Spectrophotometric Determination of Mefenamic Acid in Pharmaceutical Preparations

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Abstract

A simple, accurate and precise spectrophotometric method has been proposed for the determination of Mefenamic acid(MA) in dosage forms. Proposed method based on the reaction of cited drug with 1,2-Naphthoquinone-4-Sulfonic sodium (NQS). The optimum experimental condition have been studied. Beer's Law is obeyed in the concentration range 0.5-10.0 µg/mL at 450nm with detection limit of 0.189µg/mL. Effect of pH, reaction time, and volume of NQS on the determination of Mefenamic acid, have been examined. The proposed method has been successfully applied for the determination of Mefenamic acid in pharmaceutical preparations.

Key Words: Spectrophotometric , Mefenamic acid, 1,2-Nphatha quinona-4-Sulfonic sodium.

Introduction

Mefenamic acid (MA) is 2-[(2,3-dimethylphenyl) amino benzoic acid. MA an anthranilic acid derivative, is a member of the fenamate group of non-steroidal anti-inflammatory drugs (NSAIDs). It exhibits anti-inflammatory, analgesic, and antipyretic activities. It is used for the relief of mild to moderate pain. It is also indicated for the treatment of rheumatoid arthritis. Similar to other NSAIDs, MFA inhibits prostaglandin synthetase [1]. The drug is official in British Pharmacopoeia and the assay is based on non-aqueous titrimetric method [2]. Literature survey reveals that various analytical techniques were used for the determination of MA such as viz, UV spectrophotometry [3-6]. High performance liquid chromatography[7-10]. Therefore, the need for a fast, low cost and selective method is obvious, especially for the routine quality control analysis of pharmaceutical products containing Mefenamic acid. The proposed method was successfully applied to the determination of Mefenamic acid in bulk pharmaceutical, tablets, and capsules The results obtained by the proposed method were in excellent agreement with those given by the official method [2], proving that the method is a reliable alternative for the analysis of Mefenamic acid in pure form and in pharmaceutical preparations.

Experimental

Apparatus:

All spectrophotometric measurements were carried out using a cintra 5 GBC Scientific Equipment, Holland with 1cm matched quartz cells, sartorious BL 210S electronic balance, Gottingen- Germany and a pH meter model 3001 was used for all pH measurements.

Material and Reagent

All the chemicals used were of analytical grade and double distilled water was used for all dilution of reagent and sample.

***1,2-Naphthoquinone-4-Sulfonic Sodium (NQS).0.5%(w/v)solution:**

A stock solution was freshly prepared by dissolving 0.5gm of the reagent in 100ml of distilled water.

***Sodium hydroxide ~0.2M Solution:**

Prepared by dissolving 0.80gm of sodium hydroxide in 25ml of distilled water and diluting to 100ml in volumetric flask with distilled water.

***Potassium Chloride 0.2M Solution:**

A standard solution was prepared by dissolving 1.429gm in 20ml of distilled water and diluting to 100ml in volumetric flask with distilled water.

***Sodium hydroxide – Potassium Chloride (buffer solution) (pH~12.40):**

Prepared by mixing 60ml sodium hydroxide solution(2M) with 25ml potassium chloride solution (0.2M) and then the solution was diluted with distilled water to the mark in 100ml volumetric flask[11].

Standard Mefenamic Acid (MA) Solution (1000µg.ml^{-1}):

A standard drug (obtained from the state state drug industry company samara-Iraq (S.D.I)solution was prepared by dissolving 0.1gm of MA in 50ml of methanol and diluting to 100ml in volumetric flask with methanol. Working solutions were freshly prepared by subsequent dilutions.

***Procedure For Dosage Forms:**

The content of 10 tablets or capsules was grinded and mixed well. A certain amount of the fine powder was accurately weighted to give an equivalent to 250mg for tablet and 500mg for capsules and dissolved in 50ml of methanol, swirled, leaved to stand for 5mints and diluted to 100ml in a volumetric flask with methanol. The solution was filtered by using

whatman filler paper No.41. to avoid any suspended or un-dissolved material before use, and the first portion of the filtrate was regected . working solutions were freshly prepared by subsequent dilutions with distilled water, and analyzed by the recommended procedure.

