

Quality assessment of five brands of loperamide hydrochloride marketed in Awka capital territory Nigeria

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Abstract

Loperamide hydrochloride (LH) is widely used for the symptomatic control of diarrhoea but there is concern with regards to the efficacy and safety of the diverse generic brands currently in use. Five brands (A, B, C, D and E) of LH were evaluated using uniformity of weight, disintegration time and dissolution time tests as well as HPLC assay. The paddle method was used for the dissolution test, while the High-Performance Liquid Chromatography (HPLC) was used to determine the quantity of Loperamide hydrochloride in each capsule.

Brands A, B, D and E passed the uniformity of weight test according USP specifications, whereas brand C failed. Brands A, B, D, and E disintegrated rapidly within 3–7 minutes, demonstrating efficient breakdown of the capsule shell. Brand C however, had a prolonged disintegration time of up to 32.5 minutes. The USP (United States Pharmacopeia) maximum disintegration time is 30 minutes for capsules. Brands A and D had the fastest and most complete dissolution, reaching nearly 100% at 45 minutes. Although brands B and E released the drug slowly, they still achieved acceptable levels. However, brand C exhibited the lowest drug release, reaching only 54 % after 45 minutes. The HPLC assay revealed brands A, B, D and E had percentage mean peak area that fell between 90-110 %, (USP allowed range) while brand C had 79.28 %. Hence brand C Loperamide also failed this test.

Conclusion: Brand C Loperamide hydrochloride did not meet most of the USP specifications.

Keywords: Weight Uniformity; Disintegration; Dissolution; HPLC; USP

1. Introduction

Substandard and falsified medicines remain a major concern in global health, with studies showing a prevalence rate of 10–15 % in many low- and middle-income countries [1]. In 2025, some drug markets in Nigeria were closed by the National Agency for Food and Drug Administration and Control (NAFDAC) Nigeria (<https://nafdac.gov.ng>) due to the presence of fake and substandard drugs in those drug markets.

The economic burden of fake products is substantial, with billions lost annually due to treatment failures; extended hospital stays, and decreased patients' trust [2]. In settings where procurement decisions prioritize affordability, patients may receive suboptimal brands, potentially affecting outcomes. Furthermore, some studies highlight the importance of evaluating quality and consistency across marketed formulations [3].

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Pharmaceutical quality control parameters such as, content uniformity, disintegration time, dissolution time, and HPLC assay are essential for ensuring a dosage form delivers consistent therapeutic outcomes [4]. Dissolution test evaluates the rate and extent of drug release, which predicts in vivo bioavailability [5]. Variations in formulation, excipients, and manufacturing processes can influence dissolution characteristics and bioavailability. Disintegration test ensures the capsule or tablet breaks down appropriately in gastrointestinal fluids [5].

By identifying products that fail to meet regulatory specifications, researchers can provide evidence to guide regulatory bodies [2]. Considering the central role of Loperamide hydrochloride as anti-diarrhoea agent, evaluating the efficacy of different marketed brands is a clinical policy-relevant issue. Regulatory science addresses the outcome through product-specific bioequivalence (BE) testing [6]. Nevertheless, even when BE is mandated, differences may persist across brands highlighting the importance of independent comparative evaluations from time to time especially in settings with variable regulatory oversight and multiple generic suppliers [7]

2. Materials And Methods

2.1. Materials

2.1.1. Drug samples

The samples of Loperamide hydrochloride capsules and tablets were coded brand A – Janssen Imodium, B - Diaglow, C – Imodium copy, D - Lemotil (in tablet form) and E - Diaflush

2.1.2. Drug Sample collection and identification

Five (5) brands of Loperamide hydrochloride 2mg were obtained from various pharmaceutical chemist shops situated within Awka capital territory, Anambra state in Nigeria. The packets of the samples had the batch number, manufacturing date, expiration date and NAFDAC registration numbers [8] written on them.

