Two Novel Spectrophotometric Methods for Determination of Naproxen via a Modulation to Hydroxy Analog

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Abstract

Potassium permanganate was used for oxidation of the synthesized hydroxy analog of Naproxen by two methods. In the first method, the oxidation occurred in acidic medium, the excess of permanganate was followed at 545 nm. Beer's law is obeyed between concentrations of 10 µg/10ml-80 µg/10ml (1-8 ppm) with good sensitivity (molar absorptivity of $9.7x10^3$ l.mol^{-1}.cm^{-1}), good precision (RSD better than ±3.2 %) and high accuracy (relative error better than 1.6%). Sandell's sensitivity index is 0.0237 µg.cm^{-2}. The detection limit (LOD) is 0.075 µg·ml^{-1} and the quantitation limit (LOQ) is 0.25 µg·ml^{-1}. For the second method, potassium permanganate was used to oxidize the hydroxy analog of Naproxen in basic medium, and the manganate produced was followed at 610 nm. The linearity range was from 20 to 70 µg/10 ml (2-7 ppm) with good sensitivity (molar absorptivity of 6.8 x 10^3 l.mol^{-1}.cm^{-1}), good precision (RSD better than ±2.5%) and high accuracy (relative error better than 1.51%). Sandell's sensitivity index is 0.0338 µg.cm^{-2} while the detection limit (LOD) is 0.0098 µg·ml^{-1} and quantitation limit (LOQ) is 0.03296 µg·ml^{-1}. The two methods were applied successfully for the determination of Naproxen after extraction of the active ingredient by ethyl acetate.

Keywords: Naproxen, modulation, oxidation, potassium permanganate
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1. Introduction

Naproxen has an antipyretic and analgesic activity that targets the nucleoprotein to inhabit RNA - Naproxen association required for Naproxen function resulting in a novel antiviral against influenza type A virus [1-3]. Naproxen is a propionic acid derivative with the following chemical structure (Figure1).

Mahmood and Al-Sarraj [5] reported that Naproxen could be determined after a modification to the hydroxyl analog before coupled to the diazotized p-aminobenzoic acid in alkaline medium for forming an orange azo dye to be measured at 500 nm. Beer's law was then followed over the range from 0.5 to 32.5 µg·ml^{-1}. This method was found to be sensitive, accurate, precise and it was applied for the assay of Naproxen in tablets.

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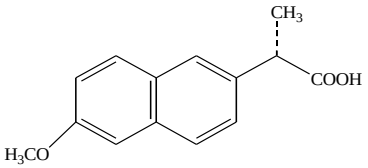

Figure 1. Chemical structure of Naproxen [4]

Naproxen sodium in combined dosage form with Sumatriptan was determined using two UV spectrophotometric methods at 272 and 284 nm as an absorptive point in the first method and at 298 nm and 335 nm as a zero-crossing point in the second method. These two methods have been applied in quality control of dosage forms [6].

A simultaneous determination of Naproxen and Esomeprazole mixture in a laboratory was reported. The method involves area under the curve in the ranges of 227-237 nm and 296.5-306.5 nm, the formation of the simultaneous equation at 232 nm and 301.5 nm, absorption correction at 232 nm λmax of Naproxen, 239.2 nm iso-absorptive point of Naproxen and Esomeprazole, 301.5 nm for absorption ratio method. The linearity for Naproxen and Esomeprazoleis 1-5 $\mu g \cdot ml^{-1}$ and 4-12 $\mu g \cdot ml^{-1}$, respectively. The method is accurate and precise for the simultaneous estimation of Naproxen and Esomeprazole in bulk formulations [7].

A simultaneous estimation of Naproxen and Pantoprazole in combined capsule dosage form has been developed. One method employs solving of simultaneous equations using 262 nm and 289 nm. The other method is Q- value analysis based on measurement of absorptivity at 262 nm and at iso-absorptive point 310 nm which shows linearity in the concentration range of 10.0-50.0 $\mu g \cdot ml^{-1}$ for Naproxen and 8.0- 18.0 $\mu g \cdot ml^{-1}$ for Pantoprazole [8].

