IN-VITRO EVALUATION OF DIFFERENT BRANDS OF DESLORATADINE TABLETS AVAILABLE IN BANGLADESHI MARKET

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Abstract: *Desloratadine, a long acting antihistamine with high selectivity for peripheral histamine H_1-receptors has a rapid onset of action and a duration of action of 24-hours. Due to difference in the formulation process for different brands different physicochemical properties may vary which ultimately leads to change in the efficacy and duration of action of the drug when given orally. The aim of this study was to analyze the quality and stability of desloratadine 5mg tablet by evaluating various in-vitro parameters. For this purpose, five different brands from different pharmaceutical companies of Bangladesh were collected. The quality control parameters including weight variation, hardness, friability, disintegration test and dissolution test were performed to get a comparison between these marketed products. As desloratadine is an INN (International Nonproprietary Names) drug, it has no specific dissolution method in USP (United State Pharmacopoeia) or BP (British Pharmacopoeia). So, a dissolution method listed by USFDA (United States Food & Drug Administration) was followed. Various results were obtained from the test and compared with the specifications. Minimum disintegration time was found 31 sec. Best Dissolution was shown 97.67% after 45 minutes. From the study, it can be concluded that the most brands of desloratadine tablets of the local brands have the desired and optimum therapeutic efficacy.*

Keywords: *Desloratadine, weight variation, friability, disintegration, potency, allergy, histamine*

Introduction

The prevalence of allergic rhinitis ranges from 10–25% worldwide, and is increasing. In the US, for example, allergic rhinitis has been seen to affect 10–30% of adults and up to 40% of children. Approximately 40–50% of individuals with allergic disorders are thought to have seasonal allergic (SAR) rhinitis and perennial allergic rhinitis (PAR), 20–30% SAR alone, and 15–30% PAR alone. Histamine H_1-receptor antagonists have been widely used in the management of allergic disorders, such as rhinitis and chronic idiopathic urticarial (CIU), for more than half a century.[1] Desloratadine is the orally active metabolite of the non-sedating antihistamine Loratadine.[2] It is a potent and selective histamine H1-receptor antagonist with a half life of 21-24 hours.[3] Its in vivo features include long duration of action with minimal sedation. The H1-receptor binding by desloratadine is reversible and that, over time, desloratadine dissociates from membrane H1-receptors. After oral administration, desloratadine selectively binds to peripheral histamine H1- receptors and thus the substance is excluded from entry to the central nervous system.[4-6] In vitro studies have shown that desloratadine inhibits the release or generation of multiple inflammatory mediators, including IL-4, IL-6, IL-8, IL-13, PGD_2, leukotriene C_4, tryptase, histamine, and the TNF-α–induced chemokine RANTES. Desloratadine also inhibits the induction of cell adhesion molecules, platelet activating factor–induced eosinophil chemotaxis, TNF- α–induced eosinophil adhesion, and spontaneous and phorbolmyristate acetate–induced superoxide generation in vitro.[7-11] This mechanism contributes to the great effectiveness and popularity for use in allergic problem of desloratadine.

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The orally administered conventional desloratadine tablet is highly acceptable because of the low cost of the therapy and case of administration lead to high levels of patient compliance. More than 50% of the drug delivery system available in the market are oral drug delivery systems. Orally administered conventional desloratadine tablets are easy to formulate compared to that of the floating tablet dosage forms. That is why desloratadine tablet is most widely formulated in the countries like Bangladesh.

Desloratadine is generally well tolerated. Bangladesh, a country of South Asian region, has shown laudable development in the pharmaceutical sector over last few years. Almost all major companies try to comply with international standard such as GMP, cGMP etc. A medicinal product must satisfy certain criteria for claiming it to be a quality product. Safety, potency, efficacy, stability and market acceptability are the principal criteria of a quality drug. The purpose of this project is to find out the current status of the quality of the marketed desloratadine preparations available in Bangladesh. This work will help to create awareness among the general people; health practitioners and drug control authority so that pharmaceutical manufacturers produce quality medicine. It provides a comprehensive knowledge about the weight variation, friability, disintegration, dissolution, percentage of potencies of desloratadine market preparations and compares these values with their official specifications.

