Academic Sciences International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 5, Suppl 4, 2013

Research Article

A NEW SENSITIVE SPECTROPHOTOMETRIC METHODS FOR DETERMINATION OF ESOMEPRAZOLE MAGNESIUM TRIHYDRATE IN DOSAGE FORMS

[1]HASNA MANDIL*, [2]AMIR ALHAJ SAKUR AND [3]AYMAN ADHAM ALLABBAN

[1]Dept. of Chemistry Faculty of Science Aleppo University Syria, [2,3]Dept. of Analytical and Food Chemistry Faculty of Pharmacy Aleppo University Syria. *Email: mandil@scs-net.org

Received: 17 July 2013, Revised and Accepted: 03 Oct 2013

ABSTRACT

A new rapid, simple, sensitive, and accurate spectrophotometric method have been developed, to determine of esomeprazole (EMZ) in its dosage forms. The method was based on the formation of a charge-transfer complexe between chloranilic acid (CAA) as a π-acceptor and EMZ as an n-donor in methanol-acetonitril medium. The maximum absorbance of the coloured complex occurred at 521-525 nm and the molar absorptivity $4.932x10^3$ $L.mol^{-1}.cm^{-1}$. The molar combining ratio and the optimum assay conditions were studied. Under optimum conditions, the stoichiometry of the reactions between EMZ and the CAA was found to be 1:2 and 1:4. The linear ranges for the proposed method were 1.250–150.00 μgmL^{-1} .The limit of detection (LOD) and limit of quantification (LOQ) was found to be 0.156$\mu g.mL^{-1}$ and 0.473 $\mu g.mL^{-1}$ respectively, with RSD was 4.6% . The proposed method was successfully applied to the analysis of esomeprazole magnesium in pure and pharmaceutical dosage forms with average recovery of 98.26–100.12% .The results obtained agree well with the contents stated on the labels.

Keywords: Esomeprazole magnesium; Spectrophotometry; Chloranilic Acid.

INTRODUCTION

Esomeprazole is bis(5-methoxy-2-[(S)-[(4-methoxy-3,5-dimethyl-2-pyridinyl) methyl] sulfinyl]-1H-benzimidazole-1-yl) magnesium trihydrate Fig.1. Its molecular formula is $(C_{17}H_{18}N_3O_3S)_2$ $Mg.3H_2O$ with molecular weight of 767.2 as a trihydrate and 713.1 on an anhydrous basis. The stability of esomeprazole magnesium is a function of pH, it rapidly degrades in acidic media, but it has acceptable stability under alkaline conditions. At pH 6.8 (buffer), the half-life of the magnesium salt is about 19 hours at 25°C and about 8 hours at 37°C**[1,2]**. It provides better acid control than current racemic proton pump inhibitors and has a favourable pharmacokinetic profile relative to omeprazole**[3]**. A detailed survey of literature revealed the estimation of omeprazole by gas chromatographic method[4], TLC[5] and several HPLC methods**[6-12]**.

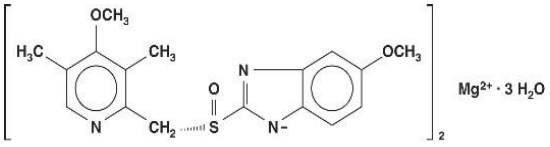

Fig. 1: Scheme of Esomeprazole magnesium trihydrate

UV spectrophotometric methods have been developed for the estimation of Esomeprazole in bulk and pharmaceutical formulations. Esomeprazole has the absorbance maxima at 303nm (Method A), and in the first order derivative spectra, showed zero crossing at 303nm, with a sharp peak at 292nm when n=1 (Method B), Method C applied was Area Under Curve (AUC) for analysis of Esomeprazole in the wavelength range of 294- 310nm. Drug followed the Beer's Lamberts range of 5-40 μgmL^{-1} for the Method A, B C. Results of analysis were validated statistically and by recovery studies and were found to be satisfactory**[13]**.

Spectrophotometric method has been developed for simultaneous estimation of esomeprazole and domperidone. The method involved solving simultaneous equations based on measurement of absorbance at two wavelengths, 301 nm and 284 nm, 'λmax of esomeprazole and domperidone respectively. Beer's law was obeyed in the concentration range of 5-20 μgmL^{-1} and 8-30 μgmL^{-1} for esomeprazole and domperidone respectively. The method was found to be precise, accurate, and specific. The proposed method was successfully applied to estimation of esomeprazole and domperidone in combined solid dosage form**[14]**.