A validated univariate and multivariate regression was developed for the simultaneous determination of a quaternary mixture of Imatinib, Gemifloxacin, Nalbuphineand Naproxen. The univariate method depends on measuring every drug in the quaternary mixture by using a ternary mixture of the other three drugs as a divisor. Peak amplitudes were measured at 294 nm, 250 nm, 283 nm and 239 nm within linear concentration ranges of 4.0-17.0, 3.0-15.0, 4.0-80.0 and 1.0-6.0 $\mu g \cdot ml^{-1}$ for Imatinib, Gemifloxacin, Nalbuphine and Naproxen, respectively. Multivariate methods adopted are partial least squares (PLS) in original and derivative mode [9].

Two spectrophotometric methods for determination of Naproxen was developed by the formation of ion-pair complex with bromocresol green at 424nm in one method and bromothymol blue at 422 nm in another method [10]. A bromophenol blue was used in the same procedure for determination of Naproxen in human serum samples with good accuracy and reproducibility [11]. There were some chromatographic methods for the estimation of Naproxen based on high-performance liquid chromatography by usage of C_{18} column were reported [12-14].

Potassium permanganate was used for determination of Famotidine in both pure form and in its dosage forms via oxidation of the drug in acid and alkaline media. Beer's law was obeyed over 0.75-7.5 and 2.5-20 ml in alkaline and acid media with a molar absorptivity value of $2.79x10^4$ and $1.62x10^4$ l $mol^{-1} \cdot cm^{-1}$, respectively [15]. Potassium permanganate was used to determine the usage of Raloxifene hydrochloride in dosage form by the formation of yellowish-brown product measured at 430 nm in acetic acid, while the other method is based on measuring the excess permanganate at 550 nm using H_2SO_4 to acidify the media [16].

In the present study, Naproxen was determined in commercially available tablet after a modulation reaction to the hydroxyl analog followed by oxidation using potassium permanganate as an oxidizing agent in an acidic medium. The excess of permanganate was followed at 545 nm as a decrease with the increase in the modulate Naproxen and in basic medium, whereas the manganate produced was followed at 610 nm as an increase with the increase in the modulate Naproxen.

2. Materials and Methods

All spectral and absorbance measurements were performed on a double-beam Jasco V-630 spectrophotometer with 1.0 cm matched quartz cells. The measurements of pH were performed using HANNA 301 pH meter, whereas BEL balance was used for weight measurements, reflux was utilized by electrothermal heater and stirring was utilized by Wisd stirrer. Chemicals used were of analytical grade.

Modification reaction of Naproxen: 0.04mol of pure Naproxen (9.2 g) was mixed with 25 ml hydrobromic acid (48%) and 25 ml acetic acid, the mixture was refluxed for 1.5 h and then was cooled, diluted with 25 ml distilled water, filtrated, dried and finally recrystallized using ethanol to produce a pink solid crystal with melting point at 190-191°C [17].

Modified Naproxen(100 µg/ml): this solution was prepared by dissolving 0.0100 g of mNaproxen in minimum amount of ethanol (2 ml), then the volume was diluted to 100 ml with distilled water in a volumetric flask. The solution was kept into a dark bottle and used for at least one month.

Pharmaceutical preparation (Naproxentablet):10 tablets of Naproxen (SDI) was ground into fine particles and a weight equivalent to one tablet was dissolved in 3 ml ethyl acetate and 1 ml HCl (3M). When two layers were separated, the organic layer was transferred to another tube and extraction was repeated 3 times, 1 ml of saturated solution of NaCl was added to organic layer and a sufficient amount of sodium sulphate was added after separation. The layer was left on-air for drying [18]; then the pure dried extract of Naproxen was modified to the hydroxyl analog as mentioned in the above step which produce pink solid crystal with melting point of 190-191°C [17] (extraction is necessary because tablets was burning during the modification reaction).

3. Results and Discussion

3.1 Modification reaction of Naproxen

The step of modification reaction of Naproxen involves a conversion of Naproxen into a hydroxy analog (mNaproxen) using hydrobromic acid in the presence of acetic acid at certain amounts as shown in Figure 2.

