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Quality control assessment and the possibility of interchangeability between multi-sourced clopidogrel tablets marketed in Nigeria

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Abstract

Background: The increasing availability of generic drug products has enhanced access to affordable medicines; however, concerns regarding their quality and interchangeability with innovator brands persist, particularly in developing countries. Clopidogrel, an antiplatelet agent, is widely used in cardiovascular therapy, making quality assurance of its multisource products essential.

Objectives: The study was aimed to assess the quality control parameters and explored the interchangeability between ten multi-sourced clopidogrel tablets marketed in Nigeria.
Methods: Quality control parameters evaluated include colour, shape, weight variation, hardness, thickness, friability, disintegration, content of active ingredient and *in-vitro* dissolution profile according to the Pharmacopoeia's standards.

Results: All the samples comply with the USP standard for thickness, weight uniformity and disintegration tests**.** Only samples A (4.35±0.34), C (5.00±0.00), I (4.80±0.92) and J (4.98 ±0.28%) passed the hardness (kg/m^2) test. All the tested samples pass the friability test with exception of samples E (1.46%) and G (7.88%). Sample F (72.40 %) failed the USP test for content of active ingredient. Comparisons of dissolution profiles of the different brands were carried out by model-independent approach: the dissimilarity factor $f1$, similarity factor $f2$ and dissolution efficiency (DE). Statistical comparison of f 1, $f2$ and DE indicated that only sample J (Torrent-clopidogrel®) was found to be similar ($p > 0.05$) to sample A (Plavix®).

Conclusion: This study therefore concludes that only Torrent-clopidogrel® is similar with Plavix® and can be used interchangeably.

Keyword: Quality Control; Interchangeability; Pharmacopoeia; Generic Drugs; Clopidogrel; Dissolution Profile

1. Introduction

There is an increasing number of generic drug products available in the market. Hence, generic drug products are the most commonly used pharmaceutical cost-containment strategies, aimed at stimulating competition on the off-patent market and thereby reducing costs without compromising quality and efficacy.[1]

Approval of a generic medicine is based on the demonstration of interchangeability or therapeutic equivalence to the innovator brand through bioequivalence studies. Bioequivalence is the absence of a significant difference in the rate

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and extent to which the active ingredient or active moiety in pharmaceutical equivalents or pharmaceutical alternatives becomes available at the site of drug action when administered at the same dose.[2]

Internationally, statistics shows that innovator drug products are dramatically prescribed, giving rise to a high cost of drug budgets. Since the use of generic drugs provides a lower cost than the innovator or branded products, great savings in health care procurement can be made.[3]

Also, availability of counterfeit drugs in most poor and developing countries has been widely noticed with generic drugs and this has also led to reduction in therapeutic effects of the generic drug product and consequently loss of public trust on some of the generic products.[4]

The manufacturers of generic drugs need FDA approval before the marketing of their drug products. To obtain FDA approval for a generic drug, it must match the innovator drug in active ingredients, strength, dosage form, route of administration, the same usage indications, bioequivalent meet, batch requirements for identity, purity, quality and be manufactured in accordance with the strict standards of FDA's good manufacturing practice regulations required for innovative products.[3]

1.1. Chemistry of clopidogrel

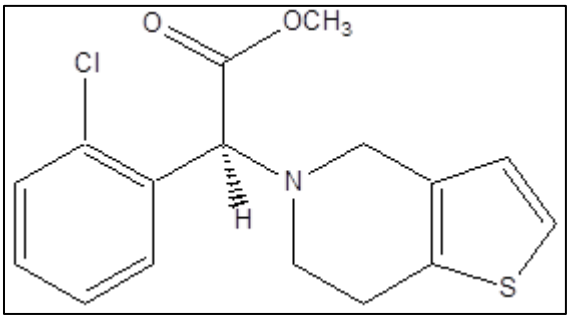

Figure 1 Chemical structure of clopidogrel

- **IUPAC Name**: Methyl (2*S*)-2-(2-chlorophenyl)-2-(6,7-dihydro-4*H*-thieno[3,2-c]pyridin-5-yl)acetate.
- **Empirical Formula**: $C_{16}H_{16}ClNO_2S.H_2SO_4$
- **Molecular Weight**: 419.9

Stereochemistry: Clopidogrel is a thienopyridine derivative, it contains a centre of dissymmetry and hence is capable of being resolved into its mirror image compounds. It has been found that only the (S)-enantiomer (dextrorotatory form) has anti-thrombolytic activity.

