dx.doi.org/10.14227/DT300123PGC1

Physicochemical Quality and In Vitro Bioequivalence of Amoxicillin Capsules Marketed in Burkina Faso, Africa

B. Gérard Josias Yaméogo[1,2*], Wendpouiré Zoungrana-Somé[1,2], B. Charles Sombié[1], Hermine Zimé-Diawara[1], Bertrand Goumbri[2], Aïssata Sanfo-Diasso[2], Elie Kabré[2], and Rasmané Semdé[1]

[1]*Laboratoire du Développement du Médicament, Centre de Formation, de Recherche et d'Expertises en Sciences du Médicament (CEA-CFOREM), Ecole Doctorale Sciences et Santé, Université Joseph Ki-Zerbo, Ouagadougou, Burkina Faso, Africa.*

[2]*Laboratoire National de Santé Publique, Ministère de la Santé, Ouagadougou, Burkina Faso, Africa.*

e-mail: josiasbyg@yahoo.fr

ABSTRACT

Amoxicillin is a penicillin antibiotic widely prescribed to treat many infections. Several brands of oral forms of amoxicillin are available on the local market. The aim of this study was to evaluate the physicochemical quality and in vitro bioequivalence of several brands of amoxicillin capsules (500 mg) marketed in Burkina Faso. Nine different brands of amoxicillin capsules (eight generic and the innovator brand) were purchased from local authorized distributors. Quality control tests (identification, uniformity of weight, disintegration, assay, and dissolution) were performed according to the *United States Pharmacopoeia* monograph. The comparison of in vitro dissolution profiles was performed in three different pH media (1.2, 4.5, 6.8) using statistical calculations of difference (f_1) and similarity (f_2) factors. All brands met *USP* specifications for physicochemical quality. Amoxicillin content was 104.60–116.04% of the label claim. Mean disintegration time was 6.12–13.44 minutes and dissolution exceeded 80% within 60 minutes. When comparing dissolution profiles, f_1 values > 15 and f_2 values < 50 were obtained for two brands at all three pH levels; these brands cannot be considered interchangeable with the innovator brand. Six out of eight tested generic brands can be considered interchangeable with the innovator product.

Keywords: amoxicillin, capsules, physicochemical quality, dissolution, in-vitro equivalence

INTRODUCTION

Amoxicillin is an antibiotic of the aminopenicillin group and ß-lactam family used to treat a wide variety of bacterial infections. It is widely prescribed in many countries due to its extended spectrum and its rapid and extensive oral absorption with good tolerability (*1*). It is used in the treatment of various infectious diseases, including upper and lower respiratory tract infections, gonorrhoea, oral infections, otitis media, skin and soft tissue infections, urogenital tract infections, biliary tract infections, anthrax, endocarditis prophylaxis, and as a part of the treatment of Helicobacter pylori infection (*2*).

Amoxicillin inhibits bacterial cell wall synthesis by blocking cross-linking between linear peptidoglycan polymer chains, which are a major component of the cell wall in Gram-positive bacteria. Amoxicillin is effective against Gram-positive and Gram-negative bacteria and is susceptible to degradation by β-lactamase-producing bacteria. Amoxicillin can be administered with clavulanic acid to decrease its susceptibility (*3*). Amoxicillin is registered in the World Health Organization (WHO) and Burkina Faso essential medicine lists (*4*, *5*).

*Corresponding author

Resistance to amoxicillin and several other families of antibiotics has rapidly developed and evolved into a significant global public health problem (*6*). The use of substandard antibiotics is often questioned in the emergence of drug-resistant microorganisms (*7*). Unfortunately, the use of generic medicines from multiple sources has been accompanied by the introduction of substandard medicines, especially in countries with weak pharmaceutical regulations (*8–13*). Therefore, monitoring the quality and efficacy of generic amoxicillin products, particularly oral solid forms, is crucial. Oral dosage forms are widely used in clinical practice because they are convenient and stable; however, bioavailability issues may result from differences in dissolution of the active pharmaceutical ingredient (API), its solubilization under physiological conditions, and its resorption through the gastrointestinal tract (*14*).

