

Optimization of Quantitative Analysis of Naproxen Sodium Using UV Spectrophotometry in Different Solvent Mediums

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ABSTRACT

A new rapid, simple and reproducible UV spectrophotometric method was developed and validated for the estimation of Naproxen Sodium (NpSd) in bulk and pharmaceutical formulation. The quantification of NpSd was done at 230 nm in methanol and in buffer of pH 6.8 and 9. Beer's law was obeyed in the concentration range of 4 - 36 ($r^2 = 0.999$) in methanol and 5 - 25 $\mu\text{g mL}^{-1}$ in buffer of pH 6.8 and 9 ($r^2 = 0.988$ and 0.997) respectively. The apparent molar absorptivity values were also calculated in all mediums. All parameters according to ICH guideline were tested and validated. The detection and quantitation limits were found to be 0.054, 0.083, 0.073 and 0.181, 0.251, 0.211 $\mu\text{g mL}^{-1}$ respectively. These methods were applied directly to the analysis of the pharmaceutical tablet preparations (Anex[®] tablet 250 mg). The results demonstrated that the procedure is accurate, precise and reproducible (relative standard deviation < 3%), while being simple, cheap and less time consuming and hence can be suitably applied for the estimation of NpSd in dosage forms and dissolution studies.

KEYWORDS

Naproxen Sodium; UV Spectrophotometry; Pharmaceutical Analysis

1. Introduction

Naproxen (NpSd), a non-steroidal anti-inflammatory drug, is chemically [(+)-2-(6-methoxy-2-naphthyl) propionic acid with anti-inflammatory, analgesic and antipyretic properties, commonly used in the treatment of rheumatoid arthritis and other rheumatic or musculoskeletal disorders, dysmenorrhea and acute gout (Figure 1). It is often preferred to acetylsalicylic acid (aspirin) because of its better absorption following oral administration and poses fewer adverse effects. It works by inhibition of both the COX-1 and COX-2 enzymes with consequent decrease in prostaglandin concentrations in various fluids and tissues. Anti-inflammatory effects of NpSd are generally thought to be related to its inhibition of cyclooxygenase and formulated in tablets or suppositories, it

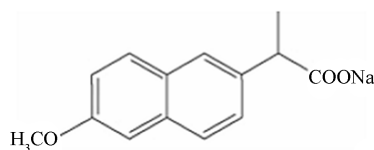


Figure 1. Naproxen sodium.

is used in the treatment of rheumatoid arthritis and other rheumatic or musculoskeletal disorders, dysmenorrhea and acute gout [1].

Naproxen in commercial formulations has been determined by coulometry [2], UV spectrophotometry [3-6], heavy atom-induced room temperature phosphorescence [7], UPLC [8] and high-performance liquid chromatography (HPLC) [9-14]. Present paper was undertaken with the aim to develop an accurate, simple and reliable UV method for estimation of naproxen API and applied to

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commercial formulations. These studies were performed in different pH environments: simulated gastric juice (0.1 N HCl) and simulated intestinal environment (pH 6.8 and 9). A detailed survey of analytical literature reveals that there is no UV spectrophotometric study on NpSd in different pH mediums simulating human body compartments. The results obtained were validated as the ICH guidelines *i.e.* Lambert and Beer's law validation, accuracy, precision, limits of detection and quantification. The proposed method is successfully applied for the analysis of the drug in bulk form and its pharmaceutical formulation. The results were in good agreement with those obtained by the official and reported methods.

2. Experimental

2.1. Instruments

Shimadzu 1801 double beam UV-visible spectrophotometer possessing a fixed slit width (2 nm) with quartz cells of 10-mm (1.0 cm) cell path length connected to a P-IV computer loaded with Shimadzu UVPC version 3.9 software and a HP Desk Jet 1200 printer were used to record the absorption spectra.

2.2. Preparation of Solutions

Three different stock solutions of NpSd reference standard ($100 \mu\text{g}\cdot\text{mL}^{-1}$) were prepared by dissolving 10 mg of NpSd in 100 mL of methanol, phosphate buffer of pH 6.8 and 9. Aliquot was diluted to a concentration range 4 - $36 \mu\text{g}\cdot\text{mL}^{-1}$ in methanol and 5 - $25 \mu\text{g}\cdot\text{mL}^{-1}$ all above mediums. Anex[®] tablets (PharmEvo (Pvt) Ltd.) were purchased from local market each containing 250 mg of NpSd. Twenty tablets were weighed to obtain mean tablet weight, then were crushed to powder and preceded in the same way. The NpSd solutions were scanned in the UV region and were quantified at 230 nm in methanol and buffer of pH 6.8 and 9, respectively.

