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Original Research Article

QUALITY ASSESSMENT OF FUROSEMIDE TABLET GENERICS USED IN A TEACHING HOSPITAL IN NIGERIA

ABDURRAHMAN UMAR[1,2]*, HALIMATU SADIYA HASSAN[1], SALISU AWWALU[1]

1. Department of Pharmaceutical and Medicinal Chemistry, Ahmadu Bello University Zaria, Nigeria.
2. Pharmacy Department, Ahmadu Bello University Teaching Hospital, Zaria, Nigeria.

ABSTRACT

The use of ineffective and poor-quality drugs endangers treatment leading to treatment failure. For the desired therapeutic effect, drugs should contain the appropriate amount of active pharmaceutical ingredients and the required physicochemical properties. This study aimed to evaluate the quality as well as the physicochemical properties of different generics of furosemide tablets used in a teaching hospital in Nigeria. Five different generics of furosemide tablets were purchased from different pharmacy units in the hospital. Their qualities were assessed via identification, assay, weight variation, friability, disintegration and dissolution tests using British Pharmacopoeia standards. All samples contain the stated active pharmaceutical ingredients, however, only two generics have furosemide within the 95 – 105% BP official limit. The weight variation test results indicated that two generics failed to comply with BP specification limits. The generics were found to be able to withstand the rigour of transportation as indicated by their friability values of less than 1 %. The generics were also found to be immediate release tablets as showed by their rapid disintegration time of less than 2 minutes. All the generics released more than 80 % furosemide within 60 minutes. Only two out of the five furosemide generics passed the quality assessment and are therefore expected to yield the desired therapeutic effect.

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INTRODUCTION

Most hypertensive patients require medication to achieve long-term blood pressure control. Antihypertensive medicines include diuretics, calcium-channel blockers, β-blockers, angiotensin-converting enzyme inhibitors, and angiotensin II receptor blockers. Calcium channel blockers and diuretics are two of the most prominent classes used to treat hypertension [1]

Furosemide is 4-chloro- 2-[(furan-2-ylmethyl) amino]-5-sulfamoylbenzoic acid (Figure 1); it is a white crystalline powder having the molecular formula $C_{12}H_{11}ClN_2O_5S$ and molecular weight 330.7 g/mol [2], commonly prescribed as a diuretic to treat edematous disorders, severe hypertension, and both acute and chronic heart failure [3].

The quality of medications is a global concern, especially in developing nations. The global market for counterfeit drugs has witnessed an epidemic-level rise in prevalence, with developing countries being the most significantly affected [1]. Because of their poor infrastructure, scarcity of qualified workers, and lax regulatory frameworks, low- and middle-income nations are particularly vulnerable to the widespread distribution of substandard and counterfeit pharmaceuticals

Corresponding author: aiu4lyf@gmail.com, +234-703 093 3143

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[4], and use of these products could endanger treatment and may lead to possible treatment failure [5].
This study aims to evaluate the physicochemical properties of different generics of furosemide tablets used in a teaching hospital in Nigeria.

MATERIALS AND METHODS

Drug Sampling

Five different generics of furosemide (40 mg) tablets were obtained from different pharmacy units of a teaching hospital in Nigeria and coded F1 to F5.

Identification Test of the Furosemide Generics

Melting Point Determination

Ten furosemide tablets from each generic were weighed and powdered using a mortar and pestle. A quantity of the powdered tablet was dissolved in 10 ml ethanol (95 %), filtered and the filtrate was air dried. This was then filled into a capillary tube by careful tapping of the capillary tube on a plain surface. The capillary tube was then placed in the melting point apparatus and the machine was operated. The melting point range was then compared with the BP melting point range [2].

Infrared Spectrophotometry

The residues obtained above were scanned 30 times within the range of 4,000 - 650 cm^{-1} at eight resolutions. The obtained spectra were then compared with the BP furosemide reference spectrum [2].