2.1.3. Apparatus

Disintegration Tester (Erweka ZT 320), USP Dissolution Apparatus Type II (Lab India DS8000), UV-Visible Spectrophotometer (Shimadzu UV-1800), Analytical Balance (Shimadzu AU220), Vernier calliper, stopwatch, pH meter and High-Performance Liquid Chromatography system with UV detector.

2.1.4. Reagents and chemicals

The reagents used in this study included 0.1 N hydrochloric acid, phosphate buffer of pH 6.8, sodium hydroxide, 95% ethanol, and distilled water. Methanol, acetonitrile, phosphoric acid, sodium, 1-hexane sulfonate, monobasic ammonium phosphate and hydrochloric acid. All reagents were of analytical grade and procured from certified suppliers.

2.2. Methods

2.2.1. Visual inspection of the samples

Prior to pharmacological analysis of the brands, visual assessment of the packets and capsules was made to determine for correctness and the legible labelling of active ingredients and dosages, expiration date, batch number and NAFDAC registration number. The appearance of the samples was also examined for discolouration.

2.2.2. Uniformity of weight content

Twenty (20) capsules from each brand were used. Each of the 20 capsules was weighed with its content, then emptied, and the empty shell weighed. The difference gave the individual content weight. The average content weight for each brand was eventually calculated (mg) and the mean weight obtained. The USP permissible percentage deviations for capsules is $\pm 10\%$ for mean weights less than 300 mg and $\pm 7.5\%$ for mean weights above 300 mg. In case of tablets USP permissible deviation is $\pm 5\%$ for mean weights above 250 mg, $\pm 7.5\%$ for mean weight 75-250 mg and $\pm 10\%$ for mean weights below 75 mg. The USP acceptance criteria also states that not more than two capsules may deviate from the mean weight by more than $\pm 10\%$ and none should deviate by more than $\pm 20\%$.

2.2.3. Disintegration time test

Six capsules from each brand were tested for disintegration time using the Erweka ZT 320 disintegration tester. Distilled water maintained at $37 \pm 0.5^\circ\text{C}$ served as the disintegration medium. Capsules and tablets were observed until complete

disintegration, which was defined as the point at which no palpable residue remained on the mesh screen of the apparatus. The USP states that not more than one capsule or tablet out of the six tested may fail to disintegrate within 30 minutes.

2.2.4. Dissolution time test

Six capsule/tablets were used for this test. The USP dissolution apparatus Type II (paddle method) was used for this study. The dissolution medium consisted of 900 ml of 0.1 N hydrochloric acid to simulate gastric conditions, followed by phosphate buffer of pH 6.8 to simulate intestinal conditions. The medium was maintained at a temperature of $37 \pm 0.5^\circ\text{C}$, and the paddle rotation speed was set at 50 revolutions per minute. Samples were withdrawn at predetermined intervals of 5, 10, 15, 30, and 45 minutes, with each withdrawn volume replaced by an equal amount of fresh dissolution medium to maintain sink conditions. The collected aliquots were filtered and analyzed using the Shimadzu UV-1800 spectrophotometer at a wavelength of 220 nm in order to determine the concentration of Loperamide hydrochloride released over time.

2.2.5. HPLC assay of Loperamide content in the brands

Twenty (20) capsules or tablets from the brand were weighed individually, and the average weight was obtained. The powdered content was removed. Then an accurately weighed quantity of the powder equivalent to 20 mg of Loperamide hydrochloride was transferred into a 100 ml volumetric flask. For the brand in tablet form, twenty tablets were weighed individually and the average weight obtained. They were then crushed together into powder. The powder equivalent to 20 mg of Loperamide hydrochloride was weighed out and transferred into a 100 ml volumetric flask. About 35 mL of 0.5 N hydrochloric acid was added into the volumetric flask, and the mixture was sonicated for 15 minutes. Thereafter, 35 mL of acetonitrile was added, and sonication was continued for another 15 minutes. The solution was then diluted to volume with a 1:1 mixture of acetonitrile and 0.5 N hydrochloric acid, mixed well, and filtered. Then 40 ml portion of this filtrate was transferred to a 100 ml. volumetric flask, diluted to volume with a 1:1 mixture of acetonitrile and water, and mixed thoroughly, this was used for the HPLC analysis. The chromatograms were recorded, and the peak responses of the major components were measured [9].