3. Method Validation

3.1. Linearity, Accuracy and Precision

The method was validated according to International Conference on Harmonization [15] for validation of analytical procedures in order to determine the linearity, sensitivity, precision and accuracy in all mediums (methanol, buffer of pH 6.8 and 9). **Table 1** summarizes the statistical results evaluated from the above observations. Precision of the method was determined by adding known amounts of pure drug (50%, 100%, and 150%) in triplicate to the solution of excipients (10% each) (**Table 2**). For the accuracy of the developed method, standard addition method was done. Different concentrations of pure drug (8, 10 and $12 \mu\text{g}\cdot\text{mL}^{-1}$) were added to a known pre-analysed formulation sample and the total concentration

Table 1. Optical characteristics and precision data.

Parameter	Methanol	Buffer of pH 6.8	Buffer of pH 9
λ_{max} (nm)	230	230	230
Linearity ($\mu\text{g}\cdot\text{mL}^{-1}$)	4 - 35	5 - 25	5 - 25
Molar absorptivity ($\text{L}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$)	2.29×10^4	1.57×10^4	1.92×10^4
Regression equation ^a			
Slope (b)	0.048	0.031	1.834
Intercept (a)	0.033	0.014	-0.14
Correlation coefficient (r)	0.999	0.988	0.997
S.D.	0.021	0.042	0.056
R.S.D	0.537	2.45	0.116
Specificity and selectivity $t_{\text{cal}}(t_{\text{crit}})^a$			
LOD ($\mu\text{g}\cdot\text{mL}^{-1}$)	0.054	0.083	0.073
LOQ ($\mu\text{g}\cdot\text{mL}^{-1}$)	0.181	0.251	0.211

^a $y = bx + a$, where x is the concentration in $\mu\text{g}\cdot\text{mL}^{-1}$.

Table 2. Precision and accuracy of the proposed method in presence of excipients*.

Drug added ($\mu\text{g}\cdot\text{mL}^{-1}$)	Predicted concentration ($\mu\text{g}\cdot\text{mL}^{-1}$)			
	Range	Mean (\pm S.D.)	% R.S.D.	% recovery
Methanol				
LC (10)	3.89 - 4.12	4.007 ± 0.062	1.55	100.17
IC (20)	19.90 - 20.08	20.96 ± 0.101	0.41	104.08
HC (30)	35.98 - 36.10	36.03 ± 0.064	0.25	100.08
Buffer of pH 6.8				
LC (5)	4.81 - 5.00	4.92 ± 0.098	0.49	98.40
IC (10)	10.04 - 10.10	10.96 ± 0.101	0.13	99.73
HC (15)	14.85 - 15.00	14.95 ± 0.086	0.29	99.80
Buffer of pH 9				
LC (5)	4.97 - 5.11	5.05 ± 0.071	1.41	100.93
IC (10)	10.02 - 10.16	10.10 ± 0.072	0.48	100.67
HC (15)	14.85 - 15.13	14.98 ± 0.146	0.56	99.93

*Solution of excipients containing 10% each as mentioned above.

was determined (**Table 3**). The percent recovery of the added pure drug was calculated as follows:

$$\% \text{ Recovery} = \left[\frac{(C_v - C_u)}{C_a} \right] \times 100$$

where C_v was the total drug concentration measured after standard addition, C_u , drug concentration in the for-

Table 3. Accuracy of the proposed method (standard addition technique)*.

Concentration of drug in formulations ($\mu\text{g}\cdot\text{mL}^{-1}$)	Concentration of pure drug added ($\mu\text{g}\cdot\text{mL}^{-1}$)	Total concentration of drug found ($\mu\text{g}\cdot\text{mL}^{-1}$)	% Analytical recovery ($\pm\text{S.D.}$)
Methanol			
10.0	8	17.89	99.41 \pm 0.063
10.0	10	20.07	100.36 \pm 0.084
10.0	12	22.12	100.54 \pm 0.084
pH 6.8			
10.0	8	17.93	99.61 \pm 0.063
10.0	10	19.84	99.19 \pm 0.077
10.0	12	22.14	100.64 \pm 0.084
pH 9			
10.0	8	17.71	98.38 \pm 0.085
10.0	10	20.18	100.90 \pm 0.211
10.0	12	21.39	97.23 \pm 0.151

*Each value is the mean result of three separate determinations.

mulation and Ca, drug concentration added to formulation. Under the experimental conditions described above, a linear regression equation (intercept and slope) for NpSd was established. The high values of the correlation coefficient and the values of Y-intercepts close to zero indicate good linearity of the calibrations.

