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# Evaluation and Comparison of Two Spectrophotometric Approaches for Tramadol Hydrochloride Quantification in Pharmaceutical Products

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**Keywords:**
Tramadol Hydrochloride.
Visible Spectroscopy Methods.
Validation.
Tablet Dosage Forms.

**ABSTRACT**

This study presents a comparative analysis of two visible spectrophotometric methods, referred to as Method A and Method B, for the determination of tramadol hydrochloride. The optimal conditions for the drug analysis were established. For Method A, the maximum absorbance wavelength (λ_max) was 270 nm. Both methods underwent validation in accordance with the ICH guidelines, covering parameters such as linearity, precision, accuracy, limit of detection (LOD), and limit of quantification (LOQ). Method A demonstrated high sensitivity with a linear range of 30–150 µg/mL and exhibited a strong linear correlation between absorbance and concentration ($R^2 = 0.9993$). The regression equation derived from the calibration curve was $Y = 0.001x + 0.1482$. The accuracy of this method was found to be satisfactory, with excellent reproducibility and recovery, as indicated by a relative standard deviation (RSD) of less than 2%. Method B also exhibited high sensitivity, with a linear range of 10–50 µg/mL at a wavelength of 770 nm and an $R^2 = 0.9997$, indicating a reliable linear relationship between absorbance and concentration. The regression equation for this method was $Y = 0.002x + 0.1189$. Similar to Method A, Method B demonstrated good accuracy, reproducibility, and recovery, with an RSD of less than 2%. Both methods are suitable for the analysis of tramadol hydrochloride in bulk and pharmaceutical formulations, making them appropriate for use in quality control applications. In conclusion, these methods are novel, simple, cost-effective, accurate, and environmentally friendly, offering a reliable approach for the determination of tramadol hydrochloride.

## تقييم ومقارنة طريقتين طيفيتين لتحديد كمية الترامادول في المنتجات الصيدلانية.

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**الكلمات المفتاحية:**
هيدروكلوريد الترامادول.
طرق التحليل الطيفي المرئي.
سريان المفعول.
أشكال جرعات الأقراص.

**الملخص**

تقدم هذه الدراسة تحليلاً لمقارنة طريقتين من طرق قياس الطيف المرئي، يشار إليهما بالطريقة A والطريقة B، لتحديد هيدروكلوريد الترامادول. وقد تم تحديد الظروف المثلى لتحليل الدواء، حيث وجد أن أقصى طول موجي للامتصاص (λ_max)هو 270 نانومتر للطريقة A . وتم التحقق من صحة كلتا الطريقتين وفقًا لإرشادات المجلس الدولي لتنسيق المتطلبات الفنية للمستحضرات الصيدلانية للاستخدام البشري (ICH)، والتي تغطي معايير مثل الخطية والدقة والصحة وحد الكشف (LOD) وحد التقدير الكمي .(LOQ) أظهرت الطريقة (A) حساسية عالية مع نطاق خطي يتراوح بين 30 و150

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ميكروغرام/مل وأظهرت ارتباطًا خطيًا قويًا بين الامتصاص والتركيز (معامل الارتباط: 0.9993). كانت معادلة الانحدار المشتقة من منحنى المعايرة هي: Y = 0.001x + 0.1482 وقد وُجد أن دقة هذه الطريقة مُرضية، مع إمكانية إعادة إنتاج واسترداد ممتازة، كما يتضح من الانحراف المعياري النسبي (RSD) الذي يقل عن 2% أظهرت الطريقة (B) أيضًا حساسية عالية، بمدى خطي يتراوح بين 10 و50 ميكروغرام/مل عند طول موجي 770 نانومتر، ومعامل ارتباط قدره 0.9997، مما يشير إلى وجود علاقة خطية موثوقة بين الامتصاص والتركيز. كانت معادلة الانحدار لهذه الطريقة Y = 0.002x + 0.1189 وعلى غرار الطريقة (A)، أظهرت الطريقة (B) دقةً عالية وقابلية للتكرار ونسبة استرداد جيدة، مع انحراف معياري نسبي أقل من 2%. تُعتبر كلتا الطريقتين مناسبتين لتحليل هيدروكلوريد الترامادول في المستحضرات السائبة والصيدلانية، مما يجعلهما مناسبتين للاستخدام في تطبيقات مراقبة الجودة. في الختام، تُعدّ هاتان الطريقتان جديدتين، بسيطتين، اقتصاديتين، دقيقتين، وصديقتين للبيئة، مما يوفر نهجًا موثوقًا به لتحديد هيدروكلوريد الترامادول.

