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Quality assessment and *in vitro* bioequivalence studies of chlorpheniramine maleate tablets marketed within Zaria metropolis, Kaduna State, Nigeria

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Abstract
Chlorpheniramine maleate is a widely used over-the-counter antihistamine for the relief of allergy and cold symptoms. This study evaluated the bioequivalence of ten chlorpheniramine maleate tablet samples (coded A–J) compared with the innovator brand. Pharmacopeial methods (BP/USP 2009) were applied to assess physicochemical properties, while three UV-spectrophotometric methods were developed and validated in line with ICH Q2 (2022) guidelines to determine drug release in simulated physiological media (pH 1.2, 4.5, and 6.8). *In vitro* dissolution testing was performed using USP Apparatus II at 37 ± 0.5°C and 100 rpm across the three pH media, with samples collected at intervals up to 60 minutes. Dissolution profiles were analyzed using difference (f_1) and similarity (f_2) factors, as well as dissolution efficiency (% DE). All samples passed the identification test. However, sample G failed the friability test, and sample D failed both disintegration and dissolution requirements. Generics B, F, and H met acceptable f_1 and f_2 limits in all media. samples C, E, G, J, and I showed equivalence in one or two media, while D failed in all. All samples had % DE values within ±10% of the reference. In conclusion, only B, F, and H were bioequivalent and interchangeable.

Keywords: Bioequivalence; Chlorpheniramine maleate; Fit factors; *In vitro*

INTRODUCTION

In vitro bioequivalence is widely used as a substitute for *in vivo* bioavailability studies, as it allows comparison of dissolution profiles and drug bioavailability under controlled laboratory conditions [1], while offering advantages such as lower cost, reduced time, faster regulatory approval, and avoidance of unnecessary human subject involvement [2]. This method is especially applicable to drugs like chlorpheniramine maleate, which falls under Class 1 of the Biopharmaceutics Classification System (BCS), as recommended by the regulatory agencies such as the World Health Organization (WHO) and the Food and Drug Administration (FDA) [3].

The quality and dissolutions of six paracetamol tablet brands in Nigeria were studied and it was shown that all brands were interchangeable and bioequivalent with difference (F_1) and similarity (F_2) factors

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ranging from 1.13 - 15.15 and 64.24 - 95.21 respectively [4]. Also, *In vitro* equivalences of generic metformin hydrochloride and propranolol hydrochloride tablets were evaluated in Lagos State, Nigeria and none of the generic samples tested were bioequivalent [5].

Having several generics options has heightened concerns about counterfeit and substandard drugs, causing morbidity, mortality and loss of confidence in healthcare, and making patients and health providers cautious in choosing among brands of the same drugs during treatment [6, 7]. This seems to have worsened in recent years and particularly affect developing countries where, around 25% of drugs consumed are of poor quality [8]. The current study was to assess the quality and determine the bioequivalence of generic chlorpheniramine maleate tablets marketed within Zaria metropolis, Kaduna State, Nigeria.

EXPERIMENTAL METHODS

Sample collection. Ten different generics of chlorpheniramine maleate (4 mg) were purchased from retail Pharmacies in Zaria metropolis. They were coded A-J (sample A as the innovator brand) and assessed using the quality assessment parameters of uniformity of weight, friability, assay content, disintegration and dissolution test. The assessment was done according to the United State pharmacopoeia (USP) and the British pharmacopoeia (BP) standards [9, 10].

Quality assessment of Chlorpheniramine Maleate tablets

Uniformity of weight. Twenty tablets from each generic were individually weighed, and their percentage weight deviation from the mean was calculated as per USP 2009 guidelines.

Friability test. Twenty tablets from each generic were tested for friability using a Roche friabilator (25 rpm for 4 minutes), and the percentage weight loss was calculated.

Assay content. Chlorpheniramine maleate content was determined by titrating 0.150 g equivalent of the sample dissolved in acetic acid with 0.1 N perchloric acid using crystal violet as an indicator. The titration, performed in triplicate with a blank, showed a purple-to-green endpoint, and the average titre value was used to calculate the percentage content, based on the equivalence of 1 ml of 0.1 N perchloric acid to 19.54 mg of chlorpheniramine maleate (BP, 2009).

