Available online on 10.01.2019 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Open Access Research Article

Development and validation of various spectrophotometric methods for naproxen as anti arthritis

Manoj Mandloi*, Gurdeep Singh, M.K. Gupta

Department of Pharmaceutical Quality Assurance, Oriental College of Pharmacy & Research, Oriental University, Indore, Madhya Pradesh, India.

ABSTRACT

The present research work discusses the development of UV-spectrophotometric method for estimation of Naproxen. Simple, specific, accurate and cost effective spectrophotometric method has been developed for estimation of naproxen sodium in bulk as well as formulation. The optimum conditions for the analysis of the drug were established. The maximum wavelength (λmax) was found to be 331 nm. The validation was performed as per ICH guidelines for linearity, accuracy, precision, LOD and LOQ. The linearity was found in the concentration range of 3-24 µg / ml for Zero, first and second order derivative spectroscopy. The correlation coefficients were found to be 0.9997, 0.9999 and 0.9998, respectively. The obtained (r^2) values show that the selected concentration range gives good linearity. All calibration curves show a linear relationship between the absorbance and concentration with coefficient of correlation 0.999. The regression of curve was Y = 0.0372 x - 0.0038. The precision of method was found to be good. The results were within the range of 99.15 ± 0.14 – 101.38 ± 0.17 and were found to be highly accurate. The proposed method will be suitable for analysis of naproxen in bulk as well as pharmaceutical formulations in quality control purpose. It is thus concluded that the proposed method is new, simple, cost-effective, safe, accurate, precise and environmental friendly

Keywords: Naproxen, Spectrophotometry, Naproxen, Linearity, Validation, LOD

Article Info: Received 23 Sep 2018; Review Completed 26 Nov 2018; Accepted 01 Dec 2018; Available online 10 Jan 2019

Cite this article as:

Mandloi M, Singh G, Gupta MK, Development and validation of various spectrophotometric methods for naproxen as anti arthritis, Journal of Drug Delivery and Therapeutics. 2018; 8(6-A):33-42

***Address for Correspondence:**

Manoj Mandloi, PG Research Scholar, Department of Pharmaceutical Quality Assurance

INTRODUCTION

Drug delivery through oral route is the most common and preferred route of drug administration both for solid and liquid dosage forms. However, solid dosage forms are popular because of the ease of administration, accurate dosage, self-medication, pain avoidance, and most importantly the patient compliance. Tablets and capsules are the most popular solid dosage forms. However, many people face difficulty in swallowing tablets and hard gelatin capsules. Orodispersible tablets are also called as orally disintegrating tablets, mouth-dissolving tablets, rapid-dissolving tablets, fast-disintegrating tablets, fast-dissolving tablets. Recently, European Pharmacopoeia has used the term orodispersible tablets. This may be defined as uncoated tablets intended to be placed in the mouth where they disperse readily within 3 min before swallowing[1]. United States Pharmacopoeia has also approved these dosage forms as orodispersible tablets. Thus, orodispersible tablets are solid unit dosage forms like conventional tablets, but are composed of super disintegrants, which help them to dissolve the tablets within a minute in the mouth in the presence of saliva without any difficulty of swallowing[2]. It offers several advantages with respect to its stability, administration without water, accurate dosing, easy manufacturing, small packaging size, and handling. Due to the presence of super disintegrants, it gets dissolved quickly, resulting in rapid absorption of drug which in turn provides rapid onset of action. Since the absorption is taking place directly from the mouth, so, bioavailability of the drug increases. Drugs present in orodispersible tablets are also not suffering from first pass metabolism. Naproxen is chemically 2-(6-methoxynaphthalen-2-yl) propanoic acid[3,4]. It is used in the treatment of Inflammations, rheumatoid arthritis, musculoskeletal disorders and gout[1]. Naproxen is a non-steroidal anti-inflammatory drug (NSAID) commonly used for the reduction of moderate to severe pain, fever, inflammation and stiffness[5]. 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 naproxen in tablet formulation[6] raw material, plasma [7], urine and intestinal perfusion samples. Since the nonspecific titrimetric assay method was specified for Naproxen API in the pharmacopoeia, hence, there was a need to develop a specific method which became the purpose of the further study. The

objective of the present work was to develop a simple, sensitive, precise and accurate UV spectrophotometric method for the determination of naproxen in bulk and semisolid formulations as per ICH Guidelines [8].

