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Simultaneous Determination 0f Naproxen Sodium and Pantoprazole Sodium in Bulk and Pharmaceutical Dosage Form by Validated Ultra-Violet Spectrophotometric Method

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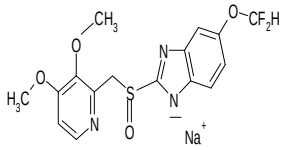
A Ultra-Violet spectrophotometric method has been developed and validated for the simultaneous estimation of Naproxen sodium (NAP) and Pantoprazole sodium (PAN) in bulk and pharmaceutical dosage form. The spectrophotometric method involves the simultaneous equation method at 232.0 and 291.0 nm over the concentration range of 10µg/ml for both by using 0.1M NaOH as solvent. The method was validated for linearity, precision, sensitivity, and specificity. The calibration curves were linear over the range of 2-10 µg/ml for both NAP and PAN, with significant high value of correlation coefficient (>0.995 for both drugs). The percentage recovery value for NAP was 100.03% and for PAN was 100.2%.

Keywords: Naproxen Sodium, Pantoprazole sodium, Ultra-Violet spectrophotometric method, Simultaneous equation, Validation.

INTRODUCTION

Pantoprazole sodium (PAN) is chemically 5-(Difluoromethoxy)-2-(3, 4-dimethoxy-2-pyridinyl) methyl) sulfinyl)-1H-benzimidazole sodium. (Fig. 1) is a potent Proton pump inhibitor used for treatment of ulcer [1, 2]. Naproxen sodium (NAP) is chemically 2-(6-methoxy naphthalen-2-yl) propanoic acid (Fig. 2) is a potent non steroidal anti inflammatory drug (NSAID) commonly used for the reduction of moderate to severe pain, fever, inflammation and stiffness [3, 4]. A novel formulation in combination of NAP 250 mg and PAN 20 mg is commercially available in Indian market for treatment of osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, fever and prevent some of the gastro-intestinal problems that NSAIDs can cause.



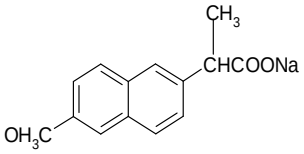


Fig. 1. Pantoprazole sodium. **Fig. 2.** Naproxen sodium

Literature survey reveals that different methods have been reported for analysis of PAN and NAP by Spectrophotometry [3-10], and HPLC [11-16], either alone or in combination with other drugs. There are fewer UV Spectrophotometry methods are reported for the simultaneous analysis of NAP and PAN in their combined dosage form. The present work demonstrates simple, rapid, accurate, reproducible and economical method for the simultaneous determination of NAP and PAN in pharmaceutical dosage form by UV Spectrophotometric method which can be used for its routine analysis in laboratories.

MATERIALS AND METHODS

Chemicals

Working standards of pharmaceutical grade PAN and NAP were obtained as generous gifts from Ajanta Pharmaceutical Ltd., Mumbai (Maharashtra, India) It was used without further purification and certified to contain 99.80 % and 99.85 % (w/w) on dry weight basis PAN and NAP respectively. Fixed dose combination of capsule containing PAN 20 mg and NAP 250 mg was purchased from Local Indian market. All other chemicals were purchased from Merck chemicals, Mumbai, India.

Apparatus

A Perkin Elmer UV-2500 UV/VIS Spectrophotometer was used with 1 cm matches quartz cell, analytical balance (shimadzu) and ultra sonic cleaner were used.

Preparation of Standard Stock Solution

Reference standard of PAN 10 mg and NAP 10 mg was transferred to 10 ml of volumetric flask and dissolved with 0.1 M NaOH. The flask was sonicated for 30 min and made up the volume with 0.1 M NaOH to obtain standard stock solution. The concentration was found to be 1000µg/ml of PAN and NAP.

