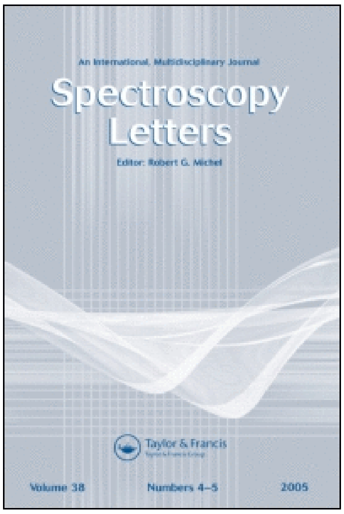

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Stability-Indicating Method for the Determination of Meloxicam and Tetracaine Hydrochloride in the Presence of their Degradation Products

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Stability – Indicating Method for the Determination of Meloxicam and Tetracaine Hydrochloride in the presence of their degradation products

Key words: Spectrophotometry; densitometry; stability-indicating method; determination of meloxicam and tetracaine hydrochloride; drug formulation.

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ABSTRACT : Sensitive, spectrophotometric and densitometric methdos are described for the determination of meloxicam I and tetracaine hydrochloride II in the presence of their degradation products.

Meloxicam was determined in the presence of its degradation products (5-methyl-2-aminothiazole) III and benzothiazine carboxylic acid IV by two methods. These methods are the first derivative spectrophotometry at 338 nm and TLC densitometric method at 365nm. The methods were applicable over the concentration range of 5-20μg.ml^{-1} and 2-10μg with mean accuracies of 99.66±0.91% and 99.99 ± 0.70% respectively.

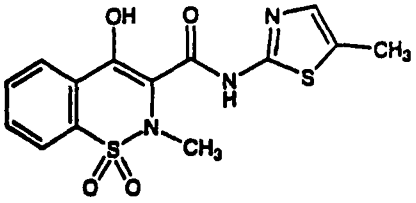
Tetracaine hydrochloride II was determined in the presence of its degradaion products, 4-(butylaminobenzoic acid) V and (N,N,-dimethylethanolamine) VI using the second and third derivative spectrophotometry at 338.6nm and 344.6 nm, respectively in the concentration range 2.5-15μg.ml^{-1} with mean accuracies of 99.91±0.60% and 99.81±0.78%, respectively. II was also determined by Glenn's method. This method gave accurate and reproducible results in the concentration range 2-10μg.ml^{-1} with a mean accuracy 99.59±0.54%.

The proposed methods were successfully applied to the determination of studied drugs in bulk powder, laboratory prepared mixtures containing different percentages of degradation products and pharmaceutical dosage forms.

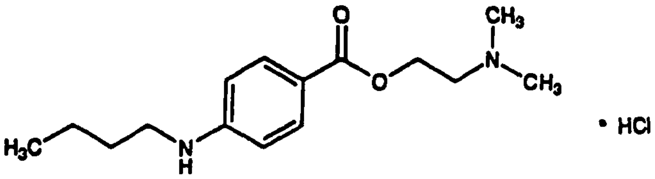
The results of the analysis were found to agree statistically with those obtained with either the official or the reported methods, furthermore the validity of the results was assessed by applying the standard addition technique.

Meloxicam I, is a nonsteroidal anti-inflammatory. Few methods have been published for the determination of I including spectrophotometry[1].

Tetracaine hydrochloride II, is used as local anaesthetic. Several methods have been reported for the analysis of II including spectrophotometry [2,3], colorimetry [4], GC[5], HPLC [6,7], potentiometry [8,9] and titrimetry [10]. The structures of I and II are shown in (Fig.1).



I - Meloxicam



II - Tetracaine Hydrochloride

Fig 1 . The structures of the studied drugs

The aim of this work is to establish simple, rapid, sensitive and reliable methods for routine quality control analysis and which can be used as stability-indicating assay.

EXPERIMENTAL

Materials :

- Meloxicam I, was kindly supplied by Boehringer Ingelheim. The purity of the sample was found to be 99.51 ±0.59% according to the reported method [1].

