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Quality assessment of five brands of ascorbic acid tablets marketed in Ogun state, Nigeria

David Gbenga BABALOLA[1*], Olusegun Ayo ADE-ADEKUNLE[2], Grace Omolola AJASA[1], Precious Adebowale DADA[2]

[1]Department of Pharmaceutical Chemistry, Olabisi Onabanjo University, Sagamu, Ogun State, Nigeria;
[2]Department of Pharmaceutical Microbiology, Olabisi Onabanjo University, Sagamu, Ogun State, Nigeria.

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Abstract
Ascorbic acid (vitamin C), a water-soluble vitamin, is an essential nutrient that plays a crucial role in the body's antioxidant defences. Since the body cannot synthesize it, ascorbic acid must be obtained through either dietary sources or supplements. The aim of this study was to assess the quality and physicochemical properties of five different brands of ascorbic acid commonly sold in several pharmacy outlets in Ogun State. The brands were analysed for their uniformity of weight, hardness, friability and disintegration time using official methods, quantitative analysis was done using dissolution test and high-performance liquid chromatography (HPLC). One out of the five brands (20%) passed the weight uniformity test ranging between 282.7 mg to 364.8 mg, four (80 %) of the five brands passed the hardness test and were within 1.5 and 6.0 KgF. All five brands passed the friability test, disintegration test and dissolution test and were within 0.0172 - 0.5691%, 0.36 - 13.52 mins and 96 - 103% respectively. The amount of API in each brand ranging from 97.25% to 103.07% were within official specifications when assayed with HPLC. This study elucidates the need for regular post market surveillance of medications to ensure the safety of consumers.

Keywords: Vitamin C tablets; Physicochemical analysis; Quality assessment; Antioxidant

INTRODUCTION

Since the early 20th century, counterfeit and substandard medicines have been a recurring problem with an undeniable effect on the health of the vulnerable population, these poor-quality drugs are harmful but a neglected issue in Nigeria's health system [1]. Production and sales of quality drugs is very essential as it guarantees the safety and efficacy of the medication [2]. Poor quality medications can result into therapeutic failure, drug resistance, worsening of consumer's health and even death, likewise a significant effect on the nation's economy [3]. According to a 2006 survey conducted by the National Agency for Food and Drug Administration and Control (NAFDAC) revealed that 70% of medications sold in the Nigeria were unregistered with 41% regarded as fake. Several studies have shown distinctively the widespread of poor-quality drugs in Nigeria [4]. For instance, a study conducted at Onitsha in 2008, evaluated the quality of five ascorbic acid brands using various tests (friability, disintegration, weight uniformity, hardness tests and assay using UV/Vis

*Correspondence. *E-mail*: babalola.d.g@gmail.com *Tel*: +234-8134915829 ISSN 0189-8442

Spectrophotometer) in accordance with the BP specification. While all brands passed weight uniformity, hardness and disintegration time tests, one brand failed friability test, and they all failed the assay according to the BP specifications. These findings suggest variability in brand quality, highlighting the need for improved quality controls [5]. In 2020, another study conducted in Sierra Leone to assess the quality of nine brands of ascorbic acid. Friability test, disintegration test, weight uniformity test, titrimetric and colorimetric assay of the samples were carried out in accordance with the BP specification. All the brands passed the weight uniformity test and friability test, only one brand failed the disintegration test and seven out of nine passed the assay according to BP specification [6].

