Ars Pharmaceutica
https://revistaseug.ugr.es/index.php/ars
E-ISSN: 2340-9894 ISSN: 0004-2927

doi: 10.30827/ars.v65i1.28908
Artículos originales

Neocuproine-Based Sensitive Flow Injection Method for Mefenamic Acid Determination in Aqueous Solutions and Pharmaceutical Formulations

Método de inyección de flujo sensible a base de neocuproina para la determinación de ácido mefenámico en soluciones acuosas y formulaciones farmacéuticas

Ali Naser Nayef[1] 0000-0003-4849-644X
Alaa Frak Hussain[1] 0000-0002-4902-2644
Dakhil Nassir Taha[2] 0000-0003-3587-6822
[1] Department of Chemistry, College of Science-University of Kerbala, Iraq
[2] Specialized Medical Sciences, University College of Al-Amal, Iraq

Correspondence
Ali Naser Nayef
E-Mail: Alielli100@gmail.com

Received: 28.08.2023
Accepted: 28.10.2023
Published: 20.12.2023

Funding
This study is a part of the PhD thesis of Ali Naser Nayef.

Conflict of interests
The authors declare no conflict of interest.

Acknowledgment
This study is a part of the PhD thesis of Ali Naser Nayef.

Resumen

Introducción: Se presenta un enfoque novedoso y preciso para la estimación del ácido mefenámico (MEF) en formulaciones farmacéuticas y soluciones acuosas, utilizando espectrofotometría de inyección de flujo. Del mismo modo, este método demuestra un alto nivel de sensibilidad y precisión

Método: Se basa en la reducción del complejo Cu (II)-2,9DMP a complejo Cu (I)-2,9DMP coloreado, mediante dos pasos de reacción. Sin embargo, en el primer paso se produce la reacción entre la neocuproína y el Cu (II) para formar un complejo incoloro de Cu (II) -2,9DMP, y en el segundo paso el ácido mefenámico redujo el complejo incoloro formado a Cu (I) - 2,9DMP con color amarillo anaranjado, se desarrolló y validó el método de inyección de flujo.

Resultados: La medición de la densidad óptica de las sustancias amarillo-naranja se realizó a una longitud de onda de 454 nm. Los gráficos de calibración muestran linealidad dentro de los rangos de concentración especificados de 1,00-80,00 µg / ml. El límite de detección (LOD) se determina en 0,360 µg/ml, mientras que el límite de cuantificación (LOQ) se encuentra en 1.093 µg/ml.

Conclusiones: la metodología propuesta exhibió atributos notables como rapidez, sensibilidad y confiabilidad, lo que la hace adecuada para la cuantificación precisa de (MEF) en formulaciones farmacéuticas y soluciones acuosas en diversas formulaciones disponibles comercialmente.

Palabras clave: Análisis de inyección de flujo continuo; ácido mefenámico; neocuproína;

Abstract

Introduction: A novel and precise approach is presented for the mefenamic acid (MEF) estimation in pharmaceutical formulations and aqueous solutions, utilizing flow injection spectrophotometry. Similarly, this method demonstrates a high level of sensitivity and accuracy.

Method: The suggested method is based on the reducing of Cu(II)-2,9DMP complex to coloured Cu(I)- 2,9DMP complex ,by two step of reaction. However, in the first step the reaction is occur between neocuproine and Cu(II) to form colorless complex of Cu(II)-2,9DMP, then in second step mefenamic acid reduced the formed colorless complex to Cu(I)- 2,9DMP with yellow orange colour, Flow Injection Method were developed and validated.

Results: The measurement of the optical density of the yellow-orange substances was conducted at a wavelength of 454 nm. The calibration graphs exhibit linearity within the specified concentration ranges of 1.00-80.00 µg/mL. The detection limit (LOD) is determined to be 0.360 µg/ mL, while the limit of quantification (LOQ) is found to be 1.093 µg/ mL.

Conclusions: the proposed methodology exhibited notable attributes such as rapidity, sensitivity, and reliability, rendering it suitable for the accurate quantification of (MEF) in pharmaceutical formulations and aqueous solutions in various commercially available formulations.

