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A Simple UV Spectrophotometric Method for the Assay of Hydrochlorothiazide in Tablet Dosage Forms and its Application in the Quality Assessment of Some Marketed Brands in Nigeria

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ABSTRACT

Aim: To carry out a simple quality assessment test on some brands of hydrochlorothiazide tablets in the Nigerian market as a check for fake and counterfeit drugs in circulation using simple UV spectrophotometric method.

Method: The British Pharmacopoeia method was used to determine the claimed content of hydrochlorothiazide in three different marketed brands of the hydrochlorothiazide tablets (B, C and D) at predetermined λmax of 273 nm with 0.1 M sodium hydroxide solution as diluents/blank.

Results: The average weight of the samples B, C and D were; 0.14 ± 2.66, 0.14 ± 2.66 and 0.16 ± 3.05 mg respectively. Sample C failed to meet the requirements of within ± 5% for weight variation while B and D passed. The disintegration times of B and D were within 60 minutes while that of C was 15 minutes. The percentage content of hydrochlorothiazide in the samples B, C and D were: 98.89%, 102.73%, and 107.57%, respectively. The results showed that sample B and C passed according to the monographs requirement while sample D insignificantly ($P< 0.05$) failed.

Conclusion: The method gave good inference on the assay of the tested brands of hydrochlorothiazide tablets and can be employed for routine assay, percentage content and the quality assessment of the tablets.

KEYWORDS: Hydrochlorothiazide, UV/visible spectrophotometric method, quality assessment.

INTRODUCTION

One of the major factors resulting to heart attack, stroke and other related diseases is hypertension which has contributed to increase in rate of public health problems in most parts of the world leading to excessive morbidity and mortality. Recently, hypertension was estimated to affect approximately 30 % of the US and European population and close to a billion people worldwide and is expected that the number will increase as population increases [1]. However, upon all the efforts in the treatment of hypertension, the rate of its increase is yet to be controlled. For example, about one third of hypertensive patients in the US have their blood pressure (BP) reduced to the recommended levels of under 140/90 mmHg for uncomplicated hypertension, and less than 130/80 mmHg for those with diabetes mellitus or renal disease [2].

At present, hydrochlorothiazide (HCT) is one of the drugs most widely used as antihypertensive combinations that block the renin-angiotensin system. Post-market surveillance in order to prevent infiltration of substandard, fake, counterfeit or spurious drug products in circulation as part of phase four study in drug development is of paramount importance.

It was reported that, determination of active ingredient and dissolution test are surrogate markers of drug quality assessment for oral dosage forms [3, 4, 5]. As a result, drugs should be sampled on regular basis from hospitals, drug market and pharmacy out-lets in order to subject them to quality

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assessment where the results will help to ascertain whether the drugs used in treating patients are of good quality, safe, efficacious and high level of purity. As this is done, it could avert the tendency of treatment failures, waste of resources in procuring drugs and subsequently death that might occur due to quality problems.

The aim of the study was to assess the quality of three brands of tablet dosage forms of hydrochlorothiazide (HCT) which are commonly found in circulation in markets, using UV spectrophotometric analytical method.

EXPERIMENTAL

Samples and Sampling

The HCT samples were purchased from pharmaceutical premises in different parts of the Federal Capital Territory, Abuja, Nigeria. The samples were labeled as A, B, C and D and stored under the specified conditions prior to analysis. Sample A was HCT reference standard; B was Esidrex® (Novartis Pharma AG) without NAFDAC registration number and the strength, 25 mg was written in red; C was Esidrex® (Novartis Farmaceutica S.A.) having NAFDAC registration number - 04-8206; while D was Hydrex® (Juhel) and is also NAFDAC registered.

Chemicals and Reagents

Reference standard of HCT was obtained from May and Baker Pharmaceutical Company PLC, Lagos. Ethyl acetate and acetone were of analytical grade purchased from Sigma Aldrich Company, ultrapure distilled water, 0.1 M sodium hydroxide solution (NaOH) used were of analytical grade.

Instrumentation

Ultraviolet (UV) Spectrophotometer (UV-160A, Shimadzu, Japan) with matched quartz cell of 1 cm path-length was used. Thin layer chromatography (TLC) plate (Silica gel GF_{254}) Capillary tubes and Whatman 125 mm filter paper were also used.