UV-Vis Spectrophotometric method for the estimation of Esomeprazole in bulk and pharmaceutical dosage form.The solvent used was methanol and chloroform (80:20) using Indigo Carmine reageants and the λ_{max} or the absorption of the drug was found to be 577 and 617 nm. A linear response was observed in the range of 5-35 $mgmL^{-1}$ with as regression coefficient of 0.9997 and 0.9989. The method was then validated for different parameters as per the I.C.H guidelines**[15]**.

The analytical method developed for the estimation of esomeprazole magnesium trihydrate in bulk fluids showed maximum absorbance λ_{max} of 203.5 nm in methanol between 200 nm and 400nm. Linearity studies indicated that estimation of esomeprazole magnesium trihydrate between 2.00 μgmL^{-1} to 10.00 μgmL^{-1} was found to be linear with regression equation of y = 0.1546X -0.00414; (r^2 = 0.999). The method developed was validated for inter and intraday variation, limit of quantitation studies. The SD values of Inter day and Intraday variation studies indicated that the variation is minimum. Limit of Quantitation of esomeprazole was found to be of 1.00 μgmL^{-1}. The above analytical parameters indicated that the developed UV Spectrophotometric method of esomeprazole was simple, accurate and reproducible**[16]**.

Simple, sensitive and selective spectrophotometric methods were developed for the determination of five antiulcer drugs namely, omeprazole (OMZ), lansoprazole (LNZ), pantoprazole (PNZ), rabeprazole (RBZ) and esomeprazole (EMZ) using neocuproine or bathocuproine as reagents. The reaction is based on the reduction of copper(II) to copper(I) by EMZ which subsequently reacts with neocuproine or bathocuproine in neutral medium to produce yellow or orange-red coloured complex with maximum absorbance at 460 or 480 nm, respectively. Beer's law was obeyed in the concentration range 0.2-4.0 μgmL^{-1} with a relative standard deviation ranging between 0.5-1.0 and 0.5-1.1 for the drugs with neocuproine and bathocuproine, respectively. The limits of detection were found to be 0.007-0.024 and 0.01-0.026 μgmL^{-1} and the limits of quantification ranged between 0.019-0.067 and 0.026-0.062 μgmL^{-1} with neocuproine and bathocuproine, respectively. The optimum assay conditions were investigated and the accuracy was found to be 99.3-100.5 % and 99.1-100.7 %, while the correlation coefficients ranged between 0.9830-1.0213 and 0.9896-0.9981 with neocuproine and bathocuproine, respectively. The colour developed was stable for 24 h at room temperature (~ 27 °C). The commonly encountered excipients and additives did not interfere in the determination. Results obtained by this method for the pure drugs and commercial tablets agreed well with those obtained by reported method**[17]**.

Two simple, sensitive and economical spectrophotometric methods have been developed for the determination of esomeprazole magnesium in commercial dosage forms. Method A is based on the

reaction of esomeprazole magnesium with 5-sulfosalicylic acid in methanol to form a yellow product, which absorbs maximally at 365 nm. Method B utilizes the reaction of esomeprazole magnesium with N-bromosuccinimide in acetone-chloroform medium to form α-bromo derivative of the drug peaking at 380 nm. Under the optimized experimental conditions, Beer's law is obeyed in the concentration ranges of 2-48 and 10-100 µg mL^{-1} with molar absorptivity of 2.11 x 10^4 and 4.57 × 10^4 L mol^{-1} cm^{-1} for methods A and B, respectively. The limits of detection for methods A and B are 0.35 and 0.46 µg mL^{-1}, respectively. No interference was observed from excipients commonly present in tablet formulations. Methods A and B are successfully applied to the commercial tablets for the estimation of esomeprazole magnesium with good accuracy and precision. The results compare favorably with the reference spectrophotometric method indicating no significant difference between the methods compared**[18]**.

UV Spectrophotometric method development different pharmaceutical dosage form using ferric chloride**[19-20]** and Indigo Carmine, Methyl orange**[21]**. Hence an attempt has been made to develop new spectrophotometric method for its estimation in bulk and pharmaceutical formulations with good accuracy, simplicity, precision and economy.

