Original Article

Quantitative Analysis of Pantoprazole Sodium Sesquihydrate in Bulk and Solid Dosage Form via UV-Spectrophotometric Method

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ABSTRACT

Pantoprazole sodium sesquihydrate, is a proton pump inhibitor, was analyzed by using UV spectrophotometry. The quantification of pantoprazole sodium sesquihydrate in distilled water was performed in the wavelength range of 290 nm at 20 μgmL^{-1}. The linearity range is 5-35 μgmL^{-1} by using UV spectrophotometry. The developed method was applied directly and easily to the analysis of the pantoprazole sodium sesquihydrate in bulk and pharmaceutical tablet preparations. The developed method was completely validated according to ICH guidelines. The accuracy of the developed method was calculated in terms of percentage recovery (99.20-101.21%) and %RSD values less than 1% were found in precision. The LOD and LOQ were 0.989 and 1.954 μgmL^{-1}, respectively. Because of simplicity, accuracy and cost-effectiveness, this validated method is helpful for a daily laboratory analysis of pantoprazole sodium sesquihydrate.

Key words: Pantoprazole sodium sesquihydrate, Proton pump inhibitor, UV-Spectrophotometer, Method development, ICH guidelines.

INTRODUCTION

Chemically, Pantopraole sodium sesquihydrate is known as sodium 5- (difluoromethoxy) - 2- [3,4 - dimethoxy - 2 - pyridyl) methylsulfinyl] - 1H benzimidazole sesquihydrate.[1] Pantopraole sodium sesquihydrate is a proton-pump inhibitors that block stomach acid by inhibiting the H^+/K^+-ATPase enzyme of the secretory caniculus parietal cell thereby curing the acid related problems. As it is unstable at low pH, therefore, available as an enteric coated tablets.[2-4] Pantoprazole sodium sesquihydrate acts as a key drug of triple therapy for Helicobacter Pylori's eradication or individually for the management of esophagus inflammation and maintenance of gastro-esophagus reflux disease, it shows similar pharmacology like other proton pump inhibitors, however shows greater consequence than Histamine H_2 antagonists.[4-8]

Few methods have been reported for the analysis of this drug in literature. Keyur and co-worker also reported the same work for the simultaneous estimation of cinitapride and pantoprazole in pharmaceutical dosage form.[9] In 2013 Sourav *et al.* reported work on the formulation and evaluation of enteric coated tablets of pantoprazole.[10] Another work published on for simultaneous estimation of pantoprazole and levosulpiride using UV spectrophotometric in capsule dosage form.[11] Ognjenka with co-worker validated HPLC method for pantoprazole pellets.[12] Utsav *et al.* reported the dual wavelength method for simultaneous estimation of ondansetron and pantoprazole in combined tablet dosage form.[13]

The published literature survey reveals that there are several analytical methods for the estimation of pantoprazole sodium sesqui-

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hydrate in a combined solid dosage form. But to the best of our knowledge, there is no method for the detection of Pantopraole sodium sesquihydrate in bulk using distilled water as solvent. Therefore, the author have made an attempt to develop modern, rapid, precise and reproducible single analytical method for the detection of pantoprazole sodium sesquihydrate in bulk for first time according to the guidelines stated by USP-39 and International Conference on Harmonization (ICH).[14,15]

Experimental

Instrumentation

UV-Spectrophotometer Model: UV-1800 240 V, Shimadzu, Japan, Electronic Balance: ATL 3000G/0.001G, Dissolution apparatus Model: GDT-6L Serial No: 14-8-95, Galvano Scientific, Pakistan. Electrical Thermostatic Water Bath 220 V 50 Hz, Power (W) 1000±10%, Temperature ranges 37–100°C, Daihan Scientific, China.

Reagent and Chemical

Pantoprazole sodium sesquihydrate kind presented by Bosch Pharmaceuticals (Pvt.) Ltd, while freshly prepared distilled water utilized in the laboratory throughout the experiment. Hydrochloric acid 37% by RCL Lab scan Limited and sodium hydroxide purchased by Daejung Chemicals and Metals Co. Ltd. Zopent tablet (20 mg) of Hilton Pharma (Pvt.) Ltd, Neege Tablet 20 mg of Sami Pharmaceuticals (Pvt.) Ltd., Panizox Tablet 20 mg of S.J. and G. Fazul Ellahie (Pvt.) Ltd. and Zentro Tablet 20 mg by Bosch Pharmaceuticals (Pvt.) Ltd was purchased from a local pharmacy.