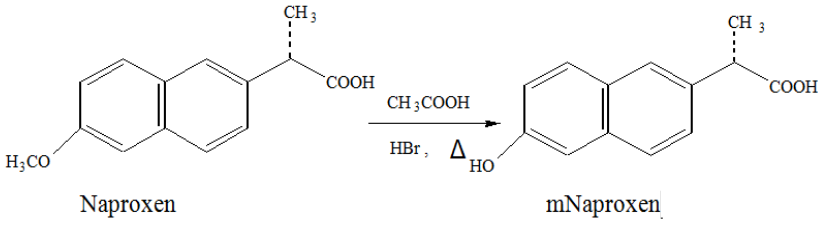

Figure 2. Modification reaction of Naproxen [17]

3.2 Procedure and calibration graph (basic medium)

Between 0.1-0.8ml of 100 µg.ml^{-1}standard of mNaproxen solution, reagents have been added in the following order: 1 ml of potassium permanganate (0.02 N), and 2 ml of H_2SO_4 (5M) has been

finally added, the volumes were completed to 10 ml, and the absorbance has been followed at 545 nm (blank against sample).

The calibration graph is linear for the concentrations from 10 to 80 µg of mNaproxen in 10 ml (1-8 ppm) with a molar absorptivity of 9.7 x 10^3 l·mol^{-1}·cm^{-1} with sensitivity index (Sandell's) equal to 0.0237 µg.cm^{-2} (Figure 3).

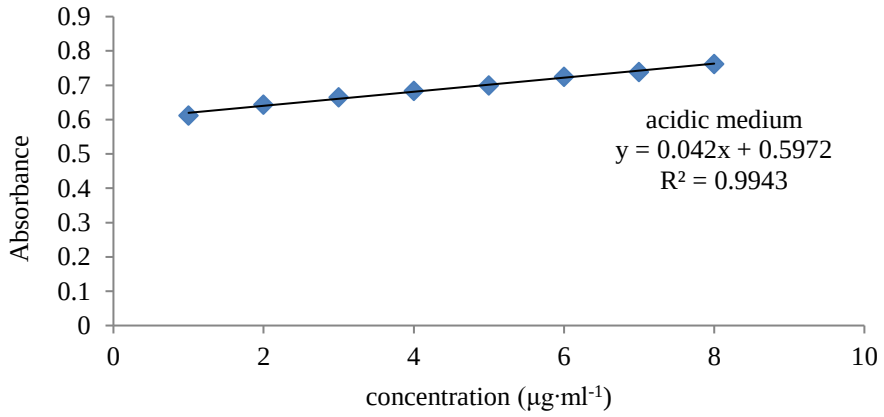

Figure 3. Calibration graph of Naproxenin acidic medium (blank against sample)

3.3 Procedure and calibration graph (basic medium)

To increase volume (0.2-0.7 ml) of 100 µg·ml^{-1} standard of mNaproxen solution, reagents have been added as follows: 3.5 ml of 0.02N potassium permanganate, and 2.5 ml of 0.1M NaOH have been added, and the volumes were completed to 10 ml in volumetric flasks. The absorbance has been measured at 610 nm against blank. The linearity range of the calibration graph is between 20 to 70 µg of mNaproxen in 10 ml (2-7 ppm) with a molar absorptivity of 6.8 x 10^3 l.mol^{-1}.cm^{-1} and the observed Sandell's index is equal to 0.0338 µg.cm^{-2} (Figure 4).

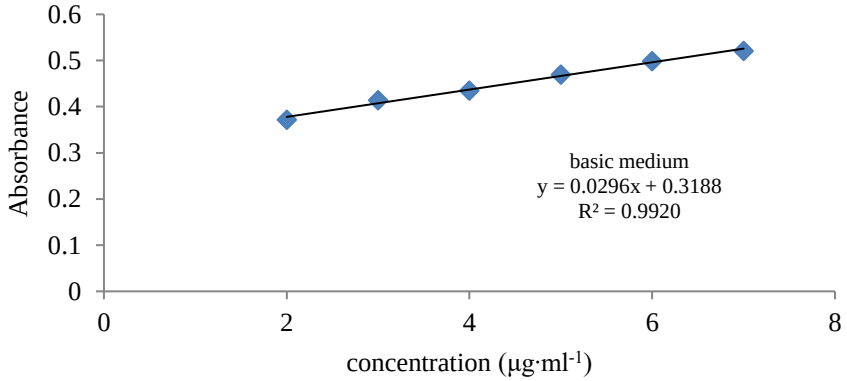

Figure 4. Calibration graph of Naproxenin basic medium (sample against blank)

