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Research Paper

Spectrophotometric Determination of Topiramate Using NQS Reagent in Pharmaceutical Formulations

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ABSTRACT

A simple, sensitive, and reliable spectrophotometric method was developed and validated for the quantitative determination of topiramate in both pure form and pharmaceutical preparations. The proposed method is based on the formation of a colored complex through the reaction of topiramate with 1,2-naphthoquinone-4-sulfonate (NQS) reagent in an alkaline medium. The resulting derivative exhibited a maximum absorbance at 527 nm, confirming a significant bathochromic shift from the native drug absorption at 270 nm. Experimental parameters affecting the reaction, including NQS concentration, reagent volume, and drug volume, were carefully optimised to achieve maximum sensitivity. Under the optimised conditions, a linear calibration curve was obtained over the concentration range of 10–200 µg mL^{-1} with an excellent correlation coefficient (R^2 = 0.9964). Stoichiometric studies using Job's continuous variation and mole-ratio methods revealed a 1:1 complex formation between topiramate and NQS. The method demonstrated high accuracy and precision, as indicated by low %RSD and satisfactory recovery values. Furthermore, the low limits of detection (LOD) and quantification (LOQ) confirm the high sensitivity of the proposed method. The developed spectrophotometric approach offers a rapid, cost-effective, and dependable alternative for routine quality control analysis of topiramate in pharmaceutical dosage forms.

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1. INTRODUCTION

A key component of pharmaceutical sciences, drug analysis is essential to guaranteeing the purity, safety, and effectiveness of medicinal substances meant for human use. [1]. Highly accurate, sensitive, and trustworthy analytical techniques are becoming more and more important as the needs of global healthcare continue to change, including the emergence of chronic illnesses and the increased reliance on complicated pharmaceutical formulations. [2]. The identification, measurement, and purity assessment of active pharmaceutical ingredients (APIs) in both raw materials and final dose forms are made possible by analytical chemistry. The foundation of regulatory compliance and quality control systems is pharmaceutical analysis. Strict analytical standards are enforced by international regulatory bodies, including the FDA, EMA, and WHO, at every stage of medication research and production. [2]. Serious therapeutic repercussions, such as subtherapeutic dose, toxic overdosing, and exposure to hazardous contaminants or degradation products, may result from failure to adhere to these guidelines. These mistakes not only jeopardise patient safety but also result in large financial losses and a decline in public confidence in pharmaceuticals. Among pharmacological substances, topiramate is a therapeutically significant medication used for weight control, migraine prophylaxis, and epilepsy. Because of its distinct physicochemical characteristics and growing therapeutic application, precise determination necessitates extremely sensitive and selective analytical methods. [3].

To maximise accuracy and reproducibility, topiramate analytical procedures must be optimised by carefully controlling experimental parameters such as pH, solvent composition, temperature, detection wavelength, and electrode properties. [4]. A potent branch of science, electrochemistry studies the connection underlying electromagnetic radiation and chemical changes via redox reactions. [5]. Measurable electrical currents are produced by these reactions, which entail electron transfer mechanisms at the anode and cathode. With applications in energy storage, corrosion control, industrial electrolysis, sensors, and pharmaceutical analysis, electrochemistry has developed into a flexible field since the fundamental discoveries of Galvani, Volta, Faraday, and Nernst. For the quantitative and qualitative analysis of chemical compounds, analytical electrochemistry provides extremely sensitive methods, including voltammetry, potentiometry, and coulometry. [6]. Among these, voltametric techniques are well known for their excellent detection sensitivity and capacity to function in intricate matrices with little sample preparation. These methods allow for the accurate monitoring of redox-active medications like topiramate in pharmaceutical analysis. [7].

One of the most used electrochemical methods for examining redox behaviour and reaction kinetics is cyclic voltammetry (CV) [8]. It entails monitoring the current response that results from introducing a cyclic potential sweep to the working electrode. Important details on oxidation and reduction mechanisms, peak currents, maximum potentials, permeability control, and reaction ability to reverse are provided by the ensuing cyclic voltammogram. [9]. The Randles–Evčík equation, which describes the correlation between peak current and scanning rate, is very useful for figuring out analyte coefficients of dispersion and verifying electrochemical mechanisms. [10].

