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PERFORMANCE EVALUATION OF DIFFERENT BRANDS OF CHLORPHENIRAMINE MALEATE (ANTIHISTAMINE) TABLETS AVAILABLE IN BANGLADESH

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Abstract: *In Bangladesh, at present about 60 pharmaceutical companies are manufacturing 90 brands of Chlorpheniramine Maleate tablets. This project work has been designed to evaluate & report the quality & stability of some marketed Chlorpheniramine Maleate tablets available in Bangladesh. The selected brands were assayed spectrophotometrically and their physical parameters (weight variation, hardness, thickness, friability, disintegration time, and dissolution rate) were analyzed according to the official (BP/ USP) pharmacopial methods to evaluate their quality. The results showed that 7 brands of tablets meet the USP specification of potency and the remaining one brand was highly potent. All but one brands showed good results when they were tested for weight variation, thickness, disintegration time, It is evident from the study that most of the brand tested showed good result but few of them are substandard. So more steps and effective measures should be taken by the authority to ensure quality medicine.*

Keywords: *Chlorpheniramine maleate, disintegration, dissolution, friability.*

Introduction

Chlorpheniramine maleate is a widely used first generation antihistamine drug. Although many companies manufacture Chlorpheniramine Maleate, not all of them produce high quality products. Some of them are sub-standard. To identify quality drugs as well as substandard drugs Chlorpheniramine Maleate tablets are evaluated according to their physical and chemical characteristics. To monitor tablet's quality, quantitative evaluations and assessments of chemical, physical and bioavailability properties must be made. Not only could all three property classes have a significant stability profile, but the stability profiles may be interrelated, i.e., chemical breakdown or interaction between tablet components may alter physical tablet properties, greatly changing the bioavailability of a tablet system[1]. The quality of drugs means the quality of treatment that ensures the well-being of the patients. According to WHO book on good practice for the manufacture and control of drugs, "the manufacturer must assume responsibility for the quality of the drugs, which they produce". A medicinal product must satisfy certain standards to claim it to be a quality drug. The principal criteria for a Quality drug product are safety, potency, efficacy, stability and market acceptability[2].

The project work was designed to study the quality evaluation of Chlorpheniramine Maleate and to inform the physicians and patients about the substandard drugs in market. This will make awareness among the peoples and physicians so that the manufacturers will produce the quality products and people may not waste their hard earning money by buying low quality substandard drugs. This project work provides us knowledge about the percent potency of these preparations and to compare these values with their claimed potencies.

Materials and Methods

The reference sample was collected from "Eskayef Bangladesh Ltd." According to their supplied information it had 99.8% potency. The samples of marketed Chlorpheniramine Maleate tablets of different companies were collected at maximum retail prices (MRP) from different regions of Dhaka city for the analytical studies. The samples were properly checked for their batch number and shelf life, name of manufacturer, manufacturing license number, and DAR number. The samples were then coded with ethics for analysis

Table 1: Apparatus and equipment used in this work

Name	Model	Source
01)Slide calipers	Wheel Brand	Shanghai, China.
02)Friability test apparatus	ERWEKA	Germany
03) "THERMONIK" Tablet Disintegration Test Unit (IP/BR/USP)		Campbell Electronics, mumbi-400025, India.
04) Electronic Balance.	Melter, Ae-100.	Switzerland.
05) Dissolution test equipment, USPXX1.		Campbell Electronics, mumbi-400025, India.
06)UV-Visible Recording Spectrophotometer,	Thermo spectronic type: Helias Gamma,	England.
07) Monsanto hardness tester		Campbell Electronics, mumbi-400025, India.
08)Volumetric flasks:10,25,50, 100, 250, 500, 1000,2000 ml.	Wheel Brand	China
09) Funnel, beaker.	Wheel Brand	China
11) Pipettes	Precicolor	Germany
12) Mortar and pestle		
13) Measuring cylinder (50,100 ml)	Wheel Brand	China