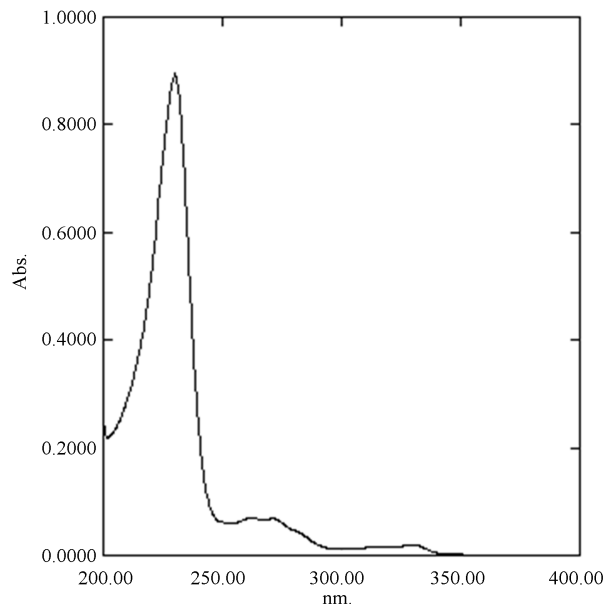
3.2. Specificity and Selectivity

NpSd solution (8, 10 and 12 $\mu\text{g}\cdot\text{mL}^{-1}$) were prepared in all selected medias along with and without common excipients (magnesium stearate, purified talc, lactose, maiz starch, povidone K 30, hydroxypropylmethyl cellulose, twin 80) all the solutions were scanned from 400 to 200 nm at a speed of 400 $\text{nm}\cdot\text{min}^{-1}$.

In a separate study, drug concentration of 10 $\mu\text{g}\cdot\text{mL}^{-1}$ was prepared independently from pure drug stock solution in selective media and analyzed ($n = 9$). Paired t-test at 95% level of significance was performed to compare the means of absorbance (Table 3).

3.3. Detection and Quantification Limits or Sensitivity

The limit of detection (LOD) is the lowest amount of analyte in a sample that can be detected, but not necessarily quantitated under the stated experimental conditions. The lower limit of detection of NpSd was shown in Table 1. Limit of quantitation (LOQ) is the lowest amount of analyte in a sample that can be determined

**Figure 2. Absorption spectrum of Naproxen sodium.**

with acceptable precision and accuracy under the stated experimental conditions [15]. The LOQ value for NpSd was shown in Table 1.

4. Results and Discussion

Naproxen sodium (NpSd) yields a characteristic curve in all mediums when scanned in the ultraviolet wavelength range. The scan (Figure 2) shows absorption maxima at 230 nm in all solvent mediums. The molar absorptivity in methanol and in buffer pH 6.8 and 9 was found to be $2.299 \times 10^4 \text{ L}\cdot\text{mol}^{-1}\text{cm}^{-1}$, 1.57×10^4 and $1.92 \times 10^4 \text{ L}\cdot\text{mol}^{-1}\text{cm}^{-1}$, which was in good agreement and hence 230 nm was chosen as the analytical wavelength. In these methods, Beer's law was valid in the concentration range of 4 to 36 $\mu\text{g}\cdot\text{mL}^{-1}$ in methanol and 5 to 25 $\mu\text{g}\cdot\text{mL}^{-1}$ in buffers (pH 6.8 and 9). The satisfactory correlation coefficient and intercept values were obtained as shown in Table 1. Precision of the method was studied in presence of standard excipients and different solvents (Table 2) and was applied to commercial pharmaceutical formulations using standard addition method whose percent recovery was shown in Table 3. The method was validated for linearity, accuracy, precision, specificity, limit of detection, and limit of quantitation. It was observed that the excipients in the tablets were not interfering in the analysis of the active compounds.

5. Conclusions

This method gave a successful result for the quantitative resolution of the reference standard and pharmaceutical dosage formulation. Using this analytical procedure, a good analytical performance was obtained for the deter-

mination of NpSd. The results suggest that this method is a powerful tool with very simple mathematical content and LLOD values 0.054, 0.083 and 0.073 $\mu\text{g}\cdot\text{mL}^{-1}$ in methanol, buffer of pH 6.8 and buffer of pH 9 respectively and is more reliable than other spectrophotometric methods and strongly encourages us to apply these calibration models for a routine analysis and quality control of commercial products.

The presented method was found to be simple, accurate and precise which gives an acceptable recovery of the analyte, which can be directly and easily applied to the analysis of the pharmaceutical tablet formulations of NpSd.

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