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Evaluation of Some Quality Parameters of Five brands of Cetirizine Hydrochloride Tablets Marketed in Abuja, Nigeria.

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ABSTRACT

Cetirizine Hydrochloride is a non-drowsy second-generation antihistamine and a derivative of piperazine with a half-life of eleven hours. It is used to relieve allergy symptoms such as runny nose, sneezing, rhinitis, urticaria and watery eyes. It is a key adjuvant therapy in management of some covid-19 related symptoms. To assess the quality of five brands of Cetirizine hydrochloride 10mg tablets marketed in Abuja. The weight variation, friability, hardness, disintegration, dissolution tests and HPLC assay were evaluated using USP methods. The hardness and friability of the samples ranged from 2.03kgF to 7.54KgF and 0.00 to 0.90% respectively. The disintegration time were within 5mins, for dissolution, 80.0 to 103.3% of the API in the samples were released within 30mins, the assay ranged from 93.1 to 101.6%. The cetirizine tablets conformed with quality standards.

Keywords: Cetirizine hydrochloride, Quality, HPLC, USP method.

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INTRODUCTION

Cetirizine Hydrochloride is a non-drowsy second-generation antihistamine and a derivative of piperazine with a half-life of eleven hours. It is used to relieve allergy symptoms such as runny nose, sneezing, rhinitis, urticaria and watery eyes [1-5]. It is a key adjuvant therapy in management of some COVID-19 related symptoms. Quality control comprises of routine tests usually carried out

on dosage forms in order to ensure that they comply with standard requirements. These requirements are usually found in official documents such as pharmacopoeias. Examples of these routine tests include weight variation, dissolution and disintegration. These tests are usually used to compare brands of a specific drug or drug products purchased from different sources in order to determine any deviation from the standard requirement.

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These tests can also be referred to as physicochemical tests which aim to evaluate the properties of the dosage form that can affect its quality, safety or efficacy [8]. The quality of a drug product can have a direct impact on its safety and efficacy which is why it is essential to ensure that a dosage form or drug product passes all the requirements laid out in the official monographs.

Quality control tests can also be used to detect fake/substandard/counterfeit/adulterated drugs when comparing between different drug products or brands. Fake/counterfeit drugs are abundant and gradually becoming a menace most especially in developing countries which is the reason why quality control of drugs is highly important in these countries [9]. Drug products that have two or more generic brands present in the market require routine quality assessment to ensure they are therapeutically equivalent to the innovator. Therefore, because of the importance of this drug and what it is designed to treat, this study aims to assess the quality of five selected brands of Cetirizine 10mg tablets based on several parameters.

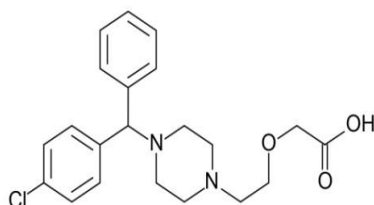


Figure 1: Structure of Cetirizine Hydrochloride

METHODS

Drug analysis involved various tests carried out following standard compendia procedures in the United States Pharmacopoeia (USP).

Materials: Porcelain mortar and pestle, stainless steel spatula, Class A glass wares (volumetric flask, beakers, pipettes (10mL, 100mL, 1000mL)), Precision pipette, membrane filters glass funnels, Friability test apparatus (Erweka®, Germany), Hardness tester (Erweka®, Germany), Analytical balance, Dissolution test apparatus (RC-6, China), High Performance Liquid Chromatography HPLC Agilent® 1200 series, Column Symmetry® 250mm x4.6mm, 5µm, Water distiller, Water filtration unit, Cetirizine HCL USP reference standard. Acetonitrile HPLC grades, Phosphoric acid, Vortex mixer, ultrasonic bath.

Sample Collection: Five different brands of Cetirizine hydrochloride 10mg tablets were purchased from different registered pharmacies in Abuja. The tablets were either round/oblong, white in colour and scored. The batch numbers, manufacturing dates, expiring dates, National Agency for Food Drug Administration and Control (NAFDAC) numbers were noted and all tablets were analyzed within their shelf life.

Weight variation test: According to the USP 40 NF 35 consideration for content uniformity occurs if dosage is < 25 mg or dose ratio is <25 % while consideration for weight variation occurs if dosage is ≥

25 mg or dose ratio is ≥ 25 %. Twenty tablets were used for this test and each tablet was weighed individually using an analytical weighing balance (Mettler Toledo®) and weight recorded. The mean and standard deviation of the weights was noted. Also, the percentage deviation at each sampling time was also calculated. [7].

$$\text{Deviation (\%)} = \frac{\text{Mean Weight} - \text{Individual weight} \times 100}{\text{Mean weight}}$$

Friability test: Ten tablets of the different brands (A, B, C, D and E) were first weighed (W1). The tablets were placed in the Friability apparatus and set at 25rpm for 4mins. The tablets were then deducted and accurately reweighed (W2). The friability was calculated as shown in this formula [7]. % Friability = $(W1 - W2)/W1 \times 100\%$ Where; W1 = Total Initial weight of tablets W2 = Total final weight of tablets **Hardness test:** Ten tablets each of the different brands (A, B, C, D and E) were subjected to hardness test using the Erweka® hardness tester. The force required to break each tablet was recorded and thereafter the mean, standard deviation and percentage deviation of the measurements at each sampling time was calculated [7].