Multiple studies have reported that some multisource amoxicillin capsules marketed in developing countries were not bioequivalent to the innovator product (*15–17*). According to the WHO, multisource pharmaceutical products that are not bioequivalent (and thus, not therapeutically equivalent) are not considered interchangeable to innovator product (*18*). For bioequivalence assessment, comparative in vivo pharmacokinetic and pharmacodynamic studies and clinical trials and comparative in vitro dissolution tests are recommended (*18*). The in vitro dissolution test is intended to determine the aptitude of dosage forms to release APIs in certain media (*19*). It is a fundamental requirement to predict in vivo performance and serve as surrogate for bioequivalence. Indeed, comparative in vitro dissolution studies may be employed to waive in vivo bioequivalence studies for Biopharmaceutical Classification System (BCS) class 1 drugs (i.e., highly soluble and highly permeable), such as amoxicillin products containing doses up to and including 875 mg (*18*, *20–23*).

This study aimed to compare the quality and dissolution profiles of several brands of amoxicillin capsules (500 mg) marketed in Burkina Faso. The in vitro dissolution test was used to evaluate in vitro bioequivalence with the innovator product. The fit factor statistical method was used to compare the dissolution profiles by calculating the similarity factor (f_2) and difference factor (f_1) (*24*, *25*).

MATERIALS AND METHODS

Materials

Amoxicillin trihydrate (USP Chemical Reference Substance [CRS]) and Prednisone 10-mg tablets (USP Reference Standard) were generously donated by the United States Pharmacopeia (USA). Sodium acetate trihydrate and anhydrous acetic acid (Carlo Erba Reagents, Val-de-Reuil, France), potassium phosphate dibasic, potassium hydroxide, and sodium hydroxide (NaOH) ≥ 99% w/w AnalaR NORMAPUR were purchased from VWR Chemical (USA), and acetonitrile (99.9%) high-performance liquid chromatography (HPLC) grade were purchased from Sigma-Aldrich (Germany). Hydrochloric acid (HCl) (0.1 N) solution was prepared from hydrochloric acid (37% w/w) purchased from PANREAC (Spain). Distilled water was freshly prepared in our laboratory.

Nine brands of amoxicillin 500-mg capsules (eight generic products and one innovator) were collected from the wholesale distributors of Ouagadougou, Burkina Faso. The details information about the samples are presented in Table 1. Clamoxyl 500-mg capsules (Glaxo Wellcome, France) was chosen as comparator following the WHO guidance (*26*). This is the leading brand of amoxicillin capsules on the market and the first brand introduced in the Burkina Faso market.

For each brand, a batch with at least one year of shelf-life remaining was collected at random. During all stages of the study, the collected samples were kept under the storage conditions specified by the manufacturer.

Table 1. *Samples of Amoxicillin 500-mg Capsules Collected for Analysis*

Sample Code	Batch No.	Country of Origin	Manufacturing Date	Expiry date
Innovator	AR5U	France	11/2019	10/2022
A	707190649	China	06/2019	05/2022
B	SZ367	France	09/2019	08/2022
C	910481	India	04/2019	03/2022
D	806	Côte d'Ivoire	12/2019	12/2022
E	AA21230	India	02/2019	01/2022
F	20BEC032	India	02/2020	01/2022
G	193131408	China	Not mentioned	05/2022
H	LN169016	India	03/2019	02/2023

Twenty-two brands of amoxicillin 500 mg capsules are registered in Burkina Faso, but only nine brands were found on the market during the study period (*27*). This lower-than-expected availability of amoxicillin brands could be explained by the fact that many registered molecules were out of stock during the study period or that some registered amoxicillin brands were not marketed for commercial reasons. India, China, and France were the main manufacturers of multisource amoxicillin capsules found in the market.

Physicochemical Quality Control

Tests for uniformity of weight, disintegration, dissolution, and API content assay were carried out for each brand as described in the *USP* (*28*).

