

## Research Article



## A Novel Validated Simultaneous Equations Method for Simultaneous Estimation of Omeprazole and Ondansetron in Bulk and Pharmaceutical Preparation

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### ABSTRACT

A simple, rapid, fast, accurate, economical and precise UV spectrophotometric method based on simultaneous equations was developed and validated for simultaneous estimation of Omeprazole and Ondansetron in tablet dosage form. Methanol was selected as a solvent for the proposed method. The method involved simultaneous equations using two wavelengths, with one being the  $\lambda_{\max}$  of Omeprazole (205 nm) and the other being the  $\lambda_{\max}$  of Ondansetron (246 nm). Beer's law was obeyed in the concentration range of 2 – 12  $\mu\text{g/mL}$  for both drugs with correlation coefficients of more than 0.99. The results of analysis have been validated statistically and by recovery studies as per ICH guidelines. The limit of detection and limit of quantification were found to be 0.29  $\mu\text{g/mL}$  and 0.90  $\mu\text{g/mL}$  for Omeprazole, respectively and 0.07  $\mu\text{g/mL}$  and 0.21  $\mu\text{g/mL}$ , respectively for Ondansetron. The mean percent recovery of triplicate samples at each level for both drugs was 99.48 - 100.3% for Omeprazole and 99.49 - 99.66% for Ondansetron. The assay results are in good agreement with the label claim; hence it could be used in routine analysis of laboratory samples and marketed formulations containing these two drugs.

**Keywords:** Simultaneous equations, Omeprazole, Ondansetron, ICH guideline, Validation.

### QUICK RESPONSE CODE →

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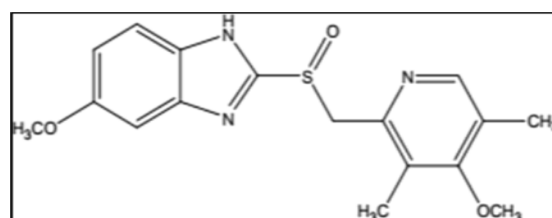


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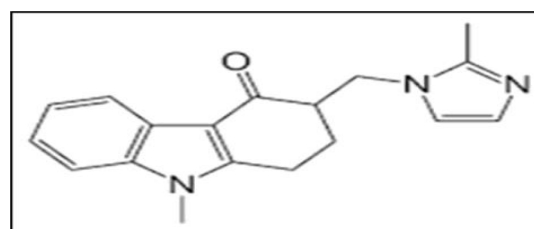
### INTRODUCTION

Omeprazole (OME) is one of the most important proton pump inhibitors (PPIs). PPIs are a group of drugs whose main action is pronounced and long-lasting reduction of gastric acid production. Omeprazole has a stereogenic center at the sulphur atom, and it exists as the two optically active forms, (S)-(-) and (R)-(+). Omeprazole.<sup>1-3</sup> It is chemically known as 6-methoxy-2-[(4-methoxy-3, 5-dimethylpyridin-2-yl) methylsulfinyl]-1H-benzimidazole. It has the molecular formula of  $\text{C}_{17}\text{H}_{19}\text{N}_3\text{O}_3\text{S}$  and a molecular weight of 345.4 gm/mol. Ondansetron (OND) is the type of the medicine called a 5HT<sub>3</sub> antagonist. OND is used to prevent the nausea and vomiting that can be caused by chemotherapy or radiotherapy for cancer, or by surgery. Chemically, it is 9-methyl-3-[(2-methylimidazol-1-yl) methyl]-2, 3-dihydro-1H-carbazol-4-one. It has the molecular formula of  $\text{C}_{18}\text{H}_{19}\text{N}_3\text{O}$  and a molecular weight of 293.4 gm/mol.<sup>4-7</sup> The chemical structure of OME and OND are shown in Figure 1. Combined treatment of OME and OND is better than either agent alone for the relief of acid-related indigestion and heartburn and to treat nausea and vomiting. OME and OND are official in many pharmacopoeias<sup>8-10</sup>. Literature

survey reveals several methods for analysis of OME alone as well as in combined dosage form with other drugs viz. UV methods<sup>11-15</sup>, HPTLC methods<sup>16-18</sup> and HPLC methods<sup>19-27</sup>. Similarly, literature survey reveals many methods for estimation of OND alone as well as in combined dosage form with other drugs viz. UV methods<sup>28-30</sup> and HPLC methods<sup>31-36</sup>. Very few analytical methods were reported for determination of OME and OND in combined dosage form.<sup>37-38</sup>. So, an attempt was made to develop simple, rapid, fast, accurate, precise, and economical spectrophotometric method based on simultaneous equations for simultaneous determination of OME and OND in tablets.



