Development and Validation of an Economical UV-Visible Spectrophotometric Method for Quantitative Determination of Ketoprofen

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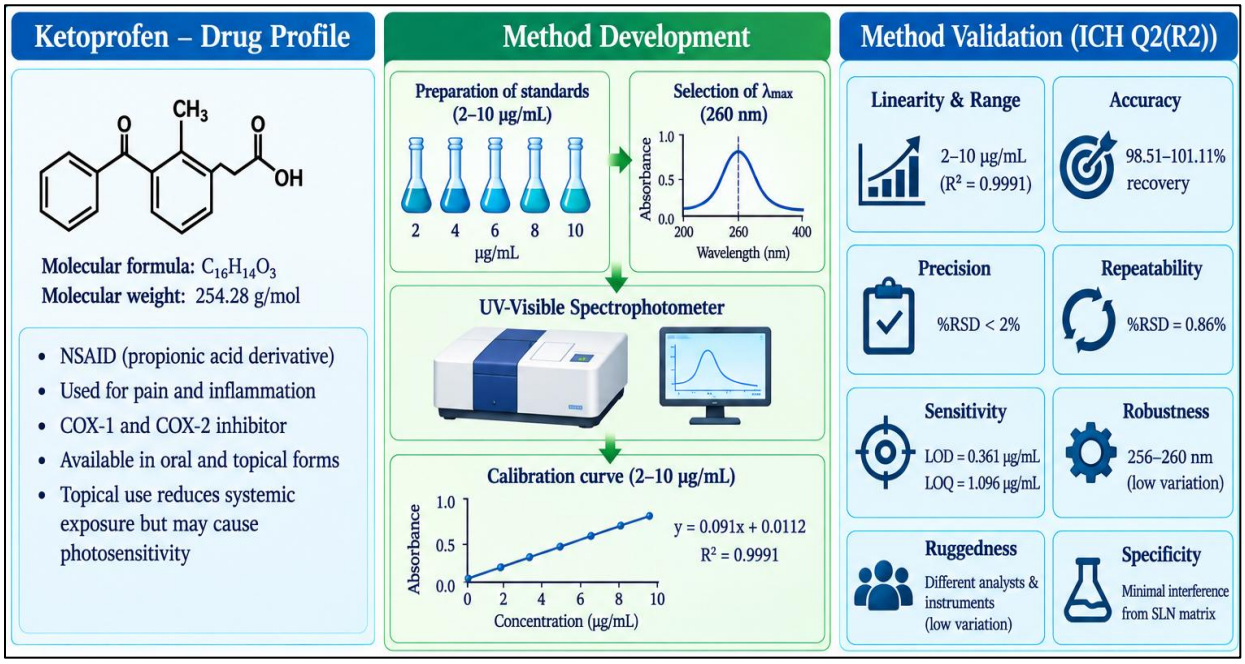
***Abstract*—Ketoprofen is a commonly used nonsteroidal anti-inflammatory agent for treating pain and inflammation. A simple and economical analytical procedure is useful for drug estimation during formulation development and related pharmaceutical investigations. In this study, a UV-visible spectrophotometric method has been developed and validated in accordance with ICH Q2(R2) principles for the quantitative measurement of ketoprofen. The drug was characterized by melting point determination, UV-Visible spectroscopy, and Fourier transform infrared spectroscopy. Phosphate buffer (pH 7.4) was selected as the working medium, and ketoprofen showed suitable absorbance at 260 nm. The method exhibited linearity over 2–10 µg/mL, with the regression equation y = 0.091x + 0.0112 and R^2 = 0.9991. Accuracy was supported by satisfactory recoveries, while precision and repeatability showed low variability. The method also demonstrated adequate sensitivity and remained reliable following small changes in wavelength and under different analyst and instrument conditions. Specificity testing showed minimal interference from the formulation matrix. Overall, the suggested study offers and provides a straightforward economical approach for routine quantitative estimation of ketoprofen in pharmaceutical research and formulation studies.**

***Index Terms*—Ketoprofen; UV-Visible spectrophotometry; Analytical method development; Method validation; Quantitative estimation.**

Abbreviations: A – Analyst; A1 – Analyst 1; A2 – Analyst 2; Abs – Absorbance, Conc – Concentration; I – Instrument; I1 – Instrument 1; I2 – Instrument 2; LOD – Limit of detection; LOQ – Limit of quantification; R^2 – Coefficient of determination; RSD – Relative standard deviation; SD – Standard deviation; SLN – Solid lipid nanoparticles.

