Spectrophotometric Method for The Micro determination of Naproxen in Pure and Pharmaceutical Dosage Forms Using bromophenol blue

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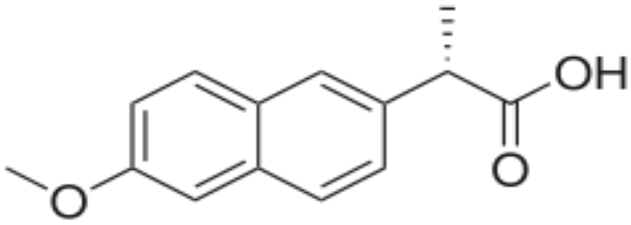
Abstract
An easy and fast spectrophotometric method has been developed for the determination of naproxen, this method depended on the reaction between the naproxen drug with bromophenol solution in present NaOH as a base to afford a color product and the high absorption at 596 nm. Beer's law was obeyed within 2-16 µg /mL concentration range, and molar absorbance value id 7.5985×103 L/mol.cm and Sandel sign value is 0.0303 µg /cm2. The limits of detection (LOD) and quantitation (LOQ) for the proposed method are 0.108 and 0.3608 µg/mL, respectively.
Keywords: Naproxen, Bromophenol blue, Sodium hydroxide, oxidative coupling reaction.

1. Introduction

Naproxen: (s)-2-(6-Methoxy naphthalen-2-yl) propanoic acid and has a synthetic formula [1]:



It is a non-steroidal anti-insomnia drug, and acts by inhibiting the action of the enzyme prostaglandin (cyclooxygenase). Also, it has analgesic, antipyretic and heat pump action [1]. Many previously reported were studied development spectrophotometric methods to detect naproxen in free form or in pharmaceutical solutions [1,2]. Mehta in 2012 [3] was developed a simple sensitive and accurate spectrophotometric method for the determination of naproxen in pure form and in the form of doses, and the high absorption at 332nm in an alkaline medium at ±25 °C, the product is stable for 7 hours, where the standard deviation is 0.1002 at 0.2%. While Kulsum et al. [4] developed two spectroscopic methods for the determination of naproxen in pure and pharmaceutical form using phenol red or green bromocresol, and the high absorption at 422 and 417 nm, respectively. then the limits of Beer's law at 80 - 60 and 160 -120 µg /mL, Sandel's significance is 0.0433 and 0.0953 µg.cm-2, and the relative standard deviation was 0.7523, 1.06. In similar, Sloka et al. [5] were able to detect naproxen by two spectroscopic methods, the first depends on the instantaneous equation in estimating the drug which a high absorption intensity at 262nm. while the second gave the high absorption at 310 nm. Also in 2009, Dowu et al [6] developed a sensitive spectrophotometric method for the determination of naproxen using nitrogenization and conjugation process to give a color compound and the high absorption at 470nm, the limits of Beer's law at 7-1 µg/ml and the reaction ratio is 2:1. Vaikunta Rao and Tirumala Rao [7], were able to the mobile phase is a mixture of C18, if the stationary phase is UHPLC naproxen in tablet form with technology. Mondal et al. [8] estimated naproxen in tablets in an easy, sensitive and fast way, using RP-HPLC technique. In 2014 Yilmaz et al [9] detected naproxen in the blood plasma by GC-MS technique and the concentration is 0.1 - 5.0 µg/ml. Also the RP-VHPLC technique was used to determine of naproxen in tablets [10]. Abdul-Moety et al [11] used TLC technology to separate naproxen from urine using silica gel as the inactive phase. Methanol and chloroform were used at a ratio of (85:15 V/V) as the mobile phase. Patil et al. [12] estimated naproxen in a fast, sensitive and simple way using HPLC technology, the mobile phase consists of ethyl acetate and acetic acid in a ratio of (0.2: 4.8), and the stationary. We wanted to extend these works by developing a simple, rapid, accurate, precise, sensitive and less time-consuming spectrophotometric method for the quantitative determination of naproxen in pure and pharmaceutical form, that can be used in laboratories where modern and expensive apparatus such as GLC and HPLC are not available.

2. Experimental

2.1 Instrumentation Used

Measurements were taken with a UV-Vis spectrophotometer.: SHIMADZU, Double beam

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model UV-1800 made in Japan, The range of wavelength (190-1100) nm, quartz cell with 1cm. path Electric Balance: Sartorius (0.0000), & PH meter: 3310, JENWAY

2.2 Materials and Solution of the Used

Everything from the substrate to the reagents employed in this study was of the highest quality. In order to dissolve and mix the solutions, distilled water was employed.

