A Quality Control Assessment of Five Brands of Chlorpheniramine Maleate Tablets Marketed In Nigeria

K.M.Ezealisiji, E.A.Omotosho

Department of Pharmaceutical and Medicinal Chemistry. Faculty of Pharmaceutical Sciences, University of Port Harcourt .Rivers State, Nigeria.

ABSTRACT

In vitro evaluations of five brands of Chlorpheniramine maleate marketed in Nigeria from companies designated A, B, C, D and E were carried out in order to determine the bioavailability of each brand. The uniformity, hardness, friability, disintegration time and dissolution test were conducted. The BP standard value of the deviation for weight uniformity is ±7.5%, hence all the samples passed the test based on specification as these respective values were obtained from each of the samples: (A = 1.48, B = 4.24, C = 3.69, D = 2.59 and E = 2.50). The hardness test values of 2, 0.775, 1.493, 1.176, 1.122KgF and disintegration values of 2.2, 1.8, 3.8, 1.1 and 2.3 were obtained for A, B, C, D and E respectively. This means that, they all passed disintegration test according to USP specification. Absolute drug content test results obtained were: A = 96.99, B = 96.57, C = 87.04, D = 74.76 and E = 92.13 showing that brands A, B and E passed the test (official acceptance range is 92.5 and 107.5%) while C and D failed it. The result obtained for dissolution test indicated that the drug content of each of the brand released with an initial increasing order and later declined as the time increased. In conclusion, this study revealed that formulation of the same dosage form of the drug varies among manufacturers.

Keyword: Chlorpheniramine maleate, *in vitro* evaluation, Dissolution test.

INTRODUCTION

Different brands of Chlorpheniramine are produced by different pharmaceutical industries. Hence there is a need to assess their bioavailability and other qualities relating to medical uses. Though different brands of chlorpheniramine in Nigeria market do possess same pharmaceutical active ingredient yet to ensure uniformity of content there is need to carry out bioavailability study. The use of *in vitro* dissolution profile studies of therapeutic agent is needed because only a few clinical response e.g. heart rate, blood pressure, electrocardiogram) can give accurate quantitative measurement. This reason has made *in vitro* dissolution profile studies an important parameter for consideration in drug administration of solid dosage form [1]

Bioavailabilities (i.e. therapeutic efficacy) of most drugs are significantly affected by formulation factors [2] For solid dosage forms, factors such as binder type or concentration, disintegrant type or concentration and/or method of incorporation, lubricant type and concentration, compression pressure, particle size of active component etc have been shown to affect the bioavailability of various drugs [3].

These factors vary from one pharmaceutical company to the other hence the differences in the bioavailability of their products. Two *in vitro* tests that are officially employed in predicting *in vitro* bioavailability of most oral dosage forms are disintegration and dissolution tests. But disintegration test does not give precise information on the rate of drug bioavailability; dissolution testing is now being used [4].

In this study, an attempt is made using *in vitro* method to ascertain the bioavailability of Chlorpheniramine tablet dosage forms marketed in Nigeria, in order to obtain the chemically equivalent brands.

Chlorpheniramine maleate an arylalkyl derivative is a short acting histamine H_1 receptor antagonist. It contains not less than 98.0 % and not more than the equivalent of 101.0 % of (RS) – 3 – (4 – chlorphenyl) – N, N – dimethyl – 3 – pyridyl – 2yl propanamine hydrogen (2) – butenedioate calculated with reference to dried substance. It is a white, crystalline powder, freely soluble in water, soluble in alcohol and slightly soluble in ether. It is supplied as 4 mg tablets [5] .

**Corresponding author: Kenneth.ezealisiji@uniport.edu.ng*

MATERIAL AND METHOD

The following drug materials were procured; five different brands of chlorpheniramine maleate tablets coded A – E were obtained commercially in the open market. Other materials include Concentrated Hydrochloric acid (BDH, England), Distilled water (Lion's water University of Nigeria, Nsukka), potassium mercuric iodide and ferric chloride (Sigma- Aldrich, St. Louis, MO, USA). UV-Vis spectrophotometer (Perkin Elmer Lambda 35, Germany), Erweka Dissolution rate Paddle apparatus (Germany).

