Original Article

Estimation of Equivalence for Quality Parameters of Metoclopramide Hydrochloride Tablets Used to Treat Emesis

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Abstract

Metoclopramide hydrochloride is used for the treatment of emesis. It is also used for chemotherapy and radiotherapy, and migraine induced nausea and vomiting. The objective of the study was the comparative assessment of different brands of metoclopramide hydrochloride. Different physiochemical tests according to USP were performed using different instruments. Scanning electron microscopy was also performed. Methanol, (Merck, Darmstadt, Germany) was used as regents. A reported method was utilized for the assay and dissolution studies. The results in weight variation test and friability ed within the pharmacopeia specified limits. The strength of the branded tablets was 6.15±0.18 to 8.77±0.38 kg. The disintegration time was within 4.1±0.52 to 7.11± 0.39 min. FT-IR and SEM analysis depicted complete compatibility between the active and excipients. The assay and dissolution results showed determination at 272 and 309 nm with USP limits. The spectrophotometric methods assess the quality and efficacy of tablets effectively, hence the evaluation provides the evidence to choose the brands for treatment.

Keywords: Scanning electron microscopy (SEM), Emesis, FT-IR, Metoclopramide hydrochloride tablets

Introduction

Metoclopramide stimulates GI peristalsis and upper colon; it speeds the passage through the gut. Metoclopramide is a benzamide used for its prokinetic properties. It possesses parasympathomimetic activity, it is a dopamine-receptor blocker, it affects the chemoreceptor trigger zone, it is also a serotonin-receptor antagonist. It is an antiemetic drug [1-4]. Metoclopramide is a BCS class III drug that is a highly soluble and low permeable drug. Metoclopramide hydrochloride is a salt and it helps in study of dopaminergic mechanisms [5]. It is utilized in treatment of nausea and vomiting caused by various reasons. It produces its effect through the inhibition of dopamine receptors of GI tract [6, 7]. After oral administration, metoclopramide is rapidly absorbed from the GIT but in case of nausea or low GI motility, absorption may be slow. It undergoes hepatic first-pass metabolism. The bioavailability of oral metoclopramide is nearly 80%. Metoclopramide with Peak plasma concentrations within 1 to 2 hours. Metoclopramide is bound to plasma protein. It freely distributes in body and passes the blood-brain barrier. Half-life is 4 to 6 hours. It is mainly excreted in the urine [7]. Chemically it is 4-Amino-5-chloro-N-(2-diethylaminoethyl)-2-methoxybenzamide [7]. The efficacy, quality, and safety of a pharmaceutical dosage form is prerequisite and it could be assured when it meets all quality parameters. The quality of any formulation depends on the manufacturing procedures, GMP, and cGMP practiced during manufacturing, and the quality of pharmaceutical formulations may be different [8]. Assay and dissolution tests are generally applied for the evaluation of quality of tablets and capsules [9].

Materials and Methods

The metoclopramide hydrochloride brands were bought from different pharmacies from Karachi. The six brands were

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marked and coded as BT1 to BT6. The reagents used was methanol, (Merck, Darmstadt, Germany). Freshly prepared distilled water was used throughout the work. All the brands were tested for uniformity in weight, friability, hardness, disintegration, dissolution test, and drug assay for the strength of active ingredient. These tests were performed according to the USP specifications [10]. Brand BT1 was considered as reference.

Physical Inspection and Evaluation of Tablets

Out of total 20 tablets were weighed from each brand using a top load analytical balance (Shimadzu, Japan). Then the mean and standard deviation was calculated. The hardness of tablets was assessed by crushing strength of twenty tablets from each brand was assessed and noted with (Erweka, Heusenstamm, Germany). The diameter of 20 tablets was determined (Digital, China). 20 tablets were chosen randomly, weighed, and then subjected to friability test (ERWEKA, Germany). The speed was 25 rpm for 4 min, the loss in the weight of tablets was calculated [10]. The disintegration assessment was performed by 6 randomly selected tablets from each brand and their time for disintegration was determined at 37 °C (ERWEKA, Heusenstamm, Germany). The Fourier transform infrared spectroscopy was conducted on Thermo Scientific iS 10 by the ATR method. The drug and the excipient analysis were analyzed. The Morphological properties of reference formulation (BT1) were examined through a scanning electron microscope, SEM (JSM-6380A, Japan). The drug release was assessed according to USP [10]. USP apparatus I was used (ERWEKA, Heusenstamm, Germany). The dissolution medium used was 900 ml of water, the temperature was maintained at 37 ± 0.5 °C, speed was 50 rpm for 30 minutes. The total dissolved amount of $C_{14}H_{22}ClN_3O_2$ was determined, absorbance was measured at the wavelength of 309 nm (UV Sectrophotometer, Shimadzu). The amount of metoclopramide hydrochloride in the samples was determined.