Table 1: Chemicals and reagents

S.No	Materials	Sources
1.	Naproxen	Ajanta Ltd Mumbai
2.	Camphor	Brucell Pvt.Ltd. Sagar
3.	Aspartame	Hi-Media Mumbai
4.	Cross Carmellose Sodium	Hi-Media Mumbai
5.	Sodium Starch Glycolate	Hi-Media Mumbai
6.	Colloidal Silicon Dioxide	Hi-Media Mumbai
7.	Mannitol	Hi-Media Mumbai

Table 2: Instruments and apparatus

S.No	EQUIPMENT	MODEL/COMPANY
1.	UV visible spectrophotometer	Model – 1372 Make ET (Double Beam)
2.	FT IR spectrophotometer	IR Affinity- 1, Shimadzu
3.	Electronic Weighing machine	DS-852 J Series Essae
4.	Melting point apparatus	Microcontroller based melting point Apparatus
5.	Tablet compression machine	Single punching machine
6.	Hardness Tester	Monsanto hardness tester
7.	Friability Test Apparatus	Roche Friabilator
8	Tablet Disintegration Tester	Model – 911 Make – E 1
9.	Tablet Dissolution Tester	6 Station programmable Model - TDT - 06L Make – Electro lab

METHODS

Identification and Characterization of Naproxen

Identification

FTIR spectrum of Naproxen

FTIR spectrum- In the preparation of Orodispersible tablet, drug and Excipient may interact as they are in close contact with each other, which could lead to the instability of drug, Preformulation studies regarding the drug-excipient interaction are therefore very critical in selecting appropriate excipients. FT-IR spectroscopy was employed to ascertain the compatibility Naproxen and the selected excipients. The pure drugs and the drug with excipients were scanned separately and results are shown in (Fig: 1)

Physiochemical Characteristics

Melting Point-M.P. of the Naproxen was found to be 152-155°C at room temperature.

Solubility- Solubility of Naproxen was shown in (Table No. 2)

Formulation

Preparation of Orodispersible tablets by Direct Compression Technique:

The term direct compression is used to define the process by which tablets are compressed directly from the powder blends of active ingredients and suitable excipients, which will flow uniformly in the die cavity and forms a film contact. In this method, addition of super-disintegrants in optimum concentrations so as to achieve rapid disintegration with good mouth feels. Super disintegrants likes sodium starch gylcolate, cross povidone, cross carmellose sodium etc. Powders of drugs were mixed/blended with camphor as subliming agent and aspartame as quickly dissolvable sugar based excipients and Mannitol as Diluents, Cross Carmellose Sodium and Sodium Starch Glycolate as super-disintegrants[9]. All ingredients were passed through mesh # 60. Then 100mg of Naproxen were compressed on tablet punching machine to get tablets, each weighing 367.5mg.

Table 3: Composition of Orodispersible tablets in (mg)

Ingredients	Fl	F2	F3	F4	F5
Naproxen	100	100	100	100	100
Comphore	-	-	2.5	12.5	25
Aspartame	2.5	2.5	-	2.5	-
Cross Carmellose Sodium	-	15	-	15	-
Sodium Starch Glycolate	15	-	15	-	15
Colloidal Silicon Dioxide	-	-	-	-	2.5
Mannitol	250	250	250	250	250
Total	367.5	-	-	-	-

Evaluation of Tablets

Preformulation studies:

1. Bulk Density and Tapped Density - Both loose bulk density (LBD) and tapped bulk density (TBD) were determined. The accurately weighed amount sample taken in 50 ml measuring cylinder of borosil measured/recorded the volume of packing and tapped 50 times on plane surface and tapped volume of packing recorded and LBD and TBD calculated by following formula.

$$LBD = \frac{\text{Mass of powder}}{\text{Volume of packing}}$$

$$TBD = \frac{\text{Mass of powder}}{\text{Tapped volume of packing}}$$

2. Angle of repose- The frictional forces in loose powder or granules can be measured by the angle of repose. This is the maximum angle possible between the surface of a pile of powders or granules and the horizontal plane.

$$\tan = h/r$$

$$\theta = \tan^{-1}(h/r)$$

Where, tan = angle of repose

h = Height

r = radius

The granules were allowed to flow through the funnel fixed to a stand at definite height. The angle of repose was then calculated by measuring the height and radius of the heap of granules formed.

Table 4: Relation between Angle of repose (θ) and flow property.

Angle of Repose (θ)	Flow property
< 25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

3. Percentage Compressibility

Percentage compressibility of powder mix was determined by Carr's compressibility index calculated by following formula.

$$\text{Carr's index \%} = \frac{\text{TBD - LBD}}{\text{TBD}} \times 100$$

Where, LBD = loose bulk density

TBD = Tapped bulk density

Table 5: Grading of the powders for their flow properties according to Carr's index

Carr's Index %	Flow
5-15	Excellent
12-16	Good
18-21	Fair to Possible
23-25	Poor
33-38	Very Poor
>40	Very-Very Poor

Post Compression Parameters:

1. Physical appearance- All the prepared tablets were visually inspected for color, size and smoothness.

2. Thickness uniformity- The aim of the present study was to check the uniformity of thickness of the formulated tablets. The thickness of the tablets was measured at 3 different points using a digital caliper and average thickness of three readings was calculated. It is expressed in mm.