Test for active ingredient of sample brands of Chlorpheniramine maleate

Each of the powdered samples was tested with potassio – mercuric iodide and ferric chloride solution and the observation recorded.

Weight Uniformity test

Ten tablets were randomly selected from each of the brands A, B, C, D and E, weighed singly and their mean weight and their deviation calculated. These were done to ascertain whether the sample conformed to the pharmacopoeia standard deviation in each.

Hardness/crushing strength test

Ten tablets from each brand were checked for crushing strength. Each of the ten tablets were placed in the lower plunger. The force expressed in KgF required to break the tablet was noted and recorded. The mean hardness was determined in each case.

Tablets friability test

Ten tablets randomly chosen from each of the brands A, B, C, D and E were weighed together and then placed in the friability chamber, closed and tightened properly. After 100 rpm (25 rpm for 4 minutes), the tablets were removed, dusted and reweighed. The difference in weight was determined and expressed as percentage w/w of the original tablet weight. The above procedure was repeated for ten tablets from the other four brands.

Disintegration time test

The disintegration time of randomly chosen five tablets from each of the brands was determined in 900ml of 0.1M HCl maintained at 37 ± 1°C using Erweka disintegration unit. The time taken for all the palpable tablet particles on the mesh to go into solution was recorded as the disintegration time. This was repeated five times.

Beer Lambert plot for pure Chlorpheniramine maleate sample

A stock solution of chlorpheniramine maleate was prepared as follows: 100 mg chlorpheniramine maleate was dissolved in 100 ml of 0.1 N HCl to stock concentration of 1mg/ml. Then 2, 4, 6, 8, 10, 12, 16 and 20 ml were diluted to 100ml each to obtain 2, 4, 6, 8, 16 and 20mg %. Their respective absorbance readings were taken with the spectrophotometer at a wavelength of 270 nm. The result obtained was used in plotting the calibration curve.

RESULTS AND DISCUSSION

Qualitatively the results obtained for the test for the presence of active ingredient, shows that all the samples produced white precipitate in the presence of potassio-mercuric iodide and yellow orange colour in the presence of ferric chloride solution. (Table 2)

There are mandatory tests in the United State Pharmacopoeia (USP) the National Formulary (NF). These tests are usually determined using two different general approaches: weight uniformity test and extent of drug content uniformity. This test also serves as a simple way to assess variation in drug dose, which makes the test useful as a quality control procedure during tablet production [6].

Table 1: General description of different brands of Chlorpheniramine maleate tablets used in this study.

Manufacturer	NAFDAC Registration Number	Lot/ Batch numbers	Manufacturing date	Expiry date	Colour
A	04 – 0252	BN7055	11/07	10/10	Light yellow
B	04 – 1268	BN0250	07/07	07/10	Deep yellow
C	04 – 7454	BN32	07/08	07/11	Light yellow
D	04 – 1118	CT8119	11/08	11/11	Yellow
E	04 – 4050	BN2963m	07/08	07/11	Light yellow

Table 2: Identification of active ingredient of sample brands of Chlorpheniramine maleate

Brands	Potassio-Mercuric Iodine	Ferric Chloride Solution
A	+	+
B	+	+
C	+	+
D	+	+
E	+	+

The official acceptance range of 92.5 - 107.5 % is used as basis for absolute drug content tests. But from the result in table 3, brands designated A, B and E passed the drug content uniformity test while C and D failed. The failure of samples C and D may be due to non-homogeneity of the batch as result of formulation and manufacturing factors. The regression equation for the Beer-Lambert plot of pure chlorpheniramine maleate was found to be y = 0.207x and the correlation coefficient [R2] of 0.9916. The Beers plot was obeyed in concentration range of 0.025 – 2.50 mg% [fig 1].