Ascorbic acid (Vitamin C), a water-soluble vitamin is a major nutrient for the body system which acts majorly as an antioxidant (non-enzymatic antioxidant). An antioxidant is a molecule capable of inhibiting the oxidation of another molecule, by breaking the free radical chain of reactions [7]. They are nature's way of defending cells against attack by Reactive Oxygen Species (ROS) which can lead to disintegration of cell membranes, damage to membrane proteins, and DNA mutations, culminating in the aging process and serving as a catalyst for several ailments such as arteriosclerosis, cancer, diabetes mellitus etc. [8]. Ascorbic acid also plays a crucial role in enhancing the functioning of the immune system, the phagocytic capabilities of neutrophils and macrophages whose deficiency can lead to a higher susceptibility to multiple infections. Furthermore, ascorbic acid enhances immune function by boosting antibody production, supporting antibacterial responses, and activating lymphocytes [9]. ascorbic acid is not synthesized in humans but can be gotten from diets and supplements, the primary dietary sources of ascorbic acid are fruits (e.g. oranges, watermelon, kiwi fruit) and vegetables (e.g. cabbage, broccoli, potatoes). It can also be synthesized in nonhuman organisms such as primate species, guinea pigs, fish and birds [10].

Ascorbic acid, a whitish or slightly yellowish crystalline powder is commonly referred to as *L*-ascorbic acid, the molecule consists of six carbon atoms in an asymmetrical arrangement which is structurally related to glucose. It has a molecular weight of 176 g/mol, melting point of 190-192ºC, density of approximately 1.65 g/cm^3. Ascorbic acid readily dissolves in water but is sparingly soluble in alcohol and insoluble in chloroform, ether and benzene. Ascorbic acid exhibits two pKa values; 4.2 and 11.6, and the pH of a 5 % w/v ascorbic acid solution is within the range of 2.2-2.5 [11,12]. It is also an organic acid that is prone to instability when exposed to factors such as light, oxygen, high temperatures humidity and heavy metals. [13]. Administration of ascorbic acid can be through the oral, parental and even topical route, the appropriate dosage depends on several factors such as the individual's medical condition, route of administration, age and weight. The healthy human body reserve of ascorbic acid is approximately 1.5 g and the body utilizes 3-4% of this reserve so a daily oral intake of 200-300 mg is advisable which can be gotten easily from fruits and vegetables. The maximum dosage for a healthy human is 2 g per day and after taking ascorbic acid the level in the bloodstream (plasma) remains relatively stable for approximately 5-6 hours before it starts to decrease [14-16].

Having noted that over 41% of medications sold in Nigeria were regarded as fake and 70% of medications sold in the Nigeria were unregistered, which reveals a crucial gap that can be addressed by ensuring drug quality and standard through: post-market surveillance, automated systems which are less prone to errors, streamlined processes at each operational step of production. [17]. This study aims to assess the quality, physicochemical properties, and chemical equivalence of five

different brands of 100 mg ascorbic acid tablets sold in Pharmacy outlets located in Ogun State.

EXPERIMENTAL METHODS

Materials. High performance liquid chromatography (Agilent series, Isocratic elution, United states), Analytical weighing balance (Adventurer-Pro, United States), Dissolution tester (RC-6, India), Ultrasonic bath, Disintegration tester (Ketan Instruments, India), Friability Tablet apparatus (DBK Instruments, Germany), Hardness tester (Ketan Instruments, India) and five brands of Vitamin C tablets (100 mg).

Sample collection. Five brands of ascorbic acid tablets were randomly purchased from different registered pharmacy outlets in Ogun state, coded and subjected to analysis before their expiration date. Physical examination was carried out on the labelling and packaging of the medications to ensure the presence of NAFDAC number, batch number, manufacturing date and expiry date. The samples were coded as VITC 1 to VITC 5 as shown in Table 1.

Determination of the uniformity of weight. Each brand had ten tablets chosen at random. The analytical balance was used to weigh each tablet. Each brand's average tablet weight was calculated. Additionally, the deviation (standard and percentage) and the percentage coefficient of variation of each weight from the average was also calculated. (USP, 2002).

Determination of tablet hardness. Ten tablets from each of the five brands were examined. Each tablet was positioned between the fixed and moveable jaws of the hardness tester, and a force was provided by rotating the screw through a spring-loaded screwdriver. The average force required to break the ten tablets from each brand (in kg/cm^2) were then determined (BP, 2008).