Metabolism: Clopidogrel is extremely metabolized *in-vivo* by carboxylesterase hydrolysis on the ester functional group resulting in the formation of clopidogrel carboxylic acid (inactive metabolite). In addition, small amount of clopidogrel is converted to pharmacologically active metabolite via the intermediate metabolite, inactive 2-oxo clopidogrel reduction then converted to active metabolite by a two-step cytochrome P450 oxidation process. Clopidogrel has been found to irreversibly bind to and alter the platelet receptor for adenosine diphosphate (ADP), thereby blocking the binding of ADP to its receptor. This binding causes the inhibition of ADP-mediated activation of the glycoprotein complex GPIIb/IIIa, and inhibiting fibrinogen binding to platelets and platelet adhesion and aggregation.[5]

In 2015, Barabde and Ambadekar developed a simple and accurate spectrophotometric and HPLC methods for determination of Clopidogrel bisulphate in tablets dosage form. The spectrophotometric method was developed by dissolving tablets in 1:1 methanol and the λ max was found to be 220nm. The developed method was used to assay three different brands of clopidogrel. The samples were found to fall within the range. The application of HPLC procedure depends on using a conventional reverse phase (C_{18}) column along with mobile phase 11 consisting of 1:1 Methanol. The advantage of these newly developed procedures which include, ease of execution and it also require less sample handling than methods described in the literature.[6]

In 2014, Mona and co-workers, conducted a study to determine counterfeit Plavix using two chromatographic methods, HPLC and TLC-densiometric methods. The developed method was proposed as a fast and reliable methods for detection and quantitation of counterfeit Plavix tablets. The proposed method was used to chemically counterfeit the tablets with Aspirin's degradation products, Salicylic acid, and metronidazole which were separated. Also, counterfeit was in packaging, strips and tablets' colour and these could be seen by visual inspection compared to original drug. The proposed methods can easily differentiate genuine from counterfeited tablets without need of prior separation. The proposed methods were validated according to ICH guidelines and applied to eleven batches, also were compared statistically with the reported one. There are numerous brands of clopidogrel in the market and many healthcare providers have complained of therapeutic failure with some brands of the medication. This would suggest that those brands do not meet the requirements for quality and the availability of those brands put numerous patients at risk of therapeutic failure.[7]

In this study, some of the most common brands of clopidogrel in Nigerian market have been chosen in order to confirm that they meet the requirements for quality. The result obtained from this study would help prescribers and pharmacists to choose the effective brand of the medication for patients without fear of failure while still maintaining an affordable cost of treatment. The study was aim to assess the quality control parameters and explored the interchangeability between ten multi-sourced clopidogrel tablets marketed in Nigeria. Objectively, the strategy was to evaluate and compare ten different brands of Clopidogrel Bisulfate which are commercially available in the Nigerian market of which the end result would help inform the regulatory bodies of the different brands which do not meet the minimum requirements for marketability in the Nigerian market in order to protect the numerous patients who used the medications daily.

Physicochemical properties of the available ten brands of Clopidogrel Bisulfate tablets were compared according to the standards of USP pharmacopoeia including uniformity of weight, friability, hardness, disintegration, dissolution rate and drug content. The content of clopidogrel in the different brands were estimated using UV spectrophotometry.

Hypothesis: Null Hypothesis H_0: Multi-sourced generic clopidogrel tablets available in Nigeria can be interchanged with the Innovator brand Plavix™ in clinical setting. Alternate Hypothesis H_1: Multi-sourced generic clopidogrel tablets available in Nigeria cannot be interchanged with the Innovator brand Plavix™ in clinical setting

2. Materials and methods

2.1. Materials

Ten commercial brands of Clopidogrel, labelled to contain 75mg per tablets, from different manufacturers were purchased and coded as A, B, C, D until J and then separated. The table below summarizes the different brands obtained

Table 1 Detailed information on clopidogrel 75 mg tablet formulations evaluated for quality