GRAPHICAL ABSTRACT



I. INTRODUCTION

Ketoprofen is a propionic acid derivative of the nonsteroidal anti-inflammatory drug (NSAID) class and is used primarily for the management of pain and inflammation. It is prescribed for conditions such as osteoarthritis and other musculoskeletal disorders affecting the joints and soft tissues. Its pharmacological action has been linked to a reduction in prostaglandin production through inhibition of the cyclooxygenase (COX)-1 and COX-2 pathways. The drug is available through different routes of administration, including oral and topical preparations. Topical delivery is particularly useful when localized treatment is desired while reducing systemic exposure associated with oral NSAID therapy. However, adverse effects such as photosensitivity may occur with topical ketoprofen and should be considered during its use.[1–4]

Accurate estimation of ketoprofen is required at different stages of pharmaceutical research, including formulation development, optimization, quality assessment, and evaluation of drug delivery systems. A number of analytical techniques have been described for its determination, including chromatographic and spectrophotometric techniques. Chromatographic methods generally provide high selectivity but may require sophisticated instrumentation, relatively elaborate sample preparation, and higher analytical expenditure. UV-Visible spectrophotometry, in contrast, can offer a practical alternative for routine analysis when an appropriate absorption wavelength and validated analytical conditions are established.[5,6]

The use of UV-based procedures for ketoprofen estimation has been reported previously. A validated flow-injection UV method, for example, employed 260 nm for quantitative determination and showed satisfactory analytical performance in pharmaceutical formulations. Other spectrophotometric methods have likewise demonstrated the applicability of UV measurements for ketoprofen analysis.[5–7] Nevertheless, the analytical response can change depending on factors such as the solvent or medium, selected wavelength, working concentration range, and formulation matrix. These considerations make validation of the specific analytical procedure important before its routine application.

Analytical validation shows that a process regularly fulfills its intended function. According to ICH Q2(R2), relevant performance characteristics should be selected based on the intended application and could comprise specificity, accuracy, precision,

linearity, range, and limits of detection and quantitation.[8] Careful assessment of these characteristics is therefore necessary when establishing the reliability of a newly developed spectrophotometric procedure.

Based on these considerations, the present work focused on developing a straightforward and economical UV-visible spectrophotometric method for ketoprofen quantification. The proposed strategy has been assessed for linearity and range, accuracy, precision, repeatability, sensitivity, robustness, ruggedness, and specificity, with the aim of establishing its suitability for pharmaceutical research and formulation-related analysis.

Drug Profile: Ketoprofen, chemically designated as 2-(3-benzoylphenyl)propanoic acid, has the molecular formula $C_{16}H_{14}O_3$ with a molecular weight of 254.28 g/mol. Its chemical structure is presented in Fig. 1. The drug is described as a white to off-white crystalline powder, with a reported melting point of approximately 94–97°C. It is practically water-insoluble but readily soluble in several organic solvents, such as ethanol, acetone, methanol, and chloroform.[9] Ketoprofen belongs to BCS Class II and is rapidly absorbed upon administration. Peak concentrations of plasma are typically reached within 0.5–2 h, while its elimination half-life is approximately 2.1 h. The drug undergoes extensive hepatic glucuronidation, and approximately 80% of the administered dose is eliminated in the urine, as glucuronide metabolites.[10]

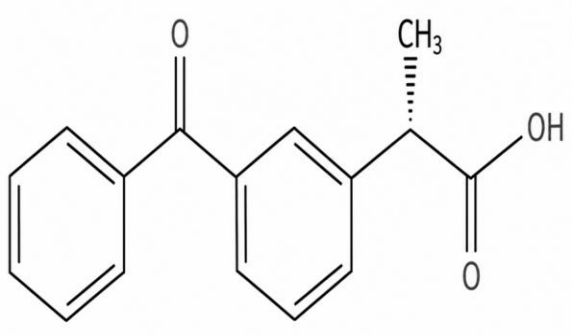


Fig. 1: Chemical structure of Ketoprofen

II. MATERIALS AND METHODS

Chemical and reagents:
Ketoprofen was acquired as a gift sample from Infinity Laboratories Pvt. Ltd., Punjab. Ethanol and methanol were procured from Bio Liqua Research Pvt. Ltd., Bengaluru, and Qualigens Fine Chem Ltd., Mumbai, respectively. The study's other chemicals and reagents were all of analytical grade.