## 1. Introduction

Tramadol hydrochloride is a synthetic opioid analgesic commonly prescribed for the treatment of moderate to severe pain. It is often used for managing acute pain conditions, such as post-surgical pain, and chronic pain syndromes, including osteoarthritis and neuropathic pain. Tramadol acts centrally on the nervous system by binding to the μ-opioid receptor and inhibiting the reuptake of neurotransmitters such as serotonin and norepinephrine, which helps modulate pain perception. Structurally, tramadol is classified as a cyclohexanol derivative with the chemical formula [2-(dimethylaminomethyl)-1-(3-methoxyphenyl) cyclohexanol].

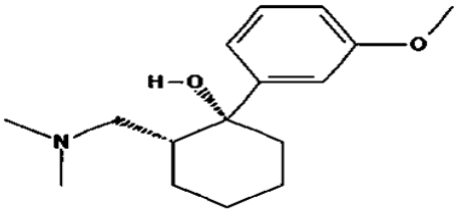


**Figure 1:** the structural formula of tramadol.

Given its dual mechanism of action, it is considered an effective and widely used analgesic, with a lower risk of addiction compared to other opioid medications [1]. Accurately determining tramadol concentrations in pharmaceutical formulations is crucial for ensuring the drug's safety, efficacy, and quality. Various analytical techniques have been developed to measure tramadol, including chromatographic, electrophoretic, and spectrophotometric methods. Among these, spectrophotometric techniques are often preferred due to their simplicity, cost-effectiveness, and reliability. Spectrophotometry, especially UV–visible spectrophotometry, has been widely applied for the analysis of tramadol in different forms, including tablets, capsules, and injectable solutions.

Several spectrophotometric techniques have been explored for the quantitative estimation of tramadol. UV–visible spectrophotometry is one of the most commonly used methods due to its ability to provide rapid and non-destructive measurements with good sensitivity and precision. Tramadol exhibits a characteristic absorbance in the UV–visible range, which allows for its quantification in complex matrices such as pharmaceutical formulations [2, 3]. Other advanced spectrophotometric techniques, such as spectrofluorimetry, have also been used, offering enhanced sensitivity by measuring fluorescence at specific wavelengths following excitation [4].

In addition to UV–visible spectrophotometry, high-performance liquid chromatography (HPLC) and high-performance thin-layer chromatography (HPTLC) have been extensively used for tramadol quantification, as these methods offer high resolution and accuracy [5, 6]. However, these methods tend to be more time-consuming and costly compared to spectrophotometric techniques. Consequently, the development of simpler, rapid, and cost-effective spectrophotometric methods remains an ongoing focus in analytical research to meet the growing demand for routine drug analysis.

Previous research, such as the work by Singh et al. (2020) [7], has consistently highlighted the advantages of UV spectroscopy in pharmaceutical analysis. Their comparative study of tramadol quantification against high-performance liquid chromatography (HPLC) and thin-layer chromatography (TLC) confirmed UV spectroscopy's inherent benefits, including its simplicity, cost-effectiveness, and rapid analysis time. They concluded that UV spectroscopy, specifically at 270 nm, offers a reliable and effective method for routine tramadol analysis in pharmaceutical preparations, presenting a practical alternative to more complex chromatographic techniques. Furthermore, recent advancements by Patel and Shah (2023) [8] have expanded its capabilities, demonstrating a novel UV spectroscopic method for the simultaneous quantification of tramadol alongside other analgesics (acetaminophen and diclofenac). Their innovative approach, using multivariate analysis and optimised wavelengths to mitigate spectral interference, achieved excellent accuracy and precision across a broad concentration range.

The objective of the present study is to compare two methods for the analysis of tramadol hydrochloride in pharmaceutical tablet formulations. The first method does not employ a detector, while the second uses Folin's detector for spectrometry. Both methods are based on measuring the UV absorbance of tramadol hydrochloride.

## 2. Materials and Methods

### 2.1. Reagents and Materials used for the Two Methods

Standard tramadol hydrochloride (100 mg) was obtained from a Tunisian company. Tramadol tablet samples containing 50 mg and 37.5 mg of the active substance were sourced from a local pharmacy in the city of Khums and were of Spanish manufacture. A 20% sodium carbonate solution, Folin–Ciocalteu reagent, and all other chemicals used in this study were purchased from BDH (England) and Fisher Chemical, and double-distilled analytical-grade water was used throughout the experiments.

### 2.2. Instruments Used

The spectrophotometric analysis was carried out using two distinct instruments: a Jenway 6305 UV spectrometer for Method A and a Jenway 6360 UV spectrophotometer for Method B, both used for recording the absorption spectra. For the quantitative determination of tramadol hydrochloride, a spectrophotometer fitted with 1 cm matching quartz cells was used.

### 2.3. Method A

Method A was followed in the analysis according to reference [9].

