RESEARCH ARTICLE / ARAŞTIRMA MAKALESİ
Journal of Advanced Research in Health Sciences /
Sağlık Bilimlerinde İleri Araştırmalar Dergisi 2024
DOI: 10.26650/JARHS2024-1238611

DETERMINATION OF MELOXICAM IN TABLETS BY THIRD DERIVATIVE UV SPECTROPHOTOMETRIC METHOD

ÜÇÜNCÜ TÜREV UV SPEKTROFOTOMETRİ İLE TABLETLERDE MELOKSİKAM TAYİNİ

Zeynep AYDOĞMUŞ[1], Faruk ALİM[1,2]

[1]İstanbul University, Faculty of Pharmacy, Department of Analytical Chemistry, İstanbul, Türkiye
[2]İstanbul University, Institute of Graduate Studies in Health Sciences, İstanbul, Türkiye

ORCID ID: Z.A. 0000-0002-6310-1197; F.A. 0000-0002-5101-7166

Citation/Atıf: Aydoğmuş Z, Alim F. Determination of meloxicam in tablets by third derivative UV spectrophotometric method. Journal of Advanced Research in Health Sciences 2024;7(1):61-67. https://doi.org/10.26650/JARHS2024-1238611

ABSTRACT

Objectives: Meloxicam (MEL) is a selective cyclooxygenase inhibitor of enolic acid class drugs with analgesic and antipyretic effects. In this study, an easy, selective, fast, and sensitive third-order derivative spectrophotometric method was developed and validated for the determination of MEL in tablet formulation.

Material and Methods: The absorption of MEL in a solution of methanol and 1 M sodium hydroxide (1:1, v/v) mixture was measured using the peak-to-zero method. This solution was found to be the most suitable for determining the drug by third-order derivative spectrometry. The wavelength at which the maximum absorption was achieved in the measurements was 341nm. The developed method has been validated in accordance with the International Conference on Harmonization guidelines (ICH).

Results: The linear working range was 1.0 - 14.0 µg/mL. The limit of detection (LOD) and limit of quantification (LOQ) values were 0.22 and 0.75 µg/mL, respectively. The method was validated for linearity, accuracy, precision, recovery, and stability. The developed method was performed for the quantification of MEL in tablets, and the recovery percentage was found to be between 97.50% and 98.12%.

Conclusion: The results show that the method is easy, simple, inexpensive, and fast compared to other published methods, in addition to being accurate and sensitive. The proposed method can be used as a very convenient alternative for the determination of MEL in pharmaceutical formulations in routine analysis in quality control.

Keywords: Third-derivative spectrophotometry, determination, meloxicam, tablets

ÖZ

Amaç: Meloksikam (MEL), analjezik ve antipiretik etkileri olan seçici bir siklooksijenaz inhibitörü enolik asit sınıfı bir ilaçtır. Bu çalışmada, tablet formülasyonunda meloksikam tayini için kolay, seçici, hızlı ve hassas bir üçüncü dereceden türev spektrofotometrik yöntem geliştirilmiş ve valide edilmiştir.

Gereç ve Yöntemler: Üçüncü türev spektrometrisi ile ilaç tayini için en uygun bulunan metanol-1 M sodyum hidroksit (1:1, v/v) çözeltisinde meloksikamın absorpsiyonu pik-sıfır yöntemi ile okundu. Ölçümlerde maksimum absorpsiyonun elde edildiği dalga boyu 341 nm idi. Geliştirilen yöntem, Uluslararası Uyumlaştırma Kılavuzuna (ICH) uygun olarak valide edilmiştir.

Bulgular: Doğrusal çalışma aralığı 1,0 - 14,0 µg/mL idi. Gözlenebilme sınırı (LOD) ve tayin sınırı (LOQ) değerleri sırasıyla 0,22 ve 0,75 µg/mL idi. Yöntem, doğrusallık, doğruluk, kesinlik, geri kazanım ve kararlılık açısından doğrulandı. Geliştirilen yöntem tabletlerde meloksikam miktar tayinine uygulanmış ve geri kazanım yüzdesi %97,50 ile %98,12 arasında bulunmuştur.

Sonuç: Sonuçlar, yöntemin doğru ve duyarlı olmasının yanı sıra, yayınlanmış diğer yöntemlere göre kolay, basit, ucuz ve hızlı olduğunu göstermektedir. Önerilen yöntem, kalite kontrolde rutin analizlerde farmasötik formülasyonlarda meloksikam tayini için çok uygun bir alternatif olarak kullanılabilir.