- Tetracaine hydrochloride II, was kindly supplied by Alcon-couvreur (Belgium). The purity of the sample was found to be 99.98 ± 0.50% according to the B.P. (1993) method [11].
- 4-(Butylaminobenzoic acid) V, was kindly supplied by Aldrich chemical company, Inc. U.S.A., its purity was labeled to be 98%.
- N,N-dimethylethanolamine VI, was kindly supplied by Aldrich chemical company, Inc. U.S.A., Its purity was labeled to be 98%.
- Mobic tablets (Boehringer Ingelheim Gmbh – Germany), batch No. 606814, 50001, labeled to contain 7.5 mg, and 15 mg meloxicam/tablet, respectively.
- Mobic capsules (Boehringer Ingetheim Gmbh-Germany), batch No. 40310, 40312, labeled to contain 7.5 mg and 15 mg meloxicam / capsule, respectively.
- Tetracaine hydrochloride ophthalmic solution (Alcon-couvreur – (Belgium), batch No. 94 H_24, 95J18, labeled to contain 0.5%.
- **Degradation products of meloxicam.**

The degradation products of meloxicam were laboratory prepared by heating 50 mg of meloxicam powder with 50 ml. 1N sodium hydroxide solution for 4hrs. The solution was cooled, neutralized with 1N hydrochloric acid, concentrated to about 2 ml and transferred to a 10-ml volumetric flask and complete to volume with methanol. 100 μl was applied in a band form on TLC plates. 10 μl of standard meloxicam solution (400μq. ml^{-1} in methanol containing 1ml 1N sodium hydroxide) was spotted. The plate was developed to 16 cm. with ethylacetate-methanol-concentrated ammonia (85:10:5 v/v) as mobile phase, then removed and air dried. The band corresponding to each of the degradation product was visualized under UV lamp at 254nm, scratched, extracted with 3 X 20 ml methanol containing 1N sodium hydroxide, filtered and evaporated just to dryness on a boiling water bath. The residue left after evaporation was used for the preparation of laboratory prepared mixtures.

Standard stock solutions.

- Meloxicam I. Weigh, accurately, about 25 mg of meloxicam into a 50-ml volumetric flask, add 0.5 ml 1 N sodium hydroxide and 30 ml methanol, shake well to dissolve the powder and complete to volume with methanol (0.5 $mg.ml^{-1}$).
- Degradation products of meloxicam 0.5 $mg.ml^{-1}$ in methanol containing 0.5 ml 1N sodium hydroxide.
- Tetracaine hydrochloride II-Dissolve an accurately weighed amount of the drug equivalent to 50 mg. Base in 10 ml water, render alkaline with ammonia and extract with 4 X 20ml chloroform. Wash the chloroform extract with water, filter over anhydrous sodium sulphate, evaporate with stream of nitrogen and dissolve in 100ml acetonitrile (0.5 $mg.ml^{-1}$) for derivative spectrophotometry.
- Tetracaine hydrochloride 40$\mu g.ml^{-1}$ in methanol for Glenn's method.
- 4-(Butylaminobenzoic acid) V,0.5 mg/ml^{-1} in acetonitrile and 40$\mu g.ml^{-1}$ in methanol.

Laboratory prepared mixtures :

A. For meloxicam.

A.i. For derivative spectrophotometric method:

Transfer accurately aliquot portions equivalent to 50-200µg of meloxicam from its stock solution (0.5 $mg.ml^{-1}$) into a series of 10-ml volumetric flasks. Add aliquot portions equivalent to 45-20 μg of degradation products from its stock solution (0.5 mg.ml^{-1}) to the same flasks. Complete to the mark with 0.1 N sodium hydroxide.

A.ii. For densitometric method :

Transfer accurately aliquot portions (0.5 – 2.25 mg) of meloxicam from its stock solution (0.5 mg.ml^{-1}) into a series of 5-ml volumetric flasks. Add from 10-90% of the degradation products using the prepared stock solution (0.5 mg.ml^{-1}).

B. For tetracaine hydrochloride :

B.i. For derivative spectrophotometric method :

Prepare mixtures of tetracaine hydrochloride and its degradation products containing 25-150μg of the first from its stock solution (0.5 mg.ml^{-1}) and 10-90% of the latter (0.5 mg.ml^{-1}) into a series of 10-ml volumetric flasks. Complete to volume with 0.001 N sodium hydroxide.

Reagents :

All chemicals used throughout this work were analytical grade.

- Acetonitrile (E. Merck).
- Methanol (E. Merck).
- Sodium hydroxide, 0.001N, 0.1N and 1N Aqueous solution.
- Hydrochloric acid, 1N Aqueous solution.
- Ethyl acetate – methanol – concentrated ammonia (85: 10: 5v/v) as mobile phase for meloxicam.

Apparatus :

- UV./VIS. Spectrophotometer SHIMADZU UV-160I PC.
- SHIMADZU – Dual wavelength flying CS-9301 PC densitometer.

- UV short wavelamp (254 nm).
- TLC plates (20 X 20cm.) with 0.25 mm thickness silica gel GE 254, (E. Merck).

Procedures :

1- For meloxicam

1.a. Spectrohotometric method.

1.a.i. Construction of calibration curves.

Transfer accurately aliquot portions equivalent to 50-200μg of meloxicam from its stock solution into a series of 10-ml volumetric flasks and complete to volume with 0.1 N sodium hydroxide. Record the first derivative curve of each solution and measure D_1 value at 338 nm. against 0.1 N sodium hydroxide as a blank.