$$\% \text{ Peak Area} = (\text{Peak Area of Sample} / \text{Peak Area of Standard}) \times 100(\text{mg})$$

3. Results

3.1. Visual inspection of the samples

All the brands satisfied the regulatory specifications except brands C which copied the brand name of the innovative brand by Janssen Pharmaceuticals Ltd though they differ in packaging (Table 1)

Table 1 Visual inspection of the brands

Sample code	Brand	Batch No	Manufacture Date	Expiration Date	NAFDAC No	Reg.	Labelled
A	Janssen Imodium ^R	22K0055	11/ 02 /2022	10/ 2027	04-2941		2mg
B	Diaglow	C12206	09/ 2024	08/ 2027	B4-6454		2mg
C	Imodium copy	222009	07/ 2024	06/ 2027	A0-4760		2mg
D	Lemotil	T2106	09/ 2024	08/ 2027	B4-0576		2mg
E	Diaflush	24PC15	08/ 2024	07/ 2027	B4-4364		2mg

3.2. Uniformity of weight test

Brand C had 3 capsules which had content weights that is below the USP acceptable range of $\pm 10\%$ of the mean. Hence brand C Loperamide failed this test (Table 2).

Table 2 Uniformity of weight using 20 capsules/tablets

S/N	Brands	USP allowed range ($\pm 10\%$ of mean wt)	Status
1	A	165.24 – 201.96	Passed
2	B	105.57 – 129.03	Passed
3	C	114.39 – 139.81(3 capsules fell outside this range)	Failed
4	D	79.61 – 92.53	Passed
5	E	111.78 – 136.62	Passed

3.3. Disintegration test

Brands A, B, D, and E disintegrated rapidly within 3–7 minutes, demonstrating efficient breakdown of the capsule shell. Brand C, however, had a prolonged disintegration time of up to 32.5 minutes, therefore it failed this test (Figure 1). The USP requires that capsules should take maximum of 30 minutes to disintegrate completely but brand C, took up to 32.5 minutes to disintegrate completely.

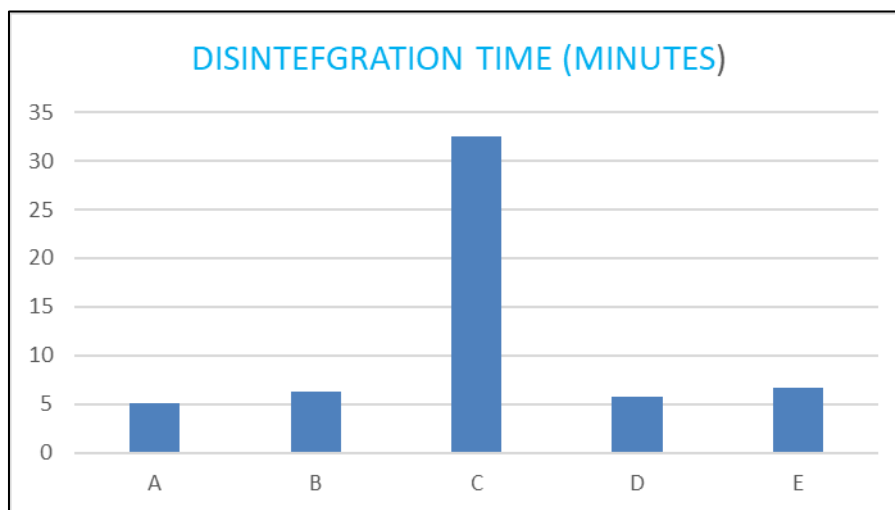


Figure 1 Disintegration time for the brands

3.4. Dissolution test

The dissolution test measures the percentage of drug released from the dosage form into solution over time. Brands A and D demonstrated the fastest and most complete drug release, reaching nearly 100 % at 45 minutes. Brands B and E released the drug more slowly but still achieved acceptable levels. Brand C however, exhibited the lowest release, reaching only 54 % after 45 minutes. The USP specifies that at least 80 % of the active drug should be released within 45 minutes for immediate release capsules. Brands A and D fully complied with this specification. However, brand C failed to meet the USP specification (Figure 2).