Anahtar Kelimeler: Üçüncü türev spektrofotometrisi, tayin, meloksikam, tablet

Corresponding Author/Sorumlu Yazar: Zeynep AYDOĞMUŞ **E-mail:** aydogmus@istanbul.edu.tr

Submitted/Başvuru: 23.01.2023 • **Revision Requested/Revizyon Talebi:** 08.05.2023 • **Last Revision Received/Son Revizyon:** 20.05.2023 • **Accepted/Kabul:** 06.07.2023 • **Published Online/Online Yayın:** 19.01.2024

INTRODUCTION

Meloxicam (MEL, 4-hydroxy-2-methyl-*N*-(5-methyl-1,3-thiazol-2-yl)-1,1-dioxo-1λ⁶,2-benzothiazine-3-carboxamide) (Figure 1), a non-steroidal anti-inflammatory, has analgesic and antipyretic properties. MEL is used in the treatment of calcification, joint pain and deformity, progressive rheumatism, acute musculoskeletal pain, symptoms of acute gouty arthritis, and relief of postoperative swelling (1-2). It is also widely used for dysmenorrhea, low back pain, postoperative analgesia, and pain related to dental interventions. MEL acts by inhibiting cyclooxygenase (COX-1 and COX-2). As COX-2 does not inhibit myocardial prostacyclin like specific products, MEL does not cause hypertension and edema (3).

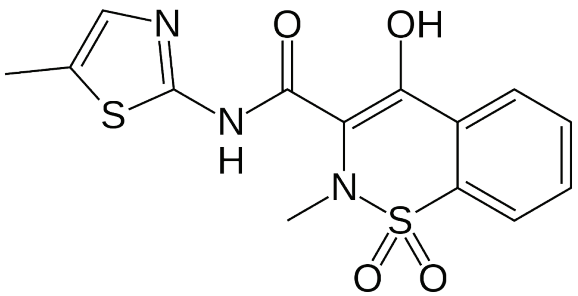

Figure 1: Chemical structure of meloxicam

Based on the literature review, some electrochemical methods (4-6) for the determination of MEL in pharmaceutical forms and several high-performance liquid chromatography (HPLC) methods for its determination in plasma (7-9) and pharmaceutical preparations alone (11-13) and simultaneously with other anti-inflammatory drugs (14-18) are available. Also, in addition to a spectrofluorometric method, there are many spectrophotometric methods based on measuring the absorbance directly in different solutions, measuring the absorbance after complexation or derivatization and chemometric measurement (19-30). Among these spectrophotometric studies, two first-order derivative spectrometry studies (31-33) and simultaneous second-order derivative spectrometry studies for MEL determination seem to be registered so far (33).

In quantitative analysis, derivative spectrophotometry provides quite an advantage over conventional absorption spectra in cases of spectral similarities, the overlap of analyte absorption bands, and broad absorption bands. In addition, derivative spectrophotometry is commonly used in drug analysis in the presence of impurities to eliminate background absorbance errors in cases of overlapping fuzzy matrices, to eliminate effects such as beam scattering, and to increase band resolution (34).

In this study, MEL was determined and validated for the first time by the third-order derivative spectroscopic method, which is much more sensitive, easier, faster, and more accurate than many existing methods. The suggested method was implemented for MEL determination in tablets with high recovery.

MATERIAL and METHODS

Apparatus

Spectrophotometric measurements were taken with an ultraviolet-visible (UV-Vis) absorption spectrophotometer (Shimadzu, UV-160 A, Japan), and 1.0 cm quartz cells were used. Spectra were acquired at a scanning range of 200-600 nm, a scanning speed of 1500 nm/min, a slit width of 2 nm, and a derivation interval (Δλ) of 2.8 nm for third-order derivative (^{3}D, d^3 A / $d\lambda^3$) spectra.

Reagents and solutions

MEL and its tablet (Melox®) were obtained from the Abdi Ibrahim Pharmaceutical Company (Istanbul). Sodium hydroxide (NaOH), hydrochloric acid (HCl, 37%), methanol, acetonitrile, and ethanol chemicals from Merck were all analytical grades. Ultra-pure water obtained from the Elga Purelab Option water purification device (Lane End, UK) was used in the analysis.