Preparation of Working Standard Solution

From the stock solution, 1ml was taken into the 10 ml volumetric flask and made up to the volume using 0.1 M NaOH. It contains 100µg/ml of PAN and NAP**.** Further pipette out 1 ml of the above stock solution into a 10ml volumetric flask and dilute up to the mark with 0.1 M NaOH. The concentration was found to be 10µg/ml of PAN and NAP.

Analysis of Marketed Formulation by Vierodt's Method

Accurately weighed twenty capsules and powder equivalent to 10mg of NAP and PAN was weighed and transferred into a dry clean volumetric flask. About 5ml of 0.1 M NaOH was added and sonicated to dissolve it completely and volume was made up to the mark with the same solvent. From the stock solution, 1ml was taken into the 10ml volumetric flask and the volume was made up to the mark using 0.1 M NaOH to contain 100µg/ml of PAN and NAP**.** Further 1ml of the above solution was pipette out into a 10ml volumetric flask and diluted up to the mark with 0.1 M NaOH. The concentration was found to be 10µg/ml of PAN and NAP.

The working standard and sample solutions were scanned within the wavelength range of 400-200 nm. The spectra of

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both the drugs were obtained to determine the λ_{max}. Two absorption maxima wavelengths were selected for NAP and PAN, that is, 232.0 nm and 291.0 nm, respectively in 0.1MNaOH. The working standard solutions of both drugs were measured at the selected wavelengths and absorptivities (a, 1%, 1cm) for both drugs at both wavelengths were determined. Concentrations in the sample were obtained using following equations:

$$CX = A2\ ay1 - A1ay2\ /\ ax2\ ay1 - ax1ay2 \quad Eq\ (i)$$

$$CY = A1\ ax2 - A2ax1\ /\ ax2\ ay1 - ax1ay2 \quad Eq\ (ii)$$

Where, A1 and A2 are the absorbance of mixture at 232.0 nm and 291.0 nm respectively, ax1 and ax2 are absorptivities of naproxen at λ1and λ2 respectively and ay1 and ay2 are absorptivities of pantoprazole at λ1 and λ2 respectively.CX and CY are concentrations of naproxen and pantoprazole respectively.

Experimental results of the λ_{max} of NAP and λ_{max} of PAN were shown in Fig (3). Amount of PAN and NAP in pharmaceutical dosage form was expressed as a percentage of label claims were shown in Table 5.

Method validation

The simultaneous equation method was validated by evaluating linearity, accuracy, method and system precision, limit of detection (LOD), limit of quantification (LOQ) and ruggedness were performed accordance with ICH guideline Q2(R1) [17].

Linearity

From the standard stock solution of concentration 100 µg/ml, 0.2, 0.4, 0.6, 0.8 and 1ml was transferred to five 10ml flasks and made up the volume with solvent. The concentrations of PAN and NAP were found to be 2-10 µg/ml. The calibration curves were plotted and shown in Fig 4, 5. The results of linearity were shown in Table 1.

Table 1: Calibration Data of Naproxen sodium and Pantoprazole sodium

S.No	Concentration (µg/ml)	NAP	PAN
1	2 µg/ml	0.1962	0.1038
2	4 µg/ml	0.8517	0.2055
3	6 µg/ml	1.6541	0.3415
4	8 µg/ml	2.3584	0.4254
5	10 µg/ml	3.3254	0.5314
Correlation Coefficient		0.995	0.995

Accuracy

Accuracy of the method was carried out by standard addition method at three levels of concentrations (80%, 100%, and 120%). The results of recovery (%) and %RSD calculated. were shown in Table 2.

