REPORT

Evaluation and comparison of different brands of domperidone tablets available in Karachi, Pakistan

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Abstract: Domperidone is an anti-dopaminergic drug used for the treatment of nausea, vomiting and dyspepsia. It has also been used in Parkinson's disease. In this study, five different brands of Domeperidone tablets were selected from the local market for evaluation of their quality as the local market is occupied of many competitors for a single generic. The evaluation of Domperidone tablets was done using various pharmacopoeial and non-pharmacopoeial tests. All the test results fell within BP specified limits for all the selected brands i.e. the results for Brands A to E for weight variation, thickness and diameter were satisfactory and within limits. For Brands A to E, the results for hardness and friability were also satisfactory i.e. 4-10kg/cm^{2}and 0.1-0.6% respectively. The results for Brands A to E for disintegration were 2-6 minutes; for dissolution and assay, the results were 89-92% and 95-99% respectively. The results of similarity factor (f_2)also showed that all brands of Domperidone have comparative dissolution profiles.

Keywords: Tablets, Domperidone, quality control, dissolution

INTRODUCTION

Domeperidone is a dopamine antagonist with anti-emetic properties and poor solubility (Barone, 1993), which undergoes extensive pre-systemic metabolism (Martindale-The extra Pharmacopoeia, 2009). It is used for human beings throughout the world for its unique pharmaceutical activity (Meuldermans *et al*., 1981; Brusa *et al*., 2006; Lan *et al*., 2006). A complete and excellent survey of the analysis of domperidone was published in two recent reviews (Gabay, 2002; Henderson A, 2003).

Domperidone (DOM) is chemically (5-chloro-1-{1-[3-(2, 3-dihydro-2-oxo-1H-benzimidazol-1-yl) propyl] -4-piperidinyl} benzimidazolin-2-one) (Indian Pharmacopoiea, 2010; British Pharmacopoiea, 2010). Currently, domperidone is approved only for the treatment of gastroparesis, nausea and vomiting in most countries, with the exception of the USA, where it is not approved (Ahmad, 2006).

Oral route of drug administration is the ideal, convenient and preferred route (Hwang, 1998).Many tests are applied to tablet formulations to deliver their optimum therapeutic effects and the techniques are well reported in the literature (Bos, 1991; Ceshel, 1999).The rationale of carrying out optimization is to opt for the best possible formulation from both pharmaceutical and consumer point of view. Various quality control tests, compendial and non-compendial, (US Pharmacopeia National Formulary USP. 2004) are employed for the formulation of a tablet so that the final tablet has all the essential properties and should be stable as well (Aulton, 2002). Proper choice of disintegrants and its steadiness of performance are essential to the formulation development of such tablets (Na Zhao and Augsburger, 2005). The compression force used to produce a tablet and the chemical component in the formula can also extend disintegration time which then affects drug dissolution rate and bioavailability.

MATERIALS AND METHODS

The chemical and pharmaceutical equivalence of five different brands of Domperidone tablets were evaluated which were collected from the local market of Karachi, Pakistan. These samples were then coded as brand A, B, C, D and E. The physical and chemical tests done for all the brands included weight uniformity, hardness test, thickness test, friability test, disintegration, dissolution, and assay for the active component. Brand A was taken as reference in this study.

Physical evaluation

Weight variation test

Analytical balance (Mettler Toledo B204-S, Switzerland) was used for the weighing of individual tablets of each Domperidone brand. The average weight and standard deviation were calculated (table 1).

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Hardness test

20 tablets from each brand were taken randomly and tested (OSK Fujiwara Hardness Tester, Tokyo, Japan). Table 1 shows mean ±S.D. results of each brand.

Thickness test

The thickness of 20 tablets was determined (Seiko Brand, 0-150 mm, China) and results are shown in table 1.

Friability test

From each brand, 20 tablets were taken randomly to determine the loss in weight (table 2), using Roche Friabilator (Erweka, Apparatobau, Germany).

