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Q-ABSORBANCE RATIO AND VIERODT'S SPECTROPHOTOMETRIC METHOD FOR THE SIMULTANEOUS ESTIMATION OF FAMOTIDINE AND OMEPRAZOLE

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Abstract

Famotidine and omeprazole are the drugs used in the treatment of gastrointestinal disorders. The current work is an analytical method for the simultaneous determination of famotidine and omeprazole and is based on the Q-absorption method and Vierodt's method. These two methods depend on the isosbestic point and the λmax of one of the two components. The isosbestic point was found to be 295 nm in ethanol. 287nm and 301nm are the λmax of famotidine and omeprazole respectively. The method is validated as per ICH guidelines.

Keywords: Famotidine, omeprazole, Q-absorbance ratio, Vierodt's Method, Isosbestic Point, λMax.

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Introduction

Famotidine is an H2-receptor antagonist that is used to treat gastroesophageal reflux disease and stomach ulcers.Chemically 3-{(2-[diaminomethylideneamino]-1,3-thiazol-4-yl) methylsulfanyl}-N-sulfamoyl propanimidamide and the empirical formula is C8H15N7O2S3 with molecular weight 337.5. Freely soluble in glacial acetic acid, slightly soluble in methanol, and ethanol, and very slightly soluble in water [2-4]. Omeprazole is a proton pump inhibitor used to treat gastric ulcer and gastroesophageal reflux disease with the chemical name 6-methyl-2-{[4-methylpyridin-2-yl] methylsulfanyl}-1*H*-benzimidazole with empirical formula C17H19N3O3S. Omeprazole is freely soluble in ethanol and methanol and very slightly soluble in water [5-8].

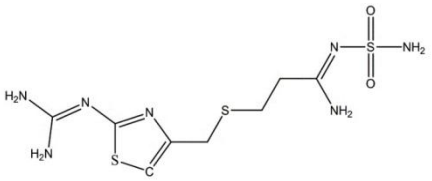

Fig no 1- Chemical structure of Famotidine

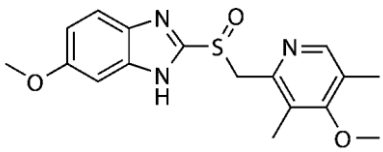

Fig no2- Chemical structure of Omeprazole

It is possible to determine an increasing number of analytes using ultraviolet and visible spectroscopy in multi-component analysis. In UV-Visible spectroscopy, the absorption of monochromatic photons between 200 to 800 nm is measured. Atoms and molecules go through an electronic transition in this area.In this work, Vierodt's approach and the Q-absorption ratio method are created for the subsequent determination of selected medications.

Q-absorption ratio method [10-12]

Consider drugs X and Y

The Q-absorption ratio approach uses the absorption ratio at two specified wavelengths, which is the isosbestic point and λmax of one of the two components. The concentration of pharmaceuticals may be determined using the following set of equations.

$$Cx=\{(Q_M-Qy)/(Qx-Qy)\} \times (A_1/ax_1)$$

$$Cy=\{(Q_M-Qx)/(Qy-Qx)\} \times (A_1/ay_1)$$

The ratiosQ_X, Q_Y, and Q_M are calculated using the average absorptivity of two medicines at a given wavelength.

$QX = ax2/ax1$

$QY = ay2/ay1$

$QM = A2/A1$

Where

- The absorptivities of X at λ1 and λ2, ax1 and ax2 correspondingly
- The absorptivities of Y at λ1 and λ2, ay1 and ay2 correspondingly
- The absorbance of the sample solution at λ1 and λ2, A1 and A2 correspondingly

Vierodt's method [13-14]

It is often referred to as the method of simultaneous equations. Vierodt's approach may be used to calculate the concentration of both medicines in a sample containing two medications, X and Y, each of which absorbs at the λmax of the other.