Results and Discussion

***Determination of Wavelength Maximum(λmax)**

To determine the λmax , an aliquot of the standard solution(100µg,ml^{-1}) containing 100µg of MA was transferred to 10ml volumetric flask, then 1ml of buffer solution (pH~12.40) and 1ml of 0.5% (w/v) NQS solution were added. The contents were mixed well and diluted to 10 ml with distilled water, then the absorbance of the colored product was measured against reagent blank in the range of 300-600nm. The maximum absorption wavelength for MA was found to be 450nm (Fig 1).

Under the experimental conditions, each reagent blank showed a negligible absorbance at the corresponding λmax.

***Method Development:(Optimization of the Experimental Conditions):**

The optimum experimental conditions were established by varying one parameter and observing its effect on the absorbance of the coloured species

***Effect of Volume of NQS Reagent:**

The effect of reagent volume on the formation colored product was studied. Varying volumes of standard reagent (0.5%w/v) NQS solutions in the range (0.2-2ml) were added and measuring the absorbances of the solutions.(Fig 2). The investigation showed that 1ml of NQS solution gave maximum absorbance due to its full intensity and further volume additions of reagent would result in a gradual decrease in the absorbance of the colored product, this is may be due to formation of new species.

***Effect of Time on Reaction before Dilution:**

The effect of time on the colour intensity of the reaction was studied by measuring the absorbance at room temperature (25±1˚C). It was found that the reaction got maximum absorbance at 5.0min and the value start to decrease gradually when reaction time raised above 5min, this may be due to decomposition of the fomed complex. (fig 3)

***Effect of the type and Amount of Added Base:**

Different base solutions such as sodium hydroxide, potassium chloride and lithium hydroxide were used to find maximum absorbance intensity. Results for that using NaOH give higher sensitivity and better reproducibly,therefore then base NaOH is used for subsequent work. On the other hand ,the optimum concentration of sodium hydroxide leading to a maximum intensity of colour was found to by 1.5ml of ~0.2M in the final volume.(fig 4).

***Effect of Temperature:**

The colour intensity of the proposed method were studied at different temperatures. The result indicate that the absorbance values reaction maximum value at 30˚C and remained constant up to 40˚C (Fig 5).

***Effect of Order Addition of Reactants:**

To obtain optimum results, the order of addition of reagents should be followed as given in the procedure below, otherwise a loss in colour intensity was observed.

***Effect of Time on the Stability of the Formed Complex**:

The reaction is instantaneous and the absorbance of the complex remained constant up to 3

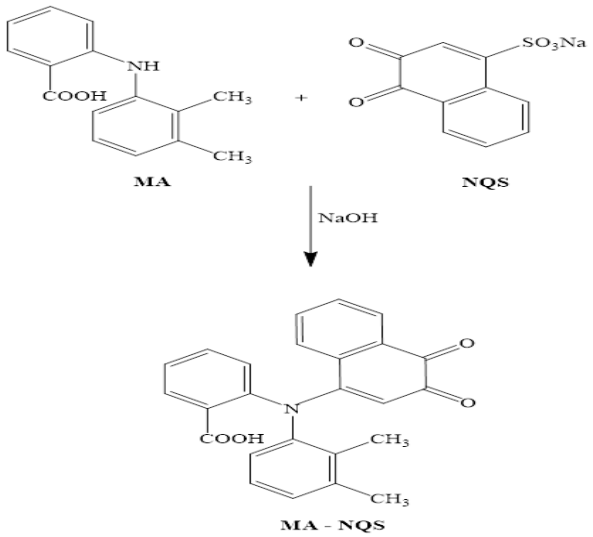
5min (Fig 6).

General Procedure and Calibration Graph:

In to a series of 10ml volumetric flasks, 1ml of 0.5%(w/v)NQS solution was added followed by the addition of increasing volume of MA ($100\mu g.ml^{-1}$)solution to cover the range of the calibration graph (0.5-10µg.ml). The resulted mixtures were shaken and 1.5ml of approximately 0.2M NaOH solution was added to each flask and the flasks were allowed to stand in dark for 5min in 30 C° in side water bath. After making up the volume of each flask to the make with distilled water. The absorbance of colored product was measured at 450nm.(Fig 7).