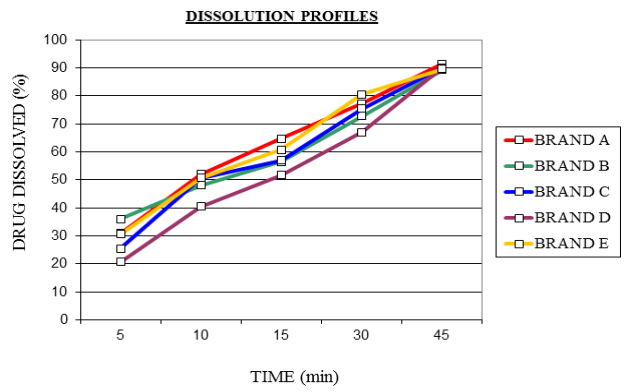
Quality control tests

Disintegration test

6 units at a time were evaluated for disintegration (Erweka ZT-2 Husenstamn, Germany) using 900 ml of distilled water, maintained at 37°C. Results are shown in table 2.

Assay of Domeperidone tablets

Twenty tablets were randomly selected, weighed and crushed. Reference and sample solutions were prepared using water and isopropyl alcohol and the solution was filtered using Wattman filter paper no. 41 (Collin Dollery, 1999**).** The absorbance of both reference and sample solutions was measured spectrophotometrically (UV Spectrophotometer 150-02, Shimadzu Corporation, Kyoto, Japan) at 286.5 nm (λ_{max}), using isopropyl alcohol as blank solution. Results are shown in table 2.



Graph 1: Graph for dissolution profiles of Domeperidone tablets.

Dissolution studies

Dissolution of Domperidone tablets was determined using USP apparatus II, at 50 rpm (Erweka DT700, Husenstamm, Germany) with six replicates. The brands were tested using 900 ml of 0.1N HCl maintained at 37°C ±5°C. Ten ml from the units were drawn at definite time intervals for each brand and replaced with fresh dissolution medium in order to maintain sink condition. Absorbance of the sample preparation and that of standard were taken at 286.5 nm using simulated gastric fluid without pepsin as blank. Drug concentrations were measured spectrophotometrically (UV Spectrophotometer 150-02, Shimadzu Corporation, Kyoto, Japan). Cumulative percentages of drugs dissolved from the different brands were calculated and the results are shown in the table 2.

Dissolution profiles comparison

The use of similarity factor (*f2*) used provides simple means to compare the data and is the model independent method. The similarity factor (*f2*) is a logarithmic reciprocal square root transformation of the sum of squared error. It is a measurement of the similarity in the dissolution % of two curves as in Eq. [1].

$$f_2 = 50 \times \log \left\{ \left(1 + \frac{1}{N} \sum_{t=1}^{n} (R_t - T_t)^2 \right)^{-0.5} \times 100 \right\} \quad (1)$$

Where:

N is the number of dissolution sample times and *Rt* and *Tt* are the individual or mean percents dissolved at each time point for the reference and test products respectively.

The difference factor can also be calculated with Eq. **2**,

$$f_1 = \left\{ \left(\sum_{t=1}^{n} |R_t - T_t| \right) / \sum_{t=1}^{n} R_t \right\} \times 100 \quad (2)$$

Where:

Rt and *Tt* are the percentage release of reference and test brands respectively.

From a statistical point of view, this method seems to be less discerning than other methods. According to the FDA guidance, *f2* values of 50-100% ensure sameness or equivalence and *f1* values less than 50% ensure the difference of two dissolution profile. The dissolution profiles may be accepted as alike without further mathematical evaluation when more than 85% of the drug is dissolved within 15 min. (Hadjiioannou, TP, 1993).