Materials and methods

Five brands of desloratadine oral tablets (5mg) were collected from retail medicine shop of different areas of Dhaka city. The samples were properly checked for their physical appearance, name of the manufacturer, batch number, manufacturing and expiry date, manufacturing license number, DAR (Drug Administration Registration) number and maximum retail price at the time of purchase. No samples were bought and analyzed whom date of expiry had already been passed. All the reagents used were of analytical grade and their sources were of China origin. Desloratadine tablets from 5 different pharmaceutical companies were coded as D01, D02, D03, D04, D05 and Deslor was used as the reference brand.

Appearance test of tablets

The tablets were tested visually at day light under a white background. In this way color of the 5 different brands of tablets were determined and observed result for each sample was recorded. Shape and surface texture were also observed.

Weight variation test

Twenty tablets were taken and each tablet was weighed individually using the electronic balance. The average weight of all the tablets was calculated and considered as the standard weight of the individual tablet. Then all the tablets were individually weighed and the percentage weight variation was calculated using the following equation.[12, 13]

$$\% \text{ of Weight Variation} = \frac{\text{Individual Wt} - \text{Avg Wt}}{\text{Avg Wt}} \times 100$$

Friability test

At first 10 tablets were taken and the tablets were carefully dusted prior to testing. Then the 10 tablets were weighed which was considered as the initial reading. After weighing the tablets, all the tablets were placed in the drum of friability tester and rotated 100 times. After 100 revolutions, the 10 tablets were removed and re-weighed. This was the final reading. Then the % of friability was calculated by the following formula.[13-16]

$$\% \text{ of Friability (f)} = \frac{\text{Initial Weight} - \text{Final Weight}}{\text{Initial Weight}} \times 100$$

Hardness test

Ten tablets were taken from each brand. Individually, a tablet was placed between two anvils, force was applied to the anvils, and the crushing strength that just caused the tablet to break was recorded. Finally the reading was taken in kg from the sliding scale.[13,14]

Disintegration Test

At first, the disintegration tester was assembled. Then 900 ml of 0.1 M HCl (pH- 1.2) was placed in each 1000 ml beaker (N.B: the volume of the liquid was such that when the assembly is in the highest position the wire mesh was at least 15 mm below the surface of the liquid and when the assembly was in the lowest position the wire mesh was at least 25 mm above the bottom of the beaker and the upper open ends of the tubes remain above the surface of the liquid). The temperature was maintained at 37^0C. Then one tablet was placed in each of the 6 tubes and the apparatus was operated for the prescribed period.

Assay

Preparation of standard curve

Hundred micrograms of desloratadine standard was measured by the electronic balance and placed in 100 ml volumetric flask and dissolved in methanol. Then the volume was made 100 ml with 0.1 N HCl. A series of standard solutions of standard desloratadine, 1 µg/ml, 2 µg/ml, 3 µg/ml, 4 µg/ml, 5 µg/ml, 8 µg/m, l0 µg/ml, were made using the same solvent. Absorbance was measured at 241.5 nm against a blank for each solution by UV-spectrophotometer. The measured absorbance was plotted against the respective concentration of the standard solutions.

Preparation of sample solution

Twenty tablets of each brands of desloratadine were weighed and powdered. Equivalent weight of 10 mg of desloratadine was weighed as sample and strength of 5 µg/ml was made using 0.1 N HCl.

Determination of potency of the sample

Absorbance was measured at 241.5 nm using UV Spectrophotometer for the samples and for the standard as well. Finally the assay was calculated by using the following equation.

$$\text{Potency of sample} = \frac{\text{Absorbance of sample} \times \text{Weight of standard}}{\text{Absorbance of standard} \times \text{Weight of sample}} \times \text{Purity of Standard}$$

In-vitro dissolution test

A suitable dissolution media is used. The flask was filled with 500 ml 0.1 N HCl. Dissolution medium was heated up to 37 ± 0.5°C by an auto heater. One tablet was put in to the basket and stirred immediately at 50 rpm. Five ml of sample was withdrawn from the flask after 15 minutes, 20 minutes, 30 minutes, 45 minutes and dissolved desloratadine was determined from UV absorbance at the wavelength of maximum absorbance at 241.5 nm of filtered portion of the solution under test after suitably diluted in comparison with a standard desloratadine solution having known concentration of USFDA for desloratadine in the same medium. Absorbance of each solution was measured at 241.5 nm by UV-specrophotometer.