3. Weight Uniformity- For weight variation test, 10 tablets from each formulation was weighed individually and the average weight was calculated. The US pharmacopoeia allows a little variation in the weight of the tablet.

Table 6: Criteria for percentage deviation in weight variation

Average Weight of Tablet	Percentage Deviation
130 mg or less	10
More than 130 mg and less than 324 mg	7.5
324 and more	5

4. Hardness-

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using Monsanto Hardness Tester. It is expressed in kg/cm^2. Three tablets were randomly picked and hardness of the same tablets from each formulation was determined. The mean and standard deviation values were also calculated.

5. Friability studies-

Friability test is performed to assess the effect of friction and shocks, which may often cause tablet to chip, cap or break. Roche Friabilator was used for the purpose. Pre weighed sample of ten tablets were placed in the Friabilator, which was then operated for 100 revolutions. After 100 revolutions the tablets were dusted and reweighed. Compressed tablets should not lose more than 1% of their weight.

Percentage Friability = (initial weight – final weight / initial weight) x 100

6. Disintegration studies-

In vitro disintegration time was performed by disintegration Apparatus at 50 rpm. 1000ml (water) was used as disintegration medium, the temperature of which was maintained at 37 ± 2°C and the time taken for complete disintegration of the tablet with no mass remaining in the apparatus was measured in seconds.

7 .Wetting time-

A piece of tissue paper (12 cm × 10.75 cm) folded twice was placed in a Petri dish (Internal Diameter = 9 cm) containing 9 m of buffer solution simulating saliva pH 7.4. A tablet was placed on the paper and the time taken for complete wetting was noted. Three tablets from each formulation were randomly selected and the average wetting time was noted.

8. In Vitro Dispersion Time-

In vitro dispersion time was measured by dropping a tablet in a 10 ml measuring cylinder containing 6 ml of buffer solution simulating saliva fluid with reference to Indian pharmacopoeial standard (pH 7.4).

For UV

Reagents and chemicals analytically pure Naproxen Jawa Pharmaceuticals (P) Ltd were available from Oasis Laboratories Jaipur, India. Double distilled water for analytical purpose was obtained from Milli-QR-O system. Naproxen was determined spectrophotometrically in bulk and marketed formulation by using 2M hydrochloric acid and 550µg/ml of potassium bromide-bromate as a strong oxidizing agent.

Preparation of standard stock solution of Naproxen: Standard stock solution prepared by accurately weighing 100 mg of Naproxen in 100 ml calibrated volumetric flask and made up the volume with distilled ethanol up to 100 ml. Preparation of the working standard stock solution: From the above standard stock solution A 10ml was pipetted using a 10ml volumetric pipette. This pipette solution was transferred carefully to another 100ml volumetric flask and dissolved further with distilled ethanol up to the 100ml mark to obtain a 100µg/ml solution (Stock solution B).

Preparation of standard solution for calibration- Plots Weigh accurately about 100 mg of Naproxen and 100 mg transfer it to a 100 ml volumetric flask. Add 50 ml of methanol, sonicate it for 5 min to dissolve the content and make up the volume with methanol to give a concentration of 1000 µgmL^{-1} of Naproxen Stock solution was further diluted to give concentration of 100 µgmL-1 of Naproxen . Stock solution was diluted with methanol to give working standard solution containing 10 µgmL^{-1} of Naproxen. These solutions were scanned in the UV region of 200-400nm in 1cm cell against methanol as a blank and the overlain spectra was recorded.

Methodology

- **Method A: Zero Order Derivative Spectroscopy**
- **Method B: First Order Derivative Spectroscopy**
- **Method C: Second Order Derivative Spectroscopy**

