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ESTIMATION OF ONDANSETRON AND ESOMEPRAZOLE IN DOSAGE FORMS BY VIERODT'S METHOD

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ABSTRACT

Aim Simple, rapid, accurate and precise UV-spectrophotometric methods have been developed for simultaneous estimation of *ondansetron* and *esomeprazole* in bulk and tablet dosage form.

Method Method involves, formation of simultaneous equation using Vierodt's Method. In dilute hydrochloric acid, *ondansetron* and *Esomeprazole* showed λ max at 248 nm and 310 nm, respectively.

Results Linearity was observed in the concentration range of 2 - 10µg/ml for *ondansetron hydrochloride* and2-10µg/ml for *esomeprazole*.The LOD & LOQ of *ondansetron*and*Esomeprazole* were0.0104484µg/ml & 0.0316196 µg/ml and 0.0106155µg/ml & 0.0321692µg/ml respectively. In our study, the percentage recovery of *ondansetron&esomeprazole* it was found to be 79.62%, 99.50%, 120.37% and 79.12%, 101.72%, 98.97% from 80%, 100% and 120% sample solutions respectively.For the precision study in the present work, the %RSD for *ondansetron* and *esomeprazole* was found to be 0.5% & 0.4% and 1.6% & 0.2% at 248 and 310nm respectively.

Conclusion The %RSD value indicates a good degree of precision within the specified range.The relative standard deviation (Ruggedness) for the sample preparations of *ondansetron* and *esomeprazole* was found to be 0.2% & 0.6% and 0.8% & 0.2% respectively. Hence the %RSD value indicates a good degree of precision within the specified range.

The methods were successively applied to tablet formulation; no interferences from the tablet excipients were found. The methods have been validated statistically and by recovery studies.

Keywords: Ondansetron, Esomeprazole, UV-spectrophotometric method,validation, simulataneous equation Vierodt's method.

INTRODUCTION:

Esomeprazole refers to the class of proton pump inhibitor that suppresses gastric acid secretion by specific inhibition of the H+/K+-ATPase in the gastric parietal cell. It is widely used as an anti-ulcer agents, enzyme inhibitors, proton-pump inhibitors, antihistamines [(1)]. *Esomeprazole* is a compound that inhibits gastric acid secretion and is indicated in the treatment of gastroesophageal reflux disease (GERD), the healing of erosive esoserotoninphagitis, and *H. pylori* eradication to reduce the risk of duodenal ulcer recurrence[(1)]. *Ondansetron* is a highly specific and selective serotonin 5-HT3 receptor antagonist, not shown to have activity at other known serotonin receptors and with low affinity for dopamine receptors [(1)].

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The serotonin 5-HT3 receptors are located on the nerve terminals of the vagus in the periphery, and centrally in the chemoreceptor trigger zone of the area postrema[29]. The serotonin then stimulates the vagal and splanchnic nerve receptors that project to the medullary vomiting center, as well as the 5-HT3 receptors in the area postrema, thus initiating the vomiting reflex, causing nausea and vomiting.

The antiemetic activity of the drug is brought about through the inhibition of 5-HT3 receptors present both centrally (medullary chemoreceptor zone) and peripherally (GI tract). This inhibition of 5-HT3 receptors in turn inhibits the visceral afferent stimulation of the vomiting center, likely indirectly at the level of the area postrema, as well as through direct inhibition of serotonin activity within the area postrema and the chemoreceptor trigger zone. It is widely used in anti-anxiety Agents, anti-emetics, anti-psychotics, serotonin antagonist, anti-pruritics, anti-psychotic agents.[(1)]

Chemistry:

The reaction of β-diketo esters with hydrazine is the most generally and prevalent method to synthesize pyrazolones. The authenticity of these compounds was confirmed by Thin Layer Chromatography. The structural conformation is done by ^{1}HNMR, using DMSO as solvent.This method of synthesis of these β-keto esters have serious drawbacks such as step-intensive, time consuming and usage of imidazoles[2].

