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Comparative Analysis of the Level of Metformin Hydrochloride in Different Tablets Brands Sold in Kano Metropolis, Nigeria

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Abstract

Metformin hydrochloride, a commonly prescribed medication for type 2 diabetes management which works by helping to restore the body's response to insulin. It decreases the amount of blood sugar that the liver produces and the intestines or stomach absorb. Manufacturing processes may lead to differences in the concentration of the active pharmaceutical ingredient (API) and quality parameters among different brands. Ensuring the quality and consistency of these brands is crucial for patient safety and treatment efficacy. The study aimed to assess and compare the identity and quality of different brands of Metformin hydrochloride tablets marketed in Kano, Nigeria using Ultra-Visible (UV) and Fourier transform infrared (FTIR) spectrophotometer among other methods. Uniformity of weight test and identification test were also conducted on the sample. The UV result showed that all samples pass the assay test with percentage purity ranging from 96.99 to 99.15 %. Similarly, the brand samples pass identification test with red-orange colour indication. The difference in average weight has 830.8g as the highest and 525.8g as the lowest. The vibrational band assignments of Metformin hydrochloride were made using FTIR measurements; and provided satisfactory vibrational band assignments of Metformin hydrochloride that gave further accuracy and reliability of the analysis. The results of the research indicated that the manufacturing processes of the assessed Metformin hydrochloride tablets adhere to specified quality standards, offering valuable Metformin hydrochloride brands to the market from the methods used.

Key words: ***Assay, Determination, I.R, Kano, Metformin, UV***

Introduction

Diabetes mellitus is a group of metabolic disorders in which the blood glucose is higher than normal levels, due to insufficiency of insulin release or improper response of cells to insulin, resulting in high blood pressure [1]. The resultant Hyperglycemia produces the classical symptoms of polyuria, polydipsia and polyphagia. It may also cause nerve problems, kidney problems, and blindness, loss of limbs, and sexual dysfunction, increase in heart attack or stroke [2]. Metformin (a biguanide derivative), decreases these

complications, by controlling blood glucose level. It is now widely prescribed as an anti-diabetic type 2 drug; however, there have been serious concerns about its adverse effects, especially ketoacidosis [3]. However, its adverse effects are negligible when compare to its benefits [4]. The drug is also used by women with polycystic ovarian syndrome which make menstrual cycles more regular and increase fertility [4]. The sudden surge of Metformin hydrochloride tablet brands in Nigeria is a source of concern about potential variations in quality. This has brought in different brands of Metformin hydrochloride in Nigeria, offered in different strengths by both the domestic and international manufacturers.

Substandard medications always fail to meet official criteria for potency, quality, purity, packaging and labeling which poses significant health risks, including treatment inefficacy, adverse reactions, and heightened rates of illness and death. However, addressing these challenges can advance pharmaceutical quality control practices and promote public health in Nigeria [5].

UV spectrometry and IR techniques offer reliable methods for quantifying pharmaceutical compounds, including Metformin hydrochloride. By evaluating these methods for different brands, the study provided valuable insights into the quality and reliability of these medications, hence contributing to improved patient outcomes and regulatory standards [6].

Material and Methods

Reagents, Chemical and Equipment

Distilled water, Sodium Hydroxide,1-Naphthol, Anhydrous sodium carbonate, Sodium Hypochlorite. All chemicals and reagents are analytical grades from Sigma-Aldric.

Equipment

Analytical weighing balance: (Mettler Philip Harris LTD. England, 2010).

Ultra Violet (UV) spectrophotometer (JEN WAY 7315, UK by Bibby scientific LTD, 2007).

Infra-Red (IR) CARY 630 FTIR spectrometer (CARRY630, USA)

Sampling Area

Medile Road (this has many Pharmacy shops and Patent medicine stores). One pack of Metformin was purchased from each of the chosen Pharmacy Shop and Patent store, at random;Yahaya Gusau, Sabuwar Gamdu Street, Yar'Aduwa Hospital way, Tal'udu Round-about, Kano Metropolis, Nigeria, were also chosen areas for the sampling. The same pattern, as done for Medile Road was used in purchasing the samples.

Sample Collection

The Reference Standard of Metformin powder of 99.8 % purity was obtained in the month of February 2024, from University of Lagos, Faculty of Pharmaceutical Sciences, Nigeria for the preparation of serial concentrations for plotting calibration curve.

Five (5) different brands of Metformin hydrochloride tablets were randomly purchased at

the different Pharmacy retail Outlets in Kano State metropolis, Nigeria in the month of January, 2024.