Keywords: Continues Flow İnjection Analysis; Mefenamic Acid; Neocuproine

Highlight

Mefenamic acid has the capacity to convert Cu^{2+} ions into Cu^{1+} ions, so the development of an analytical approach based on Neocuproine reagent by flow injection method for mefenamic acid measurement in aqueous solution and tablets is extremely promising [8]. Furthermore, the suggested technique was applied to the quantitative evaluation of mefenamic acid in the actual samples (aqueous and pharmaceutical). The suggested method's quick reaction time, straightforward chemical and equipment requirements. The drugs industry has a significant challenge today in the form of the development of quicker, cheaper, and more precise methods. novel analytical techniques to ensure drug content and detect substances in medications that pose health hazards. and eliminate (or swap out) any materials dangerous to the environment and public health. Flow systems are great instruments for handling solutions in wet chemical analysis for these reasons. since one of the main requirements for analytical chemistry is automation.

In this proposed flow injection method, we used uncommon reagents and were not tuned to achieve the lowest possible waste production, Limit of Detection (LOD), Limit of Quantification (LOQ), standard deviation (SD), maximum sensitivity and wide ranges of concentration 1.00-80.00 µg/mL.

Fundamental benefits of the suggested flow injection method for measuring mefenamic acid in pharmaceutical and aqueous solutions include speed, ease of use, precision in findings, and low cost of equipment determination samples in very low concentrations 1.00-80.00 µg/mL. Accordingly, they are easier to use as well as quicker than the majority of the documented ways. Since common excipients included in commercial preparations do not interfere with the measurement of mefenamic acid, the proposed procedures can be effectively used for routine pharmaceutical quality control and research purposes.

Introduction

Mefenamic acid consider as a class of a nonsteroidal anti-inflammatory medicine (NSAID), and owing to the powerful analgesic and anti-inflammatory qualities it has, it has garnered a large amount of interest in recent years. As a consequence of this, it is used extensively in the therapy of a wide variety of unpleasant diseases, including menstrual cramps, rheumatoid arthritis, and osteoarthritis, amongst others[1]. It contains numbing, anti-pyretic, and anti-inflammatory characteristics, at higher concentrations, this molecule reduces inflammation[2]. The chemical formula of mefenamic acid (MEF) is 2-,[(2,3,-Dimethylphenyl)amino] benzoic acid (C15H15NO2). It is a weak organic acid that also includes the related (3-hydroxyanthranilic acids), a tryptophan (a standard amino acid) natural metabolite[3].

Neocuproine is a chelating substance and heterocyclic chemical molecule $C_{14}H_{12}N_2$. The derivatives substituted at the location 2 and 9 positions are among the most researched of the substituted phenanthrolines, having been initially published in the late 19th century[22]. Similarly, In chemistry of copper(I), Neocuproine as a (NN ligands) with somewhat large substituents crucial. Because of its selectivity for copper(I) and potent visual absorbance of the $Cu(DMP)^{2+}$ adduct, 2,9-dimethyl-1,10-phenanthroline (NC) is typically the reagent chosen for the colorimetric measurement of copper(I)[14]

Water-insoluble mefenamic acid is somewhat soluble in (chloroform) and (ethers), faintly soluble in ethanol (4.6 mg/mL) and water (1:9), and more soluble in dimethylformamidee (38.5 mg/mL)[4] Mefenamic acid reduces inflammation and pain by inhibiting COX and prostaglandin synthesis since it provides cerebral and peripheral analgesia. Its nonselective COX inhibitors inhibit both COX-1 and COX-2 enzymes[5]

Mefenamic Acid (MFA) operates in the same way as other nonsteroidal anti-inflammatory medicines by which blocking the enzymatic prostaglandin synthase[6] There are several known and reported analytical methods for measuring MEF acid in biological and pharmacological products[7] Spectrophotometry[8] Gas Chromatography[9] Extraction method of Micro-electrodriven Membranes in 2 Phases[10] capillary electrophoresis with two channels[11] RP-HPLC[12] Fluorometric method[13] Hyphenated Tech-

niques[14] Electrospray Ionization Mass Spectrometry[15] Turbidity Measurement[16] flow injection method[17]

