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QUALITY CONTROL STUDIES ON CETIRIZINE HYDROCHLORIDE TABLETS AVAILABLE IN BANGLADESHI DRUG MARKET

Asif Hasan, Syed Masudur Rahman Dewan, Sayed Koushik Ahamed, Md. Masud Kaisar*

Department of Pharmacy, Noakhali Science and Technology University, Sonapur, Noakhali- 3814, Bangladesh

*Corresponding Author Email: pharmasud@operamail.com

ABSTRACT

Drugs are those Things which are directly related to the human health; therefore, quality of a drug is essential to save the human being from a severe health hazard. Various quality control parameters of pharmaceutical products i.e., weight variation, friability, content uniformity, disintegration time, and in vitro dissolution profiles can ensure their quality as well as bioavailability and optimum therapeutic activity. The present study was carried out aiming to ensure the quality and therapeutic activity of cetirizine hydrochloride tablets of different brands available in Bangladeshi pharma market. To demonstrate the differences between the commercial brands, difference (f_1) and similarity (f_2) data were analyzed. The results showed that all the selected brands met the specification given by pharmacopeia (USP-NF).

KEY WORDS

Cetirizine Hydrochloride, Disintegration, Dissolution, Quality Control, Pharmacopeia

INTRODUCTION

Quality control is a process that is carried out to ensure a desired level of quality in a product or service. It might include whatever actions a business deems necessary to provide for the control and verification of certain characteristics of a product or service. Most often, it involves thoroughly examining and testing the quality of products or the results of services. ISO 8402-1986 standard defines that quality is the totality of features and characteristics of a product or service that bears its ability to satisfy stated or implicated needs [1]. Pharmaceutically, we can say quality is checking and directing the degree and grade of experience of process and products [2]. This process is carried out to validate the product quality, to produce medication of superior efficacy, safety, and to provide assurance to physician, pharmacists and patients as well that given product performs satisfactorily and uniformly.

When a number of different formulations are available for the same drug, it becomes essential to ensure the equivalency (relationship followed by bioavailability, therapeutic response, or a set of established standards of one drug product to another [3]) of the products pharmaceutically.

Cetirizine is a long acting antihistamine and unlike conventional or first generation antihistamines it causes less sedation and psychomotor impairment and as well causes no behavioral changes. It is a major metabolite of hydroxyzine, and a racemic selective H_1 receptor antagonist used in the treatment of allergies, hay fever, angioedema, and urticaria.

The basic goal of our study was to ensure that the products (cetirizine tablets) that are saturated in Bangladeshi drug market meet specific requirements and characteristics, such

as being dependable, satisfactory, safe and fiscally sound.

MATERIALS AND METHODS

MATERIALS

Cetirizine (standard) was donated by Globe Pharmaceuticals Ltd., Bangladesh. In our study, nine commercial Bangladeshi brands (selected randomly) containing 10 mg of Cetirizine Hydrochloride were purchased from nearby retail pharmacy shop and here denoted by CTZ 1, CTZ 2, CTZ 3, CTZ 4, CTZ 5, CTZ 6, CTZ 7, CTZ 8, and CTZ 9. In the study we used 2.9 mL/L phosphoric acid in water to prepare buffer solution.

Analytical Method

Accurately weighed cetirizine was dissolved in the buffer solution in a 100 ml volumetric flask. From the mother solution, different dilutions were prepared to generate a calibration curve by measuring absorbance using UV spectrophotometer (UV- 1800, UV-VIS spectrophotometer, Shimadzu, Japan) at 230 nm. The concentration of cetirizine was calculated using the linear regression equation of the calibration curve.

Weight Variation

For each brand, ten tablets were randomly selected and weighed individually using an analytical balance (ELB 3000, Shimadzu, Japan). The average weights were determined and the percentage deviations from mean values were calculated. Then the standard deviation, and percentage of related standard deviation (RSD) were determined.

Hardness Test

The hardness of randomly selected ten tablets was determined for all the brands using 'Monsanto' type hardness tester (Intech, Korea). The mean crushing strengths were determined.

Friability Test

Ten tablets from each commercial brand were weighed individually, and each set of tablets was put into the friabilator (EF-2, Electrolab, India). Then the tablets were rotated at 100 rpm for 1 minute. Then the tablets were removed and weighed again. The friability percentage was calculated for each batch.

Test for Content Uniformity

The amount of cetirizine in each brand was determined according to USP. A standard solution and sample solutions were prepared of 20 tablets for each brand. The absorbance of each prepared solution was determined at 230 nm by UV spectrophotometer. The amount of cetirizine in each brand was calculated using the equation of the calibration curve.

