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Determination of certain proton pump inhibitors in pharmaceutical formulations using spectrophotometry

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ABSTRACT: Simple, sensitive and accurate spectrophotometric method for the determination of certain benzimidazole class of antiulcer drugs has been developed. The method is based on the reaction of omeprazole (OMZ), lansoprazole (LNZ), pantoprazole (PNZ), rabeprazole (RBZ) and esomeprazole (EMZ) with iron (III) and subsequent complexation with bathophenanthroline which yields a orange coloured product with maximum absorption at 520 nm. The commonly encountered excipients and additives along with the drug did not interfere with the determination. Antiulcer drugs in the range of 100-3500 ng ml^{-1} for LNZ, PNZ and RBZ, 60-2600 ng ml^{-1} for OMZ and 160-3400 ng ml^{-1} for EMZ can be determined by this method. Results of the analysis of commercial capsules/tablets (omelac capsule, lanpro capsule, pan tablet, rabeloc tablet and raciper tablet for OMZ, LNZ, PNZ, RBZ and EMZ, respectively) by this procedure agree well with those of the reported method.

Key words- bathophenanthroline, antiulcer drugs, spectrophotometry, determination.

I.INTRODUCTION

Antiulcer drugs are a class of drugs, exclu sive of the antibacterial agents, used to treat ulcers i n the stomach and the upper part of the small intesti ne. The proton pump inhibitors block the secretion of gastric parietal cells. Ulcer is a common disorder of the gastrointestinal system, which causes much discomfort to patients, disrupting their daily routines and causes mental agony. It is generally more common in those who keep themselves in hurry, become worry and consume curry [1] . Peptic ulcer disease can be characterized by inflamed lesions or excavations of the mucosa and tissue that protect the gastrointestinal tract. Damage of mucus membrane which normally protects the oesophagus, stomach and duodenum from gastric acid and pepsin causes peptic ulcer [2].

Various methods have been proposed for the determination of antiulcer drugs include; indirect argentometry [3], capillary electrophoresis [4], polarography [5-7], voltammetry [8,9], flow injection analysis [10,11], and high performance liquid chromatography [12-17]. Simple methods based on UV-Visible spectrophotometry have of late become an accepted analytical tool for the assay and evaluation of drugs.

Visible spectrophotometric methods are convenient, simple, sensitive and are relatively inexpensive. The spectrophotometric methods for the determination of antiulcer drugs employ different routes in the determination of chromogen produced and these are of four types. Type I method involves the oxidative coupling of the drug with an electrophilic reagent, in the presence of an oxidant and measurement of the resulting chromophore [18]; method of type II involves the use of electron acceptor and the antiulcer drug as electron donar in which the resultant product is coloured molecular complex [19]. Type III method consists in the formation of a charge transfer complex between the drug and the reagent [19]. Finally, Type IV method is based on the use of a suitable oxidant to produce colour for the spectrophotometric measurement [20]. Methods of Type I, II and III are lengthy; however, the method of Type IV although is simple and straightforward, but lacks selectivity as the coloured product is presumed to be the radical cation of the drug. Also, the above methods have not utilized a co-ordinate complex as a chromogen for the determination of antiulcer drugs. These deficiencies have encouraged the authors to develop a simple, sensitive, rapid and reliable method for the determination of antiulcer drugs.

The work describes a new method for the determination of antiulcer drugs like OMZ, LNZ, PNZ, RBZ and EMZ and it is based on the reduction of iron(III) to iron(II) by the drugs and subsequent complexation with bathophenanthroline which produces a orange coloured product having a maximum absorption at 520 nm.

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II.EXPERIMENTAL

Apparatus

UV-VIS spectrophotometer UVIDEC-610 type with 1.0-cm matched cell (Jasco, Tokyo, Japan) was employed for measuring the absorbance values.

Reagents

Omeprazole (OMZ), lansoprazole (LNZ), pantoprazole (PNZ), rabeprazole (RBZ) from Cipla, India, commercial tablets of esomeprazole (EMZ) ammonium iron(III) sulphate from BDH, India and bathophenanthroline from SRL, India were used. All other chemicals and solvents used were of analytical grade. Double distilled water used throughout. Weighed (100 mg) samples of drugs were dissolved in about 10.0 ml of alcohol and the solution was diluted with distilled water in 100-ml volumetric flask. The solutions were stored in a refrigerator and diluted daily to get the required concentrations. Aqueous solution of 0.001 N ammonium iron(III) sulphate containing few drops of dilute sulphuric acid and 0.2% (w/v) of bathophenanthroline solution were prepared in double distilled water and alcohol, respectively.