MEF is determined by different flow injection technique, it has been estimated in pharmaceuticals by flow-injection[18] and estimation of Mefenamic Acid in Aqueous Solutions Using Reverse - Continuous Flow Injection Analysis[6] determination of MEF in pharmaceuticals formulation by flow-injection Fluorometry[21]. However, in recent years there has been a growing interest in the use of Neocuproine (2,9-dimethyl-1,10-phenanthroline) as a complexing agent in analytical chemistry. Neocuproine exhibits strong and selective chelation with various metal ions, including copper (II)[18] This property has been effectively utilized in the development of novel analytical methods, particularly in flow injection analysis (FIA)[19] Similarly, in terms of mefenamic acid analysis, the creation of a sensitive flow injection technique that uses neocuproine as a complexing agent is a breakthrough[20]

Materials and methods

All materials were of the analytical reagent grade; and the solutions were prepared with deionized water.

Preparation of standard solutions

Preparation of 2,9-dimethyl 1-10 phenanthroline solution 500 µg/mL

A stock solution that prepared freshly by solvation accurate amount of 0.0500g Neocuproine from (Sigma-Aldrich) in 100 mL of used solvent (ethyl alcohol+ deionized water) in ratio 1:9 and then diluting to the other concentrations.

Preparation of Sodium hydroxide 0.03 M

0.1200 g of standardized sodium hydroxide from (Merck, Germany) were newly prepared by dissolveing them in 25 mL of (deionized water), then adding the same solvent (0.03 M NaOH) to fill a volumetric flask to a capacity of 100 mL.

Preparation of Cupper Nitrate 0.005M Solution

0.1900 g of salt from (BDH) dissolve in 30 mL of deionized water and diluting to 100mL in volumetric flask with same solvent to prepare A standard solution and then diluting to the other concentrations.

Preparation of Standard MFA (100 µg/mL)

A standard drug obtained from the state drug industry company samara-Iraq (S.D.I), and for preparation of MFA solutions, dissolve 0.0100g MFA in 25 mL of 0.03 M standardized NaOH and complete volume up to 100 mL with standardized NaOH, working solutions were freshly prepared by various subsequent dilutions.

Preparation of mefenamic acid working solutions

The powdered and combined ten capsules, an exact weighted amount of powder dissolved in 25 mL 0.03 M standardized NaOH, stirred, allowed to stand for 7 min, and then diluted to 100 mL in a volumetric flask with the same solvent 0.03 M standardized NaOH. This yielded the equivalent of 250 mg capsules. Before use, the obtained solution was filtered with Whatman filler paper no. 41 to remove any undissolved or suspended materials. Working solutions were daily made through consecutive dilutions with deionized distilled water, and they were then tested according to the proposed method.

Instrumental Condition

Flow Injection System

We used in this flow injection system double beam Shimadzuu UVa-1700 Japan for absorption measurements result, x-y Recorder type Siemens C 1032, Germany, and we used Ismatic, Germany peristaltic pump. To provide the solution fluid, the flow injection analysis system (FIA) employed in this project

consists of peristaltic pump and injection valve with 6-way port that are connected to one another by a single low-load connection, as illustrated in Figure 1.

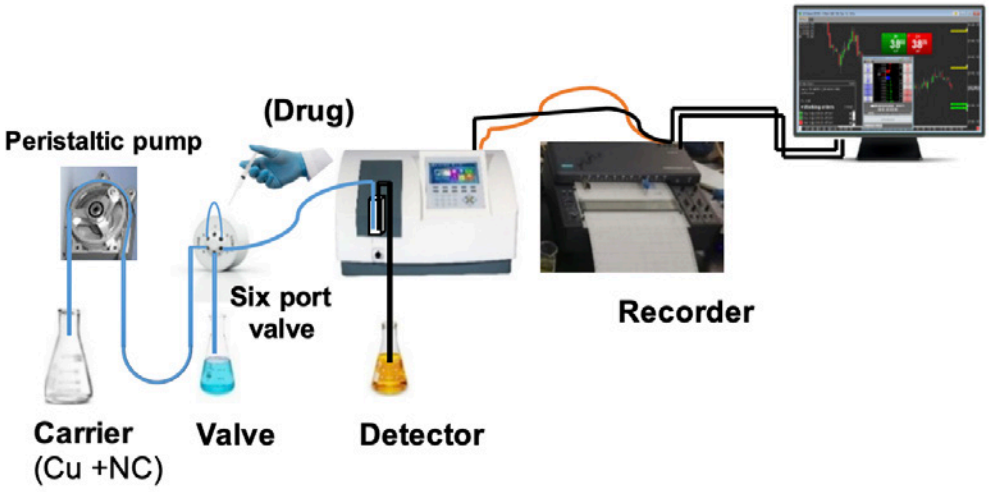

Figure 1. The model of flow injection system that we designed in our laboratory.