Assay of amoxicillin was performed in triplicate by using an HPLC chromatography system (Agilent 1260, USA) equipped with UV-Visible detector operating at 230 nm. The mobile phase was potassium dihydrogen phosphate buffer pH 5.0 ± 0.1 and acetonitrile (96:4 v/v). The chromatographic column was an RP-C18 L1 (250 × 4.0 mm, 5 µm). The flow rate was 1.5 mL/min, and injection volume was 10 µL.

Dissolution Tests

The dissolution test was conducted using the paddle method and dissolution tester (Sotax AT, France). The first test was conducted with 900 mL of distilled water at 37.0 ± 0.5 °C and 75 rpm. At 60 minutes, 10-mL samples (n = 6) were withdrawn and filtered (0.45-µm, Millipore). A UV-Visible spectrophotometer (Agilent Cary 3500, USA) was used to determine the amount of amoxicillin released at 272 nm.

As recommended in the BCS-based biowaiver approach, the comparative in vitro dissolution test was performed with 900 mL of each media, namely buffer pH 1.2 (0.1 N HCl), acetate buffer pH 4.5, and phosphate buffer pH 6.8 (*18*, *21*). These three media were prepared according to the *USP* monograph (*28*). At 10, 15, 30, 45, and 60 minutes, 10-mL samples (n = 12) were withdrawn and filtered (0.45-µm, Millipore). The volume removed at each time point was immediately replaced by the same dissolution medium to keep the volume constant during the test.

Equipment and Method Validations

The HPLC, spectrophotometer, and dissolution equipment were qualified and their

performances checked in accordance with *USP* (*28*).

The analytical methods were validated according to the ICH Q2(R1) recommendations (*29*). These include accuracy, specificity, linearity, repeatability, and precision. Amoxicillin CRS from the USP was used for this purpose.

For dissolution method, one unit of amoxicillin capsule was introduced into each vessel of apparatus containing the required volume of a buffer medium pH 1.2, 4.5, or 6.8 maintained at 37 ± 0.5 °C, with 75 rpm. Other vessels containing only the buffer media were used as control. Samples were collected at 60 min and processed exactly as described earlier. The linearity was evaluated on the Reference Standard range and range of the test product. For each range, three independent points and three different test samples are taken, the three points being 20%, 50%, and 100% concentration of the fully dissolved product. The accuracy was deduced from the data from the linearity of the ranges of the Reference Standard and the test product. Specificity was calculated to ensure that the signal measured comes only from the API. Intermediate precision was evaluated using three different samples of the Reference Standard and test product at 100% concentration (n = 6).

Data Analysis

To assess for linearity, the linear regression coefficient of variation (R^2) must be greater than 0.980. For accuracy, typical acceptance criteria in dissolution and assay tests is 97–103% of the label claim. For repeatability and specificity, the coefficient of variation must be less than or equal to 1% and 2%, respectively.

For comparative dissolution tests, if both products (test and comparator) demonstrate 85% dissolution in at least 15 minutes, then the profiles are considered similar (*18*). Otherwise, the fit factor statistical method is used to calculate the relative error between two dissolution curves, i.e., f_1 (difference factor) and f_2 (similarity factor) (*18*, *21*, *25*). Cumulative dissolution values (mean %) are used to calculate f_1 and f_2. To use mean data, the coefficient of variation at the early time point should not be more than 20% and at other time points should not be more than 10%. When the two profiles are identical, $f_1 = 0$ and $f_2 = 100$; f_1 values up to 15 and f_2 values greater than 50 indicate similarity and f_1 values greater than 15 and f_2 values lower than 50 indicate possible differences in the in vivo performance (*18*, *21*).

RESULTS AND DISCUSSION

Physicochemical Quality Comparison

Table 2 shows results of pharmaceutical quality assessments for the collected brands of amoxicillin 500 mg capsules, including the innovator brand. Comparative assessment of pharmaceutical quality is a prerequisite for the determination of bioequivalence. Results for weight variation, disintegration time, HPLC retention time, API content, and dissolution rate, for all tested brands of amoxicillin 500-mg capsules complied with *USP* specifications.