1.a.ii. Assay of laboratory pepared mixtures :

Record the first derivative spectrum of laboratory prepared mixtures containg different ratios of meloxicam and its degradation products. Measure D_1 value at the previously chosen wavelength. Calculate the concentration of meloxicam from the regression equation. Results obtained are shown in (Table 1).

1.b. Densitometric method :

1.b.i. Construction of calibration curves:

Transfer accurately aliquot volumes equivalent to (0.5-2.25 mg) of meloxicam from its stock solution (0.5 $mg.ml^{-1}$) to a series of 5-ml volumetric flasks then complete to volume with methanol. Apply 20μl of each solution to a high performance thin layer chromatographic plate (20 X20cm.) using a 20μl pipette. Develop the plate to 16 cm using ethyl

Table (1) : Comparison between the proposed methods and the official and reported methods for the determination of meloxicamand tetracaine hydrochloride in the presence of their degradation products.

Exp. No.	% of Degradation product	Meloxicam			Tetracaine hydrochloride		
		First derivative	Denistometric method	Reported method	Second derivative	Third derivative	Official method
		Recovery, %	Recovery, %	Recovery, %	Recovery, %	Recovery, %	Recovery, %
1	10	100.22	99.48	104.51	99.21	100.40	110.00
2	30	99.21	98.91	107.22	99.60	100.29	130.31
3	50	99.53	100.30	110.00	100.42	99.91	151.25
4	70	100.01	100.45	112.13	100.10	99.83	160.43
5	80	99.89	99.82	124.50	99.42	100.50	175.11
6	90	109.2**	99.71	135.75	108.11**	109.56**	190.61
	Mean	99.77	99.78		99.75	100.19	
	C.V.	0.40	0.56		0.50	0.30	

** Rejected %.

acetate-methanol – concentrated ammonia (85 : 10 : 5v/v) as mobile phase then air dried. Detect the spots under UV lamp and scan at 365 nm (Photomode : reflection, scan mode : zigzag). Plot the calibration curve represinting the relationship between the recorded area under the peak and the corresponding concentration.

1.b.ii. Assay of laboratory prepared mixtures :

Apply 20 µl of different samples of the laboratory prepared mixtures to a high performance thin layer chromatographic plate. Proceed as mentioned under calibration curves 1,b.i. starting from "Develop the plate to 16 cm..."

1.c. Dosage forms:

1.c.i. Tablets :

Weigh accurately twenty tablets and grind to fine powder. Transfer a weight of powder equivalent to 25 mg of meloxicam into a 50–ml volumetric flask, add 0.5 ml 1 N sodium hydroxide, 30 ml methanol shake well and complete to volume with methanol. Filter and complete as under 1,a spectrophotometric method starting with the words "Tranfer accurately aliquot portions equivalent to 50-200µg of meloxicam .." and as under 1,b. Densitometric method starting with the words "Transfer accurately aliquot volumes equivalent to (0.5 –2.25 mg).......".

1.c.ii. Capsules :

Evacuate the contents of 20 capsules, mix thoroughly, weigh, and calculate the average weight in each capsule. Transfer an accurate weight of the mixed sample, equivalent to 25 mg of meloxicam into a 50 – ml volumetric flask, complete as under 1,c,i. Tablets starting with the words "add 0.5 ml 1 N sodium hydroxide....".

1. For tetracaine hydrochloride :

2.a. Spectrophotometric method.

2.a.i. Construction of calibration curve.

Transfer accurately aliquot portions equivalent to 25-150μg of tetracaine hydrochloride from its stock solution (0.5 $mg.ml^{-1}$) into a series of 10-ml volumetric flasks then complete to volume with 0.001 N sodium hydroxide. Record the second and third derivative curves of each solution and measure D_2 and D_3 values at 338.6nm and 344.6nm, respectively against 0.001 N sodium hydroxide as a blank.

2.a.ii. Assay of laboratory prepared mixtures :

Record the second and third derivative curves of laboratory prepared mixtures containing different ratios of tetracaine hydrochloride and its degradation products. Measure D_2 and D_3 values at the previously chosen wavelengthes. Calculate the concentration of tetracaine hydrochloride from the regression equation. Results obtained are shown in (Table 1).

2.a.iii. Dosage forms

Ophthalmic formulations

Transfer an accurately measured volume of II equivalent to 50 mg base into a 100 – ml separating funnel, complete as under stock solution of tetracaine hydrochloride II starting from "render alkaline with ammonia.." Determine II spectrophotometry as under 2.a.i.

