2024
T_G	Film-coated tablets	White	India	500	July 2023
T_H	Film-coated tablets	Pink	India	500	February 2024
T_I	Film-coated tablets	White	India	500	December 2024
T_J	Film-coated tablets	White	India	500	February 2025
C_A	Hard gelatin capsule	Green	Nigeria	250	March 2024
C_B	Hard gelatin capsule	Turquoise blue	India	250	December 2023
C_C	Hard gelatin capsule	Green	Nigeria	250	March 2024
C_D **(Innovator)**	Hard gelatin capsule	White	Italy	250	June 2024

Organoleptic Properties and Presentation

Each dosage unit (tablet or capsule) was visually examined for defects such as discolouration, chips, or breakages. The mode of presentation, including packaging and labelling, was also recorded.

Weight Variation Test

Weight variation was evaluated separately for tablets and capsules in accordance with official compendial standards.[15,16] For tablets, twenty units were randomly selected per brand and weighed individually using a Mettler balance. The mean weight was calculated, and the percentage deviation for each tablet was determined using Equation (1):

$$\% \text{ Weight deviation} = \frac{(\text{Mean weight}) - (\text{Weight of individual tablet})}{\text{Mean weight}} \times 100 \quad (1)$$

Tablets with a weight of 500 mg complied with the test if no individual tablet deviated by more than ±5 % and not more than two deviated by ±10 %.

For capsules, twenty units per brand were weighed individually. The contents were then removed, and the empty shells were reweighed. The net weight of each capsule was determined as:

$$\text{Net weight} = (\text{Weight of intact capsule}) - (\text{Weight of empty capsule shell}) \quad (2)$$

The mean net weight and percentage deviation were calculated. Capsules complied with the test if not more than two deviated by ±15 %, and at least 18 did not deviate by more than ±7.5 %. The deviations were also plotted to illustrate weight variation trends.

Friability Test

Ten tablets from each brand were collectively weighed (initial weight) and placed in a friability tester (Labtronics Microprocessor LT-710, Panchkula, India) operating at 25 rpm for 4 min. After dedusting, tablets were reweighed (final weight), and the percentage friability was calculated using Equation (3):

$$\% \text{ Friability} = (\text{Initial weight} - \text{Final weight})/(\text{Initial weight}) \times 100 \quad (3)$$

Determinations were performed in triplicate, and mean values ± standard deviations were reported.

Hardness Test

Tablet hardness was measured using a hardness tester (Labtronics LT-780, Panchkula, India). Three determinations per brand were performed, and results were expressed as mean ± standard deviation.

Disintegration Test

The disintegration test was performed using Apparatus A (basket-rack method) as described in the BP and USP,[15, 16] A tablet disintegration apparatus (Labtronics, Microprocessor LT-731, Panchkula, India) was employed, with distilled water maintained at 37 ± 0.5 °C as the medium. Six tablets from each brand were tested, and disintegration was defined as the point at which no residue remained on the basket screen. Results were expressed as mean disintegration time ± standard deviation.

The same procedure was applied for capsule dosage forms. However, in capsules, disintegration was recorded once the gelatine shell ruptured or dissolved, followed by the release of contents.

Dissolution Test

The dissolution test was performed using the paddle apparatus as described in the British Pharmacopoeia.[15] Tablets and capsules were evaluated using a dissolution test apparatus (Labtronics Microprocessor LT-720, Panchkula, India) with phosphate buffer pH 7.5 as the dissolution medium, maintained at 37 ± 0.5 °C and stirred at 100 rpm. Dissolution medium (5.0 mL) was withdrawn at predetermined time intervals (0.5, 1, 2, 5, 10, 15, 20, 25, 30, and 40 min) and replaced immediately with an equal volume of fresh medium to maintain sink conditions. The concentration of azithromycin in the withdrawn samples was determined using UV-Visible spectrophotometry at 210 nm (Inesa UV/Vis L6S, Shangfen, China).