Equipment:
Absorbance measurements were obtained using a double-beam UV-Visible spectrophotometer (UV-1800, Shimadzu, Japan) equipped with Spectra Manager software. Quartz cuvettes with a 1-cm optical path length were used. An electronic balance (WENSAR, Essae Teraoka Ltd., Chennai) for weighing the chemicals. An FTIR spectrophotometer (1700S, Shimadzu, Japan) was used to conduct the FTIR analysis, while the melting point was determined using a melting point apparatus (Secto Ltd., Bengaluru).

Characterization of pure drug:
The supplied ketoprofen sample was characterized by melting point determination, UV-Visible spectroscopy, and FTIR analysis. The experimental results were contrasted with the reported characteristics of ketoprofen to assess its conformity with the expected properties of the drug.[12,23]

Determination of melting point:
The melting point was determined by the capillary fusion method. Finely powdered ketoprofen was introduced into a sealed-end glass capillary and placed in the melting point apparatus. The temperature at which complete melting of the sample was observed was recorded.[11,12]

Identification by UV-Visible spectrophotometry:
A ketoprofen solution of 100 µg/ml was prepared in 75% methanol and scanned in the range of 200 to 400 nm using 75% methanol as the blank. The maximum absorption wavelength was recorded in comparison to the reported value in the Indian Pharmacopoeia (2022).[12]

FTIR Spectrophotometric Analysis:
For characterization using FTIR, ketoprofen was triturated with spectroscopic-grade potassium bromide (KBr) to obtain a uniform mixture. Approximately 100 mg of the mixture was compressed at a 10-ton pressure to prepare a transparent KBr pellet. The spectrum was recorded over 4000–400 cm^{-1}, and the distinctive absorption bands were compared with the reported spectral features of ketoprofen.[13,14]

Analytical Experimental Method
Preparation of phosphate buffer, pH 7.4:
Potassium dihydrogen phosphate (6.8 g) and sodium hydroxide (1.564 g) were dissolved in distilled water and transferred to a 1000-ml volumetric flask. The volume was adjusted to the mark with distilled water. The pH was measured using a calibrated pH meter and adjusted to 7.4 when required.[7,15]

Determination of λmax of Ketoprofen:
Ketoprofen (10 mg) was initially dissolved in 10 ml ethanol and transferred to a 100-mL volumetric flask. The volume was brought up to the mark with phosphate buffer (pH 7.4), resulting in a final concentration of 100 µg/ml. The wavelength that corresponded to maximal absorption was chosen for further study after the solution was scanned using phosphate buffer as a blank.[7]

Preparation of Calibration Standards:
For the primary stock solution, 25 mg of ketoprofen was dissolved in ethanol and diluted to 25 ml to obtain a concentration of 1000 µg/ml. A secondary stock solution of 100 µg/ml was prepared by taking 1 ml of the primary stock into a 10-mL volumetric flask, then making up the volume with phosphate buffer (pH 7.4). Calibration standards of 2, 4, 6, 8, and 10 µg/ml were prepared by transferring 0.2, 0.4, 0.6, 0.8, and 1.0 ml, respectively, of the stock-2 solution into separate 10-mL volumetric flasks and diluting with phosphate buffer. Absorbance was measured at 260nm in triplicate. Values for mean absorbance were plotted against the corresponding ketoprofen concentrations using Microsoft Excel.[16,17]

Analytical Method Validation:
The developed method was validated as per the applicable principles of ICH Q2(R2).[8] Linearity and range, accuracy, precision, repeatability, sensitivity, robustness, ruggedness, and specificity were evaluated.[24]

Linearity and range:
Five calibration standards covering 2–10 µg/ml were analyzed. A calibration plot was developed with concentration as the independent variable and absorbance as the dependent variable. Linear regression was applied, and the slope, intercept, and coefficient of determination (R^2) were used to evaluate the linear response.[7,8,20]

Accuracy:
Accuracy was investigated by recovery studies at 80%, 100%, and 120% levels relative to the nominal sample concentration of 10 µg/ml. Ketoprofen standards corresponding to 8, 10, and 12 µg/ml were added to the pre-analyzed sample solution. The solutions prepared were examined using the proposed method, and percentage recovery was calculated.[18,19]
Using the formula given below, the % recovery was determined. $\% \text{ Recovery} = [(SPS - S) / SP] \times 100$
where, SPS - amount determined in the spiked sample; SP - amount of standard added; S - amount present in the original sample

Precision:
Precision was assessed under intra-day and inter-day conditions. For intra-day precision, replicate analyses were performed on the same day, whereas inter-day precision was evaluated on three consecutive days under comparable experimental conditions. The obtained results were expressed as a percentage relative standard deviation (%RSD).[6,20]