Naproxen standard solution (1000 µg.ml-1)

This solution was made by dissolving 0.1000 g of Naproxen powder in ethanol and bringing the volume up to the mark in a 100 ml volumetric flask [13]. The concentration of 100 g/ml was achieved by adding 10 ml of the standard solution (1000 g/ml) to the same solvent and bringing the volume up to the mark.

The 1.49103 M solution of blue bromophenol was made by dissolving 0.100 gram in a small volume of distilled water and then bringing the volume up to 100 ml.

Preparing a 0.1 M sodium hydroxide solution required dissolving 0.400 grams in a small volume of distilled water and then bringing the volume up to 100 ml with more distilled water.**[14]**

Infusion of drug preparation solution (500 mg Tablets – DELORBIS)

First, ten tablets are weighed (500 mg/Tablet), crushed until the grains are fine, and then a specific weight of the powder is taken, which is equivalent to 0.1g of Naproxen. Next, the powder is dissolved in and filtered to separate the insoluble components, if any, and then transferred to a volumetric flask with a capacity of 100 ml, and the volume is completed to the mark with distilled water. Finally, 10 ml of this solution is taken

3. Results and Discussion

3.1. Preliminary study:

A color product was formed after addition (1 mL) of (1.49 × 10-3 M) of bromophenol blue solution to (1.5mL) of naproxen solution (100 µg/mL), and then add (1mL) of sodium hydroxide solution (0.1M) and complete the volume to 25mL of distal water. The absorption spectrum of the solution was measured after 10 min [15], and was gave a high value at 596nm result is showed the figure 1.

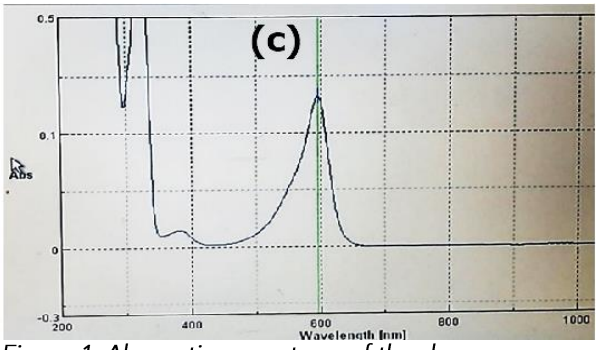

Figure 1: Absorption spectrum of the drug naproxen–bromophenol blue dye

3- Effect of order of addition

For choose the best sequence for adding the reactants, the chosen sequences are listed table 3. It was found through the recorded results that arrangement 3 is the best to form a color product, and accordingly it was chosen in the subsequent experiments.

Examining Optimal Reaction Conditions 3.2

To achieve maximum sensitivity and absorbance, the optimum circumstances for doing so were investigated and chosen. Follow-up tests were conducted with (1.5mL) of naproxen solution (100 g / mL), with the volume brought up to 25 mL, and the absorbance of solutions was measured at 596 nm relative to a blank solution using:

First, the impact of colorant concentration

In order to quantify the effect of the dye, different volumes of solution (3-0.2 ml) of blue bromophenol (1.49 103 M) were added to 1.5 mL of naproxen solution (100 g/mL), followed by 1 mL of sodium hydroxide solution (0.1 M) in a final volume of 25 ml, and the absorption at wavelength 596 nm was measured [16]. The results are shown in figure 1.

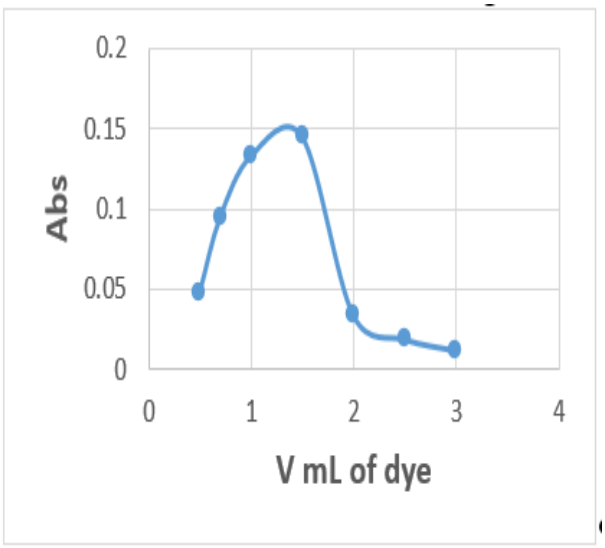

Figure 2. The effect of quantity of blue bromophenol solution.