Assay of Azithromycin

The assay was performed according to USP/NF [16] using a high-purity azithromycin reference standard on an HPLC system with UV detection at 210 nm. The column used was 4.6 mm × 25 cm, 5 µm packing, maintained at 50 °C, with a flow rate of 2 mL/min. The mobile phase consisted of acetonitrile and phosphate buffer (65:35 v/v, pH 7.5). Standard solutions (1 mg/mL) were prepared in the mobile phase. In contrast, sample solutions were prepared by pooling, finely powdering, and dissolving at the same concentration from not fewer than 20 dosage units per brand. The HPLC method was validated in accordance with the ICH Q2(R2) guidelines.[17] The method exhibited linearity over the concentration range of 1-100 µg/mL with a calibration equation of y = 0.0045 x - 0.0079 (R^2 = 0.9908). Repeatability and intermediate precision showed % RSD values below 2 %. The LOD and LOQ were 3.67 µg/mL and 11.11 µg/mL, respectively. The percentage of labelled azithromycin content was calculated as:

$$\% \text{ Drug content} = \left(\frac{ru}{rs}\right) \times \left(\frac{Cs}{Cu}\right) \times P \times F \times \pi r^2 \times 100 \quad (4)$$

Where r_u = peak response of azithromycin from the sample solution

r_s = peak response of azithromycin from the standard solution

c_s = concentration of azithromycin in the standard solution

c_u = nominal concentration of azithromycin in the sample solution

P = Potency of reference standard (µg/mg)

F = Conversion factor, 0.001mg/µg

Each determination was performed in duplicate. Dosage forms were considered compliant if they contained 90 - 110 % of the labelled amount.

Microbiological Analysis

Antimicrobial activity of the azithromycin dosage units was assessed using the pour plate method[18] against *Staphylococcus aureus* ATCC 6571, *Escherichia coli* ATCC 25922, *Bacillus subtilis* NCTC 3366, Pseudomonas aeruginosa ATCC 27853, *Salmonella typhi* ATCC 14028, and *Klebsiella pneumoniae* ATCC 700303. Sterile distilled water and gentamicin (0.1 µg/mL) were included as controls.

Tablet samples were powdered, and capsule contents were emptied and powdered, and solutions with

concentrations corresponding to 100, 50, 25, 12.5, and 6.25 µg/mL were prepared. Overnight bacterial cultures were diluted 1:100 in sterile distilled water to achieve the 0.5 McFarland standard, and 0.2 mL was inoculated into nutrient agar at 45 ^{o}C, poured into sterile Petri dishes, and allowed to solidify. Wells (6 mm diameter) were bored and filled with sample solutions and controls. Plates were pre-diffused for 2 hours, incubated at 37 ^{o}C for 24 hours, and zones of inhibition were measured in millimetres. All determinations were performed in duplicate.

Statistical Analysis

All experimental determinations, including weight variation, friability, hardness, and disintegration time, were performed in triplicate. Data are presented as mean ± standard deviation (SD). Statistical comparisons among the different brands were conducted using one-way analysis of variance (ANOVA) followed by Tukey's post hoc test to identify significant differences between groups. A p-value < 0.05 was considered statistically significant. All calculations and statistical analyses were performed using Microsoft Excel 2019 (Microsoft Corp., Redmond, WA, USA) and GraphPad Prism 9 (GraphPad Software, San Diego, CA, USA).

RESULTS

Physicochemical Properties of Azithromycin Brands

All tablets were 500 mg strength, while capsules were 250 mg. The innovator brand (CD) was a 250 mg capsule, allowing uniform comparison among capsule forms. All tablets were intact, evenly coloured, and free from chips or breakages. Capsules exhibited uniform colouration with intact shells. All 14 brands were NAFDAC-registered. Eight brands were manufactured in India (seven tablets, one capsule), one tablet brand from Pakistan, and four brands (two tablets, two capsules) were locally produced in Nigeria; the innovator brand originated from Italy. Most tablet brands were film-coated, except TF, which was a conventional uncoated tablet. The capsules had a similar visual appeal.

The weight variations are presented in Figures 1 and 2. All brands passed the pharmacopeial criteria.[12,15] Tablets TH (> +5.0 %) and TI (> +9.0 %) had minor deviations in two out of twenty units but remained within acceptable limits. Capsule brand CB exhibited the highest deviations (+3.0-5.0 %), followed by CC (> +3.0 %), while CA showed minor multiple deviations (> +2.0 %). The innovator brand showed only one capsule slightly exceeding +3.0 %, demonstrating excellent weight uniformity.