Brand Code	Brand Name	Manufacturer	Country of Origin	Inscription	Labelled Strength (mg)	Batch Number	NAFDAC Reg. Number	Expiry Date	Price/75 mg Tablet (N)	Price/75 mg Tablet
A	Plavix™	Sanofi	France	75	75	AA510	A4-7682	Feb.-2023	478.57	(N)
B	Pidogrel™	Zolon	India	-	75	T0064	A4-6556	Jan.-2023	80.00	478.57
C	Plagerine™	Micro Labs LTD	India	MICRO	75	PANH0073	A4-5107	Dec.-2022	70.00	80.00
D	Nigrel™	Baroque pharmaceuticals P VT. LTD.	India	-	75	GD18686	B4-5747	Feb.-2022	65.00	70.00
E	Instaclop™	Ajanta Pharma LTD	India	-	75	PA1138F	A4-2716	May-2021	79.00	65.00

F	Clopidogrel™	Bafna Pharmaceuticals LTD	India	-	75	F20266002	C4-0853	June-2023	58.00	79.00
G	Clodorel™	Lark Laboratories LTD	India	-	75	TCD-05	B4-9451	July-2023	60.00	58.00
H	Clopidogrel™	Ecomed Pharma LTD	Nigeria	KA	75	8JC47004	A11-0301	Aug-2021	60.71	60.00
I	Predogrel™	Fredun Pharmaceuticals LTD	India	-	75	FC0022	B4-4354	Feb-2023	30.00	60.71
J	Clopidogrel™	Torrent Pharma	UK	-	75	1010777	NIL	Sept-2023	78.57	30.00

Pure samples of Clopidogrel were also obtained from AK scientific, India, and used for the purpose of this study.

Instruments and Equipment: Analytical weighing balance, (Kern and Shon GmbH/ Germany), Monsanto Hardness tester (Bexco/USA), Friabilator (Erweka, Germany), Micrometer screw-gauge, Volumetric flasks (10 & 100 ml), Measuring Cylinders (50 and 1000 ml) (Pyrex/USA; Minghe/China), Disintegration apparatus & DT60 Dissolution tester (Erweka, Heusenstamm/ Germany), UV spectrophotometer (), Pipette, Mortar and pestle, Thermometer, Whatmann's filter paper (25 mm).

Chemicals and Reagents: A 0.1N Hydrochloric acid (HCl) and Distilled water.

Methods: Six brands of ciprofloxacin 500 mg tablets were used in the study. Identity, weight uniformity, dissolution test and assay for the content of active ingredients were done as described in the British Pharmacopoeia, 2004. All the assays were carried out in triplicate except the dissolution tests which were done six times as indicated in BP. Dissolution profiles were constructed for each drug product.

Weight Uniformity Test: Weight uniformity test was performed on the different brands of Clopidogrel as described in the British pharmacopoeia 2005. Twenty (20) tablets were selected randomly from the batch and weighed using an analytical weighing balance. The average weight of the tablets and standard deviation was then calculated.

Hardness Test: Ten (10) tablets each from the evaluated brands were tested using a Monsanto hardness tester. The crushing strength in kg/m^2 for each tablet was obtained and recorded. The mean hardness and the standard deviation were calculated.

Friability Test: Ten (10) tablets were dusted and weighed prior to testing and subjected to a uniform tumbling motion for a period of 4minutes at 25revs/min in a fixed geometry closed chamber called a friabilator. They were then dedusted and reweighed. From the results obtained, weight lost was calculated and expressed in percentage.

Thickness Test: The thickness of the brands of Clopidogrel was each obtained by measuring the thickness of 10 tablets from each brand using a micrometer screw-gauge. The values obtained in mm were recorded and used to compare against standard values.

Disintegration Test: The EREWKA disintegration test apparatus was used based on the British Pharmacopoeia 2005 method. The disintegration medium was filled with 0.1N HCL to 700 ml and temperature maintained at 37±1°C all through the testing process. Six (6) tablets of each product were selected and placed separately on the six cylindrical tubes of the basket, and a disc was placed to act as a stopper. The time taken for each tablet to completely disintegrate and pass through the net into the disintegration medium was recorded and inferences made.

Preparation of Standard Stock Solution: A 100 mg of the pure sample of Clopidogrel was completely dissolved in 100 ml of 0.1N HCl maintained at a pH of 1. A stock solution with a concentration of 1mg/ml of pure Clopidogrel Bisulfate was thus prepared.