The findings of this work reveals that all the brands conform to both USP and BP standards for weight uniformity, since none of the samples deviated from the standard value of ±7.5%. Hence all the samples passed the test based on the BP specification (Table 4).

Ta

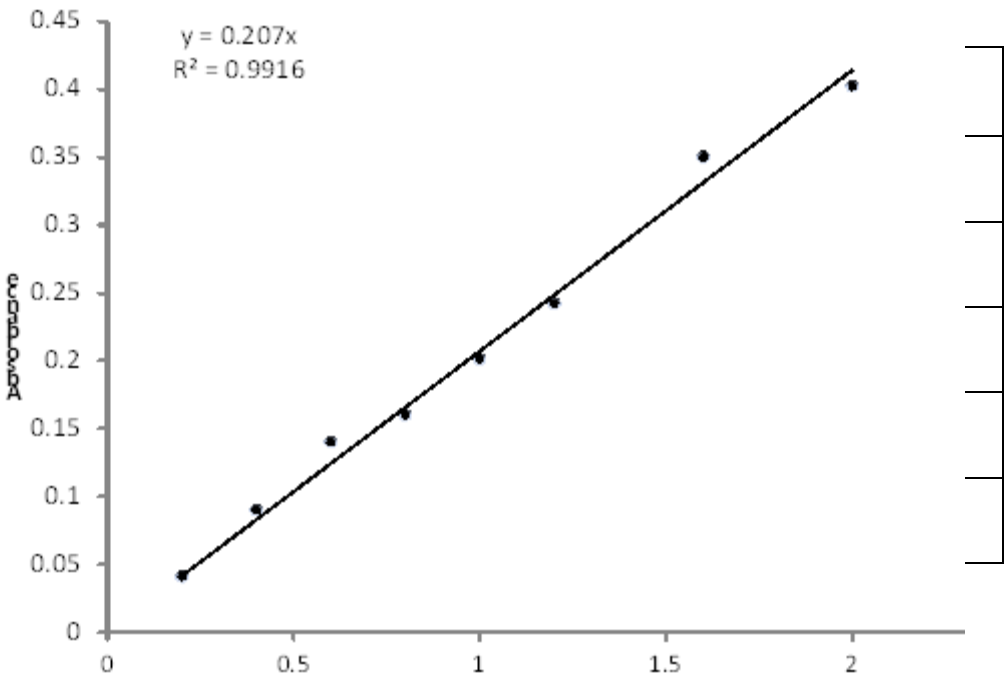

Fig 1: Beer's plot of Chlorpheniramine maleate at 270 nm

Table 4 Weight Uniformity of sample brands of Chlorpheniramine maleate

Brands	Mean weight (mg)	Standard deviation (mg)	Standard Error of Mean (mg)	% coefficient of variation
A	139.90	1.48	0.47	1.06
B	128.30	4.24	1.34	3.31
C	132.60	3.69	1.17	2.78
D	171.60	2.59	0.82	1.51
E	198.78	2.50	0.79	1.26

The crushing strength is more closely related to the compressional force. The hardness test result showed that most of the samples may not withstand much stress during handling, transportation and shipping. Only sample D has an acceptable value (Table 5). This recorded failure may be due partly to low compression force, as employed during the compression of the tablet, insufficient binder, improper granulation of the powder before compression and too much fines in the granules, as evident in their various containers.

For pharmaceutical products the friability values should fall within 0.8 – 1.0 %. This test is capable of providing a measure of a tablets plasticity or elasticity. Thus it enables the manufacturers of the product to detect incipient capping or chipping of the tablet. Samples A, B, have lower values while C, D and E were of higher than value than the acceptable range which means that, samples C, D and E may be able to withstand crumbling during transportation, handling and friction between tablets and walls of the containers but in the area of drug dissolution and drug release there may be some challenges.

