



Development and validation of naproxen in bulk and tablet dosage form

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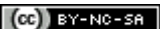
ABSTRACT

A simple, accurate, precise and sensitive UV-Spectrophotometric method was developed for the determination of naproxen. The solvent used was ethanol and the wavelength corresponding to maximum absorbance of the drug was found at 242 nm. Beer's law was obeyed in the concentration range of 10-60 µg/mL with correlation coefficient of 0.9984. The method was validated for several parameters like linearity and range, accuracy, precision and specificity as per International Conference on Harmonization guidelines. The value of the relative standard deviation and %recovery was found to be satisfactory, indicating that the proposed method is precise and accurate and hence can be used for the routine analysis of naproxen.

Keywords: Naproxen, Spectrophotometric, Correlation coefficient, Regression method, Standard deviation.

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INTRODUCTION

Naproxen is used for reduction of pain, fever, inflammation and stiffness caused by migraine, osteoarthritis, kidney stones, gout and menstrual cramps. It works by inhibiting COX-1 and COX-2 enzymes. They work by reducing the levels of prostaglandins, chemicals that are responsible for pain, fever, and inflammation. Naproxen is chemically 2-(6-methoxynaphthalene-2-yl) propanoic acid. It is used in the treatment of inflammations, rheumatoid arthritis, musculoskeletal disorders and gout. Naproxen is a non-steroidal anti-inflammatory drug (NSAID) commonly used for the reduction of moderate to severe pain, fever, inflammation and stiffness. It works by inhibiting both the COX-1 and COX-2 enzymes. Literature review revealed that some spectrophotometric and HPLC methods have been reported for the estimation of the naproxen in tablet formulation, raw materials, plasma, urine and intestinal perfusion samples.

Since the nonspecific titrimetric assay method was specified for Naproxen API in the pharmacopeia, hence, there was a need to develop a specific method which became the purpose of the further study.

Main objective is to develop and validate UV-visible method using Absorption Q Ratio method which is accurate and commercial.

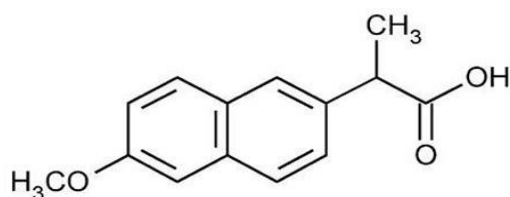


Figure 1: Structure of naproxen

VALIDATION

Establishing documentation evidence, which provides a high degree of assurance that specific process, will consistently produce a product meeting its predetermined specifications and quality attributes.

System Suitability: It is a checking of a system to ensure system performance before or during the analysis of unknowns. System solubility tests are an integral part of UV methods and they verify the resolution and reproducibility of the system are adequate for the analysis to be performed %RSD.

Accuracy: For accuracy determination, three different concentrations were prepared separately i.e. 50%, 100%, and 150% for the concentration of absorbance values are recorded for the same.

MATERIALS AND METHODS

Instrumentation: A Shimadzu 1601 UV-Visible Spectrophotometer with spectral bandwidth of 2.0 nm and wavelength accuracy of ± 0.5 nm with automatic wavelength correction and a pair of 10 mm quartz cells were used for the absorbance measurements connected with Analytical Technologies software.

Materials: The Naproxen (assigned purity 99.68%) was kindly supplied as a gift sample by Syncrop Labs Pvt. Ltd., Hyderabad, India. All chemicals and solvents used in the spectrophotometric analysis were of analytical reagent grade obtained from Rankem Ltd, India.

Methods

Preparation of standard solution: Standard stock solution (100 $\mu\text{g}/\text{mL}$) was prepared by transferring 10 mg of naproxen into a 100 mL volumetric flask, 30 mL of ethanol was added, and the mixture was sonicated to dissolve and make up the volume with ethanol.

Determination of Absorption Maxima: Accurately weigh 100 mg (0.1gms) of drug in 100 ml of volumetric flask. To this add 75ml of diluent (Ethanol) and sonicate it and further make up the volume with diluent. From this take 3 ml and make up to 10 ml. The solutions were scanned in the range of 200-400 nm in 1cm cell against ethanol as blank.