Assay of the Tablets

After the relevant literature review validated method for assay for metoclopramide hydrochloride on spectrophotometer was used for the assay of tablets [11]. Tablets of the referenced brand were crushed and powder equal to 100 mg of metoclopramide hydrochloride was weighed and then transferred to a volumetric flask (100mL). The powder was mixed with methanol (50mL), it was agitated until completely dissolved and volume was made with methanol (100mL). 20 tablets were randomly selected weighed and crushed to powder. Powder equal to 25 mg of metoclopramide hydrochloride was taken into a 100 mL volumetric flask, about 10 mL of methanol was mixed. The solution was sonicated for about 15min. Methanol was used to make up the volume in solution was filtered through Whatman filter paper. Methanol was added to obtain a concentrated solution of 1.2µg/mL. Quantitative determination was performed by UV spectrophotometer [11]. The Similarity factor (*f2*) of the model-independent method was employed to compare the dissolution profiles for tablets in test (Eq. 1). The Similarity factor (f2) is the logarithmic reciprocal square root transformation of the sum of squared error. It is an assessment of similarity in % dissolution amid both curves. The value falls between 50 and 100, profiles are considered similar. A descending f2 value indicates dissimilar dissolution profiles [12].

$$f_2 = 50 \times \log\left\{(1 + {}^{1}/_{N}\sum_{i=1}^{n}(R_i - T_i)^2)^{-0.5} \times 100\right\} \quad (1)$$

Where, Ti is % of test drug dissolved, Ri is % of reference drug dissolved, the number of samples is represented by N.

Results and Discussion

The results and outcomes of the current study represented that all brands qualified for USP criteria of the quality control and quality assurance. Six brands of metoclopramide hydrochloride tablets were tested for weight variation and uniformity as shown in **(Figure 3)** diameter, friability, disintegration time, assay, and dissolution profiles **(Table 1)**. represents the physical parameters.

Table 1. Physical Parameters of Tablet

Brand of Tablets (BT)	Weight variation ±SD (mg) (S.D.) n=20	Diameter (mm) (S.D.) n=20	Hardness (kg) Mean (S.D.) n=20	Friability (%)
BT1	100.01±0.27	777.19±0.017	6.15±0.18	0. 0.53
BT2	101.22±0.78	7.07±0.001	8.49. ±0.71	0.21
BT3	101.23±1.38	8.21±0.033	8.77±0.38	0.62
BT4	99.73±0.67	6.58±0.097	6.32±0.59	0.55
BT5	105 39±0.99	9..02±0.010	9.11±0.47	0.78
BT6	102.54±1.62	8.45±0.002	7.98±0.66	0.64

The weight variation test of brands showed values that followed the pharmacopeia specified limits for weight variation and none of the branded tablets deviated by up to ±5% from the mean [10, 13, 14]. The drug release profile of different brands is mention in **Figure 1**.

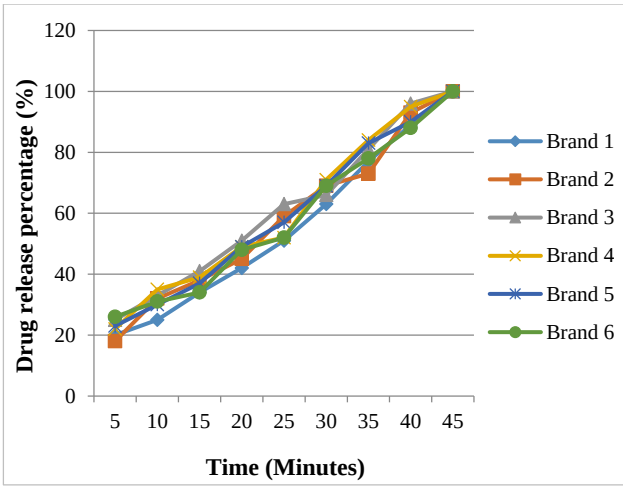

Figure 1. Drug Release Profile of Metacholpromide's Brands

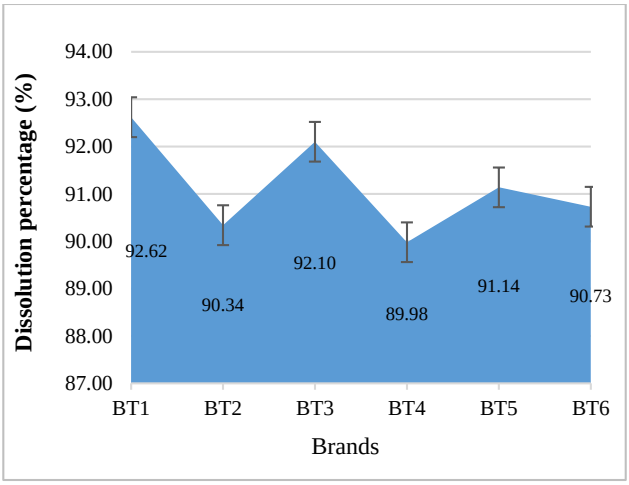

Figure 2. Dissolution Profile of Metacholpromide's brands

The friability test was also conducted. It was found less than 1% for all the tested brands, however, the difference in values may be due to variation in manufacturing process or nature of excipients [15-17]. All the branded tablets showed crushing strength between 6.15±0.18 to 8.77±0.38 kg. The dissolution profile of different brands is given in **(Figure 2)**.

