RADS-JPPS Vol 3 (2), December 2015, 89-93

Pharmaceutical Equivalenceand Bioequivalence Study of Domperidone by Using UV Spectrophotometric Technique

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ABSTRACT

Domperidone is a dopamine receptor antagonist that is used to relieve symptoms of nausea and vomiting in adults and children by inhibiting Chemoreceptor triggerzone's (CTZs). It is also used to relieve symptoms of indigestion or feelings of discomfort or fullness in the stomach mostly in adults. Assay of Domeperidone through simple spectrophotometric method comparison has been made between their two brands (Drug A and B) dispersible tablets having same wavelength 222nm, by making various dilutions of both brands and examining their efficacy and effectiveness under the acidic and basic medium.

Keywords: *Domperidone,Chemoreceptor trigger zone's (CTZs),Spectrophotometric Method*

INTRODUCTION

Domperidone(5-chloro-1-(1-(3-(2-oxo-1-Benzimidazolinyl)propyl)-4-piperidyl)-2-benzimidazolinone), [1]It hasmolecular formula (C22H24ClN5O2) and (pKa Strongest Acidic value is 12.52) while (pKa Strongest Basic value is 7.03).[1] Itis a weak base havinggood solubility in acidic pH whereas in alkaline pH its solubility is mostly reduced. [1]Domperidone is basically a dopamine-2 receptor antagonist. It acts as an antiemetic and a prokinetic agent by producing its effects on the chemoreceptor trigger zone (CTZ) and motor function of the stomach and small intestine. [1] It does not cause any adverse neurological symptoms because it has minimal penetration through the blood-brain barrier.[1] Thus, it provides an excellent safety profile for long-term administration orally in the prescribed doses[3]. Officially Domperidoneis used for the treatment of gastro paresis (reduced GI symptoms and hospitalizations, enhanced quality of life, and accelerated gastric emptying of a solid meal to a normal rate, successfully treats on a long-term outcome basis and has an excellent safety profile.)[1], dyspepsia, heartburn, epigastric pain and any condition that cause chronic nausea and vomiting. [3] Domperidone does not exaggerate the extra pyramidal side effects of neuroleptic drugs. [1]In Parkinson's disease it has also been used. [1]The marked differences occur in the effect of intra cerebrally and systemically administered domperidone in antagonizing the behavioral effects of dopamine. [5]At 10-30 minutes peak plasma concentrations are achieved after IM and oral administration while at 1 to 2 hrsafter rectal administration of suppositories. Systemic bioavailability of IM domperidone is about 90%, whereas oral is 13 to 17%.[4]Due to 'first pass' and hepatic gut wall metabolism the systemic bioavailability is probably low.[5]The plasma protein binding of tritiateddomperidoneinhumanisapproximately 92%.[5]By hydroxylation and oxidative N-dealkylationDomperidone undergoes rapid and extensive biotransformation.[2]That part

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of the dose recovered in the urine is inthe greatest proportion in the form of glucuronide conjugates of the metabolite formed by oxidative N-dealkylation.[5]Domperidone has elimination half-life of 7.5 hours in healthy subjects and may prolong to up to 20.8 hours in patients having severe renal dysfunction.[5]

QT interval prolongation may cause sudden cardiac death and usually occur due to the worsening of existing heart conditions which leads to ventricular arrhythmia (VA) that caused by Domperidone. [1] Estimation of domperidone involves absorbance measurement at 285 nm corresponding to the respective absorption maxima. [1]

The most prescribed brand of domperidone is Drug B (by Janssen-Cilag Pharmaceutica, Belgium) and another brand Drug A (by Atco Laboratories Pakistan). Drug B is multinational brand while Drug A is local brand of domperidone.

EXPERIMENTAL

Assay

UV visible 1601 Shimadzu double beam spectrophotometer was used to measurement of spectra. The solvent which are used for the assay was water.

Material and Reagents

Pyrex glass wares were used which includes measuring cylinder, volumetric flask and pipette, mortar and pestle, weighing machine and. For initially washing of glass wares we use chromic acid afterward we use water and finally rinsed with double distilled water (freshly prepared) and the tablets of different brands of Domeperidone.