No brand had a weight variation of more than 7.50%. Indeed, for capsules with an average weight of more than 300 mg, the weight uniformity test is compliant if the individual weights of no more than two units deviate from the average weight by more than ± 7.50% and if no unit deviates by more than ± 15.00% (*28*).

Table 2. *Quality parameters of Tested Brands of Amoxicillin (500 mg) Capsules*

Sample	Mean weight (mg)	Maximum weight deviation (%)	Disintegration time (min)	API t_R (min)	API Content (%)	Dissolution within 60 min (%)
Innovator	580.17 ± 4.08	1.70	9.20 ± 0.52	5.459	109.91 ± 0.04	88.40 ± 0.87
A	590.01 ± 4.73	1.71	6.12 ± 1.01	5.457	107.33 ± 0.02	94.51 ± 3.84
B	579.16 ± 3.87	0.99	10.26 ± 0.95	5.459	113.13 ± 0.09	84.73 ± 3.09
C	575.47 ± 3.55	4.39	13.44 ± 1.17	5.458	116.04 ± 0.10	83.21 ± 3.12
D	591.67 ± 4.00	1.06	8.13 ± 0.79	5.457	107.65 ± 0.08	92.99 ± 2.07
E	582.55 ± 3.71	2.87	7.86 ± 1.15	5.457	104.60 ± 3.82	90.01 ± 4.11
F	586.00 ± 3.54	1.51	9.06 ± 0.44	5.456	114.94 ± 0.06	92.49 ± 3.10
G	583.39 ± 4.12	1.23	6.22 ± 0.19	5.456	108.63 ± 0.07	94.93 ± 2.33
H	582.25 ± 4.04	1.80	8.07 ± 1.21	5.458	109.19 ± 0.02	89.20 ± 2.88

Values are mean ± SD unless otherwise noted.
Specifications: < 7.50% mean weight deviation, ≤ 30.00 mins disintegration time, 5.457 mins API t_R, 90–120% API content, and ≥ 80% dissolution within 60 mins.
API: active pharmaceutical ingredient, t_R: chromatographic retention time.

Mean disintegration time for all brands was consistent (6.12–13.44 mins). Product C had the highest disintegration time (13.44 min), which correlated with the lowest dissolution rate (83.21% in 60 min) compared to the other samples.

All capsule brands contained the indicated API (104.60–116.04% of label claim), and retention times of amoxicillin were nearly identical for all samples (range: 5.456–5.459 mins).

All samples released more than 80% of API within 60 minutes of dissolution, as required by the *USP*.

These results are consistent with a prior study in Ethiopia (*16*). In contrast, Kyriacos et al. reported that 56% of amoxicillin capsules in Arab countries did not meet *USP* requirements (*8*).

In Vitro Dissolution Profile Comparison

Validation of the dissolution method demonstrated that it is capable of accurately and reliably measuring amoxicillin over the specified pH range. Indeed, a linear relationship was obtained and the data of accuracy, specificity, repeatability, and intermediate precision were as one would expect.

The dissolution release profiles of each brand of amoxicillin capsules are given in Figure 1. Approximately 70–100% of amoxicillin was released within the first 15 minutes and more than 80% was released within 60 minutes in pH 1.2, 4.5, and 6.8.