Results and discussion

All the brands of desloratadine tablets used in this investigation were within their shelf life. All tablets collected from local market were subjected to a number of tests in order to assess quality parameters like potency, weight variation, friability, hardness, dissolution and disintegration time.

The appearance of the brands of desloratadine tablets was thoroughly analyzed and found brownish, sky blue, pick, brownish and sky blue for D01, D02, D03, D04 and D05 respectively.

Among the five brands shape of D02 was rectangle and others were round shape. Surface textures of all the brands were smooth.

The weight variation of 5 different brands of desloratadine tablets were determined according to the procedure discussed (Table 1).

Table 1: Weight variation of 5 brands of desloratadine tablet

Sample code	Number of tablets taken	Average weight per tablet (mg)
D01	20	126.9
D02	20	137.6
D03	20	150.5
D04	20	109.7
D05	20	141.5

The combined effect of the weight variation test is to ensure that all tablets in a batch are within the reasonable limits, of the same batch. Tablets are required to meet a weight variation test were the active ingredient comprises a major portion of the tablet and were control of weight may be presumed to be an adequate control of drug content uniformity. It is necessary that the tablets meet the specification indicating the uniform distribution of the active ingredient within the tablets.[12, 13]

According to BP and USP allowable range for the weight variation of tablets up to 130 mg is ±10%. It is observed from the results that all brands complied with the specification. When the weight variation is within the specifications the tablets are thought to contain uniform active ingredient to give desired therapeutic response. But if the weight variation does not meetWith the specification, the tablets are thought to contain less or more active ingredient to give ineffective therapeutic response or toxic effect respectively.[14-17]

Friability tests were done for the market preparations and the data are presented in a table (Table 2).

Table 2: Friability of various brands of desloratadine tablets.

Sample Code	Observed friability %(w/w)
D01	0.70
D02	0.92
D03	0.66
D04	0.75
D05	0.45

Friability is important to determine the loss of weight during packaging and shipment. Tablet friability may be profoundly affected by the moisture content of the tablet granulation and the finished tablets. Very dry granulation and tablets containing less than 0.5 to 1.0 percent of moisture may be much more friable than tablets contain 2 to 4 % of moisture.[10] USP/BP and specification for friability of tablets allowed range =1.0% (w/w). From the above results it is appeared that all brands of desloratadine tablets complied with the specification of friability[16-18].
Result of hardness test of desloratadine tablets (Table 3):

Table 3: Hardness of desloratidine tablet

Name	Hardness (kg/cm^2)	SD
D01	4.00	1.5
D02	4.45	0.88
D03	4.05	1.82
D04	5.00	0
D05	4.75	1.50

Tablet hardness serves both as a criterion to guide product development and as a quality-control specification. Tablets should not be too hard or too soft.[19, 20]Hardness can affect the disintegration. So if the tablet is too hard, it may not disintegrate in the required period of time and if the tablet is too soft, it will not withstand the handling during subsequent processing such as coating or packaging. Tablet hardness should lies between 5 to 10 kg/cm2.[21] All marketed brands were within the accepted range of hardness for oral tablets.

Disintegration times for samples are given in the Table 4.