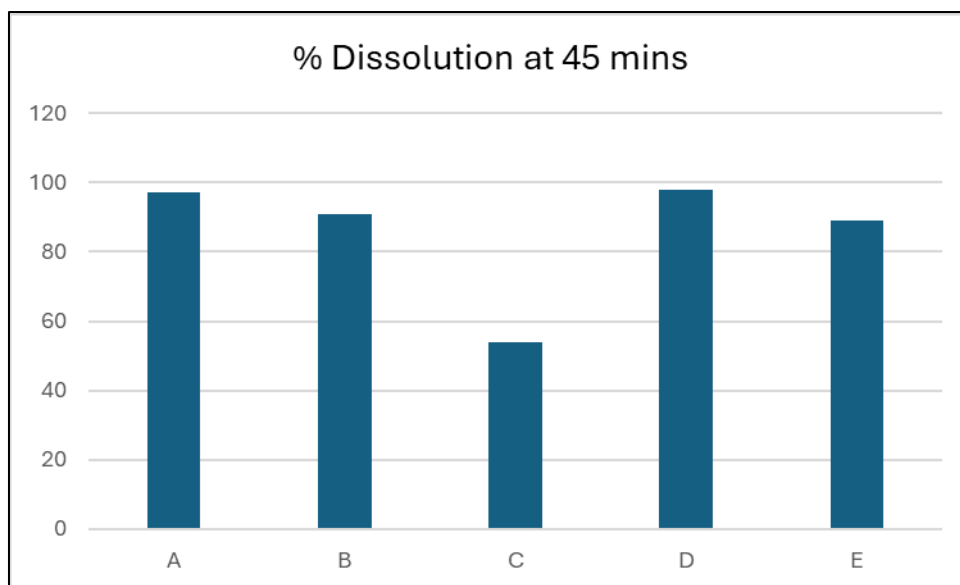


Figure 2 Percentage dissolution at 45 minutes

3.5. HPLC assay of Loperamide hydrochloride content in the brands:

The average peak area of the standard was 3171.003, and the acceptable USP range for mean % peak area of Loperamide is 90 %–110% (for both capsules and tablets). Brands A, B, D and E all satisfied this specification. However, the average percentage peak area for brand C was 79.28 % which was lower than 90 %. Therefore, brand C failed this test (Figure 3).