Wavelength Selection

About 200 ppm solution of two brands of Domeperidone (Drug B and Drug A) were accurately prepared in distilled water . These solutions were scanned in the 200-400 nm UV region. The wavelength maxima (λmax) was observed at 222 nm and this wavelength was adopted for absorbance measurement.

Sample Preparation

The two different brands (Drug B and Drug A).The tablets of each brand have same batch number and were labelled to contain Domeridone 10mg per tablet.

10 tablets of each brand of Domeperidone (Drug B, Drug A) from the marketed sample were weighed and crushed uniformly with the help of a mortar and pestle. By calculating the average weighed sample powder equivalent to 20 mg of Domepridonewas transferred into a volumetric flask containing 10mL distilled water. The solutions were sonicated for about 5 min and than make up volume up to 100 ml with water to produce 200ppm solution.

Dilutions

Prepare serial dilutions of 100ppm, 50ppm and 25ppm from 200ppm solution. Take 50ml from 200ppm solution in a volumetric flask and make-up the volume upto 100ml with distilled water to produce 100ppm solution. Then from 100ppm solution take 50ml solution in a volumetric flask and make-up the volume upto 100ml with distilled water to produce 50ppm solution. Now take 50ml again from 50ppm solution in a volumetric flask and make-up the volume with distilled water upto 100ml to produce 25ppm solution.

Procedure

After preparation of tablet solutions, strength of solution 200 ppm, 100ppm, 50ppm, 25ppm in 100 ml, absorbance of the each sample preparations in 1cm cell at the wavelength of maximum absorbance at about 222nm, using a spectrophotometer, using the blank solution.

ACID-BASE

Material and reagents

Pyrex glass wares were used which includes test tubes, volumetric flask, pipette. For initially washing of glass wares we use chromic acid afterward we use water and finally rinsed with double distilled or DI water (freshly prepared).

.Analytical grade reagents were used which includes 0.1N Sodium hydroxide, 0.1N Hydrochloric acid and de-ionized water or double distilled water and the tablets of different brands of Domeperidone.

Instruments

UV-visible Spectrophotometer with a quartz cuvette (Ultraviolet Lamp: Serial NO: N 045571, LF-204.LS, '4W-254 and 365 nm', T80 UV-VI spectrometer) 'PG Instrument', Weighing Balance (Item PA214C) of Pioneer OHAIUS, and Water Bath with 'HH-4' (digital and constant temp tank.)

Preparation of 0.1 N Sodium hydroxide and Hydrochloric acid

4 grams of sodium hydroxide was transferred in 100ml volumetric flask and was dissolved in small quantity of water and finally the volume was made up to mark of the flask with de-ionized water.

8.3ml analytical grade hydrochloric acid having 37% purity and 12N normality was transferred in a volumetric flask and the final volume was made up to the mark of flask with DI water.

Preparation of solution of different brands ofDomeperidone (Drug B&Drug A)

10 tablets of each brand of Domeperidone(Drug B, Drug A) from the marketed sample were weighed and crushed uniformly with the help of a mortar and pestle. The required amount of the powder material was weighed on the weighing balance to prepare the solution of 100ppmequivalent to 10 mg of Domeperidoneand was dissolved in small quantity of DI waterformaking the solution. Finally the volume was made up to the mark with de-ionized water. Shake for even distribution.

Procedure for study

To determine the effect of acid and base on

Observations:

Table 1. Absorbance of different brands of domperidone

Drug B		Drug A	
Concentration	Absorbance	Concentration	Absorbance
200	1.017	200	1.027
100	0.569	100	0.616
50	0.316	50	0.368
25	0.121	25	0.169

Table. 2. Absorbance of different dilutions of two brands of domperidone in different pH and at different time interval

	Drug B		Drug A	
Time (min.)	0.1N HCl	0.1N NaOH	0.1N HCl	0.1N NaOH
0	1.466	0.841	1.165	1.54
30	0.179	-0.03	0.056	0.223

Domeperidone, 5 ml of 100 ppm solution of Domeridone brands (Drug B&Drug A) were transferred into two separate test tubes then 5 ml of 0.1 N hydrochloric acid was added in one test tube and 5 ml of 0.1 N sodium hydroxide was added in another test tube respectively of each brand. Then we take their absorbance at time zero by using spectrophotometer at wavelength max 222nm. Then the tubes were left for 30 minutes. The absorbance of the solutions was determined using spectrophotometer at wavelength max 222nm.