Structure of Omeprazole



Structure of Ondansetron

Figure 1: Chemical structure of OME and OND



## MATERIALS AND METHODS

### Instrumentation

Double beam UV-visible spectrophotometer (Shimadzu, model-1700, Japan) having two matched quartz cells with 1 cm light path were used for spectral measurements. UV probe 2.0 software was loaded on to UV-visible spectrophotometer.

### Chemicals and reagents

Omeprazole (OME) and Ondansetron (OND) pure drug powder were gifted from Intas Pharma, Ahmedabad, Gujarat. Methanol of AR Grade was procured from S.D. Fine Chemicals Ltd., Mumbai, India. Whatman filter paper no 41 (Millipore, USA) was also used.

### Preparation of solutions

#### Preparation of standard stock solutions (100 µg/mL)

The quantity of OME (10 mg) and OND (10 mg) was accurately weighed and transferred to 100 mL volumetric flasks separately and dissolved in a little amount of methanol. Then the flasks were shaken for few minutes and the volume was made up with methanol to obtain standard stock solution having concentration of 100 µg/mL each and filtered with 0.22 µm filter.

#### Preparation of working standard solutions

It was assembled in 2-12 µg/mL range of both OME and OND. Standard stock solutions of OME and OND were precisely measured (0.2, 0.4, 0.6, 0.8, 1.0, 1.2 mL) separately and transferred both of drugs in 10 mL volumetric flask and mitigated with methanol. The aliquots of the above stock solutions were diluted further with methanol to get concentrations of 2- 12 µg/mL for both OME and OND.

#### Preparation of sample solution

Twenty tablets were weighed accurately and average weight was determined. The tablets were powdered and tablet powder equivalent to OME (10 mg) and OND (4 mg) was weighed accurately and transferred to 100 mL volumetric flask. About 40 mL methanol was added to the flask and sonicated for 10-15 mins. The final volume was adjusted with the methanol and filtered through Whatman filter no 41. Then, the resulting solution was suitably diluted to the final sample solution of OME (10 µg/mL) and OND (4 µg/mL).

## RESULTS AND DISCUSSION

The main objective of this study was to develop a new spectrophotometric method based on simultaneous equations for simultaneous estimation of OME and OND in tablets and validated it as per ICH guidelines.

In the simultaneous equations method, the standard stock solutions (10 µg/mL) of both OME and OND were scanned in the range of 200 – 400 nm against methanol as a blank. The overlain spectra of OME and OND (10 µg/mL) is shown in Figure 2. Maximum absorbance was obtained at 205 nm

and 246 nm for OME and OND, respectively. Calibration curves for OME and OND were plotted and absorptivity for both drugs were calculated at two wavelengths 205 nm ( $\lambda_{max}$  of OME) and 246 nm ( $\lambda_{max}$  of OND) and concentration of OME and OND in the sample solutions were calculated using equations (1) and (2).

$$C_x = (A_2aY_1 - A_1aY_2) / (aX_2aY_1 - aX_1aY_2) \dots \dots \dots (1)$$

$$C_y = (A_1aY_2 - A_2aX_1) / (aX_2aY_1 - aX_1aY_2) \dots \dots \dots (2)$$

Where  $C_x$  and  $C_y$  are concentrations of OME and OND, respectively.  $A_1$  and  $A_2$  are absorbances of sample solution at 205 nm and 246 nm, respectively.  $aX_1$  and  $aX_2$  are absorptivities of OME at 205 nm and 246 nm.  $aY_1$  and  $aY_2$  are absorptivities of OND at 205 nm and 246 nm.

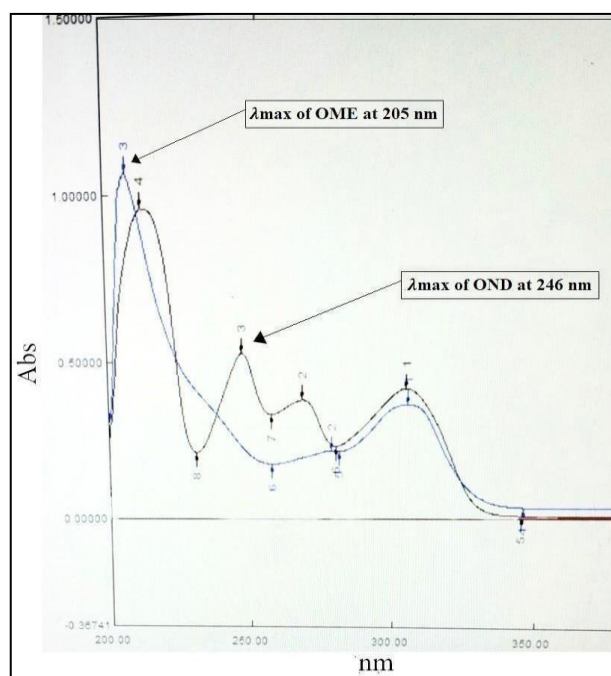


Figure 2: Overlain spectra of OME and OND (10 µg/mL)