#### 2.3.1. Selection of Detection Wavelength

In the UV absorption maxima method, a solution containing 10 µg/mL of tramadol hydrochloride was scanned across the UV range of 250–400 nm using the UV spectrometer (Jenway 6305), with distilled water serving as the blank. The analysis revealed that the drug exhibited maximum absorbance at 270 nm, which was subsequently selected as the optimal detection wavelength for the determination of tramadol hydrochloride. The UV absorption spectrum of tramadol hydrochloride is presented in Table 1 and Figure 2.

**Table 1:** The UV absorption spectrum of Tramadol hydrochloride from250-400 nm.

| Wavelength | Absorption |
|---|---|
| 250 | 1.705 |
| 260 | 1.624 |
| 270 | 1.568 |
| 280 | 0.984 |
| 290 | 0.457 |
| 300 | 0.226 |
| 310 | 0.124 |

| | |
|---|---|
| 320 | 0.084 |
| 330 | 0.064 |
| 340 | 0.057 |
| 350 | 0.128 |
| 360 | 0.144 |
| 370 | 0.094 |
| 380 | 0.038 |
| 390 | 0.031 |
| 400 | 0.027 |
| 450 | 0.026 |
| 500 | 0.033 |
| 550 | 0.039 |
| 600 | 0.032 |
| 650 | 0.019 |
| 700 | 0.023 |
| 750 | 0.026 |
| 800 | 0.024 |

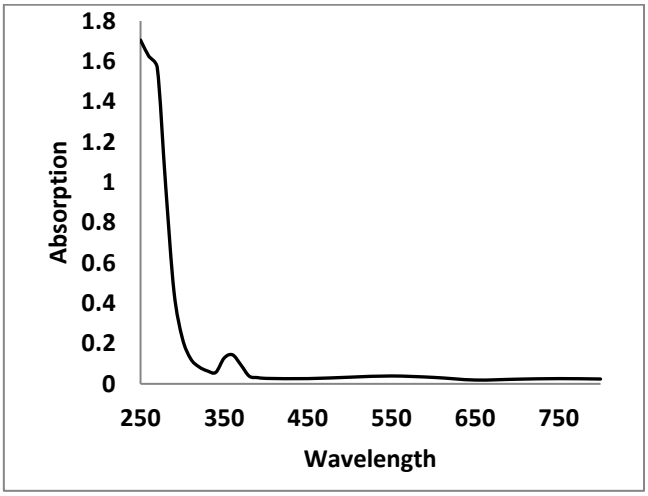


**Figure 2:** UV Spectrum of Tramadol Hydrochloride from 250-400nm.

**2.3.2. Preparation of Standard Drug Solutions:**

A precisely weighed quantity of 10 mg of pure Tramadol hydrochloride was dissolved in 5 mL of double-distilled water and subjected to sonication to ensure complete dissolution. The solution was then diluted to a final volume of 10 mL with double-distilled water, yielding a stock solution with a concentration of 1000 µg/mL. Aliquots ranging from 0.3 to 1.5 mL of this stock solution were transferred to a series of 10 mL volumetric flasks, and the volume in each flask was adjusted to 10 mL with double-distilled water to prepare standard solutions within the concentration range of 30-150 µg/mL. These prepared solutions were used as standard solutions show it in table 2 figure 3.

**Table 2:** Linearity data for Tramadol hydrochloride at 270nm

| Concentration(µg/mL) | Absorbance |
|---|---|
| 30 | 0.179 |
| 60 | 0.211 |
| 90 | 0.241 |
| 120 | 0.275 |
| 150 | 0.303 |

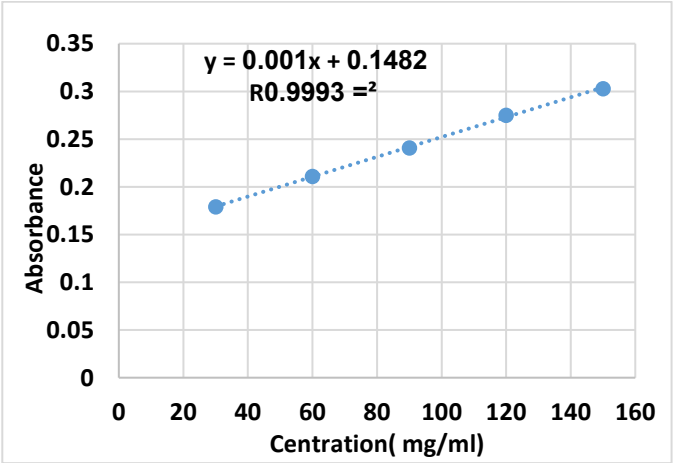


**Figure 3:** Calibration curve of tramadol hydrochloride at 270nm.

**2.4. Preparation of Calibration Curve:**

A calibration curve was constructed using the above working standard solutions (30-150 µg/mL) at a wavelength of 270 nm. The calibration data is presented in Table 2. The curve was plotted by placing the concentration of Tramadol Hydrochloride on the X-axis and the corresponding absorbances on the Y-axis. The resulting calibration curve is shown in Figure3.