Table 5: Hardness test of sample brands of Chlorpheniramine maleate

Brands	Mean Hardness (KgF)	Standard Deviation (KgF)	Standard error (KgF)	%Coefficient of Variation
A	2.000	0.082	0.025	4.100
B	1.200	0.203	0.064	16.967
C	3.050	0.268	0.085	8.787
D	5.260	0.243	0.077	4.619
E	3.080	0.181	0.057	5.877

Table 6 Friability test of sample brands of Chlorpheniramine maleate

Brands	Initial weight (W_o) (g)	Final Weight (W) (g)	Abrasion Resistance (B)
A	1.400	1.390	0.714
B	1.290	1.280	0.775
C	1.340	1.320	1.493
D	1.700	1.680	1.176
E	1.960	1.938	1.122

Table 7: Disintegration test of sample brands of Chlorpheniramine maleate

Brands	Mean Disintegration time (Mins)	Compliance
A	2.20	Passed
B	1.80	Passed
C	3.80	Passed
D	1.12	Passed
E	2.30	Passed

Table 8 Drug release profile for the tablets of different brands of Chlorpheniramine maleate at pre-determined time interval in 0.1N HCl (%)

Time (min) / **Brands**	5	10	20	40	60	80	100	120
A	37.27	41.61	44.01	47.71	40.64	37.75	31.66	29.72
B	44.21	48.18	50.61	43.51	42.50	38.53	33.16	30.06
C	41.33	42.43	43.71	47.51	51.68	45.87	40.08	35.93
D	46.31	50.04	52.07	52.80	51.32	45.37	39.57	36.79
E	40.83	44.08	48.54	50.93	48.20	43.21	38.27	34.63

Disintegration tests are one useful means of assessing the potential importance of formulation and process variables on the biopharmaceutical properties of the tablets and as a drug quality control procedure [7,8]. Surprisingly based on the friability test results with respect to the USP specification, all the samples passed the disintegration test. The USP specifies that chlorpheniramine maleate tablets should disintegrate within 30 minutes, which all the samples complied with. (Table 7)

The dissolution test result (Table 8), shows the drug release profile of the sampled chlorpheniramine brands used in this work. The result indicates that the drug content is released at a faster rate when compared to the release rate of the drug after 40min for the brands tested. This means that at different time intervals, a particular quantity of the drug is released (fig 2)..

CONCLUSION

It is thus concluded that formulations of the same dosage form of the same drugs varied among manufacturers. This may be due to variation in the type or concentration of excipients or formulation procedure adopted. Hence proper quality assurance has to be done for different batches of tablets meant for public consumption. The raw material and the active pharmaceutical ingredients (API) in terms of quality should meet the specified official stipulated official stipulated standard. More attention should be made to see that the products active ingredient strength is stated clearly and excipients mixed properly and at the right proportion. Proper labeling with adequate information about the product should always accompany the product packaging material.