In the present work, spectroscopic analytical study for the analysis of esomeprazole in pure and its Syrian pharmaceutical dosage forms through complexation with chloranilic acid in methanol-acetonitrile medium has been applied.

MATERIALS AND METHODS

Apparatus

Spectrophotometric measurements were made in Jasco company (Japan) model V530. UV-Visible spectrophotometer with 1.00 cm quartz cells. The pH measurement was performed with EUTECH coperscan-500. A ultrasonic processor model powersonic 405 was used to sonicate the sample solutions. The solution was kept in a thermostat at 30°C. The diluter pipette model DIP-1 (Shimadzu), having 100 µL sample syringe and five continuously adjustable pipettes covering a volume range from 20 to 5000 µL (model PIPTMAN P, GILSON), were used for preparation of the experimental solutions.

Reagents

Esomeprazole magnesium (98.6%) was of pure from Parabolic Drugs-INDIA, the purity 95.52% as esomeprazole(EMZ), which was determined by HPLC method[22]. Chloranilic acid (CAA) was of analytical grade, alcohols and acetonitril were of extra pure from Merck. A stock solution 3.62x10^{-4} M (250µg.mL^{-1} esomeprazole eq. 258.37µg.mL^{-1} esomeprazole magnesium) was prepared in methanol. This solution was found to be stable for several weeks, if kept in the dark and stored at −4°C. A chloranilic acid 0.0836% (4.10^{-3}M) was prepared in methanol-acetonitril (1:9).

Working standards were prepared daily by added different volumes of stock solutions to 3 mL of reagent chloranilic acid 4.10^{-3}M and diluting to 10 mL with methanol-acetonitril (1:9). The concentration of EMZ (0.750, 0.937, 1.875, 3.75, 7.50, 12.50, 25.0, 50.0, 75.0, 100.0, 125.0, 137.5, 150.0 µg.mL^{-1}). Were used for the analysis of EMZ by the spectrophotometric method after 30 min. The method was based on the formation of a charge-transfer complexe between CAA and EMZ in methanol-acetonitril medium. The colored product was quantified spectrophotometrically using absorption bands at 521 nm.

Sample preparation

A commercial formulations (capsule) were used for the analysis of esomeprazole by using spectrophotometric analysis. The following commercial formulations were subjected to the analytical procedures:

(1) **S-Omepral** (caps), Asia pharmaceutical industries(Aleppo–SYRIA), each tablet contains: 20 or 40mg esomeprazole.

(2) **S-Omepral** (caps), Ibn Al Haytham, Pharma Industries Co. (Aleppo–SYRIA), Each capsule contains: 20 mg esomeprazole.

(3) **New omeprazole** (caps).Syria pharma for medicaments(Aleppo–SYRIA), Each tablet contains: 20 mg esomeprazole.

Crushed eight capsules (or the contents of eight capsules) of each studied pharmaceutical formulations, mix well and weigh equivalent one capsule from powder (contain 20mg or 40 mg EMZ), solve it in 10 ml methanol & 40mL acetonitril by using ultrasonic, filtered over a 100 mL flask and diluting to 100 mL with acetonitril (Stock solution of pharmaceutical formulations).The stock solutions content: 400, 200 and 200µg.mL^{-1} of esomeprazole for pharmaceuticals. Known volumes (2 mL) of the prepared solution were added to 3 mL of reagent chloranilic acid 0.0836% (4.10^{-3}M) and diluting to 10 mL with methanol-acetonitril (1:9). Were used for the analysis of EMZ by the spectrophotometric method after 30 min.

RESULTS AND DISCUSSION

The different experimental parameters affecting the produced color of EMZ: CAA complex were extensively studied in order to determine the optimal conditions for the determination of EMZ.

Spectrophotometric results

UV-Vis spectra by using methanol-acetonitril (1:9) as blank were studied. The esomeprazole magnesium $(EMZ)_2Mg$ solutions do not absorb in range 400-700 nm. The chloranilic acid (CAA) solutions has absorption only at 441 nm. When the EMZ:CAA complex solutions has absorption at 521 nm. The method was based on the formation of a charge-transfer complexe between chloranilic acid (CAA) as a π-acceptor and EMZ as an n-donor in methanol-acetonitril medium.the molar absorptivity are 4.932x10^3 L.mol^{-1}.cm^{-1} (Fig.2).