Repeatability:
Repeatability was evaluated using six replicate preparations of ketoprofen at the selected working concentration (6 µg/ml) under identical analytical conditions. The outcomes were expressed as the mean, standard deviation, and %RSD.[13,14]

Sensitivity:
Sensitivity was assessed in terms of the limit of detection (LOD) and the limit of quantification (LOQ), and the parameters were calculated using the standard deviation of the response and the slope of the calibration curve according to:

LOD = 3.3σ/S and LOQ = 10σ/S
where σ represents the standard deviation and S represents the slope of the calibration curve.[6,8]

Robustness:
Robustness was tested by introducing a small, deliberate variation in the detection wavelength. Ketoprofen solutions were analyzed at 256, 258, and 260 nm, and the resulting values were compared using the mean, SD, and %RSD.[21]

Ruggedness:
Ruggedness was evaluated by analyzing the drug solution under comparable conditions using different analysts and instruments. The results were compared using mean, SD, and %RSD to assess the reproducibility of the analytical response.[20,22]

Specificity:
Specificity was investigated by measuring the responses of the blank, drug-free SLN placebo, ketoprofen standard, and ketoprofen-loaded SLN formulation at 260 nm. Phosphate buffer pH 7.4 served as the blank, while drug-free SLN was used to evaluate possible matrix interference. The formulation sample was suitably diluted with phosphate buffer before analysis.[22,24]

III. RESULTS AND DISCUSSION

Melting Point:
The measured melting point of ketoprofen was 95°C, comparable with the reported melting range of the drug, supporting the expected physicochemical characteristics of the supplied sample.

Identification by UV-Visible Spectroscopy:
The UV–Visible spectroscopic analysis of ketoprofen showed a maximum absorption wavelength (λmax) of 257.49 nm, with a corresponding absorbance of 0.657, as displayed in Fig. 2. The observed λmax was in strong agreement with the pharmacopoeial value (258 nm and 0.66) reported in the Indian Pharmacopoeia (IP) 2022, Volume II. This close agreement supported the identification of ketoprofen and demonstrated consistency with the reported spectrophotometric characteristics of the drug. [12]

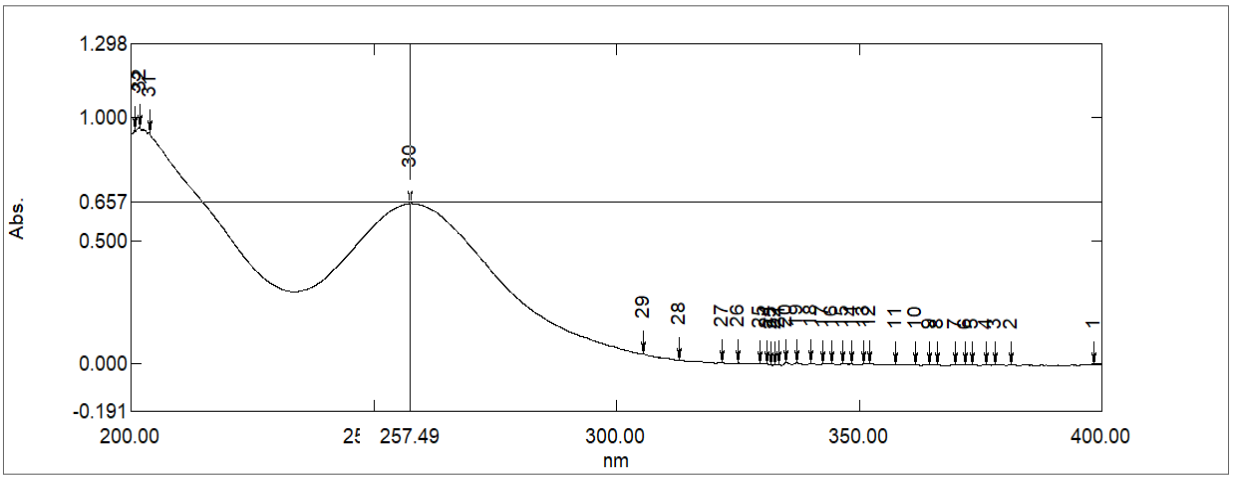


Fig. 2: Overlay spectrum of ketoprofen from the UV-Visible spectrophotometric identification test