Disintegration test: Six tablets each of the different brands (A, B, C, D and E) were subjected to a disintegration test with the disintegration apparatus set at 29-32 cycles per minute at temperature of $37 \pm 1^\circ\text{C}$ with 900 mL medium of distilled water [7]. The time for each tablet to disintegrate and pass through the mesh was recorded

alongside the mean, standard deviation and percentage standard deviation.

Chromatographic conditions: The HPLC-UV Agilent 1200 series was used. The conditions utilized was as follows: Column C18 250mmx 4.6mm, 5 μm , detection wavelength 230nm, injection volume 10 μL , flow rate 1.0mL, DAD, auto sampler.

Identification test: Retention time of the major peak area of the sample solution corresponds to that of the standard solution as obtained in the assay

Mobile phase preparation and diluent preparation: Buffer (2.9mL/L of phosphoric acid in water): Acetonitrile 2:3 for dissolution. For assay, Diluent was prepared using Solution A (2N sulphuric acid and water (2:33): Acetonitrile: water (1:100:100). Acetonitrile: Buffer (3:7) [7]

System suitability: System suitability parameters of the HPLC method were assessed by six replicate injections of the reference standard as working standards (11 $\mu\text{g/mL}$) and three replicate injections of control standard following the USP method, the tailing factor, number of theoretical plates and the percent relative standard deviation was recorded in accordance with USP method [7]

Dissolution media: 2.9mL/L Phosphoric acid: water

Dissolution test: The dissolution media was filtered and degassed before setting up the dissolution vessel (RC-6) (Apparatus 2) with the paddle rotating at 50 rpm and the temperature stabilized at

37°C. 5mL of the samples was withdrawn at different time intervals: 5mins, 10mins, 20mins and 30mins, after which it was filtered through a 0.45µm membrane filter into already labelled sample bottles. The aliquot was subjected to the analysis as stated in the monograph (isocratic HPLC method) [7].

Results of the dissolution test is calculated with this formula= $(Ru/Rs) \times (Cs/L) \times V \times 100$ Where Ru=peak response from sample; Rs=peak response from standard, Cs = Concentration of USP Cetirizine Reference standard solution (mg/mL), L= label claim of tablet (mg/tab), V= Volume of medium =900mL.

Assay: It involves the random selection of not less than 20 tablets from a particular batch which are then weighed together and crushed. The weighed powdered tablet was dissolved in the diluent (0.2 mg/mL), placed in an ultrasonic bath for 10 mins then filtered. The aliquot was subjected to the assay method stated in the monograph using the isocratic HPLC method [7]. Results of the Assay is calculated with this formula= $(Ru/Rs) \times (Cs/Cu) \times 100$ Where Ru=peak response from sample; Rs=peak response from standard, Cs = Concentration of USP Cetirizine Reference standard solution (mg/mL), Cu= nominal concentration of Cetirizine HCl (mg/mL).