The tablets were labelled to contain 500 mg of Metformin hydrochloride as the Active Pharmaceutical Ingredient. The samples were coded brand A- E and stored at room temperature.

The Name, Manufacturer, Production and Expiry date, NAFDAC registration number and Batch were recorded as shown in Table 1.

Table 1. Sample of Metformin hydrochloride tablets (500 mg) randomly selected from the collection areas in Kano Metropolis, Nigeria

Brand	Country of manufacure	Batch Number	NAFDAC Reg. NO.	MFG Date	Expiry Date
A	India	PAF01721	04-8247	Apr. 2023	Apr. 2026
B	India	(10)G031004	B4-2429	Jun. 2021	May 2024
C	Spain	E208653	04-6233	Apr. 2021	Mar. 2026
D	Malaysia	CC07739	04-0810	Jul. 2022	Jun. 2025
E	Nigeria	S43012	04-7968	Aug. 2023	Feb. 2026

Physical and Chemical Identification of Metformin Hydrochloride

Physical Appearance Test

A blister containing 20 tablets for each of the samples were randomly selected, the blisters were broken to expose the tablets. The tablets were opened and each sample was powdered and examined for colour, texture and taste. The same tests were conducted for Standard Sample [7].

Weight Uniformity

The tablets were weighed individually and collectively as described in BP 2009 [7]. The individual weights were compared with the average weight. The Mean weight was calculated and weight uniformity was recorded in table 3.

Identification Test

Solution A: This was prepared by dissolving 1 g of 1-naphthol in a solution containing 6 g of Sodium Hydroxide and 16 g of anhydrous Sodium Carbonate in 100 mL of distilled water.

Sodium Hydroxide (5M) Preparation

A 2 g portion of sodium hydroxide was dissolved into 10 mL volumetric flask with small amount distil waters, and then shaken to completely dissolve the solute; it was then filled to the mark with distil water.

Sample solution: A 0.083 g amount of powered tablets equivalent to 50 mg of Metformin hydrochloride was dissolved with 10 mL of distilled water, filtered and the filtrate was used for the analysis.

Reference Standard solution: This was prepared by dissolving 0.05 g of Reference Standard in 10 mL of distilled water and filtered. The filtrate was used for analysis.

Identification Analysis: To 5 mL of the sample solution, 1.5 mL of 5 M sodium hydroxide solution was added followed by 1 mL of solution A. Then 0.5 mL of Sodium hypochlorite solutions was added drop-wise with shaking [8]. The same test was conducted for the Reference Standard.

Assay

All chemical used were of analytical grades and all solutions were freshly prepared.

Preparation of 10 µg/mL Standard Metformin Hydrochloride Solution

This was prepared by dissolving 0.01 g of Standard Metformin hydrochloride into 10 mL volumetric flask with distill water. Then 1 mL of it was transferred into 100 mL volumetric flask and distilled water was diluted used to mark using ditilled water. This solution was labelled solution A.

Preparation of Standard Solutions

From solution A, a concentrations of 8 µg/mL, 6 µg/mL, 4 µg/mL, 2 µg/mL were prepared for calibration curve.

Preparation of Samples Solutions

Using weighing balance, 20 tablets were weighed and finely powdered, 0.1662 g equivalent to 100 mg Metformin hydrochloride of Sample A was transferred into a 100 mL volumetric flask. From this solution 70 mL was added and shaken by mechanical means for 15 minutes. It was then diluted with distilled water to final volume and filtered by discarding the first 20 mL of the filtrate.

From the filtrate 10 mL was diluted with distilled water to 100 mL of volumetric flask. The concentration of this solution is 10 µg/mL [8] and this preparation was done to the rest of the samples.

Procedure for Assay

Series of serial dilutions of Reference Standard solutions with known concentrations were prepared and labelled as solutions RS1 (10 µg/mL), RS2 (8 µg/mL), RS3 (6 µg/mL), RS4 (4 µg/mL), and RS5 (2 µg/mL). The Absorbance of each standard solution was measured using the UV spectrophotometer at 232 nm wavelength. A graph of Absorbance versus Concentration was plotted as shown in figure 1. The calibration curve was used to determine the Concentration of samples by measuring their Absorbance corresponding to their concentrations.

Infra Red (IR) Procedure

The IR machine (CARY 630 model) was calibrated according to manufacturer's manual. The Standard sample was loaded in the clean and dry sample compartment. The parameters for spectral range, resolution and number scan were set. The result of

of the scan appeared and printed. The procedure was repeated for all the brands samples.