MATERIALS & METHODS:

Instrumentusedis best UV spectrophotometric Schimadzu with equipped detector. Data acquisition was made with lambda25 software and analytical balance (company) was used for the weighing purpose.The standard *ondansetron* and *Esomeprazole* was procured from was obtained as a gift sample from Glow chem. Industries ltd. Jadcherla, Hyderabad. A.P. India. Methanol, Acetone, distilled water was used throughout the study. Pharmaceutical dosage form, tablet was obtained from local market manufactured and supplied by Mankind pharmaceuticals pvt. Ltd. as brand name of VOMICET and ZOFRAN (4mg and 40mg). Further the estimation of both the formulations was done using vierodt's method.[3]

EXPERIMENTAL SECTION

Preparation of ondansetron stock solution:

Preparation of stock solution of *ondansetron* is done by taking quantity containing 100mg of *ondansetron* standard in to 100ml volumetric flask and then about 10 ml of 1N HCl is added, after dissolving it completely the volume was made up to the mark with 1N HCl to obtain 1000µg/ml. About 10ml was taken from standard stock solution in to a 100ml volumetric flask and the volume was made up to the mark with 1N HCl to obtain 100µg/ml concentration of *ondansetron*. From the 100µg/ml stock solution, 10ml was taken and transferred in to 100ml volumetric flask and the volume was made up to the mark with 1N HCl to obtain 10µg/ml concentration of *ondansetron*[4].

Preparation of esomeprazole stock solution:

Preparation of stock solution of *Esomeprazole* is done by taking quantity containing 100mg of *Esomeprazole* standard in to 100ml volumetric flask and then about 10 ml of 1N HCl is added, after dissolving it completely the volume was made up to the mark with 1N HCl to obtain 1000µg/ml. About 10ml was taken from standard stock solution in to a 100ml volumetric flask and the volume was made up to the mark with 1N HCl to obtain 100µg/ml concentration of *ondansetron*. From the 100µg/ml stock solution, 10ml was taken and transferred in to 100ml volumetric flask and the volume was made up to the mark with 1N HCl to obtain 10µg/ml concentration of *Esomeprazole*[3].

Preparation of sample solution:

The quantity equivalent to 100mg of *ondansetron* and *Esomeprazole* was weighed and transferred in to a dry 100ml volumetric flask and then about 10 ml of 1N HCl is added, after dissolving it completely the volume was made up to the mark with 1N HCl to obtain 1000µg/ml. About 10ml was taken from sample stock solution in to a 100ml volumetric flask and the volume was made up to the mark with 1N HCl to obtain 100µg/ml. From the 100µg/ml stock solution, 10ml was taken and transferred in to 100ml volumetric flask and the volume was made up to the mark with methanol to obtain 10µg/ml[3,4].

The stock solutions of 10µg/ml *Ondansetron* and *Esomeprazole* were scanned in wavelength range of 200-400nm. By this maximum wavelengths of two drugs were selectedfor formulations. The absorptivities (A1%, 1cm) of both the drugs at the wavelengths were determined. The absorbance and absorptivities values at the particular wavelength were substituted in the following to obtain the concentration of x and y drugs.

$$Cx = \frac{A_2\ a_{y1} - A_2\ a_{y2}}{A_{x2}\ a_{y1} - a_{x1}\ a_{y2}}$$

$$Cy = \frac{A_1\ a_{x2} - A_2\ a_{x1}}{A_{x2}\ a_{y1} - a_{x1}\ a_{y2}}$$

From the stock solution of 100µg/mL, working standard solutions of drugs were prepared by appropriate dilution and were scanned in entire UV range to determine the λmax. *ondansetron* has λmax of 248nm while *esomeprazole* has µmax at 310nm respectively (Fig.1). Standard solutions were prepared having concentration 10µg/mL for *ondansetron* and 10µg/mL for *esomeprazole*. The absorbances of these standard solutions were measured at 248nm and 310 nm and calibration curves were plotted at these wavelengths. Two simultaneous equations (in two variables C1 and C2) were formed using these Absorptivity coefficient values.

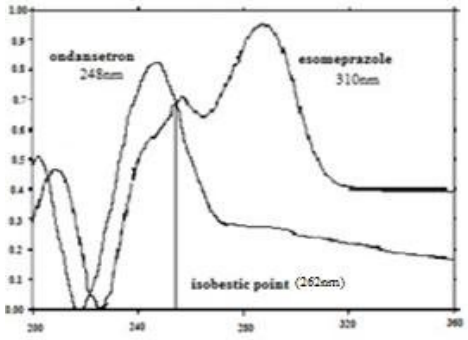
A1 = (0.4548) C1 + (0.4071) C2

A2 = (0.5510) C1 + (0.5620) C2

RESULTS AND DISCUSSION

1. Determination of λ max:

λ max is the wavelength at which maximum absorption takes place. The λmax is the characteristic of drug molecules. From this figure no.1 absorption maxima (λmax) for *ondansetron* was observed at 248nm whereas for *Esomeprazole* was observed at 310nm. Here both spectra were coincided at 310nm (isobestic point), hence suitable wavelength for detection is 257nm.