Table 4: Disintegration time of desloratadine Tablets

Sample code	Disintegration time (Sec)	SD
D01	73	1.82
D02	63	1.88
D03	31	1.50
D04	100	3.08
D05	92	2.50

BP specification for disintegration time is not more than 15 minutes for uncoated tablets. To be compliant with the USP standards, the tablets must disintegrate, and all particles must pass through the 3 inches long glass tubes and held against a 10-mesh screen in the time specified.[18, 22, 23] The onset of action of a dosage form of a drug depends on the time to be taken by the tablets to release the active ingredients into the digestive fluid. The tablets should be disintegrated in the appropriate time, otherwise the prescribed course will be affected and the drug may not exert its effect properly. It is seen from the above results that none of the samples exceeded the specification for disintegration time. Therefore, it can be said that all the studied samples complied with the specification for tablet disintegration time.[23, 24]

The potency of 5 different brands of desloratadine tablets was determined within their shelf-life according to the procedure.

Table 5: Potency of desloratadine tablets

Sample code	Potency %	SD
D01	100.33	2.52
D02	88.53	1.88
D03	97.47	3.78
D04	101.46	1.08
D05	90.16	1.50

The ingredients of tablets exert the therapeutic effect. The deficient potency will result in less therapeutic response or even the product may be ineffective. For highly potent low dose drug such as

desloratadine, the potency according to the USP should be within 90% -110%.[15, 25] From the result, we can say that only D02 did not comply with the specification.

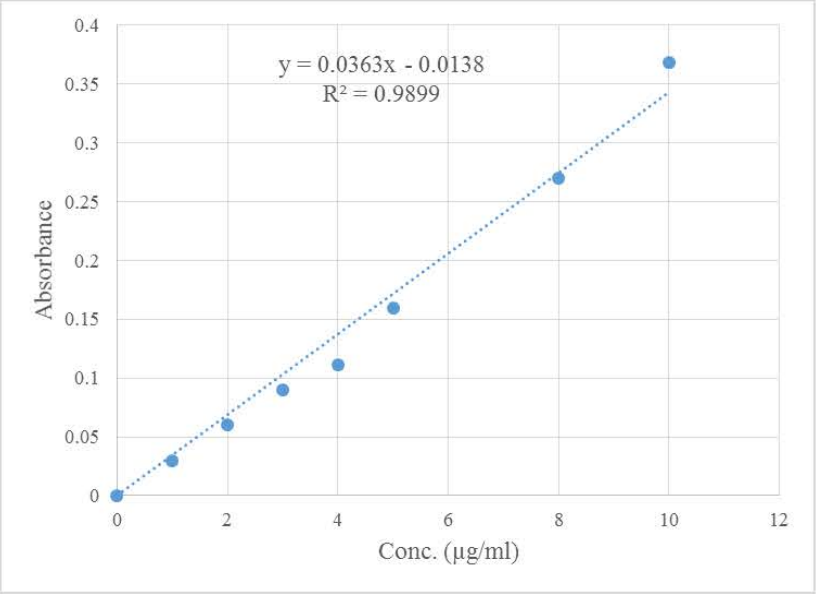

Figure 1: Standard curve of desloratadine

Table 6: Dissolution Rate of various brands of desloratadine Tablets.

Sample Code	Drug Release (%)	
	After 30 minutes	After 45 minutes
D01	92.14	97.67
D02	84.38	94.47
D03	87.16	95.47
D04	85.84	95.77
D05	86.46	95.87

According to BP, at least 75% of the active substance needs to be released within 45 min. In cases where a longer release time than that recommended above limits of 2 time intervals may be specified. All the samples were found within the acceptance range.[23, 26]

Conclusion

Among the samples of five locally available brands of desloratadine, D02 failed to meet the specified potency. Other brands of Desloratadine tablets evaluated in this study could be regarded as being pharmaceutically and chemically equivalent and can therefore be freely interchanged. The result of weight variation (10%), friability (1%), disintegration time (30 minutes), hardness (4-5 kg/cm^2), and dissolution (90-97% in 0.1 N HCl within 45 minutes) potency(90-110)% shows that except the sample D02 all the brands were within the specified acceptance value. The present study, although performed in a limited scale, yet the data reported in this study can help the Drug Control Authority to get an idea about the quality status of the marketed desloratadine preparations in Bangladesh as well as will help increasing awareness among general people. This study can be helpful for the manufacturers to be more cautious in maintaining quality while manufacturing their products. Further large scale study is necessary to get the actual picture.

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