Result

The physical Appearance results for both Standard and that of Samples are shown below in table 2. Reference Standard and brand Samples have all pass according to B.P. 2009 [7].

Table 2: The physical appearance test

Samples	Colour	Taste	Texture	Shape
A	White	Bitter	Fine powder	Oval
B	White	Less bitter	Fine powder	Round
C	White	Less bitter	Fine powder	Round
D	White	Less bitter	Fine powder	Round
E	White	Bitter	Fine powder	Round
RS	White	Bitter	Crystalline	Granules

Table 3 shows the result of weight uniformity for the brands of samples under review, which showed compliance according to the BP 2009.

Table 3: Weight uniformity of different brands of Metformin hydrochloride.

Samples	Weight w1(mg)	Weight w2(mg)	Average weight(mg)
A	830.8	830.8	830.8
B	617.7	617.6	617.7
C	526.4	526.3	526.4
D	525.8	525.8	525.8
E	534.3	534.2	534.3

Identification Result

The result for identification test on selected samples of Metformin hydrochloride, and Reference Standard (RS) is presented below in Table 4.

Table 4 Identification test reading for all the selected samples and Reference Standard (RS)

Samples	Results
A	An orange-red colour was produced that is darkens on standing
B	An orange-red colour was produced that is darkens on standing
C	An orange-red colour was produced that is darkens on standing
D	An orange-red colour was produced that is darkens on standing
E	An orange-red colour was produced that is darkens on standing
RS	An orange-red colour was produced that is darkens on standing

Assay Result

The Absorbance of each of the five (5) brands are shown below from which corresponding concentrations were obtained from the calibration Curve plotted.

Table 5: Assay for all the selected samples of Metformin hydrochloride studied.

Sample	Concentration (µg/mL)	Percentage (%) Content
A	56.03	96.98
B	55.84	96.98
C	55.86	97.00
D	55.86	97.00
E	55.85	96.99

Construction of Calibration Curve

The calibration curve for standard Metformin hydrochloride powdered was constructed as shown in Fig. 1