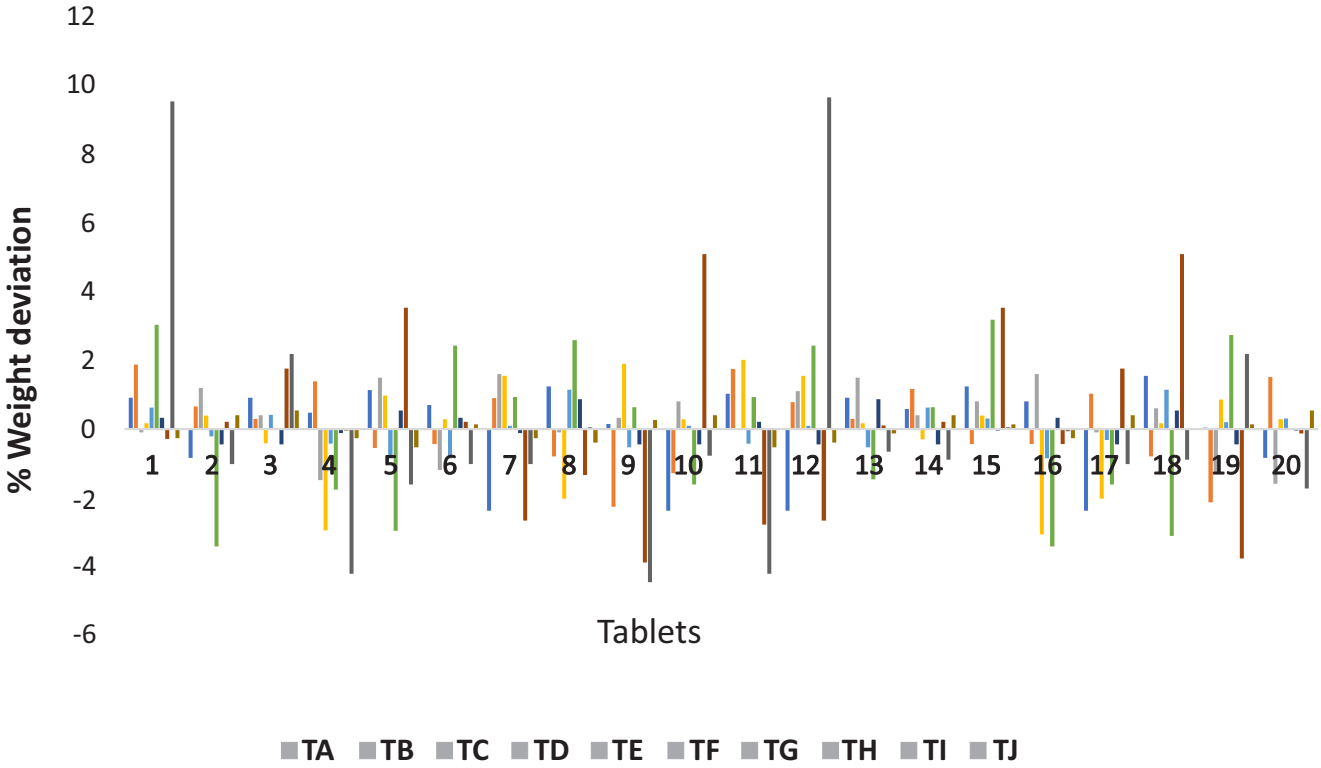


Figure 1: Percentage weight deviation of the brands of azithromycin 500mg tablets