Uniformity of Weight Test

Twenty tablets from each generic were selected randomly and their weights were recorded. The average weight and percentage deviation of each tablet weight from the mean were calculated [2].

Assay of the Furosemide Generics

A quantity of the powdered tablet equivalent to 200 mg was dissolved in a conical flask (500 ml) containing 300 ml of 0.1M sodium hydroxide, shaken and then made to volume with 0.1 M sodium hydroxide. The solution was filtered, and a portion (5 ml) was further diluted to 250 ml using 0.1M sodium hydroxide. The absorbance of the resulting solution was taken at 271 nm. The content of furosemide was calculated using 580 as the value of A (1%, 1 cm) [2].

Friability Test

Ten tablets from each generic were collectively weighed and subjected to abrasion by using Erweka friability at 25 revolutions per minute (rpm) for 4 minutes. The tablets were then dedusted and weighed, the difference in the weights was determined and the percentage friability was then calculated [2].

Disintegration Test

Six tablets from each generic were selected and placed in six tubes of a Euweka disintegration apparatus containing distilled water (900 ml) at 37 ± 0.5 °C. The time taken for each tablet to break up from its whole mass and pass through the sieve was recorded [2].

Dissolution Test

Furosemide release from six tablets of each generic was analysed using a dissolution tester equipped with rotary paddles (USP Apparatus II) operated at 50 revolutions per minute. The dissolution medium was 900 ml phosphate buffer (pH 5.8) maintained at 37 ± 0.5 °C. The sample (10 ml) was taken at 30 minutes, filtered and diluted using the medium. The amount of the dissolved drug was determined using a UV-visible spectrophotometer at the wavelength of 274 nm.

RESULTS

Identification test of the Furosemide Generics

The melting point ranges of the furosemide recovered from the generics sample are shown in Table 1, and their FTIR spectra are placed against the furosemide BP reference IR spectrum in Figures 2–6. It was found that all of the generics' melting points fell within the range of the active pharmaceutical ingredient (API) for furosemide.

Uniformity of Weight Test

The uniformity of weight of furosemide generics is shown in Table 2. It was observed that generics F2, F3, and F5 comply with the weight uniformity test, as no more than two of the individual tablets should differ from the average mean by ± 7.5% [2].

Friability Test

Table 3 displays the friability values of generic furosemide; the values obtained ranged from 0.51 to 0.85. According to the British Pharmacopeia, uncoated tablets must have friability ratings below 1% to resist abrasion during handling and transit [2].

Disintegration Test

The disintegration times of furosemide generics are shown in Table 4. Values obtained for all the generics were less than 15 minutes, which is the British Pharmacopeial set limit for uncoated tablets.

Dissolution Test

The percentage release of the generics is shown in Table 3. All the generics release up to 80% of the furosemide active pharmaceutical ingredient within 30 min.

DISCUSSION

All the generics were suspected to contain furosemide active pharmaceutical ingredient (API) as indicated by their melting points (Table 1) which fall within the BP official range (206 –

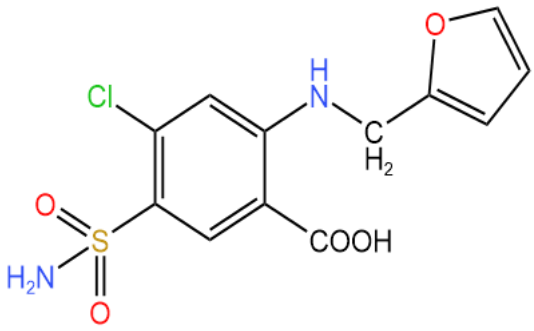

Figure 1: Furosemide

Table 1: Melting points of the furosemide tablet generics.