Table 2: Reagent used in this Experiment

Name	Source	Specification
1) Hydrochoric acid(HCl)	Merck, Germany.	36% extra pure
2) Sulphuric acid	Merck, Germacy.	95-97%
3) Reference sample	Eskayef Bangladesh Ltd	99.8%
4) Whatman filter paper	E.MERK, Germany.	
5) Distilled water		

Table 3: Specification for different test

Test	Specification	Reference
1) General appearance	No specification	
2) Weight variation	± 5 %	British Pharmacopoeia
3)Hardness test	Not more than 7kg	British Pharmacopoeia
4)Friability	Not more than 1%	British Pharmacopoeia
5) Disintegration time	Not more than 15 minutes	British Pharmacopoeia
6) Dissolution	Not less than 75% in 45 minutes	USP
7) Potency determination	10%	USP

Physical Parameters Analysis

General Appearance: The Tablets were destripped or deblistered carefully. The tablets were observed visually with care at day light on a white surface. For packaging control, the outer pack and blister/strips were also checked, especially cuts, and ruptures, imprinting problems and the quality of packaging materials (paper/aluminium).

Thickness test of tablet: Thickness of 10 tablets of each sample was measured with a slide calipers. The average thickness of the tablets was determined and then thickness variation was calculated. In this way the thickness variation of 6 different brands of tablets was determined and the observed result for each sample was recorded.

Diameter Tests of Tablets: Ten tablets of each sample were taken and determined individual diameter, average diameter and standard deviation.

Weight variation test of tablets: 10 tablets of each brand were taken and weighed individually by an analytical balance. The average weight of the tablets was calculated. Then % of weight variation is calculated by using the following formula.

$$\% \text{ of weight variation} = \frac{\text{Individual weight} - \text{average weight}}{\text{Average weight}} \times 10 \times 100$$

In this way the weight variation for 8 different brands of tablets were measured and the observed value for each sample was recorded[3].

Friability: Four tablets of each brand were taken and weighed by an analytical balance. Then the tablets were put in a friabilator and the machine is allowed to rotate at 25 rpm for four minutes. After that the tablets were weighed again. The percent friability was calculated by the following formula:

$$\% \text{ of friability} = \frac{\text{Initial weight-final weight}}{\text{Initial weight}} \times 100$$

In this way % friability was determined for 8 different brands of tablets and the observed value was recorded.

Disintegration: The disintegration machine consists of 6 glass tubes that are 3 inches long, open at the top and held against a 10-mesh screen at the bottom and of the basket rack assembly. The basket rack is positioned in a 1-liter beaker of medium (water) at $37^0C \pm 0.5^0C$, such that the tablets remain 2.5 cm below the surface of the liquid on their upward movement and descend not closer than 2.5 cm from the bottom of the beaker. A standard motor-driven device is used to move the basket assembly containing the tablets up and down through a distance of 5 to 6 cm at a frequency of 28 to 32 cycles per minute. There are also six perforated plastic discs, which may be used on top of the tablets to impart an abrasive action to the tablets if necessary. The disks are useful for tablets that float. The disintegration time of 3 tablets of each brand was determined and the average disintegration time was calculated. In this way disintegration time for eight different brands were calculated and recorded[4].

Chemical Analysis

Dissolution rate test of tablet: In general, a single tablet is placed in a small wire mesh basket fastened to the bottom of the shaft connected to a variable speed motor. The basket is emerged in the dissolution medium (0.1N hydrochloric acid, 500ml) contained in a 1000 ml flask. The flask is cylindrical with a hemispherical bottom. The flask is maintained at a $37^0C \pm 0.5^0C$ by a constant temperature. The motor is adjusted to turn at the specified rpm.

