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Statistical assurance of process validation by analytical method development and validation for omeprazole capsules and blend.

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ABSTRACT

A new simple, rapid and reliable UV Spectrophotometry method was developed and validated for the estimation of Omeprazole in blend & Capsules formulations. The method was based on simple UV estimation in cost effective manner for regular laboratory analysis. The instrument used was Perkin Elmer, UV Spectrophotometer (Lambda 25) and using 0.1 N NaoH as solvent system. Sample were analysed using UV Win Lab 5.2.0 Software and matched quartz cells 1 cm and was monitored at 302 nm. Linearity was obtained in the concentration range of 2 - 10 mg mL–1 for Omeprazole. The validation parameters, tested in accordance with the requirements of ICH guidelines, prove the suitability of this method. Spectrophotometric interferences from the Capsules excipients were not found. The results of blend uniformity and content uniformity, done on process validation batches samples.

Key Words: UV Spectrophotometer, Omeprazole, Process Validation, Capsules Formulations, Quantitative analysis.

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INTRODUCTION

Omeprazole is chemically known as 6-methoxy-2-[(4-methoxy-3, 5- dimethylpyridin-2-yl) methylsulfinyl]-1Hbenzimidazole. Omeprazole is a used as an antiulcer drug and against other acid-related diseases [1]. This blocks the final and common step in gastric acid secretion. Literature survey reveals that USP 2007 and IP 2007 [2, 3] report HPLC method for assay of omeprazole. Analytical methods reported for the estimation of omeprazole are HPLC [4-12], LC-MS [13, 14] and HPTLC [15]. The present paper describes a simple, accurate and precise method for estimation of omeprazole in capsule dosage form. So far, no analytical methods are reported for analysis which is looking to pharmacokinetic characteristics of drug i.e. having t_{max} of 1 – 2 hour. The objective of this investigation is to develop, two simple, accurate and economical UV-spectrophotometric methods for estimation of Omeprazole using 0.1 N NaOH in which drug have good solubility. Process validation samples (blend and Capsules) are withdrawn at all stages and for all three validation batches for which analysis was performed using developed method.

EXPERIMENTAL

Instrument

For method, Perkin Elmer UV-Vis spectrophotometer (Lambda 25, spectral bandwidth 1nm) with 10 mm matched quartz cells; Shimadzu, Electronic Weighing Balance (AUX – 220), Oscar Ultrasonic Cleaner, Sonicator (Micro Clean 103) were used.

Reagent

Sodium Hydroxide (A.R.)

Procedure:

Method of analysis

Standard stock solution of omeprazole was prepared by dissolving 55 mg drug in 100 mL 0.1 N NaoH (i.e.550 µg/mL). Aliquot of these solutions were further diluted to obtain concentrations of 5.5 µg /mL for omeprazole and scanned in the UV-range. From the spectra, wavelength 302 nm (λmax of omeprazole) was selected. As reported in Figure1. The linearity was observed in the concentration range of 2- 10 µg/mL for omeprazole. The absorptivity coefficient of drug at desired wavelengths was determined and the results are presented in Table1. The spectral data from this scan was used to determine the concentration of drug in blend and Capsules sample solutions.

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Table: 1 Absorptivity A (1%, 1Cm) Values of Omeprazole at 302 nm

Concentration µg/ml	Absorbance	A(1%,1cm) Mean ± S.D	Molar Absorptivity (Mean ± S.D)
6	0.5874	979.11 ± 0.270	36234.93 ± 11.87

*Mean of Six Concentrations.

Analyses of Process validation samples (Blend and Capsules formulation)

Twenty Capsules were weighed ,crushed in to powder and an amount of powder equivalent to 250 mg omeprazole was transferred to a 100 mL calibrated volumetric flask, extracted with 0.1 N NaoH by shaking mechanically (for Content Uniformity). Similarly blend equivalent to 250 mg omeprazole was transferred to a 100 mL calibrated volumetric flask, extracted with 0.1 N NaoH by shaking mechanically (for Blend Uniformity). The solution was diluted to mark with the same solvent and filtered through Whatmann filter paper. (no. 41). Aliquot portion of this solution was diluted to get concentration of 6 µg/mL of omeprazole. Absorbance of the sample solutions were recorded, at 302 nm respectively (Perkin Elmer, Lambda 25). And, the concentrations of drug in samples were determined, by using calibration curve. The concentration of each drug was determined by analysis of spectral data of the sample solutions with reference standards. The results are reported in Table 2.