Preparation of Solutions

Stock solution: 0.02 g of pantoprazole sodium sesquihydrate was weighed accurately, transferred to a volumetric flask (100 mL) and dissolved in 20 mL distilled water. The volume of the flask was made up to the 100 mL and was shaken well. From stock standard solution, 5 mL of pantoprazole sodium was transferred to a volumetric flask (50 mL) and the volume of the flask was made to mark 50 mL with distilled water and was shaken well.

Preparation of sample solution: Transfer about 0.02 g of pantoprazole sodium sesquihydrate accurately weighed to a volumetric flask of 100 mL, dissolved in 20 mL distilled water and then diluted with diluents to volume and mixed. After even mixing, the final 20 μgmL^{-1} concentrated solutions were prepared by pipetting out 5 mL aliquot of this solution in another 50 mL volumetric flask and diluted it with diluent to calibration mark. Shake the contents to get homogenous dilution.

MATERIALS AND METHODS

Analytical method development using UV-Spectrophotometer

Different aliquots were scanned via UV-Spectrophotometer to determinate the wavelength having maximum absorbance.

Medium suitability of pantoprazole sodium sesquihydrate with distill water

The sample preparation was left up to a specified period of about 24 hrs and stability of pantoprazole sodium sesquihydrate with the distilled water was assessed by comparing solution preparations at different time intervals to that of initial. The solutions were scanned at different time intervals like 2, 4, 8 and 24 hrs and spectra of respective peaks were recorded.[14,15]

Analytical method validation of proposed method

The validation of proposed method was based on ICH guidelines and USP-39.[14,15]

Linearity

The calibration curve was plotted in the range of 5 to 35 μgmL^{-1} to determine the correlation coefficient and y-intercept. The sample solution was serially diluted from 5 to 35 μgmL^{-1} in distilled water and scanned at 290 nm wavelength to get the absorbance of respective dilution.[16]

Precision

Intraday precision was determined by estimating the response of six samples of 20 μgmL^{-1} on the same day.[14-16]

Accuracy

The accuracy of the method was determined by calculating the percentage recoveries. So, these 10, 15, 20, 25 and 30 μgmL^{-1} dilutions were analyzed thrice to assess the percentage recoveries.[14,15]

Ruggedness

For the determination of intermediate precision 20 μgmL^{-1} dilution was analyzed on three consecutive days by three different analysts without changing the parameters and instrument. The results were reported in terms of relative standard deviation %RSD.[14]

Robustness

Robustness of the stated method was evaluated by deliberate variation in the solvent and temperature. Deliberately changed tap water instant of distill water and temperature 25°C±5. Scanned the standard solu-

tion following the both samples to find out the robustness of the method. [14]

Limit of Detection and Limit of Quantification

By using below equation, the LOD of our developed method of pantoprazole sodium sesquihydrate in bulk was determined. Limit of detection [LOD] =3.3 σ/S. Limit of quantification was determined by using this equation. Limit of quantification [LOQ] =10 σ/S.

Specificity of the proposed method was determined by analyzing the standard dilution and the placebo. [16]

Assay of marketed available pantoprazole sodium tablets

20 tablets from each brands were accurately weighed and grinded them to a fine powder. Transferred powder equivalent to 100mg of Pantopraole sodium sesquihydrate into 50mL volumetric flask. Add 20 mL of distill water and stir to dissolve the contents. Make up the volume to the mark with diluents and mixed well. Then all the dilutions were scanned at 290nm by using UV-Spectrophotometer. Then, absorbance of all the four test solutions was recorded.[17]

RESULTS AND DISCUSSION

Analytical Method Development Using UV-Spectrophotometer

Solution with 20 μgmL^{-1} concentration was considered as standard dilution of pantoprazole sodium sesquihydrate and wavelength of 290 nm was selected as quantitative wavelength (Figure 1).

Medium suitability of pantoprazole sodium sesquihydrate with distill water

It was evaluated that the pantoprazole sodium sesquihydrate with water showed satisfactory behavior during the 24 hr (Table 1) (Figure 2).

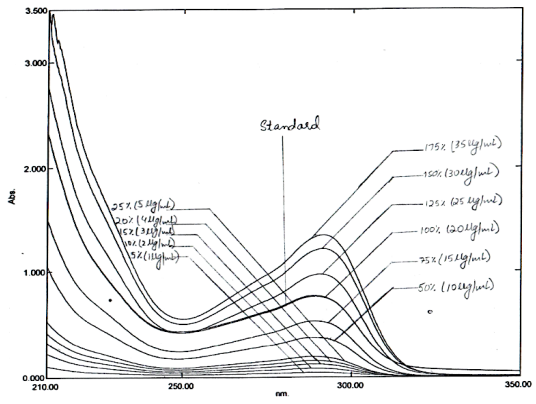

Figure 1: Analytical method development using UV-spectrophotometer scheme.