The results of disintegration were between 4.1±0.52 to 7.11± 0.39 minutes, all results were within specified USP limits [10]. FT-IR analysis showed perfect compatibility between active and excipients. SEM image of the sample displayed uneven and asymmetrical surface of particles shown in **Figure 4**. The USP method for the assay illustrates determination with different diluents and detection wavelength, we used an already reported spectrophotometric method [11].

Table 2. Assay of Tablets

Brands	Disintegration test n= 6 Dissolution test) Minutes	Dissolution test n= 6 (%)	Assay (average drug content) n=20 (%)	f2 results (%)
BT1	6.56±0.87	92.62%±0.37	100.5%±0.89	Reference
BT2	5.39±0.73	90.34%±0.85	99.7%±0.72	63.54
BT3	7.11±0.39	92.10%±0.70	101.7%±0.31	57.59
BT4	4.1±0.52	89.98%±0.67	100.7%±0.37	56.91
BT5	5.34±0.83	91.14%±0.86	97..4%±0.96	62.73
BT6	6.44±0.96	90.73±0.17	98.6%±1.11	64.25

As aforesaid the variability of values might be due to variations in manufacturing procedures according to product master formula, different behavior of ingredients, and process parameters Shown **(Figures 2 and 3)** the dissolution profiles were tested for each brand; however, the results were within the specified limits [10]. The USP specified limits of assay were 90 % to 110 % and assay values of all branded tablets were within 90% to 110%. Hence, the vetted results assured the label claim quantity of active therapeutic ingredient.

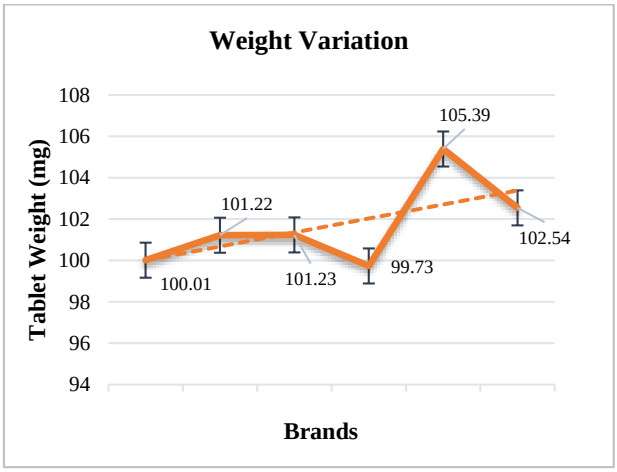

Figure 3. Weight Variation in Different Brands

Since the antiemetic properties of medicines containing metoclopramide hydrochloride depends on the release characteristics of the drugs and timely release helps in onset of action on the release of the drug [18-23]. In the present investigation, the dissolution studies exhibit timely release of the drugs. All branded tablets were calculated for similarity factor (f_2) and all brands were similar in drug release.

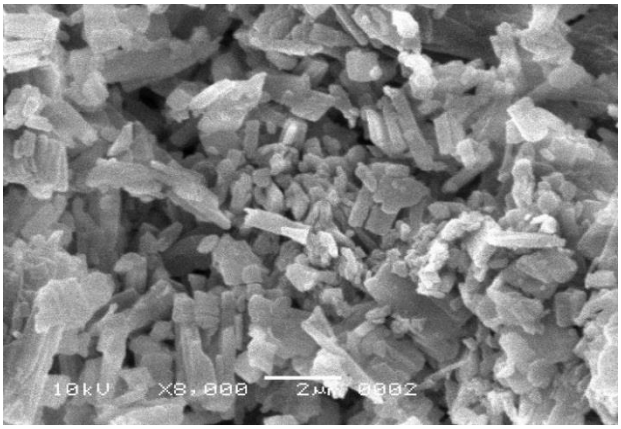

Figure 4. SEM of referenced brand

It was revealed that absorption was observed at various wavelengths. However, at 272 nm the absorbance was good, the results were observed at this wavelength [11].

Conclusion

The current study provides an effective analysis method of metoclopramide hydrochloride branded tablets to decide their efficacy and quality. These spectrophotometric methods are easy to operate for evaluation. Such evaluations are helpful in the determination of the quality of a brand.