RESULT AND DISCUSSIONS

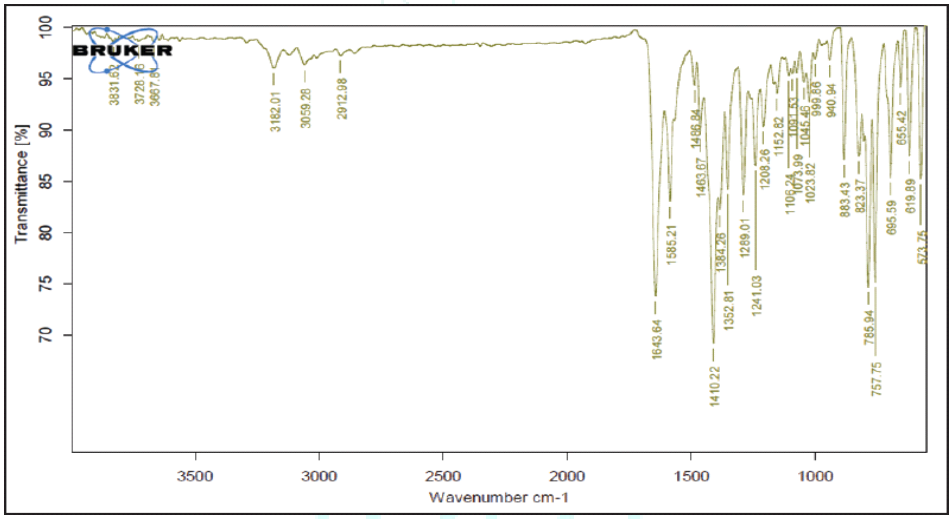

Figure 1: Result of FTIR Spectra of Naproxen

Table 7: Interpretation of FTIR of Naproxen

S.No.	Functional Groups	Peak Wave No. cm^{-1}
1	C=O Streching	1726
2	O-H Streching	3200
3	O-H Bend	1419
4	O-H Streching	1720
5	O-H Bend	1018
6	C=O Streching	1720

Table 8: Solubility profile for Naproxen

S.No.	Solvent	Result
1	Methanol	Soluble
2	Ethanol	Insoluble
3	Water	Soluble
4	Acetone	Insoluble
5	Ether	Insoluble

6.3.-Preparation of Orodispersible tablets –

Table 9: Pre-compression Parameter of Orodispersible tablets

S.No.	Pre-compression studies	Formulation				
		F_1	F_2	F_3	F_4	F_5
1.	Angle of repose(θ)	40.69°	30.26°	28-22°	25.56°	20.09°
2.	Bulk Density (g/ml)	0.78	0.82	0.73	0.75	0.70
3.	Tap Density (g/ml)	0.95	0.94	0.92	0.90	0.82
4.	Compressibility index (%)	9.8	7.3	5.8	9.0	6.9
5.	Hausners ratio	0.86	0.85	0.83	0.87	0.75

Table 10: Post-Compression Parameter of Orodispersible tablets

S.No.	Pre-compression studies	Formulation				
		F_1	F_2	F_3	F_4	F_5
1	Uniformity of thickness (n=3) mm	5.3±0.33	5.6±0.78	5.4±0.77	5.6±0.78	5.5±0.78
2	Hardness(n=3) kg/cm²	2.0±0.33	1.5±0.40	1.6±0.42	1.0±0.57	1.0±0.57
3	Friability %(n=6)	1.16	0.24	0.20	0.22	0.10
4	Weight Variation (n=10)	449±2.12	450±2.12	453±2.12	443±2.10	444±2.10
5	Drug content in (mg) (n=3)	98.55±0.2	99.55±2.2	98.65±3.2	98.47±1.2	97.4±1.32
6	Disintegration on tine in sec. at 37°	46	48	45	46	53
7	Wetting time in sec (n=3)	75±2.4	45±2.2	35±1.5	25±1.3	15±1.2
8	In-vitro Dispersion time (sec)	150	115	90	75	45

6.4. Result of Analysis of Orodispersible Tablet Formulation –

Table 11: Assay of Orodispersible Tablet Formulation

Formulation	NAPROXEN	
	Lable Claim (mg)	%Purity
F_5	100	98.78

Method A: Zero Order Derivative Spectroscopy

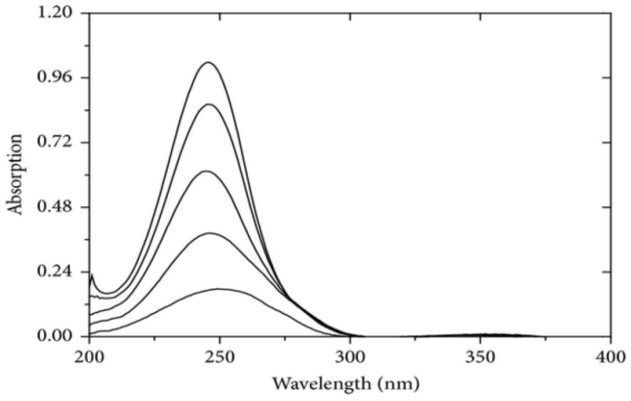

Figure 2: Zero order spectra of Naproxen at 331nm

Table 12: Results of calibration curve at 331 nm for Naproxen by Zero order Spectroscopy

S. No.	Conc. (µg/ml)	Absorbance at 253 nm
1	0	0
2	3	0.112
3	6	0.221
4	9	0.328
5	12	0.438
6	15	0.458
7	18	0.662
8	21	0.779
9	24	0.90

Table 13: Optimum conditions, Optical characteristics and Statistical data of the Regression equation in Zero order Spectroscopy