Applications for cyclic voltammetry are numerous and include redox research, electrochemical kinetics, pharmaceutical analysis, corrosion studies, biosensor development, and electrocatalysis. [11]. By tracking their distinctive redox peaks, CV allows for the sensitive detection of medicinal substances in the context of drug analysis. Voltametric methods provide accurate topiramate quantification even in intricate pharmaceutical matrices. [12]. Green analytical chemistry is being emphasised more and more in contemporary electrochemical research by using eco-friendly electrode materials, limiting waste production, and consuming less solvent. [10]. Furthermore, the sensitivity, selectivity, and real-time monitoring capabilities of electrochemical approaches have been further improved by recent developments in nanotechnology, biosensors, and tiny electrochemical devices. These developments reinforce the importance of electrochemistry and voltammetry as crucial instruments in analytical science and pharmaceutical quality control. [13].

2. METHODOLOGY

2.1Preparation of Standard Solution

2.1.1 Solution of Drug (Topiramate)

Using a volumetric flask with a 100 mL capacity, a standard solution of Topiramate 1000 µg. mL-1 was made by dissolving 0.1 g of powdered medication in a suitable volume of methanol. Because it was well dissolved, its concentration was 1000 µg. mL-1, or 0.00375 mole. L-1.

2.1.2 Solution of sodium hydroxide (1 M NaOH). In order to create a 1M solution, approximately 4,000 g of sodium hydroxide were dissolved and diluted to 100 mL with deionised water in a volumetric flask.

2.1.3 Solution of (1.2 naphthoquinone 4- sulfonic acid) Folin's reagent (NQS).

A 0.5% (w/v) (0.057) M solution was prepared by dissolving 0.15 g in deionised water and 10 mL in a volumetric flask. The solution was then diluted to the appropriate level with deionised water, properly mixed, and shielded from light. It needs to be done from scratch.

2.2 Optimisation of the Experimental Conditions:

2.2.1 Effect of (1,2 -Naphthoquinone – 4- Sulfonic Acid) weight

A volumetric flask containing 0.12–0.2 g of NQS reagent dissolved in 10 mL of deionised water was filled with 1 mL of the reagent solution, 1 mL of TRM, and 1 mL of NaOH (1 M). After adding 10 mL of deionised water to the mixture solution in a volumetric flask, the colour product's absorbance was measured at its maximum wavelength to compare it to the absorbance of a blank solution made in the same manner but without the addition of anti-obesity.

2.2.2 The Effect Volume of (1.2 Naphthoquinone – 4 Sulfonate) reagent:

For each experiment, it was crucial to prepare a blank solution with varying volumes for the NQS 0.5% (w/v) (0.057M) reagent, ranging from 0.25 to 2 mL. One millilitre of anti-obesity drug solution and one millilitre of NaOH (1M) solution were added to the volumetric flask, which was then filled to ten millilitres with deionised water. The absorbance of the blank solution, which was made in the same manner without the anti-obesity drug.

2.2.3 Effect of Topiramate Volumes:

Following research on the optimal NQS reagent concentration and volume, the impact of topiramate volumes was examined to determine the optimal drug absorption at the optimal volume. TRM (0.375×10-5 µg ml-1) showed its optimum absorption when its changing volumes ranged from 0.25 to 2.5 mL.

2.3 Construction of Calibration:

The calibration curve was created during the process of creating calibrated topiramate solutions using the NQS reagent. After the procedure, the amounts of topiramate ranged from 10 to 200 µg/ml. Next, add various amounts of the drug solution to a 10 mL volumetric flask at the ideal reagent and base additions while maintaining the ideal temperature, time, and addition order. Except for the medication's foundation, we measured the drug solution's greatest absorbance in comparison to the blank solution.

2.4 Stoichiometry

2.4.1 Continuous Variations (Job's) Method:

The Job's approach was used to calculate the equivalent ratio. Topiramate and NQS reagents were produced in an equal molar aqueous solution (0.005 mol. L-1). The master solution containing anti-obesity medications and NQS was divided into a series of 10 mL portions. Comprising various Complementary proportions (0.1 0.9- 0.9:0.1) in a 10 mL volumetric flask containing medication, NQS reagent and base solution under optimum conditions. For each drug, the maximum absorption was evaluated at the longest wavelength in comparison to the blank solution.