### Method Validation<sup>39</sup>

#### Linearity

The linearity was evaluated by analyzing different concentrations of the standard solutions of OME and OND and it was found to be linear in the range of 2- 12 µg/mL for both OME and OND. The visual characteristics such as linearity range, standard deviation on slope and intercept, correlation coefficient and regression linear equation were calculated, and are summarized in Table 1.

#### Accuracy (% Recovery)

The accuracy of proposed method was determined by % recovery. Standard addition was used for accuracy determinations at three levels (80%, 100% and 120%) of concentrations; involving analysis of formulation of the samples containing 5 µg/mL of OME and 2 µg/mL of OND to which certain amounts of authentic drugs were added. The % recovering for OME and OND were found to be  $100.1 \pm 0.49$  and  $99.29 \pm 0.57$ , respectively as shown in Table 2.

**Precision****Method precision (Repeatability)**

Repeatability was studied by calculating the RSD for six determinations of the concentration of about 10 µg/mL and 4 µg/mL for OME and OND, respectively, performed on the same day and under same experimental conditions. The % RSD for OME and OND was found to be 0.49 % and 0.95%, respectively as shown in Table 1.

**Intermediate precision (Reproducibility)**

Intraday and inter day variations were determined by three solutions (4, 6, 8 µg/mL) of both OME and OND

within the same day and three different days over a period of week. The %RSD for OME and OND was found to be less than 2.0% as shown in Table 1.

**Limit of Detection (LOD) and Limit of Quantification (LOQ)**

LOD and LOQ for both drugs were calculated theoretically using following equation as per ICH guidelines. These data show that the method is sensitive. The corresponding results are reported in Table 1.

$$LOD = 3.3 \times \sigma/S \text{ and } LOQ = 10 \times \sigma/S$$

Where  $\sigma$  is the standard deviation of the response and S is the slope of the calibration curve.

**Table 1:** Summary of method validation parameters for OME and OND

Parameters	Simultaneous equations method			
	OME		OND	
	205 nm	246 nm	205 nm	246 nm
Calibration range (µg/mL)	2 -12	2 -12	2 -12	2 -12
Regression equation $y = mx + c$	$Y=0.1025x + 0.0833$	$Y=0.0239x + 0.0195$	$Y=0.0738x + 0.0949$	$Y=0.0558x + 0.065$
Slope	0.1025	0.0239	0.0738	0.0558
Intercept	0.0833	0.0195	0.0949	0.065
Correlation coefficient	0.9997	0.9992	0.9992	0.9993
Precision (% RSD)	Repeatability	0.49	0.59	0.54
	Intraday	0.10-0.50	0.72-1.32	0.55-0.84
	Interday	0.53-0.78	0.58-1.75	0.37-0.84
LOD (ug/mL)	0.29	0.03	0.12	0.07
LOQ (ug/mL)	0.90	0.09	0.39	0.21

**Table 2:** Accuracy studies of OME and OND (% Recovery)

Drug	Spiked level (%)	Amount taken (µg/mL)	Amount added (µg/mL)	% Recovery ± S.D (n = 3)
OME	80%	5	4	100.2 ± 0.10
	100%	5	5	100.3 ± 0.62
	120%	5	6	99.48 ± 0.76
OND	80%	2	1.6	99.49 ± 0.53
	100%	2	2	98.73 ± 0.92
	120%	2	2.4	99.66 ± 0.52

**Table 3:** Analysis of marketed formulation by proposed methods

Drug	Simultaneous equation method	
	OME	OND
Label claim (mg)	10	4
Assay (content in mg)	9.956	3.999
% Assay (Mean* ± S.D, n=6)	99.56 ± 0.89	99.98 ± 0.88

**CONCLUSION**

The simultaneous equations method for simultaneous determination of OME and OND in combined dosage form were developed and validated as per ICH guidelines. Linearity was observed in the range of 2-12 µg/mL for both OME and OND with correlation coefficient ( $r^2 = 0.999$ ). The % recoveries of OME and OND were in the range of 98-102% which was within the acceptance criteria. The %RSD was not more than 2% which proved the precision for the developed method. Results of validation of proposed



method indicates that the method is simple, precise, sensitive, accurate, rapid and economical for the determination of OME and OND in combined dosage form. The assay results showed that the method can be successfully applied for routine analysis of OME and OND in combined dosage form.

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