Disintegration Time Test

USP-30 [4] disintegration apparatus (Electrolab, India) containing 6 glass tubes that are 3 inches long, open at the top and held against a 10-mesh screen at the bottom end of the basket rack assembly was used in the study. To test for disintegration time, one tablet was placed in each tube and the basket rack is positioned in a 1L beaker containing buffer solution at 37^0C, such that the tablets remain 2.5 cm below the surface of the media on their upward movement and descent not closer than 2.5 cm from the bottom of the beaker. A standard motor driven device is settled to move the basket assembly containing tablets up and down through a distance of 5.3 to 5.7 cm at a frequency of 29 t o 32 cycles per min. The disintegration time of each tablet was determined and the average disintegration time was calculated.

***In vitro* Dissolution Rate Studies**

The dissolution studies were carried out according to the USP paddle method [5]. The stirring rate was 50 rpm at 37 ± 0.5^0 C. the dissolution medium was 900 ml buffer solution. The samples were withdrawn at ten minute

intervals up to 30 minutes and assayed spectrophotometrically at 230 nm. The percentage of cumulative drug release of each tablet was determined using the linear regression equation of the calibration curve.

Comparison of Dissolution Profiles

As model-independent approaches, here, two fit factors (f_1 and f_2) that compare the dissolution profile of a pair of drug products were applied to the dissolution data. Values of f_1 between 0 and 15, and values of f_2 between 50 and 100 are used to define equivalence of two dissolution profiles [6].

$f_1 = \{[S_{t=1}^{n} (R_t - T_t)] / [S_{t=1}^{n}. R_t]\}. 100$

$f_2 = 50. Log \{[1 + (1/n). S_{t=1}^{n} (R_t - T_t)^2]^{-0.5}. 100\}$

Where, n is the number of dissolution sample times, and R_t and T_t are the mean percent dissolved at each time point t for the reference and test dissolution profiles respectively.

RESULTS AND DISCUSSION

Calibration Curve

The calibration curve (**Figure 1**) of cetirizine HCl was obtained by using the method which was explained in 'analytical method' section.

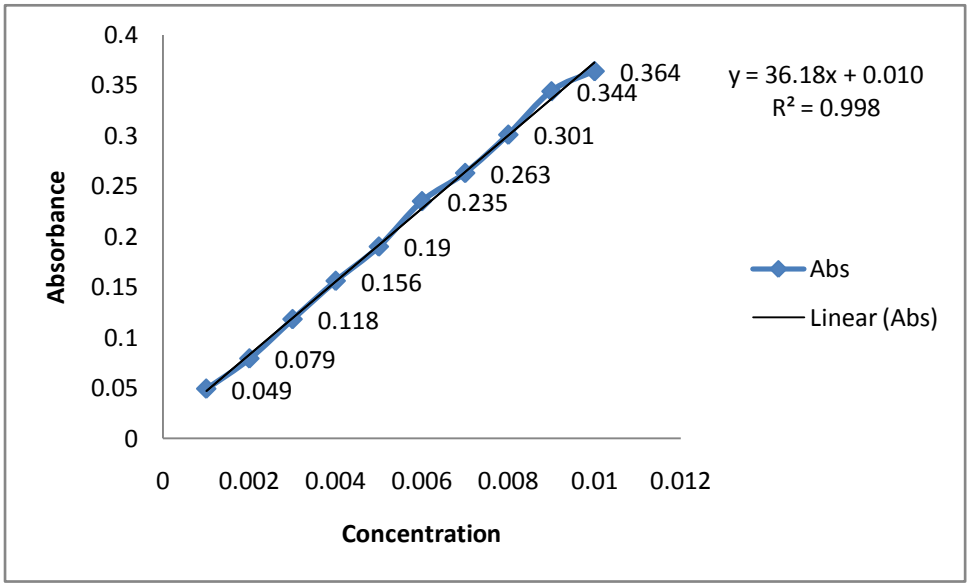

Figure 1: Calibration curve for cetirizine HCl

Weight Variation

According to USP, the weight variation range for each cetirizine tablet is ±5% (w/w), and the weights from different brand products showed in **Table 1**, were within the acceptance limit.

Hardness Test

Tablet hardness is defined as the force required for breaking a tablet in a diametric compression test. If the tablet is too hard, it may not disintegrate in the required period of time to meet the dissolution specification. Conversely, hardness should not be so low that tablets are soft and friable. For a satisfactory tablet quality, hardness should be between 4 and 8 kg [7]. Results of the brand products (**Table 2**) for hardness test were satisfactory.