Results and discussion

The current work employs as a novel method for determination of MEF. However, when the Cu(II) reacted with Neocuproine reagent, the colorless complex will form Cu(II)-Neocuproine, this formed complex will react with mefenamic acid (reduced form) to produce yellow-orange products Cu (I)-Neocuproine[22] As showed in Figure 2.

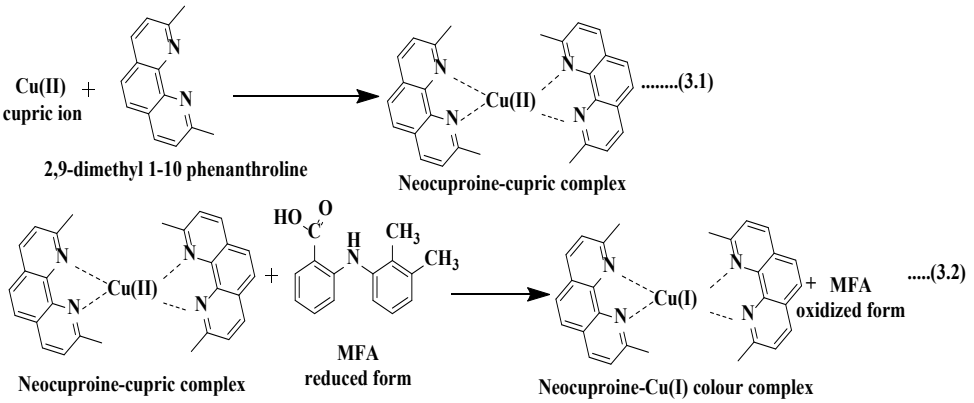

Figure 2. Schematic diagram for proposed method

Determination of maximum wavelength (λmax)

Absorbance of coloured products was measured in the 190-1100 nm range against a reagent blank. However, we conclude that Mefenamic acid absorption has a maximum wavelength of 454 nm. Under the testing circumstances, each reagent blank had a negligible absorbance at the relevant λ_{max}.

Experimental Conditions for Optimization

To estimate the better potential experimental condietions, we monitored many parameters and its influences on absorbance of coloured species.

The rate flow effect

flow rate's impact on the creation of coloured products was investigated by changing flow rate (10 - 70) mL/min and calculating the absorption of the coloured product generated, this study revealed that first broad peack from the base have the highest peak, but we discard here because incomplete mixing. However, the optimal flow rate, which results in the nicest beak shape and the maximum absorption, was 2.3 mL/min with a peack height of 4.3 cm. Due to the greater amount of time that speed required, two were selected above the other options.

The Influence of Neocuproine Reagent Concentration

The impact of adjusting the reagent concentrations on the reaction was investigated in this study. Similarly, these data have been collected using a variety of Neocuproine reagent concentration (50-500) µg/mL, and high concentrations cause a decrease in absorbance. However, this was possibly caused by an increase in particle density, which could have resulted in the buildup of precipitate particles in front of the detector.

The findings indicated that the optimal absorption occurs when the reagent concentration is 50 µg/mL.

The influence of pH changes

To investigate the effect of pH (1.0-9.0) on peak Hight (cm) and coloured complexes, various amounts 0-2 mL of 0.004 M standardized hydrochloric acid solution were added to an aliquot of solution containing 50 µg/mL of MFA as shown in Figure 3.