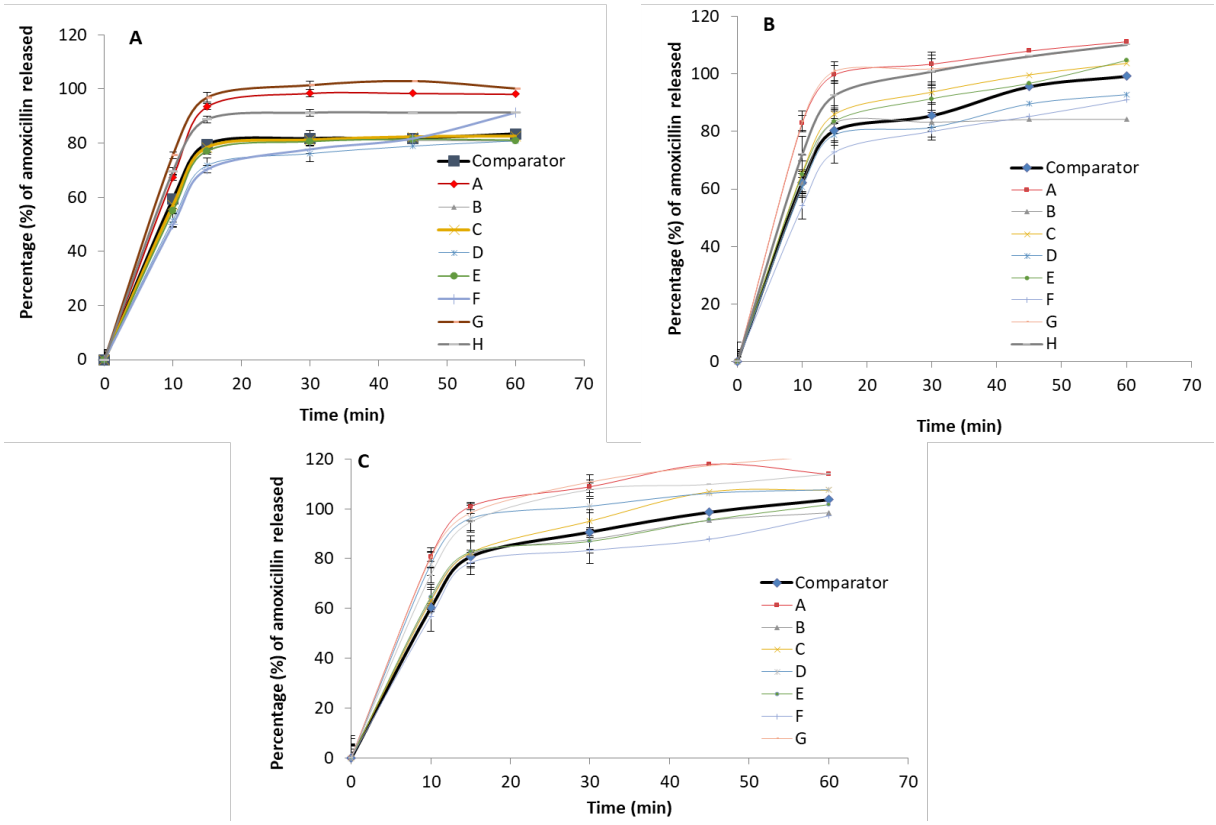

Figure 1. *Dissolution profiles of amoxicillin (500-mg capsules) in pH 1.2 (**A**), 4.5 (**B**) and 6.8 (**C**).*

Figure 1 shows dissolution profiles with similar but not superimposable patterns for all different brands of amoxicillin capsules. Overall, there was less drug released at pH 1.2 compared with pH 4.5 and 6.8. The release of amoxicillin after 60 minutes was not complete at pH 1.2 for all brands, whereas amoxicillin was fully released at pH 4.5 and 6.8 for most brands.

Dissolution of API was faster in pH 6.8, which is consistent with the USP recommendations for quality control dissolution testing of amoxicillin capsules in aqueous media (*28*). The coefficient of variation for mean dissolution was less than 10% at all times for all samples, indicating good homogeneity of amoxicillin dissolution.

The difference and similarity factors are frequently used in vitro bioequivalence studies to compare the dissolution profiles of different brands of dosage forms with the innovator product. It is a relatively fast and inexpensive technique for predicting the in vivo performance of pharmaceutical dosage forms. The fit factor method requires identical sampling points for the calculation of two factors from the individual raw data of two profiles, a minimum of three points over time (excluding time zero), and 12 individual values for each time point for each formulation. The WHO recommends, as a first condition, to use data with less than 20% variance at the first time point and less than 10% variance at subsequent time points (*18*, *21*). This condition was met as variances obtained at all time points for all brands were less than 10%.