Preparation of standard solutions

The stock solutions of HCT were prepared by dissolving 50.0 mg of the powdered HCT tablets in 100.0 mL of 0.1 M NaOH medium to obtain 500 µg/mL solutions and were adjusted to pH of 1.24. The working standard solutions were obtained by diluting the stock solutions with the same diluents (0.1 M NaOH) to obtained 5, 10, 15, 20 and 25 µg/mL, respectively and analyzed at 273 nm in order to check linearity of the method [6].

Method validation

Exactly 50.0 mg of the powdered tablet was dissolved in 10 ml of 0.1 M NaOH, diluted and made-up to 100.0 mL with distilled water.2.0 mL of the solution was diluted to 100.0 mL with 0.1 M NaOH and mixed thoroughly by shaking together before being scanned in the UV within 250 to 350 nm wavelength in which the solution showed absorption maxima at 273 nm and at 323 nm. The standard and the sample solutions were analyzed at 273 nm as the maximum wavelength of absorption for analyzing hydrochlorothiazide [6,7, 9].

Test for identity

Test for identity was carried out using a normal phase TLC method with 100 ml of ethyl acetate as the mobile phase. The reference and the samples were processed by weighing 10 mg of each using analytical balance and triturated with 10 ml of acetone and filtered to obtain 0.1 % w/v of each and labeled A, B, C and D, respectively. A 0.5 µl quantity of each of the processed samples were spotted on the activated TLC plates labeled A, B, C and D using a capillary tube. The plates were air-dried and developed, followed by examination under the UV lamp at 254 nm.

Weight uniformity of test

Twenty tablets were selected randomly and each weighed, followed by weighing the 20 together. This was performed for each of the three brands using analytical balance. Average weight, standard deviation, and percentage deviation for each of the three brands of HCT tablets were calculated. Allowable percentage deviation of 5 % for tablet weights greater than 250 mg was taken as acceptable limit [8].

Dissolution Test

The Basket method was adopted using a dissolution rate apparatus (DT 80, Erweka, Germany) for the test [6]. 500 ml of 0.1 N HCl of pH of 1.24 was used as the dissolution medium, maintained at the temperature of $37.0^{o}C \pm 2.0^{o}C$ and speed of 100 rpm throughout the test period. 5 ml samples were withdrawn at intervals of 2, 5, 10, 15, 30, and 60 minutes, filtered and diluted with the stock solution of 0.1 N HCl and then analyzed for HCT content at 273 nm using a UV spectrophotometer (UV-160A, Shimadzu, Japan). The withdrawn samples were immediately replaced with equal volumes of fresh medium. All the measurements were done in triplicates.

Data Analysis

The data obtained were analyzed by two-way ANOVA and Student's *t*-test where the values obtained at $P< 0.05$ were considered significant.

RESULTS AND DISCUSSION

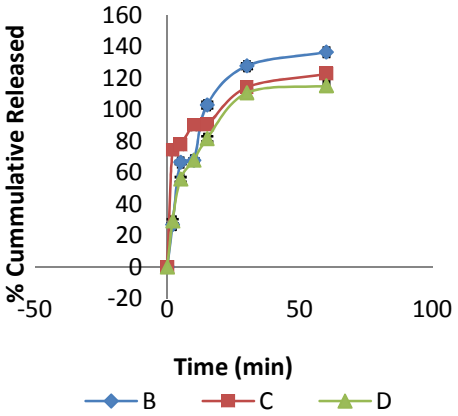

Fig.1: Dissolution profiles of the hydrochlorothiazide tablet formulations.

Figure 1: shows the dissolution profile of three brands of hydrochlorothiazide tablets (B, C and D). All the brands exhibited typical dissolution rate curves of progressive release of the active ingredient into the dissolution medium with time. Although the release from B (unregistered brand) was initially lower than that of C (NAFDAC registered), it eventually became higher than the others from the fifteenth (15^{th}) and maintained the lead throughout the test period. The registered brand (C) initially releases faster than the other two brands (D and B) within the first fifteen (15) minutes after which it drop to be lower than B but maintain higher release rate than D (Hydrex) through the test period. Batch D maintained progressive and steady release rate than the other two brands (C and B) throughout the dissolution test. The overall rate of dissolution of the three was in this order; B (unregistered) > C (registered) > D (registered).