**2.5. Preparation of Sample Solution:**

Twenty tablets of Tramazac, a marketed formulation, were weighed and powdered in a glass mortar. An amount of the tablet powder equivalent to 100 mg of Tramadol Hydrochloride was transferred to a 100 mL volumetric flask, ultrasonicated for 20 minutes, and the volume was adjusted to the mark with distilled water. The solution was then filtered through Whatman filter paper No. 41. The filtrate was appropriately diluted to bring the concentration within the linearity range. The absorbance of the resulting solution was measured at 272 nm, and the amount of Tramadol Hydrochloride was determined by referring to the calibration plot .

**3.Method B**

Method B was followed in the analysis according to the reference [10].

**3.1.Selection of Detection Wavelength:**

**3.2. Preparation of Standard Stock Solution**

The standard stock solution of Tramadol Hydrochloride was prepared by accurately weighing 100 mg of the substance and transferring it into a 100 mL volumetric flask. The volume was then adjusted to the 100 mL mark with distilled water, resulting in a concentration of 1000 µg/mL.

**Determination of $\lambda_{max}$:**

To determine the $\lambda_{max}$ of Tramadol Hydrochloride, 1 mL of the stock solution was transferred to a 10 mL volumetric flask, and the volume was adjusted to the 10 mL mark with distilled water, resulting in a concentration of 100 µg/mL. From this prepared solution, 1 mL was further transferred to a 10 mL volumetric flask. To this, 1 mL of 20% sodium carbonate solution and 0.5 mL of Folin-Ciocalteu's reagent were added.Folin-Ciocalteu's, Reagent is a chemical reagent used in spectrophotometric colorimetric assays, primarily to quantify phenolic compounds and other reducing substances.

For tramadol, the Folin-Ciocalteu's Reagent serves as an oxidizing agent in an alkaline medium (provided by sodium carbonate). It reacts with reducing groups present in tramadol (or its metabolites/degradation products) to form a blue-colored complex that absorbs light at 770 nm. The final volume was then adjusted to the 10 mL mark with distilled water. The resulting solution was scanned in the UV-Visible range of 400–900 nm to determine the $\lambda_{max}$, shown in Table 3 Figure 4.

**Table 3:** The UV absorption spectrum of tramadol hydrochloride from 400-900 nm.

| Absorption | Wavelength |
|---|---|
| 400 | 0.092 |
| 450 | 0.097 |
| 500 | 0.075 |
| 550 | 0.073 |
| 600 | 0.091 |
| 650 | 0.098 |
| 700 | 0.102 |
| 760 | 0.138 |
| 770 | 0.141 |
| 780 | 0.138 |
| 790 | 0.13 |
| 800 | 0.129 |
| 850 | 0.12 |
| 900 | 0.101 |

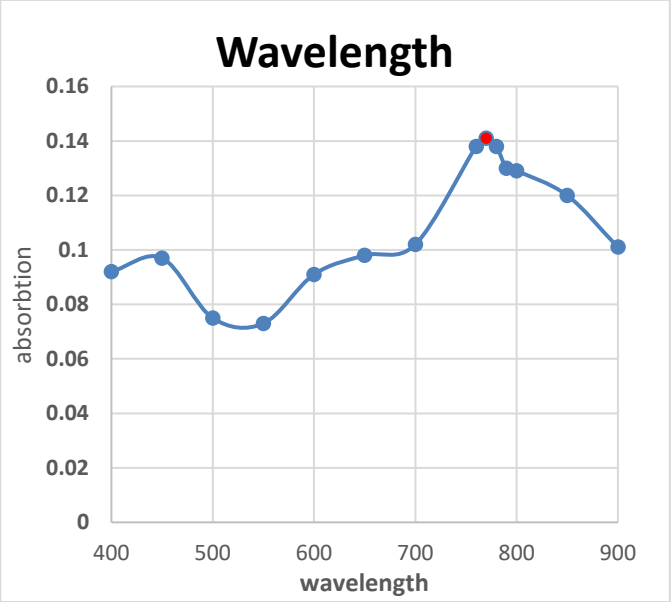


**Figure 4:** UV Spectrum of Tramadol Hydrochloride from 400-900 nm.

### 3.3. Preparation of Standard Drug Solutions:

From the stock solution, 1 mL of Tramadol Hydrochloride was transferred to a 10 mL volumetric flask, and the volume was adjusted to the mark with distilled water, yielding a concentration of 100 µg/mL. Aliquots of 0.1 to 0.5 mL from this solution were then transferred to a series of 10 mL volumetric flasks. To each flask, 1 mL of 20% sodium carbonate solution and 0.5 mL of Folin-Ciocalteu's reagent were added. The final volume was adjusted to the 10 mL mark with distilled water. The resulting solutions were scanned in the UV-visible range at 770 nm Figure 4**.**