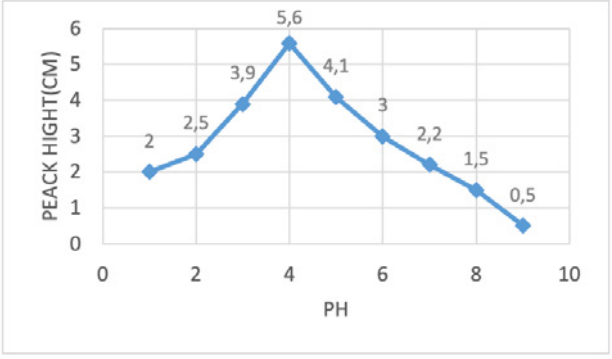

Figure 3. The Effect of pH changes, λmax= 454nm, NC.Conc. = 50 µg/mL, Cu(II)Conc.=350 µg/mL ,Flow rate =2.3 mL/min , MEF Conc.=50 µg/mL

As shown above the optimum pH with higher absorption intensity at peack Hight 5.6 cm at pH 4.0 due to good intensity.

Cu(II) Concentration effect on absorbance

Effects of copper (II) concentration (50-500) µg/mL on complex's absorbance was studied. It was observed that 350 µg/mL of Cu(II) gave the highest absorption with peack Hight 6 cm, which is strongly suggested for experimental procedures as we showed in Figure 4.

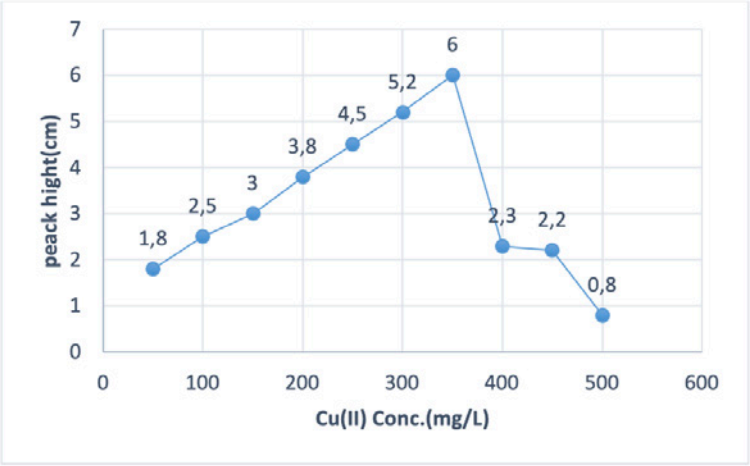

Figure 4. The Effect of Cu(II) concentration , λmax= 454nm,NC.Conc. = 50 µg/mL , pH=4.0, Flow rate =2.3 mL/min, MEF Conc.=50 µg/mL

As shown above the optimum Cu(II) Conc µg/mL with higher absorption intensity at peack Hight 6.0 cm due to good intensity.

Standard Calibration Curve for Mefenamic Acid in Aqueous Solution

This is done by preparation a series of solutions containing the concentrations in the range from (1.0 to 80.0) µg/mL and by using the optimum conditions which is used in this project. The results we are getting shown in Figure 5.

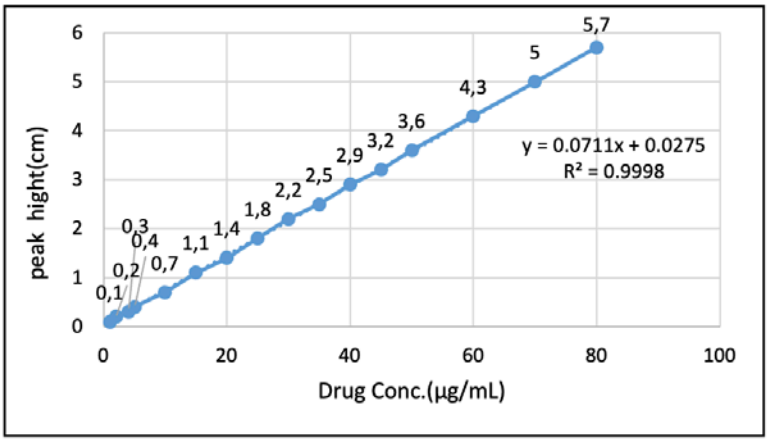

Figure 5. standard Calibration curve of Mefenamic acid, λmax= 454nm, NC.Conc. = 50 µg/ ml pH=4.0 , Cu(II)Conc. 350 µg/ ml, Flow rate =2.3 ml /min, MEF Conc.=50 µg/ ml

The statistical properties for our proposed method and Optimum conditions illustrated in Table 1.