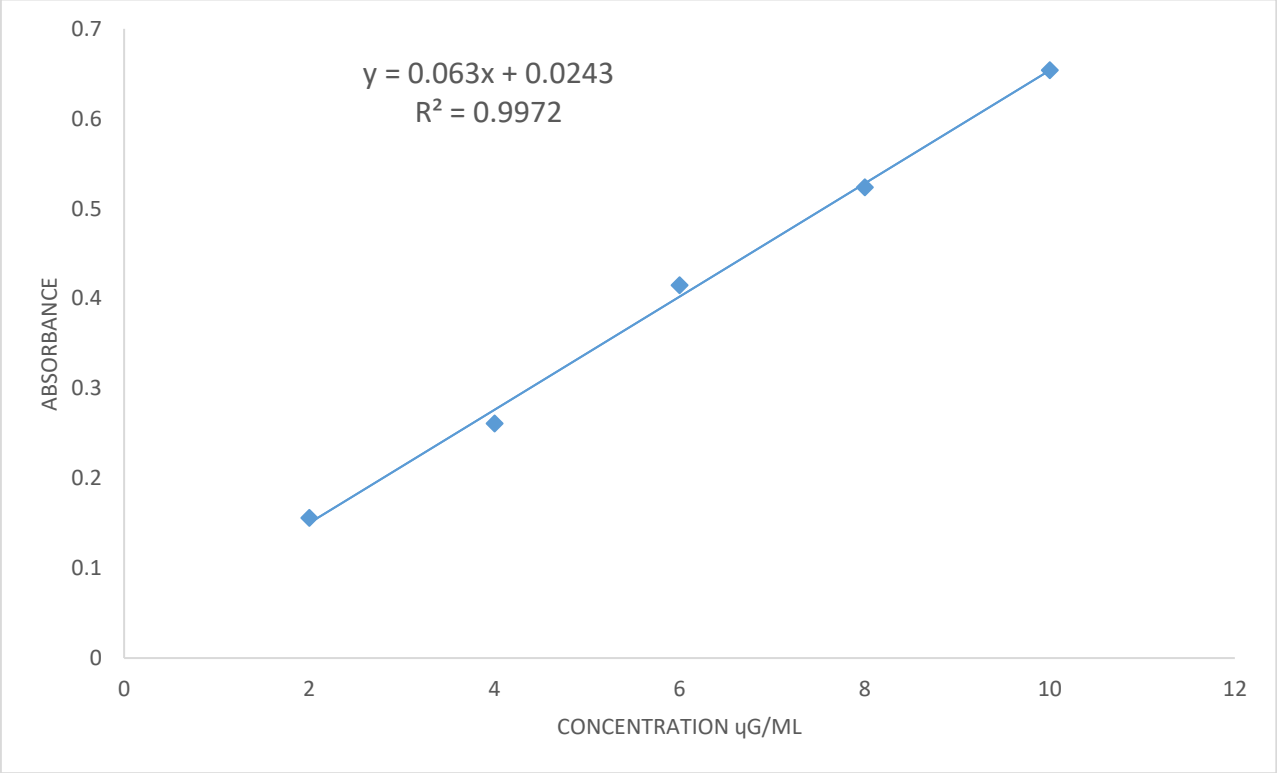

Figure 1: Calibration Curve for Standard Metformin powder

Infra-red (IR) Result

Below are the figures showing the Infra-red Spectrum of the Reference Standard and Samples of Metformin hydrochloride.The infra-red spectra of the Metformin hydrochloride Reference Standard reveals characteristic peaks consistent with the known functional groups of the compound with their respective frequencies were observed.

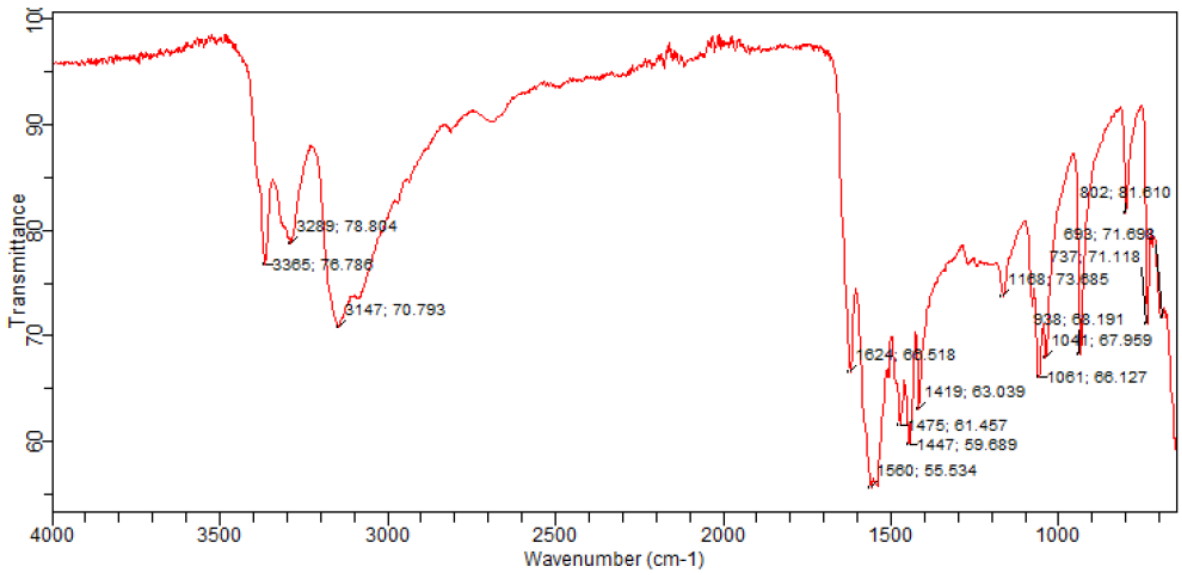

Figure 2: Infra-red spectrum of Reference Standard

The infra-red spectra of the Metformin hydrochloride Reference Standard revealed characteristic peaks consistent with the known functional groups of the compound. The N-H stretching peak appeared around 3300-3500 cm^{-1}, indicating hydrogen bonding interactions, while C-H stretching peaks were observed in the range of 3000-2800 cm^{-1}. Peaks corresponding to C=N and C-N functional groups were identified around 1626 and 1583 cm^{-1} stretching vibration. The spectrum demonstrated conformity to the expected molecular structure of Metformin hydrochloride, providing a baseline for comparison with other brands (A-E).