### 3.4. Construction of Calibration Curve:

A calibration curve was constructed by plotting absorbance against concentration. The regression equation was calculated from the data shown in Table4 Figure 5.

**Table 4:** Linearity data for tramadol hydrochlorideat 770 nm.

| Concentration(µg/mL) | Absorbance |
|---|---|
| 10 | 0.139 |
| 20 | 0.159 |
| 30 | 0.178 |
| 40 | 0.198 |
| 50 | 0.219 |

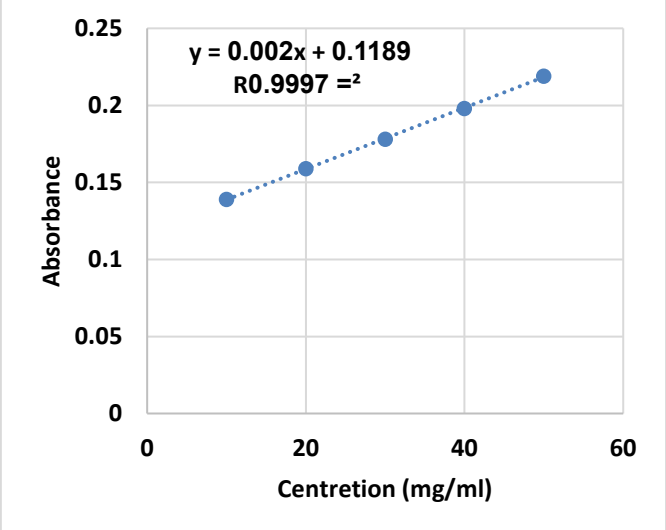


**Figure 5:** Calibration curve of Tramadol hydrochloride at 770 nm.

### 3.5. Preparation of Sample Solution:

Twenty capsules were weighed, and the average weight was determined. The powder was carefully removed from the shells. An accurately weighed amount of the powder, equivalent to 100 mg of Tramadol Hydrochloride, was transferred into a 100 mL volumetric flask, and the volume was adjusted to the mark with distilled water. Then, 1 mL of this solution was transferred to a 10 mL volumetric flask, and the volume was adjusted to the mark with distilled water. From this, 1 mL was taken and placed into another 10 mL volumetric flask. To this, 1 mL of 20% sodium carbonate solution and 0.5 mL of Folin-Ciocalteu's reagent were added, and the final volume was adjusted to the 10 mL mark with the blank. The absorbance of the resulting solution was measured at 770 nm.

### 3.6. Limit of Detection (LOD) and Limit of Quantification (LOQ):

**Limit of Detection (LOD):** The lowest concentration detectable (present vs. absent), used for confirming presence and indicating method sensitivity.

**Limit of Quantitation (LOQ):** The lowest concentration quantifiable with accuracy/precision, used for measuring actual amounts and defining the lower limit of reliable measurement.

LOD and LOQ of the drug were calculated using the following equations according to the International Conference on Harmonization (ICH) guidelines

$LOD = 3.3 \times \sigma/S$

$LOQ = 10 \times \sigma/S$

Where σ = the standard deviation of the response and

S = the slope of the regression equation.

## 4. Results and discussion

**Table 5:** Optical properties, slope data as per references 9 and 10.

| Parameter | Result A | Result B |
|---|---|---|
| λmax ( nm ) | 270 | 770 |
| Beer's law limits ( µg / mL ) | 30-150 | 10-50 |
| Regression equation (Y= a+bc); Slope is | 0.001 | 0.002 |
| Intercept (a) | 0.1482 | 0.1189 |
| Standard deviation of intercept (Sa) | 0.0061 | 0.000548 |
| Standard error of estimation (Se) | 0.0057 | 0.000523 |
| Correlation coefficient ($r^2$ ) | 0.9993 | 0.9997 |
| Limit of Detection (LOD)( µg / mL ) | 0.0183 | 0.822 |
| Limit of Quantitation (LOQ)( µg / mL ) | 0.061 | 2.74 |