3.4 Study of conditions (acidic medium)

The chemical reaction can be expressed as follows.
General reaction of MnO_4^- in acidic medium: $MnO_4^- + 8H^+ + 5e^- = Mn^{2+} + 4H_2O$
The oxidation reaction of mNaproxen (Figure 5):

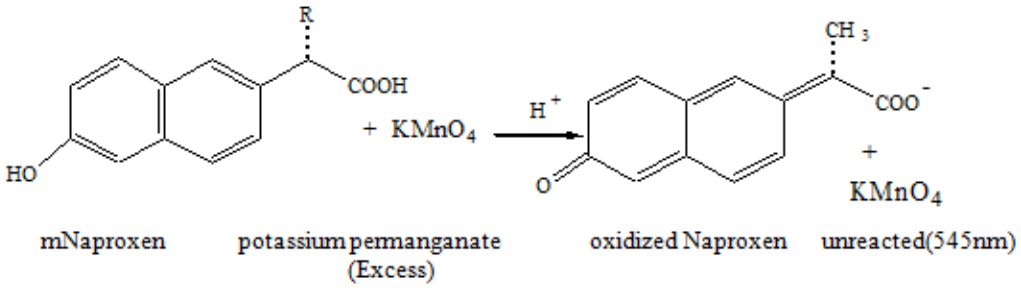

Figure 5. The oxidation reaction of mNaproxen in acidic medium

3.4.1 Effect of $KMnO_4$

The effect of (0.5-1.5) ml of potassium permanganate (0.02 N) has been followed against 20-80 µg of mNaproxen/10 ml and 1 ml H_2SO_4 (5M). The determination coefficient has been evaluated. Table 1 shows that 1 ml of $KMnO_4$ solution gives the best sensitivity.

Table 1. Effect of $KMnO_4$ amount on the sensitivity

Volume (ml) of 0.02N $KMnO_4$	Absorbance/µg of mNaproxen				R^2
	20	40	60	80	
0.5	0.207	0.212	0.220	0.229	0.9849
1.0	0.445	0.478	0.503	0.537	0.9968
1.5	0.569	0.618	0.646	0.689	0.9903

3.4.2 Selection of acid and its amount

Potassium permanganate act as a stronger oxidizing agent in acidic medium, therefore effect of different amount of three acids on the absorption intensity of the coloryield has been studied (Table 2).The results showed that the intensity of the maximum absorptions of the colored product was resulted from adding 2 ml of H_2SO_4, therefore, it is kept for further use.

Table 2. Selection of acid and its amount for acidifying the medium

Acid used (5M)	Absorbance/ml of acid				
	0.5	**1.0**	**1.5**	**2.0**	**2.5**
H_2SO_4	0.462	0.478	0.602	0.673	0.664
H_3PO_4	0.033	0.037	0.040	0.039	0.033
CH_3COOH	0.030	0.031	0.037	0.038	0.037

3.4.3 Study of order of addition

A study of the influence of the orders D+OX+A and D+A+OX (Drug- D, Oxidant- OX, Acid- A) shows no significant difference between them. The order D+OX+A was used in the previous and subsequent steps.

3.4.4 Effect of surfactant

In some reactions the presence of surfactants increases the absorption intensities of the color complex, this may be due to the correlation between chemical structures and surface properties [19], while there is no detailed discussion of surfactant behavior because of the wide range of possible environments for surfactant molecules [20].

In the present work, 1ml of (1×10^{-3}M) of cationic [(cetylpyridinium chloride, CPC), (cetyltrimethylammonium bromide, CTAB)] and 1 ml of anionic [sodium dodecyl sulphate, (SDS)] surfactants were added to the reaction mixture in different order. Table 3 indicates that there are no enhancements in the absorption intensity.

