**World Journal of Pharmaceutical Sciences**
ISSN (Print): 2321-3310; ISSN (Online): 2321-3086
Available online at: http://www.wjpsonline.org/
**Original Article**

# Development and validation of naproxen in bulk and tablet dosage form

Afshanurooj*, N. Balaraju, B. Swathi, P. Sainath, D. Vijaya Laxmi, Rajeswar Dutt, K.N.V. Rao

Nalanda College of Pharmacy, Cherlapally, Nalgonda, Telangana, India

***Received: 19-03-2019 / Revised Accepted: 17-04-2019 / Published: 01-05-2019***

## 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.

**Address for Correspondence:** Afshanurooj, Nalanda College of Pharmacy, Cherlapally, Nalgonda, Telangana, India; E-mail: afshanurooj9@gmail.com

**How to Cite this Article:** Afshanurooj, N. Balaraju, B. Swathi, P. Sainath, D. Vijaya laxmi, Rajeswar Dutt, K.N.V. Rao. Development and validation of naproxen in bulkand tablet dosage form. World J Pharm Sci 2019; 7(5): 95-101.

## 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-methoxynapthalene-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 (NASID) 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, urineand 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.

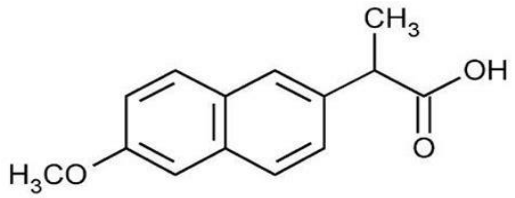



**Figure 1: Structure of naproxen**

## 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 µg/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 of 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.

a. **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.
b. **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.
c. **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 7.5µg/ml ofNaproxen 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 λmax 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 10µg to 60µg 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 and 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 µg /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.