Analytical method validation of developed method using UV-Spectrophotometer

Linearity

The linearity of developed method was evaluated at seven different concentrations from 5 to 35 μgmL^{-1}. Correlation coefficient, intercept and slope value were also determined for statistical investigation. The observed absorbance of each test sample was plotted against the corresponding concentration and a controlled linear line was obtained (Figure 3) with linear regression equation 0.03 and correlation coefficient 0.99 in the concentration from 5 to 35 μgmL^{-1} range. So, it is concluded that the proposed method is linear in the specified range of concentrations.[18]

Accuracy

Accuracy was determined by analyzing known amounts of analyses and it was calculated as the % recovery of the analytes. Each sample was analyzed three times from concentrations 50, 75, 100, 125 and 150%. Table 2 results revealed that the developed analytical method is highly accurate for the analysis of pantoprazole sodium sesquihydrate in bulk.

Precision

Six readings of 20 μgmL^{-1} were taken as to calculate the intra-day precision. The % recoveries were from 98.81 to 100.52%. On behalf of %RSD range which is less than 1%, it was concluded that the developed method had good precision (Table 3 and Figure 4).

LOD and LOQ

The distinctive study verifies the no interference of degradation or impurity and solvent in absorbance of Pantoprazole sodium sesquihydrate (Figure 5). As per ICH guidelines, LOD and LOQ were found to 0.989 and 1.954 μgmL^{-1}, respectively.

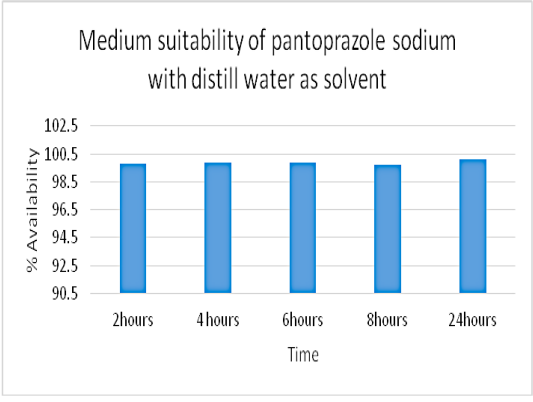

Figure 2: Medium Suitability of Pantoprazole Sodium with Distilled Water.

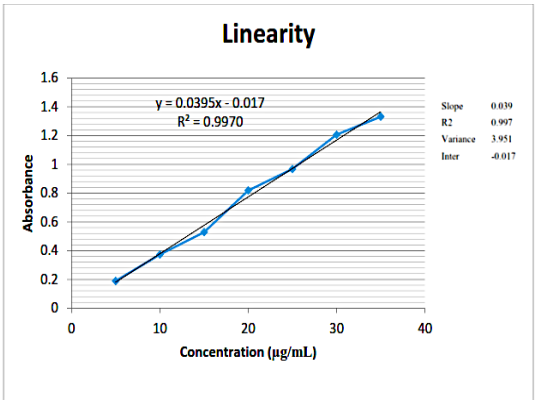

Figure 3: Linearity curve of developed method.

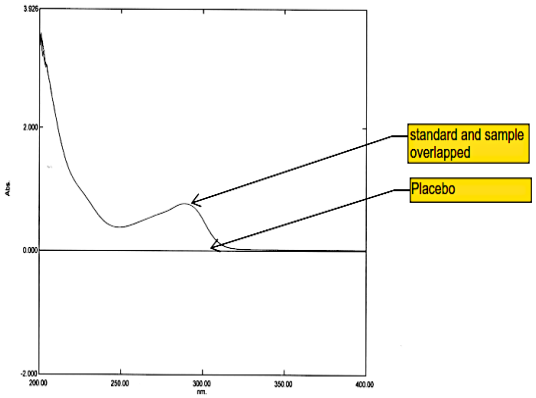

Figure 5: Specificity of Developed Method.

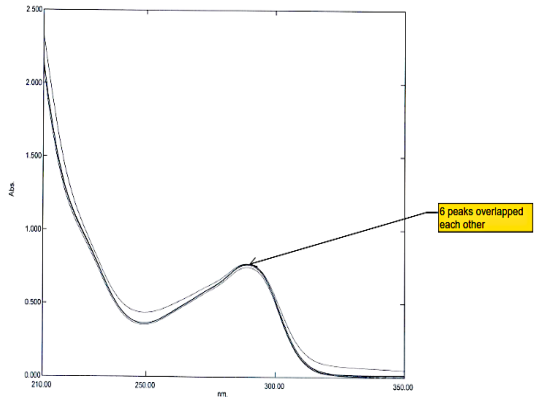

Figure 4: Precision of developed method.