The effect of temperature: The effect of temperature on the produced adduct was studied. It was found that heating at 30°C was better than heating at a higher temperature.

The effect of time: The effect of time on formation of complex was studied. It was found that better time was 30-60 min.

The effect of solvent: the better solvent was methanol: acetonitril (1:9).

The effect of concentration of CAA: The effect of concentration of CAA on formation of complex was studied. It was found that better concentration was more than 10 times of concentration EMZ.

Composition of $(EMZ)_2Mg$:CAA complex: The composition of EMZ:CAA complex was determined by Job's method of continuous variation method as follows:

Molar ratio method: The stoichiometry of EMZ:CAA complex by molar ratio method according to following equation: A_{max}= f([CAA]/[EMZ], confirms that the ratio of complex EMZ:CAA is equal to 1:2 and 1:4. Where the concentration of $(EMZ)_2Mg$ is constant (2×10^{-4} M) and the concentrations of CAA is change from 0 to 18x 10^{-3} M (Fig. 3).

Calibration curve

The calibration curves for EMZ in pure form through complexation with CAA {$(EMZ)_2Mg$: CAA complex} showed excellent linearity over concentration ranges of 1.250–150.00 µgmL^{-1}, see Fig 4 & 5. The spectra characteristics of the EMZ:CAA solutions as ε, ⌊max, Beer's law, the equation (y=0.00714x+0.0014; y=absorbance, x=concentration of EMZ in µg.mL^{-1}, 0.0014 = intercept and 0.00714 = slope) and the correlation coefficient (R^2=0.9999) are summarized in Table-1.

Analytical results

Spectrophotometric determination of EMZ through complexation with CAA in methanol:acetonitril (1:9) in optimal conditions using calibration curve was applied. The results, which summarized in Table 2 showed that, the determined concentration of EMZ was rectilinear over the range of 1.250 to 150.00 µg.mL^{-1} with relative standard deviation (RSD) was not more than 4.6%. The limit of detection (LOD) and limit of quantification (LOQ) was found to be 0.156µg.mL^{-1} and 0.473 µg.mL^{-1} respectively. The proposed method was validated statistically and through recovery studies. The method was successfully applied for the determination of EMZ in pure and dosage form with percent recoveries from 98.26% to 100.12%. The results obtained from the proposed method have been compared with the official HPLC method[6] and good agreement was found between them.

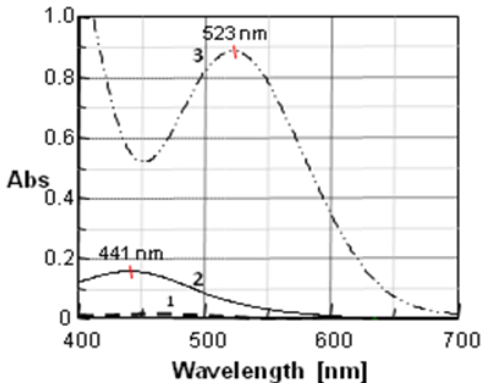

Fig. 2: Vis spectore of: 1. 18x10^{-5} M EMZ, 2. 2-12x10^{-4} M CAA, 3. 18x10^{-5} M complex (18x10^{-5} M EMZ with 12x10^{-4} M CAA; ℓ =1cm)

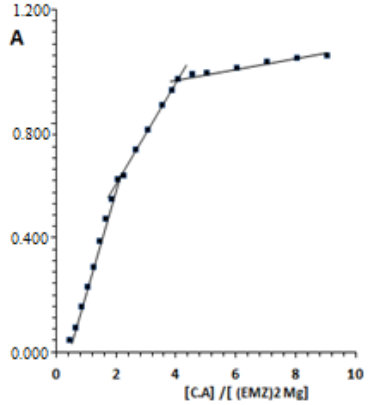

Fig. 3: Molar ratio method to calculate coupling ratio for EMZ:CAA complex (by using methanol: acetonitril 1:9 as blank, C_{EMZ} = 2x10^{-4}M, ℓ =1 cm, λmax = 521 nm).