*Suggested reaction scheme[12,13]:

Mefenamic acid molecule contains only one center (secondary amino group) available for this condensation reaction, which replaces the sulfonic acid group of NQS. The most probable mechanism of nucleophilic substitution reaction of MA with NQS is shown in scheme1.



Scheme (1)

*Spectral Characteristics of the Proposed Method:

Under the experimental conditions described, Beer's Law, molar absorptivity and Sandell's sensitivities for MA are given in Table1. Data of the regression analysis using the least squares method made for the calibration curves are also given in the same table(1).

*Precision and Accuracy of the Proposed Method:

The precision of the proposed methods was determined by replicate analysis of five separate sample solutions at three concentration levels of MA. The relative standard deviations (RSD%) were 1.29-2.14% , on the other hand the accuracy of the proposed methods was evaluated by calculating the relative error percentage (R.E%) table(2).

The results indicated good accuracy of the method at each concentration level.

*Interference Studies:

The results of the interferences study showed that no interferences were found from any of the excipients studied Lactose, Magnesium stearate and Starch, Sucrose, Fructose and Glucose. The recovery of MA was ranged 99.80- 100.80%. Table(3) indicated the absence of interferences from these excipients.

***Application of the Proposed Method to Analysis of MA in pharmaceutical Formulation:**

To increase the insurance, the proposed spectrophotometric method was applied for the determination of MA in pharmaceutical preparation sample following the standard addition technique, (Fig 8-13) shows the standard addition plot and table(4) shows the result of accuracy in term of relative error percent, and reveals that the method was reasonably accurate.

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Table No.(1): Optical characteristics and statistical data for the determination of MA

Parameter	Under univariate conditions
λmax (nm)	450
Color	Brownish yellow
Linear range (µg.ml^{-1})	0.5 – 10.0
Regression equation	A =0.1409[MA µg.ml^{-1}] + 0.0009
Slope (L.mg^{-1}.cm^{-1})	0.1409
Intercept	0.0009
Molar bsorptivity (L.mol^{-1}.cm^{-1})	3.40×10^4
Corr. Coefficient	0.9995
Detection Limit (µg.ml^{-1})	0.187
Sandell's Sensitivity (µg.cm^{-2})	0.0071

Table No.(2): Precision and Accuracy of the Proposed method

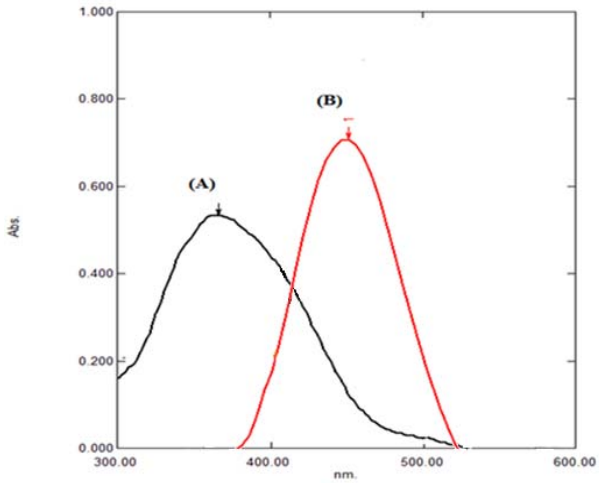
Taken Conc. µg.mL^{-1}	Found Conc. µg.mL^{-1}					Average	R.E %	R.S.D %
2	2.0332	2.0110	1.9571	1.9466	2.0383	1.9972	-0.13889	2.1459
5	5.0161	4.9771	5.1004	4.8730	4.9906	4.9915	-0.1709	1.6372
8	8.1939	7.9080	7.9941	8.0448	8.0352	8.0352	0.4400	1.2922

Table No.(3): Effect of the interference on the determination of the drug (MA) 10µg.mL^{-1} the Proposed method

Excipients	Mefenamic Acid Conc. Taken 10 µg.mL^{-1}	
	Conc. Fond µg.mL^{-1}	% Recovery
Lactose	9.993	99.93
Magnesium Stearate	9.98	99.8
Starch	10.06	100.6
Sucrose	9.99	99.9
Fructose	10.08	100.8
Glucose	9.987	99.87