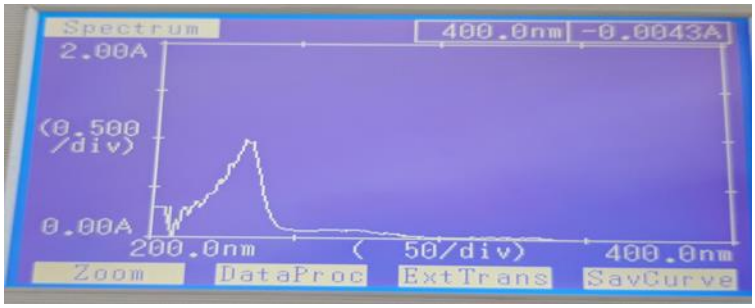



**Figure 2: Shows UV spectrum of Naproxen standard**

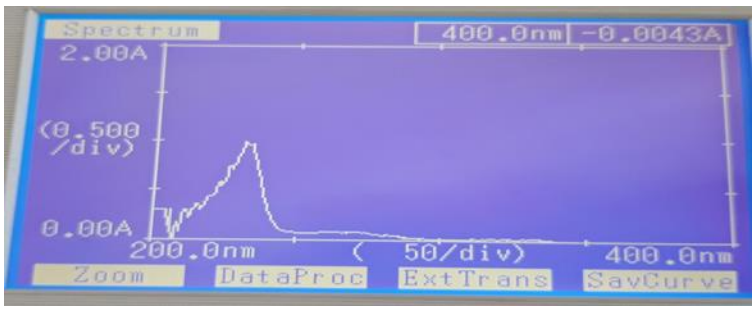



**Figure 3: Shows UV absorption spectrum of Naproxen standard**

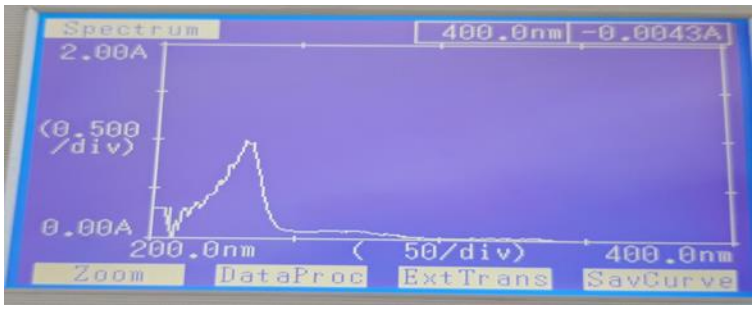



**Figure 4: Shows UV absorption spectrum of Naproxen sample**

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

**Accuracy**

**Table 2: Shows % Accuracy Recovery of Naproxen**

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

**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 ad 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**

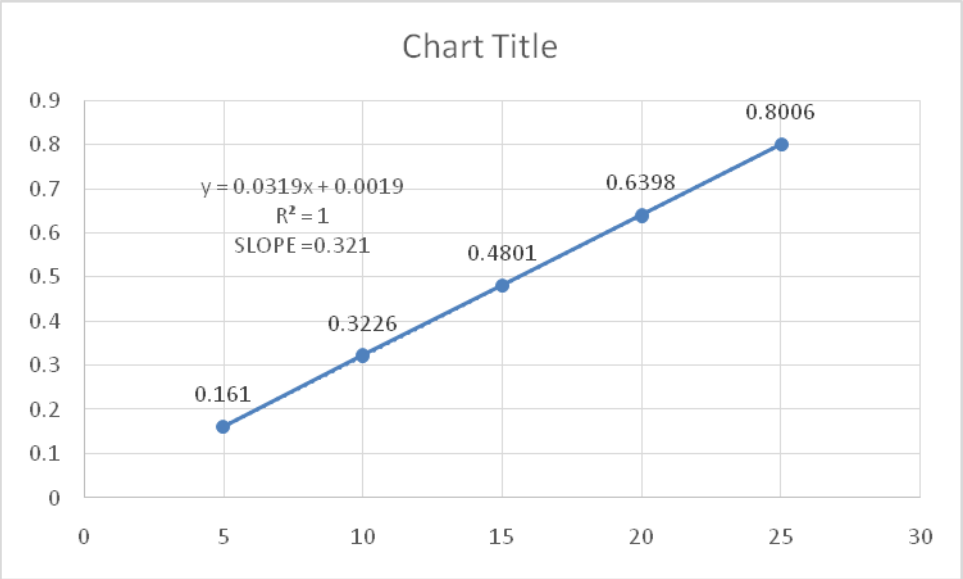
**Table 6: Shows result of Intra Day**

| 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 I the experimental conditions such as changes in the wavelength

**Table 8: Shows results of Robustness**

| S No | Parameters | Absorbance |
|---|---|---|
| 1 | Robust wavelength240 nm | 0.3444 |
| 2 | Robust wavelength241 nm | 0.3321 |
| 3 | Robust wavelength242 nm | 0.3231 |
| 4 | Robust wavelength243 nm | 0.3133 |
| 5 | Robust wavelength244 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 b 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 =3.3x 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 x 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.

## REFERENCES


1. Skoog, West, Holler, Analytical chemistry, Har court publishers. New Delhi, 7$^{th}$ed.. 1-9
2. B.K. Sharma, Instrumental methods of chemical Analysis, Goel publishers. 23$^{rd}$ed,. 286-321
3. R.M. Verma, Analytical chemistry, CBS publishers, New Delhi, Third ed…3-31
4. http://chem,yonsei.ac.kr/-mhmoon/pdf/AnalChem/Chl/pdf-ch1
5. Y,R Sharma elementary Organic spectroscopy, Goel publishers,23$^{rd}$ ed…3-9
6. Hobort H. Willard, instrumental of analysis, CBS publishers New Delhi second ed,118-141
7. http://en.wikipedia.org/wiki/Ultraviolet%E2%80%93visible_spectroscopy
8. http://blamp.sites.truman.edu/files/2012/03/322-UV-Vis-Instrumentation.pdf
9. Shynderkirckland, Glajch, Practical HPLC method development, John Wiley India Pvts.ltd New Delhi, second ed..3-19,685-706.
10. Ahuja, Seypinski, Hand book of Modern Pharmaceutical Analysis. Elsevier publishers New Delhi, vol(3),419-428
11. P.D.Sethi, HPLC Quantitative Analysis of Pharmaceutical Formulations CBS publishers New Delhi,2006 ed., 11-27
12. https://www.google.co.in/'poharmaceutical process validation-pdf
13. G.Vidya sagar, Basics of drug Analysis. Pharma med press Hyderabad,2009 ed..21-27
14. http://www.drugbank.ca>drugs
15. https://en.m.wikepedia.org>wiki>pantoprazole
16. Prateek Kumar Mishra, Savita Upadhayay,Avinash C. Tripathi, Shaiendra K. Saraf, Stability Indicating HPLC-UV Method for Simultaneous Estimation of Naproxen Domperidone and Drotaverine. International Journal of Pharma Tech Research,8(5),2015,912-23
17. J.Subba Rao, S. Vidyadhara. A. Ramu. B. Venkateshwara Rao and Vanaja. A novel RP-HPLC method development and validation for the simultaneous estimation of domperidone and Naproxen in bulk and pharmaceutical formulations, Journal of chemical and pharmaceutical research, 7(12) 2015, 640 – 646
18. Byendla Mahender Amarnath and medidi Srinivas Method Development and validation of RP – HPLC Method for the simultaneous Estimation of andondanseNaproxen tronHydrocholride in bulk and in a synthetic mixture, international journal of pharmatech research, 6 (6), 2014, 1794 – 1802
19. Lakshmidurga k, ram mohan reddy t. ajitha a and umamaheshwarrao v. analytical method development and validation for simultaneously and estimation of Naproxenand mosapride in pharmaceutical dosage form by RP – HPLC Method, journal of pharmacy and chemistry ,8(4) 2014, 14 – 20
20. B Siddhartha and I. Sudheer babu, analytical method development and method validation for the estimation of in tablet dosNaproxen age form by RP – HPLC, Der pharma 5(4), (2013), 99-104.