Determination of tablet friability. Ten tablets from each brand were weighed collectively before being put in a friabilator. For four minutes (100 revolutions), the friabilator was run at 25 revolutions per minute. After which the tablets were taken out, dusted, and reweighed using the analytical Balance. A percentage of weight loss was used to express the test's results (BP, 2008). The percentage friability was calculated as the difference in weight of the tablet before and after friabilation divided by the weight before friabilation and then multiplying the result by 100.

Determination of tablet disintegration. Disintegration rate of tablets was determined using disintegration test apparatus containing distilled water which was maintained at 37 ± 0.5°C. The disintegration chamber consists of six glass tubes closed at the lower end by 10 mesh rust-less wire gauze. The tube was raised and lowered in distilled water at a constant frequency. The rate of disintegration of 5 tablets from each of the 5 brands used for this research was determined at once by placing one tablet in each of the 5 glass tubes of the disintegration chamber and left to disintegrate (leaving a soft palpable core). The disintegration time for each of the tablets was recorded and mean disintegration time of each brand was calculated (USP, 2002).

Dissolution test. The dissolution vessel was filled to the 900 mL mark and was set to 37°C buffered with phosphate buffer (pH 6.8) then allowed to reach thermal equilibrium in the dissolution paddle apparatus. The rotation speed was then adjusted to 50 rpm, at predetermined time points (5, 10, 20, 30, 45, and 60 minutes), 5 mL aliquots were withdrawn from the dissolution medium and filtered using syringe filters. To maintain sink conditions, an equivalent volume of fresh medium was replaced. The filtered samples were then diluted 1:50, and their absorbance was measured at 265 nm using a UV spectrophotometer. The content of ascorbic

acid was then determined and recorded. This process was replicated for two additional tablets from each batch to obtain triplicate determinations, ensuring accurate and reliable results [18].

Assay of ascorbic acid tablets. The quantitative assay test was carried out using high performance liquid chromatography using United States Pharmacopeia method (2023). Analytical method verification was also performed. The buffer was prepared by weighing 2.04 g of monobasic potassium phosphate per 1000 mL of water then adjusted with phosphoric acid to a pH of 3.0 which served as the mobile phase (isocratic mode). The diluent was prepared by weighing 0.56 g of edetate disodium dihydrate and 2.04 g of monobasic potassium phosphate per 1000 mL of water which was then adjusted with phosphoric acid to a pH of 3.0.

Chromatographic conditions.
Mode: Liquid chromatography; Mobile Phase: 2.04 g of potassium phosphate per 1000 mL of water (pH 3.0); Detector: UV 245 nm; Column: 4.6 mm x 25 cm; 5 µm packing L1; Flow rate: 1.0 mL/min; Injection volume: 5 µL Temperature: 25°C

Preparation of standard solution. USP ascorbic acid standard (25 mg) was weighed accurately into 100 mL volumetric flask made up to 100 mL mark on the volumetric flask with the diluent to form the standard stock solution, thereafter 1.0 mL of the standard stock solution was transferred accurately into a 10 mL volumetric flask, 2.5 mL of diluent and 1.0 mL of water was added into the 10 mL volumetric flask and made up to the 10 mL mark with the diluent to form 0.025 mg/mL of USP ascorbic acid reference standard solution (25 µg/mL). The prepared standard was then used for analytical method verification (determining system suitability and as well as for preparing the linearity or calibration curve).