Table No.(4):the result application of pharmaceutical

Sample	Amount of drug (mg)		Concentration ($\mu g.ml^{-1}$)		R. E.%
	Labeled	Found	Taken	Found	
Mefril 250 mg Bangalore-India	250	254.68	1.0	1.0238	2.3800
			5.0	5.0682	1.3640
Ponstidin 250mg SDI-Iraq	250	251.30	1.0	1.0165	1.6500
			5.0	4.9695	-0.6100
Mefex 500 mg Neopharma -UAE	500	507.12	1.0	1.0148	1.4800
			5.0	5.0683	1.3657



Figuer No.(1): Absorption spectra of : (A) Reagent blank agants + distilled water. (B) Reaction product (MA =6µg.ml^{-1}) aganst blank.

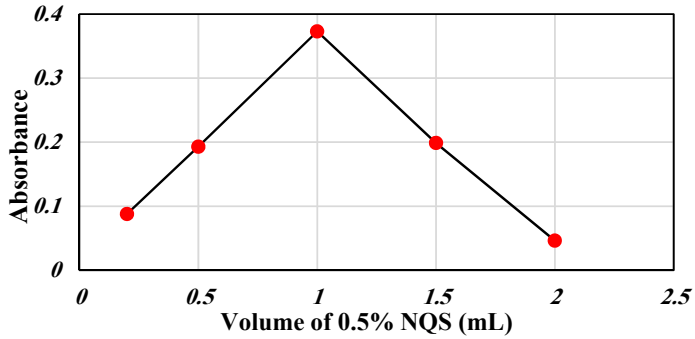


Figure No.(2): Effect of Volume reagent 0.5% NQS on the absorbance of the reaction product.

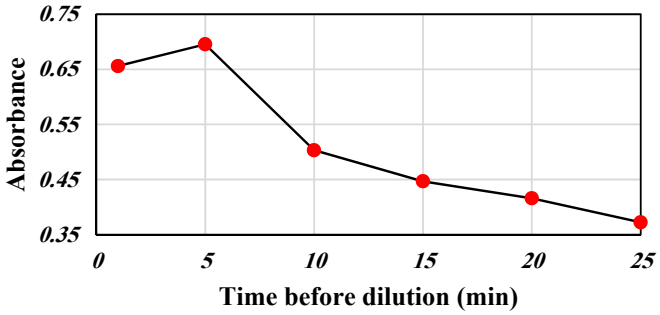


Figure No.(3): Effect time on the formation of the reaction product.

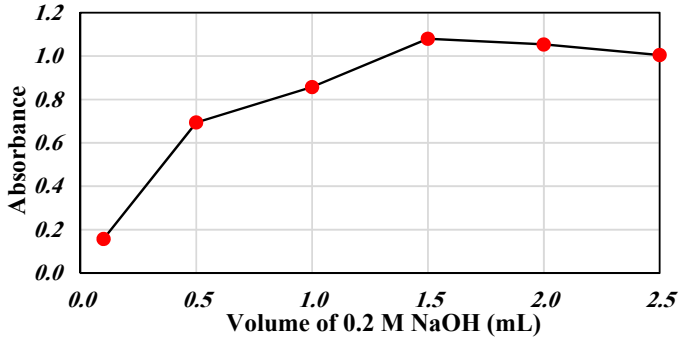


Figure No.(4): Effect of volume of sodium hydroxide on the absorbance of the reaction product.

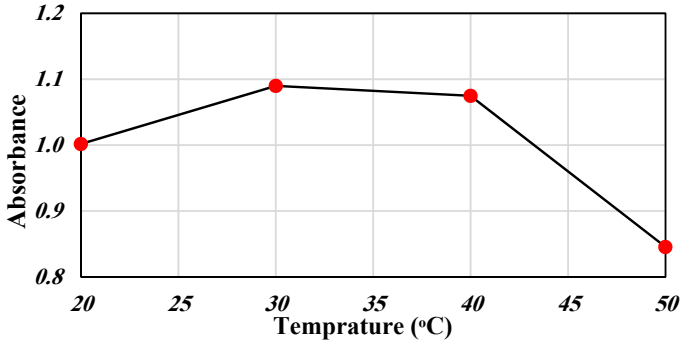


Figure No.(5) : Effect of temperature on the formation of the reaction product.