The observed initial lower rate of the unregistered Esidrex at 15 min may be due to error during formulation, probably as a result of noncompliance with GMP. Even though batch B is not NAFDAC registered, it may not be counterfeit since it also passed the percentage of active ingredient test. At the end of one hour dissolution test period there were no particles of sample C tablet remaining, while trace of undissolved excipients was observed for samples B and D. This observation may also be associated with the type of excipients used and formulation efficiencies of the various brands of tablets.

Table 1 shows the results of the percentage of stated dose assay and other physicochemical characteristics of the selected generic and branded HCT tablets in Nigerian market. The Rf value for the reference standard (A) Hydrochlorothiazide (HCT) was 0.62 which was the almost same for the different brands of the samples; B (0.62), C (0.62) and D (0.62). This confirms the identity of the samples as hydrochlorothiazide (HCT) since they have the same Rf as the reference sample, therefore, this requirement was fulfilled. Sample B and C falls within the range for percentage (%) content test therefore it has passed, while D failed by an insignificant ($P< 0.05$) margin, because it was out of the range for percentage (%) content of the hydrochlorothiazide (HCT) which was stated as 92.5 to 107.5 %[10]. The tablets weight variation of samples C failed to meet the requirements of within -5 % to +5 %, while B and D passed. These results may further be verified to establish the veracity of the findings under the experimental conditions.

Table 1: % stated dose assay and other physico-chemical characteristics of the selected HCT tablets in Nigerian market.

Brands	TLC Exam. [Reference (A)Rf= 0.62]	AVERAGE wt. per tablet	Uniformity of weight	Description	% stated dose assay
Esidrex Unregistered (B)	Similar Rf as reference(Rf =0.62)	0.14	-2.66% to +2.66%	White smooth round tablet, which dissolves in dilute solution of NaOH	98.89.
Esidrex registered (C)	Similar Rf as reference (Rf=0.62)	0.14	-2.69% to +2.69%	White smooth round tablet, which dissolves in dilute solution of NaOH	102.73
Hydrex Registered (D)	Similar Rf as reference (Rf=0.62)	0.16	-3.05% to +3.05%	White smooth round tablet, which dissolves in dilute solution of NaOH	107.57

*** Innovator** HCT®

CONCLUSION

The outcome of the study indicated that, sample D insignificantly ($P< 0.05$) failed, the registered Esidrex (C) and the unregistered Esidrex (B) tablets

of HCT selected from the Nigerian market, passed the percentage of stated dose assay and other physicochemical characteristics tested. Therefore it the method could be used for determination of the hydrochlorothiazide (HCT) in dosage forms without interference from commonly used excipients and could be easily used in a quality control laboratory for drug analysis.

Appendix 1: Percentage Released Per Time

Time (min)	% Released B	C	D
0	0	0	0
2	26.88±1.5	74.56±2.0	29.28±1.8
5	66.56±0.9	77.76±1.6	55.84±1.3
10	67.84±1.0	90.24±1.8	67.84±1.5
15	103.04±1.2	90.56±0.8	81.6±0.9
30	127.84±2.1	114.24±2.4	110.72±1.7
60	136.64±1.8	122.88±1.4	115.2±3.1

Appendix 2: Uniformity of weight test for HCT tablets samples B, C and D

Serial Number	Esidrex Sample B (g)	Esidrex Sample C(g)	Hydrex Sample D (g)
1	0.1393	0.1417	0.1622
2	0.1408	0.1410	0.1635
3	0.1401	0.1878	0.1610
4	0.1392	0.1186	0.1610
5	0.1404	0.1407	0.1600
6	0.1392	0.1634	0.1566
7	0.1402	0.1292	0.1534
8	0.1393	0.1415	0.1526
9	0.1394	0.1421	0.1582
10	0.1413	0.1410	0.1581
11	0.1396	0.1421	0.1540
12	0.1413	0.1420	0.1588
13	0.1425	0.1414	0.1603
14	0.1373	0.1405	0.1570
15	0.1397	0.1410	0.1555
16	0.1399	0.1405	0.1519
17	0.1412	0.1413	0.1588
18	0.1389	0.1406	0.1588
19	0.1427	0.1397	0.1602
20	0.1395	0.1408	0.1597
Average weight	**0.1401**	**0.1415**	**0.1579**

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