2.b. Glenn's method :

2.b.i. Contruction of calibration curves :

In 10 ml volumetric flasks, prepare mixtures of tetracaine hydrochloride II and its degradation product V. Dilute with methanol so that the concentration of either compound is in the range cited in (Table 2). Measure the absorbance (A_1 and A_2) of the mixture in a 1cm cell at 303nm, and 311nm. Calculate the concentration of the two compounds from the following equations :

$C_X = A_1 / \alpha_1 (b-m) / (b-a)$.

$C_y = A_2 / B_2 [b(m-a) / m(b-a)]$

Where C_x is the concentration of tetracaine hydrochloride in g/100 ml and C_y is the concentration of its degradation product V in g/100ml α_1 and α_2 are $A^{1\%}_{1cm}$ values for II at λ_1 and λ_2 respectively; B_1 and B_2 are the $A^{1\%}_{1cm}$ values for degradation product V at λ_1 and λ_2 respectively/ $m = A_2/A_1$; $a = \alpha_2/\alpha_1$; and $b = B_2/B_1$.

2.b.ii, For ophthalmic formulation.

Transfer an accurately measured volume of drops equivalent to 40μg.ml^{-1} of tetracaine hydrochloride to 100-ml volumetric flask and dilute to the mark with methanol. Proceed as under 2.b.i. Construction of Calibration curves.

RESULTS AND DISCUSSION

1- For meloxicam

Two degradation products were separated from alkaline hydrolysis of meloxicam namely, 5-methyl-2- aminothiazole III which was identified by Marshal reagent and benzothiazine carboxylic acid IV. Zero-order absorption spectrum of III showed slight interference at λ max of meloxicam 365.nm while IV had no absorbance at the same wavelength (Fig.2). To overcome this interference, derivative

Table (2): Performance data for the determination of tetracaine hydrochloride in the presence of 4-(butylaminobenzoic acid) by Glenn's method.

Compound	Concentration Range ($\mu g.ml^{-1}$)	$\lambda_1 = 303$ nm				$\lambda_2 = 311$ nm			
		$A^{1\%}_{1cm}$*	Intercept	Slope	Correlation coefficient	$A^{1\%}_{1cm}$	Intercept	Slope	Correlation coefficient
Tetracaine hydrochloride	2-10	946.30	0.02	0.09	0.9996	1010.00	-0.007	0.103	0.9998
4-(butylamino-benzoic acid)	2-8	1220.71	-0.04	0.131	0.9992	1055.70	-0.06	0.12	0.9996

*Average of seven determination.

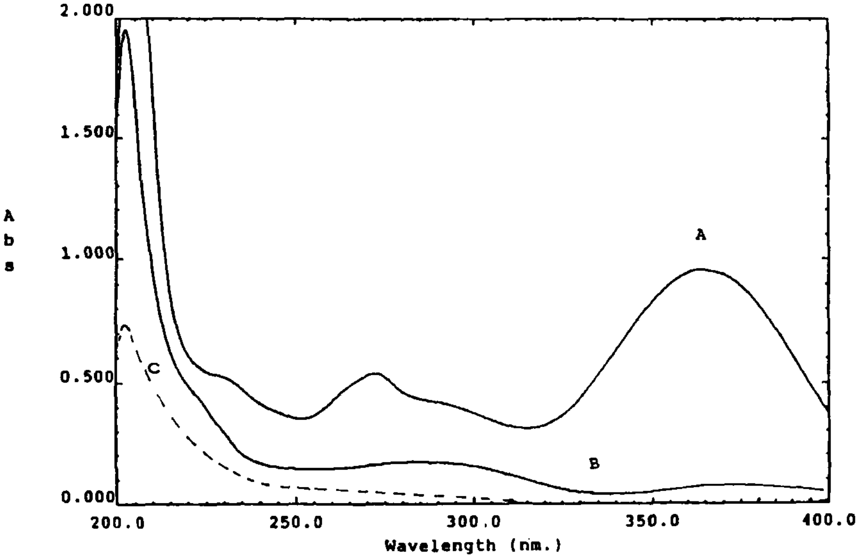


Fig 2 : Zero Order Absorption Spectra of Meloxican (A) and its Degradation Product (B) & (C) in 0.1N Sodium Hydroxide. 20μg. ml^{-1} of each

spectrophotometry and densitometric stability-indicating methods were developed for the determination of intact I in the presence of its degradation products III and IV.

1.a. Derivative spectrophotometric method

The principle advantage of derivative spectrophotometry is the improvement of resolution of overlapping absorption bands, the accuracy and precision of UV absorption methods are considerably improved.