System suitability. The above standard stock solution (1 mL) was transferred into a 10 mL volumetric flask and made up to mark with the diluent (25 µg/mL ascorbic Acid). Six replicates' injections of 5 µL of the final concentration were injected for analysis to as to ensure the repeatability of the HPLC system (ability of the system to produce consistent results under the same conditions.) The percentage relative standard deviation of the peak area was determined and recorded. The criterion for accepting system suitability requirements is Relative standard deviation: NMT 1.0%

Linearity (calibration) curve. Concentrations of 50, 100, 150, 200, 250, 300, 350, 400, 450 and 500 ug/mL of ascorbic acid were made by transferring 0.5 mL, 1.0 mL, 1.5 mL, 2.0 mL, 2.5 mL, 3.0 mL and 3.5 mL respectively of the above stock solution into a 10 mL volumetric flask and made up to mark with diluent. 5 µL of each concentration were injected for the linearity. The linear equation was derived from the graph of peak area (AUs) against concentration (µL/mL). Least square linear regression analysis was determined using the slope, y-intercept and the correlation coefficients of the standard plots. Using $y = mx + c$; where x is the amount in µg/mL and y is the area. Twenty tablets of each brand were weighed using an electric weighing balance and their average weight was calculated. The tablets were then finely powdered using a mortar and pestle. A portion from the 20 finely powdered tablets was then transferred from the mortar, nominally equivalent to about 25 mg of ascorbic acid, then into a 100 mL volumetric flask. The diluent (60 mL) was added to the previous solution, the mixture was mixed mechanically for 15 minutes, the diluent was then used to make the solution up to volume, then mixed well. The resulting solution was filled into the HPLC vials through a syringe attached to a 0.45 µm filter and 5 µL of the final concentration was injected for analysis (25 µg/mL of ascorbic acid). This procedure

was carried out two more times on each brand to obtain triplicate results. The quantification of the samples was based on comparison of the peaks of the standards with those of the samples.

RESULTS

Five brands of ascorbic acid (vitamin C) 100 mg tablets were randomly selected from pharmacy outlets in Ogun State, physical and chemical tests were carried out on each brand. Table 1 shows the packaging information of the five brands. The packaging information included the brand name, batch number, NAFDAC number, manufacturing date, expiration date, and tablet description. At the time of the investigation, every brand of ascorbic acid tablet used in the study was still within its recommended shelf life. All of the samples complied with the packaging specifications, which included details on the dosage form's description, manufacturing and expiration dates, active ingredient names, strengths, and NAFDAC numbers. Every sample was seen be attractive. The result of the weights of ten 10 randomly selected tablets from each brand of the five brands of ascorbic acid tablets examined at 100 mg is shown in Table 2. However, the experimental results indicates that only one brand (VITC 3) out of the five brands successfully passed the weight uniformity test which shows that the ingredients were not evenly distributed in most brands thus causing inconsistencies in the bioavailability of the active ingredient which could be as a result of insufficient blending, the tableting conditions in the rotary tableting machine or using a faulty analytical balance and even high moisture content [19].

Table 2 shows the result of the hardness test of ten randomly chosen tablets from each brand of ascorbic acid under study. In reference to the 2008 British Pharmacopeia, VITC 1, VITC 2, VITC 4, VITC 5 failed the test with mean hardness of 2.74KgF, 2.46KgF, 2.03KgF and 3.48KgF respectively, while only VITC 3 passed the hardness test with mean hardness of 5.36KgF.

Table 1: Packaging information for ascorbic acid brands investigated

Brand code	Batch number	NAFDAC number	Manuf. date	Expiry date	Tablet description
VITC 1	2193C	04-1453	07/2023	07/2026	White, round tablet & convex
VITC 2	0523VWI9	A11-0106	05/2023	04/2026	White, round tablet & convex
VITC 3	VCK323	04-3232	07/2023	07/2026	White, round tablet & convex
VITC 4	16G	04-5250	07/2023	06/2026	White, round tablet & convex
VITC 5	RVCO523A	04-3486	03/2023	08/2024	White, round tablet & convex

Table 2: Mechanical and physical parameters of brands of ascorbic acid tablets investigated