Preparation of Standard curve: 100 mg of standard Chlorpheniramine Maleate BP was taken in a volumetric flask and the volume was adjusted with 0.1 N HCl. From this stock solution 0.5;1;2;4;8 ml was taken and kept in different 100 ml volumetric flask and the volume was adjusted with the same solvent. Ultimately the concentration obtained was 5;10;20;40;80 µgm/ml. Then absorbance of the prepared solution was taken by UV spectrophotometer and absorbance were plotted against the concentration which give a straight line as given below

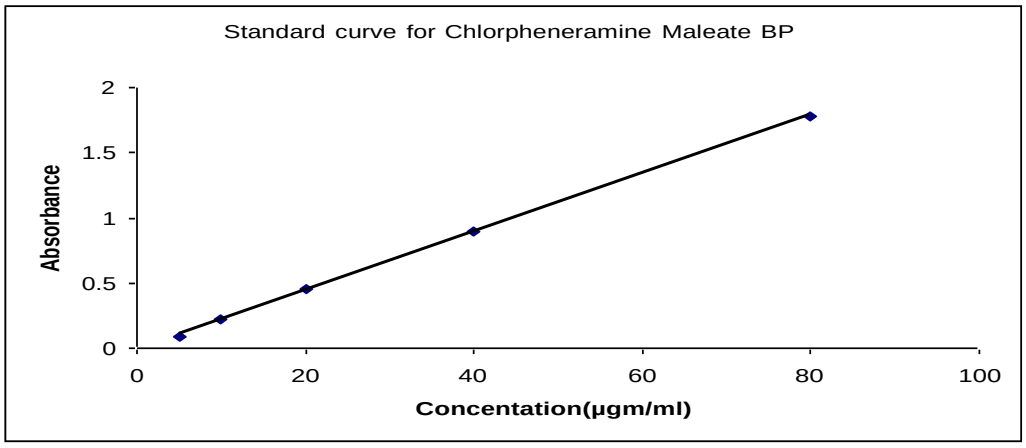

Figure 1: Standard curve for Chlorpheniramine Maleate for dissolution

Dissolution Procedure: The flask was filled with 500 ml of 0.1N HCl .The dissolution medium was heated up to $37^0C \pm 0.5^0C$ by an auto heater. One tablet was put into the basket and stirred immediately at 50rpm.20 ml of sample was withdrawn from the flask after 30 minutes and also 20 ml solvent was added to the flask to remain the environment similar to the specification. The dissolved Chlorpheniramine Maleate was determined from UV absorbance at the wavelength maximum absorbance at about 265 nm of filtered portion of the solution under test in comparison with a standard solution having known concentration of USP Chlorpheniramine Maleate in the same solvent[5].

$$\% \text{ Dissolution} = \frac{\text{Absorbance of sample} \times \text{dilution of standard}}{\text{Absorbance of standard} \times \text{dilution of sample}} \times \text{Purity of standard} \times (\text{tablet weight}/4)$$

Potency determination: For larger dose drugs in tablet from the official potency range that is permitted is not less than 95% and not more than 105% of the label amount. In general official potency analytical methods require that a composite sample of the tablets be taken, ground up, mixed, and analyzed to produce an average potency value.

Preparation of standard solution: 100 mg of standard Chlorpheniramine Maleate RS was weighed and taken in a 100 ml volumetric flask. Dissolve it by 0.05M H_2SO_4 of and make the volume up to 100 ml by the same solvent. Dilute 0.5; 1; 2; 4 and 8 ml of the above solution to 100 ml with the same solvent that yield 5; 10; 20; 40 and 80 µgm/ml concentration. A standard curve was produced by taking absorbance of different known concentrations of Chlorpheniramine Maleate at 265 nm and then putting them against corresponding concentration on a graph paper [5].

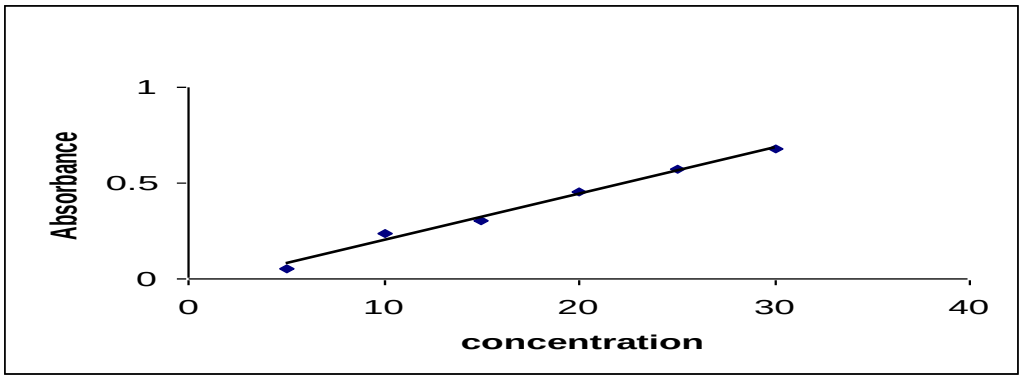

Figure 2: Concentration versus absorbance curve for standard curve for potency determination