RESULTS

In this study, various pharmacopoeial and non pharmacopoeial tests i.e. were employed on five different brands of Domperidone tablets whose results are shown in tables 1 and 2. The results show that these formulations, though having Domperidone as their active ingredient, demonstrate slightly different performance but all within specification limits (BP, 2010). The results for Brands A to E for weight variation, thickness and diameter were within limits. For Brands A to E, the results for hardness and friability were also satisfactory i.e. 4-10kg/cm^{2}and 0.1-0.6% respectively. All Domeperidone tablets disintegrated in 6 minutes whereas for dissolution and assay, the results were 89-92% and 95-99% respectively. Comparative dissolution profiles were observed for all brands of Domperidone after calculating results of similarity factor (f_2).

Table 1: Assessment of various parameters for different brands of Domeperidone tablets

Formulation	Weight variation (mg) (S.D.) n=20	Diameter (mm) (S.D.) n=20	Hardness (kg) Mean (S.D.) n=20	Thickness (mm) Mean (S.D.) n=20	Friability (%)
A.	99.79±0.81	6.50±0.004	7.15±0.40	2.99±0.01	0.1
B.	193.29±1.27	7.03±0.014	9.85±0.75	4.37±0.02	0.5
C.	100.83±1.19	6.07±0.083	4.25±0.51	3.01±0.01	0.3
D.	181.19±1.50	8.03±0.018	6.70±0.56	3.54±0.02	0.4
E.	159.81±1.03	7.22±0.015	6.35±0.69	4.01±0.01	0.6

(*n=20 tablets for all above tests)

Table 2: Assessment of different parameters for various brands of Domeperidone tablets

Formulation	Disintegration test n= 6 (min)	Dissolution test n= 6 (%)	Assay (average drug content) n=20 (%)	f2 results (%)
A.	5.95±0.78	91.38%±0.95	99.2%±0.96	-*
B.	3.33±0.22	89.77%±0.82	97.4%±0.70	63.761
C.	3.18±0.57	89.95%±0.63	96.3%±0.40	67.262
D.	2.70±0.43	90.28%±0.45	95.7%±0.37	50.117
E.	2.31±0.80	89.77%±0.91	95.3%±1.2	78.364

(*Brand A taken as standard for f2 calculations)

DISCUSSIONS

During the manufacturing process of the tablets, difference in use of excipients, particle size distribution of granules, etc can affect tablet performance to a great extent (Pifferi G, 1999; Pifferi G and Restani P, 2003; Fichtner F, 2005; Rohrs BR, 2006; Virtanen S, 2010)**.** The weight variation test is a valid indication of the corresponding difference in the drug content (Rawlins EA, 1995)**.** Analysis of weight variation showed that mean weights from Brand A to E were within BP specified limit. Hardness was found to be 4-10 kg/cm^2. The diameter and thickness of all the tablets was also satisfactory (table 1). All the brands of Domperidone tablets showed satisfactory friability test results as well (table1).

Disintegration test is employed to ensure that the drug substance is fully available for dissolution and absorption from the gastrointestinal tract (Block LH and Yu ABC, 2001)**.** All Domperidone tablets disintegrated rapidly in less than 6 minutes (table 2). The test for content uniformity showed 90-110% results within 45 minutes (table 2) rendering the results as satisfactory for all the brands. The dissolution test is *in vitro* control procedure that measures the time required for certain percentage of the drug substance in a tablet to go into solution under a specified set of conditions; the pH of the medium used should be controlled and should simulate the biological conditions (Siewert M, 2003). Dissolution test results for all Domperidone brands showed satisfactory % release (table 2). f_2 (similarity factor) test was applied taking Brand A as reference standard and results from table 2 show that it was greater than 50% for all the brands. (graph 1) presents the dissolution profiles of various Domperidone brands, showing comparable results for all of them.

CONCLUSION

The evaluation on different brands of generic drugs available in the local market should be encouraged to have a check on their quality and also market price. Such studies will be helpful to promote rational drug therapy and will also minimize health burden in the community. Further *in vivo* studies can also be performed to evaluate the pharmacokinetic parameters of the tablets.

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