Table: 2 Results of Assay.

Result Of Assay Label Claim (mg/Tab)	% Label Claim*	± SD	%RSD	SE
250mg	100.74	0.88	0.83	0.14

* Mean of Five Estimation.

Recovery Studies

The recovery studies were carried out at three different level i.e. 80,100 and 120%. It was performed by adding known amount of standard drug solutions of omeprazole to preanalysed Capsules solutions. The resulting solutions were then reanalyzed by proposed methods. The results of recovery studies are shown in Table 3.

Table: 3 Results of Recovery studies.

S.No	Amount Of Drug Added (µg/mL)	% Recovery* ± SD	%RSD
1	3.2	99.58± 0.41	0.41
2	4.0	99.1± 0.60	0.64
3.	4.8	98.8 ± 0.88	0.89

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RESULTS AND DISCUSSION

The proposed methods are simple, sensitive, accurate, precise, reproducible, economic and rapid for simultaneous analysis of omeprazole in Capsules. Accuracy of the method was evaluated by carrying out recovery studies. Low values of %RSD are indicative of high precision of the methods. The repeatability and ruggedness study signifies the reproducibility of the method as shown in Table 4.

Based on the validation study data, it can be concluded that the proposed method is accurate and precise for the analysis of drug. No interference was found from excipients used in Capsules formulation and hence the method is suitable for analysis of blend and Capsules formulation. Process validation samples, blend uniformity was found to be good within and between all three validation batches as shown in Table 5. Formation of Capsules, sample for content uniformity were collected at three stages (initial, mid, end) for all three validation batches, results for which show that there is uniformity in dosage units within batch and similarity between batches as shown in Table 6.

Table: 4.Results of Repeatability and Ruggedness studies.

Parameters	% Recovery*+ RSD
Precision %RSD	
Intra-Day (n=3)	0.40-1.46
Inter-day (n=3)	0.72-1.39
Repeatability (n=6) % RSD	0.89
Ruggedness (n=5)	
Analyst I	0.65
Analyst II	0.74

Table: 5.Blend Uniformity * (% Assay for Each Sample)

	Batch I	Batch 2	Batch 3
Mean	100	98.4	102.1
Min.	98.6	98.1	101.5
Max	0.77	0.3	0.53

*Final blend analysed for 6 locations from Rapid Mixing Granulator.

Table: 6.Content Uniformity * (% Assay for Each Sample)

S.No	Batch 1 Stage			Batch 2 Stage			Batch 3 Stage		
	1	2	3	1	2	3	1	2	3
Mean	99.9	100.2	100.1	99	100.3	101.3	102.7	103	103.2
Min	99.9	99.5	99.6	97.4	98.4	100.2	102	102.6	102.7
Max.	98.9	100.6	100.6	100.2	102.3	103.8	104.1	103.9	102.6
%RSD	0.50	0.4	0.3	1.1	1.2	0.7	0.7	0.5	0.4

* Ten Units individual assay was analyzed for each stage of all the batches.

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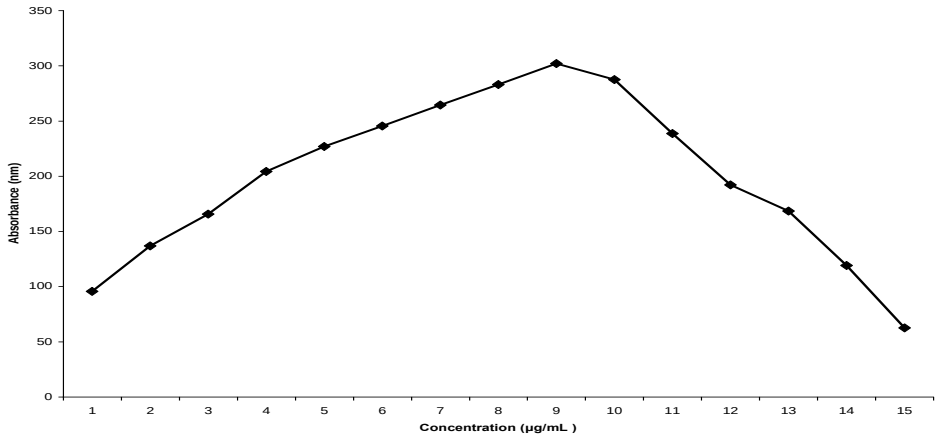

Figure: 1. Spectra of Omeprazole API

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