Table 2: Accuracy results for the Naproxen sodium and Pantoprazole sodium

Drug	Level (µg/ml)	Amount added (µg/ml)	Total Amount (µg/ml)	Amount recovery	%recovery
NAP	80	5	85	84.9	99.2%
	100	5	105	105.2	101.3%
	120	5	125	124.6	99.6%
PAN	6.4	5	11.5	11.9	101.2%
	8	5	13	12.9	99.8%
	9.6	5	14.6	14.5	99.7%

Table 3: Precision results for the Naproxen sodium and Pantoprazole sodium

S. No	NAP	PAN
1	3.3178	1.0977
2	3.3141	1.0842
3	3.3092	1.0831
Avg.	3.3137	1.0883
S.D	0.00431	0.0081
%R.S.D	0.147%	0.74%

Method and System Precision

Precision of the method was verified by repeatability (system precision) and intermediate (method precision) studies. Repeatability studies were performed by three replicate absorbances of PAN and NAP on the same day. The studies were replicated on different days to determine intermediate precision. The results of the system and method precision were shown in Table 3,4.

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

The limit of detection (LOD) is the lowest amount of analyte in a sample that can be detected, but not necessarily quantified, under the stated experimental conditions. LOD & LOQ was calculated by using standard deviation and slope values obtained from calibration curve.

Table 4: Precision results for the Naproxen sodium and Pantoprazole sodium

S.NO	NAP		PAN	
	Day 1	Day 2	Day 1	Day 2
1	3.3247	3.3178	1.0977	1.0249
2	3.3992	3.3141	1.0842	1.0192
3	3.3017	3.3092	1.0831	1.0153
Avg	3.3085	3.3137	1.0883	1.0198
S.D	0.0140	0.00431	0.0081	0.00482
%R.S.D	0.66	0.147	0.74	0.47

Avg- Average, S.D- Standard deviation, %R.S.D- Relative standard deviation

RESULTS AND DISCUSSION

A rapid, simple and economical UV method was developed for the simultaneous estimation of NAP and PAN in bulk and pharmaceutical dosage form. In the proposed method, NAP and PAN showed the maximum absorbance at 232.0 nm for NAP and 291.0 nm for PAN in 0.1 M NaOH, respectively. Isobestic point was found to be 257 nm (Fig.3). Both analytes, i.e. .NAP and PAN obeys the Beer's law at a

concentration range between 2 and10 µg/ml. assay values of NAP and PAN was displayed in Table 1 and Fig. 4, 5. The developed method was validated as per ICH guidelines.

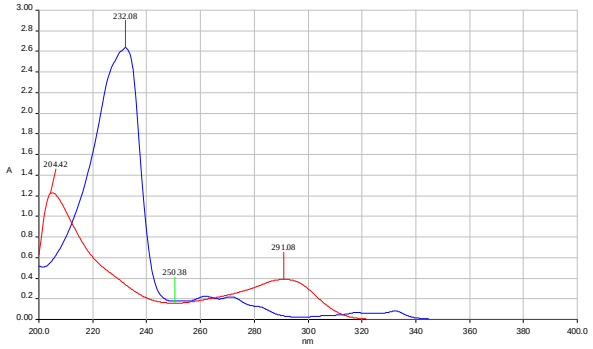

Fig. 3. Spectra for the isobestic point of Naproxen sodium and Pantoprazole sodium

Accuracy is a measure of the closeness of test results obtained by a method to the true value. It indicates the deviation between the mean value found and the true value. In our study, the percentage recovery of NAP was found to be 99.2%, 101.3%, and 99.6% from 80%, 100% and 120% sample solutions respectively. For PAN it was found to be 101.2%, 99.8% and 99.7% from 80%, 100% and 120% sample solutions respectively. The obtained percentage recovery of both drugs was found to be within the range. This indicates the proposed method was more accurate than the existing methods. The results were displayed in table 2.

Table 5: Assay results for the Naproxen sodium and Pantoprazole sodium

Drug	Labeled amount	Amount present	% of drug found
NAP	250	248.97	99.5
PAN	20	19.97	99.8

The precision of an analytical method is the degree of agreement among individual test results obtained when the method is applied to multiple sampling of a homogenous sample. Precision is a measure of the reproducibility of the whole analytical method (including sampling, sample preparation and analysis) under normal operating circumstances. Precision is determined by using the method to assay a sample for a sufficient number of times to obtain statistically valid results (i.e. in between 5-10). The precision is then expressed as the relative standard deviation. Acceptance criteria for the precision of the method, the %RSD should not be more than 2%. In the present study, the % RSD for NAP and PAN was found to be 0.147%, 0.74% respectively. The % RSD value indicates a good degree of precision within the specified range (Table 3, 4).