Also, WHO states that if the innovator and generic products dissolve very quickly (≥ 85% within 15 min), a profile comparison is not necessary (*18*). Mean dissolution of samples A, G, and H was above 85.00% at 15 min in all three media; however, mean dissolution of the innovator product was approximately 80% in all media. Samples B–F also did not have very fast

dissolution (< 85% in 15 min) in at least two pH levels. Therefore, the similarity factor calculation was applied to compare the eight multisource products with the innovator brand.

Amoxicillin brands B–F and H were similar to the innovator brand, i.e., f_2 values were greater than 50 and f_1 values were less than 15 in all dissolution media; however, brands A and G had f_2 values below 50 and f_1 values above 15 (Table 3). Thus, the dissolution profiles for the latter two samples cannot be considered similar to the innovator sample. The differences observed for these two brands could be related to the formulation. These two brands had faster disintegration times (on the order of 6 min) and very fast drug release (> 85% in 15 min).

Table 3. *Similarity Factor Analysis for Amoxicillin Dissolution Profiles at pH 1.2, 4.5, and 6.8.*

Sample	pH 1.2		pH 4.5		pH 6.8		Comparison with Innovator Brand
	f_1	f_2	f_1	f_2	f_1	f_2	
A	18.13	48.43	19.64	44.80	20.23	43.37	Not similar
B	2.43	86.24	7.37	59.68	3.75	77.56	Similar
C	1.37	93.20	6.13	68.97	4.75	71.98	Similar
D	6.98	67.43	4.57	73.35	12.60	52.27	Similar
E	2.85	83.01	4.35	74.77	3.47	79.55	Similar
F	7.95	63.31	9.32	60.84	7.05	64.26	Similar
G	23.61	43.18	18.83	45.34	21.53	42.69	Not similar
H	11.94	57.88	14.05	52.24	14.86	50.36	Similar

In this study, six out of eight brands were considered similar and thus interchangeable with the innovator brand. This interchangeability rate is higher than that obtained for similar studies in Ethiopia, which reported that most products were not interchangeable with the comparator product (*15*, *16*). On the other hand, a study in Nigeria examined seven brands of amoxicillin/clavulanic acid tablets and found that only one was not bioequivalent to the innovator product (*30*).

In Burkina Faso, Semdé et al. evaluated 20 marketed generic forms of antibacterial drugs and found that all products were interchangeable with the reference products (*31*). High interchangeability rates in some countries but not others could be explained by the establishment of effective marketing authorization and surveillance systems for pharmaceutical products, especially in Burkina Faso in recent years. These pharmaceutical regulatory efforts must be continued for the well-being and health of our populations. Maintaining quality controls at import and post-marketing surveillance are effective ways to ensure the pharmaceutical quality of medicines marketed in resource-limited countries.

CONCLUSION

The dissolution test is essential in the evaluation of quality medicines because it provides in vitro data that can be extrapolated to predict the in vivo behavior of the drug. In this study, all tested brands of amoxicillin 500 mg capsules met *USP* requirements for physicochemical quality. Comparison of dissolution profiles showed that two out of eight generic brands of amoxicillin are not interchangeable with the innovator brand (Clamoxyl) based on statistical calculations of f_1 and f_2.

In view of these observations, it is important that the national drug regulatory authority insists on bioequivalence studies of generic products before any marketing authorization is granted.

It should also strengthen post-marketing surveillance of sensitive medicines such as antibiotics to ensure that they retain their pharmaceutical quality and effectiveness. For a broader view of the quality of amoxicillin capsules, testing unlicensed brands of amoxicillin, imported under special authorization, could be considered.

FUNDING

This work was financially supported by the CEA-CFOREM of Université Joseph Ki-Zerbo (Burkina Faso).

CONFLICT OF INTEREST

The authors disclosed no conflicts of interest related to this article.