An amount of 2.0 mg of MEL was weighed exactly, dissolved in methanol :1 M NaOH (1:1, v/v), and made up to 100 mL (stock solution, 20 µg/mL). It was used by making various dilutions in the analysis. Stock solutions were kept refrigerated, and we worked with a freshly prepared solution every week.

Calibration curve

For the calibration curve, 0.5, 2, 4, 5, 6, and 7 mL of the stock solution containing 20 µg/mL MEL (equivalent to 1, 4, 8, 10, 12, and 14 µg/mL, respectively) were transferred into 10 mL flasks and completed to volumes with the selected methanol:1M NaOH (1:1 v/v) mixture solution. The UV spectra of these solutions were taken against the blank solution (methanol:1M NaOH, 1:1 v/v) in the 200-600 nm range and operated to obtain its third-order derivative (^{3}D). The peak absorption ($d^3A/d\lambda^3$) was measured by the peak-to-zero technique (*height* of *peak* from *zero*) at 341 nm. The calibration curve was established by drawing the third derivative absorbance versus the concentration of MEL, and the regression analysis was performed. The calibration curve was created by replicating at least six separate analyzes.

Determination in tablets

Ten tablets containing 7.5 mg of MEL, trade name Melox®, were weighed one by one, and the average tablet weight was determined and ground into powder in a mortar. An amount of tablet powder equivalent to the weight of one tablet was precisely weighed. It was transferred to a 100.0 mL flask and kept in an ultrasonic bath for 60.0 min with 70.0 mL of a methanol:1 M NaOH (1:1, v/v) mixture. It was then completed to its volume and filtered through blue banded filter paper. One mL of tablet solution was taken, and after completion to 10.0 mL (7.5 µg/mL) with the same solution, it was worked out as in the section on the calibration curve study.

RESULTS

Appropriate solvent and wavelength selection

Solvents, wavelengths, and derivative spectrophotometry scans

Table 1: Spectral parameters of MEL in different solvents

Tested solution	MEL µg/mL	^{0}D, λ nm	Absorbance	^{3}D, λ nm	Absorbance
Methanol	10	366	0.358	345	0.685
1 M NaOH	10	360	0.690	341	0.991
MeOH:1M HCl (1:1, v/v)	10	343	0.408	323	0.742
Acetonitrile	10	365	0.298	348	0.603
MeOH:1M NaOH (1:1, v/v)	10	360	0.822	341	1.285
MeOH:water (1:1, v/v)	10	363	0.254	341	0.570

MeOH: Methanol; NaOH: Sodium hydroxide; HCl: Hydrochloric acid

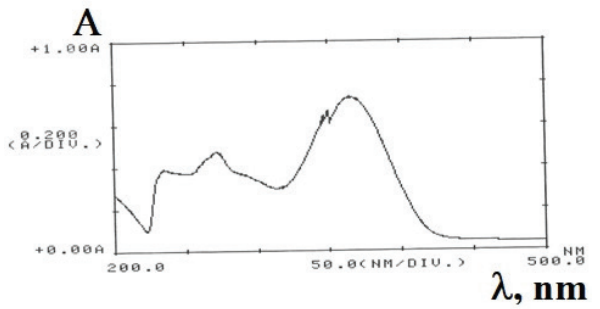

Figure 2: The zero-order spectrum of meloxicam at 10.0 µg/mL in methanol:1 M sodium hydroxide (1:1, v/v)

were investigated to obtain the most appropriate conditions for the method. For MEL determination, firstly the spectra between the zero-order and fourth derivatives were taken. Considering the high absorption response proportional to the concentration and a well-separated peak, the 3rd derivative spectrometry method was determined to be the most appropriate, so studies were continued with this method. To determine the appropriate solvent for which the MEL gives the highest absorbance, the third derivative (^{3}D) absorption values of MEL at 10.0 µg/mL concentration were recorded in methanol, 1 M NaOH, methanol:1 M HCl (1:1, v/v), acetonitrile, methanol:1 M NaOH (1:1, v/v), and methanol: water (1:1, v/v). Under these conditions, the highest absorbance value was obtained in methanol:1 M NaOH (1:1, v /v) solvents. The absorption and wavelength (λ) values of MEL obtained by a zero-order (direct, ^{0}D) and ^{3}D spectrophotometric methods in the tested solvent systems are summarized in Table 1. The maximum absorbance wavelength recorded in the spectrum with the peak-to-zero technique was 341 nm. The ^{0}D and ^{3}D spectra of the drug recorded in the selected solution are given in Figures 2 and 3.