Brand code	Uniformity of weight (g)	Hardness (Kg/cm)	Friability (%)	Disintegration time (minutes)
VITC 1	0.3060±0.013(F)	2.74±0.49(F)	0.10(P)	1.20±0.83(P)
VITC 2	0.3040±0.012(F)	2.46±0.59(F)	0.57(P)	6.95±2.62(P)
VITC 3	0.3483±0.007(P)	5.36±0.36(P)	0.017(P)	8.82±3.71(P)
VITC 4	0.3462±0.020(F)	2.03±0.28(F)	0.24(P)	10.14±2.77(P)
VITC 5	0.3261±0.018(F)	3.48±0.88(F)	0.17 (P)	1.48±0.71(P)

P = Pass, F = Fail

Table 3: Percentage content of **ascorbic acid** in different brands of **ascorbic acid** tablets

Brand Name	Theoretical value (µg/mL)	Recovered amount (µg/mL)	Label Claim (mg)	Percentage content	Remark
VITC 1	250	254.06±2.65	100	101.59±1.10	Passed
VITC 2	250	247.48±2.41	100	99.26±1.56	Passed
VITC 3	250	245.61±2.13	100	98.46±1.51	Passed
VITC 4	250	251.84±1.85	100	99.84±3.64	Passed
VITC 5	250	255.34±2.54	100	102.46±1.19	Passed