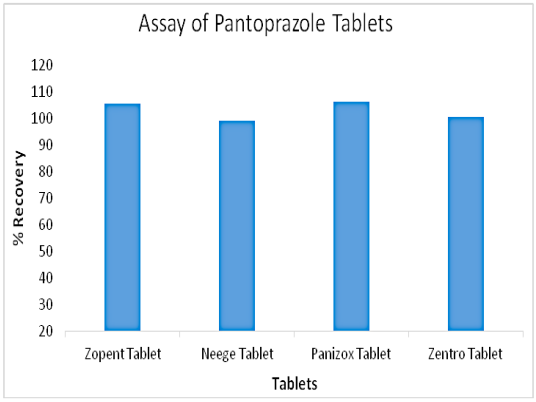

Figure 6: Assay of Pantoprazole Sodium Tablets.

Ruggedness

The ruggedness of the analytical method was estimated by an inter-day experimental condition. Three days practical was performed by three different analysts under the same conditions with the same instrument. The resulting scheme in Table 4 presented a good ruggedness of the method.

Robustness

The robustness of the developed method in this experimental work was evaluated by changing the solvent from distilling water to tap water and temperature 25°C ± 5. The results represented that no critical change was recorded as mention in Table 5.

Assay of pantoprazole sodium sesquihydrate tablets

According to USP-39, the assay limit of pantoprazole sodium sesquihydrate enteric coated tablet is NLT 90% and NMT 110.0%.[16] Table 5 shows the assay results of Zopent, Neege, Panizox and Zentro. Neege and Zentro have 99.08% and 100.52% close to each other whereas Zopent and Neege showed results above 100% (Table 6, Figure 6). All the % availabilities were in limit and all brands pass the assay results.

CONCLUSION

A simple, selective, rapid, accurate and precise analytical method by using UV-spectrophotometer for estimation of pantoprazole sodium sesquihydrate in bulk was developed and validated according to USP-39 and ICH guidelines. Commonly and easily available solvent and

Table 1: Medium suitability of pantoprazole sodium with distilled water

S No.	Time (hrs)	Absorbance		%Recovery
		Sample	*Standard*	
1	2	0.758	0.767	99.82
2	4	0.766	0.767	99.86
3	6	0.766	0.767	99.86
4	8	0.76	0.767	99.73
5	24	0.768	0.767	100.13

Table 2: Accuracy of Developed Method Using UV-Spectrophotometer

S No.	Concentration		Absorbance		%Recovery
	µg/mL	*%*	*Sample*	*Standard*	
1	10 (*n*=3)	50	0.383	0.382	100.26
			0.384	0.382	100.52
			0.385	0.382	100.78
2	15 (*n*=3)	75	0.575	0.573	100.34
			0.580	0.573	101.21
			0.579	0.573	101.04
3	20 (*n*=3)	100	0.759	0.764	99.34
			0.759	0.764	99.34
			0.765	0.764	100.13
4	25 (*n*=3)	125	0.951	0.958	99.26
			0.959	0.958	100.10
			0.950	0.958	99.16
5	30 (*n*=3)	150	1.150	1.146	100.34
			1.149	1.146	100.26
			1.146	1.146	100.00

Table 3: Precision of Developed Method Using UV-Spectrophotometer

S No.	Concentration		Absorbance		%Recovery	%RSD
	µgmL^{-1}	%	Sample	Standard		
1	20	100	0.766	0.762	100.52	0.625
2	20	100	0.763	0.762	100.13	
3	20	100	0.765	0.762	100.39	
4	20	100	0.753	0.762	98.81	
5	20	100	0.761	0.762	99.86	
6	20	100	0.759	0.762	99.60	

Table 4: Ruggedness of Developed Method Using UV-Spectrophotometer

S No.	Analyst	Day	Absorbance		%Recovery	% RSD
			Sample	*Standard*		
1	A	Day-1	0.761	0.760	100.13	0.370
2			0.761		100.13	
3			0.759		99.86	
1	B	Day 2	0.769	0.769	100.00	
2			0.768		99.86	
3			0.767		99.73	
1	C	Day 3	0.765	0.766	99.86	
2			0.762		99.47	
3			0.758		98.95	