Table 3. Effect of surfactants on the absorption intensity

Surfactant solution (1×10^{-3}M)	**Absorbance/order of addition***		
	I	**II**	**III**
SDS	0.620	0.619	0.606
CTAB	Turbid	Turbid	Turbid
CPC	Turbid	Turbid	Turbid

Note: Absorbance without surfactant = 0.681
* I. Drug (D) + surfactant (S) + $KMnO_4$ (OX) + H_2SO_4 (A),
II. D+OX+S+A,III. D+OX+A+S

3.4.5 Effect of time of oxidation

An oxidation time of the reaction solution has been allowed for 12 min before dilution. It was found that 3 min was sufficiently enough for oxidation, therefore it is followed in subsequent steps.

3.4.6 Stability of reaction

A stability time (60 min) of the colored product after preparation of the sample completely (after dilution) has been followed. The reaction solution was still stable with an absorbance of 0.67.

3.4.7 Absorption Spectrum

The absorption spectrum of the colored product against blank is shown in Figure 6. The maximum absorption intensity is exhibitedat 545 nm. This wavelength has been used in subsequent investigations.

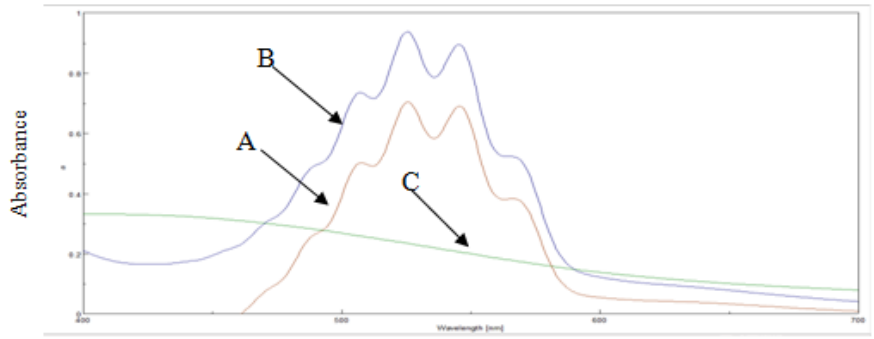

Figure 6. Measurement of absorption spectrum of 100 µg/10 ml of m Naproxen
A = blank against sample, B = blank against distilled water and C = sample against distilled water

3.4.8 Limit of detection and limit of quantification (LOD and LOQ)

In order to calculate the limit of detection (LOD) and limit of quantification (LOQ), 10 solutions of thelowest concentration (within the calibration) of Naproxen have been prepared according to the optimum reaction conditions and measured at 545 nm. The results in Table 4 show that the lowest content of mNaproxen that can be distinguished from background noise and measured with reasonable statistical certainty (LOD) is 0.075 $\mu g \cdot ml^{-1}$ and the lowest concentration on the calibration curve that can be measured with an acceptable level of accuracy and precision (LOQ) is 0.25 $\mu g \cdot ml^{-1}$.

3.4.9 Accuracy and precision of the calibration graph

Three different concentrations of mNaproxen is prepared for determination. The results are listed in Table 5, which indicates good accuracy and precision.

3.4.10 Application of the method for the determination of Naproxen in tablets

To test the applicability of the present method, it has been applied for determiningNaproxen after extraction from pharmaceutical preparations. The results in Table 6 exhibit good applicability of the method.

Table 4. Calculation of LOD and LOQ of the method

The absorbance of C_{low} (Xi)	$X_i - \bar{X}$	$(X_i - \bar{X})^2$
0.598	$-1.3x10^{-3}$	$16.9x10^{-7}$
0.600	$7x10^{-4}$	$4.9x10^{-7}$
0.599	$-3x10^{-4}$	$0.9x10^{-7}$
0.601	$1.7x10^{-3}$	$28.9x10^{-7}$
0.599	$-3x10^{-3}$	$0.9x10^{-7}$
0.599	$-3x10^{-4}$	$0.9x10^{-7}$
0.599	$-3x10^{-4}$	$0.9x10^{-7}$
0.598	$-1.3x10^{-3}$	$16.9x10^{-7}$
0.599	$-3x10^{-4}$	$0.9x10^{-7}$
0.601	$1.7x10^{-3}$	$28.9x10^{-7}$
$\bar{X} = 0.5993$		$\sum(X_i - \bar{X})^2 = 1.01x10^{-5*}$