Preparation of assay solution: 5 tablets were weighed and crushed for powder with a mortar and pestle. Then an amount of powder transferred equivalent to 2 mg of Chlorpheniramine Maleate in a 100ml volumetric flask. 60 ml of 0.05 M H_2SO_4 was added and shaken mechanically for 20 minutes. The volume was adjusted up to the mark with the same solvent and filter. Anticipated concentration was 2.0 mg / 100 ml.

Table 4: Absorbance of different concentration of standard Chlorpheniramine Maleate solution measured at 265 nm

Concentration µg/ml	Absorbance	Average of absorbance
5	0.088 0.083 0.830	0.085
10	0.191 0.199 0.197	0.196
20	0.434 0.437 0.446	0.439
40	0.933 0.933 0.936	0.934
80	1.833 1.847 1.845	1.842

Measurement: The absorbance of both the standard and assay solution were measured in a suitable UV-Visible spectrophotometer having 1—cm cell at 265 nm using 0.05 M H_2SO_4 as blank. Each sample was run in duplicate and average of the results was taken to consideration. The potency was calculated by the following equation

$$\text{Potency of sample} = \frac{\text{Absorbance of sample} \times \text{weight of standard}}{\text{Absorbance of standard} \times \text{weight of sample}} \times \text{potency of standard}$$

In this way the potency of 8 brands was determined and the observed value for each sample was recorded.

Result

Physical Parameters Analysis: General Appearance: The general appearance of all brands of Chlorpheniramine Maleate tablets has been thoroughly analyzed and the results show that there is not much difference between the brands except color. As there is no specification about the color of tablets in BP/USP, the manufacturers can use any coloring agents in tablet formulation permitted by the concerned authority.

Table 5: Weight variation of various brands of Chlorpheniramine Maleate Tablets

Sample code	No of tablets	Average weight	Percent deviation	Inference
CM 01	10	114.41	+5.41to-1.93	Satisfied
CM 02	10	135.7	+3.32to -3.39	Satisfied
CM 03	10	98	+3.06to-3.06	Satisfied
CM 04	10	109.13	+2.26to-3.6	Satisfied

CM 05	10	144.32	+1.72to -4.24	Satisfied
CM 06	10	169.71	+1.41to-0.71	Satisfied
CM 07	10	78.46	+4.9to-2.12	Satisfied
CM 08	10	114.79	+2.45to-7.13	Satisfied

USP specification of weight variation for tablets of 130 mg or less: ±10
USP specification of weight variation for tablets of 130-324 mg: ±7.5

Table 6: Friability (% loss) of Chlorpheniramine Maleate tablets

Sample Code	No. of tablet	Initial weight (mg)	Final weight (mg)	%of friability	Specification
CM-01	4	454.1	451.3	0.62	Satisfied
CM -02	4	541	537	0.73	Satisfied
CM -03	4	395	390	1.26	Dissatisfied
CM -04	4	434.7	433.1	0.36	Satisfied
CM -05	4	579.8	578.3	0.25	Satisfied
CM -06	4	681.3	677.2	0.60	Satisfied
CM -07	4	310.8	308.3	0.80	Satisfied
CM -08	4	477	473	0.83	Satisfied

Specification: BP/USP specification 0.5 to 1 % loss of their weight.

Table 7: Disintegration Test of Chlorpheniramine Maleate Tablets.