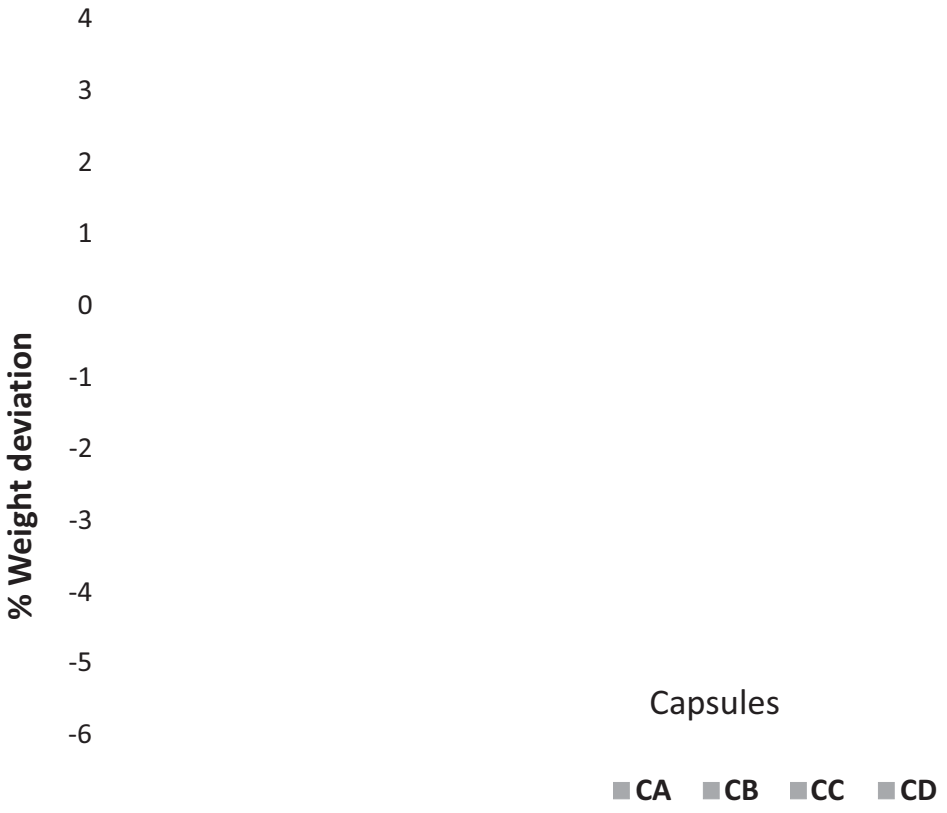


Figure 2: Percentage weight deviation of the brands of azithromycin 250 mg capsules

The tablet friability values are presented in Table 2. All tablet brands except TB and TD met the acceptance limit for percentage friability.

The tablet hardness, reflecting mechanical strength, presented in Table 2, showed that eight brands exceeded 100 N, while T_C and T_J showed lower values (83.8 N and 79.73 N, respectively). The uncoated brand demonstrated high hardness (128.27 N).

Table 2: The mechanical and drug release properties of azithromycin tablets and capsules

Formulation code	% Friability	Hardness value (N)	D_t (min)	t_{50} (min)	t_{80} (min)	Azithromycin content (%)
T_A	0.4420	159.53	7.20	0.25	27.0	95.21
T_B	5.0687	102.90	1.15	0.15	26.5	93.64
T_C	0.0203	83.8	2.54	0.25	7.5	103.79
T_D	2.2558	122.47	3.22	8.25	40.0	98.56
T_E	0.0043	153.17	27.45	5.3	27.5	96.72
T_F	0.1946	128.27	3.97	14.2	27.0	99.30
T_G	0.0197	124.63	5.60	15.0	31.0	103.34
T_H	0.0022	151.37	2.80	12.0	28.5	98.80
T_I	0.0164	150.83	2.56	3.5	13.6	86.52
T_J	0.0288	79.73	1.97	8.5	17.7	83.71
C_A	-	-	3.85	13.0	25.4	98.15
C_B	-	-	1.53	5.0	31.8	88.45
C_C	-	-	2.67	6.5	12.6	96.23
C_D	-	-	17.78	10.5	24.0	99.70

Disintegration and Dissolution Times

The disintegration times (Dt) are presented in Table 2. All brands complied with pharmacopeial specifications, disintegrating within 30 minutes.[15] The innovator brand C_D exhibited the longest disintegration time. The dissolution profiles of the tablets and capsules are presented in Figures 3 and 4, including the t_{50} (time for 50 % azithromycin release) and t80 (time for 80 % azithromycin to be released). Tablet brands T_E, T_F, T_G, T_H, and capsule C_A exhibited relatively high t_{50} and t_{80} values, while the innovator brand C_D showed moderate values, indicating steady drug release. All brands except T_D met the USP/NF[16] dissolution criteria (≥ 80 % dissolved within 30 min).