First derivative technique is used to resolve such spectral overlapping as shown in (Fig.3). By applying the first derivative technique, zero-crossing points for the degradation products were

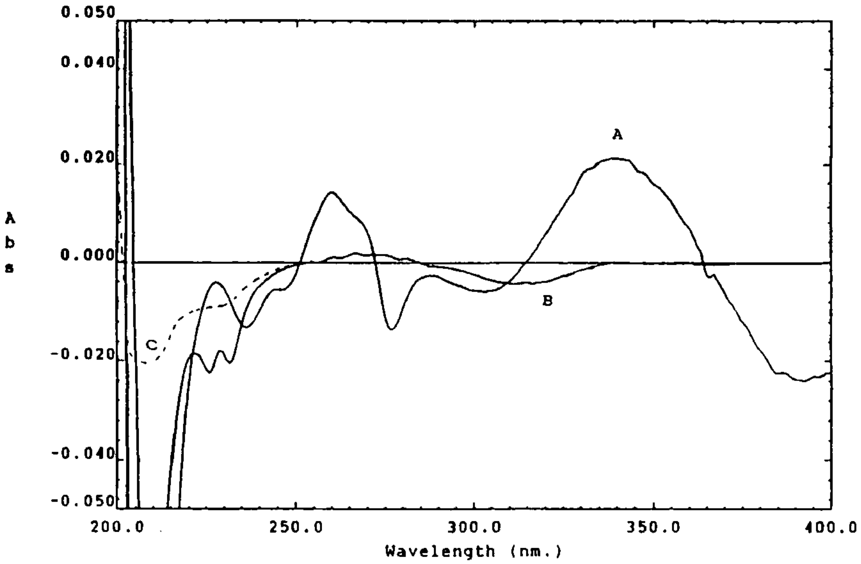


Fig 3 : First Derivative Spectra of Meloxican (A) and its Degradation Product (B) & (C) in 0.1N Sodium Hydroxide . $20 \mu g . ml^{-1}$ of each

showen at 338 nm. and a linear correlation was obtained between D_l value and the concentration range of (5-20 $\mu g.ml^{-1}$) for intact meloxicam from which the linear regression equation was calculated.

$D_l = 0.001 + 0.001\ C$, $r = 0.9991$.

Where D_l is the first derivative value, C is concentration in $\mu g.ml^{-1}$ and r is correlation coefficient.

The proposed method is valid and applicable for the determination of intact meloxicam in presence of up to 80% of its degradation products, with mean percentage recovery of 99.77 ± 0.40%.

1.b. Densitometric method

TLC is known to be one of the simplest chromatographic separation technique, the quantitative TLC scanning allows the application of the method for microquantitative analysis. Thus, a densitometric method was suggested for the determination of meloxicam in the presence of its degradation products. Complete separation was obtained using ethyl acetate-methanol – concentrated ammonia (85 : 10 : $5^{v}/_{v}$) as a mobile phase. Meloxicam shows R_f value 0.38 while its degradation product III has R_f value 0.78 and IV has zero R_f. Quantitatively the chromatogram was scanned at 365 nm.

By applying this technique a linear correlation was obtained between the area under the peak and concentration in the range of (2-10 μg) from which the linear regression equation was calculated.

$$A = 0.15 + 0.645\ C, \qquad r = 0.9991$$

Where A is the area under the peak, C is concentration in μg and r is correlation coefficient.

The proposed method is valid for the determination of meloxicam in presence of up to 90% of its degradation products, with mean percentage recovery of 99.78 ± 0.56%.

2- For tetracaine hydrochloride

Tetracaine solution suffers hydrolytic degradation which results in the formation of p-n-butylaminobenzoic acid and diethylaminoethanol. P-n-Butylaminobenzoic acid is sparingly soluble in water and it can cause crystal deposition in tetracaine hydrochloride solution on storage[12]. Therefore, it was necessary to develop simple analytical methods to determine the intact drug in the presence of degradation products.

2.a. Derivative spectrophotometric method

Zero-order absorption spectra of tetracaine hydrochloride II and its degradation product V in 0.001 N sodium hydroxide showed certain overlapping which interferes with the direct determination of intact II as shown in (Fig.4) while the degradation product VI showed an absorbance at 205 nm which is far from the λ max of the intact II (305 nm). To ovecome this overlapping derivative spectrophotometry was used for the determination of intact II in presence of its degradation product V (Fig. 5,6). Different molarities of sodium hydroxide were tried, 0.001 N was found to be the optimum.

Applying the second and third derivative technique showed zero-crossing points for the degradation products at 338.6 nm and 344.6 nm, respectively. Linear correlation were obtained between D_2 and D_3 values and the concentration range of 2.5 – 15 $\mu g.ml^{-1}$ for D_2 and D_3 from which the linear regression equation was calculated.