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References

1. Nazareth C, Pereira S. A Review on Chiral Stationary Phases for Separation of Chiral Drugs. Int. J Pharm Phytopharmacol Res. 2020;10(3):77-91.
2. Jafar M, Alshaer FI, Adrees FA. Cyclodextrin Ternary Inclusion Complexation: A Strategy to Improve Solubility of Poorly Soluble Drugs. Int J Pharm Phytopharmacol Res. 2018;8(6):8-17.
3. Soboleva MS, Loskutova EE, Amelina IV. Improvement of pharmaceutical consultation process in drugstores. J Adv Pharm Educ Res. 2020;10(1):136-42.
4. Najafi ML, Nasiri M. Review of drug abuse patterns and their association with some individual and social variables among addicts. J Adv Pharm Edu Res. 2019;9(2):99-101.
5. Varillas MA, Brevedan MI, González Vidal NL. Pharmaceutical Equivalence and Similarity Studies of Metoclopramide Tablets. Dissolut Technol. 2018;25(1):14-21.
6. Huque S, Brishti NR, Noor M, Das S, Akhter R, Gorapi MZ, et al. Comparative in vitro equivalence evaluation of some Desloratadine generic tablets marketed in Bangladesh. IJAR. 2017;3(2):288-93.
7. Brayfield A. Martindale: The complete drug reference. Pharmaceutical Press; 2017.
8. Weise AM, Liu CY, Shield AF. Fatal liver failure in a patient on acetaminophen treated with sunitinib malate and levothyroxine. Ann Pharmacother. 2009;43(4):761-6.
9. Yogananda R, Nagaraja TS, Snehalatha JK, Vijay Kumar MM. Comparative in vitro equivalence studies of designed, branded and generic tablets of ciprofloxacin-250. Int J Pharm Sci. 2009;1(1):28-34.
10. Noor S, Salam FB, Hima HN, Bhuiyan MS, Chowdhury S. Comparative in-vitro quality evaluation of some brands of Metronidazole tablet available in Bangladesh. Int J Appl Res. 2017;3(7):753-8.
11. Thangamani A, Anton Smith A, Vedhapriya B. Development of analytical method for metoclopramide using uv-spectrophotometry. Int J Pharm Chem Biol Sci. 2014;4(3):551-5.
12. Jung-Cook H, Mayet-Cruz L, Girard-Cuesy ME. Comparative in vitro dissolution and in vivo bioavailability of commercial amlodipine tablets. Trop J Pharm Res. 2018;17(9):1685-91.
13. Joda AE, Tayo F, Aina BA. Quality assessment of ciprofloxacin tablets obtained from community pharmacies in Lagos, Nigeria. Ife J Sci. 2018;20(1):155-68.
14. Alsaifi A, Alyahawi A. Quality assessment of different brands of paracetamol tablets in Yemeni market. J Pharm Res. 2018;3(4):39-43.
15. Grdešič P, Vrečer F, Ilić I. Flow and compaction properties of hypromellose: new directly compressible versus the established grades. Drug Dev Ind Pharm. 2016;42(11):1877-86.
16. Shah RB, Tawakkul MA, Khan MA. Comparative evaluation of flow for pharmaceutical powders and granules. Aaps Pharmscitech. 2008;9(1):250-8.
17. Alyahawi A, Abdulmajed A. Quality control assessment of different brands of ciprofloxacin 500 mg tablets in Yemen. Univ J Pharm Res. 2018;3(4):31-6.
18. Othman GQ. Quality assessment of seven brands of albendazole tablets marketed in Yemen. Yemeni J Med Sci. 2017;11(1):46-52.
19. Igboasoiyi AC, Offor AC, Egeolu AP. Quality assessment of various brands of ciprofloxacin hydrochloride tablets sold in Uyo Metropolis. Niger J Pharm Appl Sci Res. 2018;7(2):89-93.
20. Osonwa UE, Abali SO, Chukwu KI. Quality assessment of fifteen different brands of ciprofloxacin hydrochloride tablets marketed in Anambra State. Nigeria. Afr J Pharm Res Develop. 2016;8:1-8.
21. FDA U. Guidance for industry: dissolution testing of immediate-release solid oral dosage forms. Food and Drug Administration Center for Drug Evaluation and Research (CDER), USA; 1997.
22. Rahman MM, Jahan FI, Fahim NF, Paul N, Jahan N, Harun-Or-Rashid M, et al. In vitro comparative quality evaluation of leading brands of metronidazole tablets available in Bangladesh. In vitro. 2020;2:63-72.
23. Sarker MR, Deb AK, Chowdhury M, Hossain MI. Investigation and evaluation of the quality features related to comfort of casual shoes in Bangladeshi leading retail brands using physical and chemical standard test methods. Leather Footwear J. 2019;19(1):11.