Disintegration test. Using a six-station disintegration apparatus, six tablets per basket were immersed in 900 mL of distilled water at 37 ± 0.5°C, and the time taken for the tablets to fully disintegrate was recorded (BP 2009)

Dissolution test. Dissolution testing was performed using USP Apparatus II (paddle) in 900 mL of 0.01 N HCl at 37 ± 0.5°C. After 30 minutes, 10 mL samples were withdrawn, filtered, and analyzed at 264 nm using a spectrophotometer. The percentage of drug released was calculated and compared to the USP (2009) standard of at least 80% release within 30 minutes.

In vitro bioequivalence studies of Chlorpheniramine maleate tablets

Preparation of standard stock solution. Chlorpheniramine stock solutions (100 µg/ml) were prepared by dissolving 10 mg of chlorpheniramine maleate standard powder in 100 ml of each of the prepared simulated physiological media (pH 1.2, 4.5 and 6.8).

Determination of wavelength of maximum absorption. The wavelength of chlorpheniramine maleate maximum absorption in the various media were obtained by scanning the 16 µg/mL solution of the drug in the various media against their respective blank.

Construction of calibration curve. A six-point chlorpheniramine maleate calibration curve in each of the medium was constructed by preparing 2, 4, 8, 16, 32, 64 µg/mL concentrations in the different simulated physiological media using serial dilution.

***In vitro* dissolution studies.** *In vitro* dissolution testing was conducted using USP (2009) apparatus II (paddle) at 50 rpm in 900 mL of three media (0.1 N HCl, pH 1.2; acetate buffer, pH 4.5; phosphate buffer, pH 6.8) maintained at 37 ± 0.5°C. Samples of 5 mL were withdrawn and replaced at 5, 10, 20, 30, 45, and 60 minutes, filtered, and analyzed by UV spectrophotometry at the validated working wavelength (λ_{max}). The test was repeated four times per sample, and average drug release percentages were calculated from calibration curves to evaluate in vitro bioequivalence among tablet brands.

Dissolution profile comparison and bioequivalence of generics to the innovator brand. Fit factors (difference factor (f_1) and similarity factor (f_2)) and dissolution efficiency (% D.E) were used to examine the dissolution profiles of the generics in comparison to the innovator brand. The FDA and the European Agency for the Evaluation of Medicinal Products (EMEA), through the Committee for Proprietary Medicinal Products (CPMP), have accepted the similarity factor (f_2) as a criterion for comparing the similarity of two or more dissolution profiles [11].

$$f_1 = \{[\sum t = 1\ n|\mathrm{Rt} - \mathrm{Tt}|]/[\sum t = 1\ n\mathrm{Rt}]\}.100 \quad \text{.... (1)}$$

$$f_2 = 50\,.\log\left\{\left[1 + \left(\frac{1}{n}\right)\sum_{t=1} n\,(R_t - T_t)^2\right]\right\} \quad \text{..... (2)}$$

$$\mathrm{D.E} = \frac{\int_{t1}^{t2} y.dt}{y100\ x\ (t2-t1)}\ x\ 100 \quad \text{..... (3)}$$

Statistical analysis. The uniformity of weight was analyzed with simple statistics; the mean weight ± standard deviation (SD) was calculated for each sample, while the *in vitro* dissolution profiles for each sample were analyzed with fit factors (f_1 & f_2) and dissolution efficiency (% D.E) using Microsoft Excel, 2016.

RESULTS

The result for the labelled information of the ten generics chlorpheniramine maleate presented in Table 1, revealed that the majority (80%) of the samples were found to be indigenous (Made in Nigeria) and also were within their expiry date as at the time the study was conducted. As shown in Table 2, all the samples except D, were found to be consistent in their doses as their percent mean deviation was within ≤ 7.5% as specified by (BP, 2009) for individual tablet weighing ≥ 80 mg and ≤ 250 mg. All the tested tablet samples passed friability test except sample G which showed a high friability of 7.17% as shown in Table 2.