$D_2 = 0.0068 + 0.0246C, \quad r = 0.9996.$

$D_3 = 0.017C - 0.002, \quad r = 0.9995.$

where D_2, D_3 is the second and third derivative values, C is concentration in $\mu g.ml^{-1}$ and r is correlation coefficient.

The proposed method is valid for the determination of II selectively in presence of up to 80% of its degradation products V with mean percentage recovery of 99.75 ± 0.50% and 100.19 ± 0.30% for D_2 and D_3, respectively.

2.b. Glenn's method.

The zero-order spectra of tetracaine hydrochloride and its degradation product V in the range 200-350nm wavelength region are shown in (Fig.7). It can be seen that the absorption spectra of II and V are very similar and show prominent peaks that can not be used for

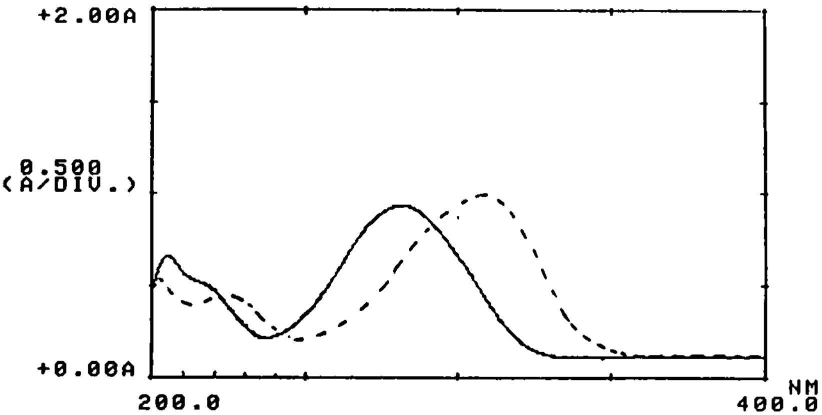


Fig 4 : Zero-Order Absorption Spectra of Tetracaine Hydrochloride (. . .) and its Degradation Product (—) in 0.001 N Sodium Hydroxide. 10μg. ml^{-1} of each

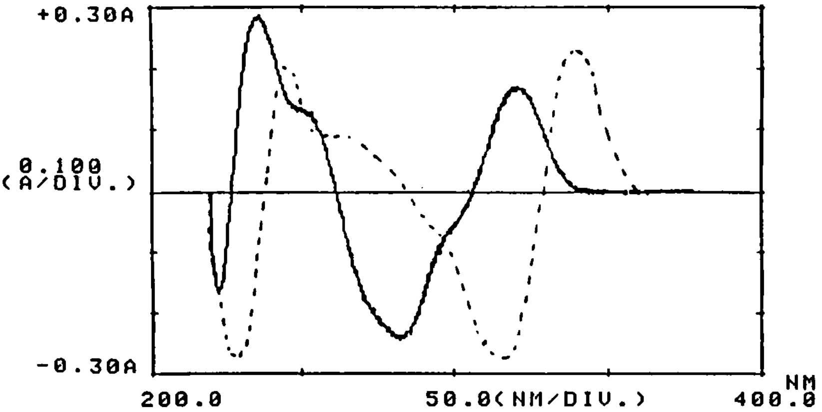


Fig 5 : Second Derivative Spectra of Tetracaine Hydrochloride (. . .) and its Degradation Product (—) in 0.001N Sodium Hydroxide. 10μg. ml^{-1} of each

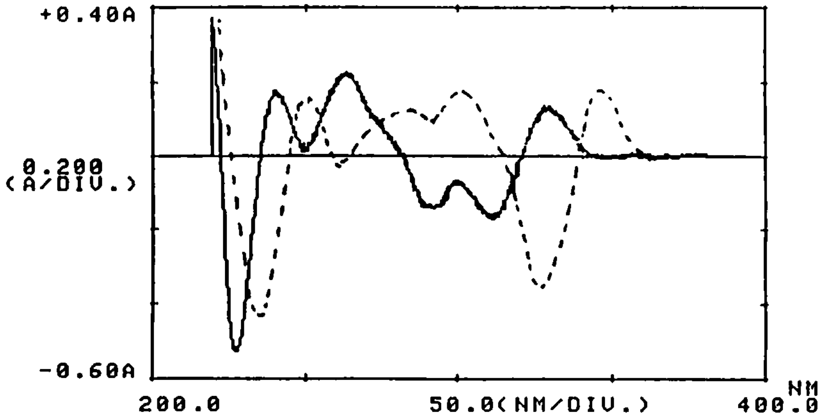


Fig 6 : Third Derivative Spectra of Tetracaine Hydrochloride (. . .) and its Degradation Product (——) in 0.001N Sodium Hydroxide 10μg. ml^{-1} of each