Note: $^{*}\sigma = \sqrt{\frac{10.1\times10^{-6}}{10-1}} = 1.05 \times 10^{-3}$

Limit of Detection LOD = 3 σC(lowconcentration) / Slope =$(3\times 1.05 \times 10^{-3} \times 1)/0.042 = 0.075$ µg.ml^{-1}

Limit of QuantificationLOQ = 10 σC(low concentration)/slope = $(10\times 1.05 \times 10^{-3} \times 1)/0.042 = 0.25$ µg.ml^{-1}

Table 5. Accuracy and precisionof calibration graph

Amount of mNaproxen (µg/10 ml)	Amount mNaproxen found (µg/10 ml)	Relative error %*	Relative standard deviation %*
20	19.58	-2.1	± 3.2
40	40.52	+1.3	± 2.7
60	60.96	+1.6	± 1.9

*Average of five determinations

Table 6. Application of the method for the determination of Naproxen in Tablets

Amount of mNaproxen (µg /10 ml)	Recovery(%) of Naproxen*		
	Naproxen (tablet 500 mg) - Inaprolfort,Bilim, Turkey	Naproxen (tablet 250 mg)-S.D.I,Iraq	Naprox(tablet 500mg) - Medical Bahri Company, Damascus, Syria
20	98.6	97.5	98.2
40	99.3	97.9	99.4
60	98.8	97.4	98.6

*Average of three determinations

3.4.11 Comparison of the method with standard method and t-testcalculation

Both the present method and British Pharmacopeia method [21] have been applied at the same time for t-test calculation [22] and the value compared with statistical tables for four degrees of freedom at a 95% validation level. The result in Table 7 indicates no real difference between the two methods.

Table 7. Comparison of the method and T-test calculation

Drug	Recovery * (%)		t-exp
	Present method	British Pharmacopeia method**	
Naproxen (tablet 500 mg)-INaproxenrolfort, Bilim, Turkey	98.9	99.9	-2.14
Naprox (tablet 500mg) -Medical Bahri Company, Damascus, Syria	98.7	97.4	1.06

* Average of three determinations

**500 mg of Naproxen was dissolved in 70ml of absolute methanol and diluted after 30minto 100ml in a calibrated flask, further dilutions with absolute methanol were used to prepare 1000 ppm of Naproxen and measured at 331nm.

3.5 Study of conditions (basic medium)

The chemical reaction can be expressed as follows.
General reaction of MnO_4^- in basic medium: $4MnO_4^- + 4OH^- + e^- \rightarrow 4MnO_4^{2-} + 2H_2O + O_2$
The oxidation reaction of mNaproxen (Figure 7):

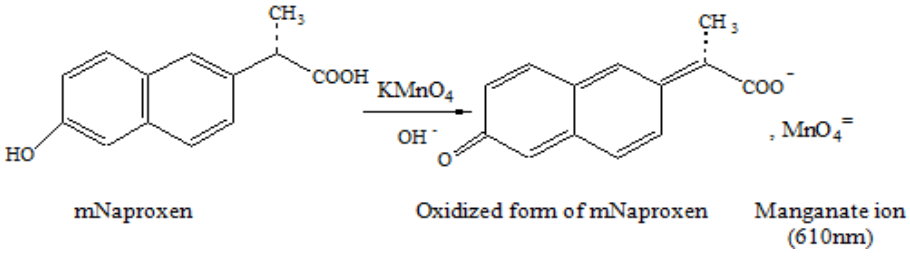

Figure 7. The oxidation reaction of mNaproxen in basic medium

3.5.1 Study ofthe effect of $KMnO_4$

The effect of 0.02N potassium permanganatehas been studied against 10-70 µg of mNaproxen/10 ml and the determination coefficient has been evaluated. Table 8 shows that 3.5 ml of $KMnO_4$ solution gives the best sensitivity.