The concentrations of X and Y in the diluted sample are Cx and Cy, respectively, and may be determined using the formula

$$\mathbf{Cx} = \frac{\mathbf{A2ay1 - A1ay2}}{\mathbf{ax2ay1 - ax1ay2}}$$

$$\mathbf{Cy} = \frac{\mathbf{A1ax2 - A2ax1}}{\mathbf{ax2ay1 - ax1ay2}}$$

Material and method

Chemicals and reagents

Famotidine and Omeprazole - Brought from Yarrowchem chemicals, Mumbai, India

Ethanol and Methanol

Equipment

Electronic balance- Tandem TJ series

UV spectrophotometer-Shimadzu, UV1700, Japan, andis connected to a UV probe 2.0 computerprogram, two matched quartz cells measuring 1 cm in length and wavelength precision of 0.5 nm.

Simultaneous estimation of famotidine and omeprazole by UV spectrophotometric method

Preparation of standard stock solution

The medications were precisely weighed and then transferred to separate 100 ml volumetric flasks where they were dissolved in ethanol and then diluted to the right volume with ethanol to achieve a concentration of 1000 µg/ml. This solution serves as the initial stock for further dilution.

Preparation of working standard solution

To create a working standard solution with a concentration of 100 µg/ml, the first stock of famotidine and omeprazole were transferred individually from a 1 ml volumetric flask to a 10 ml volumetric flask.

Preparation of calibration curve of standard Famotidine and Omeprazole

Aliquots of omeprazole (0.2, 0.4, 0.6, 0.8, and 1.0 ml) and famotidine (0.4, 0.8, 1.2, 1.6, and 2.0 ml) were transferred separately in a series of 10 ml volumetric flasks from the aforementioned working standard solution. Using ethanol, adjust the amount to the desired level, obtaining a famotidine and omeprazole concentration of 4–20 µg/ml and 2–10 µg/ml, respectively. Using ethanol as a blank, the absorbance is measured between 200 and 400 nm.

Preparation of synthetic in synthetic mixture

A synthetic mixture containing 10 mg of HPMC, 10 mg of lactose, and 5 mg of talc was created by correctly weighing 50 mg of famotidine and 25 mg of omeprazole, respectively.

Preparation of sample solution

To create a 500 µg/ml famotidine and 200 µg/ml omeprazole solution, a quantity equal to 50 mg famotidine and 20 mg omeprazole was transferred to a 100 mg volumetric flask, dissolved in ethanol, and then sonicated for 20 minutes. The final concentration of the solution was 8 µg/ml of famotidine and 4 µg/ml of omeprazole after it had been filtered through Whatman filter paper no. 41 and further diluted. At a given wavelength, the response of the sample solution was tested in comparison to a blank.

Simultaneous estimation of Famotidine and Omeprazole using the Q absorbance ratio method

In this method absorbance at the selected wavelength is 295 nm, the isosbestic point, and 287 nm the λmax of famotidine was selected for estimation. Working standard solution having concentrations of 4, 8, 12, 16, and 20µg/ml of famotidine and 2,4,6,8, and 10µg/ml of omeprazole in ethanol is measured for absorbance at 295nm and 287nm. Using a calibration curve, the absorptivity coefficient was obtained, and the following equation was used to estimate the concentration of two medicines in the synthetic mixture.

$$Cx = \left\{\frac{QM - QY}{QX - QY}\right\} \times \left(\frac{A1}{ax1}\right)$$

$$Cy = \left\{\frac{QM - QX}{QY - QX}\right\} \times (A1/ay1)$$

Where, A1 and A2 are the absorbances of the mixture at 295nm and 287nm; ax1 and ay1 are the absorptivities of Famotidine and Omeprazole at 295 nm; ax2 and ay2 are the absorptivities of Famotidine and Omeprazole at 287nm

Vierodt's methodof quantification of Famotidine and Omeprazole using the Q absorbance ratio method

Working standard solutions comprising 2, 4, 6, 8, and 10 µg/ml of omeprazole and 4, 8, 12, 16, and 20 µg/ml of famotidine were scanned in the UV region between 200 and 400 nm. Omeprazole displays a λmax of 287 nm and famotidine displays a max of 301 nm. The synthetic mixture is then measured for absorbance at various wavelengths, and the concentration is calculated using a series of simultaneous equations based on the drug's overlaid spectrum's absorptivity coefficient at the chosen wavelength.