RESULTS

Table 1: Physical parameters of Cetirizine 10mg tablets brands

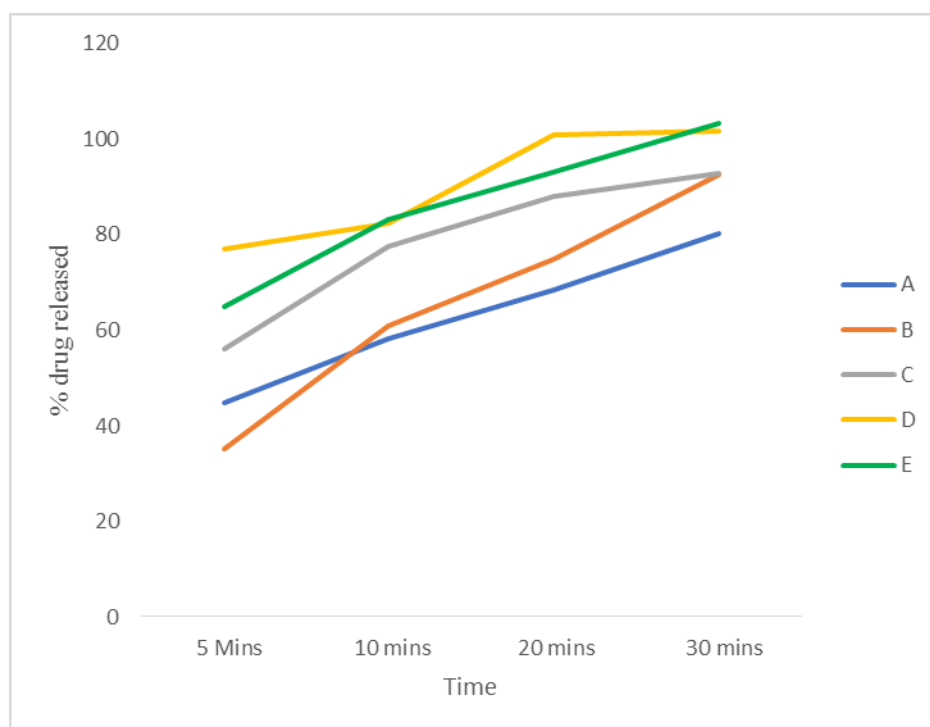
Sample/Parameter	A	B	C	D	E
Uniformity of weight (mg)	119.75±0.02	119.30±0.04	120.90±0.03	182.10±0.03	187.10
Hardness (kgF)	7.54	5.83	2.03	6.46	±0.01
Friability (%)	0.25±0.08	0.00±0.00	0.17±0.01	0.00±0.00	0.90±0.01
Disintegration time (min)	3.98±0.43	3.03±0.49	2.73±0.99	0.45±0.20	0.34±0.04
Assay (%)	93.2±1.90	101.6±1.60	99.9±2.90	94.7±1.70	93.5±0.30
USP 90.0-110.0%					

Table 2: Dissolution of Cetirizine 10mg tablets showing percent released API with time

Percent release/sample Time (Mins)	A %	B %	C %	D %	E %
5 (mins)	44.76	35.22	56.14	77.03	65.03
10 (mins)	58.26	60.92	77.50	82.41	83.27
20 (mins)	68.57	74.76	87.94	100.99	93.09
30 (min)	80.32	92.72	92.91	101.76	103.36

Table 3: System suitability Parameters for Chromatographic conditions for Cetirizine Hydrochloride Reference standard

Parameters	Found Mean Assay	Found Mean Dissolution	USP Acceptable Limits
Theoretical plates (n=6)	1827.8±27.8	3427.8±64.1	NLT 1000
USP Tailing factor (n=6)	0.6±0.00	0.4±0.00	NMT 2.0
Repeatability			RSD% NMT 2.0%
Peak Area (n=6)	1.5%	0.2%	

**Figure 2:** Dissolution plot cetirizine HCl release over time

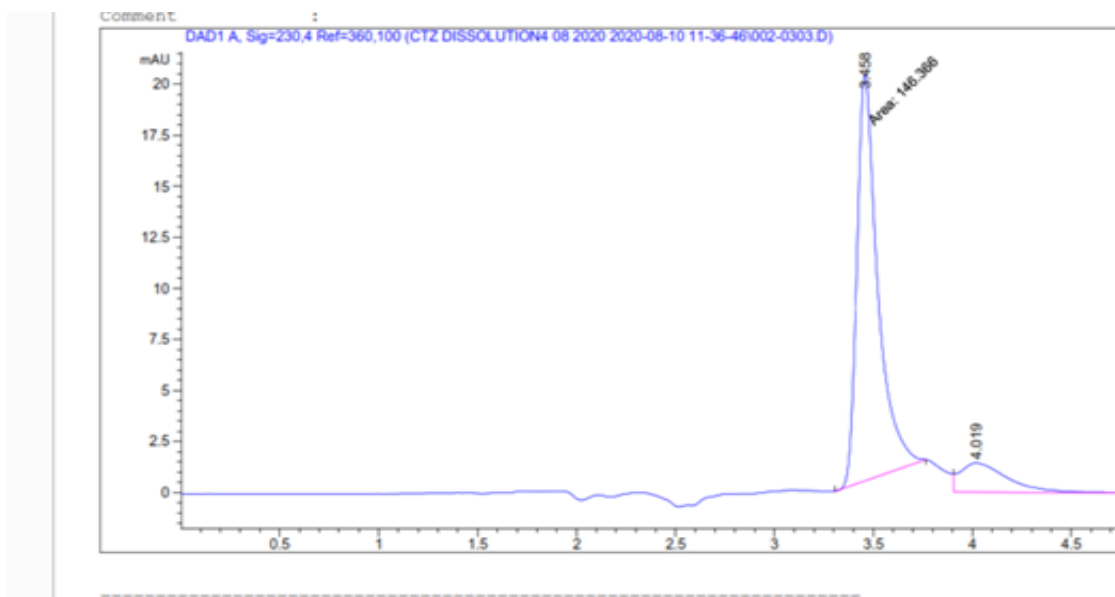


Figure 3: Chromatogram plot of cetirizine HCl reference standard (working standard) using the HPLC