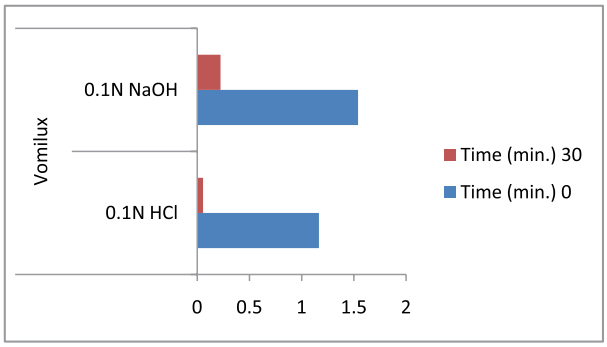

Fig. 1. Brand A

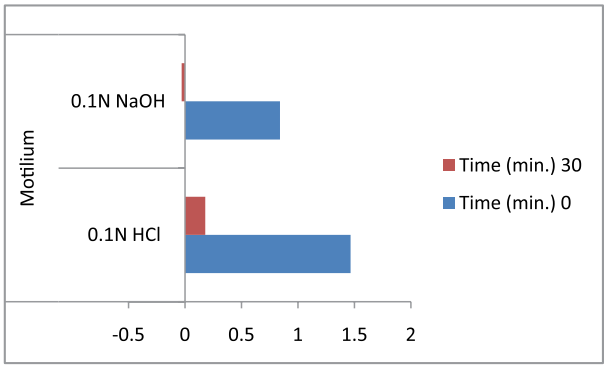

Fig. 2. Brand B

RESULT AND DISCUSSION

Pharmaceutical assay was carried out by using spectrophotometer on two brands of domperidone(Drug B and Drug A). About 200 ppm solution of two brands of Domeperidone were accurately prepared in distilled water and observed the maximum wave length which is 222nm . Prepare serial dilutions of 100ppm, 50ppm and 25ppm solutions. After the preparation of different strength of solution, take absorbance at 222nm by using spectrophotometer against the solvent blank and the assay was determined by comparing with the absorbance of available brands. Our result reveals that among all the two brands of Domperidone that is Drug B and Drug A. In Alkaline medium Drug B shows was highest percent assay which is 60 % as compare to acidic medium, while the percent assay of the Drug A in acidic medium shows highest 40% as compare to alkaline medium.

The main objective of this study is to determine the effect of acidic and basic medium of two different brands (Drug B and Drug A) of domperidone. For this reason we prepared a 200ppm solution of two different brands of Domperidone. To determine the effect of acid and base on domperidone the 200 ppm solution of Drug B and Drug A was transferred in to four separate test tubes that contain 5ml of acid Hcl and base NaOH separately. After preparing the test tubes we determined the absorbance at time "0" initially and after that thetubes were left for 30 minutes. The absorbance of the solutions was determined using spectrophotometer at wavelength max 222nm. The result reveals that the drug(Drug B) is degraded more in acidic medium at time "0" and 30 mints as compare to basic medium,while the other brand of the drug which is Drug A is degraded more in basic medium at time "0" and 30 mints as compare to acidic medium. The absorbance of solution (Drug B) was increased at time 0 to 1.466 and after 30 mints 0.179 when subjected to acidic medium and when the solution was subjected to alkaline medium the absorbance decreases many folds as compared to acidic medium see Fig. 1&2. In alkaline medium the absorbance was found to be 0.841 at time 0 and -0.03 at 30 mints. on the other hand the absorbance of solution(Drug A) was increased at time 0 to 1.54 and after 30 mints 0.223 when subjected to basic

medium and when the solution was subjected to acidic medium the absorbance decreases many folds as compare to acidic medium . In acidic medium the percent availability of the Drug B was 25% and in alkaline medium the percent availability was 60% while the percent availability of the Drug A in acidic medium 40% and in alkaline medium the percent availability was 25%.We have done these categories of studies in our previous investigations.[6-9]

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