Table 1. The Optimum conditions and statistical features for the proposed method

parameter	value
λ_{max}	454 nm
flow rate	2.3 mL/min
pH of carrier solution	4.00
Neocuproine Conc.	50 µg/ ml
Cu(II) Conc.	350 µg/ ml
Linearity range	1.00-80.00 µg/ ml
Regression equation	y = 0.0711x + 0.0275
Regression coefficient (R^2)	R^2 = 0.9998
Standard Deviation (SD)	0.0078
Standard Error	0.0074
Standard Error for Intercept	0.0103
LOD	0.360 µg/ ml
LOQ	1.08µg/ ml

Repeatability

We discovered the reproducibility of the suggested method by taking 6 samples solution having 50 µg/ ml of mefenamic acid, the result which gotten was highly degree of repeatability and extremely excellent as shown in Table 2.

Table 2. Repeatability of Mefenamic acid

Drug Conc. (µg/ ml)	Peak Height (Cm)						Mean Y\	SD	RSD%
50	3.7	3.8	3.7	3.7	3.8	3.7	3.73	0.0471	1.2638

Dispersion of Mefenamic Acid

By conducting two studies to determine the dispersion value of MEF contained in (50µg/mL and 70 µg/ ml), we evaluated the dispersion of mefenamic acid. Mefenamic acid at a concentration of 50 µg/mL comes first. The current experiment depicts the intensity response of the sample that enters the analysis (H_{max}). Mefenamic acid and Neocuproine were combined before being introduced into a manifold unit; the outcome demonstrates no convection or diffusion-related dispersion impact. This illustration depicts (H^o). It is possible to compute dispersion (D) by applying dispersions equation as shown: (($D^\circ = H^o/H_{max}$)) ,D= 1.057 and by doing the same procedure for the second mefenamic acid concentration (70 µg/ml) we get dispersion value equal to D= 1.081 as shown below in Table 3.

Table 3. Disperssions of mefenamic acid

Drug Conc. (µg/ml)	Peak Height (cm)		Dispersion(D)
	H^0	H_{max}	
70 µg/ml	5.3	4.9	1.081
50 µg/ml	3.7	3.5	1.057

LOD and LOQ

The sensitivity of the technique utilized in this method to identify mefenamic acid by the presentation limit of detection (L.O.D) and limit of quantification (L.O.Q) was highlighted. The fact that this FIA method could estimate the lowest concentration of mefenamic acid to be (1 µg/mL).

The limits of detection (LOD) and limit of quantitation (LOQ) were assessed as equation 3.3 and 3.4[22]

$$LOD=3.3\ S_o/b \quad \ldots\ldots\ldots\ldots 3.3$$

$$LOQ=3\ LOD \quad \ldots\ldots\ldots\ldots 3.4$$

Where:

b: Slope

So: Standard deviation of the regression line.

Application of Mefenamic Acid in Aqueous Solutions

We can determine unknown concentrations of aqueous solutions of mefenamic acid, three unknown aqueous solutions where prepared to determine concentrations. Then, we measured the absorbance according to the optimum conditions that we used in our project, as shown in Table 4.

Table 4. Application of Mefenamic Acid in aqueous Solutions

Conc. µg/ml		Error %	Rec %	RSD %
present	found			
10	10.1	0.0333	101.00	0.5716
20	19.94	0.0208	99.700	0.1808
30	29.95	0.0173	99.833	0.0578

Pharmaceutical Application of Mefenamic Acid Use in Pharmacological Dosage Forms

The applicability of the proposed flow injection procedure was tested by commercial dosage form from different brands.in addition, the result shows that finding where to be constant as showed in label of pharmaceutical dosage form, as shown in Table 5.