Method Validation

For the validation of the developed method, the following parameters were examined in accordance with the recommendations of the International Council of Harmonization (35).

Linearity and sensitivity

From the calibration curve obtained by plotting the third-order derivative absorbance values read against the concentrations of the MEL solutions, the dynamic linear range of the MEL was

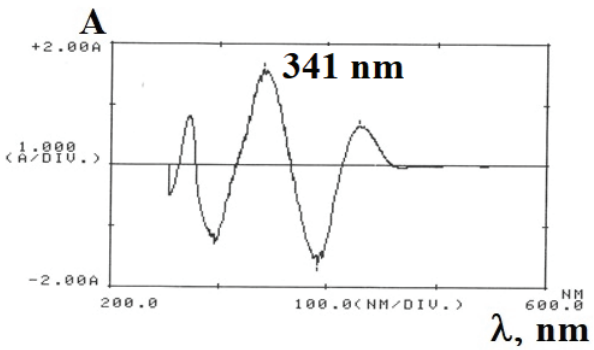

Figure 3: The third-order derivative spectrum of meloxicam at a concentration of 14.0 µg/mL in methanol:1 M sodium hydroxide (1:1, v/v)

Table 2: Analytical figures of merit for the presented method

Parameters	Standard solution
^{3}D (nm)	341
Beer's law range (µg/mL)	1.0-14.0
Regression equation (n= 6)[a]	y=0.1107C + 0.0135
Slope ± SD	0.1107±0.0017
Intercept ± SD	0.0135±0.016
LOD (µg/mL)	0.22
LOQ (µg/mL)	0.75
Correlation coefficient, R^2	0.9998

ay= aC + b (where C is the concentration of the drug in µg/mL. y is absorbance, a is slope, and b is intercept). aAverage of six determinations for six concentration levels. SD: Standard deviation, LOD: The limit of detection, LOQ: Limit of quantification.

determined to be between 1.0 and 14.0 µg/mL. The regression equation corresponding to this curve was calculated as y ($d^3A/d\lambda^3$) = 0.1107C(µg/mL) + 0.0135 (Figure 4). The correlation coefficient (R^2) value of this equation is 0.9998, indicating perfect linearity (Table 2).

The LOD and LOQ values were calculated with the following formulas: LOD = 3 x SD/m and LOQ = 10 x SD/m. Here, SD is the standard deviation of the y-intercept of the calibration line, and m is the slope of the calibration line. The LOD and LOQ values

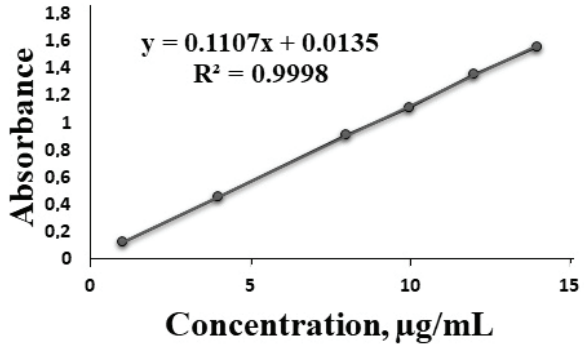

Figure 4: Calibration curve of meloxicam

calculated according to the given equations were found to be 0.22 and 0.75 µg/mL for MEL, respectively.

Precision study

To ascertain the intraday and interday precision, MEL solutions prepared daily at two different concentrations (2.0 and 12.0 µg/mL) were taken and studied on the same day and on six different days (n= 6), as described in the "Calibration Curve" section.

In the intraday repeatability study, the standard deviation (SD) and percent recovery values ranged from 0.033 to 0.074 and 97.5% to 100.93%, respectively. *Relative standard deviation* (RSD%) was found to be between 0.61% and 1.69%. In the interday reproducibility study, SD and % recoveries values were found to be between 0.041-0.071 and 97.65%-99.59%, respectively. The RSD% was between 0.60% and 2.12%, indicating excellent precision (Table 3).

Table 3: Intraday and interday analysis of MEL (n=6)

	Intraday		Interday	
Concentration (µg/mL)	**Recovery[a] (%) ± SD[b]**	**RSD[b] (%)**	**Recovery[a] (%) ± SD[b]**	**RSD[b] (%)**
2.0	97.50±0.03	1.69	97.65±0.04	2.12
12.0	100.93±0.07	0.61	99.59±0.07	0.60
Mean	99.22±0.20	1.15	98.62±0.06	1.36

[a]Mean of five determinations (n=5), [b]SD is the standard deviation and RSD% is the relative standard deviation.