- Preparation of 50% solution:** About 12.5mg of Naproxen was weighed and transferred to 25ml volumetric flask. Add 10ml of mobile phase, sonicate for 10min make up to the mark with same solvent. Further 3ml of above solution was diluted to 10ml with the diluents to get 50% level solution.
- Preparation of 100% solution:** About 25mg of Naproxen was weighed and transferred to 25ml volumetric flask. Add 10ml of mobile phase, sonicate for 10min make up to the mark with same solvent. Further 3ml of above solution was diluted to 10ml with the diluents to get 100% level solution.
- Preparation of 150% solution:** About 25mg of Naproxen was weighed and transferred to 25ml volumetric flask. Add 10ml of mobile phase, sonicate for 10min make up to the mark with same solvent. Further 3ml of above solution was diluted to 10ml with the diluents to get 150% level solution.

Acceptance criteria: the method is considered accurate if the average recovery is not less than 98% and not more than 102%.

Precision: Accurately weigh and transfer 25mg Naproxen working standard into 25ml clean dry volumetric flask add diluents and sonicate to dissolve it completely and make volume up to the mark with the solvent. Further pipette 3ml of above stock solution into a 10ml volumetric flask and dilute up to the mark with diluent. Then the standard solution was placed into cuvettes for six times and measured for all six-concentration absorbance value by using λ max in UV. The %RSD for the area of six replicate concentrations was found to be within the specified limits.

Repeatability: Repeatability was determined by preparing six replicates of standard and sample separately to determine the system precision and method precision respectively and the

Intermediate Precision: Intermediate precision was determined by the typical variations to be studied on different days (day1 and day 2) by different analysts (analyst 1 and analyst 2).

The tests were carried out by preparing drug solutions of concentration 7.5 μ g/ml of Naproxen and analysed.

The results were reported as %RSD. The precision result showed a good reproducibility with percent relative standard deviation less than 2.

Linearity and Range: appropriate aliquot of standard naproxen stock solution was taken in 50ml volumetric flask and resultant solution was diluted up to the mark with diluent to obtain final concentration of naproxen. This solution was placed into cuvettes. By using λ max concentration were obtained and absorbance values was determined for each concentration of drug solution. Calibration curve was constructed by plotting peak area against applied concentrations. The slope intercept and correlation coefficient (r^2) were also

determined. Linearity of the analytical method for assay by placing the linearity solution prepared in the range of 10 μ g to 60 μ g of test concentration into the cuvettes covering minimum 6 different concentrations. Draw a plot between the concentration vs absorbance of naproxen. Report the slope intercept and regression coefficient from the plot.

Robustness: Robustness of analytical procedure is a measure of its capacity to remain unaffected by small, but deliberate variations in method parameters and provides indications of its reliability during normal usage. Wavelength was varied between -2. The solution was made in triplicates and were analysed the %RSD is determined.

Standard solution of 30 μ g /ml naproxen was analysed at varied wavelength of 2nm plus and 2nm minus.

Limit of detection (LOD): The detection limit is determined by the analysis of samples with known concentration of analyte and by establishing that minimum level at which the analyte can reliably detected.

Limit of qualification: The qualification limit is generally determined by the analysis of sample with known concentrations of analyte and by establishing the minimum level at which the analyte can be quantified with acceptable accuracy and precision.

RESULTS AND DISCUSSION

Development and optimization of the spectrophotometric method: Proper wavelength selection of the methods depends on the nature of the sample and its solubility. To develop a rugged and suitable spectrophotometric method for the quantitative determination of naproxen, the analytical conditions were selected after testing the different physical properties.

Table 1: shows solubility study of Naproxen

Trial no	Solvent	Result
1	Water	Insoluble
2	Ether	Slightly soluble
3	Methanol	Soluble
4	Chloroform	Soluble

Selection of wavelength: The standard stock solution was scanned from 200 – 400 nm and the absorption spectra's were recorded at 242nm.