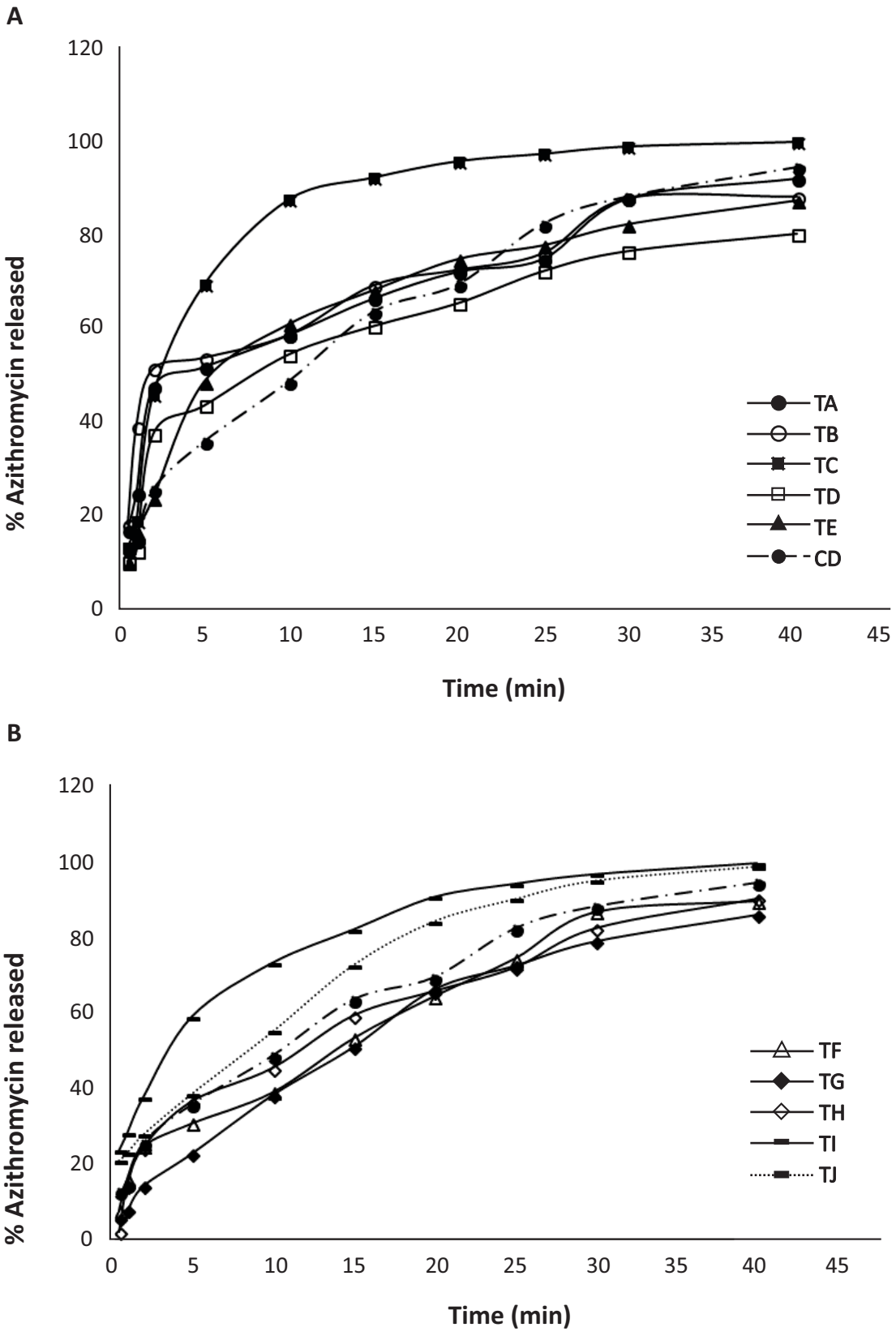


Figure 3 A&B: Dissolution profiles of azithromycin tablet brands in comparison with the innovator brand C_D