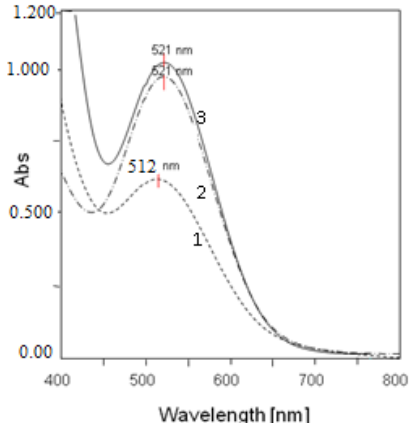

Fig. 4: UV-Vis spectra of 2x10^{-4} M EMZ with CAA; 1 to 3 concentration of CAA were as the follow as: 1- 4x10^{-4}; 2- 8x10^{-4}; 3-18x10^{-4} (methanol: acetonitril 1:9; ℓ =1cm).

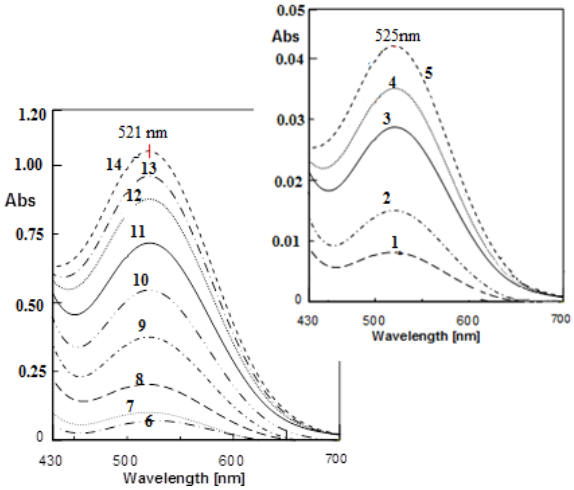

Fig. 4: UV-Vis spectra of 2x10^{-4} M CAA with EMZ; 1 to 9 concentration of EMZ were as the follow as: 1-0.937; 2- 1.250; 3- 1.875; 4- 3.75; 5- 5.63; 6-7.50 ; 7- 12.5; 8- 25; 9- 50; 10- 75; 11- 100 ; 12- 125; 13-137.5; 14 (methanol:a-150 µg.mL^{-1} (in acetonitril 1:9; ℓ =1cm).

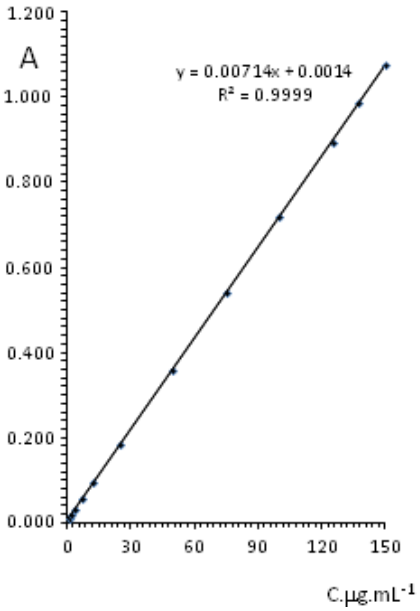

Fig. 5: Calibration curve for determination EMZ through complexation with CAA (methanol: acetonitril 1:9; ℓ =1cm).

Table 1: The optimum parameters established for spectrophotometric determination of EMZ in pure form through complexation with CAA in methanol:acetonitril (1:9).

Parameters	Operating modes
Time of maximum color intensity	30-60 min
λ_{max} of complex	521 nm
Solvent	Methanol: Acetonitril (1:9).
Stability (h)	24
Molar absorptivity (L $mol^{-1}cm^{-1}$)	$4.932x10^3$
Temperature of solution	30 ± 0.5°C
Concentration of CAA	≥10 C_{EMZ}
Beer's Law Limit, µg.mL^{-1}	1.250 - 150.00
LOD(3.3SD),µg.mL^{-1}	0.156
LOQ (10SD),µg.mL^{-1}	0.473
Regression equation:	y=0.00714x+0.0014
Slope	0.00714
Intercept	0.0014
Correlation coefficient (R^2)	0.9999
RSD%	4.6

Table 2: Spectrophotometric determination of EMZ in pure form through complexation with CAA in methanol:acetonitril (1:9).