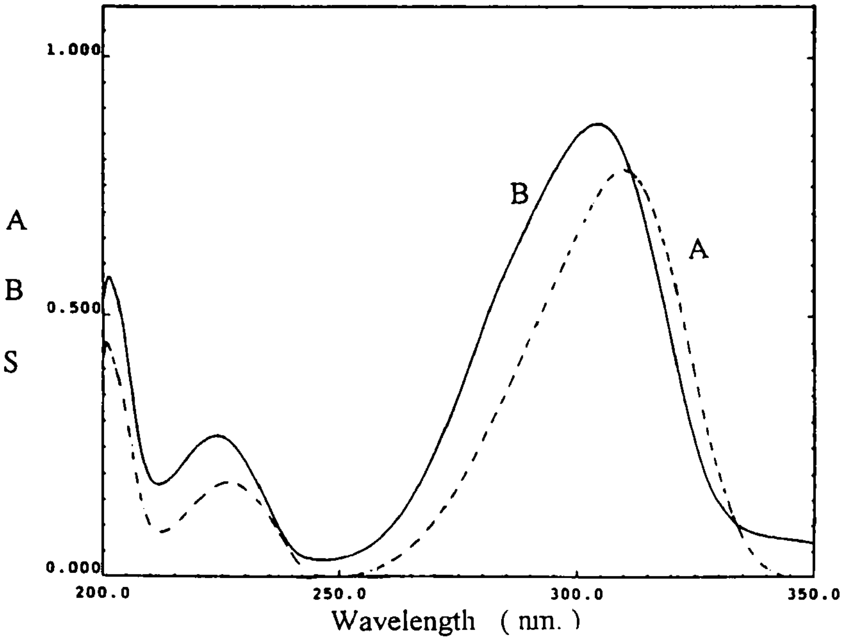


Fig 7 : Absorption Spectra of (A) Tetracaine hydrochloride,

(B) 4- Butylaminobenzoic acid (7μg.ml)

Table (3) : Application of Glenn's method for the analysis of tetracaine hydrochloride and 4-(butylaminobenzoic acid).

	Added ($\mu g.ml^{-1}$)		Recovery, %	
	Tetracaine hydrochloride	4-(butylamino-benzoic acid	Tetracaine hydrochloride	4-(butylamino-benzoic acid)
Authentic sample				
1	4.00	0.40	100.23	99.79]
2	4.00	1.00	99.81	100.11
3	4.00	2.00	98.77	99.23
4	4.00	3.00	99.69	99.56
5	4.00	3.60	99.45	99.74
Mean			99.59	99.69
C.V.			0.54	0.32
Tetracaine Hydrochloride Ophthalmic Solution (0.5%)				
- B.N 94 H24	4.00	1.00	99.12	98.78
	4.00	2.00	101.15	99.55
	4.00	3.60	99.61	99.32
Mean			99.96	99.22
C.V.			1.06	0.39
B.N. 95 J18	4.00	1.00	99.57	99.51
	4.00	2.00	99.64	98.96
	4.00	3.60	100.12	99.44
Mean			99.78	99.30
C.V.			0.30	0.30

reliable direct absorption measurements of the mixture. (Fig. 7) shows that 303 and 311 nm are suitable wavelengths for measurement. The performance data for the analysis of the mixture by Glenn's method are shown in (Table 2). The results obtained from the analysis of authentic mixture, are given in (Table 3).

To assess the stability – indicating efficiency of the proposed methods, the degradation products of I and II were mixed separately with their authentic samples in different ratios and analysed by the proposed sepectrophotometry and densitometric methods. The results obtained are shown in (Table 1,3).

Table (4) : Comparison between the proposed methods* and the reported method** for the determination of meloxicam in pure and in dosage forms.

Preparations	First derivative method	Standard addition	Densitometric method	Standard addition	Reported method
	Found % ± C.V.	Recovery, % ± C.V.	Found % ± C.V.	Recovery, % ± C.V.	Found % ± C.V.
- Pure sample	99.66 ± 0.91		99.99± 0.70		99.51 ± 0.59
- Mobic tablets 7.5 mg/tablet	99.81 ± 0.50	100.21 ± 0.42	99.36 ± 0.36	99.51 ± 0.60	100.40 ± 0.31
- Mobic tablets 15mg/ tablet	100.26 ± 0.49	99.09 ± 0.51	99.80 ± 0.31	99.22 ± 0.60	99.26 ± 0.49
- Mobic capsules 7.5 mg/capsule	99.61 ± 0.39	99.49 ± 0.56	99.11 ± 0.20	99.79 ± 0.29	99.51 ± 0.62
- Mobic capsules 15 mg/capsule	99.40 ± 0.20	100.50 ± 0.62	100.50 ± 0.62	99.91 ± 0.60	99.71 ± 0.90

• Mean of three determinations.