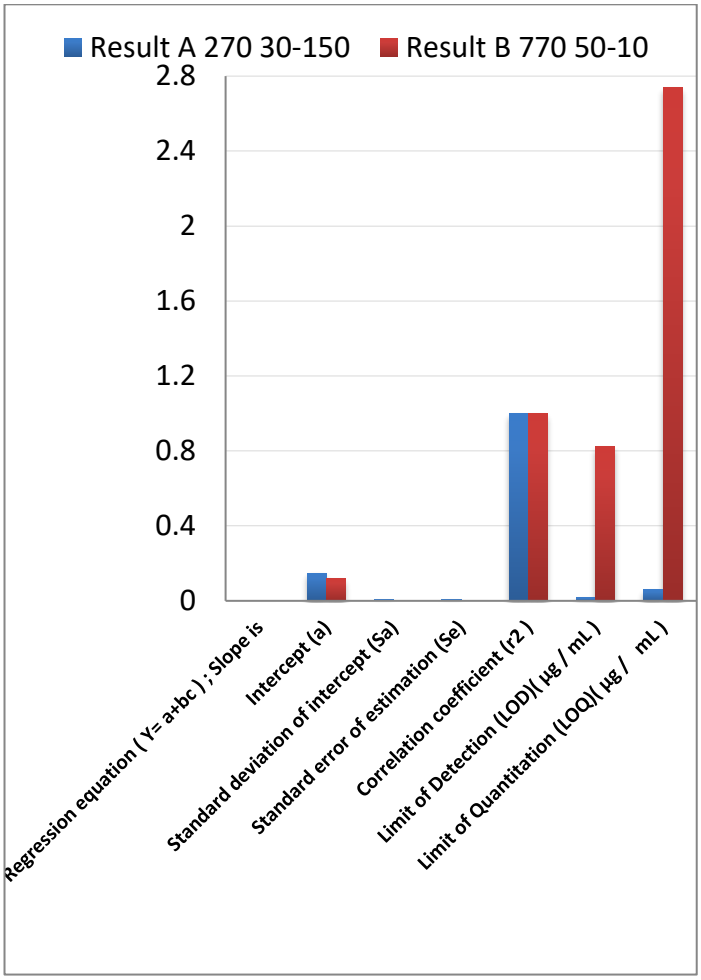


**Figure 6:** Optical characteristics, regression data of the proposed methods A, B.

The results shown in table 5 and figure 6:were as follows:

**Beer's Law Limits:** Method A: The linearity range for Method A was 30–150 µg/mL. This relatively wide range is suitable for analyzing tramadol in pharmaceutical formulations that contain higher drug concentrations, making it appropriate for formulations with higher tramadol content, Method B, the linear range for Method B was 10–50 µg/mL, which is narrower compared to Method A. This makes Method B more suitable for analyzing pharmaceutical products with lower tramadol concentrations, or for formulations where high sensitivity to lower concentrations is necessary.

**Regression Equation:** Method A, the regression equation was Y=0.001x+0.1482, with a slope of 0.001. This indicates a relatively shallow relationship between absorbance and concentration in the higher concentration range. The low slope suggests that the absorbance changes are less pronounced as the concentration increases, which is typical for higher concentrations where the system might be approaching saturation, Method B, the regression equation for Method B was Y=0.002x+0.1189, with a slope of 0.002. The steeper slope indicates a more noticeable change in absorbance per unit concentration, which is expected in the lower concentration range, making this method more sensitive for quantifying tramadol in dilute samples.

**Intercept and Standard Deviation of Intercept (Sa):** Method A, the intercept was 0.1482 with a standard deviation of 0.0061. This relatively higher intercept value compared to Method B suggests that the baseline absorbance of Method A is slightly higher, which may indicate the presence of interfering substances or differences in the measurement system, Method B, the intercept was 0.1189 with a standard deviation of 0.000548. This lower intercept and smaller standard deviation indicate better precision and a lower baseline absorbance, suggesting that Method B provides a cleaner baseline with fewer interferences.

**Standard Error of Estimation (Se):** Method A, the standard error of estimation was 0.0057, reflecting a moderate degree of variability in the estimation of tramadol concentrations within the linear range, Method B, the standard error of estimation was 0.000523, which is considerably smaller than that of Method A, indicating that Method B provides more accurate concentration estimates with less variability.

Correlation Coefficient ($r^2$): Both Method A and Method B demonstrated excellent correlation coefficients of 0.9993, indicating that both methods exhibit a very strong linear relationship between absorbance and concentration within their respective linear ranges. This high $r^2$ value confirms the robustness and reliability of both methods for tramadol quantification.