Table 4: The accuracy of the method by standard addition method (n=6)

Taken tablet amount (µg/mL)	Added standard MEL amount (µg/mL)	Total found amount (µg/mL)	Recovery%	SD[a]	CV[b](%)
1.0	1.0	1.97	98.32	0.047	2.39
5.0	5.0	9.84	98.43	0.050	0.51
13.0	5.0	17.46	97.01	0.164	0.94

[a]SD is the standard deviation, [b]CV % is the coefficient of variation.

Accuracy studies

The accuracy of the study was assessed with the standard addition technique by adding standard MEL solution (at 1.0 and 5.0 µg/mL) to the tablet solution (at 1.0, 5.0, and 13.0 µg/mL) and analyzing at three different concentration levels in the calibration curve range. The results represent the average of six separate analyses. The percent recovery was calculated by the equation [% = [[(Ct-Cu)/Ca]x100]: where Ct = total concentration of MEL found; Cu = MEL concentration of tablet solution; and Ca= added standard solution. The recovery % of the drug varies between 97.01% and 98.43%. RSD% values were between 0.51% and 2.43% (Table 4). The high recovery rate indicates the accuracy of the method, and the MEL is unaffected by any additives used in the tablet formulation.

Stability studies

For determination of the stability of MEL in bulk, the solutions at 10.0 µg/mL were kept at 4 °C and room temperature for 1, 2, 4, 6, and 24h and then analyzed. Recovery results of the drug showed no significant difference within 24 hours. In the analysis results given in Table 5, the mean SD and RSD% values were 0.06 and 0.55% for room temperature holding, and 0.17 and 1.66% for 4°C storage, respectively. Recovery percentages were found to be 100.86% and 99.32% for the bulk solution of MEL

Table 5: Stability results for MEL at different conditions

		Room temperature	+4 °C
Duration (hour)	**Concentration Taken µg/mL**	**Concentration Found µg/mL**	**Concentration Found µg/mL**
1	10.0	10.14	10.18
2	10.0	10.14	9.96
4	10.0	10.09	9.91
6	10.0	10.05	9.87
24	10.0	10.01	9.74
Mean values		10.09	9.93
SD[a]		0.06	0.17
RSD%[b]		0.55	1.66
Recovery%		100.86	99.32

[a]SD is the standard deviation, RSD%[b] is percentage relative standard deviation

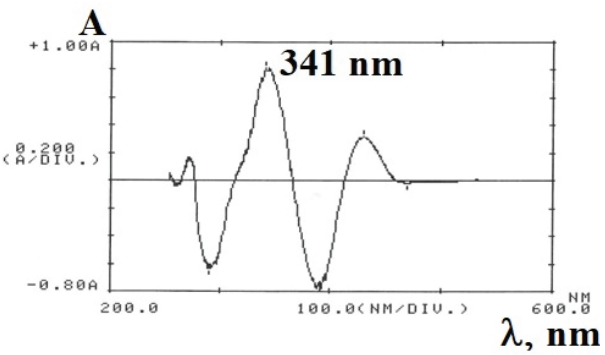

Figure 5: The third-order derivative spectrum of a tablet solution containing 7.5 µg/mL meloxicam, taken under selected conditions

at room temperature and at 4˚C, respectively. These results can indicate that the MEL is stable in the chosen solvent of analysis (methanol: 0.1 M NaOH, 1:1 v/v) at room temperature and refrigerator and is also resistant to sunlight and in moderate alkaline conditions.

Determination of MEL in tablets

To see the feasibility of the developed and validated method, MEL determination was carried out on tablet samples (Figure 5). The determination of tablet content was calculated by putting the absorbance values in the regression equation prepared with the standard MEL solution, and then their recovery was found. As a result of at least 6 separate analyses, the average recovery of MEL in tablets was found to be 97.50%. The SD and RSD% were 0.14 and 1.93%, respectively.

DISCUSSION

In this study, a series of preliminary experiments were conducted to determine the most suitable conditions for the determination and validation of MEL drug in tablets by a new third-order derivative spectrophotometric method.