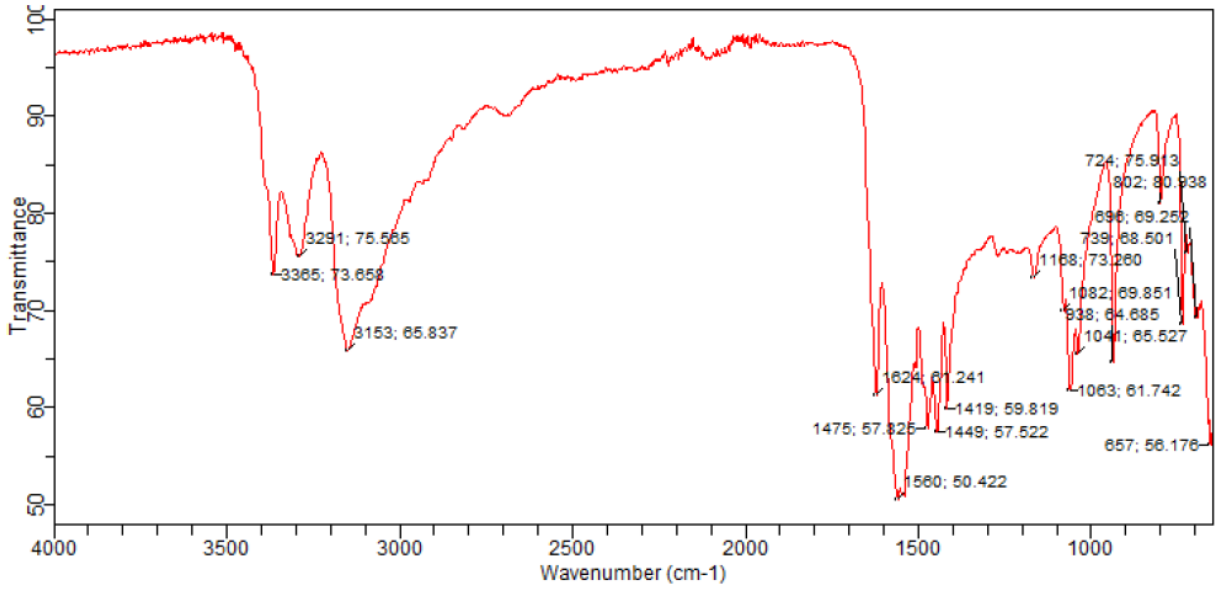

Figure 3: Infra-red spectrum of Sample A

Brand A: The N-H stretching peak at 3100-3400 cm-1 closely matched the reference standard, indicating similar hydrogen bonding interactions. C-H stretching peaks were observed around 3000-2800 cm^{-1}, consistent with the Standard. Peaks corresponding to C=N and C-N groups were also in agreement with the Reference.

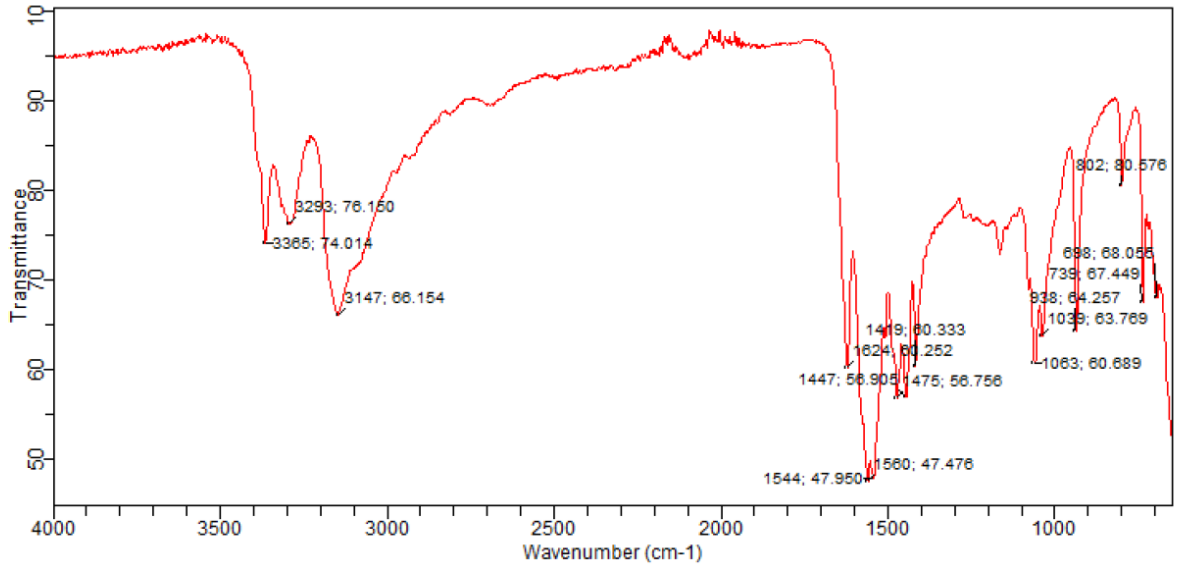

Figure 4: Infra-red spectrum of Sample B

Brand B: Similar N-H stretching and C-H stretching peaks were observed at 3400 and 3100 cm^{-1} compared to the reference standard. Peaks attributed to C=N and C-N functional groups exhibited minor shifts but remained comparable to the standard with a stretching vibration at 1626 and 1583 cm^{-1}