Generics	Range (°C)
F1	205 – 207
F2	205 – 206
F3	207 – 209
F4	204 – 206
F5	206 – 208

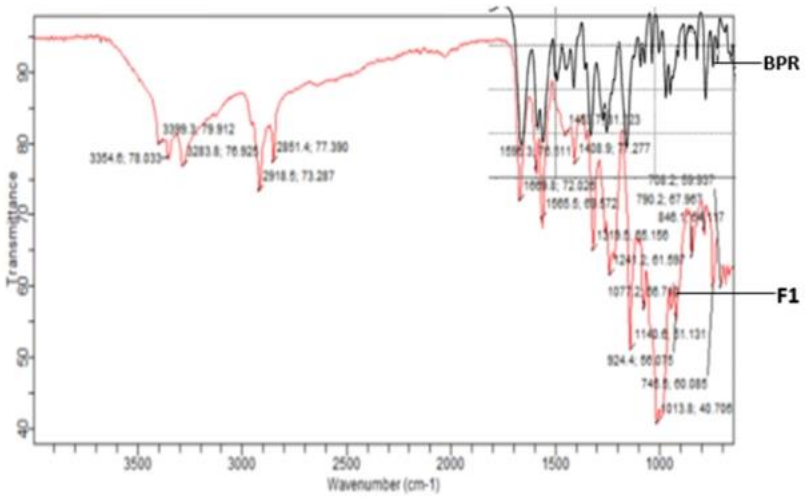

Figure 2: Superimposed FTIR Spectra of Generic F1 and Furosemide BP Reference.

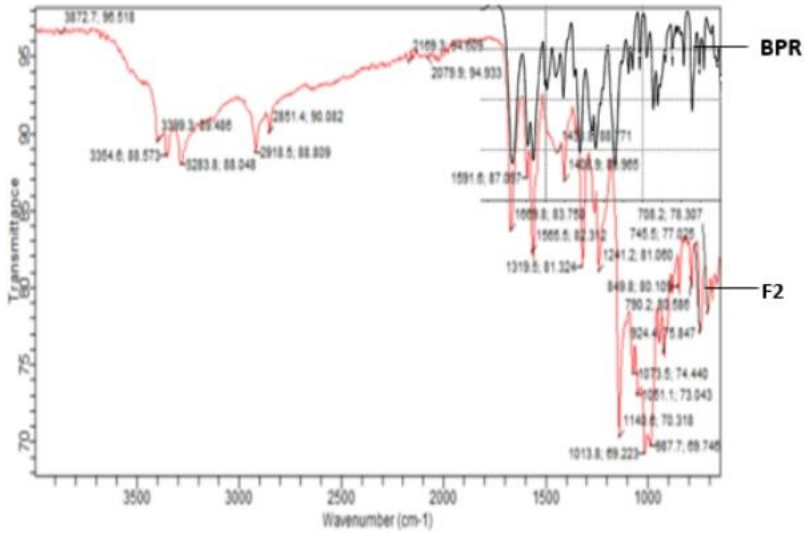

Figure 3: Superimposed FTIR Spectra of Generic F2 and Furosemide BP Reference.

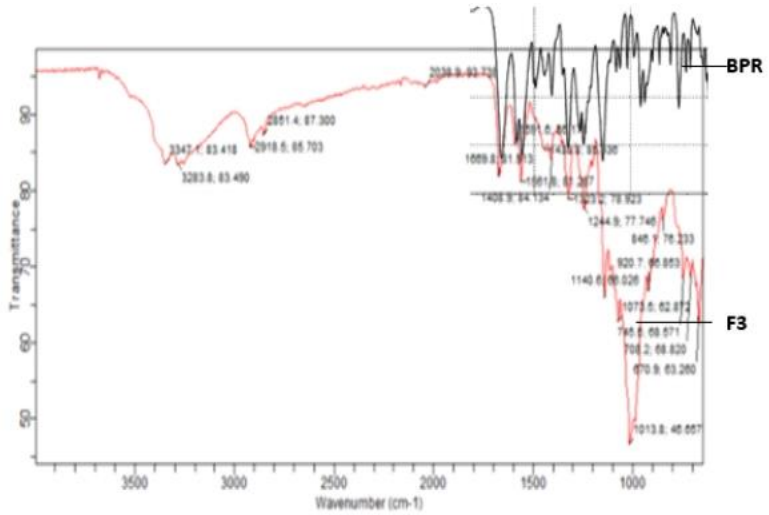

Figure 4: Superimposed FTIR Spectra of Generic F3 and Furosemide BP Reference.