Determination of Absorbance Maximum and Beer-Lambert's Curve: From the stock, aliquot of 0.5 ml, 1.0 ml, 1.5 ml, 2.0 ml, 2.5 ml, and 3.0 ml were respectively measured out using a pipette and transferred to previously rinsed 10 ml volumetric flasks. They were them made up to 10 ml to obtain concentrations of between 0.05 mg/ml and 0.30 mg/ml. The spectrum was then recorded between 400 – 200 nm and the optimum wavelength/absorption maxima of 240 nm

selected. The samples were then analyzed using a UV spectrophotometer at a set wavelength of 240 nm. The values gotten were then used to determine the Beer's plot and calibration curve obtained.

Content of Active ingredient test: Twenty (20) tablets for each batch were randomly selected, weighed using an analytical weighing balance and their average weight equivalent to the weight of one tablet calculated. The tablets were then crushed in a mortar and pestle until a smooth powder was gotten. The average weight which is equivalent to the average theoretical content (100 mg) of each tablet was then weighed out from the crushed sample. The weighed sample was then dissolved in 100 ml of 0.1N HCl acid to get a stock solution with a concentration of 1 mg/ml, the solution was then filtered using the non-absorbent filter paper. A 0.1ml of the filtrate was withdrawn and transferred to a 10 ml volumetric flask, it was made up to 10 ml using 0.1N HCl acid. The diluted samples for each batch were then analyzed using a UV spectrophotometer at 240 nm. The obtained values were used to calculate the actual content of active ingredient of the different brands.

Dissolution Test: The dissolution rate tests were carried out on the different brands of Clopidogrel Bisulfate tablets using USP apparatus 2 (DT60 dissolution tester, Erweka, Heusenstamm, Germany). A 900 mL volume of 0.1N HCl acid maintained at a temperature of 37 ± 0.5^{0}C was used. The rotation speed of the paddles was set at 50 rpm. 5mL volumes of the samples were withdrawn at 5, 10, 15, 20, 25, 30, 40, 50 and 60 minutes by a an already calibrated pipette. After withdrawal of the sample, fresh dissolution medium was simultaneously replaced in the vessel to maintain a constant dissolution volume. The collected samples were filtered and 1 ml was transferred to a volumetric flask and made up to 10 ml with 0.1N HCL acid. The actual concentration of the different batches were therefore determined using a UV spectroscopy at a wavelength of 240 nm. Using the standard curve already prepared, the percentage of drug released was determined for the tablets. Model-independent were also employed for this comparison. The methods used include: Similarity factor ($f2$), Difference factor ($f1$) and Dissolution efficiency (DE%).

Statistical Analysis: Data generated were statistically analyzed using a software called SPSS. Thus, statistical comparisons of the profiles were carried out. In order to evaluate both dissimilarity and the similarity factors between test and reference dissolution profiles, both $f1$ and $f2$ were calculated.

3. Results and discussion

Table 2 shows the physicochemical parameters such as colour, shape, weight uniformity, thickness, hardness, friability, disintegration time and assay of different brands of clopidogrel tablet collected from local market in Nigeria.

In this study, sample quantification was based on the previously constructed calibration curve. The calibration curve has correlation coefficient (r) of 0.9961 and linear equation (y) of 1.4862x. It is linear in the ranges of 0.05 – 0.30 mg/ml.

Table 2 Physicochemical Parameters of Different brands of clopidogrel tablet collected from local market in Nigeria

Brand Code	Colour	Shape	Weight Uniformity (mg) ± SD N=20	Thickness (mm) ± SD N=10	Hardness (Kg/cm) ± SD N=10	Friability (%) N=10	Disintegration Time (min) ± SD N=6	Assay (%)
A	Pink	Round	255.05 ± 2.06	4.92 ± 0.03	4.35 ± 0.34	0.117	8:50 ± 0.01	100.03
B	Orange	Round	308.85 ± 5.05	5.69 ± 0.06	2.62 ± 0.63	0.129	4:20 ± 0.09	85.11
C	Peach	Round	332.45 ± 12.33	5.57 ± 0.04	5.00 ± 0.00	0.119	3:00 ± 0.06	116.05
D	Peach	Round	209.85 ± 4.28	4.89 ± 0.04	2.10 ± 0.32	0.000	3:23 ± 0.05	95.05
E	Peach	Round	259.40 ± 11.23	4.94 ± 0.07	3.05 ± 0.37	1.460	7:30 ± 0.08	103.00
F	Pink	Oval	329.75 ± 29.13	5.75 ± 0.08	2.28 ± 0.56	0.274	3:47 ± 0.04	72.40
G	Red	Round	322.80 ± 39.17	6.51 ± 0.09	1.15 ± 0.41	7.882	2:15 ± 0.06	112.74
H	Red	Oval	674.85 ± 19.24	4.33 ± 0.07	13.95 ± 0.16	0.090	17:39 ± 0.05	115.50
I	White	Oval	309.65 ± 6.21	4.86 ± 0.04	4.80 ± 0.92	0.032	7:07 ± 0.05	99.48
J	Pink	Round	259.25 ± 3.48	4.92 ± 0.03	3.95 ± 0.28	0.116	2:53 ± 0.05	85.97