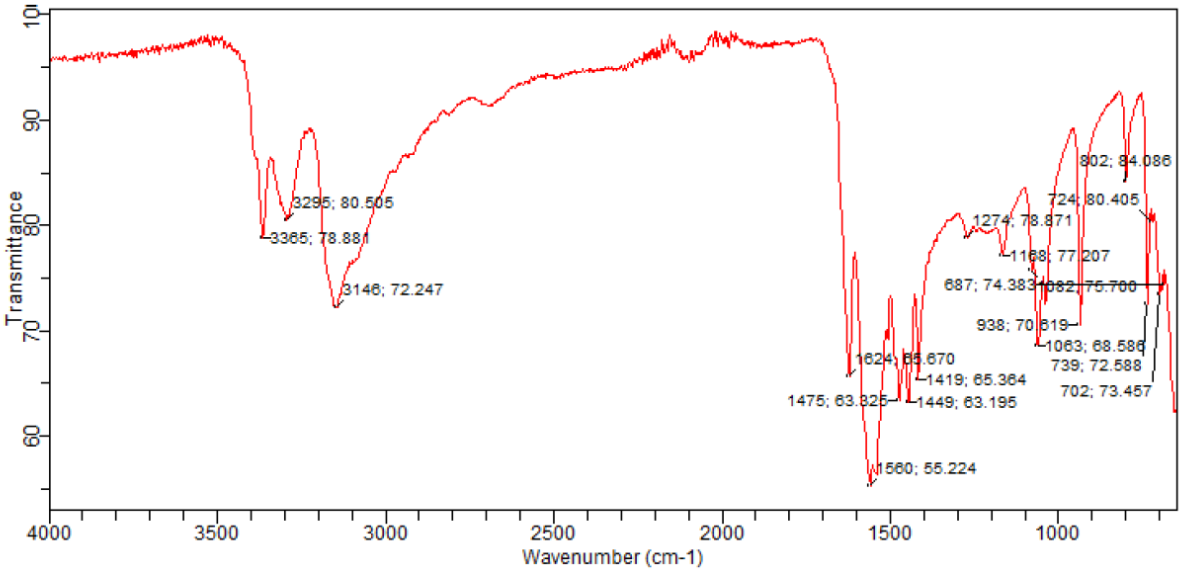

Figure 5:Infrared spectrum of Sample C

Brand C: The N-H stretching peak is slightly broader compared to the reference, suggesting variations in hydrogen bonding interactions. However, peaks related to C-H stretching, C=N, and C-N groups aligned well with the Reference Standard.