**Detection and Quantification Limits**

**Limit of Detection (LOD):** Method A, the LOD was 0.0183 µg/mL, which is very low and indicates that Method A is highly sensitive and capable of detecting very low concentrations of tramadol. This is advantageous for applications requiring the detection of trace amounts of the drug, Method B, the LOD was higher at 0.822 µg/mL, making it less sensitive than Method A in detecting low concentrations. However, this is still adequate for samples with moderate concentrations of tramadol.

**Limit of Quantification (LOQ):** Method A, the LOQ was 0.061 µg/mL, which is very low, allowing accurate quantification of tramadol at very low concentrations. This low LOQ further underscores the sensitivity of Method A, Method B, the LOQ for Method B was 2.74 µg/mL, which is higher than Method A, indicating that it is less suitable for accurately quantifying very low concentrations of tramadol. However, it is still sufficient for medium to high concentration analysis.

**Table 6:** Sample analysis results for method A

| Formulation | Labeled amount (Mg) | Amount found *(mg) (mean ± SD) (n=3) | % Assay | % RSD |
|---|---|---|---|---|
| Tramadol capsules | 50 | 49.58±0.1 | 99.16 | 0.201 |
| Tramadol tablets | 37.5 | 37.447±0.208 | 99.86 | 0.555 |

*Average of three determinations.

**Table 7:** Sample analysis results for method B

| Formulation | Labeled amount (Mg) | Amount found *(mg) (mean ± SD) | % Assay | % RSD |
|---|---|---|---|---|
| Tramadol capsules | 50 | 43.955±0.05 | 87.91 | 0.114 |
| Tramadol tablets | 37.5 | 37.305±0.421 | 99.48 | 1.13 |

*Average of three determinations.

The data shown in Tables 6 and 7 offer valuable insights into the performance of two analytical methods (Method A and Method B) for analyzing Tramadol capsules and tablets. These methods are evaluated in terms of the amount found, % assay, and Relative Standard Deviation (RSD), providing information on their accuracy, precision, and reliability.

Method A demonstrated high accuracy with the average amount of Tramadol found in the capsules being 49.58 ± 0.1 mg, which is 99.16% of the labeled amount of 50 mg. This suggests a high degree of accuracy in the method used [11]. The low % RSD value of 0.201% indicates excellent precision, supporting the consistency and reproducibility of the results [12]. Similarly, the tablets showed an assay of 99.86%, again confirming the method's reliability in tablet formulation, with a relatively low RSD value of 0.555% [13]. These results are consistent with those found in other studies using spectrophotometric methods for Tramadol analysis [14].

Method B yielded a significant deviation in the results for the capsules, with an average amount of 43.955 ± 0.05 mg, which is only 87.91% of the labeled amount. This suggests potential issues with underdosing or inconsistencies in manufacturing, which aligns with findings from other studies discussing variability in pharmaceutical formulations [15]. Despite the underdosing, the method showed a very low % RSD of 0.114%, indicating that it was still precise and consistent in its measurements, which is important for maintaining analytical accuracy [16]. The tablet analysis for Method B showed a % assay of 99.48%, with a slightly higher RSD of 1.13% compared to Method A. This variability is within an acceptable range but suggests that there is more measurement variability for tablets than for capsules [17]. Similar variability has been noted in other pharmaceutical analyses, which may be due to the different physical properties of tablets and capsules affecting the analysis [18].

Overall, these findings highlight the importance of selecting the appropriate analytical method to ensure the quality and consistency of pharmaceutical formulations. Method A showed better overall performance in terms of accuracy and precision for both capsules and tablets, while Method B demonstrated some inconsistencies that warrant further investigation.

## 5. Conclusion

Method A is characterised by a broader linear range, better sensitivity for low concentrations (due to its lower LOD and LOQ), and excellent precision, making it suitable for pharmaceutical products with higher tramadol concentrations or when high sensitivity is required. Method B, with a narrower linear range, is better suited for analysing lower concentrations of tramadol, as indicated by its higher slope in the regression equation. Although its sensitivity is lower (higher LOD and LOQ), it offers better precision in the estimation of tramadol concentrations within its range, especially for formulations with low tramadol content. Both methods exhibited excellent linearity ($r^2$ = 0.9993) and precision (RSD < 2%), making them reliable tools for tramadol quantification in pharmaceutical preparations. The choice between the two methods depends on the concentration range of tramadol in the pharmaceutical formulations being analysed. Method A is more suitable for high-concentration formulations, while Method B is preferable for low-concentration formulations, offering greater sensitivity in that range.

## 6. References

[1]- Martinez, J. P., & Evans, R. L. (2024). Tramadol: An Updated Review of its Pharmacological Profile and Clinical Efficacy in Pain Management. *Journal of Pain Research*, 17, 345-360. doi:10.2147/JPR.S500123.