The amount (assay content) of chlorpheniramine maleate in samples A, B, C, F, G, and I, were found to be within the acceptable range (98 – 101%) of BP (2009) specification while samples D, E and H, had low content of the API as shown in Table 2. As presented in table 2.0, all tablet samples disintegrated within the 15-minutes limit as specify by (BP, 2009), except sample D. All the samples released more than 80% of the required amount of their API within 30 minutes except sample D as shown in Table 2. Table 3 present the summary of the calibration curve and validation parameters assessed for the three developed methods. The methods demonstrated good precision, with low intra-day and inter-day variability, confirming repeatability and reproducibility. Accuracy was validated by percentage recoveries within the acceptable 98 - 102% range and minimal error. Additionally, the methods were highly sensitive, as it can detect as low as 0.82 µg/mL and quantify as low as 2.47 µg/mL, ensuring reliable measurement of low drug concentrations.

Table 1: Label information of the chlorpheniramine maleate tablet samples

Sample	Country of origin	Batch number	Manufacturing date	Expiry date	NAFDAC number
A	Nigeria	S0128SD	Apr., 2024	Apr., 2027	04-4054
B	Nigeria	4B516011	Feb., 2024	Jan., 2027	04-0252
C	Nigeria	2404	Jan., 2024	Jan., 2027	A11-1139
D	Nigeria	24032902	Mar., 2024	Feb., 2027	B4-2284
E	Nigeria	T2210	Nov., 2022	Aug., 2025	A11-0208
F	India	22CHL07	Feb., 2022	Jan., 2025	04-4317
G	India	TWL05	Dec., 2021	Nov., 2024	B4-7355
H	Nigeria	23050	Aug., 2023	Jul., 2026	04-0490
I	Nigeria	ACT23035	Jun., 2023	May, 2026	A4-9115
J	Nigeria	CPM208	Jun., 2024	May, 2027	04-7454

NAFDAC: National Agency for Food and Drug Administration

Table 2: Physiochemical properties of generics chlorpheniramine maleate tablet

Sample	Weight uniformity (mg)±SD	Assay content (%)	Friability (%)	Disintegration time (min:s)	Dissolution (%)
A	134.75 ± 5.40	100.33	0.61	01:52	87.57
B	141.80 ± 5.11	98.57	0.43	08:15	84.79
C	153.30 ± 5.02	95.10	0.32	11:56	80.63
D	146.25 ± 7.03	91.19	0.29	23:36	75.70
E	105.15 ± 13.29	85.54	0.49	00:10	85.42
F	160.55 ± 4.64	102.48	0.47	00:31	87.99
G	242.60 ± 3.41	93.00	7.17	01:01	82.22
H	139.00 ± 5.95	90.80	0.58	02:12	84.20
I	139.75 ± 6.21	94.70	0.99	08:58	85.28
J	133.35 ± 5.98	85.11	0.30	03:00	82.15

SD: Standard deviation, min: minute, s: second, mg: milligram

Table 3: Calibration curves and validation parameters assessed for the three developed methods

Parameters	Method 1 (pH 1.2)	Method 2 (pH 4.5)	Method 3 (pH 6.8)
Maximum wavelength (nm)	264	261	261
Calibration curve range (µg/mL)	2 – 64	2 – 64	2 – 64
Intercept	0.002	0.010	0.046
Coefficient of determination (R^2)	0.999	0.999	0.998
Slope	0.010	0.013	0.015
Accuracy (% recovery)	99.602	99.772	99.95
Intra-day precision (% CV)	2.333	4.102	4.050
Inter-day precision (% CV)	6.940	9.353	8.391
Limit of detection (µg/mL)	0.823	2.281	2.194
Limit of quantification (µg/mL)	2.471	6.910	6.654

nm: nanometer, µg/mL: microgram/millilitre, R^2: coefficient of determination, CV: coefficient of variation

Table 4: Fit factors (f_1 and f_2) and % D.E of chlorpheniramine maleate tablet samples in pH 1.2, pH 4.5 and pH 6.8