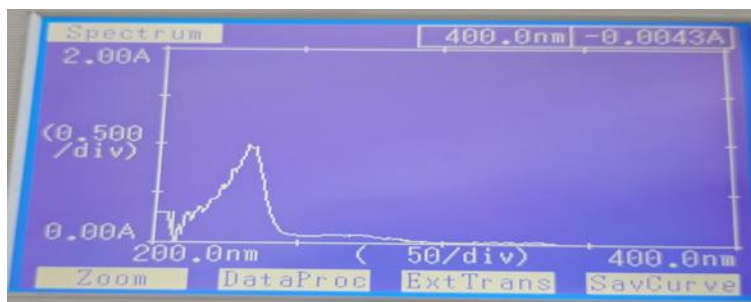


Figure 2: Shows UV spectrum of Naproxen standard

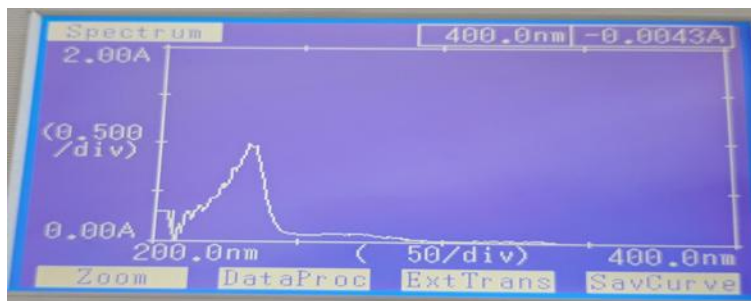


Figure 3: Shows UV absorption spectrum of Naproxen standard

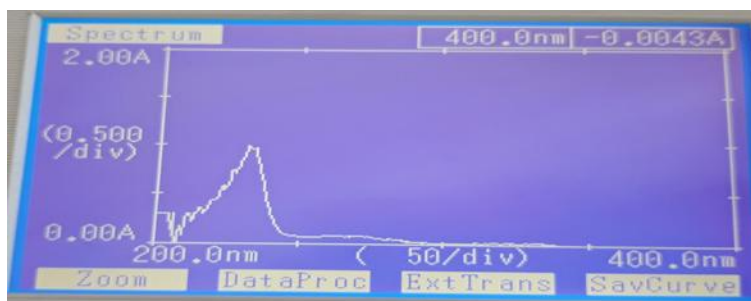


Figure 4: Shows UV absorption spectrum of Naproxen sample

From the above spectrum the wavelength selected for estimation of drug is 242nm as λ_{max} of Naproxen.

Accuracy

Table 2: Shows % Accuracy Recovery of Naproxen

Concentration level	Amount added (mg)	Amount found (mg)	% Recovery	Average % recovery
50%	12.5mg	12.5mg	100.25%	100.33%
	12.5mg	12.5mg	100.25%	
	12.5mg	12.6mg	100.5%	
100%	25mg	25.25mg	100.22%	100.20%
	25mg	25.02mg	100.3%	
	25mg	25.07mg	100.1%	
150%	37.5mg	37.6mg	100.3%	100.13%
	37.5 mg	37.5mg	100.09%	
	37.5mg	37.5mg	100.01%	

Result: The accuracy for the average of triplicate in each concentration samples are within the limit.

Table 3: Shows % recovery of Naproxen.

Amount added (mg)	Amount found (mg)	Average % recovery
25mg	25.2mg	100.22%

Precision: Repeatability studies were done by taking 30µg/ml in six replicates and the absorbance was observed and the %RSD was calculated. %RSD was found to 0.999.

Acceptance criteria: A method is said to be precise if the %RSD is < 2%, the result show %RSD for repeatability studies was < 2% which indicates the results meet the acceptance criteria and hence the method is said to be precise.

a) System precision

Table 4: Shows results of system precision

Concentration (µg/mg)	Absorbance of Naproxen
30	0.3230
30	0.3201
30	0.3199
30	0.3228
30	0.3224
30	0.3228
Mean	0.321
Standard deviation	0.001435
%RSD	0.447

Result: The precision values are found within the limit.

Intermediate precision

a) Intra day

Table 5: Shows results of Inter day

Concentration (µg/ml)	Analyst -1		Analyst - 2	
	DAY1	DAY2	DAY1	DAY 2
30	0.0324	0.0256	0.0462	0.0662
30	0.0313	0.0245	0.0451	0.0651
30	0.0302	0.0234	0.0440	0.064
Mean		0.0579	0.10596	0.065
S.D	0.011	0.0011	0.0011	0.0011
%RSD	1.4	1.8	1.03	1.6

Acceptance criteria: A method is said to be precise if the %RSD IS < 2% the result show % RSD for the intermediate precision as within the limits and hence the method is said to be precise.