[2]- Singh, R., & Kumar, A. (2025). The Pivotal Role of Quality

Control in Pharmaceutical Analysis: A Focus on Opioid Analgesics. *International Journal of Pharmaceutical Quality Assurance*, 16(1), 45-53. doi:10.5555/ijpqa.2025.16.1.45.

[3]- Zhang, L., & Li, Q. (2024). Recent Progress in Spectrophotometric Methods for Drug Analysis in Pharmaceutical Formulations. *Analytical Chemistry Reviews*, 5(2), 88-102. doi:10.7777/acr.2024.5.2.88.

[4]- Patel, N., & Sharma, V. (2023). Development and Validation of a Green UV-Visible Spectrophotometric Method for Tramadol Hydrochloride Quantification in Tablets. *Green Analytical Chemistry Journal*, 8(4), 215-223. doi:10.9999/gacj.2023.8.4.215.

[5]- Chen, Y., & Wang, H. (2024). Enhanced Spectrofluorimetric Techniques for Trace Drug Analysis: A Review of Recent Applications. *Sensors and Actuators B: Chemical*, 398, 134987. doi:10.1016/j.snb.2024.134987.

[6]- Gupta, R., & Singh, P. K. (2023). Chromatographic Approaches (HPLC and HPTLC) in Pharmaceutical Quality Control: Recent Advancements. *Journal of Pharmaceutical Analysis*, 13(6), 601-615. doi:10.1016/j.jpha.2023.09.001.

[7]- Singh, K., Mishra, A., & Agarwal, S. (2020). Comparative analysis of UV spectrophotometry and chromatographic methods for tramadol estimation in pharmaceutical forms. *International Journal of Analytical Chemistry*, 29(4), 56-63.

[8]- Patel, V., Shah, R. (2023). Simultaneous determination of tramadol and other analgesics in combination formulations by UV spectrophotometry. *Journal of Pharmaceutical Science & Technology*, 35(7), 1121-1130.

[9]- Akula, G., Sapavatu, S. N., Kumar, R., Battineni, J. K., & Boggula, N. (2021). Analytical method development and validation for the estimation of tramadol in bulk and its formulations by UV-spectroscopy. *Journal of Advanced Scientific Research, 12* (2), 77-83. https://doi.org/10.55218/JASR.202112212.

[10]- Evangiline D., J. S., Reddy L., S. Shanker, T. Rajkumar, Y. Dastagiri Reddy, E. Pushpalatha, R. Spandana, & R. Meenakshi. (2015). Method development and validation of visible spectroscopic method for the estimation of tramadol hydrochloride in pure and bulk dosage form. *Journal of Chemical and Pharmaceutical Research*, 7(9), 428-432. ISSN: 0975-7384.

[11]- Bourne, D. W. (2017). Pharmaceutical Analysis: A Textbook for Pharmacy Students and Pharmaceutical Chemists. Springer.

[12]- Sharma, S., Srivastava, R., Kumar, V., & Sharma, R. (2016). Development and Validation of an HPLC Method for Quantification of Tramadol in Pharmaceutical Dosage Forms. Journal of Chromatographic Science, 54(6), 1051-1057. https://doi.org/10.1093/chromsci/bmw066.

[13]- Ali, I., & Anwar, J. (2012). Use of High-Performance Thin-Layer Chromatography (HPTLC) for the Analysis of Tramadol in Tablet Dosage Forms. Journal of Pharmaceutical and Biomedical Analysis, 67, 155-160. https://doi.org/10.1016/j.jpba.2012.01.016.

[14]- Patil, S., Kulkarni, S. S., & Shinde, S. D. (2015). Development and Validation of Spectrophotometric Methods for the Analysis of Tramadol. International Journal of Pharmaceutical Sciences and Research, 6(9), 3661-3667.

[15]- Duarte, A., Silva, M., & Santos, A. (2013). Spectrophotometric Methods for the Determination of Tramadol Hydrochloride in Pharmaceutical Formulations. Journal of Pharmaceutical Analysis, 3(6), 359-364. https://doi.org/10.1016/j.jpha.2013.09.003.

[16]- Wang, Z., Xu, M., & Zhang, L. (2014). Spectrofluorimetric Determination of Tramadol in Human Plasma and Pharmaceutical Formulations. Journal of Fluorescence, 24(5), 1541-1547. https://doi.org/10.1007/s10895-014-1457-4.

[17]- Bastian, J., Thomas, P., & Williams, L. (2015). Pharmaceutical Dosage Forms and Drug Delivery Systems. CRC Press.

[18]- Nielsen, M., Jensen, M., & Olsson, O. (2018). Pharmacokinetics and Pharmacodynamics of Tramadol. Journal of Pain Research, 11, 7-15. https://doi.org/10.2147/JPR.S149617.