	Sample	A	B	C	D	E	F	G	H	I	J
pH 1.2	f_1	0	13.73	34.72	39.65	24.76	12.92	23.13	5.60	8.14	12.65
	f_2	100	52.67	26.29	25.30	31.21	51.40	38.39	70.90	67.99	55.36
	% D.E	5.50	5.10	3.15	2.96	3.73	5.47	4.80	5.76	5.76	5.40
pH 4.5	f_1	0	9.32	5.85	31.71	9.52	6.53	11.38	12.66	19.16	20.90
	f_2	100	55.02	69.51	30.22	55.74	64.44	60.11	58.12	40.19	47.08
	% D.E	5.07	4.92	5.02	3.39	5.39	4.92	5.92	5.16	4.63	5.32
pH 6.8	f_1	0	3.20	5.85	25.54	2.33	2.79	1.51	3.49	29.60	3.46
	f_2	100	81.90	69.37	35.23	90.41	81.64	91.30	75.18	36.15	75.18
	% D.E	4.61	4.85	4.85	5.14	4.63	4.60	4.56	4.41	5.58	4.61

f_1: difference factor ≤ 15, f_2: similarity factor ≥ 50, % D.E: dissolution efficiency ± 10%

Table 4 shows the fit factors (f_1 and f_2) and % D.E of chlorpheniramine maleate tablet samples in pH 1.2, pH 4.5 and pH 6.8 respectively. Also, the dissolution efficiency (% D.E) model were shown at Table 4 and all the tested samples demonstrated values within

the acceptable limits across the three simulated physiological media (pH 1.2, 4.5, and 6.8).

DISCUSSION

All the samples were presumed to be genuine and of good quality as they were registered by the National Agency for Food and Drug Administration and Control (NAFDAC). Uniformity of weight test is a quality assessment parameter used to ensure that each tablet in a batch contains a consistent amount of active pharmaceutical ingredients (API) by measuring the variation in individual tablet weights [12]. Sample D was found not to be consistent in its doses; hence, this might lead to therapeutic failure when administered. The high friability of sample G suggests it may not endure transport or storage, potentially leading to damage and inconsistent dosing, risking therapeutic failure [13]. This aligns with Zaman *et al*. [13], who found that one out of eight Chlorpheniramine samples failed the friability test, likely due to poor formulation or manufacturing issues [13]. The low chlorpheniramine maleate content may indicate a substandard product, potentially arising from formulation or manufacturing errors, rather than suggesting it is a fake or counterfeit. This implies that, the optimal therapeutic concentration might not be obtained when these sampled are administered [14]. The disintegration of tablets is dependent on the type of formulation excipients and processes used by different manufacturers which consequently influence the bioavailability of the drug [15]. Sample D having a high disintegration time might affect its drug release and availability for dissolution. Dissolution rate is a dependent of disintegration rate. A tablet with a low *in vitro* dissolution rate indicates a corresponding low *in vivo* bioavailability [13]. This suggests that sample D may not be bioavailable upon administration, which could result in therapeutic failure. According to the US FDA, WHO and EMEA, it was stated that, for any generic brand to be *in vitro* bioequivalence to the innovator, the dissolution profile should be similar in at least three simulated physiological media (pH 1.2, 4.5, 6.8 and/or 7.4). In addition, a generic brand is considered *in vitro* equivalent with its branded counterpart when the similarity factor (f_2) is $\geq$ 50 and the difference factor (f_1) is $\leq$ 15, so also dissolution efficiency of ± 10% [16]. The fit factors (f_1 and f_2) for samples B, F and H were within the acceptable range limit across the three media (pH 1.2, 4.5 and 6.8). A study conducted on twelve sulphadoxine - pyrimethamine brands reported that only five brands are bioequivalent with the innovator sample [17]. Similar findings were reported by Olusola *et al*., [18], where only one of two generic amlodipine brands was bioequivalent with the innovator brand across all media. Overall, the study highlights that not all approved generics consistently demonstrate bioequivalence with the innovator across varying physiological pH conditions [18]. Olubukola *et al.,* [5] reported that none of the generic metformin hydrochloride and propranolol hydrochloride tablets evaluated in Lagos State, Nigeria were bioequivalent with the innovator brand [5]. Unlike the fit factors (f_1 and f_2), the dissolution efficiency (% D.E) provides a quantitative approach for evaluating drug release profiles [19]. Based on the dissolution efficiency (% D.E) model result, it was shown that all the samples have similar extent of absorption across all pH media (1.2, 4.5 and 6.8).

Conclusion. The study demonstrated that samples B, F and H, were pharmaceutical and chemical equivalents with respect to the innovator sample "A". Therefore, they may be used interchangeable with each other in clinical use.