UV spectra of Ondansetron and Esomeprazole in1N HCl

2. Assay:

Assay determines the content of specific components such as *ondansetron* and *Esomeprazole* in the given formulation (brand name) by means of measuring the absorbance and absorptivities values at the particular wavelength of *ondansetron* and *esomeprazole*. The results were shown the following table and are the values obtained are substituted in following formula, $C_x$and C_y

Name of drug	248nm	310nm
Ondansetron	0.4548	0.4071
Esomeprazole	0.5510	0.5620
Formulation	1.3483	0.9712

Therefore Cx = 0.099145µg/ml & Cy =0.096702576µg/ml

The percentage purity of *ondansetron* is 99.14% and *Esomeprazole* is 98.35%. As the assay limit should lie between 98%- 101% hence the method is reliable.

VALIDATION PARAMETERS:

Validation of an analytical procedure is the process by which it is established, by laboratory studies, that the performance characteristics of the procedure met the requirements for its intended use.

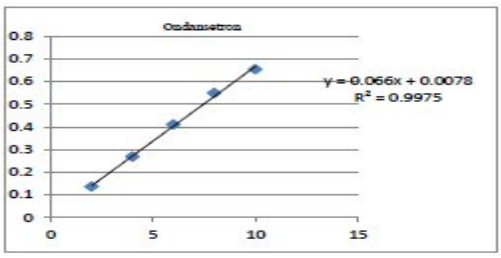
1. Linearity studies:

The linearity of calibration curves (Absorbance Vs Concentration) in pure solution was checked over the concentration ranges of about 2-10µg/ml for *ondansetron* and *Esomeprazole* respectively and the results for linearity values of ondansetron and Esomeprazole were shown in the following table.

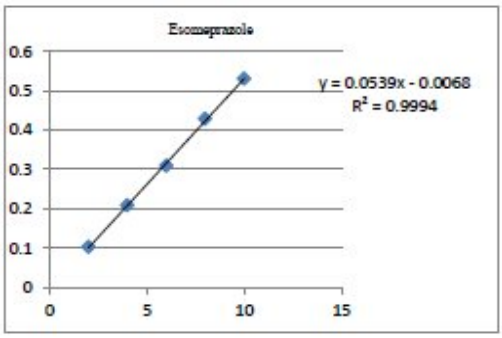
Linearity studies of pure samples

Concentration (µg/ml)	Absorbance	
	Ondansetron	Esomeprazole
2	0.136	0.103
4	0.268	0.209
6	0.410	0.310
8	0.550	0.429
10	0.655	0.532

The relationship between the concentration and the peak response of *ondansetron* and *Esomeprazole* was linear in the specific range and the regression coefficient was found to be 0.997 & 0.999 for both *Ondansetron* and *Esomeprazole* respectively.



Linearity of Ondansetron



Linearity of Esomeprazole

2. Range:

The range of method can be defined as the lower and upper concentrations for which the analytical method has adequate accuracy, precision, and linearity. The Beer's law limit for *ondansetron* and *Esomeprazole* is 2-10µg/ml.

The relationship between the concentration and the peak response of *ondansetron* and *Esomeprazole* was linear in the specific range of 2-10µg/ml.

3. LOD & LOQ:

The LOD and LOQ values for the *ondansetron* and *Esomeprazole* were calculated and results are tabulated in the following table

Parameters	Ondansetron	Esomeprazole
LOD	0.01044µg/ml	0.01061µg/ml
LOQ	0.03161 µg/ml	0.03216µg/ml

The LOD & LOQ of *ondansetron* was 0.0104484µg/ml & 0.0316196 µg/ml and LOD & LOQ of *Esomeprazole* was 0.0106155µg/ml & 0.0321692µg/ml. The method is reliable as the LOD value should not exceed LOQ and should obey the linearity range.

4. Accuracy:

Accuracy of the method was determined by recovery experiments. To the formulation, the reference standards of the drug were added at the level of 80%, 100% & 120%. The recovery studies were carried out three times and the percentage recovery and percentage relative standard deviation of accuracy data of *ondansetron* and *esomeprazole* were calculated and shown in tables.

Acceptance criteria for the percentage recovery should be within ±2.5%. In our study, the percentage recovery of *ondansetron* was found to be 79.62%, 99.50%, 120.37% from 80%, 100% and 120% sample solutions respectively. For *ondansetron* it was found to be 79.12%, 101.72%, 98.97% from 80%, 100% and 120% sample solutions respectively. The obtained percentage recovery of both drugs was found to be within the limit. This indicates the proposed method was more accurate.