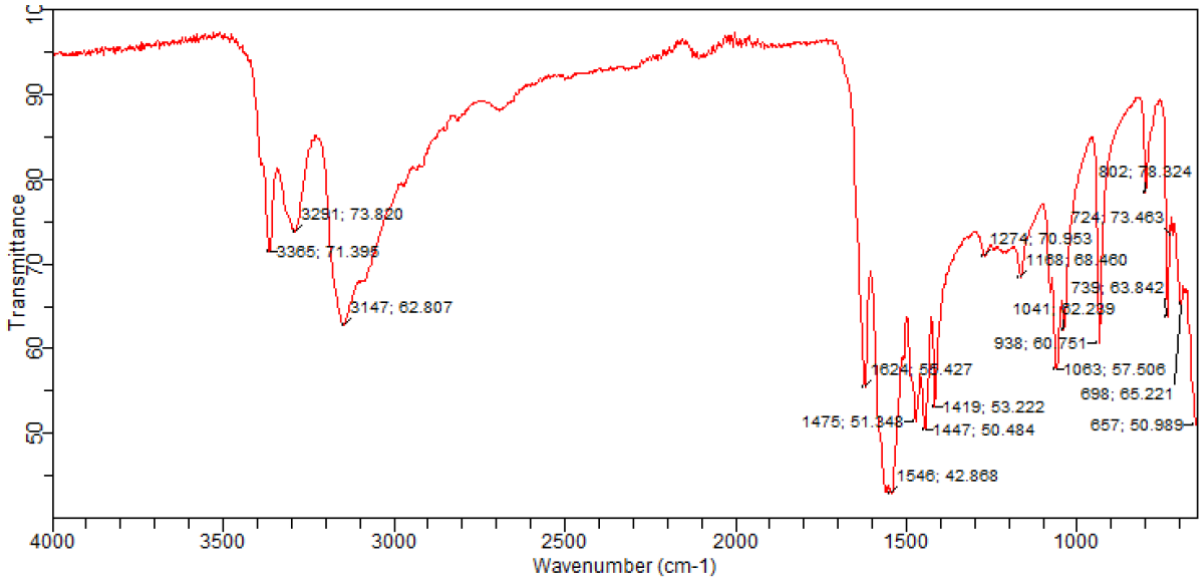

Figure 6: Infra-red spectrum of Sample D

Brand D: N-H stretching and C-H stretching peaks closely resemble those of the Reference Standard. Peaks associated with C=N and C-N functional groups showed slight variations but remain consistent with the standard.

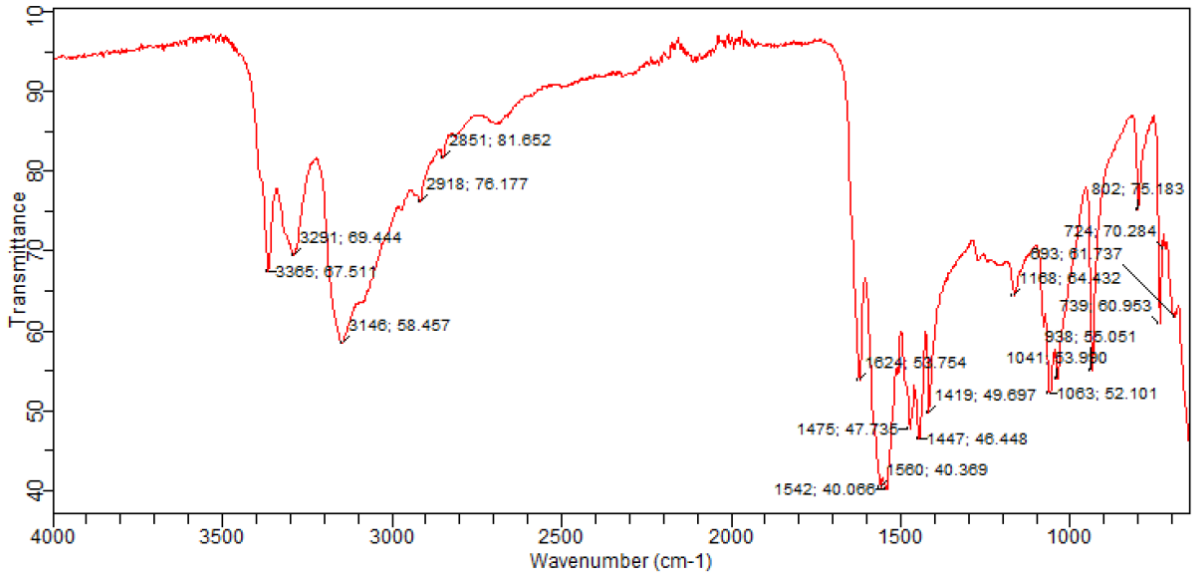

Figure 7: Infrared spectrum of Sample E

Brand E: The N-H stretching peak exhibited minor differences in intensity compared to the Reference, while C-H stretching peaks were in good agreement. Peaks corresponding to C=N

and C-N groups showed slight shifts but are comparable to the standard

Discussion

The samples of Metformin hydrochloride analyzed were approved by NAFDAC and posses satisfactory shelf-lives. The Reference Standard and Samples exhibited desirable visual characteristics of white colour, odourless and has a bitter taste as illustrated from the table 1. This has met the requirements of organoleptic properties according to B.P 2009 [7].

The average weight of the different brands of Metformin hydrochloride tables are shown in Tables 2. These table showed that brand A had the highest average weight of 830.76 mg per tablet while brand D had the lowest average weight of 525.8 mg per tablet. For most tablets, including Metformin, the acceptable weight variation is usually around ±5% of the average weight of the tablets according to Food Drug Administration, FDA or pharmacopoeias like the USP. The differences in weight could be attributed to variations in the amount of inactive ingredients used as fillers, binders, or coatings, which can vary between different manufacturers or formulations. Additionally, differences in tablet size or shape could also affect the overall weight. The purpose of this test was to ensure consistency across all batches, reflecting the uniformity of the drug content in each formulation batch [9,10].