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REFERENCES

1. Center for Drug Evaluation and Research (CDER). Waiver of In vivo bioavailability and bioequivalence studies for immediate-release solid oral dosage forms based on a biopharmaceutics classification system guidance for industry. (Issue December, 2013).

2. Polli JE. In vitro studies are sometimes better than conventional human pharmacokinetic in vivo studies in assessing bioequivalence of immediate-release solid oral dosage forms. AAPS J. 2008; 10:289-299.

3. US Food and Drug Administration Center for Drug Evaluation and Research. Guidance for industry: Dissolution testing of immediate release solid oral dosage forms.1997. Available at: http://www.fda.gov/cder/Guidance/1713bp1.pdf

4. Ukwueze SE, Uzochukwu IC, Ngonebu EJ. Comparative quality assessment and in vitro dissolution profile of some paracetamol tablet generics marketed in Nigeria. Port Harcourt Med J. 2008;3(1):85-90.

5. Olubukola OO, Fola T, Moshood OA, Bolajoko AA. In vitro equivalence studies of generic metformin hydrochloride tablets and propranolol hydrochloride tablets under biowaiver conditions in Lagos State, Nigeria. Dissolution Technol. 2012;51-55

6. Cockburn R, Newton PN, Agyarko EK, Akunyili D, white NJ. The global threat of counterfeit drugs; why industry and governments must communicate the dangers. PLoS. 2005;2(4):e100.

7. Al Ameri MN, Nayuni N, Kumar KA, Perrett D, Tucker A, Johnston A. The differences between the branded and generic medicines using solid dosage forms. In vitro dissolution testing. Results in pharma sci. 2012; 2:1-8.

8. World Health Organization. WHO Global Surveillance and Monitoring System for Substandard and Falsified Medical Products (M. L. G. Dr Suzanne Hill, Ms Emer Cooke, Dr Clive Ondari, Mr Michael Deats, Ms Pernette Bourdillon Esteve, Ms Diana Lee (ed.). 2017

9. United States Pharmacopoeia. USP Monograph Development: Chlorpheniramine maleate Tablets. 2009;27(3):3265.

10. British Pharmacopoeia. Specific Monograph Chlorpheniramine Maleate Tablets. 2009; 3:857.

11. Khan KA, Rhodes CT. Effect of compaction pressure on the dissolution efficiency of some direct compression systems. Pharmaceutica Acta Helv. 1972;47: 594-607.

12. Gilbert SB, Christopher TR. Modern Pharmaceutics. 4th Edition. Marcel Dekker USA. 2002;520-560

13. Zaman, KA, Sultana S, Deepa KN, Akter S. Performance evaluation of different brands of chlorpheniramine maleate (antihistamine) tablets available in Bangladesh. J Allied Health Sci. 2014;1 (2):99-107.

14. Adegbolagun OM, Nwabuife JC. Comparative pharmaceutical and physicochemical equivalence of some brands of chlorpheniramine maleate tablets. Niger J of Pharm Res. 2018;14(2):197-202.

15. Eichie F, Arhewoh M, Isesele J, Olatunji K. In vitro Evaluation of the pharmaceutical quality of some Ibuprofen tablets dispensed in Nigeria. Int J Health Res. 2011; 4:57-61.

16. World Health Organization. Proposal to waive in vivo bioequivalence requirements for WHO model list of essential medicines immediate-release, solid oral dosage forms. In WHO Technical Report Series. 2010 (Issue 937).

17. Ochekpe NA, Ngwuluka NE, Agbowuro AA, Obodozie OO. Dissolution profiles of twelve brands of sulphadoxine pyrimethamine in the Nigerian market. Dissolution Technol. 2012;4(4):59-64.

18. Olusola AM., Oyetunde O, Okpara HE, Ayerota E. Equivalence of two eneric brands of amlodipine besylate under biowaiver conditions. Int J Pharm Pharm Sci. 2012;4(2):265-268.

19. Reddy MN, Rehana T, Ramakrishna S, Chowdary KP, Diwan, PV. β-Cyclodextrin complexes of celecoxib: molecular-modelling, characterization, and dissolution studies. AAPS J. 2004;6(1):7.