FTIR Spectroscopic Characterization:
The FTIR spectrum of ketoprofen exhibited absorption bands characteristic of its principal functional groups (Fig. 3). A broad absorption region from 2500 to 3300 cm^{-1} was observed, corresponding predominantly to carboxylic acid O–H stretching with overlapping C–H absorption. The spectrum also showed prominent bands at 1703.20 and 1653.05 cm^{-1}, together with an aromatic C=C band at 1597.11 cm^{-1} and a C–O absorption at 1282.71 cm^{-1}. Bands at 731.39 and 708.20 cm^{-1} were observed in the lower wavenumber region and were associated with aromatic C–H out-of-plane vibrations. Overall, the observed spectral pattern was in line with the characteristic FTIR profile reported for ketoprofen (Table 1).[25]

Table 1: Characteristic FTIR absorption bands of pure Ketoprofen.

Sl. No.	Functional group	Standard peak values of pure Ketoprofen (cm^{-1})	Observed peak values of pure Ketoprofen (cm^{-1})
1.	O–H stretching (carboxylic acid)	2500-3300	2997.48, 2733.22, 2652.21
2.	C=O stretching (carboxylic acid)	1680–1720	1703.20
3.	C=O stretching (ketone)	1640–1660	1653.05
4.	Aromatic C=C stretching	1500–1600	1597.11
5.	C–O stretching (carboxylic acid)	1210–1320	1282.71
6.	Aromatic C–H bending	700–750	731.39, 708.20

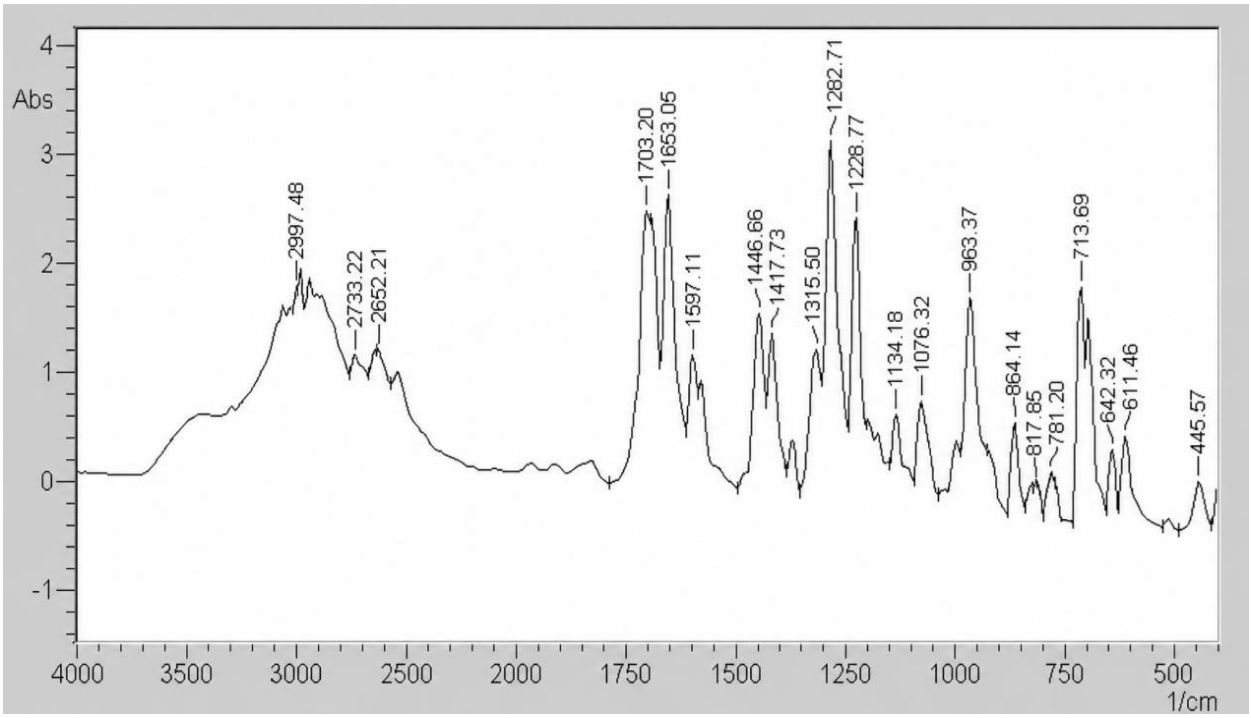


Fig. 3: FTIR spectrum of pure Ketoprofen showing characteristic absorption peaks.