Parameter	UV method
λ_{max} (nm)	331
Beer's law limits (µg / ml)	3-24
Molar extinction coefficient (L mol^{-1} cm^{-1})	0.03653 $X10^4$
Sandell's sensitivity (µg / cm^2-0.001 absorbance units)	0.02737
Regression equation (Y*)	Y = 0.0372 x - 0.0038
Slope (b)	0.0372
Intercept (a)	-0.0038
Correlation coefficient (r^2)	0.9997
Intraday Precision (% RSD**) Interday Precision (% RSD**)	0.342 0.395
Limit of detection (µg / ml)	0.107
Limit of quantitation (µg / ml)	0.325

*Y = bx + a where x is the concentration of Naproxen in µg / ml and Y is the absorbance at the respective $\lambda_{max.}$

**Average of Six determinations.

Table: 14. Determination of Accuracy results for Naproxen at 331nm by Zero order Spectroscopy

Brand used	Amount of sample (µg / ml)	Amount of drug added (µg / ml)	Amount Recovered	% Recovery ± SD**
Aleve	10	7.5	7.46	99.46 ± 0.012
	10	15	15.23	101.53 ± 0.042
	10	22.5	22.25	98.85 ± 0.021
Naprosyn	20	7.5	7.56	100.80 ± 0.014
	20	15	14.92	99.46 ±0.037
	20	22.5	22.46	99.89 ± 0.028

**Average of six determinations.

Table: 15- Determination of Precision results for Naproxen at 331 nm by Zero order Spectroscopy

Conc. (µg / ml)	Inter-day Absorbance Mean ± SD**	% CV	Intra-day Absorbance Mean ± SD**	% CV
3	0.1120 ± 0.001414	1.26	0.1135 ± 0.001871	1.64
6	0.2231 ± 0.002639	1.18	0.2241 ± 0.002229	0.99
9	0.3273 ± 0.001633	0.49	0.3255 ± 0.001872	0.57
12	0.4371 ± 0.001472	0.33	0.4366 ± 0.001633	0.42
15	0.5463 ± 0.00216	0.39	0.5451 ± 0.001472	0.34
18	0.6625 ± 0.001871	0.28	0.6643 ± 0.001751	0.28
21	0.7758 ± 0.002317	0.29	0.7761 ± 0.001941	0.25
24	0.9110 ± 0.005657	0.62	0.9128 ± 0.006795	0.74

**Average of Six determinations

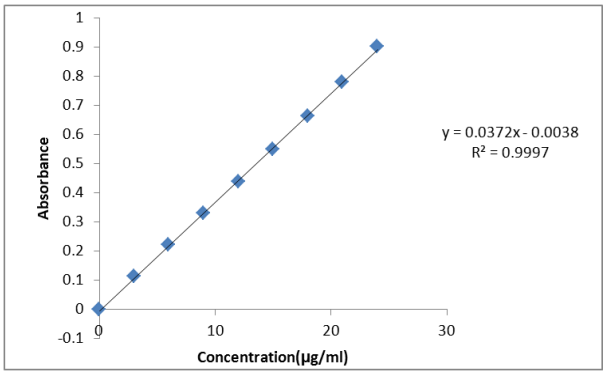

Figure 3: Linearity curve for Naproxen at 331 nm by Zero order Spectroscopy

Table: 16: Ruggedness results for Naproxen at 331 nm by Zero order Spectroscopy

Brand used	Label claim (mg/ml)	Analyst I		Analyst II	
		Amount found** (mg/ml)	% Recovery ± SD**	Amount found** (mg/ml)	% Recovery ± SD**
Aleve	20	20.28	101.42 ± 0.0170	19.34	99.67 ± 0.0294
Naprosyn	20	20.14	101.04 ± 0.0294	19.97	99.07 ± 0.0281

**Average of six determinations.

Method B: First Order Derivative Spectroscopy

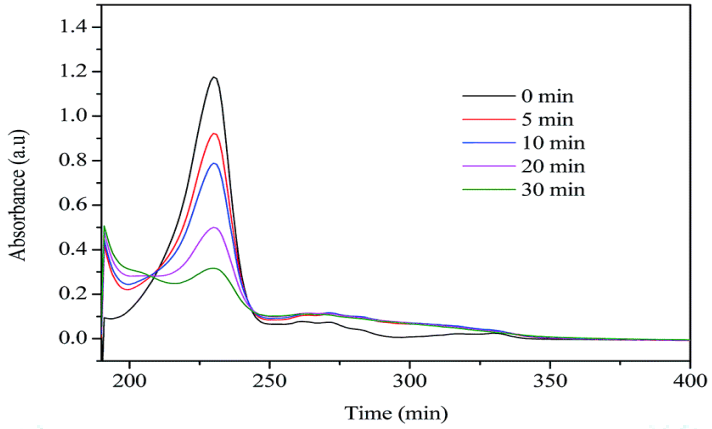

Figure 4: First order derivative spectra of Naproxen at 310 nm

Table: 17: Results of calibration curve at 310 nm for Naproxen by First order derivative Spectroscopy