x_i, µg.mL^{-1} (taken)	$*\overline{X}$, µg.mL^{-1} (found)	SD, µg.mL^{-1}	Analytical standard error, $\frac{SD}{\sqrt{n}}$, µg.mL^{-1}	Confidence limits $\frac{-}{x} \pm \frac{t.SD}{\sqrt{n}}$ µg.mL^{-1}	RSD %
0.937	0.946	0.0530	0.0237	0.946± 0.0681	5.6
1.250	1.238	0.0569	0.0255	1.238± 0.0707	4.6
1.875	1.872	0.0660	0.0295	1.872 ± 0.0819	3.5
3.750	3.750	0.1170	0.0523	3.750 ± 0.1453	3.1
7.500	7.485	0.1918	0.0858	7.485 ± 0.2381	2.6
12.50	12.22	0.282	0.126	12.22 ± 0.350	2.3
25.00	25.16	0.480	0.215	25.16 ± 0.596	1.9
50.00	50.20	0.775	0.347	50.20 ± 0.392	1.5
75.00	75.13	0.838	0.375	75.13 ± 1.040	1.1
100.00	100.23	0.925	0.414	100.23 ± 1.148	0.9
125.00	125.26	1.123	0.502	125.26 ± 1.394	0.9
137.50	137.67	1.395	0.623	137.67 ± 1.731	1.1
150.00	150.18	1.624	0.726	150.18 ±2.016	1.1

* n=5, t= 2.776

Applications

Many applications for the determination of $(EMZ)_2Mg$ in some Syrian pharmaceutical preparations with a spectrophotometric method through complexation with CAA in methanol:acetonitril (1:9). In optimal conditions were proposed. Regression equations and correlation coefficients were included in Table 1. Calibration curve and Standard addition curves for determination of EMZ in different Syrian pharmaceutical preparations were used. The amount of EMZ in one capsule by mg/caps., The results of quantitative analysis for EMZ were calculated by calibration curves and the standard addition methods, see Table 3.

Table 3: Spectrophotometric Determination of cefixime in syrian pharmaceuticals through complexation with CAA in methanol:acetonitril (1:9).

Commercial name	Contents	Calibration curve			Standard addition		
		$*\overline{X}$, mg/caps	RSD%	Recovery %	$*\overline{X}$, mg/caps.	RSD%	Recovery %
S-Omepral, caps. Asia pharmaceutical industries Aleppo – SYRIA	40 mg/caps.	41.6	1.8	104.0	40.6	1.6	101.15
S-Omepral, caps. Asia pharmaceutical industries Aleppo – SYRIA	20 mg/caps.	20.8	2.3	104.4	20.4	4.3	102.0
S-Omepral, caps. Ibn Al Haytham, Pharma Industries Co. Aleppo–SYRIA	20 mg/caps.	19.8	2.5	99.9	20.2	4.4	101.0
newomeprazole, caps. Syria pharma for medicaments Aleppo–SYRIA	20 mg/caps.	21.0	2.2	105.0	20.6	4.6	103.0

* n=5

CONCLUSION

Spectrophotometric determination of $(EMZ)_2Mg$ in pure and its Syrian pharmaceutical formations through complexation with CAA in methanol:acetonitril (1:9), has been developed. The method was based on the formation of a charge-transfer complexe between chloranilic acid (CAA) as a π-acceptor and EMZ as an n-donor in methanol-acetonitril medium.The maximum absorbance of the coloured complex occurred at λ= 521-523 nm and the molar absorptivity is $4.932x10^3$ $L.mol^{-1}.cm^{-1}$. Reaction conditions have been optimized to obtain the complex. The linear range of the calibration curve was 1.250–150.00 μgmL^{-1} with correlation coefficients ≥0.9999 in all cases. Overall recoveries were of the order of 98.26–100.12%.The limit of detection (LOD) and limit of quantification (LOQ) was found to be 0.156 $\mu g.mL^{-1}$ and 0.473 $\mu g.mL^{-1}$, respectively. The proposed method was simple, economic, accurate and successfully applied to the determination of EMZ in pharmaceutical formulations and the results obtained agree well with the contents stated on the labels. The results obtained by this method were validated by HPLC[6].