Level	Amount (µg/ml)	Absorbance	Mean	Amount recovery	%recovery
80%	10	0.109	0.086	6.37	79.62%
		0.070			
		0.079			
100%	10	0.154	0.134	9.9506	99.50%
		0.142			
		0.107			
120%	10	0.224	0.195	14.44	120.37%
		0.192			
		0.169			

Recovery study of Ondansetron

Level	Amount (µg/ml)	Absorbance	Mean	Amount recovery	%recovery
80%	10	0.204	0.1956	6.33	79.12%
		0.196			
		0.187			
100%	10	0.329	0.3143	10.17	101.72%
		0.315			
		0.299			
120%	10	0.378	0.3670	11.87	98.97%
		0.369			
		0.354			

Recovery study of Esomeprazole

5. Precision:

Precision is determined by using the method to assay a sample for a sufficient number of times to obtain statistically valid results. The precision is then expressed in term of relative standard deviation. Acceptance criteria for the precision of the method is the %RSD should not be more than 2%. The results for intraday and interday were shown in the table

Intraday precision (1st day)

Concentration (µg/ml)	Ondansetron		Esomeprazole	
	248nm	310nm	248nm	310nm
10	0.6826	0.6943	0.5432	0.5762
	0.6781	0.6856	0.5429	0.5756
	0.6647	0.6790	0.5318	0.5697
Average	0.6751	0.6863	0.5393	0.5738
S.D	0.009	0.007	0.003	0.003
%RSD	1.3%	1.1%	0.6%	0.6%

Intraday precision (3rd day)

Concentration (µg/ml)	Ondansetron		Esomeprazole	
	248nm	310nm	248nm	310nm
10	0.5526	0.5691	0.4882	0.4895
	0.5489	0.5762	0.4910	0.4798
	0.5440	0.5799	0.4950	0.4905
Average	0.5485	0.5750	0.4914	0.4866
S.D	0.002	0.004	0.003	0.005
%RSD	0.5%	0.7%	0.6%	1.02%

Intraday precision (5th day)

Concentration (µg/ml)	Ondansetron		Esomeprazole	
	248nm	310nm	248nm	310nm
10	0.4956	0.4583	0.4219	0.4517
	0.4937	0.4551	0.4184	0.4501
	0.4901	0.4549	0.4087	0.4495
Average	0.4931	0.4561	0.4163	0.4504
S.D	0.002	0.009	0.0068	0.001
%RSD	0.5%	0.4%	1.6%	0.2%

The %RSD should not be more than 2%. For the precision study in the present work, the %RSD for *ondansetron* and *esomeprazole* was found to be 0.5% & 0.4% and 1.6% & 0.2% at 248 and 310nm respectively. The %RSD value indicates a good degree of precision within the specified range.

6. Ruggedness:

Ruggedness is the degree of reproducibility of results obtained by the analysis of the same sample under a variety of normal test conditions i.e.; different analysts. Acceptance criteria for ruggedness, the %RSD should not more than 2%. Results for ruggedness data of *ondansetron* and esomeprazole were shown in table

Analyst	Ondansetron		Esomeprazole	
	248nm	310nm	248nm	310nm
1	0.5421	0.5691	0.4082	0.3480
2	0.5417	0.5762	0.4110	0.3492
3	0.5398	0.5799	0.4150	0.3472
Average	0.5412	0.5750	0.4114	0.3481
S.D	0.001	0.004	0.003	0.001
%RSD	0.2%	0.6%	0.8%	0.2%

Ruggedness

The relative standard deviation for the sample preparations of *ondansetron* and *esomeprazole* was found to be 0.2% & 0.6% and 0.8% & 0.2% respectively. The %RSD should not be more than 2. Hence the %RSD value indicates a good degree of precision within the specified range.

CONCLUSION

A more rapid, simple, precise, sensitive, economic and reproducible spectrophotometric method for simultaneous estimation of *ondansetron* and *esomeprazole* by vierodt's method was developed and validated for specificity, linearity and range, accuracy, precision, LOD & LOQ, ruggedness as per ICH guidelines.

No interference was observed from 1NHCl and excipients of the formulation. Calibration curve was constructed for 2µg/ml - 10µg/ml for both *ondansetron* and *esomeprazole*. The linearity 2ppm-10ppm and correlation coefficient was found to be 0.997 & 0.999 for *ondansetron* and *esomeprazole*.

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