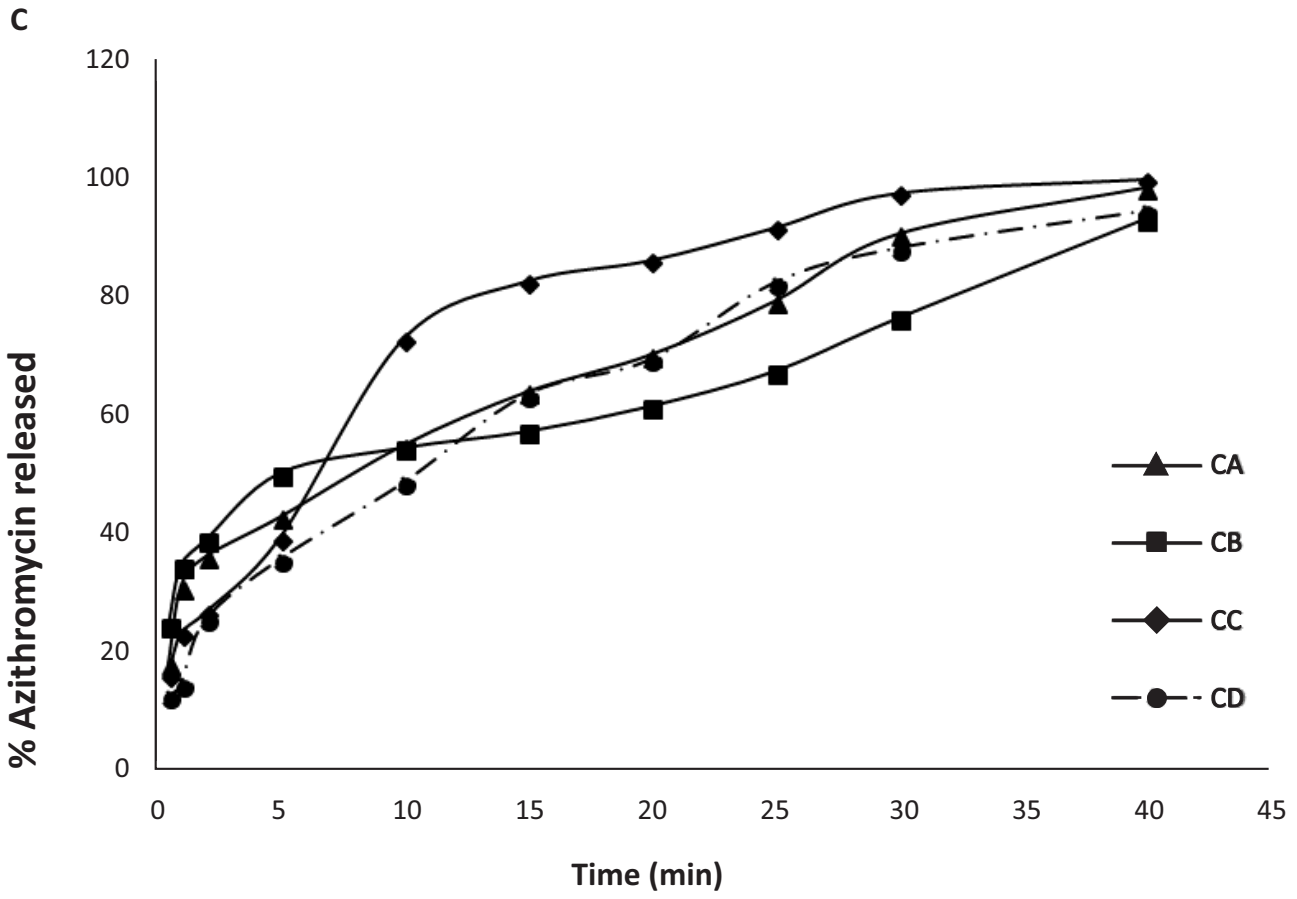


Figure 4: Dissolution profiles of azithromycin capsule brands C_A, C_B and C_C in comparison with the Innovator brand C_D

Assay of Azithromycin Dosage Units

The result of the assay is presented in Table 2. All but two tablet brands (T_I and T_J) and one capsule brand (CB) met the 90 - 110 % w/w azithromycin content requirement. T_I and T_J contained 86.52 % and 83.71 %, respectively, which are below the minimum acceptable limit. All other brands, including the innovator C_D (99.70 %), complied with content specifications.

Microbiological Sensitivity

Microbiological potency results are shown in Figures 5 and 6. The innovator brand C_D exhibited the highest potency across all bacterial species. Most generic brands demonstrated good activity, with tablet brand T_C and capsule brands C_A and C_C showing comparable efficacy. As expected, bacterial sensitivity decreased with lower antibiotic concentrations. Salmonella typhi and Klebsiella pneumoniae were less susceptible than other species. Overall, most brands demonstrated effective antimicrobial activity at 25 - 100 µg/mL. Relative potency ranking was: $C_D > C_A > C_C > T_C > T_G > T_F > T_E > T_D > T_H > C_B > T_B > T_A > T_I > T_J$.