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 days, different analysts, laboratories, instruments, reagents, assay temperatures, different days etc. (i.e. from laboratory to laboratory, from analyst to analyst). Acceptance criteria for ruggedness, the %RSD for the area of five standard injections should not be more than 2%. Results of this study showed that the % RSD of three samples was 0.66, 0.147 for NAP and 0.74, 0.47 for PAN respectively indicating a good intermediate precision of the method.

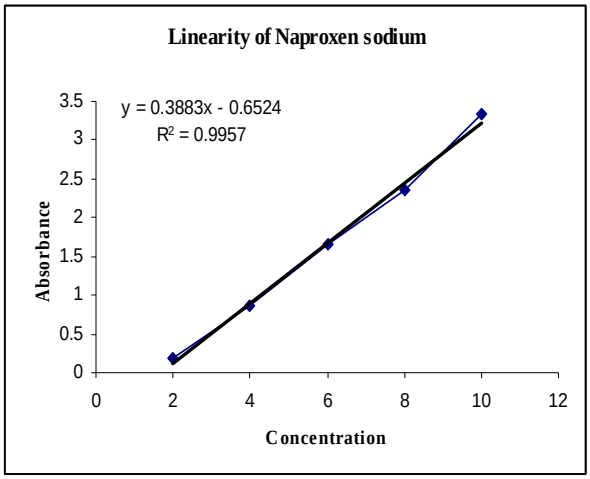

Fig. 4. Calibration plot of Naproxen sodium

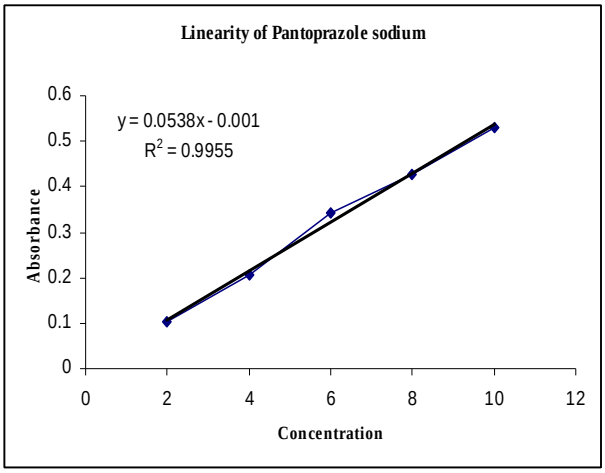

Fig. 5. Calibration plot of Pantoprazole sodium

LOD and LOQ were calculated by from standard deviation and slope values obtained from calibration curve using non instrumental method. The LOD and LOQ value for PAN were 0.0042 µg/ml, 0.0129 µg/ml respectively and for NAP were 0.011 µg/ml, 0.0042 µg/ml, respectively.

Concentration of the individual drug present in the marketed formulation was determined by solving the simultaneous equation at 232.0 nm and 291.0 nm using the respective absorptivity value. The drug content was found to be 99.8% for PAN and 99.5% for NAP. It indicates that there is no interference from the excipients present in formulation. Literature survey revealed that the previous methods used methanol as a solvent for the analysis of NAP and PAN. But in this proposed method 0.1 M NaOH was used as the solvent, so the cost of the analysis can be greatly reduced. The results show that the proposed method is accurate and precise.

In conclusion, an economic, simple and rapid UV Spectrophotometric method has been developed for simultaneous determination of NAP and PAN in capsule dosage form. The method was validated for linearity, precision, accuracy, LOD and LOQ as per ICH guidelines. Therefore, the proposed method could be applied for the routine analysis of pharmaceutical dosage forms containing NAP and PAN.

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