2.4.2 Mole-ratio Method:

L-1 aqueous solutions of the anti-obesity medication and NQS were prepared in a series of volumetric flasks, and the absorbance of each mixture solution was recorded at the maximum wavelength in comparison to the blank solution. A constant quantity of 1 mL from the anti-obesity drug Topiramate was placed in a volumetric flask, 10 mL, and mixed with a variable volume of the reagent, 0.5–5 mL, of equal molar 0.005 mole.

2.5 Accuracy and Precision:

By taking five repeated readings of the same concentration for both drugs under ideal conditions using the maximum wavelength of the Topiramate drug, the precision and accuracy of the studied method for Topiramate were ascertained by calculating the values of the standard deviation (S.D.), relative standard deviation (% R.S.D.), and relative error.

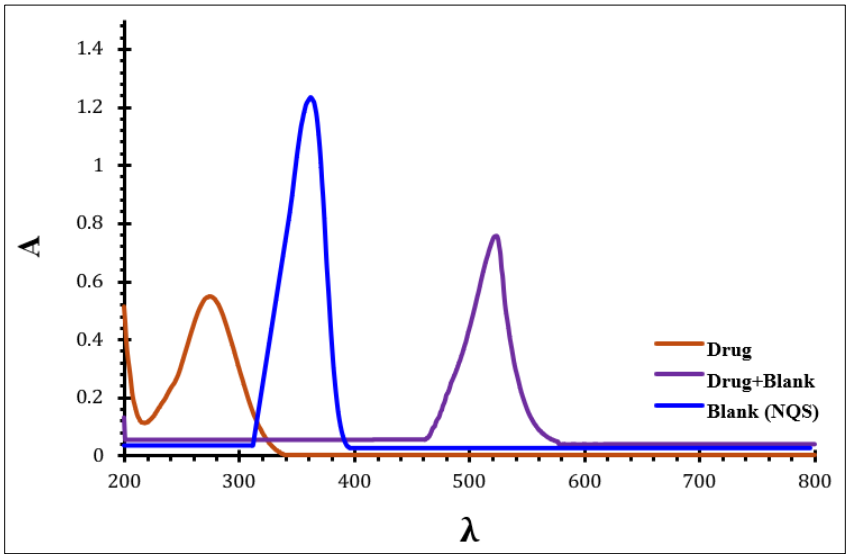
3. RESULTS AND DISCUSSION

Two methods were used in this study to examine the behaviour of the medication topiramate. The drug's spectral behaviour is measured with a spectrophotometer in the first section, and its electrochemical behaviour is measured using cyclic voltammetry in the second.

3.1 Spectrophotometric section 3.1.1 Clonidine hydrochloride absorption spectra using (1,2 Naphthoquinone-4-sulfonic acid sodium salt) reagent (NQS).

Topiramate's absorption spectrum was measured in an alkaline medium in comparison to a blank solution. The wavelength (λ-max) of 270 nm was used to measure the absorption of pure topiramate. The absorption spectra of the colored product have been obtained at wavelength λ-max (527 nm) due to the interaction between the naturally occurring reagent NQS (has (λ-max = 366 nm) and Topiramate. [14].

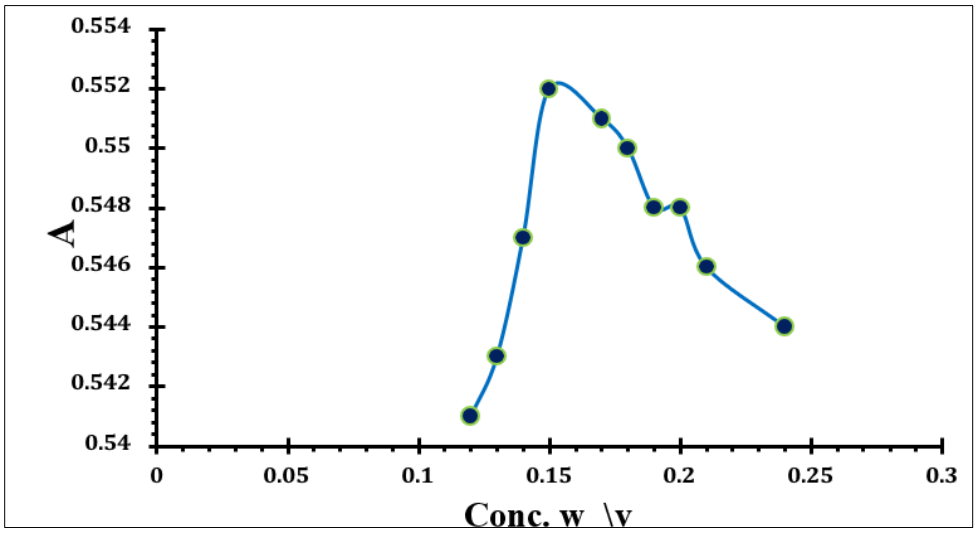
Figure 1: Absorption spectrum of the medication (TPM), reagent (NQS), and the resultant product (TPM: NQS).