REFERENCES

1. http://www.rxlist.com/nexium-drug.htm updated on 11/07/2010.
2. Andersson T, Hassan -Alin M , Hasselgren G ,Rohss K , Weidolf L, Pharmacokinetic studies with Esomeprazole, the (S)-Isomer of omeprazole.Clinical Pharmacokinetics 2001;40:411-26.
3. Scott LJ , Dunn CJ , Mallarkey G , Sharpe M .Esomeprazole – A review of its use in the management of acid-related disorders. Drugs 2002;62:1503-38.
4. Petersen KU, Schmutzler W. Proton pump inhibitors release of active substance from various preparations. Detsche Apotheker Zeitung 1999;139:68-9.
5. Dogrukol AK, Tunalier Z, Tuncel M. TLC densitometric determination of omeprazole in pharmaceutical preparations. Pharmazie 1998;53:272-3.
6. Sluggett GW, Stong JD, Adams JH, Zhao Z, Omeprazole determination using HPLC with coulometric detection . J Pharm Biomed Anal 2001;25,357-61.
7. Ding L, Yang J, Yan HL, Zhang ZX, An DK, Determination of omeprazole and its pharmacokinetics in human plasma by an improved HPLC method. Chinese J Pharm Anal 1999;17:458-61.
8. Shim SH, Bok SJ, Kwon KI. Determination of omeprazole in rat plasma by HPLC with column switching. Arch Pharm Res 1994;17:458-61.
9. Zhi XJ, Hunang J, Zhang JH, Wang HT, Zhang LL. Determination of omeprazole and its metabolites in plasma by RP-HPLC. Chinese J Pharm 1999;30:166-8.
10. Cass QB, Lima VV, Oliveira RV, Cassiano NM, Degani ALG, and Pedrazzoli J, Enantiomeric determination of the plasma levels of omeprazole by direct plasma injection using high-performance liquid chromatography with a chiral–chiral column-switching. J. Chromatogr. B 2003.798: 275-281.
11. Kanazawa H, Okada A, Matsushima Y, Yokota H, Okubo S, Mashige F, and Nakahara K, Determination of omeprazole and its metabolites in human plasma by liquid chromatography–mass spectrometry. J. Chromatogr. 2002. A 949: 1-9.
12. Cheng FC, Ho YF, Hung LC, Chen C F, Tsai TH, Determination and pharmacokinetic profile of omeprazole in rat blood, brain and bile by microdialysis and high-performance liquid chromatography. J. Chromatogr. A, 2002.949: 35-42
13. Kelani KM, Aziz AM, Hegazy MA, and Fattah LA, 2002. UV-spectrophotometric stability indicating methods for the quantitative determination of cimetidine, famotidine, and ranitidine hydrochloride in the presence of their oxidative. Anal. Let. 35: 1055-1073.
14. Priti D, Trivedi DG, Maheshwari KB, Institute The method involved Q-absorption analysis based on the measurement of absorbance at two wavelengths, i.e λmax of Esomeprazole (301 nm) and Iso-absorptive point of both drugs (290 nm). International Journal of ChemTech Research.2010,2.1598-1605.
15. Ozaltin N, Kocer A. Determination of omeprazole in pharmaceuticals by derivative spectroscopy. J Pharm Biomed Anal 1997;16:337-42.
16. Prabu SL, Shirwaikar A, Shirwaikar A, Kumar D , Joseph A, and Kumar R, Simultaneous Estimation of Esomeprazole and Domperidone by UV Spectrophotometric Method. Indian Journal of Pharmaceutical Sciences., 2008,70(1), 128–131.
17. Akheel AS, Ayesha S, Neocuproine and bathocuproine as new reagents for the spectrophotometric determination of certain proton pump inhibitors, Chemical Society of Ethiopia, 2007, 21, 315-321.
18. Nafisur R, Zehra B , Syed N H A, Spectrophotometric Determination of Esomeprazole Magnesium Using 5-Sulfosalicylic Acid and N-Bromosuccinimide. Journal of the Chinese Chemical Society, 2008, 55, 557-566 India
19. Putta RK, Somashekar S, Mallikarjuna GM, Shanta SMK, Physico-chemical characterization, UV spectrophotometric method development and validation studies of Esomeprazole Magnesium Trihydrate, *J. Chem. Pharm. Res., 2010, 2,484-490*.
20. Patil SS, Dhabale PN, Kuchekar BS, Development and Statistical Validation of Spectrophotometric Method for Estimation of Esomeprazole in Tablet Dosage Form, Asian J. Research Chem. 2009,2, 154-156.
21. Azza AMM, Spectrophotometric methods for the determination of lansoprazole and pantoprazole sodium sesquihydrate. Journal of Pharmaceutical and Biomedical Analysis. February 2000, 22, 45-58.