Compared to previously reported methods in terms of LOD, the current method was found to be significantly more sensitive to reported derivative spectrometry studies, most chemically pretreated UV-visible spectrophotometric methods, ^{0}D

Table 6: Comparison of the statistical performances of the proposed method with published spectrophotometric methods of MEL

Methods	Analysis medium	λ (nm)	LOD/LOQ, µg/mL	Linearity, µg/mL	Ref.
^{3}D-*UV*	Methanol:1 M NaOH (1:1 v/v)	341	0.22 /0.75	1.0 - 14.0	Proposed
^{0}D-UV ^{1}D-*UV* ^{2}D-*UV*	0.1 M NaOH	270.0 339.6 315.6	1.30/3.50 1.0/3.50 1.20/3.80	4.0 - 14.0	33
^{0}D-UV ^{1}D-*UV* ^{2}D-*UV* UV-vis	0.1 M NaOH Ethanolic solution:0.1 M HCl Borax: phosphate buffer pH 8.0 safranin T:borax-phosphate pH 8.0	339.9-384.7 322-368 343.2-385.6 518	0.11/2.0 0.07/1.0 0.1/1.0 0.33/4.0	2.0-10.0 1.0-10.0 1.0-10.0 4.0-12.0	19
^{1}D-*UV* TLC:densitometric	0.1N NaOH	338 365	Not given	5-20 2-10	31
^{0}D-UV UV-AUC ^{1}D-*UV*	0.1N NaOH	269 253-279 275	Not given	5-30 5-30 50-300	32
^{0}D-UV	0.1 M NaOH	365	0.12/0.38	2.0- 12.0	20
^{0}D-UV	Methanol:0.1M HCl	346.0	0.13/0.41	5.0-150	21
^{0}D-UV	Etanol	365	1.28/2.0	2.0 -18.0	22
UV-vis- Flow-injection (UV)	Fe (III) [2Meloxicam/Fe (III)]: methanolic solution 0.1 M NaOH	570 362	0.47/-1.51 0.72 /2.52 0.04/0.13	2.0-200 5.00-250 0.5-20	23
Direct flow injection (UV) Indirect flow Injection (UV)	Diazotized procaine Benzylpenicillin:alkaline MEL:p-methylaminophenol sulfate	492 656	2.73/4.21 5.26/ 9.62	5-80 15-225	24
UV-vis	Acetonitrile: methanol (50:50): 1% aluminium chloride	375	0.68/ 2.25	5-30	25
^{0}D-UV UV-vis Hydrotropic (UV)	0.1M NaOH 0.1M NaOH:5% ferric chloride % Trisodium citrate in water	269 476 269	0.038 / 0.11 0.33/ 0.94 0.038/0.11	5- 30 50- 250 5-30	26
UV-vis	Sodium nitroprusside:Hydroxylamine HCl:sodium carbonate Ferric chloride:1,10-Phenanthroline	363 343	0.16/ 0.23 0.49/0.71	4-20 10-50	28
UV-vis	Phosphate buffer (pH=7.5)	350	0.88/2.9	3.5-19.6	30
UV-vis ^{0}D-UV	Methanol:Ferric Ammonium sulfate: 0.1 N NaOH	396 354	Not given	5-30 3-12	*29*

LOD/LOQ: The limit of detection/ limit of quantification, NaOH: Sodium hydroxide, UV-vis: ultraviolet- visible spectrophotometer, ^{0}D-UV: Zero order derivative ultraviolet absorption, MEL: Meloxicam, TLC: Thin layer chromatography

methods and flow spectrophotometric methods (Table 6) (19, 22-26, 28, 30, 32). As given in Table 6, LOD and LOQ values were not given in some studies with a linear working range at high concentrations. When the determinations were compared in terms of linear ranges, it was found that our developed method was mostly more sensitive and/or had a wider range than almost all of them. Furthermore, a comparison of the LOD and linear range values of the developed method with those obtained by some published HPLC methods, which are much more expensive, time-consuming, and require greater solvent consumption, revealed that the developed method is fairly sensitive (11-16). Moreover, the absence of any additives in the absorbance of the tablet solution because of the solvent and possible tablet additional ingredients proves the selectiveness of the method and contributes to high recovery (Figures 3 and 5).

CONCLUSION

In this study, a new selective, stable, accurate, and simple third-order derivative spectrophotometric method using a peak-to-zero measurement technique was developed for the determination of MEL in bulk and tablets. The new method was more sensitive than some reported spectrophotometric and HPLC-UV methods when compared with the detected LOD value of 0.22 µg/mL and the wide linear range of 1.0-14.0 µg/mL. The current method is very quick and cheap compared to complex and expensive advanced HPLC and HPLC/MS methods that are not available in every analytical laboratory. The developed method offers significant advantages due to its easy and fast sample preparation, which requires no processing and uses a low amount of non-destructive solvents. Its practicality and precision make it a preferable choice for routine analysis of MEL in both pure and tablet forms, compared to the reported methods.