Table 5. Analysis of mefenamic acid in capsule formulations

pharmaceutical application					
Mefenamic acid	Conc. µg/mL		Error %	Rec %	RSD %
	present	found			
Ponstidin Capsule (250 mg)	50	49.98	0.005	99.96	0.0200
	40	39.97	0.008	99.93	0.0382
	30	29.95	0.005	99.83	0.0333
	20	20.03	0.035	100.15	0.3036
Mefril (250 mg)	50	49.97	0.011	99.94	0.0400
	40	39.98	0.005	99.95	0.0250
	30	29.94	0.003	99.82	0.0192
	20	19.91	0.017	99.55	0.1506

Discussion

This novel injection technique, characterized by its simplicity, accuracy, inexpensive and speed and time reducing was developed to determine mefenamic acid in aqueous solutions and pharmaceutical dosage form by using flow injection technique, the proposed method involved a direct redox reaction between Cu(II) and NC reagent, followed by an instantaneous reaction of Cu(II)-NC with mefenamic acid. However, this method has the potential to detect drugs at extremely at low concentrations (1µg/ ml) in aqueous solutions and pharmaceutical dosage form. On the other hand, based on the findings, statistical analysis revealed a standard deviation was equal to (SD) 0.0078 and This FI unit's data repeatability was accurate at low RSD levels. Additionally, the (LOD) was 0.360 µg/ mL, while the limit of quantification (LOQ) was 1.08 µg/ mL. The standard error was calculated to be 0.0074 µg/ml. Furthermore, the relationship between drug concentration in aqueous solutions and peak height (cm) was represented by the straight-line equation y = 0.0711x + 0.0275. The correlation equation for the standard specification yielded a value of 0.9998, indicating a strong linear relationship. Lastly, the linearity of this method was confirmed within the 1.00–80.00 µg/mL. The results of the calibration curve demonstrated a strong correlation coefficient, indicating a high degree of linearity. This suggests a robust relationship between the peak height (measured in centimeters) and the concentration (measured in micrograms per milliliter.

Conclusions

Based on the redox reaction, an effective, selective and precise flow injection technique for the measurement of mefenamic acid in aqueous solutions and pharmaceutical formulations was developed. The suggested approach, which has an excellent analytical performance, sensitive enough to enable estimation of lower amounts of (mefenamic acid), highly degree of repeatability, so can be used as a substitute method for the regular analysis of mefenamic acid in aqueous solutions and pharmaceutical raw and forms of medication. In conclusion, these flow injection techniques offer the benefits of increased selectivity, quick, straightforward performance, and low cost.

References

1. Duc K, Case Le. Report: Persistent Pulmonary Hypertension of the Newborn and Narrowing of the Ductus Arteriosus After Topical Use of Non-Steroidal Anti-Inflammatory During Pregnancy. Front Pharmacol. 2021;12(3): 1–5. Doi:10.3389/fphar.2021.756056

2. Wasito H, Purnamasari D, and Fareza MS. Mefenamic acid determination in tablet formulations using a selective and accurate spectrophotometric method based on Prussian blue formation. Malaysian J Anal Sci. 2021;25(1):71–80.

3. Omer ME, Qandil AM, Ali AS, and Habib HJ. Preparation and solubility profile study of sodium and potassium salts of mefenamic acid: The effect of pH and polarity. Dig J Nanomater Biostructures, 2021;16(2): 443–454. Doi: 10.15251/DJNB.2021.162.443

4. Hayes S and Org SH. Book reviews J Med Lib Assoc, 2014;102(3), 220–221. Doi: 10.3163/1536-5050.101.4.008

5. Otsuka M, Nishizawa J, Shibata J and Ito M. Quantitative Evaluation of Mefenamic Acid Polymorphs by Terahertz–Chemometrics. J Pharm. Sci. 2010;99(9):4048-4053. Doi: 10.1002/jps.22194

6. Al-Ameer LR, Al Sultani K. K and Taha D. N. Determination of Mefenamic Acid in aqueous Solutions Using Reverse - Continuous Flow Injection Analysis. J Pharm Negat Results, 2022;13(3):165–171. Doi: 10.47750/pnr.2022.13.03.026

7. Santini AO, Pezza HR and Pezza L. Development of a potentiometric mefenamate ion sensor for the determination of mefenamic acid in pharmaceuticals and human blood serum. Sensors Actuators, B Chem, 2007;128(1):117–123. Doi:10.1016/j.snb.2007.05.039