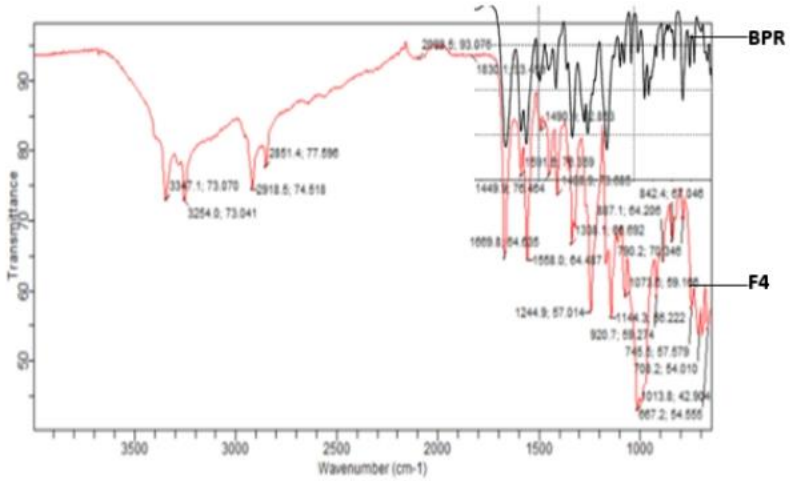

Figure 5: Superimposed FTIR Spectra of Generic F4 and Furosemide BP Reference.

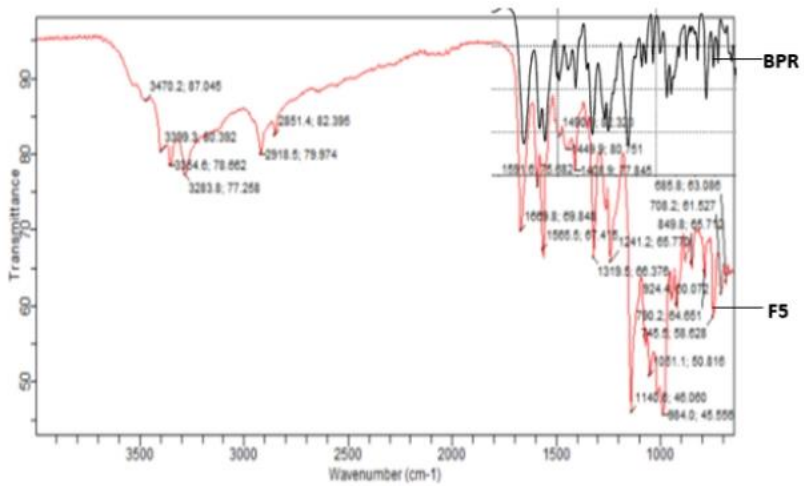

Figure 6: Superimposed FTIR Spectra of Generic F5 and Furosemide BP Reference.

Table 2: Weight uniformity of various generics of furosemide tablet

Codes	Average weight (mg)	No. of Tablet that failed to comply
F1	186.50	3
F2	179.05	2
F3	189.10	0
F4	192.30	4
F5	189.30	0

Table 3: Assay, Friability and Drug release of the various generics

Generic	Content (%)	Friability (%)	Drug release (%) ± SD, n = 6
F1	109.48	0.52	95.74 ± 1.67
F2	115.30	0.56	87.00 ± 0.74
F3	98.28	0.51	96.05 ± 0.45
F4	118.97	0.56	99.27 ± 1.23
F5	104.74	0.85	93.08 ± 2.41