According to the results shown in the table above, the optimal volume of the reagent solution is 1.5 mL.

Picking a solid foundation

The effect of various 1 ml solutions of bases with a concentration of around 1 x 10-1 M on absorption intensity was investigated. The tabulated outcomes are displayed below (1).

Table (1): Choosing of best base	
Base Solution 1×10^{-1} M	Abs at 569 nm
KOH	0.11
NaOH	0.145
Na_2CO_3	0.110

3- Quantity-at-Base Effect

Also, the impact of base concentration was investigated by adding varying quantities of 0.1 M sodium hydroxide solution (3-0.3 ml) to 25 ml

volumetric flasks containing 1.5 ml of bromophenol solution (1.49103 M) and 1.5 ml of solution naproxen focused (100 g/mL). The findings of the absorbance measurement at 596 nm may be shown in table 2. The high absorption value [17] may be explained by the amount of added base, which is 2 ml.

Table 2: Effect of the amount of the added base solution								
V ml of NaOH	0.3ml	0.5 ml	0.8ml	1.0ml	1.5ml	2.0ml	2.5ml	3.0ml
Abs at 569 nm	0.025	0.0423	0.0736	0.135	0.123	0.155	0.061	0.0527

Table 3: Effect of the addition sequence on the absorbance of the resulting solution		
Abs at 596 nm	Order of addition	Order No
0.0824	R+B+D	1
0.155	D+R+B	2
0.169	D+B+R	3
0.132	B+D+R	4
R: dye; D The property to be valued, B The rule used.		

4- Effect Temperature on the product formed

For the chosen reaction conditions, the impact of temperature (20-50oC) on absorbance of the solution was investigated. We found that 30 degrees Celsius was best, and those numbers are shown in table 4.

Table 4: Effect of temperature on the absorbance of the resulting solution							
50	45	40	35	30	25	20	Temp °C
0.095	0.112	0.139	0.156	0.171	0.161	0.151	Abs at 596 nm

3.4. Stability of the color product

The stability time of the color product was studied using 1.5 mL of naproxen solution (100 µg/mL) with add (2 mL) of 0.1M of sodium hydroxide solution and add (1.5 mL) of bromophenol solution and complete the volume to 25 mL. The solution absorption was measured at 596 nm vs. blank solution. We noted that the absorption value of the color product is stable for a period of time 50 minutes, which is an appropriate time to complete many measurements and the results are recorded in the table 5.

Table 5: The stability of the output formed							
60	50	40	30	20	10	0	Time/min
0.168	0.169	0.172	0.173	0.174	0.174	0.0858	Abs

3.5. Approved working method and calibration curve:

By combining (0.5 - 4 mL of 100 g/mL) with a 1.5 mL bromophenol solution (1.49 103 M), followed by (2 mL) of sodium hydroxide (0.1 M), and bringing the total volume to 25 mL, a series of increasing concentrations of naproxen solution (2-20 g/mL) were prepared under optimal conditions for previous experiments. After 10 minutes, the absorbance of these solutions was measured at 596 nm; the resulting calibration curve is shown in Figure 3; it conforms to Beer-law Lambert's over a concentration range of 2–16 g/mL, and its molar absorbance value is 7.5985103 L/mol.cm, while its Sandel sign value is 0.0303 g/cm2 [18].

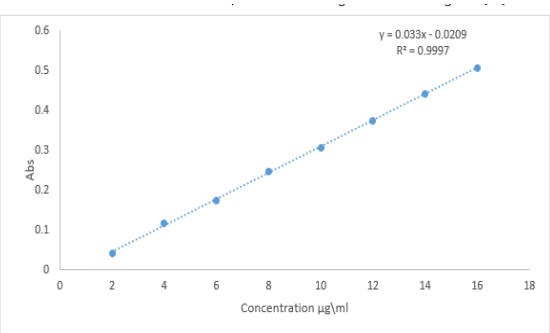

Figure 3: Calibration curve for naproxen

3.6. Accuracy and precision

The optimal circumstances for using this technique to verify the precision and accuracy of the calibration curve. Six Values for three Naproxen Concentration Solutions Calibration was performed within the range established by Ber's law-Lambert (See table 6). By calculating the recovery rate and relative standard deviation (RSD%), we found that this technique offers a very precise and agreeable result. The average, regression, and relative standard deviation were calculated mathematically as follows:

Table 6: Accuracy and precision			
RSD%	Recovery%	Found Nb µg/ml	Taken Nb µg/ml
0.4438	99.166	5.95	6
0.3867	101.10	10.11	10
0.3354	99.41	11.93	12

3.7. The detection limit (LOD) and quantitative limit

The detection limit (LOD) was measured as the lowest concentration calculated from the calibration curve, succession six times at similar conditions, and the results are listed in table 7.

Table 7: Detection Limit				
LOQ µg.ml-1	D.Lµg.ml-1	S	X	Conc. of Naproxen
0.3608	0.108	0.03849	2.1333	2

3.8. Set the equivalence of the output

To investigate the product-formed nature and the property's correlation percentage with dye, Job method [2] used a similar concentration of naproxen solution and dye (1×10-4 M). Different volumes of the naproxen solution was used within (0.1-0.9mL) and added the volume by dye solution in (25 ml) volumetric with added 2 ml of the base and completed with distilled water. The absorbance of these solutions was measured at 596 nm vs. blank solution and figure 4 shows that the molar ratio is 1:1 between naproxen and dye.

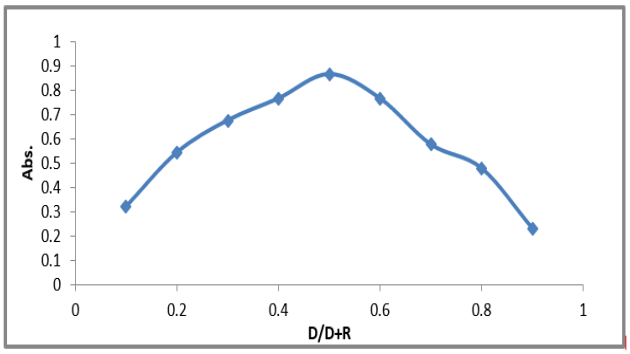

Figure 4: Continuous variations method

3.9. Application of the proposed method:

This method can be successfully applied to the naproxen pharmaceutical form (500 mg pills Cypriot). Three different concentrations of naproxen solution (10, 12, 16 µg/ml) were taken and these solutions were treated in similar steps used in preparing the calibration curve, and the absorption was measured at 596 nm against the blank solution and the return was calculated as well as the relative standard deviation and the results are listed in table 8.

Table 8: Application of the proposed method for drug estimation to pharmaceutical preparations				
RSD%	Recovery%	Found Nap µg/ml	Taken Nap µg/ml	Preparative Drug
0.374	100.40	10.04	10	Delorbis
0.2602	102.58	12.31	12	
0.1357	99.85	13.98	14	

3.10. Comparing the method with other methods

The analytical parameters for this current method for detecting naproxen were compared with other spectroscopic detecting methods and the results of that comparison are listed in table 9.

Table 9: Comparing the method with other methods			
Literature Method (38)	Literature Method (39)	Present method	Analytical Parameters
480	432	596	λmax (nm)
Water	Methanol	Water	Solvent
1-Naphthylarnine	BPB	BPB	Reagent
-	3.0	10	pH
10-65	1-10	2-16	Beers Law rang(ug/ml)
0.0128	0.47619	0.03033	Sandell's sensitivity
0.996	0.997	0.9997	Correlation coefficient (r2)
0.0452	0.006	0.033	Slope
0.033	0.348	0209.0	Intercept
17986.9	9.75×103	7.59858×103	(L.mol-1.cm-1)£
-	0.292	0.3608	LOD [µg/ml]

Based on these findings, it is clear that the present approach has several benefits over the other methods stated in table 9, including low cost, no need for an extraction procedure, enough time to do many tests, a large linearity range, high precision, and compatibility.

4. Conclusions

This study proved that pure Naproxen and its dose formulation can be identified using visible spectroscopy and ion complexation reaction. Naproxen The suggested procedures were statistically analyzed and were found to be easy to implement, accurate, exact, economical, and time efficient; moreover, the findings obtained are accurate, precise, sensitive, and free from the interferences of other additives present in formulations.

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