Selection of Analytical Wavelength:

When ketoprofen was analyzed in phosphate buffer (pH 7.4), the absorption spectrum showed a distinct maximum at 260.16 nm, with an absorbance of 0.387 (Fig. 4). Although the wavelength slightly differed from that obtained from identification test (257nm) using in 75% methanol (Fig.2), the response at 260 nm was distinct and reproducible in the selected analytical medium, and is also helpful in various formulation studies of ketoprofen. The USP monograph specifies 260 nm for the UV determination of ketoprofen using phosphate buffer at pH 7.4. Therefore, 260 nm was selected as the working analytical wavelength for subsequent quantitative estimation of ketoprofen in the present study.[26]

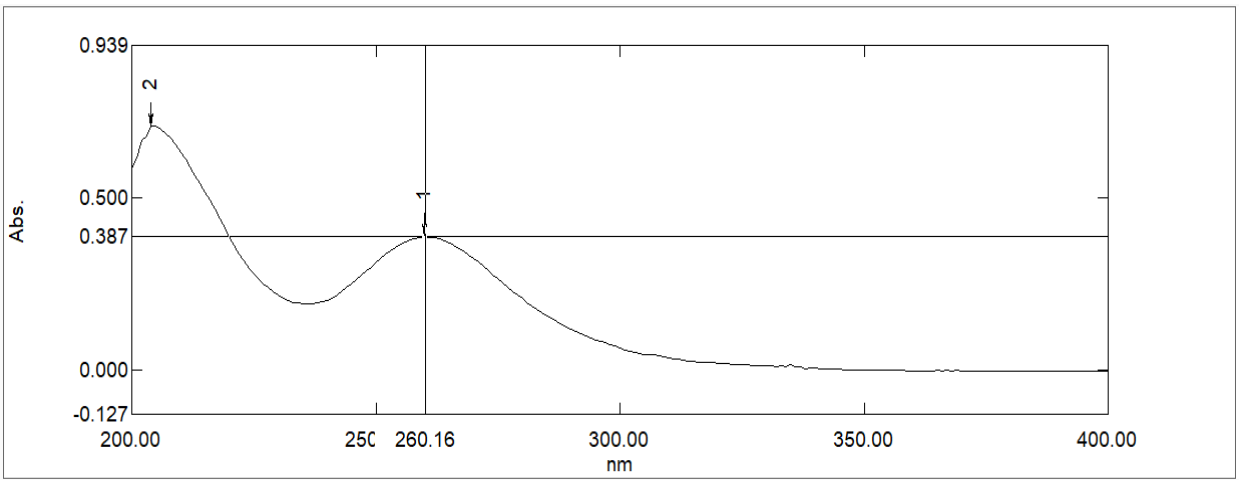


Fig. 4: UV–Visible absorption spectrum of Ketoprofen showing maximum absorption.

Calibration curve of ketoprofen:

A progressive increase in absorbance was observed with increase in ketoprofen concentration over the range of 2–10 µg/ml at 260 nm as ICH Q2(R2) states that linearity should be evaluated across the working range and recommends a minimum of five appropriately distributed concentrations for assessing a linear response.[8] The calibration plot showed a strong linear response, with a coefficient of determination of 0.9991 (Table 2 and Fig. 5). The obtained result shows that the suggested approach provided a consistent, concentration-dependents spectrophotometric response within the investigated range.

Table 2: Standard calibration curve of Ketoprofen at 260 nm.

Conc. (µg/ml)	Absorbance			Mean absorbance	SD	% RSD
	n=1	n=2	n=3			
2	0.202	0.207	0.204	0.204	0.0025	1.23
4	0.378	0.371	0.368	0.372	0.0051	1.38
6	0.569	0.558	0.565	0.564	0.0056	0.99
8	0.750	0.754	0.744	0.749	0.0050	0.67
10	0.906	0.912	0.910	0.909	0.0031	0.34