Table 4: Disintegration time of the furosemide tablet generics

Generics	Mean Disintegration Time ± SD (min)
F1	0.42 ± 0.88
F2	0.81 ± 0.29
F3	1.30 ± 0.11
F4	0.89 ± 0.26
F5	0.52 ± 0.32

210°C), Furosemide functional groups, such as N-H Bending vibration (Near 1515 cm^{-1}), O=S=O Stretching (1390-1290 cm^{-1}), C=O Stretching vibration (1600-1800 cm^{-1}), O-H Bending vibration (1440-1395 cm^{-1}) and C-Cl Stretching vibration (850-550 cm^{-1}) were found to be present in the generics (F1-F5). These groups were fully superimposed on their FTIR spectra against the furosemide BP reference IR spectrum, indicating the presence of furosemide active pharmaceutical ingredient (API) (Figure 2 - 6).

The consistency of the active pharmaceutical ingredient (API) in a particular tablet formulation is indicated by tablet weight uniformity [1]. To pass the uniformity of weight test, a tablet weighing more than 80 mg, but less than 250 mg must have no more than two individual tablets that deviate from the average mean by more than ± 7.5% [2]. Failure of the weight variation test indicates inconsistent API concentration, which may result in toxicity, inefficacy, and unpredictable therapeutic effects [1]. Generics F1 and F4 fail the weight variation test (Table 2) as more than two tablets fall outside the 7.5 % BP percentage limit

while generics F2, F3 and F5 passed the test. In contrast, Chinaka and Nwachukwu assessed five generics of furosemide (40 mg) tablets marketed in Port Harcourt, Nigeria and reported that all the generics passed the weight variation test [6]. According to Brevedan et al, all eight of the evaluated generics (40 mg) in the quality assessment of furosemide marketed in Argentina passed the weight variation test [7]. Abebe et al, reported satisfactory results of weight variation on various generics of furosemide marketed in northwest Ethiopia [1].

Only two generics (F3 and F5) were able to pass the assay test (Table 3), as their furosemide concentration fell between the official range of 95 and 105.0 % [2], implying the products ought to achieve the expected therapeutic effect. Furosemide toxicities notably dehydration, decreased blood volume, and electrolyte abnormalities [8], can occur from the generics (F1, F2, and F4) that failed this test. All five generics of furosemide tablets examined passed the per cent content test, according to a study conducted in Port Harcourt, Nigeria [6]. All the generics passed the friability test (Table 3) as all their percentage friability (0.51 – 0.85 %) were less than the 1% BP limit [1]. Hence the furosemide tablets are of good strength and could withstand shocks during transportation and handling. One of the five generics of furosemide assessed by Chinaka and Nwachukwu failed the friability test [7].

Tablet disintegration is an important step in the bioavailability of a drug as it affects tablet dissolution and subsequently therapeutic efficacy of the medicine. The disintegration test revealed that all the generics (F1-F5) rapidly disintegrated (Table 4) in less than fifteen minutes (15 min) as required by BP, 2009 for the immediate release of un-coated tablets. Hence, furosemide API will be available for absorption in the gastrointestinal tract.

All generics passed dissolution studies as more than 80 % of furosemide was dissolved within 30 minutes (Table 3). Therefore, all generics are expected to have a good bioavailability profile to elicit pharmacological action. Chinaka and Nwachukwu reported that all the five generics of furosemide evaluated passed the dissolution test [7].

CONCLUSION

Only two out of the five furosemide generics passed the quality assessment and are therefore expected to yield the desired therapeutic effect.

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AUTHORS' CONTRIBUTION

Umar Abdurrahman: Designed and carried out the Lab work, analyzed data and drafted the manuscript. Awwalu Salisu: Designed, supervised the work and proofread the manuscript. Hassan Halimatu Sadiya: Supervised the work and proofread the manuscript.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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