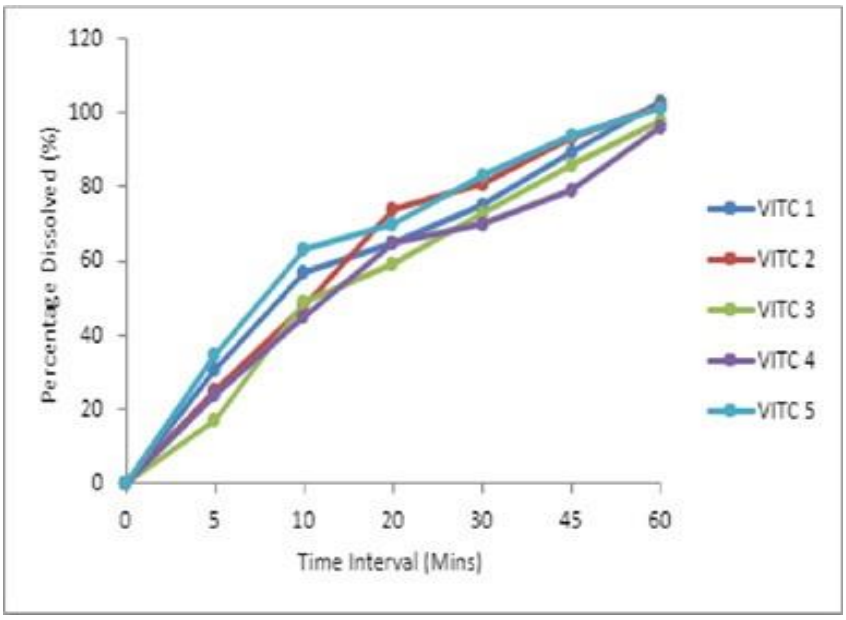

Figure 1: Drug released profile of ascorbic acid-tablets

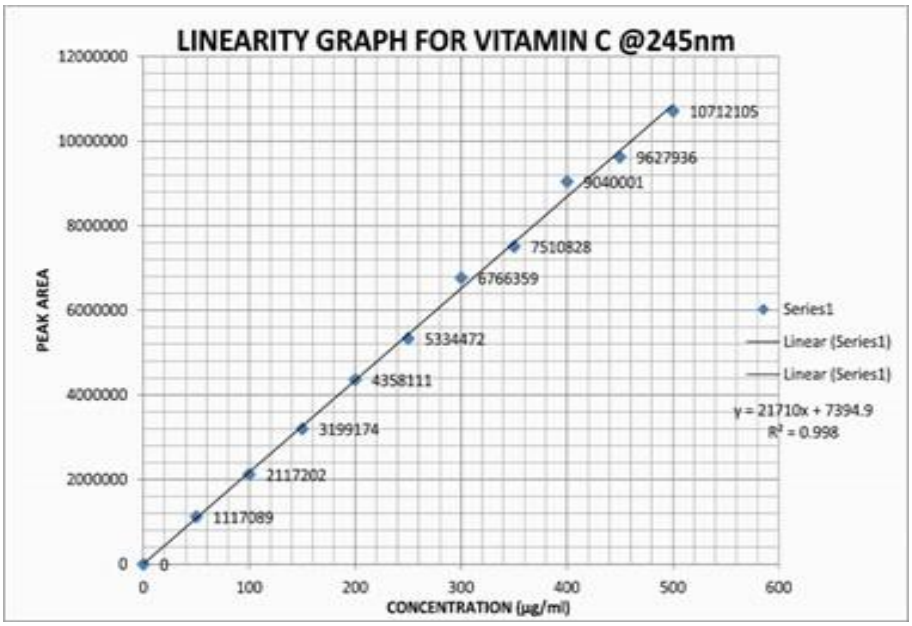

Figure 2: Calibration curve of ascorbic acid analysis

Table 2 also shows the result of friability test on all the brands of ascorbic acid 100 mg tablets indicating that all the brands passed the friability test according to the 2019 United State Pharmacopoeia. The percentage friability of the tablets ranged between 0.0172% and 0.5691%

The result of the disintegration tests conducted on all the brands of ascorbic acid 100 mg tablets is shown in Table 2. The disintegration time ranged from 1.2 to 10.14 minutes indicating that all the brands passed the disintegration test which was within the standard specification for coated tablet.

The results presented in Table 3 show the percentage content of ascorbic acid in the brands that were studied. indicate that all the brands of ascorbic acid tablets studied (VITC 1, VITC 2, VITC 3, VITC 4, VITC 5) successfully passed the HPLC assay analysis

for percentage content. VITC 3 exhibited the lowest concentration (98.46%), while VITC 5 showed the highest concentration (102.46%).

Figure 1 shows that the drug dissolved percentage of all the brands which are coated tablets ranged between 96 % and 103 % which indicates that all brands passed the dissolution test according to 2019 British Pharmacopeia.

DISCUSSION

Evaluation of the five brands of ascorbic acid involved the determination of their uniformity of weight, friability test, hardness test, disintegration test and dissolution assay. The uniformity of weight observed in each brand serves as a crucial indicator when assessing the uniformity of dosage units, which indirectly or directly gauge the quantity of the drug substance in the tablet [20]. The deviation in weight among the brands, which also reflects the tablet sizes, may raise concerns among patients and clinicians regarding the bioequivalence of these different brands. According to the United States Pharmacopoeia (2019) standards, not more than two tablets should exceed a percentage deviation beyond ±5%, and none should differ by more than double the relevant percentage deviation (i.e., above ±10%) and it was shown that only one brand (VITC 3) out of the five brands passed the test. A study showed that only 20% of the tablets tested met the USP criteria for uniformity of dosage units. Another study showed that 30% of the tablets tested failed to meet the USP criteria while in contrast, the current study deduced that only 1 out of 5 brands (20%) passed the test, which is consistent with the findings of these similar studies [21, 22].

The tablet's crushing strength, which indicates the hardness of a tablet, relies on factors such as the manufacturing process, the type and quality of the binding agent utilized. According to the United States Pharmacopoeia 2019, a recommended crushing strength falls within the range of 5-8 kp/cm² (kilopond/square centimetre) which is equivalent, according to calculations, to 5–8 kg/cm^2 (kilogram/square centimetre) and it was shown that only one brand (VITC 3) passed the test out of the five brands. The low level of hardness depicted in most brands of these ascorbic acid could be as a result of insufficient, low quantity of binders in the tablet formulation, and even the compression force used during compression of the tablets. Addition of binders in the right proportion is essential in the formulation of a tablet with adequate hardness. An excessively hard tablet could significantly prolong disintegration time, consequently affecting dissolution and bioavailability (United States Pharmacopoeia, 2019). The hardness of a tablet also has effect on the friability of the tablet. Ascorbic acid, being a supplement, is likely stored for extended periods. Prolonged storage under unsuitable conditions, such as improper temperature and humidity, can impact the tablet's hardness [23].