Sl. no.	Conc. (µg / ml)	Absorbance
1	0	0
2	3	0.043
3	6	0.089
4	9	0.137
5	12	0.188
6	15	0.232
7	18	0.275
8	21	0.322
9	24	0.368

Table : 18- Optimum conditions, Optical characteristics and Statistical data of the Regression equation in First order derivative Spectroscopy

Parameter	UV method
λ_{max} (nm)	**310**
Beer's law limits (µg / ml)	3-24
Molar extinction coefficient (L mol^{-1} cm^{-1})	0.0154 X10^4
Sandell's sensitivity (µg / cm^2 - 0.001 absorbance units)	0.0646
Regression equation (Y*)	Y = 0.0154 x - 0.0018
Slope (b)	0.0154
Intercept (a)	-0.0018
Correlation coefficient(r^2)	0.9999
Intraday Precision (% RSD**) Interday Precision (% RSD**)	0.842 0.885
Limit of detection (µg / ml)	0.146
Limit of quantitation (µg / ml)	0.442

*Y = bx + a where x is the concentration of Naproxen in µg / ml and Y is the absorbance at the respective $\lambda_{max.}$

**Average of Six determinations.

Table: 19. Determination of Accuracy results for Naproxen by First order derivative Spectroscopy

Brand used	Amount of sample (µg / ml)	Amount of drug added (µg / ml)	Amount Recovered	% Recovery ± SD**
Aleve	15	12	12.21	101.75 ± 0.030
	15	15	14.93	99.53 ± 0.045
	15	18	18.24	101.33 ± 0.027
Naprosyn	12	12	11.92	99.33 ± 0.034
	12	15	15.31	102.06 ± 0.056
	12	18	18.14	100.77 ± 0.044

**Average of six determinations.

Table: 20: Determination of Precision results for Naproxen at 310 nm by First order derivative Spectroscopy

Conc. (µg / ml)	Inter-day Absorbance Mean ± SD**	% CV	Intra-day Absorbance Mean ± SD**	% CV
3	0.0428 ± 0.001169	2.72	0.0423 ± 0.001211	2.86
6	0.0888 ± 0.001472	1.65	0.0888 ± 0.001751	1.98
9	0.1368 ± 0.001722	1.25	0.1363 ± 0.00216	1.58
12	0.1835 ± 0.001871	1.01	0.1836 ± 0.00216	1.17
15	0.2333 ± 0.002066	0.88	0.2333 ± 0.001966	0.84
18	0.2741 ± 0.002366	0.86	0.2738 ± 0.002408	0.87
21	0.3236 ± 0.00216	0.66	0.3241 ± 0.002317	0.71
24	0.3645 ± 0.002074	0.56	0.3656 ± 0.002338	0.63

**Average of Six determinations

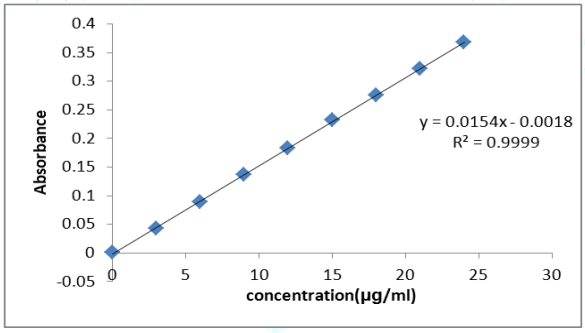

Figure 5: Calibration curve for Naproxen at 310 nm by First order derivative Spectroscopy

Table 21: Ruggedness results for Naproxen at 310 nm by First order derivative Spectroscopy

Brand used	Label claim (mg/ml)	Analyst I		Analyst II	
		Amount found** (mg/ml)	% Recovery ± SD**	Amount found** (mg/ml)	% Recovery ± SD**
Aleve	20	20.20	102.16 ± 0.0544	20.25	101.58 ± 0.0848
Naprosyn	20	20.91	99.40 ± 0.0581	20.11	100.73 ± 0.0728