The study was based on ten (10) different brands of clopidogrel randomly purchased from registered Pharmacies in the southern part of Nigeria, with their detailed information table 1. All of the sampled tablets were either round or oval in shape, film-coated and had a declared dose (expressed as the clopidogrel base) of 75 mg. The quality control tests for tablet dosage forms are usually categorized into pharmacopoeia and non-pharmacopoeia tests. The non-pharmacopoeia test includes the organoleptic tests, thickness, diameter, hardness and friability. The non-pharmacopoeia test has no standardized prescribed limit. The different manufacturers set the limit for their products. It was shown in table 3 that the colour of samples studied varied from white, peach, red-like or orange (organoleptic property). Table 3 showed that all the tested samples pass the thickness test since most literature prescribed that the thickness should be controlled within ±5% variation of the individual tablet average thickness. Hardness test, also called crushing test was carried out. Crushing force is the force required to break a tablet in a diametric compression test. Tablets are expected to be hard enough to withstand pressure from handling, shipping and distribution, yet soft enough to be disintegrated after being swallowed. Hence, hardness can affect disintegration, such that if the tablet is too hard, it may not disintegrate in the required period of time and if too soft, it may not be able to withstand handling during subsequent processing such as coating or packaging. [8] From table 3.2, it is shown that result of the experiment carried out on samples A, C and I complied with the standard specifications, while samples B, D, E, F, G and H did not meet the specification of either the minimum or maximum force. In fact, samples B, D, E, F and G required a lesser force to break the tablet than the prescribed minimum force while the force required to break sample H tripled the force required to break the tablet of sample A, innovator brand, though the diameter and the thickness of the sample H is twice and two-third that of innovator brand respectively. The hardness of sample H is expected to be high as displayed in the result, this can be deduced from the fact that the hardness of the tablet depends on both the force of compression and the mass of the granules compressed, moreover there is a direct relationship between the applied force and both the mass and the radius of the compressed tablet. The failure of the samples to meet the prescribed force may be due amongst many other reasons to the congressional force applied when compressing the tablet, the characteristics of the granules to be compressed, the amount and type of binder and/or lubricant used, granulation method adopted in preparing the tablet and the space between the upper and lower punches at the time of compression.[9]

It must be stated that hardness test alone is not enough parameter to reject a batch, the rejection of a batch can only be valid if the hardness test results is combined with that of disintegration test. Friability is a phenomenon where the surface of the tablet is damaged or show a site of damage due to mechanical shock or vibration. The friability test is performed to determine the ability of tablets to withstand abrasion during packaging, handling, and shipping processes. The idea behind this test is to mimic the kind of forces caused by phenomena such as collisions and sliding of tablets towards each other, which a tablet is subjected to during coating, packaging, handling and shipping. The USP specification for friability test is a percentage loss not greater than 1% and the test is also rejected if any tablet caps, laminates or breaks up in the course of the test.[10] From the result in table 3, batch E and G failed the test. During the experiment, the tablets of sample G broke which indicates that it failed the test. Tablet friability can be influenced by the moisture content of the tablet granulation in the finished tablets. A low but acceptable moisture level frequently serves to act as a binder. Very dry granulation that contain only fractional percentages of moisture will often produce more friable tablets than will granules containing 2% to 4% moisture.[10]