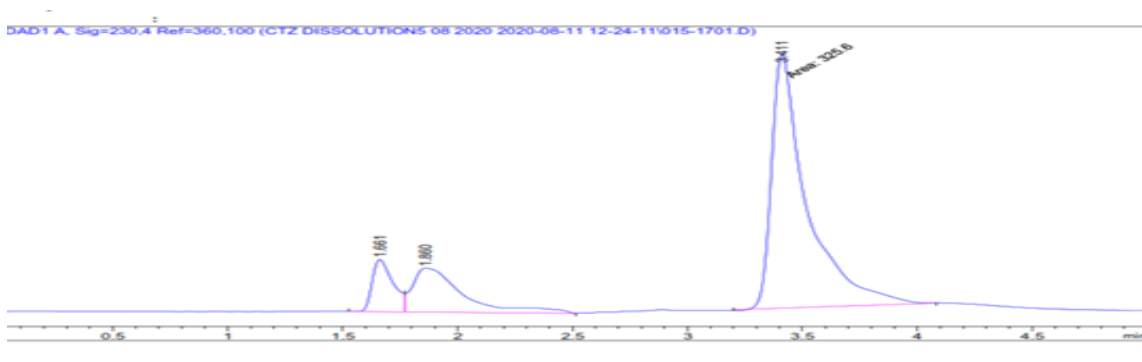


Figure 4: A Chromatogram plot of cetirizine HCl tablet using the HPLC

DISCUSSION

Weight variation test seeks to ensure that each tablet contains the correct amount of drug although it is not a direct measure of drug content except in formulations where the active ingredients form the bulk of the content [10]. When the weight of each tablet is compared to the average the variation is then determined. From the results obtained, all the brands met the USP specifications of weight

variation of not more than 10%. Hardness/crushing strength is an important parameter that helps to assess the mechanical strength of the tablet and hence its ability to resist stresses it may encounter throughout its shelf life. It is required that tablets be of sufficient hardness but not extreme such that it cannot disintegrate. Also, there is the possibility of correlation between hardness, disintegration and dissolution and also friability.

The hardness can be controlled during basic steps of the tablet manufacturing process. The hardness of a non-coated tablet should be between 4-8kgF but that of coated tablets such as zidovudine can be outside this range up to 10kgF [11]. The hardness test results were within 4-10gF which is indicative that the tablet can withstand erosion, fracture, chipping or fragmentation of tablets in the course of packaging, transportation and handling.

Friability test measures the ability of the tablet to overcome abrasion/chipping when exposed to mechanical stresses. This therefore means the tablet does not lose some of its weight when it encounters stresses of all forms. It is required that the % loss in weight of the tablets, an indicator of its friability should not be more than 1 % for it to pass this test [7] From results obtained Friability test all the tablets were less than 1% which affirms a good manufacturing practice by the manufacturers.

Tablet disintegration is important as it leads to subsequent dissolution and absorption of drug. Therefore, it is necessary to assess a dosage form disintegration as it can to some extent help predict its absorption/bioavailability [10]. According to the USP (7) all normal release tablets should not exceed 15mins disintegration time. The disintegration test for all the brands tested was less than 15mins.

Dissolution is another property of oral dosage form which is essential for drug absorption and bioavailability. A drug has to possess adequate aqueous solubility in order to elicit a therapeutic effect. Therefore, the drug dissolution profile is also known as the drug release profile as it tells of the amount of drug released with time.

Although it is worthy to note that this does not always predict *in vivo* absorption of bioavailability [10]. According to the USP (USP 40 NF 35) dissolution test for zidovudine, it is expected that not less than 80 % of the labelled amount of Cetirizine (active pharmaceutical ingredient) is released within 30 minutes. All the brands passed the dissolution test. The system passed the System suitability test before proceeding to run the analysis on the HPLC-UV. The relative standard deviation expressed in percentage for the peaks of the reference standards was less than 2.0% which within specification and the tailing factor was less than 2.0 for both the assay and dissolution test. The content of the Active Pharmaceutical Ingredient for all the brands tested was within the USP acceptable limit of 90.0 to 110.0%.

CONCLUSION

The results obtained on these five samples of Cetirizine hydrochloride complied with the acceptance criteria as stated by the USP, hence the quality of these samples has been ascertained. However, periodic routine analysis should be carried out on these drug samples to monitor their compliance with monograph acceptance criteria, as Cetirizine hydrochloride tablets is key as an adjuvant therapy in management of some covid-19 related symptoms.

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