**Average of six determinations.

Method C: Second Order Derivative Spectroscopy

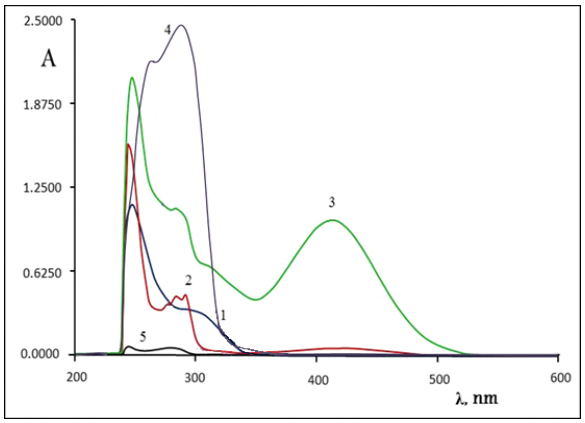

Figure 6: Second order derivative spectra of Naproxen at 353 nm

Table 22: Results of calibration curve at 278 nm for Naproxen by Second order derivative Spectroscopy

S. No.	Conc. (µg / ml)	Absorbance
1	0	0
2	3	0.007
3	6	0.015
4	9	0.023
5	12	0.031
6	15	0.039
7	18	0.047
8	21	0.054
9	24	0.062

Table 23: Optimum conditions, Optical characteristics and Statistical data of the Regression equation in Second order derivative Spectroscopy

Parameter	UV method
λ_{max} (nm)	354
Beer's law limits (µg / ml)	3-24
Molar extinction coefficient (L mol^{-1} cm^{-1})	0.0026 X 10^4
Sandell's sensitivity (µg / cm^2 - 0.001 absorbance units)	0.3846
Regression equation (Y*)	Y = 0.0026 x – 0.0004
Slope (b)	0.00026
Intercept (a)	-0.0004
Correlation coefficient(r^2)	0.9998
Intraday Precision (% RSD**) Interday Precision (% RSD**)	1.422 1.460
Limit of detection (µg / ml)	0.575
Limit of quantitation (µg / ml)	1.743

*Y = bx + a where x is the concentration of Naproxen in µg / ml and Y is the absorbance at the respective λ_{max}.

**Average of Six determinations.

Table: 24-Determination of Accuracy results of Naproxen by Second order derivative Spectroscopy

Brand used	Amount of sample (µg / ml)	Amount of drug added (µg / ml)	Amount Recovered	% Recovery ± SD**
Avele	8	12	12.18	101.5 ± 0.071
	8	15	15.31	102.06 ± 0.06
	8	18	17.93	99.61 ± 0.045
Naprosyn	12	12	11.96	99.55 ± 0.591
	12	15	14.88	99.66 ± 0.042
	12	18	18.22	101.22 ± 0.068

**Average of six determinations.

Table: 25- Determination of Precision results for Naproxen at 354 nm by Second order derivative Spectroscopy

Conc. (µg / ml)	Inter-day Absorbance Mean ± SD**	% CV	Intra-day Absorbance Mean ± SD**	% CV
3	0.0068 ± 0.000408	5.97	0.0071 ± 0.000408	5.69
6	0.0156 ± 0.000516	3.29	0.0146 ± 0.000516	3.52
9	0.0223 ± 0.000516	2.31	0.0230 ± 0.000632	2.74
12	0.0321 ± 0.000753	2.34	0.0315 ± 0.000548	1.73
15	0.0375 ± 0.000548	1.46	0.0385 ± 0.000548	1.42
18	0.0451 ± 0.000753	1.66	0.0455 ± 0.000548	1.20
21	0.0525 ± 0.000837	1.59	0.0538 ± 0.000753	1.39
24	0.0630 ± 0.000894	1.41	0.0618 ± 0.000751	1.21

**Average of Six determinations

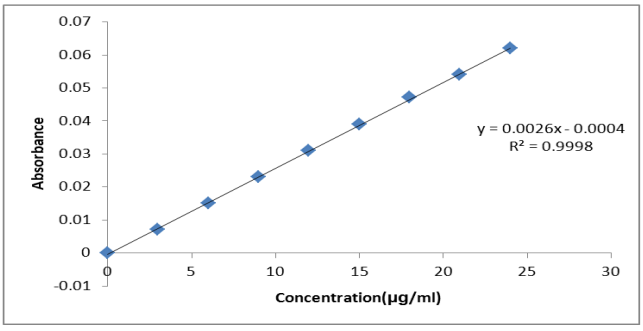

Figure 7: Calibration curve for Naproxen at 354 nm by Second order derivative Spectroscopy

Table: 26- Ruggedness results for Naproxen at 354 nm by Second order derivative Spectroscopy

Brand used	Label claim (mg/ml)	Analyst I		Analyst II	
		Amount found** (mg/ml)	% Recovery ± SD**	Amount found** (mg/ml)	% Recovery ± SD**
Aleve	20	20.26	102.01 ± 0.0679	20.14	101.14 ± 0.0563
Naprosyn	20	20.98	99.86 ± 0.0146	20.17	101.13 ± 0.1381

**Average of six determinations.

CONCLUSION

From the above discussion it can be concluded that the proposed method is specific, precise, accurate, linearand robust. Results are in good agreement with labelclaim which indicates there is no interference of excipients. Therefore the proposed method can be used for routine analysis of Naproxen in drug substances and formulation.