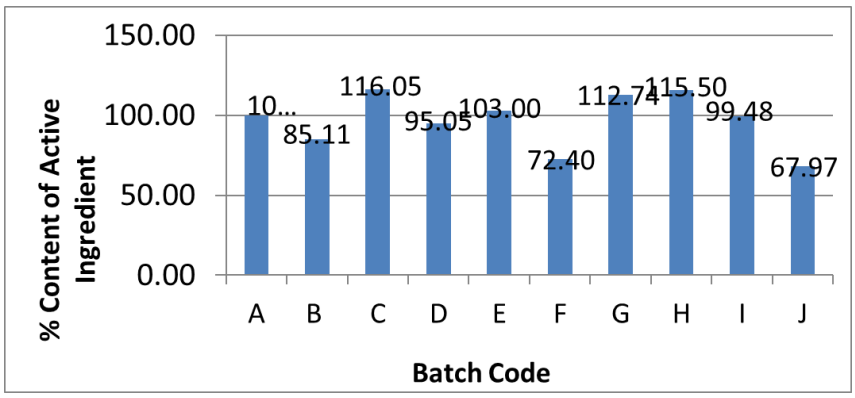

Figure 2 Percentage of Active content of Different Brands of clopidogrel Bisulphate Tablets marketed in Nigeria

Uniformity of weight of a drug is important because it ensures that every tablet contains the amount of drug substance intended, with little variation among tablets within a batch. With the exception of sample D whose average weight is less than 250 mg although more than 80 mg (the limit of which is 7.5%), the remaining samples had an average weight of 250 mg or more. when weighed singly, the samples were not expected to have that more than two of the tablets deviating from the average weight by a percentage greater than ± 5% and none should deviate by more than twice that

percentage. The result shown in table 3 implies that all the samples complied with the standard limit stipulated above, except that of samples E and G, where more than two tablets weight deviated from the mean weight by more than ± 5% and some of the samples also deviated by more than ± 10%. The rate of drug absorption as well as the therapeutic efficacy of the drug is dependent upon the disintegration time. The disintegration time is one of the measures of the drug quality, if the disintegration time is too long, it may imply that the force of compression is too high, amongst other reasons. An inconsistent disintegration time within a batch could imply lack of uniformity within the batch. According to USP, 2013 specifications, the disintegration time should be less than 30 minutes for film coated tablets. Hence, from the results in table 3, all the samples pass the test according to the result despite the fact that with exception of sample H which had a longer disintegration time as 17.39 min. However, other samples disintegrated within 10 min. In this study, the disintegration result of sample H was not referred to as an aberration because of the significantly ($p > 0.05$) higher values of average diameter and weight of sample H when compared to the rest of the samples. Factors such as; the type and concentration of binder used, method of incorporation, the presence of excessive and overly mixed lubricant, and compression force may affect the way tablets disintegrate. The content of active ingredient is an important quality measure of the final solid dosage form. It ensures that a consistent dose of the API is maintained between batches so that the patient receives the correct dose. The active ingredient needs to be evenly distributed throughout the tablet to ensure that if the tablet is split into half, each half of the tablet has an equal dose.[11] According to the USP specification, the requirements for content uniformity are met if the amount of active ingredient in nine (9) of the ten (10) tablets lies between the range of 75% - 125% of the label claim. From the result obtained as shown in table 3, all the samples passed the test except sample F (72.40%) that failed the test. The failure of sample F may be as a result of uneven distribution of the drug in the powder and granules or segregation of the powder mixture in granulation during formulation processes.

Table 3 Dissolution Profile of Ten Brands of clopidogrel Bisulphate Tablets

Time (min)	A	B	C	D	E	F	G	H	I	J
5	61.69	88.11	53.76	27.28	23.92	30.62	9.41	22.73	35.20	68.95
10	67.14	96.54	74.98	89.83	48.86	50.44	44.67	25.58	75.35	83.73
15	82.97	97.76	77.81	86.95	75.95	70.72	84.49	31.17	101.75	92.18
20	92.86	98.43	80.64	96.74	77.01	80.24	87.45	37.94	101.20	93.58
25	94.44	99.69	81.11	100.20	79.72	86.19	88.37	40.26	102.30	94.13
30	98.28	100.32	81.59	100.77	86.57	96.77	88.86	45.94	103.40	95.77
40	97.17	101.62	82.06	103.08	86.04	100.55	90.80	57.31	106.70	95.77
50	97.72	104.19	82.53	103.71	81.79	101.30	90.80	69.42	107.25	97.41
60	99.90	105.92	83.47	103.71	94.47	102.20	91.90	81.94	108.90	99.05