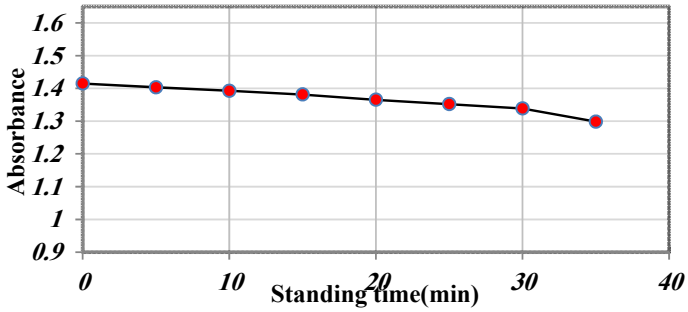


Figure No.(6): Effect of time on the stability of the formed complex.

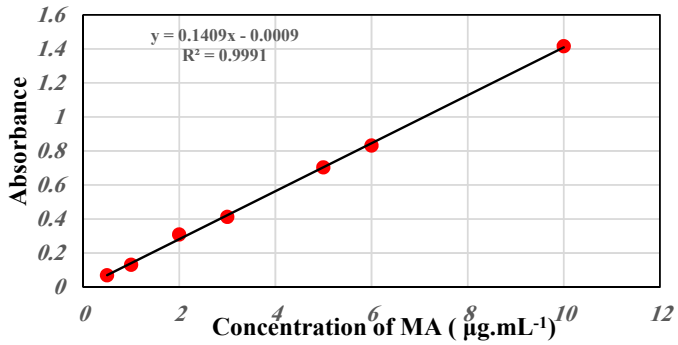


Figure No.(7): Calibration graph for determination of Mefenamic acid.