Sample Code	No. Of Tablet	Disintegration Time (min)	BP specification
CM-01	6	3 minutes19 sec	Satisfied
CM -02	6	4 minutes 50 sec	Satisfied
CM -03	6	2 minutes 38 sec	Satisfied
CM -04	6	2 minutes 17 sec	Satisfied
CM -05	6	3 minutes 50 sec	Satisfied
CM -06	6	4 minutes 35 sec	Satisfied
CM -07	6	3 minutes 37 sec	Satisfied
CM -08	6	2 minutes 49 sec	Satisfied

It is seen from the above results (Table 7) that none of the samples exceeded the specification for disintegration time. Therefore, it can be said that all the studied samples complied with the BP/USP specification for tablet disintegration time.

Chemical Analysis

Table 8: Dissolution Rate of Chlorpheniramine maleate Tablet.

Sample Code	%0f Drug Release After 10 Minutes	%0f Drug Release After 30 Mins	%0f Drug Release After 45 Minutes	USP Specification
CM -01	84.1	95.01	95.75	Satisfied
CM -02	63.05	93.25	93.75	Satisfied
CM -03	86.25	88.75	88.77	Satisfied
CM -04	83.05	94.15	94.75	Satisfied
CM -05	62.5	97.5	100	Satisfied
CM -06	88.5	99.1	99.75	Satisfied
CM -07	87.35	97.5	97.5	Satisfied
CM -08	87.25	96.48	99.65	Satisfied

USP specification not less than 75% of the labeled amount of Chlorpheniramin Maleate should be dissolved in 45 minutes.

Table 9: Potency of Chlorpheniramine Maleate Tablet.

Sample Code	Potency (%)	Percent Deviation	USP Specification
CM-01	96.62	3.38	Satisfied
CM -02	98.66	1.34	Satisfied
CM -03	103.44	-3.44	Satisfied
CM -04	95.02	4.98	Satisfied
CM -05	101.16	-1.16	Satisfied
CM -06	107.30	-7.3	Satisfied
CM -07	99.27	0.73	Satisfied
CM -08	112.75	-12.75	Dissatisfied

USP Specification: 90-110% for Chlorpheniramine Maleate Tablet.

Discussion

From the above results (table 6), it appears that 7 brands out of 8 complied with the BP/USP specification of friability, but one brand does not comply. This noncompliance of 1 brand in respect of friability may be due to less binding agent used in the tablet or improper processing. 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 % of moisture may be much more friable than tablets containing 2 to 4 % of moisture[6].

It is seen from the above results (Table 8) that every sample fulfills the USP specification for tablet dissolution rate. The rate of drug absorption is determined by the rate of drug dissolution from the dosage form. For this reason, in vitro drug dissolution rate is important to achieve high peak blood levels for a drug. Good co-relation exits between in vitro dissolution rate and in vivo bioavailability of a tablet product. Tablet has high in vitro dissolution rate shows high in vivo bioavailability[7].

From the table 9, it is clear that one out of eight brands (10%) of Chlorpheniramine Maleate did not comply with the specification. This one brands failed to contain the specified amount of Chlorpheniramine Maleate claimed at it. The highly potent brand arises due to the mistake in weighing of active ingredient while manufacturing. This over potency may give high therapeutic response and consequently give toxic effect[8].

Conclusion

There is no alternative to quality medicine for good health. After the implementation of National Drug Policy in 1982, no doubt, the quality of medicine is improved, but not as expected. This project work was designed to evaluate the current status of the marketed Chlorpheniramine Maleate tablets because very often we found in various news media about the spurious and substandard drug in Bangladesh.

The present study although performed on a limited scale, yet on the basis of professional judgment, the data reported in this project paper can help the Drug Control Authority to get an idea about the quality status of the marketed Chlorpheniramine Maleate tablet preparations in Bangladesh. From the above result it is assumed that although most of the brands meet with specification, few brands do not satisfy the specification. So the Drug Control Authority should take proper measure to control quality of marketed drug in any situation. Sub-standard drugs cause not only wastage of money but also are responsible for health hazards which are sometimes so acute that may cause death. So the drug control authority should strengthen their visiting team to visit frequently the manufacturing plant and establish more effective analytical measures to analyze the marketed drugs.

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