B) Inter day

Table 6: Shows result of Intra Day

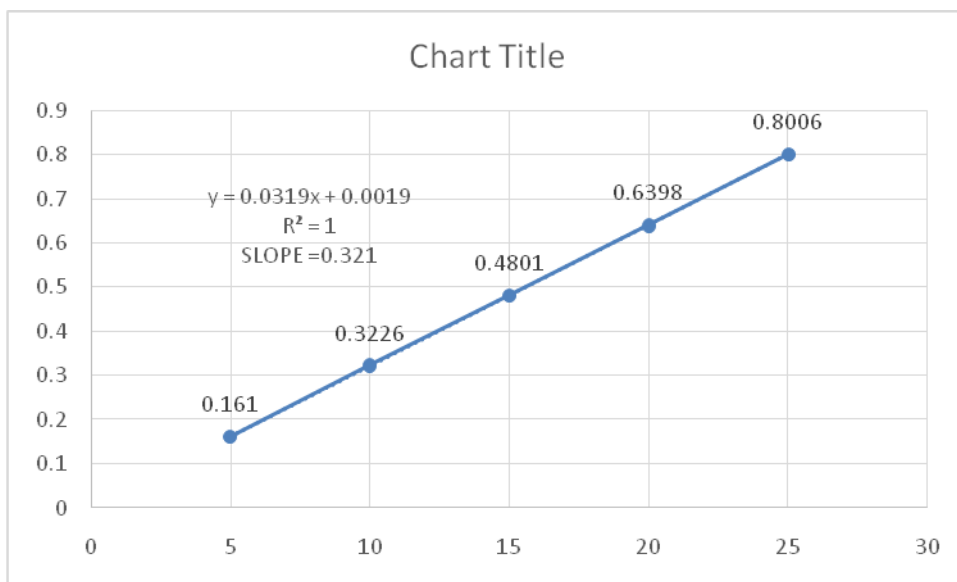
Concentration(µg/ml)	ABSORBANCE	
	DAY-1	DAY-2
30	0.2532	0.2524
30	0.2526	0.2522
30	0.2543	0.2548
Mean	0.590	0.253
S. D	0.000424	0.000141
%RSD	0.07	0.055

Acceptance criteria: A method is said to be precision if the percentage RSD is less than 2% the result show RSD of intermediate precision within the limits and hence the method is said to be precise

LINEARITY AND RANCE

Stock solutions were prepared within the methanol to give concentrations from 10-60 µg/ml Naproxen. The calibration curve was obtained by plotting absorbance on X-axis against concentration on Y-

axis regression equation was found $Y=0.3003X+0.0153$ and the correlation coefficient was found to be 0.999. The results are shown in Table No.11 and the calibration curve of Naproxen.



Result: From the above graph. It can be concluded that the relationship between the concentration and peak response Naproxen peak is linear in the range examined as all the points lie in a straight line with

the regression coefficient of 0.999 for Naproxen which is within the limits. Hence the developed method is linear in the specified range for estimation of Naproxen.

Table 7: Shows linearity results of Naproxen

S.no	Linearity level	Concentration	Area
1	I	5	0.1610
2	II	10	0.3226
3	III	15	0.4801
4	IV	20	0.6398
5	V	25	0.8006
Correlation Coefficient			0.9999

ROBUSTNESS: The robustness of the method was determined by making slight changes in the experimental conditions such as changes in the wavelength

Table 8: Shows results of Robustness

S No	Parameters	Absorbance
1	Robust wavelength 240 nm	0.3444
2	Robust wavelength 241 nm	0.3321
3	Robust wavelength 242 nm	0.3231
4	Robust wavelength 243 nm	0.3133
5	Robust wavelength 244 nm	0.3012
Mean		1.37214
Standard deviation		0.016806
%RSD		1.2

CONCLUSION

UV Spectrophotometric Method Development Naproxen is an NSAIDS This tablet was considered for analytical method development and validation for determination of Naproxen assay By UV spectroscopy method exhibited maximum absorption at 242 nm. The estimation was done by

using mobile phase as ethanol Accuracy parameter is considered if the average recovery is not less than 98% and not more than 101% in precision parameter RSD of six replicate injections should be NMT 2%. Robustness of an analytical procedure is a measure of its capacity to remain unaffected by small, but deliberate variations in method parameters and provides an indication of its

reliability during normal usage> Wave length was varied between +2, The solutions were made in triplicates and were analysed the 5RSD is determined.

Precision parameter RSD for the assay values of 6 sample preparations of some batch should not be more than 2.0%. The LOD are calculated from the calibration curve by using the formulas $LOD = 3.3 \times SD/b$ where, SD- the estimate is the standard deviation of the peak area of the drugs b- is slope of the corresponding calibration curve passed. The LOQ are calculated from the calibration curve by

the using the formulas $LOQ = 10 \times SD/b$ where, SD-THE estimate is the standard deviation of the peak area of the drugs. B-is slope of the corresponding calibration curve the %recovery varies in the rage of 98-101% LOD & LOQ values are found within the limits. These result shows the method is accurate, precise, sensitive, economic & rugged. The UV method is more rapid. The propose method is successfully applied to the tablet dosage form the method was found to be having suitable application in routine laboratory analysis with high degree of accuracy and precision.

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