The identification of all the brands and Reference Standard produced an orange - red colour that was darkens on standing, which is an acceptance criterion for Identification of Metformin hydrochloride according to USP 32. this result proved that the brands have contained Metformin as Active Pharmaceutical Ingredient (API), an indication towards quality products.

The assay result for the selected samples have the following as percentage purity of brand A, B, C, D, and E being 96.98 %, 96.98 %, 97.00 %, 97.00 % and 96.99 % respectively. According to the United States Pharmacopoeia [8], the percentage purity of the Metformin Hydrochloride should be in the acceptance range of 95.0% to 105.0%. Therefore, all the brands tested have passed this important quality criteria. This is similar to the study done by Agnes *et al.* [11], whose assay test result showed percentage purity of 99.15 %, 99.03 %, 99 %, 99.66 %, 99.42 %, and 99.38 % respectively for all the Metformin brands tested.

Similarly, the percentage purity Reference Standard was found to be with range of 98.5 % to 101.0 %, with reference to the same USP 32 [8]. This consistency of percentage purity is clear indication that many Metformin manufacturers are across the world are putting their best in following Good Manufacuring Practice (GMP) to produce qualitative drugs that give desire pharmacological effect to patients.

The analysis of infrared spectra for the Metformin hydrochloride Reference Standard and all the brands studied offered consistency and quality of these products.

The Metformin hydrochloride Reference Standard exhibited characteristic peaks corresponding to known functional groups, such as N-H stretching, C-H stretching, C=N, and C-N bonds, in agreement with literature values [12]. This consistency with the expected molecular structure of Metformin hydrochloride validates the use of the Reference Standard as a reliable benchmark for assessing the quality and composition of other brands.

For brands (A-E) of the Infra-red (IR) results shown, all the brands possessed the characteristic peaks consistent with the known functional groups of the compound of the Metformin hydrochloride Reference Standard. However. Brand C and E have N-H stretching peak slightly broader compared to the Reference Standard, suggesting variations in hydrogen bonding interactions. This is could be due to variations in formulation, manufacturing processes, or raw materials used by individual manufacturers [13].

This is similar to the study done by Agnes *et al.* [11] using seven samples of Metformin hydrochloride with N-H stretching vibrations found in the region 3300- 3500cm^{-1}, the C-H stretching vibration generally occurring in the region 3500- 3300 cm^{-1} and in the region of 3200-3000 cm^{-1}. There is C-N stretching vibration generally occurring in the region of 1500-1000 cm-1 with the peak at 1416 cm^{-1}. Another similar research also shown that Metformin Hydrochloride N-H stretching of C=N–H group occurs in the region 3400 - 3100 cm^{-1} [14]. Therefore, the results obtained for this work is in conformity with the reports of other researchers.

In comparing, the two methods, UV spectrometry and IR spectroscopy are both analytical techniques used in pharmaceutical analysis. UV spectrometry quantified compounds with conjugated double bonds which was used for both identification and assaying of the drug; while IR spectroscopy provided functional group information and was used for identification test of the drug. From this study, UV Spectrometry is more preferred for quantifying Metformin hydrochloride and IR was used for identifying Metformin hydrochloride more effectively.

Conclusion

The research findings support that there is no significant variance in the quantitative determination and quality control of Metformin hydrochloride brands marketed in Kano State Metropolis, Nigeria. UV spectroscopy proved more effective and reliable for quantification of Metformin hydrochloride content. Equally, FTIR spectral measurements provided satisfactory vibrational bands for proper identification of Metformin hydrochloride through understanding of its chemical structure and composition.

Recommendations

1. Further research is needed to investigate the implications of observed spectral variations on the pharmacokinetic and Pharmacodynamic properties of Metformin hydrochloride brands.

2. In light of the recently introduced Mega drug distribution system by the Federal Government in Nigeria, there is a pressing need to establish and maintain quality control laboratories in all states of the federation. These laboratories will play a crucial role in ensuring the distribution of safe and effective drugs throughout the entire distribution chain, safeguarding public health and promoting confidence in the healthcare system.
3. Regulatory agencies in Nigeria should prioritize the enforcement of strict quality and effectiveness standards for pharmaceutical products. It is imperative to prevent counterfeit or substandard drugs from entering the community, as they pose significant risks to patient safety and undermine public trust in the healthcare system. Encouraging greater vigilance and accountability among regulatory agencies will help uphold the integrity of the Pharmaceutical market and protect the health and well-being of the Nigerian population.

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