Ethics Committee Approval: Ethics committee approval is not required since our study is a quantification of the drug in tablet formulation and is not a clinical study.

Peer Review: Externally peer-reviewed.

Author Contributions: Conception/Design of Study- Z.A., F.A.; Data Acquisition- F.A., Z.A.; Data Analysis/Interpretation- F.A., Z.A.; Drafting Manuscript- Z.A., F.A.; Critical Revision of Manuscript- Z.A., F.A.; Final Approval and Accountability- Z.A., F.A.; Material and Technical Support- Z.A., F.A.; Supervision- Z.A.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: This work was supported by the Scientific Research Project Coordination Unit of Istanbul University, Project number, and ID are 37460 and 1150, respectively.

REFERENCES

1. Davies NM, Skjodt NM. Clinical pharmacokinetics of meloxicam. Clin Pharmacokinet 1999;36(2):115-26.
2. Zobdeh F, Eremenko, II, Akan, MA, Tarasov VV, Chubarev VN, Schiöth HB, et al. Pharmacogenetics and Pain Treatment with a Focus on Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and Antidepressants: A Systematic Review. Pharmaceutics 2022;14(6):1190.
3. Xu S, Rouzer, CA, Marnett LJ. Oxicams, a class of nonsteroidal anti-inflammatory drugs and beyond. IUBMB Life 2014;66(12):803-11.
4. Šelešovská R., Hlobeňová F, Skopalová J, Cankař P, Janíková L, Chýlková J. Electrochemical oxidation of anti-inflammatory drug meloxicam and its determination using boron doped diamond electrode. J Electroanal Chem 2020;858:113758.
5. Eroğlu ME, Bayraktepe DE, Polat K, Yazan Z. Electro-oxidation mechanism of meloxicam and electrochemical sensing platform based on graphene nanoparticles for its sensing pharmaceutical sample. Curr Pharm Anal 2019;15(4):346-54.
6. Radi AE, Ghoneim M, Beltagi A. Cathodic adsorptive stripping square-wave voltammetry of the anti-inflammatory drug meloxicam. Chem Pharm Bull 2001 49(10):1257-60.
7. Bae JW, Kim MJ, Jang CG, Lee SY. Determination of meloxicam in human plasma using a HPLC method with UV detection and its application to a pharmacokinetic study. J Chromatogr B 2007;859(1):69-73.
8. Liew KB., Loh GO. K, Tan YTF, Peh KK. Improved protein deproteinization method for the determination of meloxicam in human plasma and application in pharmacokinetic study. Biomed Chromatogr 2014;28(12):1782-8.
9. Tian Y, Wu X, Zhang M, Zhao L, Xiong Z, Qin F. Quantitative determination of meloxicam in dog plasma by high performance liquid chromatography–tandem mass spectrometry and its application in a pharmacokinetic study. Biomed Chromatogr 2018;32(7):e4228.
10. Miyamoto A, Aoyama T, Matsumoto Y. The measurement of meloxicam and meloxicam metabolites in rat plasma using a high-performance liquid chromatography-ultraviolet spectrophotometry method. Chem Pharm Bull 2017;65(2):121-6.
11. Sahoo NK, Sahu M, Rao PS, Rani NS, Devi JNV, Ghosh G. Validation of assay indicating method development of meloxicam in bulk and some of its tablet dosage forms by RP-HPLC. Springerplus 2014;3(1):1-6.
12. Bandarkar FS, Vavia PR. A stability indicating HPLC method for the determination of meloxicam in bulk and commercial formulations. Trop J Pharm Res 2009;8(3):257-64.
13. Ahmad S, Deepika S, Amol P, Kapil W, Usman MR M. Novel RP-HPLC Method Development and Validation of meloxicam suppository. IJPER 2017;51(4):644-9.
14. Taha EA, Salama NN, Fattah LESA. Stability-indicating chromatographic methods for the determination of some oxicams. AOAC Int 2004;87(2):366-73.
15. Vignaduzzo SE., Castellano PM, Kaufman TS. Method development and validation for the simultaneous determination of meloxicam and pridinol mesylate using RP-HPLC and its application in drug formulations. J Pharm Biomed Anal 2008;46(2):219-25.
16. Induri M, Mantripragada BR, Yejella RP, Kunda PR, Arugula M, Boddu R. Simultaneous quantification of paracetamol and meloxicam in tablets by high performance liquid chromatography. Trop J Pharm Res 2011;10(4):475-81.
17. Ji HY, Lee HW, Kim YH, Jeong, DW, Lee H S. Simultaneous

determination of piroxicam, meloxicam and tenoxicam in human plasma by liquid chromatography with tandem mass spectrometry. J Chromatogr B 2005;826(1-2):214-9.