$$Cx = \frac{A2ay1 - A1ay2}{ax2ay1 - ax1ay2}$$

$$Cy = \frac{(A1ax2 - A2ax1)}{(ax2ay1 - ax1ay2)}$$

A1 and A2 are the absorbances of the mixture at 295nm and 287nm

Method validation

Linearity

Famotidine and omeprazole serial dilutions were made. By establishing a graph of absorbance (y-axis) vs. concentration, the calibration curve was created (x-axis). Equation of linear regression found over concentration range: Y=mx+c

Accuracy and precision

Accuracy was expressed as a percentage of the recovery. 2 µg/mL of omeprazole and 4 µg/mLof famotidine are spiked at levels of 80, 100, and 120%.

By repeatedly scanning and measuring absorbance without modifying the method's parameters, the precision of the method was evaluated.

Reproducibility

By examining the matching responses three times on the same day and three times on three different days over the course of a week for three different concentrations of a standard solution of Famotidine and omeprazole, the intraday and interday precision was ascertained.

Limit of detection (LOD) and Limit of quantification (LOQ)

The LOD and LOQ of the drug were derived by calculating the signal-to-noise ratio.

$$LOD = 3.3 \times (standard\ deviation/slope)$$

$$LOQ = 10 \times (standard\ deviation/slope)$$

Result and discussion

The absorbance of the serial dilution of Famotidine (4-20 g/ml) and Omeprazole (2-10 g/ml) was measured in the UV range of 200-400 nm.Famotidine's absorption maxima were determined to be 287 nm and omeprazole's to be 301 nm, with the isosbestic point being at 295 nm.Famotidine and Omeprazole are able to meet the primary condition for the absorbance ratio approach, which is that the entire spectrum adheres to Beer's lamberts law across the board. The two wavelengths used for the analysis are 295 nm, the isosbestic point, and 287 nm, the famotidine absorption maximum, at which the calibration curves for the two medications were created. The graphic displays the overlapped UV absorption spectra of omeprazole and famotidine while also displaying isosbestic spots.

In the Vierodt's method, the absorbance of the medications Famotidine in the range 4-20 µg/mL and Omeprazole in 2-10 µg/mL was assessed at 287 nm and 301 nm.

For the suggested method, the validation parameters were investigated at all wavelengths. Recovery and the mean calculations were used to establish accuracy, while repeatability calculations were used to estimate precision for both medicines. The synthetic mixture's absorbance is measured, and the devised method was used to quantify the amounts of famotidine and omeprazole**.**