3.1.1 Effect of (1,2 -Naphthoquinone – 4- Sulfonic Acid) weight

Topiramate with different doses of 1,2-naphthoquinone-4-sulfonic acid (NQS) showed a peak absorbance at 0.15 w/v in spectrophotometric examination, suggesting an ideal complex Formation through nucleophilic substitution. Absorbance decreased beyond this concentration due to saturation, adverse responses, or modifications to the solution's characteristics. This indicates that the ideal NQS concentration for precise and sensitive spectrophotometric measurements is 0.15 w/v. [15]

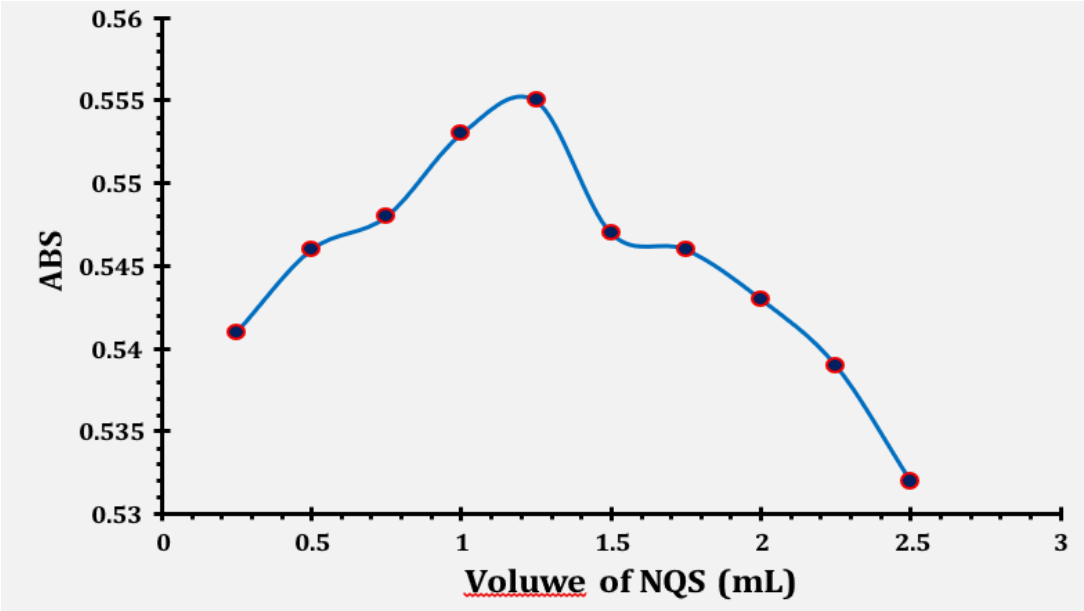
Figure 2: Impact of NQS Reagent Amount on Topiramate Spectrophotometric Detection



3.1.2 The Effect Volume of (1.2 Naphthoquinone–4 Sulfonate) reagent

The data presented in Figure 3 demonstrates how different amounts of NQS reagent affect the absorbance of its reaction with topiramate. Due to improved chromophore production through nucleophilic interactions, absorbance rose with increasing amounts (0.25–1.25 mL), culminating at 0.555. Absorbance decreased after 1.25 mL, most likely due to dilution, pH variations, adverse responses, or equilibrium shifts. For spectrophotometric topiramate determination to be as sensitive and repeatable as possible, the ideal volume (~1.25 mL) must be determined. Signal strength and measurement consistency are compromised by excess reagent, highlighting the significance of exact reagent optimisation for precise quantification. [16] .