Table 8. Effect of $KMnO_4$ amounton thesensitivity

Volume of 0.02N $KMnO_4$ (ml)	Absorbance/µg of mNaproxen				R^2
	10	30	50	70	
2.5	0.136	0.220	0.271	0.293	0.9341
3.0	0.139	0.232	0.308	0.368	0.9907
3.5	0.143	0.244	0.334	0.399	0.9910
4.0	0.091	0.176	0.252	0.306	0.9905

3.5.2 Selection of base and its amount

Different amounts of different bases on the absorption intensity of the resulted complex has been studied. The results in Table 9 show that 2.5 ml of NaOH gives the intensity of maximum absorptions of the colored product, therefore, it is used for the following steps.

Table 9. Selection of base and its amount to alkaline reaction medium

Base used (0.1M)	Absorbance/ ml of base					
	0.5	1.0	1.5	2.0	2.5	3.0
NaOH	0.168	0.269	0.334	0.379	0.413	0.370
KOH	0.088	0.131	0.161	0.162	0.174	0.176
Na_2CO_3	0.038	0.053	0.058	0.058	0.054	0.054
$NaHCO_3$	0.020	0.020	0.020	0.014	0.007	0.001

3.5.3 Order of addition

Different order of addition has been checked for predicting the best absorbance value.The order D+ OX+B gives the best results.

3.5.4 Effect of surfactant

One ml of cationic [cetylpyridinium chloride (CPC),cetyltrimethylammonium bromide (CTAB)] and anionic [sodium dodecyl sulphate (SDS)] surfactants with different order of additions has been followed (as shown in Table 10) in order to examine the effect on absorbance values.The results in Table 10 show that the presence of surfactant decreases the absorbance intensity of manganate or cause in turbidity; thiscan be explained by the decrease in oxidizing power of permanganate or formation of insoluble species respectively.

Table 10. Effect of surfactants on the absorbance intensity

Surfactant solution (1×10^{-3}M)	Absorbance/order* of addition		
	I	II	III
SDS	0.402	0.399	0.400
CTAB	Turbid	Turbid	Turbid
CPC	Turbid	Turbid	Turbid

*Absorbance without surfactant = 0.412,
I. =mNaproxen (D) + surfactant (S) + MnO_4 (OX) + NaOH(B), II. = D+OX+S+B, III. = D+ OX+B+S

3.5.5 Effect of time of oxidation

The reaction mixture needs 10 min as an oxidation time, which is sufficient enough for oxidation. These results have been concluded by allowing the reaction mixture before dilution to 15 min.

3.5.6 Absorption spectrum

The absorption spectrum of the colored product against blank is shown inFigure 8.The maximum absorption intensity is at 610 nm, andthis wavelength has been used in subsequent investigations.

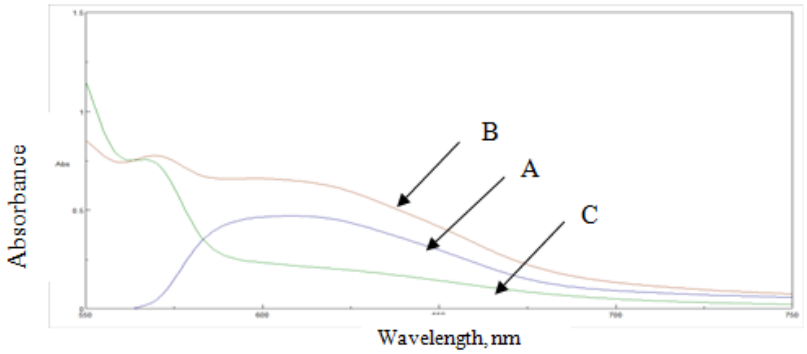

Figure 8. Measurement of absorption spectrum of 40 µg/10 ml of mNaproxen
A = Sample against blank, B = sample against distilled water and C = blank against distilled water

3.5.7 Limit of detection and limit of quantification (LOD and LOQ)

The blank solution exhibits a certain value of absorbance as shown in the absorptionspectrum, therefore to calculate the limit of detection (LOD) and limit of quantification (LOQ), 10 solutions of blank have been prepared according to the optimum reaction conditions and measured at 610 nm. The results in Table 11 show that the lowest content of analyte that can be distinguished from background noise and measured with reasonable statistical certainty (LOD) is 0.00988 $\mu g \cdot ml^{-1}$ and the lowest concentration on the calibration curve that can be measured with an acceptable level of accuracy and precision (LOQ) is 0.0329 $\mu g \cdot ml^{-1}$.