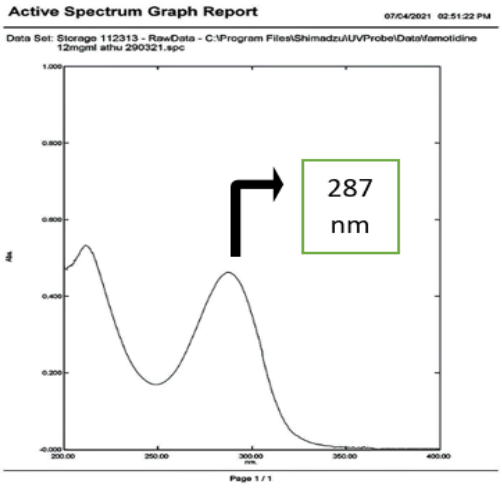

Fig no 3- UV spectrum of Famotidine
With λmax of 287 nm

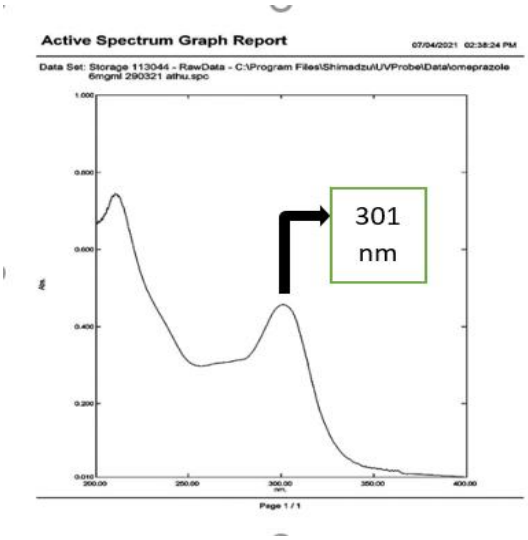

Fig no 4- UV spectrum of Omeprazole With λmax of 301 nm

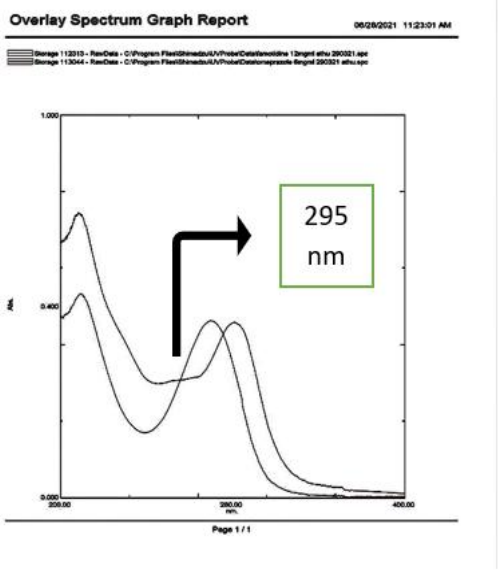

Fig no 5- iso-absorptive point of Famotidine

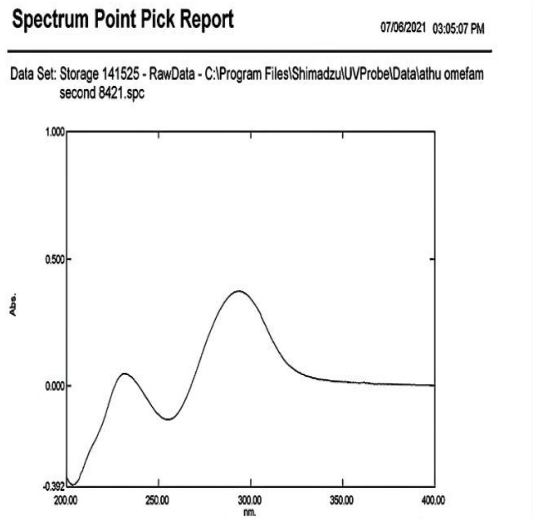

Fig no 6- UV spectrum of synthetic mixture and Omeprazole

Table No 1- Concentration Vs Absorbance of Famotidine and Omeprazole

Famotidine			Omeprazole		
Concentration (µg/ml)	absorbance		Concentration (µg/ml)	absorbance	
	Q-absorbance ratio	Viero dt's method		Q-absorbance ratio	Viero dt's method
4	0.235	0.231	2	0.235	0.222
8	0.348	0.348	4	0.311	0.329
12	0.454	0.462	6	0.431	0.447
16	0.584	0.584	8	0.584	0.571
20	0.698	0.697	10	0.698	0.662