REFERENCES

1. Kaur, S. P.; Rao, R.; Nanda, S. Amoxicillin: a broad-spectrum antibiotic. *Int. J. Pharma Sci.* **2011**, *3* (3), 30–37.
2. Sweetman, S. C. *Martindale: The Complete Drug Reference*, 7th ed.; The Pharmaceutical Press, 2007.
3. Ogawara, H. Antibiotic resistance in pathogenic and producing bacteria, with special reference to beta-lactam antibiotics. *Microbiol. Rev.* **1981**, *45* (4), 591–619.
4. World Health Organization Model List of Essential Medicines, 21st ed., World Health Organization, 2019.
5. Ministry of Health Liste Bationale des Médicaments Essentiels et Autres Produits de Santé. Ministry of Health: Burkina Faso, 2020.
6. Carle, S. La résistance aux antibiotiques : un enjeu de santé publique importante. *Pharmactuel* **2009**, *42* (2), 6–21.
7. Ouédraogo, A. S.; Jean Pierre, H.; Bañuls, A. L.; Ouédraogo, R.; Godreuil, S. Émergence et diffusion de la résistance aux antibiotiques en Afrique de l'Ouest: facteurs favorisants et évaluation de la menace. *Méd. Santé Trop.* **2017**, *27* (2), 147–154.
8. Kyriacos, S.; Mroueh, M.; Chahine, R. P.; Khouzam, O. Quality of amoxicillin formulations in some Arab countries. *J. Clin. Pharm. Ther.* **2008**, *33* (4), 375–379. DOI: 10.1111/j.1365-2710.2008.00926.x.
9. Hailu, G. S.; Gutema, G. B.; Asefaw, A. A.; Hussen, D. A.; Hadera, M. G. Comparative assessment of the physicochemical and in vitro bioavailability equivalence of co-trimoxazole tablets marketed in Tigray, Ethiopia. *Int. J. Pharm. Sci. Res.* **2011**, *2*, 1000–1008.
10. Menegola, J.; Steppe, M.; Schapoval, E. E. Dissolution test for citalopram in tablets and comparison of in vitro dissolution profiles. *Eur. J. Pharm. Biopharm.* **2007**, *67* (2), 524–530. DOI: 10.1016/j.ejpb.2007.02.009.
11. Ferraz, H. G.; Carpentieri, L. N.; Watanabe S.P. Dissolution profile evaluation of solid pharmaceutical forms containing chloramphenicol marketed in Brazil. *Braz. Arch. Biol. Technol*. **2007**, 50, 57–65. DOI: 10.1590/S1516-89132007000100007.
12. Byakika-Kibwika, P.; Lamorde, M.; Kalemeera, F.; D'Avolio, A.; Mauro, S.; Di Perri, G.; Ryan, M.; Mayanja-Kizza, H.; Khoo, S.; Back, D.; et al. Steady-state pharmacokinetic comparison of generic and branded formulations of stavudine, lamivudine and nevirapine in HIV-infected Ugandan adults. *J. Antimicrob. Chemother.* **2008**, *62* (5), 1113–1117. DOI: 10.1093/jac/dkn290.
13. Stuart, A. V.; Zuo, J.; Löbenberg, R. Investigating the dissolution profiles of amoxicillin, metronidazole, and zidovudine formulations used in Trinidad and Tobago, West Indies. *AAPS PharmSciTech* **2014**, *15* (5), 1060–1069. DOI: 10.1208/s12249-014-0132-9.
14. Al Ameri, M. N.; Nayuni, N.; Anil Kumar, K. G.; Perrett, D.; Tucker, A.; Johnston, A. The differences between the branded and generic medicines using solid dosage forms: In-vitro dissolution testing. *Results Pharma Sci.* **2011**, *2*, 1–8. DOI: 10.1016/j.rinphs.2011.12.001.
15. Kassaye, L.; Genete, G. Evaluation and comparison of in-vitro dissolution profiles for different brands of amoxicillin capsules. *Afr. Health Sci*. **2013**, *13* (2), 369—375. DOI: 10.4314/ahs.v13i2.25.
16. Hailu, G. S.; Gutema, G. B.; Hishe, H. Z.; Ali, Y. S.; Asfaw, A. A. Comparative In vitro Bioequivalence Evaluation of Different Brands of Amoxicillin Capsules Marketed in Tigray, Ethiopia. *Int. J. Pharma. Sci. Nanotechnol.* **2013**, *6* (1), 1966–1971. DOI: 10.37285/ijpsn.2013.6.1.7.
17. Al-Tabakha, M. M.; Fahelelbom, K. M. S.; Obaid, D. E. E.; Sayed, S. Quality Attributes and In Vitro Bioequivalence of Different Brands of Amoxicillin Trihydrate Tablets. *Pharmaceutics* **2017**, *9* (2), 2–11.