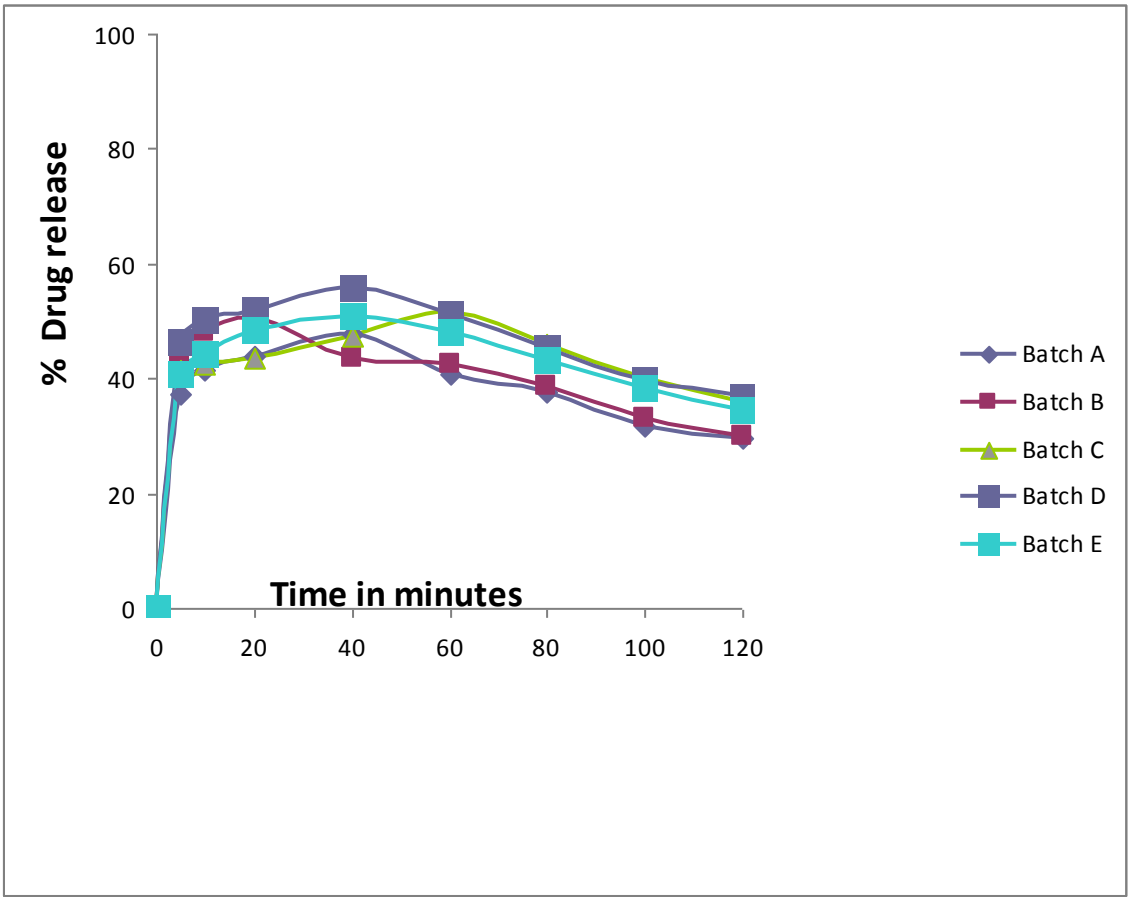

Figure 2:Drug release profile for the Chlorpheniramine maleate tablets of different brands

REFERENCES

[1] Aulton.M.E, (1988), Pharmaceutics: The Science of Dosage form Design. (Churchill Livingstone London). Pp 250 – 280.

[2] Ofoefule, S I (2002). A textbook of Pharmaceutical technology and Industrial Pharmacy, Samakin Nigeria Enterprises, Lagos .pp 2 – 14, 60 – 65, 283 – 285.

[3] Koch –Wesser, J.(1974). Bioavailability of drugs. New England, J. Med., 291: 233 – 237

[4] Olaniyi AA (2000).Principle of drug quality assurance and Pharmaceutical analysis, Mosuro Publishers Ibadan. pp 399 – 404.

[5]The United State Pharmacopoeia. XXIII, 1995 and the National Formulary (18th Edition). The United States Pharmacopeia Convention, Inc. Rockville, MD, pp 1790 – 1794.

[6] Gilbert S. Banker, Christopher T Rhodes Ed. (2002) Modern Pharmaceutics. 4th Edition. Marcel Dekker USA. Pp 520-560

[7] Lloyd V Allen, Jr., Nicholas G. Popovich, Howard C Ansel (2011) Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems.9th Edition. Lippincott Williams & Wilkins pp 205-251

[8] Kalakuntla R, Veerlapati U, Chepuri M, Rapavla R (2010) Effect of various super-disintegrant on hardness, disintegration and dissolution of drugs from forms. J Adv. Sci. Res. 2010. 1(1): 15-19