Table 11. Calculation of limit of detection and limit of quantification of the method

Absorbance of Blank (Xi)	$X_i - \bar{X}$	$(X_i - \bar{X})^2$
0.215	$5x10^{-4}$	$2.5x10^{-7}$
0.214	$-5x10^{-4}$	$2.5x10^{-7}$
0.214	$-5x10^{-4}$	$2.5x10^{-7}$
0.215	$5x10^{-4}$	$2.5x10^{-7}$
0.215	$5x10^{-4}$	$2.5x10^{-7}$
0.215	$5x10^{-4}$	$2.5x10^{-7}$
0.215	$5x10^{-4}$	$2.5x10^{-7}$
0.215	$5x10^{-4}$	$2.5x10^{-7}$
0.214	$-5x10^{-4}$	$2.5x10^{-7}$
0.213	$1.5x10^{-3}$-	$22.5x10^{-7}$
$\overline{X}$ =0.2145		$\sum(X_i - \bar{X})^2$=$4.5x10^{-6}$*

*$\sigma = \sqrt{\frac{4.5\times10^{-6}}{10\text{-}1}} = 7.07 \times 10^{-4}$

Limit of Detection (LOD) = 3 σ /0.2145 = 0.00988 µg·ml^{-1}

Limit of Quantification (LOQ) = 10 σ/ slope = 0.03296 µg·ml^{-1}

3.5.8 Accuracy and precision of the calibration graph of mNaproxen

To evaluate the accuracy and precision of the calibration graph, determining mNaproxen at three different concentrations was measured; the results are shown in Table 12, which exhibits good accuracy and precision.

3.5.9 Application of the method for the determination of Naproxen in tablets

The application of the method is shown in Table 13. The results show a good applicability range of the method.

3.5.10 Validation of the method

A comparison between the present method and British Pharmacopeia method [21] have been followed for determination of 500mg Naproxen tablet of two pharmaceutical company by application of the two methods at the same time followed by t-test calculation [22] and the value has been compared with statistical tables for four degrees of freedom at a 95% validation level. The results are shown in Table 14.

The result in Table 14 indicates no real difference between the suggested method and the method adopted in British pharmacopeia.

Table 12. Accuracy and precision of the calibration graph of mNaproxen

Amount mNaproxen taken (µg/10 ml)	Amount mNaproxen found (µg/10 ml)	Relative error %*	Relative standard deviation %*
20	20.30	+1.51	± 2.5
40	40.54	+1.37	± 1.45
60	60.59	+0.99	± 1.11

*Average of five determinations

Table 13. Application of the method for the determination of Naproxen in Tablets

AmountofmNaproxen (µg /10 ml)	Recovery(%) of Naproxen*		
	Naproxen (tablet 500 mg) - Inaprolfort,Bilim, Turkey	Naproxen (tablet 250 mg)- S.D.I,Iraq	Naprox (tablet 500mg) - Medical Bahri Company, Damascus, Syria
20	98.7	100.4	98.3
40	98.2	99.3	100
60	98.1	99.5	98.6

*Average of three determinations

Table 14. Comparison of the method and T-test calculation

Drug	Recovery * (%)		t-exp
	Present method	British Pharmacopeia method	
Naproxen (tablet 500 mg)- INaprolfort,Bilim, Turkey	98.3	99.9	-3.48
Naprox (tablet 500mg) - Medical Bahri Company, Damascus, Syria	98.9	97.4	1.25

* Average of three determinations

4. Conclusions

A modulate Naproxen has been oxidized by potassium permanganate in acidic medium (method 1), the excess of permanganate was followed at 545 nm as a decrease with the increase in the modulate Naproxen. Beer's law was obeyedbetween concentration valuesof 1-8 ppm. In a basic medium (method 2), the manganate produced was followed at 610 nm as an increase with the increase in the modulate Naproxen. The linearity range was between 2-7 ppm. The two methods areprecise, accurate, sensitive and applicable for pharmaceuticals. It does not need any organic reagent, does not need an extensive technique but it requires an extraction step.

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