Comparatively, a study reported that 60% of tablets met the recommended hardness range, while another study found that 40% failed to meet the range while our study revealed a lower compliance rate, with only 20% of brands (VITC 3) meeting the recommended hardness range, indicating a significant disparity in tablet quality [24, 25].

For friability testing, according to the United State Pharmacopoeia 2019, a maximum weight loss not more than 1% after fibrillation is required for coated tablets of which all the brands used in this analysis are coated, and from our analysis we could deduce that all brands passed the friability test. This test is used to evaluate the ability of the tablet to withstand pressure, abrasion, resist chipping and break under storage, transportation. All brands passing the test indicates that the tablets are less likely to deteriorate during handling and storage, manufacturing processes are adequate, and they will maintain their physical integrity ensuring consistent dosage. A study comparing the friability of tablets

manufactured using different excipients and found that tablets with a friability loss of less than 1% showed improved mechanical strength and stability, another review article highlighted the importance of friability testing in ensuring tablet quality and noted that a friability loss of not more than 1% is generally considered acceptable [26, 27].

According to the United State Pharmacopoeia 2019, it is required that a disintegration test should be performed on all tablets and capsules as a criterion of its performance, and all uncoated and coated tablets are required to disintegrate in water within the first 15 minutes and 30 minutes for sustained release tablets. It was seen that all brands passed the disintegration test. This corroborates with a study conducted in 2017 which evaluated the disintegration time of various Ascorbic acid tablet formulations and found that all formulations disintegrated within 5-12 minutes, similar to this study [28].

According to the 2019 British pharmacopoeia, after 60 minutes, the acceptable drug dissolved % should be 95 % to 105 % and all brands passed this. Dissolution test is used to understand the rate at which the drug would dissolve in the body or a biological medium for optimum therapeutic response. This result indicates that all brands are likely to have optimal absorption, similar bioavailability and therapeutic efficacy [29, 30]. This similarly aligns with a study that showed all tested brands of tablets met the 95 % - 105 % dissolution criteria. Another study reported comparable dissolution profiles among different brands of tablets, suggesting similar in vivo performance [31, 32].

The widely used high-performance liquid chromatography (HPLC) method serves the purpose of separating compound mixtures, identifying, assessing purity, and quantifying components within a mixture. The assay's primary objective is to ensure the presence of the required amount of the active ingredient, as substantial variations or deviations might result in either ineffective therapeutic drug levels or overdosing, potentially leading to toxicity [33]. In accordance with the USP 2019, the acceptable limit range for the assay is set at 90% - 110% of which all the brands passed. A 2018 study presented HPLC assay findings for Vitamin C tablets sourced from various manufacturers, revealing a concentration range of 95.2-104.5% which were within specifications, another review article published highlighted the importance of HPLC assay in ensuring the quality of Vitamin C tablets and noted that concentrations within the 90-110% range are generally considered acceptable [34, 35].

This investigation into the physicochemical equivalence of various Vitamin C brands underscores the necessity for continuous and routine monitoring of drug products to ensure quality and manufacturer's compliance with the current good manufacturing practice (cGMP) standard. This study explored potential variations in the physicochemical properties of five Vitamin C tablet brands sourced from diverse retail pharmacy outlets in Ogun State, Nigeria.

Conclusion. This study reveals that while most Vitamin C brands met the required standards in the friability, disintegration, dissolution, and assay tests, only VITC 3 passed both the hardness and weight uniformity tests. This indicates that VITC 3 is the only brand exhibiting consistent physical and chemical quality. To ensure ongoing batch-to-batch consistency, routine comprehensive analyses of Vitamin C brands are recommended. Furthermore, manufacturers should strengthen quality control processes by conducting rigorous evaluations of raw materials and finished products before and after production.

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