DO : 10.3390/pharmaceutics9020018.
18. WHO Expert Committee on Specifications for Pharmaceutical Preparations. *Multisource (generic) Pharmaceutical Products: Guidelines on Registration Requirements to Establish Interchangeability*. WHO Technical Report Series, No. 1003, Annex 6; World Health Organization, 2017; pp 193–231.
19. Dissolution test of solid dosage forms. In *European Pharmacopoeia*. European Directorate for the Quality of Medicines and HealthCare, 2020; pp 354-361.
20. *Guideline on the Investigation of Bioequivalence*, CPMP/EWP/QWP/1401/98 Rev. 1. Committee for Medicinal Products for Human Use (CHMP), European Medicines Agency; 2010.
21. *Waiver of In Vivo Bioavailability and Bioequivalence Studies for Immediate-Release Solid Oral Dosage Forms Based on a Biopharmaceutics Classification System*; Guidance for Industry. U.S Department of Health and Human Services, Food and Drug Administration. 2017.
22. WHO Expert Committee on Specifications for Pharmaceutical Preparations. *Proposal to Waive In Vivo Bioequivalence Requirements for WHO Model List of Essential Medicines Immediate-Release, Solid Oral Dosage Forms.* WHO Technical Report Series, No. 937, Annex 8; World Health Organization, 2006.
23. Thambavita, D.; Galappatthy, P.; Mannapperuma, U.; Jayakody, L.; Cristofoletti, R.; Abrahamsson, B.; Groot, D. W.; Langguth, P.; Mehta, M.; Parr, A.; Polli, J. E.; Shah, V. P.; Dressman, J. Biowaiver monograph for immediate-release solid oral dosage forms: amoxicillin trihydrate. *J. Pharm. Sci.* **2017**, *106* (10), 2930–2945. DOI: 10.1016/j.xphs.2017.04.068.
24. Moore, J. W.; Flanner, H. H. Mathematical comparison of curves with an emphasis on in-vitro dissolution profiles. *Pharm. Technol.* **1996**, *20* (6), 64–74.
25. Shah, V. P.; Tsong, Y.; Sathe, P.; Liu, J. P. In vitro dissolution profile comparison--statistics and analysis of the similarity factor, f2. *Pharm. Res.* **1998**, *15* (6), 889–896. DOI: 10.1023/A:1011976615750.
26. WHO Expert Committee on Specifications for Pharmaceutical Preparations. *Guidance on the selection of comparator pharmaceutical products for equivalence assessment of interchangeable multisource (generic) products*. WHO Technical Report Series, No. 902; World Health Organization, 2002.
27. Nomenclature Nationale des Spécialités Pharmaceutiques et Médicaments Génériques Enregistrés au Burkina Faso. Ministry of Health, Burkina Faso, 2020.
28. Monograph for amoxicillin capsules. In *USP41–NF36*, United States Pharmacopeial Convention, Inc., 2018; pp 276-278.
29. International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use. *Validation of analytical procedures: Text and Methodology, Q2 (R1);* ICH Harmonised Tripartite Guideline, 2005.
30. Olanrewaju, O. J.; Paul, A. C.; Olusola, A. M. Quality assessment of amoxicillin-clavulanate potassium tablets in Lagos, Nigeria. *J. Chem. Pharm. Res.* **2012**, *4* (12), 5032–5038.
31. Semdé, R.; Ouédraogo, H. W.; Guissou, I. P.; Amighi, K. [Bioequivalence in vitro evaluation of some antibacterial generic dosage forms] [Article in French]. *J. Pharm. Belg.* **2005**, *60* (2), 51–55.