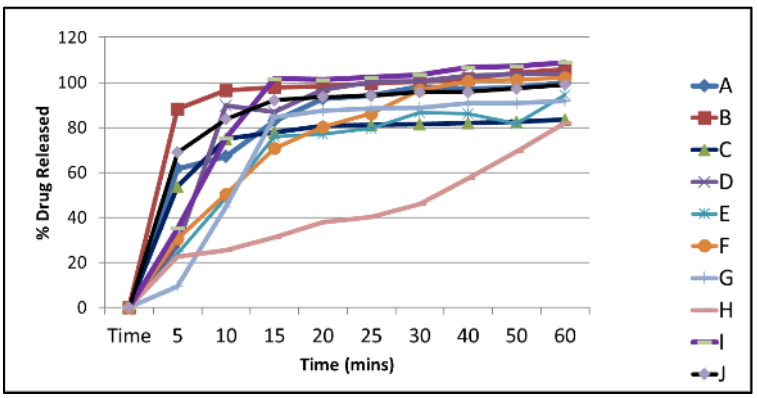

Figure 3 Drug Release study of Ten Different Brands of clopidogrel Bisulphate

Dissolution test is an important *In-vitro* qualitative and quantitative tool, which can provide important information about bioavailability of a drug as well as batch-to-batch consistency. The ultimate aim of performing dissolution tests is

to predict the extent of release and absorption of the administered drug *in-vivo*, (*in-vivo-in-vitro* correlation). The results of the dissolution profile in the pH 2.0 HCl buffer was shown in table 3, while Figure 3 shows the mean drug release profiles of the assayed products. The dissolution test described in USP 39 for clopidogrel tablets indicates that not less than 80% of the labelled amount of API should be dissolved in 30 minutes.[11] Only sample H (Δ % DF = 29.29) as shown in table 3 did not comply with the Pharmacopeial specification, thus, the other nine samples complied in terms of drug release rate. However, the dissolution profiles shown in Figure 3 indicate that the products had differences in dissolution performance, with the compendial medium providing good discrimination among the different formulations.

Table 4 Dissimilarity factor *(f1)* and similarity factor *(f2)* of each brand of Clopidogrel bisulphate 75mg with respect to the innovator brand

PAIR COMPARISON	***f2***	***f1***
B vs A	43.13	11.80
C vs A	43.75	14.40
D vs A	40.14	11.80
E vs A	36.11	17.90
F vs A	40.77	12.80
G vs A	33.52	15.50
H vs A	48.28	17.60
I vs A	42.23	13.50
J vs A	59.25	4.30

Similarity factor (*f*2) should be higher than 50% and dissimilarity factor (*f*1) less than 15% in the medium is predicted a successful bioequivalence profile of the product. As shown in table 3.4, the *f*1 values for samples E, G and H were less than 15 while *f*1 values for samples B, C, F and I were less than 15. But the closer the *f*1 value is to zero value the lesser the dissimilarity between the product, thus sample J with the lowest value of *f*1 (4) is most similar to the reference sample (innovator product) in terms of dissolution profile than any of the remaining samples. Meanwhile only one *f*2 values was greater than 50 (sample J) and eight *f*2 values were lower than 50 (samples B - I). Therefore, the *f*2 values for sample J seemed to support dissolution profile similarity with innovator product "sample A" (Plavix®). Based on the results from this study it can be said that only sample J showed similarity to the innovator brand (sample A) and therefore can be interchanged with the innovator product.

Table 5 Dissolution Efficiency (%DE) of each brand of Clopidogrel bisulphate 75mg

BATCH CODE	%DE	Δ %DF
A	86.44	-
B vs A	90.36	3.92
C vs A	90.19	3.75
D vs A	85.93	0.51
E vs A	76.34	10.1
F vs A	79.03	7.41
G vs A	81.86	4.58
H vs A	57.15	29.29
I vs A	84.76	1.68
J vs A	89.32	2.88

%DF = Test product – Reference product.

The Dissolution Efficiency (DE) is the area under the dissolution curve up to a certain time, t, expressed as a percentage of the area of the rectangle described by 100% dissolution in the time.