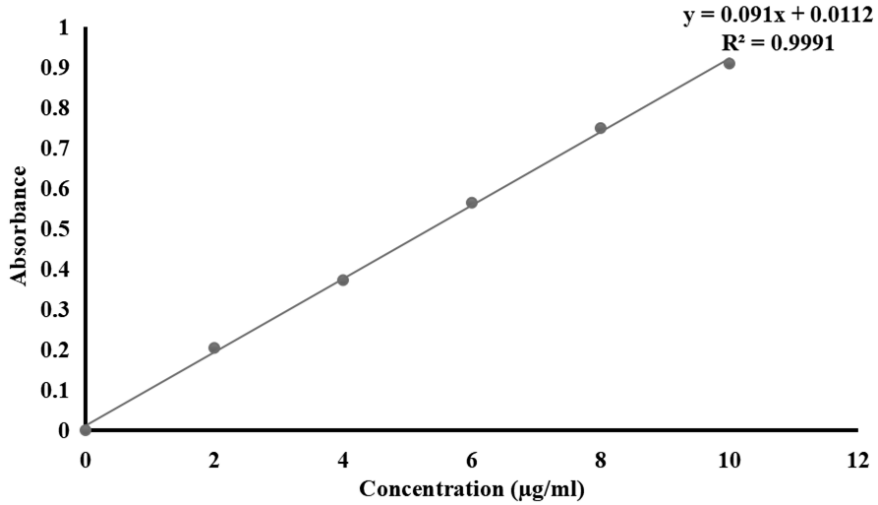


Fig. 5: Calibration curve of Ketoprofen in the conc. range 2–10 µg/ml at 260 nm.

Analytical method validation

Linearity and Range:

The method demonstrated linearity over 2–10 µg/ml, with the regression equation: y = 0.091x + 0.0112 and R^2 = 0.9991. The high coefficient of determination indicates a close relationship between ketoprofen concentration and measured absorbance over the selected analytical range. The obtained range was therefore deemed appropriate for the intended quantitative estimation.[27]

Accuracy:

The recovery study showed satisfactory agreement between the measured and expected ketoprofen concentrations. The mean recoveries were 98.51% at the 80% level, 100.40% at the 100% level, and 101.11% at the 120% level (Table 3). The values remained close to 100% at each of the three levels, showing satisfactory accuracy of the proposed procedure.[18,19]

Table 3: Accuracy study showing recovery profile of Ketoprofen.

Recovery Level (%)	Amount added (µg/ml)	Amount found in spiked sample (µg/ml)			% Recovery			Average % Recovery
		N=1	N=2	N=3	N=1	N=2	N=3	
80	8	17.79	17.88	17.91	97.90	98.80	99.10	98.60
100	10	20.16	19.96	19.99	101.60	99.60	99.90	100.36
120	12	22.17	22.29	22.26	101.70	102.90	102.60	102.40

Note: Recovery calculation based on a 10 µg/ml pre-analyzed sample and the corresponding standard additions of 8, 10, and 12 µg/ml.

Precision:

The method displayed little fluctuation during both intra-day and inter-day assessments (Table 4). The replicate measurements obtained under the respective conditions were closely comparable, indicating that the analytical response remained consistent during repeated measurements and across different analytical days.[6,20]

Table 4: Intra-day and Inter-day precision study.

Conc (µg/ml)	Intra-day observation						Inter-day observation					
	Morning	Afternoon	Evening	Mean Abs	SD	%RSD	Day 1	Day 2	Day 3	Mean Abs	SD	%RSD
2	0.202	0.195	0.198	0.198	0.0035	1.77	0.202	0.204	0.197	0.201	0.0036	1.79
4	0.378	0.373	0.381	0.377	0.0040	1.07	0.378	0.370	0.364	0.370	0.0070	1.89
6	0.569	0.559	0.562	0.563	0.0051	0.91	0.569	0.557	0.552	0.559	0.0087	1.56
8	0.750	0.739	0.744	0.744	0.0055	0.74	0.750	0.736	0.731	0.739	0.0098	1.33
10	0.906	0.902	0.909	0.905	0.0035	0.39	0.906	0.899	0.894	0.899	0.0060	0.67

Repeatability:

The repeatability assessment produced closely comparable absorbance responses among the six replicate determinations. The resulting %RSD was 0.86% (Table 5), demonstrating low variability under identical analytical conditions and confirming good repeatability of the method.[13,14]

Table 5: Repeatability study of the developed method.

Conc. (µg/ml)	Absorbance (n=6)	Mean absorbance	SD	% RSD
6	0.569	0.565	0.0047	0.83
6	0.558			
6	0.565			
6	0.571			
6	0.563			
6	0.568			

Sensitivity:

The calculated LOD and LOQ were 0.361 µg/ml and 1.096 µg/ml, respectively (Table 6). The LOQ was less than the lower limit of the validated calibration range, indicating that the method possessed adequate sensitivity for quantitative determination within the intended application. [6,8] The calculations obtained were: LOD = 3.3 × 0.00997 / 0.091 = 0.361 µg/ml and LOQ = 10 × 0.00997 / 0.091 = 1.096 µg/ml

Table 6: Sensitivity parameters of the developed UV spectrophotometric method.