Procedure

Assay with iron(III) and bathophenanthroline: Aliquots of standard solutions of OMZ, LNZ, PNZ, RBZ and EMZ were transferred into calibrated flasks (25-ml). To each flask was added ammonium iron(III) sulphate (2.0 ml) and bathophenanthroline (2.0 ml). The flasks were kept aside for 10 min. The solutions were made up to the volume with distilled water. The absorbance was measured at 520 nm against the corresponding reagent blank and calibration graphs were constructed. The optical characteristics are presented in Table 1.

Table 1: Optical characteristics of the antiulcer drugs as determined using bathophenanthroline

Parameters	**OMZ**	**LNZ**	**PNZ**	**RBZ**	**EMZ**
Colour	Orange	Orange	Orange	Orange	Orange
λ_{max} (nm)	520	520	520	520	520
Stability (h)	24	24	24	24	24
Beer's law (ng ml^{-1})	60-2600	100-3500	100-3500	100-3500	160-3400
Recommended drug concentration (ng ml^{-1})	1400	2000	2200	2000	2000
Molar absorptivity (L mol^{-1} cm^{-1})	8.91 x 10^4	8.10 x 10^4	7.22 x 10^4	7.13 x 10^4	6.99 x 10^4
Sandell's sensitivity (µg cm^{-2})	0.008	0.005	0.005	0.008	0.006
Regression equation*					
Slope (a)	0.3176	0.3345	0.2754	0.2134	0.3891
Intercept (b)	-0.0064	0.0098	0.0256	0.0432	0.0245
Correlation coefficient	0.9767	0.9874	0.9453	0.9421	0.9851

*y=ax+b where x is the concentration of OMZ, LNZ, PNZ, RBZ or EMZ in µg ml^{-1}

Pharmaceutical preparations

Twenty capsules each of omeprazole and lansoprazole were emptied carefully and the mass of the collected contents was determined. The capsule contents were finely powdered in a mortar. In case of pantoprazole, rabeprazole and esomeprazole twenty tablets each were finely powdered. An accurately weighed 50 mg of the powdered drug was dissolved in about 10.0 ml of alcohol and filtered through a Whatman No.42 filter paper. The filtrate was made up to 100 ml with distilled water in a volumetric flask. A suitable volume of the filterate was accurately diluted with water so as to obtain a sample concentration of 10 µg ml^{-1}. An aliquot of this solution was treated as per the procedure described earlier for the determination of antiulcer drugs.

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III.RESULTS AND DISCUSSION

Omeprazole (OMZ), lansoprazole (LNZ), pantoprazole (PNZ), rabeprazole (RBZ) and esomeprazole (EMZ) belong to a class of antisecretory compounds. These compounds are acid labile and reversibly transformed in acidic medium to a sulfenamide [21]. They are referred to as proton pump inhibitors (PPI) being introduced for the management of duodenal ulcer, gastric ulcer or pathogenic hyper secretory condition [22]. Gastric PPI is a prodrug that requires an acid induced activation. It is a weak base that is converted to its active form by gastric acid before acting on the proton pump. It inhibits gastric acid secretion by covalently binding to the proton pump ($H^{+/}K^{+}$ AT Pase) [23].

Bathophenanthroline is used as a bacteriostatic, fungistatic, antifibrillating agent, inactivator, paint and oil drier, enzyme inhibitor and activator, antihelmintic and bactericidal agent, polymerization agent, catalyst and electroplating agent [24].

The method for the determination of antiulcer drugs involves the reaction of these drugs with iron(III) salts, in the presence of bathophenanthroline to produce a orange colour with maximum absorption at 520 nm. The reaction involves the reduction of iron(III) to iron(II) by OMZ, LNZ, PNZ, RBZ and EMZ which subsequently reacts with bathophenanthroline to give a orange colour in neutral medium.

Beer's law limits, molar absorptivity, sandell's sensitivity, regression equation and correlation coefficients obtained by least squares treatment of these results are given in Table 1.