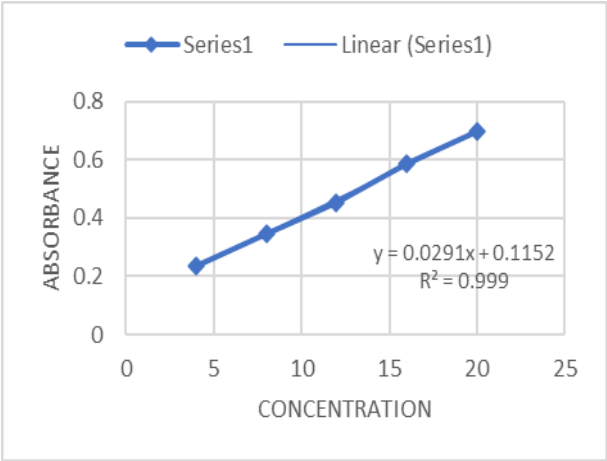

Fig No 7 - Calibration curve of Famotidine

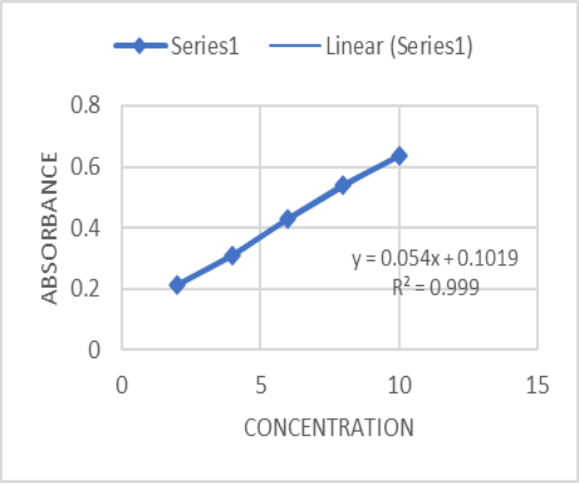

Fig No 8 - Calibration curve of Omeprazole, Q-absorbance ratio method

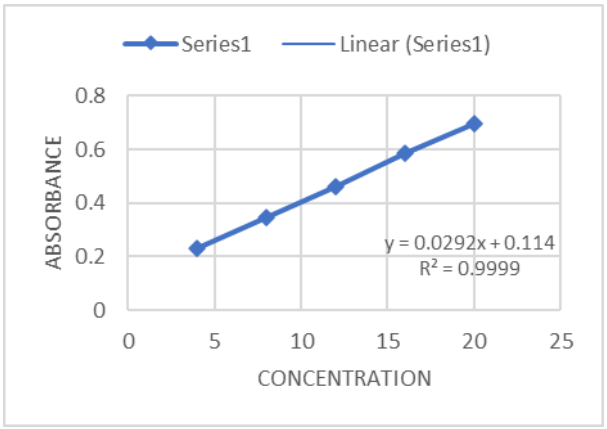

Fig No 9- Calibration curve of Famotidine method

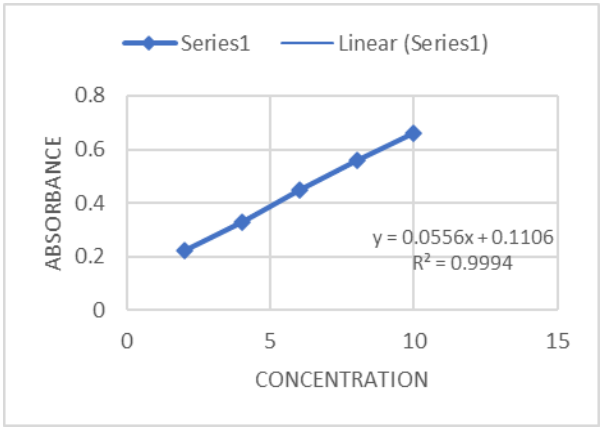

Fig No 10- Calibration curve of omeprazole, Vierodt's

Table No 2- Assay of Synthetic mixture

Drug name	Drug content(%±SD)	
	Q absorbance method	Vierodt's method
Famotidine	98.8032±0.0009	97.9034±0.0013
Omeprazole	97.3056±0.0008	99.5087±0.0024

Table No 3- Intra-day precision with mean, standard deviation, relative standard deviation

Concentration (n=6)	**Absorbance**			
	FAMOTIDINE (287nm),12µg/ml		**OMEPRAZOLE (301nm), (6µg/ml)**	
	Q-absorbance ratio	**Vierodt's method**	**Q-absorbance ratio**	**Vierodt's method**
1	0.454	0.461	0.433	0.457
2	0.456	0.460	0.435	0.456
3	0.457	0.462	0.438	0.458
4	0.455	0.463	0.432	0.457
5	0.458	0.460	0.433	0.456
6	0.454	0.462	0.431	0.456
MEAN	0.455	0.461	0.433	0.456
SD	0.001	0.0012	0.002	0.0081
RSD (%)	0.307	0.262	0.461	0.178

Table No 4- Interday day precision, Q-absorption ratio method

Drugs (n=3)	Concentration (µg/ml)	Interday precision Absorbance		Interday precision Absorbance	
		Mean±SD	%RSD	Mean±SD	%RSD
FAM	4	0.231±0.0008	0.387	0.230±0.003	0.353
	8	0.374±0.0007	0.200	0.374±0.005	0.280
	12	0.461±0.0001	0.262	0.461± 0.0001	0.328
OME	2	0.222±0.0008	0.402	0.221±0.0009	0.443
	4	0.329±0.0008	0.080	0.327±0.0008	0.273
	6	0.456±0.0008	0.178	0.452±0.0007	0.166