Parameter	Result
Calibration range	2–10 µg/ml
Slope (S)	0.091
Intercept	0.0112
R^2	0.9991
Residual SD (σ)	0.00997
LOD	0.361 µg/ml
LOQ	1.096 µg/ml

Robustness:

The robustness assessment showed that small changes in detection wavelength produced only limited changes in the analytical response. Measurements performed at 256, 258, and 260 nm showed low variability across the investigated concentrations (Table 7). These findings indicate that the method was reasonably tolerant to minor wavelength variations around the selected analytical condition. [21]

Table 7: Robustness study under deliberate variation of the detection wavelength.

Conc. (µg/ml)	Abs at different wavelength			Mean absorbance	SD	% RSD
	256 nm	258 nm	260 nm			
2	0.208	0.205	0.202	0.205	0.0030	1.46
4	0.373	0.386	0.378	0.379	0.0066	1.73
6	0.562	0.574	0.569	0.568	0.0060	1.06
8	0.745	0.764	0.750	0.753	0.0098	1.31
10	0.908	0.928	0.906	0.914	0.0122	1.33

Ruggedness:

Comparable analytical responses were obtained when the procedure was performed by different analysts and using different instruments (Table 8). The low %RSD values indicated limited variability between analysts while a slightly higher degree of variation was seen between the instruments; however, the overall response remained consistent. The findings therefore demonstrate satisfactory reproducibility of the procedure under normal laboratory variations. [20,22]

Table 8: Ruggedness study by two different analysts and two different instruments.

Conc. (µg/mL)	Abs measured by different Analysts		Abs measured by different Instruments		Mean Absorbance		SD		%RSD	
	A1	A2	I1	I2	A	I	A	I	A	I

2	0.202	0.206	0.202	0.207	0.204	0.204	0.0028	0.0035	1.39	1.73
4	0.378	0.385	0.378	0.387	0.381	0.382	0.0049	0.0063	1.30	1.66
6	0.569	0.574	0.569	0.581	0.571	0.575	0.0035	0.0084	0.62	1.48
8	0.750	0.747	0.750	0.769	0.748	0.759	0.0021	0.0134	0.28	1.77
10	0.906	0.911	0.906	0.928	0.908	0.917	0.0035	0.0155	0.39	1.70

Specificity:

The specificity assessment indicated minimal interference from the SLN formulation matrix (Table 9). The blank showed no measurable absorbance, while the drug-free SLN placebo produced only a low response at 260 nm. In comparison, the ketoprofen standard and drug-loaded SLN formulation showed clear analytical responses. The relatively low placebo response suggests that the lipid and surfactant components did not significantly impede ketoprofen measurement at the selected wavelength. Thus, the technique was thought to be appropriate for the quantitative estimation of ketoprofen in the investigated SLN formulation.[8,27]

Table 9: Specificity of the developed method for ketoprofen.

Sample for Specificity study	Sample used	Abs at 260 nm
Blank	Phosphate buffer, pH 7.4	0.000
Placebo	Drug-Free SLN	0.039
Ketoprofen Standard	Conc. 6 µg/ml	0.564
Ketoprofen Formulation	Drug-loaded SLN upon dilution	0.397

IV. CONCLUSION

A simple and economical UV-Visible spectrophotometric method was developed for the quantitative determination of ketoprofen and evaluated using relevant analytical validation parameters. The method showed a linear response over 2–10 µg/mL at 260 nm, with a high coefficient of determination (R^2 = 0.9991). The satisfactory recovery values and low variability observed during precision and repeatability studies demonstrated reliable analytical performance. The method also showed adequate sensitivity, with LOD and LOQ values of 0.361 and 1.096 µg/ml, respectively.

The procedure remained consistent following small changes in detection wavelength and under variations in analysts and instruments. Specificity assessment further indicated that the formulation matrix produced only minimal interference at the chosen wavelength. These results collectively show that the proposed technique is appropriate for the regular quantitative estimation of ketoprofen, particularly during pharmaceutical formulation development and analysis of the investigated SLN formulation. Its simple procedure, conventional instrumentation, and relatively low analytical requirements make it a practical alternative for laboratories where economical routine drug estimation is required.

DECLARATION

Artificial Intelligence (AI) tool was used in assistance to generate graphical abstract.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest related to this work.

ETHICAL CLEARANCE

No ethical clearance was required as this research work do not involve any kind of studies on animals.

DATA AVAILABILITY

All data is within this manuscript and no supplementary data is available.

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