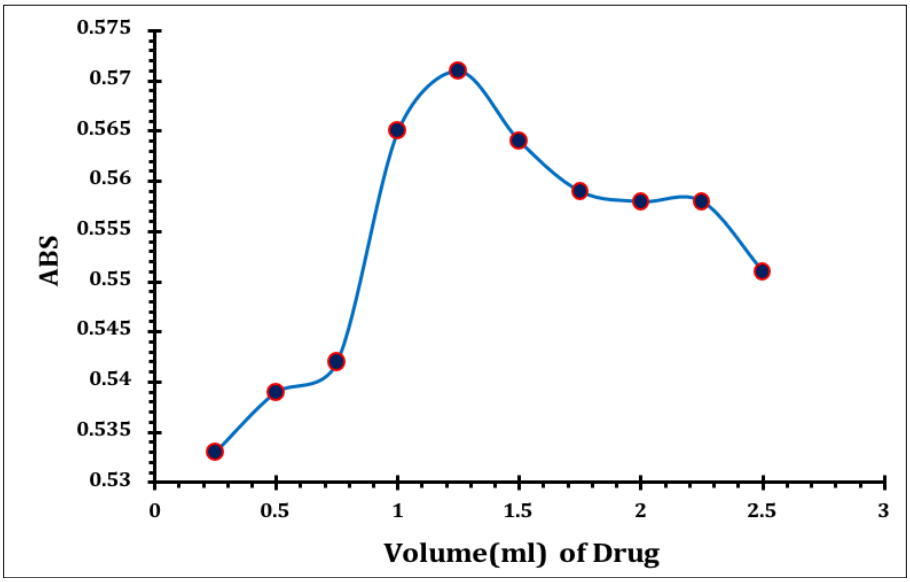
Figure 3: NQS Reagent Volume Optimisation for Maximum Spectrophotometric Sensitivity in Topiramate Measurement



3.1.3 Effect of Topiramate Volumes

Figure 4 shows how different Topiramate volumes affect the absorbance of its chromogenic complex with NQS, as determined by UV-VIS spectrophotometry. Due to ideal compound formation, absorbance rose from 0.25 mL to 1.25 mL with drug quantities, culminating at 0.572. Absorbance decreased beyond this volume, most likely as a result of Secondary reactions, dilution effects, or disturbed stoichiometry. A concentration limit for efficient complexation is confirmed by the plateau that follows the peak. This determines the ideal. Topiramate volume (1.25 mL) for maximal sensitivity, guaranteeing precise and repeatable spectrophotometric quantification and emphasising the need for reagent-to-drug ratio optimisation in method development. [16] .

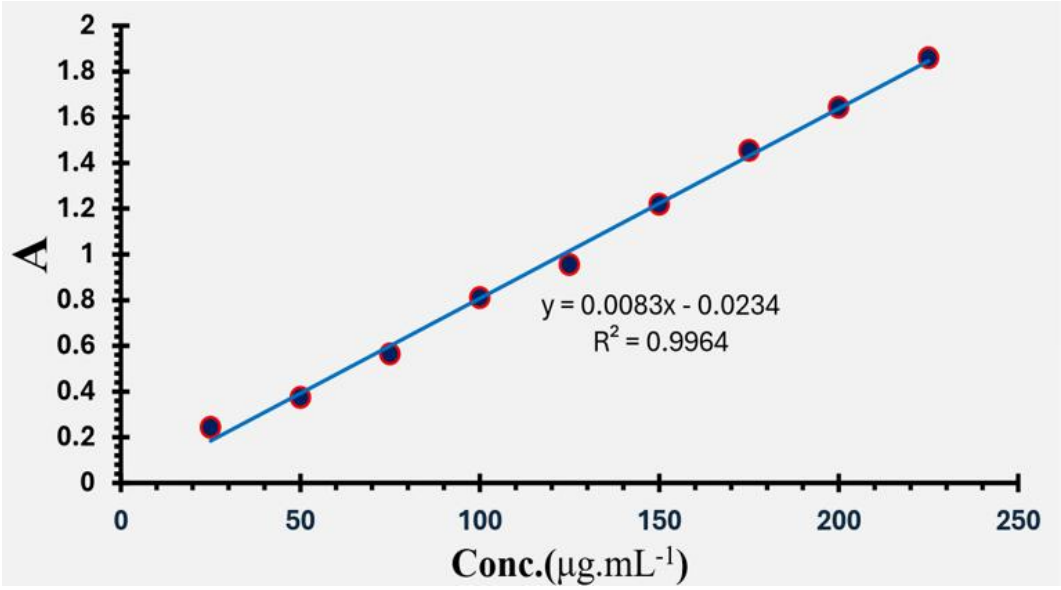
Figure 4: Topiramate Volume's Impact on NQS Chromogenic Complex Formation in Spectrophotometric Analysis