Table 5: Robustness of Developed Method

S No.	Concentration		Solvent	Temperature (°C)	Absorbance		% Recovery
	*µg/m*L	%			Sample	Standard	
1	20	100	Tap Water	20°C	0.763	0.768	99.35
				25 °C	0.768		100.00
				30°C	0.770		100.26
2	20	100	D.I Water	20°C	0.765		99.61
				25 °C	0.769		100.13
				30°C	0.772		100.52

Table 6: Assay of Pantoprazole Sodium Tablets

S No.	Brand	Absorbance	Limit	Result
1.	Zopent Tablet	0.806	*NLT 90% and NMT 110%	105.35
2.	Neege Tablet	0.758		99.08
3	Panizox Tablet	0.812		106.14
4.	Zentro Tablet	0.769		100.52

- Not less than (NLT) and Not more than (NMT)

technique was adopted for the experimental work. So, we can say that the developed analytical method is also cost-effective. On the basis of above results and discussion, the developed method for determination of pantoprazole sodium sesquihydrate in bulk can be used in routine analysis. The pantoprazole sodium sesquihydrate solution is stable up to 24 hrs under normal environmental condition. Moreover, the developed method is also successfully applied for the determination of pantoprazole sodium sesquihydrate in solid dosage form. The marketed brands passed the pharmacopoeial test.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

LOD: Limit of detection; **LOQ:** Limit of quantification; **mL:** Milliliter; **UV**: Ultra violet.

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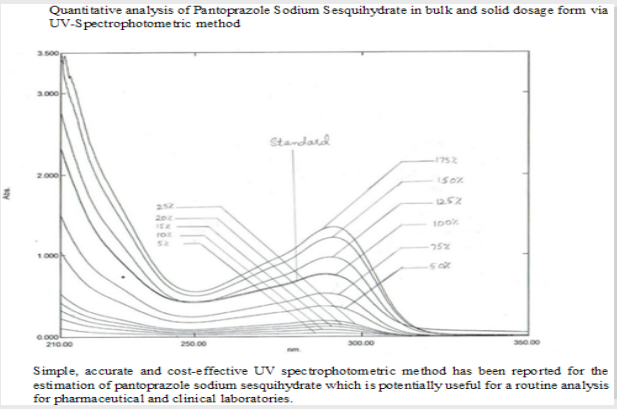
PICTORIAL ABSTRACT



SUMMARY

Simple, accurate and cost-effective UV spectrophotometric method has been reported for the estimation of pantoprazole sodium sesquihydrate which is potentially useful for a routine analysis for pharmaceutical and clinical laboratories.

About Authors

Asma Rafiq has completed her M.Phil., with specialization in the field of Pharmaceutical method development via spectroscopy and stability studies. Currently she is working as an Assistant Manager Regulatory Affairs, Nabi Qasim Industries Pvt. Ltd. She actively participates in research and presents her research work in different National and International conferences.

Prof. Dr. Somia Gul is working as an Associate Professor of Pharmaceutical Chemistry. Her field of specialization is Drug-Drug interaction studies, Drug-Metal complexes and Organic synthesis of drug molecules of biological interest. Currently, she is involved in green synthesis of molecules of biological interest against Multi Drug Resistant Pathogens. Dr. Somia has more than 70 international publications in refereed journals. Her one book has been published while another is in pipeline. She has already produced 6 M.Phil. students and 1 Ph.D. student. Besides teaching and research, she is also serving as reviewer and examiner for different reputed journals, universities and research funding bodies.

Ms. Arzoo Ajaz is pursuing her M. Phil. in Pharmaceutical Chemistry under the supervision of Dr. Somia Gul. Her current focus is on synthesis of different drug metal complexes as strong antimicrobial agents against MDR bacteria. She also served as a lecturer in Nazeer Husain University and presented a number of research works in different national and international conferences.

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Dr. Agha Zeeshan Mirza is working as an Assistant Professor and his research broadly fall in the area of Organic, Pharmaceutical and Analytical Chemistry. Particularly he specialized in developing new methods and protocols for *in vitro* analysis of drug-drug interactions. He also researched for six months as a Visiting Scholar at Purdue University, USA. At Purdue, his focus was on the development of nanoparticles for biosensing and targeted drug delivery for cancer therapeutics. At Umm Al Qura University, he completed the project related with the Drug Design of Isoxazolidine Nucleosides Derivatives with Potential Antiviral and Anticancer Activities and now involved in the proposal with Drug Design of bifunctional Hybrid agents. He published 45 research articles in national and international journals.

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