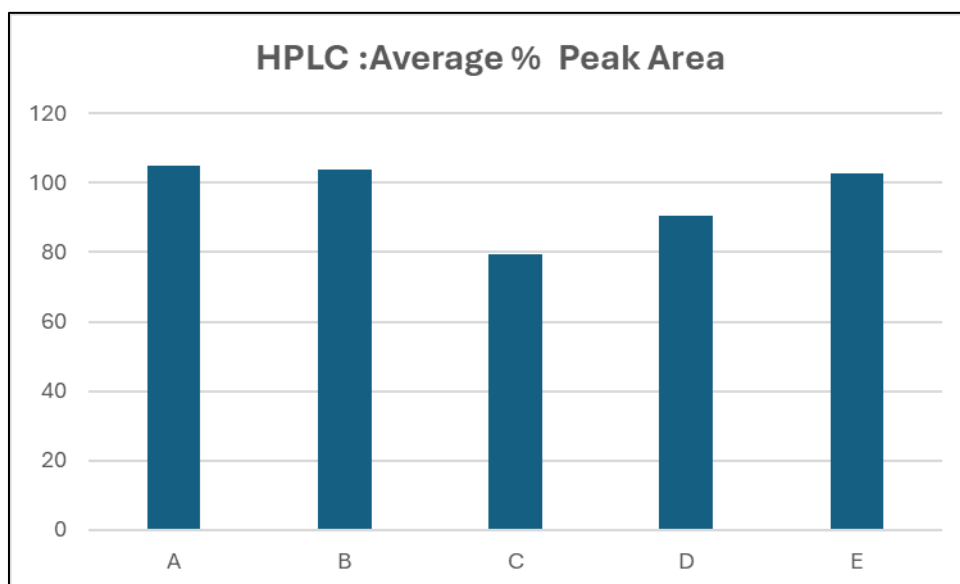


Figure 3 Average percentage peak area of the brands

4. Discussion

Uniformity of weight is a fundamental indicator of manufacturing precision and dosage uniformity [10]. It is a preliminary but vital quality indicator in solid oral dosage forms [11]. In this study, brand C Loperamide hydrochloride failed uniformity of weight test. Weight non-uniformity often signals the absence of standard manufacturing controls [12]. This could be due to lapses in manufacturing process such as inadequate filling or inconsistent capsule size. Inconsistent filling of active ingredient in each capsule or tablet can affect efficacy and safety of the drug. Disintegration testing further highlighted inter-brand variability in performance. Genuine brands display disintegration times within pharmacopeia limits, thereby supporting their bioavailability and therapeutic potential. Brand C also failed this test.

Prolonged disintegration time could lead to reduced bioavailability and variable absorption which could eventually lead to ineffectiveness and therapeutic failure. Ensuring proper disintegration is crucial for effective medication delivery and patient outcome. Prolonged disintegration time may also be attributed to poor excipient selection, inappropriate compression forces, or intentional substitution of inactive fillers, as has been previously reported in counterfeit [13].

Drug administered orally has to dissolve before it can be absorbed. Poor dissolution rate could be due to poor granulation, insufficient disintegrant, poor solubility due to particle size and pH related issues. Poor dissolution could lead to poor bioavailability and potential treatment failure manifesting in inconsistent treatment outcomes, and increased healthcare cost. Brand C had poor dissolution and did not meet the USP criteria. Complete dissolution suggests adequate solubilisation of the active pharmaceutical ingredient (API), which can be linked to standard excipient quality or even the adequate quantity of therapeutic agent itself like loperamide hydrochloride. Previous quality-control investigations into falsified medicines have similarly reported poor dissolution as a hallmark of counterfeiting, with dissolution failure directly correlating with therapeutic inefficacy [14].

High-Performance Liquid Chromatography (HPLC) is one of the most robust, sensitive, and reliable analytical tools in pharmaceutical analysis [15]. The acceptable USP range for mean % peak area for Loperamide is 90 –110%. However, the average percentage peak area for brand C was 79.28 % which was lower than 90 %. Therefore, brand C failed this test. Degradation and improper storage conditions can affect the assay value in HPLC study [16]. Stability can be compromised by environmental factors such as humidity and temperature [16]. Therefore, inconsistent filling of the capsule, loss of active ingredient due to improper storage conditions could have resulted in this failure. Failing HPLC assay could lead to dosing variability which can impact treatment outcomes. These observed variabilities in the results obtained in this study across the brands reflects the documented phenomenon of inter-brand differences in pharmaceutical formulations. Generic formulations, while required to meet pharmacopeia specifications, may occasionally display variations often attributed to differences in excipients, manufacturing technologies and or storage conditions [14]. This underscores the importance of continuous post-market surveillance and reinforces the role of monitoring of marketed pharmaceuticals [17]

5. Conclusion

Brand C Loperamide hydrochloride failed in almost all the tests used in this study. Therefore, within the limits of this study the contents of the Loperamide hydrochloride capsules as claimed by the manufacturer may not be justified.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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