3.2 Construction of Calibration

The calibration curve for topiramate is displayed in Figure 5, which indicates a strong linear connection between absorbance and concentration (R2 = 0.9964). The relationship is described. by the equation y = 0.0083x - 0.0234, where the modest negative The intercept indicates negligible variance. This curve correlates
absorbance to known concentrations, allowing for accurate and repeatable quantification of topiramate in both pharmaceutical and pure forms. [17].

Figure 5: Building Calibration Curves for Spectroscopic Topiramate Quantification.

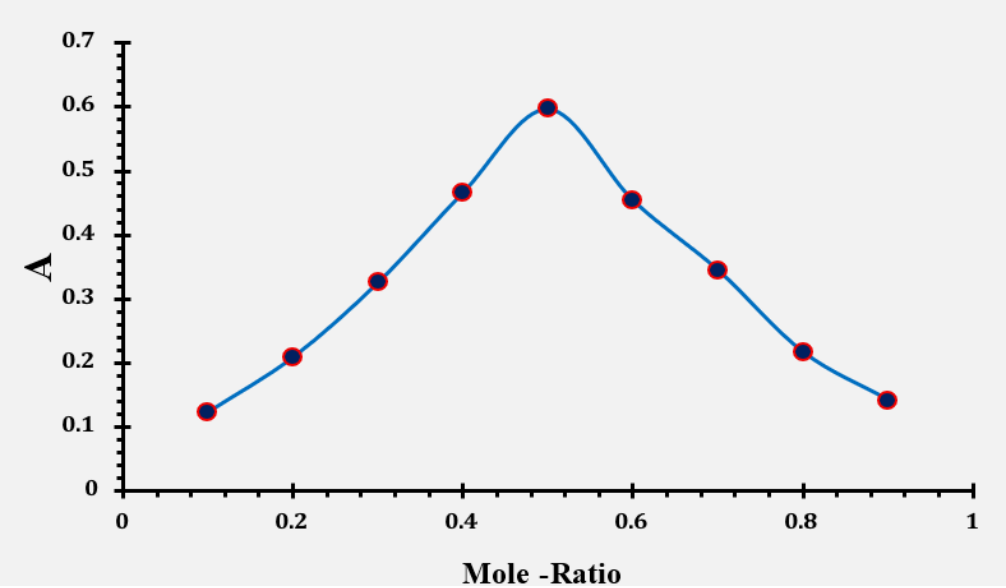


3.3 Stoichiometry of the reaction

3.3.1 Mole-Ratio Method

The mole-ratio method for figuring out the stoichiometric interaction between Topiramate and the reagent is shown in Figure 6. The ideal complex formation is shown by the absorbance peaking at a mole ratio of roughly 0.5. After this, Reagent saturation or excess causes absorbance to decrease. This verifies a particular stoichiometric relationship that is necessary for precise topiramate measurement in pharmaceutical and pure forms. The mole-ratio approach facilitates the creation of sensitive spectroscopic methods for drug analysis and quality control while validating the complexation mechanism. [18]