18. Zaman M, Murtaza H. Development and validation of RP-HPLC method for simultaneous estimation of tizanidine HCl and meloxicam in bilayer mucoadhesive buccal films. Acta Pol Pharm -Drug Res 2018;75(4):851-9.
19. Hassan EM. Spectrophotometric and fluorimetric methods for the determination of meloxicam in dosage forms. J Pharm Biomed Anal 2002;27(5):771-7.
20. Induri M, Mantripragada BR, Yejella RP, Kunda PR, Nannapaneni DT, Boddu R. Dissolution studies and quantification of meloxicam in tablet dosage form by spectrophotometry. Pak J Pharm Sci 2012;25(1):283-7.
21. Hasan SH, Othman NS, Surchi KM. Development and Validation of a UV-Spectrophotometric Method for Determination of Meloxicam in Bulk and in Tablet Formulations Int J Pharm Sci Res 2015;6(7):1040-5.
22. Chaudhary KB, Bhardwaj K, Verma G, Kumar P. Validated Analytical Method development for the determination of Meloxicam by UV Spectroscopy in API and Pharmaceutical dosage form. AJPER 2018;7(2):60-9.
23. García MS, Sánchez-Pedreño C, Albero MI, Martí J. Spectrophotometric methods for determining meloxicam in pharmaceuticals using batch and flow-injection procedures. Eur J Pharm Sci 2000;9(3):311-6.
24. Abed RI, Hadi H. Determination of meloxicam using direct and indirect flow injection spectrophotometry. Curr Pharm Anal 2021;17(2):254-64.
25. Mandrescu M, Spac AF, Dorneanu V. Spectrophotometric determination of meloxicam. Rev Chim 2009;60(2):160-3.
26. Dhandapani B, Eswara MS, Susrutha N, Rama S, Rani S, Sarath T, et al. Spectrophotometric estimation of meloxicam in bulk and its pharmaceutical formulations. Int J Pharm Sci Res 2010;1(4):217-21.
27. Rao RN, Meena S, Rao AR. An overview of the recent developments in analytical methodologies for determination of COX-2 inhibitors in bulk drugs, pharmaceuticals and biological matrices. J Pharm Biomed Anal 2005;39(3-4):349-63.
28. Gurupadayya BM, Trinath MN, Shilpa K. Spectrophotometric determination of meloxicam by sodium nitroprusside and 1, 10-phenanthroline reagents in bulk and its pharmaceutical formulation. Indian J Chem Technol 2013;20(3):111-5.
29. Basu, SK, Mandal S. Spectrophotometric methods for the estimation of meloxicam in dosage forms. Asian J Chem 2009;21(7):5184-8.
30. Salazar-Rojas D, Intilangelo A, Vignaduzzo SE, Maggio RM. Development and validation of a green method for dissolution monitoring of pharmaceutical combinations. Meloxican and Pridinol. J Pharm Biomed Anal 2019;170:228-33.
31. Bebawy LI. Stability-indicating method for the determination of meloxicam and tetracaine hydrochloride in the presence of their degradation products. Spectrosc Lett 1998;31(4):797-820.
32. Redasanı VK, Patel CF, Chhajed CF, Surana SS. Quantitative Determination of Meloxicam in bulk and in tablet by UV Spectrophotometry. Int J Pharm Drug Anal 2014;2(3):246-50.
33. Pomykalski A, Hopkała H. Comparison of classic and derivative UV spectrophotometric methods for quantification of meloxicam and mefenamic acid in pharmaceutical preparations. Acta Pol Pharm 2011;68(3):317-23.
34. Kus S, Marczenko Z, Obarski N. Derivative UV-VIS spectrophotometry in analytical chemistry. Chem Anal 1996;41(6):889-927.
35. ICH, I. Q2 (R1): Validation of analytical procedures: text and methodology. In International conference on harmonization, Geneva, 2005. pp.1-13.