The reference and test product can be said to be equivalent if the absolute difference between their dissolution efficiencies is within appropriate limits (±10%, which is often used). Hence, as shown in table 5, the samples had dissolution efficiency greater than 70% and therefore could be considered quality products except sample H (57%) with less than 70% DE which could be considered a less quality product. However, comparing the % DF, it can be seen that the values obtained for samples E and H were greater than 10 making them not similar to the innovator brand, sample A (Plavix®), and thus they are not interchangeably with the innovator brand. Based on the above discussion only sample J may be interchange with the innovator product sample A

4. Conclusion

This study clearly demonstrated that not all the brands of Clopidogrel bisulphate (75mg) marketed in the Nigerian market met the official requirement in the quality control tests. From the results which compared the dissolution performance of several clopidogrel multi-source products available in Nigeria with the innovator brand (Plavix®), some of the evaluated samples were found to comply with the requirements of the dissolution test of the USP 39 and were considered pharmaceutical equivalents to Plavix®. However, the dissolution profiles of the tested products were not superimposable to that of Plavix®. Indeed, only sample J is similar to Plavix® in terms of similarity factor and dissolution efficiency (p> 0.05). However, in order to confirm any correlations with the *in vitro* performance of the clopidogrel multisource products tested and to demonstrate their interchangeability with the innovator brand the *in vivo* bioequivalence studies should be conducted. For good quality of pharmaceutical products, it is therefore imperative for regulatory bodies to be more stringent in product evaluation before giving approval for sale and use. Furthermore, there is need for periodic assessment of pharmaceutical products, proper consideration of all the physiochemical properties of the drug and excipient to ensure good quality which in turn infers safe and therapeutically active products. It is also evident from the study that only Torrent clopidogrel® can be interchanged for the innovator product "Plavix®" unfortunately it is not a registered drug product in Nigeria by NAFDAC.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare that they have no known competing financial or non-financial interests, personal relationships, or affiliations that could have appeared to influence the work reported in this paper.

References

[1] Rathe J, Sondergaard, J., Jarbol, D., Hallas, J., Andersen M., (2014). Patients´concerns about their medicine after a generic switch: a combined cross-sectional questionnaire and registrer study. *Pharmacoepidemol Drug Safety*, 23: 965-973.

[2] Lewek P., (2010). *The Journal of family practice*, 59 (11): 634-640.

[3] Nelson AL, Cohen JT, Greenberg D, Kent DM., (2019). Much cheaper, almost as good: decrementally cost-effective medical innovation. *Ann Intern Med* 2009; **151**: 662– 7.

[4] Olusegun A., (2013). Counterfeit drugs in Nigeria: A threat to public health. *African Journal of Pharmacy and Pharmacology,* 7 (36): 2571-2576.

[5] Kazui M., Nishiya Y., Ishizuka T., Hagihara K., Farid N.A., Okazaki O., Ikeda T., Kurihara A., (2010). Identification of the human cytochrome P450 enzymes involved in the two oxidative steps in the bioactivation of clopidogrel to its pharmacologically active metabolite. Drug Metab. Dispos. 2010; 38 : 92–99.

[6] Barabde GR, Ambadekar S. R., (2015). Comparative Study of Estimation of Clopidogrel Bisulphate from Commercial Sample by UV–Visible Spectrophotometer and HPLC Method. *Journal of Research in Pharmaceutical Science,* 2 (9): 17-20.

[7] Mona E. ElTantawy, Lories I. Bebawy, Rafeek F. Shokry, (2014). Chromatographic determination of clopidogrel bisulfate; detection and quantification of counterfeit Plavix® tablets, *Bulletin of Faculty of Pharmacy, Cairo University,* 52 (1): 91-101.

[8] Felton L. A., (2012) Remington Essentials of Pharmaceutics. UK: *Pharmaceutical press.*

[9] Adeline Stew, (2016). Dissolution testing Pharmaceutical Technology. *Pharmaceutical Technology,* 40 (11): 56,64.

[10] Davinder K, Jasbir S, Mamta A, Virender K., (2016). Quality control of tablets: A Review. *International Journal of Universal pharmacy and Bio science.* 5 (4): 54-63.

[11] United States Pharmacopeia (USP) (2016a). Monograph: clopidogrel tablets. In The United States Pharmacopeia and National Formulary USP 39-NF34 (Spanish version); U.S. Pharmacopeial Convention, Rockville, M. D.