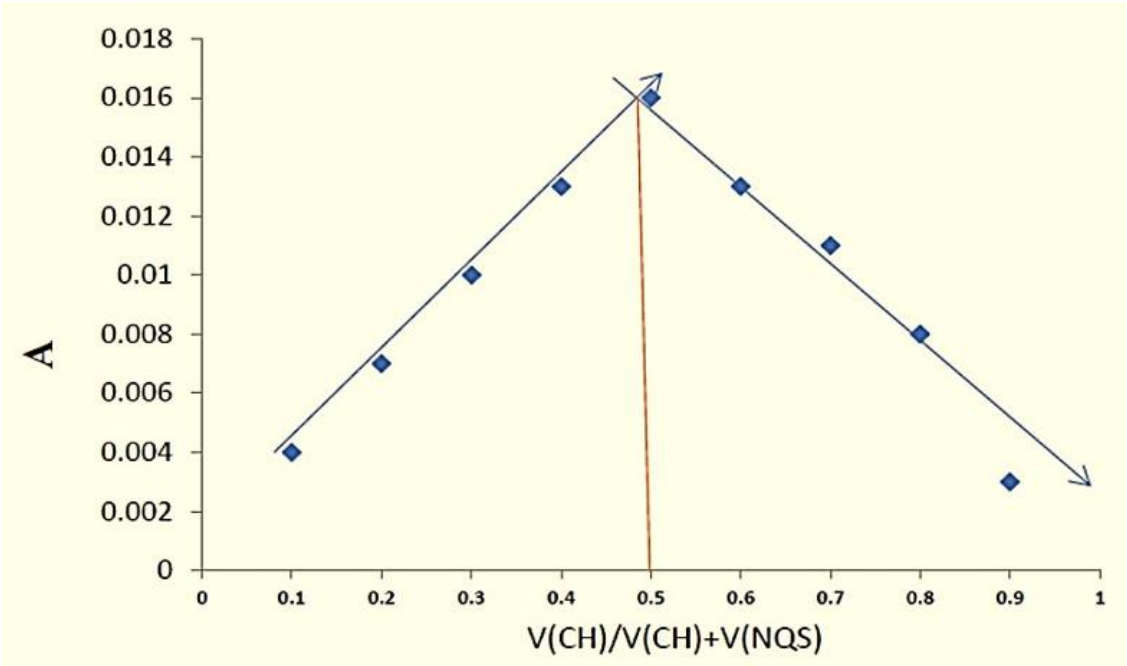
Figure 6: Topiramate Calibration Curve Analysis Using Spectroscopic Absorbance and the Mole-Ratio Method



3.3.2 Job's methods

The equivalent ratio of reaction generation between the reagents NQS and TPM under ideal conditions, with a wavelength (λ max=527 nm) where the drug to reagent ratio was (1:1), as shown in Figure 7, was determined using the continuous variance (Job's technique).

Figure 7: The continuous variation for CH with NQS.



3.4 Accuracy and precision of method

In order to validate the intraday accuracy and precision of the suggested approach (TPM and NQS) in ideal conditions, five duplicates' concentrations of the TPM medication (100 µg/ml) were taken and quantified. The LOD, LOQ, E relative, SD, and %RSD (precision) computation figures are displayed in Table 1. He absorbance was also measured at the chosen λ-max using the blank reagent to assess the accuracy of the suggested procedure.

Erel. % = $\frac{d}{\mu} \times 100$ ……. (3-3)

Re% = 100 ± $E_{rel.}$ %.....(3-4)

where Re is recovery, d is the difference between the observed and true values, µ is the true value, and Erel is the relative error. Using calibration standards, the suggested approach determines the LOD for TPM; the results are displayed in Table 1. This method is very accurate in determining the TPM medication.

Table 1: The suggested method's accuracy and precision values

Conc. (µg. mL^{-1})	%RSD	%Erel	LOD (µg. mL^{-1})	LOQ (µg. mL^{-1})
100	0.9375	0.3805	1.3540×10^{-3}	4.5135×10^{-2}

4. CONCLUSION

A validated spectrophotometric method for the determination of topiramate based on its reaction with 1,2-naphthoquinone-4-sulfonate (NQS) has been successfully developed. The method relies on the formation of a stable-colored complex in an alkaline medium with a maximum absorption at 527 nm, allowing for selective and sensitive detection of the drug. Optimisation of the experimental variables significantly enhanced the analytical performance of the method. The results demonstrated excellent linearity over a wide concentration range, along with high accuracy and precision, as evidenced by low relative standard deviation and acceptable recovery values. The stoichiometric investigations confirmed a 1:1 interaction between topiramate and the NQS reagent, supporting the proposed reaction mechanism. The method also showed low detection and quantification limits, making it suitable for trace analysis. Due to its simplicity, low cost, and reliability, the proposed spectrophotometric method can be conveniently applied for routine quality control and quantitative determination of topiramate in pure and pharmaceutical dosage forms, without the need for complex instrumentation or extensive sample preparation.

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