Table 1: Weight variation Measurement (n = 10)

Brand products of Cetirizine	Average weight (mg)	Standard Deviation (SD)	% Relative Standard deviation (RSD)
CTZ 1	195.39	0.016	0.003
CTZ 2	129.40	0.004	0.003
CTZ 3	178.47	0.009	0.005
CTZ 4	195.29	0.004	0.002
CTZ 5	135.59	0.014	0.010
CTZ 6	103.49	0.015	0.014
CTZ 7	194.38	0.005	0.003
CTZ 8	200.10	0.011	0.005
CTZ 9	83.96	0.003	0.004

Table 2: Results of hardness, friability, content uniformity, disintegration time, and dissolution tests

Brand products of Cetirizine	Hardness (kg-ft) (mean ± SD)	Friability (%)	Content Uniformity (%)	Average Disintegration time (min)	Average Drug release (%) after 30 minutes
CTZ 1	7.25 ± 0.39	0.56	95	4.86	102.39
CTZ 2	4.09 ± 1.14	0.78	97	0.38	101.29
CTZ 3	4.77 ± 1.32	1.00	102	3.54	91.95
CTZ 4	4.65 ± 1.44	0.78	99	1.77	106.63
CTZ 5	4.20 ± 1.99	0.51	103	10.96	80.88
CTZ 6	4.88 ± 1.35	0.58	99	8.39	90.70
CTZ 7	7.82 ± 0.35	0.89	95	2.88	90.56
CTZ 8	4.85 ± 1.29	0.95	109	19.04	80.70
CTZ 9	6.41 ± 1.09	0.71	105	8.65	93.66

Friability Test

For satisfactory tablet, the friability value must be less than 0.5 – 1 % [8]. From **Table 2**, it is shown that all brands were within the friability limit.

Content Uniformity

According to USP 36 [5], contents of cetirizine tablets must be not lower than 90.0 % and not more than 110.0 % of the labeled amount of active drug. The results (**Table 2**) show that, all the brand products meet the criteria.

Disintegration time (DT) test

It has been established that no correlation can be established between disintegration and dissolution. Disintegration is used as a guide to the formulator in the preparation of a satisfactory tablet formula and as an in-process control test. So, to ensure lot-to-lot product uniformity, DT test is very important.

According to USP, it is said that the disintegration time must not more than (NMT) 30 minutes. The results, shown in **Table 2** for the brand products, meet the criteria.

Dissolution Rate Studies

Oral bioavailability of a drug fully depends on the dissolution rate of the drug. So, it is very important to evaluate the dissolution data and comparison of dissolution profiles for different available market products. **Table 2** shows the average percentage of drug release after an hour. Difference (f_1) and similarity (f_2) tests were

applied to the release rate, and are shown in **Table 3**.

Table 3: f_1 (Difference) and f_2 (similarity) factors for reference (CTZ 4) vs. test products (CTZ 1, 2, 3, 5, 6, 7, 8 and 9)

Factors	CTZ 1	CTZ 2	CTZ 3	CTZ 5	CTZ 6	CTZ 7	CTZ 8	CTZ 9
f_1	13.64	14.23	35.14	37.59	42.79	44.54	35.23	14.98
f_2	89.19	87.90	47.94	39.74	47.79	49.19	38.91	87.94

According to USP, the dissolution rate for cetirizine tablets should not be less than 80 % within 30 minutes, and the brand products meet the requirement (**Table 2**).

Table 2 shows that CTZ 4 released the maximum amount of drug (106.63 %), whereas CTZ 8 released the lowest amount of drug after 30 min. So, CTZ 4 was considered as the reference for maximum drug release. **Table 3** indicates that the dissolution profile of CTZ 1, CTZ 2 and CTZ 9 are similar to the profile of reference (CTZ 4), whereas the profiles of CTZ 3, 5, 6, 7 and 8 are not similar to that of the reference.

CONCLUSION

The investigation shows that the marketed cetirizine HCl tablets manufactured by the Bangladeshi pharmaceutical companies are of satisfactory quality. They met the USP standards in all aspects. Though, the results indicate the differences for release profiles, all the brand products released 80% of drug labeled amount according to USP, so they can satisfy patient needs. In fine, further investigation is suggested to establish *in vivo-in vitro* correlation to reveal the accurate pattern of drug release *in vivo* environment from marketed cetirizine formulations.

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***Corresponding Author:**
Syed Masudur Rahman Dewan*
Department of Pharmacy
Noakhali Science and Technology University
Sonapur, Noakhali- 3814
Bangladesh
E-mail: pharmasud@operamail.com
Contact number: +8801716026148