REFERENCES

1. Tripathi KD. Essentials of Medical Pharmacology. New Delhi: Jaypee Brothers Medical Publishers Pvt.Ltd; 2004. P. 176.
2. Monser L, Darghouth F. Assay of naproxen by high-performance liquid chromatography and identification of its photoproducts by LC-ESI MS: J. Pharm. Bio Ana. 2003; 32: 1087.
3. Kulsum S, Padmalatha M, Sandeep S, Saptasila B, Vidyasagar G. Spectrophotometric methods for the determination of naproxen sodium in pure and pharmaceutical dosage forms, Int. J. Res Pharm Biomed Sci. 2011; 3: 1303.
4. Haque T, Talukder MU, Fatema S.L, Kabir AKL. Simultaneous estimation of naproxen and ranitidine HCl by using UV spectrophotometer, Stamford .J. Pharm. Sci. 2008; 18: 1 -2.
5. Dinc E, Ozdemir A, Aksoy H, Ustundag O, Baleanu D. Chemometric determination of naproxen sodium and pseudoephedrine hydrochloride in tablets by HPLC. Chem Pharm Bull 2006, 54, 415.
6. Ekpe A, Tong JH, Rodriguez L. High-performance liquid chromatographic method development and validation for the simultaneous quantitation of naproxen sodium and pseudoephedrine hydrochloride impurities. J Chromatogr Sci, 2001; 39: 81.
7. Nielsen Kudsk F. HPLC determination of some anti-inflammatory, weak analgesic and uricosuric drugs in human blood plasma and its application to pharmacokinetics, Acta Pharmacol Toxicol, 1980; 47: 267.
8. Ling TL, Yee JP. A multiple dose pharmacokinetic comparison of naproxen as a once daily controlled release tablet and a twice-daily conventional tablet, J. Clin. Pharma. 1987; 27(4): 325-329.
9. Irin Dewan, Sadiya Afrose Jahan, Mahjabeen Gazi, Joydeb Nath, Asaduzzaman Md, Maksud Al- Hasan, Design, Preparation, Evaluation, Compatability and in-vitro studies of Naproxen and Esomeprazole multilayer tablets by layer technology. World Journal of Pharmaceutical research, 2015; 4(6): 472-492.
10. Kumar Ashutosh S, Debanth Mandip and Dr Rao seshagiri J.V.L.N. Simultaneous estimation of Esomeprazole and Naproxen in bulk as well as in pharmaceutical formulations by using RP-HPLC, Int. J. Pharm Sci Res, 2013;(8):2988-2999.
11. Czech B, Oleszczuk P. Sorption of diclofenac and naproxen onto MWCNT in model wastewater treated by H2O2 and/or UV. Chemosphere. 2016; 4(4):272-278.
12. Palazzini E, Galli G, Babbini M. Pharmacokinetic evaluation of conventional and controlled release product of Naproxen, Drug under experimental and clinical research, 1990; 16(5): 243-247.
13. Dahl TC, Bormeth AP. Naproxen controlled release matrix tablets, fluid bed granulation feasibility, Drug. Dev, Ind. Pharm, 1990; 16(4): 581-590.
14. Dahl TC, Calderwood, Bormeth A, Trimble K, Piepmeier E. Influence of physicochemicalproperties of hydroxy propyl methyl cellulose on naproxen release fromsustained release matrix tablets, J. Cont. Rel, 1990; 14: 1-10.
15. Wadher S, Pathankar P, Puranik M, Ganjiwale R, Yeole P. Simultaneous Spectrophotometric Estimation of Paracetamol and Metoclopramide Hydrochloride in Solid Dosage Form, Indian J. Pharm. Sci. 2008; 70(3): 393-5.
16. Swapna Y, Nagarjun Reddy G, Chandra K Sekhar. A new RP - HPLC method for simultaneous estimation of naproxen and sumatriptan in tablet dosage form, Int .J . Pharm .Bio Sci, 2013; 3(1): 179-185.
17. Kamepalli Sujana, Gowri Sankar D, Konda Abbulu. Simultaneous estimation of sumatriptan succinate and naproxen sodium by RP-HPLC in bulk and pharmaceutical dosage form. Int .J. Pharm Sci Res, 2012; 3(9): 3433-3437.
18. Ampati S, Lagishetti S, Bairi AG. Development and validation of RP-HPLC method for simultaneous estimation of naproxen sodium and esomeprazole in pharmaceutical tablet dosage form. Int. J. Pharm, 2014; 4(3):95-104.