Table No 5- Accuracy of Q-absorbance ratio method- % recovery with mean plus standard deviation, relative standard deviation

Drug	Accuracy level (%)	Amount			% Recovery	Mean+ S	% RSD
		Actual(µg/ml)	Added(µg/ml)	Found(µg/ml)			
FAM	80%	4	3.2	7.1	98.61	97.52±0.973	0.997
	100%	4	4	7.7	96.25		
	120%	4	8.7	8.6	97.72		
OME	80%	2	1.6	3.4	97.22	97.48±0.204	0.209
	100%	2	2	3.9	97.5		
	120%	2	2.4	4.3	97.72		

Table No 6- Interday day precision, Vierodt's method

Drug S(n=3)	Concentration (µg/ml)	Interday		Interday	
		Mean ±SD	%RSD	Mean± SD	%RSD
FAM	4	0.233±0.001	0.307	0.235±0.0009	0.382
	8	0.348±0.001	0.287	0.345±0.001	0.289
	12	0.455±0.001	0.219	0.452±0.001	0.221
OME	2	0.215±0.002	0.930	0.212±0.002	0.943
	4	0.301±0.002	0.664	0.299±0.002	0.668
	6	0.433±0.002	0.461	0.430±0.002	0.465

Table No 7- Accuracy of Vierodt's method- % recovery with mean plus standard deviation, relative standard deviation

Drug	Accuracy level (%)	Amount			%Recovery	Mean±SD	%RSD
		actual(µg/ml)	added(µg/ml)	Found(µg/ml)			
FAM	80%	4	3.2	7.0	97.22	98.27±0.916	0.932
	100%	4	4	7.9	98.75		
	120%	4	8.7	8.7	98.86		
OME	80%	2	1.6	3.5	97.22	97.48±0.250	0.257
	100%	2	2	3.9	97.5		
	120%	2	2.4	4.3	97.72		

Table No 8– Linearity, Correlation coefficient, Accuracy, precision, LOD, LOQ of developed methods

Parameters	Vierodt's method		Q-adsorption method	
	Famotidine	Omeprazole	Famotidine	Omeprazole
Linearity (µg/ml)	4-20	2-10	4-20	2-10
Correlation coefficient	0.9996	0.9950	0.9990	0.9968
% Recovery (Means)	98.27±0.916	97.48±0.250	97.52±0.973	97.48±0.204
Accuracy(%RSD)	0.932	0.257	0.997	0.209
Precision(%RSD)	0.262	0.178	0.307	0.461
Limit of detection (LOD) (µg/ml)	0.9718	0.6345	0.739	0.5870
Limit of quantification (LOQ) (µg/ml)	2.945	1.923	2.241	1.779

Conclusion

Endoscopic reflux esophagitis, Barret's esophagus, and recurrent acid regurgitation are symptoms of gastroesophageal reflux disease (GRED), a disorder. Famotidine and Omeprazole together increased the length of and time to reach intragastric PH >4 in healthy, Helicobacter pylori-negative volunteers, according to a randomised clinical trial. Compared to famotidine alone, the combined therapy was superior[15-16]. As a result, a method for the simultaneous quantification of omeprazole and famotidine utilizing UV Spectrophotometry was established in this work.The Q-absorbance ratio method was the first developed technique; Famotidine exhibits a linearity range of 4–20 g/ml in this technique, and correlation coefficients were discovered to be 0.9990. The linearity range for omeprazole was found to be 2–10 g/ml, and the correlation coefficient was 0.9968. The second approach was Vierodt's, which had a linearity range comparable to the simultaneous equation method and discovered that the correlation coefficients for famotidine and omeprazole were, respectively, 0.9996 and 0.9950.

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Conflict of Interest

No Conflict of Interest

Funding

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Author contribution

All authors are contributed equally

Ethical Considerations

Not Applicable

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