Spectral characteristics

An orange coloured product with maximum absorbance at 520 mm was formed when OMZ reacts with ammonium iron(III) sulphate, in the presence of bathophenanthroline in neutral medium.

Optimization of analytical variables

Maximum and constant absorbance values were obtained when the standard flasks were kept aside for 10 min after adding the reagents to the drug solutions which remained stable for 24 h. It was found that a 0.001N ammonium iron(III) sulphate in the range 1.0-3.0 ml, 0.2% (w/v) of bathophenanthroline in the range of 1.0-4.0 ml were necessary to get maximum intensity of colour and stability. Hence, 2.0 ml each of ammonium iron(III) sulphate and bathophenanthroline solutions were found appropriate.

The sequence of addition of ammonium iron(III) sulphate, bathophenanthroline and drug solution was studied via the formation of the orange complex. Absorbance or colour of the product did not change appreciably when the order of addition of these reactants was varied.

Table 1 shows the linear calibration ranges and equation parameters for different drugs. Separate determinations at different drugs. Separate determination at difference concentrations of each drug gave a coefficient of variation not exceeding 2%.

Stability

The coloured product remained stable for 24 h.

Interference

The effect of common ingredients usually present in pharmaceutical preparations was studied, by taking omeprazole as a representative drug. Commonly encountered pharmaceutical additives and excipients such as glucose, lactose, dextrose, starch, sodium alginate and sodium lauryl sulphate did not interfere, while vitamin C was found to interfere seriously. The results are presented in Table 2.

Table 2: Recovery of omeprazole (OMZ) in the presence of excipients and other substances

Material	Amount (mg)	% Recovery of OMZ* ±RSD**
Glucose	50	100.2 ± 0.45
Lactose	50	99.8 ± 0.76
Dextrose	50	99.4 ± 0.86
Magnesium stearate	50	100.6 ± 0.78
Starch	50	98.2 ± 1.04
Gum acacia	50	97.5 ± 0.84
Talc	50	100.8 ± 0.62
Vitamin B_6	50	99.4 ± 0.74
Carboxyl methyl cellulose	50	98.6 ± 0.70

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Sodium alginate	50	99.4 ± 0.96
Vitamin C	10	#>50<60

*1000 ng ml^{-1} of OMZ taken, ** relative standard deviation (n=5), #erratic values

Analysis of pharmaceutical formulations

Commercial formulations (capsules/tablets) containing OMZ, LNZ, PNZ, RBZ and EMZ were subjected to analysis by the proposed new method. The values obtained by the proposed and the reference methods for the pharmaceutical preparations were compared statistically using the F- and t- tests and no difference was found significantly. The results are summarized in Table 3.

Table 3: Determination of certain antiulcer drugs in commercial samples by the proposed method using bathophenanthroline

Drug	Label claim (mg per drug)	*Recovery% ± SD**	Additional analyte added (mg)	*Recovery% ± SD**	Reported method found%
Omelac capsule (Omeprazole)	20	100.4± 0.86 F=3.67(4.34) t=2.94 (1.82) (n=5)	20	100.2 ± 0.86	99.4 ± 0.88 (n=5)
Lanpro capsule (Lansoprazole)	15	99.4 ± 0.98 F=3.56(4.67) t=2.87 (3.54) (n=5)	15	98.6 ± 0.65	99.6 ± 0.78 (n=5)
Pan tablet (Pantoprazole)	20	100.8 ± 0.70 F=3.86(5.32) t=3.44 (2.38) (n=4)	20	99.4 ± 0.56	100.5± 0.82 (n=4)
Rabeloc tablet (Rabeprazole)	20	98.5 ± 0.86 F=2.87(2.12) t=3.24 (2.86) (n=7)	20	100.8 ± 1.14	98.4 ± 0.74 (n=7)
Raciper tablet (Esomeprazole)	20	98.6 ± 0.78	20	98.6 ± 0.64	-

*proposed method **standard deviation

The figures in parentheses are the tabulated F- and t-values at 95 % confidence level

IV.CONCLUSION

Ulcer has a known history for morbidity and mortality in humans. Ever since the age of Hippocrates and till present times, drastic changes were seen in disease pathophysiology and treatment goals. Ulcer has a known history for morbidity and mortality in humans. Ever since the age of Hippocrates and till present times, drastic changes were seen in disease pathophysiology and treatment goals.

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