** Mean of three determinations.

Table (5) : Comparison between the proposed methods* and the official method** (B.P. 1993) for the determination of tetracaine hydrochloride in pure and in dosage forms.

Preparations	Second derivative method	Standard addition	Third derivative method	Standard addition	Official method**
	Found % ± C.V.	Recovery, % ± C.V.	Found % ± C.V.	Recovery, % ± C.V.	Found % ± C.V.
- Pure sample	99.91 ± 0.60		99.81 ± 0.78		99.98 ± 0.50
- Tetracaine hydrochloride ophthalmic solution	100.22 ± 0.31				
- B.N 94 H24	99.89 ± 0.49	99.90 ± 0.54	99.52 ± 0.83	100.72 ± 0.19	100.60 ± 0.32
- B.N. 95 J18		100.00 ± 0.31	99.11 ± 0.70	100.40 ± 0.31	99.91 ± 0.72

* Mean of five determinations.

** Mean of three determinations.

Table (6) : Statistical comparison between the determination of meloxicam and tetracaine hydrochloride by the proposed and the official and reported method.

	Meloxicam			Tetracaine hydrochloride			
	First derivative method	Densitometric method	Reported method	Second derivative method	Third derivative method	Glenn's method	Official Method
Range of concentration	5 – 20 $\mu g.ml^{-1}$	2-12 μg	5-20 $\mu g.ml^{-1}$	2.5-15 $\mu g.ml^{-1}$	2.5-15 $\mu g.ml^{-1}$	2 – 10 $\mu g.ml^{-1}$	30 – 300 mg
C.V	0.91	0.70	0.59	0.60	0.78	0.54	0.50
Correlation coefficient	0.9991	0.9991		0.9996	0.9965	0.9998	
Variance	0.83	0.49	0.35	0.36	0.61	0.29	0.25
N	5	7	6	5	5	5	6
F	1.03 (5.2)	1.49 (5.0)		1.44 (5.2)	2.43 (5.2)	1.16 (5.2)	
t	0.50 (2.262)	1.22 (2.201)		1.13 (2.262)	0.44(2.262)	1.11 (2.262)	

The proposed methods were applied to the analysis of meloxicam and tetracaine hydrochloride in their dosage forms, the results obtained are shown in (Table 3,4,5).

The validity of the proposed methods was assessed by applying the standard addition technique as well as in the presence of degradation products. The results are presented in Table (3,4,5).

(Table 6) shows statistical comparison of the results obtained by applying the proposed methods and official and reported methods, from which the calculated t and F are less than that the corresponding theoretical values indicating that there is no significant difference between the two methods with respect to both precision and accuracy.

The main advantage of the suggested methods over other methods is that, with the exception of the HPLC, they are applicable in the presence of the degradation products. Also, they give accurate and reproducible results when applied to the analysis of pharmaceutical preparations. Moreover, the methods are inexpensive, rapid, sensitive and selective.

REFERENCES

1- Spectrophotometry manufacturer procedure supplied by Boehringer Ingelheim by personal communication.

2- M. I. Arufe Martinez and J.L. Romero Palanco, J. Anal. Toxicol., 12(4), 192-196 **(1988)**.

3- M.I. Arufe Martinez, J.L. Romero Palanco, J. Gamero Lucas and M.A. Vizcaya Rojas, J. Anal. Toxicol., 13 (6), 345-349 **(1989)**.

4- M.E. El-Kommos and M.B. Sidhom, Arch. Pharm. Chemi, Sci. Ed., 10(2-3), 57-60 **(1982)**.

5- M. Culea, N. Palibroda, Z. Moldovan, A.D. Abraham and P.T. Frangopol, Chromatographia, 28 (1-2), 24-26 (1989).

6- M. Bauer, C. Degude and L. Mailhe, J. Chromatog. 315, 457-464 **(1984)**.

7- D.P. Wang, Y.H. Tu. And L.V. Allen Jun, Chung hua Yao Hsueh Tsa Chih, 40 (3), 143-150 **(1988)**.

8- H. Satake, T. Miyata and S. Kaneshina, Bull. Chem. Soc. Jpn., 64 (10), 3029-3034 **(1991)**.

9- N.A. Zakhari, S.M. Ahmed and K.A. Kovar, Pharmeuropa, 3(4), 269-273 **(1991)**.

10- M. Qiu, Yaoxue Tongbao, 21(3), 144 **(1986)**.

11- British Pharmacopeia, Her Majesty's Stationery Office, London, p. 36 **(1993)**.

12- K. Florey (Ed.), Analytical profiles of Drugs Substances, vol. 18, pp. 379-411. Academic Press, New York **(1989)**.

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