8. Rashad IQ and Bakir MH. Spectrophotometric Determination of Mefenamic acid using Metol reagent by Oxidative Coupling Reaction," IOP Conf Ser Mater Sci Eng. 2021;1058(1):120-125. Doi:10.1088/1757-899X/1058/1/012081

9. Jalbani NS, Solangi AR, Khuhawar MY, Memon S, Junejo R, and Memon AA. Gas chromatographic and spectrophotometric determination of diclofenac sodium, ibuprofen, and mefenamic acid in urine and blood samples, Turkish J Pharm Sci. 2020;17(5):465–473. Doi: 10.4274/tjps.galenos.2019.42243

10. Hanapi NS. Rapid Determination of Non-steroidal Anti-inflammatory Drugs in Aquatic Matrices by Two-phase Micro-electrodriven Membrane Extraction Combined with Liquid Chromatography, J Chromatogr Sci. 2018;56 (2):166–176. Doi: 10.1093/chromsci/bmx092.

11. Le MD, Duong HA, Nguyen MH, Sáiz J, Pham HV and Mai TD. Screening determination of pharmaceutical pollutants in different water matrices using dual-channel capillary electrophoresis coupled with contactless conductivity detection, Talanta, 2016;160: 512–520. Doi: 10.1016/j.talanta.2016.07.032

12. Alfeen MA. Determination of Mefenamic Acid in Pharmaceutical Drugs and Wastewater by RP-HPLC, J Anal Bioanal Sep Tech. 2017;2(2):85–88. Doi:10.15436/2476

13. Ashira TV, Rafeeque TM, Maanvizhi S, Kathirvel S, Indukala PC, Safeetha S. Review for Analytical Methods for the Determination of Mefenamic Acid. J Pharm Res Int. 2021;426–437.

14. Siddiqui MR, AL Othman ZA, and Rahman N. Analytical techniques in pharmaceutical analysis: A review," Arab J Chem. 2017;10(3): S1409–S1421. Doi: 10.1016/j.arabjc.2013.04.016

15. Abdelhamid HN and Wu HF. Soft ionization of metallo-mefenamic using electrospray ionization mass spectrometry, Mass Spectrom Lett. 2015;6(3):43–47. Doi: 10.5478/MSL.2015.6.2.43

16. Turkie NS and Kadhim MK. Determination of Mefenamic Acid Using a New Mode of Irradiation (Array of Six Identical LEDs) and Detection (Twin Solar Cells) Through Turbidity Measurement by CFIA, J Sci. 2016; 57(2B):1052–1070.

17. Farhood AS. and Taha DNA new merging-zone flow injection system for the quantification of ferrous and ferric ions in aqueous solution and sludge of wastewater," Anal Scine Techno. 2022;35(5):1-10. Doi: 10.5806/AST.2022.35.5.1

18. GarcõÂa S, PedrenÄo CS, Albero I, and GarcõÂa C. Flow-Injection Spectrophotometric Determination of Diclofenac or Mefenamic Acid in Pharmaceuticals, Mikrochim Acta. 2021;136: 67-71

19. Saleem BA and Alnuaimy LA. Spectrophotometric Determination of Mefenamic acid in pure and Pharmaceutical Preparations, J Phys Conf Ser. 2021;1853(1):1-12. Doi: 10.1088/1742-6596/1853/1/012048

20. da Silva JC, Suarez WT, and Franco OK. Flow-Injection Spectrophotometric Determination of Methimazole in Pharmaceuticals Using a Charge Transfer Complex Cu(I)–Neocuproine, J Anal Chem. 2018;73(3):243–248. Doi: 10.1134/S1061934818030061

21. Hamed M, Hammood MK. Simultaneous. Determination of Trace Mefenamic Acid in Pharmaceutical Samples via Flow Injection Fluorometry, IJDDT,2020;10 (3):395–401. Doi: 10.25258/ijddt.10.3.16

22. Basavaiah K, Somashekar BC. Quantitation of rantidine in pharmaceuticals by titrimetry and spectrophotometry using dichromate as the oxidimetric reagent. J Iranian Chem Soc. 2007;12(4):78-88. Doi.org/10.1007/BF03245806