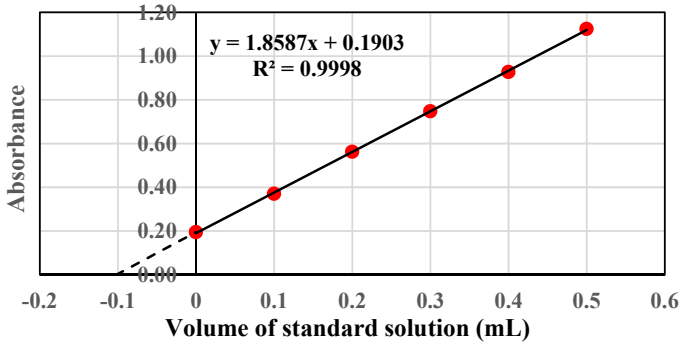


Figure No.(8) :Determination of MA in capsule Mefril –India

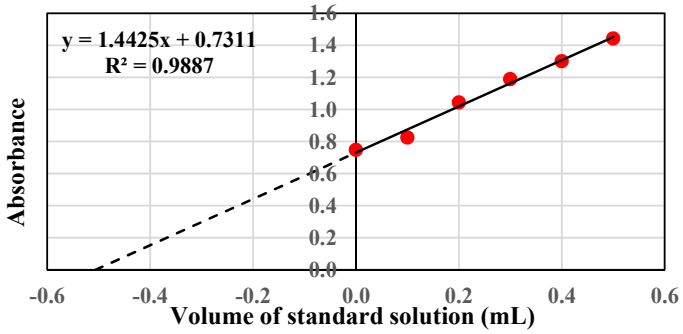


Figure No.(9) :Determination of MA in capsule Mefril -India

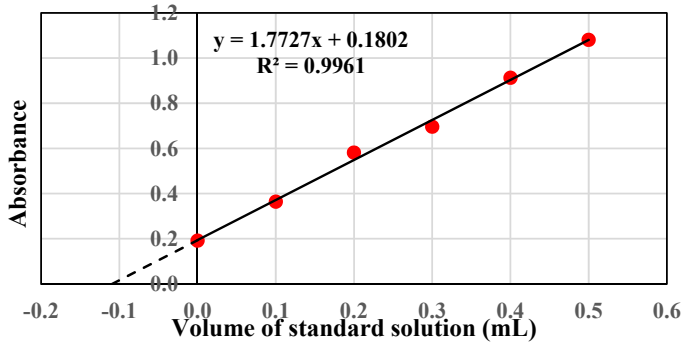


Figure No.(10):Determination of MA in capsule ponstidin

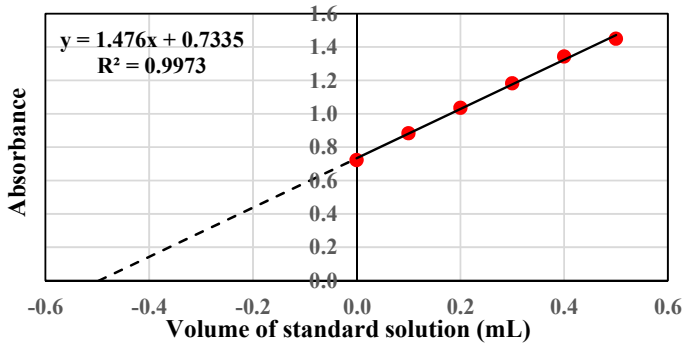


Figure No.(11):Determination of MA in capsule ponstidin.

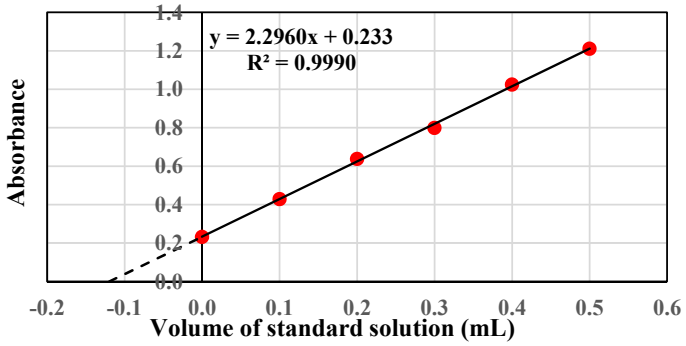


Figure No.(12) :Determination of MA in tablets Mefex

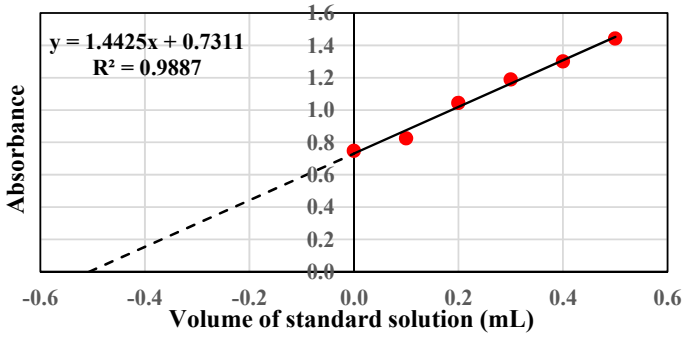


Figure No.(13) :Determination of MA in tablets Mefex.

التقدير الطيفي لعقار حامض الميفيناميك في مستحضراته الصيدلانية

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الخلاصة

اقترحت طريقة طيفية بسيطة ,دقيقة ومضبوطة لتقدير حامض الميفيناميك(MA) في صورتها النقية وفي المستحضرات الصيدلانية . الطريقة المقترحة تستند الى تفاعل العقار مع الكاشف 2,1-نفثاكوينون 4- سلفونيك الصوديوم (NQS). درست الظروف الفضليات من تأثير حجم الكاشف و الدالة الحامضية, زمن التفاعل الافضل لتكوين المعقد الناتج وكانت مطاوعة قانون بير في مدى تراكيز يتراوح بين 0.5-10.0 مكغم.مل$^{-1}$ عند الطول الموجي 450 نانومتر, وحد الكشف 0.189 مكغم.مل$^{-1}$. الطريقة المقترحة طبقت بنجاح لتقدير حامض الميفيناميك في مستحضراته الصيدلانية.

الكلمات المفتاحية: التقدير الطيفي , حامض الميفيناميك, 2,1-نفثاكوينون 4- سلفونيك الصوديوم(NQS)