DISCUSSION

A greater number of tablet dosage forms were collected than capsules, reflecting the higher market prevalence of tablets. The diversity of brands and countries of manufacture provides an opportunity to examine potential relationships between origin and product quality. Most tablet brands were film-coated, enhancing aesthetics and handling, while capsules provided a similar visual appeal. The differences in colour and presentation may provide signs for detecting potential defects or counterfeit products for healthcare professionals familiar with expected appearances. The percentage variation for tablets weighing more than 250 mg should not exceed ±5%, while for capsules weighing 250 mg, the variation limit should not exceed ±7.5 %.[19,20] The weight variation of the brands tested indicated generally acceptable consistency, with minor variations in a few of the generics: T_H and T_I. T_B and T_D may be more susceptible to mechanical stress during handling or transport, potentially compromising product quality, as they failed the friability test ($p > 0.05$), which measures tablet weakness. Film coating has been shown to increase tablet hardness up to 50 - 140 %,[19] enhancing abrasion resistance. Overall, tablets demonstrated adequate mechanical strength, since the hardness values exceeded 4 kgF, i.e. 39.23 N, which is generally considered satisfactory for tablets.[19]

The compendial requirement for the disintegration time of film-coated tablets and capsules is 30 mins, while for unconventional tablets it is 15 mins.[15] All the brands passed the DT test despite their hardness. An immediate-release film-coating polymer may have been used, which is a thin protective layer designed for fast dissolution so that the contents in the tablet core can be rapidly released.[20] The in vivo bioavailability of an oral drug can usually be predicted from in vitro dissolution studies, as opposed to *in vitro* disintegration tests, with poor correlation.[21] All the brands released 50 % of azithromycin within 15 mins (t_{50}), and only TD overshot the compendial requirement of 80 % release of azithromycin (t_{80}) within 30 mins ($p > 0.05$). Thus, indicating that the antibacterial agent would be released in a short period to reduce the bacterial load in an infected person to affect treatment.

T_I, T_J and C_B failed the drug assay findings ($p = 0.05$). These had drug content below the minimum 90 % recommended, thus suggesting a high chance of therapeutic failure, with implications of increased health costs and possible development of drug resistance, as an antibacterial agent.

It is not surprising that the same brands with poor drug content also had poor microbiological potency. The three brands had no activity against *K. pneumoniae*, while T_I and T_J additionally had no activity against *S. typhi*, and only T_J had no activity against *P. aeruginosa*.

Minor weight variations, lower hardness, poor friability, delayed dissolution, and substandard content were observed in select tablets and capsules. These deficiencies are particularly concerning given azithromycin's widespread use in treating respiratory, enteric, and sexually transmitted infections, as well as its role in mass drug administration programs. Substandard products may result in subtherapeutic exposure, treatment failure, and the emergence of antimicrobial resistance. Most generics demonstrated microbiological potency comparable to the innovator drug, indicating therapeutic equivalence. However, brands with reduced potency highlight the need for routine post-marketing surveillance, especially in low- and middle-income countries with high circulation of substandard antibiotics. Post-marketing surveillance allows regulatory authorities such as NAFDAC to identify and withdraw non-compliant products, enforce quality standards, and safeguard public health.

CONCLUSION

Most of the azithromycin brands tested in Ibadan, South-Western Nigeria, met pharmacopeial standards for physical characteristics, weight uniformity, friability, hardness, disintegration time, dissolution time, drug content, and antimicrobial potency. However, a few generic brands exhibited deviations that could compromise therapeutic efficacy. These findings thus emphasise the need for continuous quality monitoring of widely used antibiotics like azithromycin to maintain efficacy, prevent treatment failures, and mitigate antimicrobial resistance.

ACKNOWLEDGEMENT

The authors thank the Alexander von Humboldt Foundation, Bonn, Germany, for the equipment grant to OAO's Drug Delivery Research Laboratory.

REFERENCES

1. Gupta MM, Khoorban SA, Ali A, Ramlogan O, Talukdar D. (2020). Comparative quality control study of different brands of diclofenac sodium tablets available in local and government

pharmacies by in-vitro testing. *Cereus* 11348: 1-8. DOI: 10.7759/cereus.

2. Mittal B. (2020). How to Integrate Quality by Efficient Design (QbED) in Product Development: A Volume in Expertise in Pharmaceutical Process Technology. Chapter 4: Qbd: A Welcome Evolution, pp. 87-114.
3. Okereke M, Anukwu I, Solarin S, Ohuabunwa MS. (2021). Combatting Substandard and Counterfeit Medicines in the Nigerian Drug Market: How Industrial Pharmacists Can Rise Up to the Challenge. *Innovations in Pharmacy* 12(3): Article xx. DOI: https://doi.org/10.24926/iip.v12i3.4233. Accessed September 27, 2022.
4. Ozawa S, Evans DR, Bessias S, Haynie DG, Yemeke, TT, Laing SK, Herrington JE. (2018). Prevalence and estimated economic burden of substandard and falsified medicines in low-and middle-income countries: a systematic review and meta-analysis. *JAMA Network Open* 1(4): e181662-e181662. doi:10.1001/jamanetworkopen.2018.1662
5. Kournoutou GG, Dinos G. (2022). Azithromycin through the Lens of the COVID-19 Treatment. *Antibiotics* 11: 1063. https://doi.org/10.3390/antibiotics11081063.
6. Pai MP. (2018). Macrolides, Azalides, and Ketolides. Drug Interactions in Infectious Diseases: Antimicrobial Drug Interactions. Cham: Springer International Publishing, pp. 57-86, doi:10.1007/978-3-319-72416-4_2, ISBN 978-3-319-72415-7.
7. Raghuram J, Appalaraju N, Kumar VK (2015). Development and application of liquid chromatographic method for the determination of azithromycin in fixed dosage form. *International Journal of Pharmaceutics* 5(4): 1139-1143.
8. Mekasha YT, Chali BU, Feissa AB, Godena GH, Hassen HK, Wega SS. (2013). Quality evaluation of the Azithromycin tablets commonly marketed in Adama, and Modjo towns, Oromia Regional State, Ethiopia. *PLoS ONE* 18(3): e0282156. https://doi.org/10.1371/journal. pone.0282156 E.
9. World Health Organization (2017). 1 in 10 medical products in developing countries is substandard or falsified. 28 November 2017, News release, Geneva. Accessed 10th November, 2022.
10. Newton PN., Green MD, Fernández FM, Day, NP, White NJ. (2006). Counterfeit anti-infective drugs. *The Lancet Infectious Diseases* 6(9): 602-613. https://doi.org/10.1016/S1473-3099(06)70581-3.
11. Nayyar, GM, Breman, JG, Newton, PN, Herrington J. (2012). Poor-quality antimalarial drugs in Southeast Asia and sub-Saharan Africa. *The Lancet Infectious Diseases*, 12(6), 488-496.https://doi.org/10.1016/S1473-3099(12)70064-6
12. Akinyandenu O. (2013). Counterfeit drugs in Nigeria: A threat to public health. *African Journal of Pharmacy and Pharmacology* 7(36): 2571-2576. https://doi.org/10.5897/ajpp12.343.
13. Adedapo, AD, Akunne, OO. (2021) Patterns of Antimicrobials Prescribed to Patients Admitted to a Tertiary Care Hospital: A Prescription Quality Audit. Cureus 13(6): e15896. doi: 10.7759/cureus.15896.
14. Akin-Ajani OD, Mustapha AD, Adebisi OP, Odeku OA. (2025). Comparative quality assessment of selected fluconazole brands in Ibadan, Nigeria. *West African Journal of Pharmacy* 36(1): 53-64.
15. British Pharmacopoeia (2020). Volumes I-V, London: British Pharmacopoeia Commission.
16. USP 43/NF 38: (2020) The United States Pharmacopoeia, the National Formulary, Rockville, Md., The United States Pharmacopeial Convention.
17. International Council for Harmonisation. (2023). Validation of analytical procedures Q2(R2) (ICH Harmonised Guideline). https://database.ich.org/sites/default/files/ICH_Q2(R2)_Guideline_2023_1130.pdf
18. Dahal P. (2022). Pour Plate Method- Definition, Principle, Procedure, Uses. *Microbe Notes*.https://microbenotes.com/pour-plate-technique-procedure-significance-advantages-limitations/. Accessed 29 June, 2023.
19. Stanley P, Rowe RC, Newton JM. (1981). Theoretical considerations of the influence of polymer film coatings on the mechanical strength of tablets. *Journal of Pharmacy and Pharmacology* 33(1): 557-560.
20. Ma, M., Nassar, M., Teckoe, J., Zeitler, J. A. (2025). Film coating density and thickness: Critical quality attributes for immediate-release tablet disintegration control. *International Journal of Pharmaceutics* 682: 125925.
21. Nakamura, K., Kambayashi, A., Onoue, S. (2022). Quantitative assessment of disintegration rate is important for predicting the oral absorption of solid dosage forms containing poorly soluble weak base drugs. *European Journal of Pharmaceutics and Biopharmaceutics* 180: 23-32.