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SPECTROSCOPIC METHODS FOR THE DETERMINATION OF FLURBIPROFEN AND TIAPROFENIC ACID

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ABSTRACT

Flurbiprofen and tiaprofenic acid reacted easily and quantitatively with copper acetate forming bluish green precipitates. The drugs were determined colourimetrically by extracting the formed precipitates in chloroform and measuring the absorbance at 686 nm for flurbiprofen and 696 nm for tiaprofenic acid.

To improve the sensitivity of the method the formed precipitates of these drugs with copper were dissolved in the least amount of dilute ammonia and the copper content was determined via reaction with sodium diethyldithiocarbamate. The formed yellow colour was measured at 447 nm. Flurbiprofen was also estimated using atomic absorption spectrometer procedure through the determination of the copper content of the precipitate. The optimum conditions for precipitation have been carefully studied. The molar ratio of the reactants were accertained. Statistical analysis of the results obtained were compared with the official methods. Results obtained were of equal accuracy and repreducibility. The proposed methods were successfully applied for determination of flurbiprofen and tiaprofenic acid in their pharmaceutical dosage forms and the results obtained were in good agreement with those of the official methods.

INTRODUCTION

Both flurbiprofen and tiaprofenic acid are propionic acid derivatives of significant advantages for patients over aspirin, indomethacin and pyrazolones as analgesics anti-inflammatory agents, since they are usually better tolerated[1]. Several methods have been recommended for their determination, including titrimetric[2], spectrophotometric[3-5], and high pressure liquid chromatographic mehods [6-9].

Previously, copper (II) was used for the determination of tiaprofenic acid by atomic absorption spectrometer[10], and used as analytical reagent for spectrophotometric anylsis[11] of ibuprofen, naproxen and ketoprofen.

In the present work a colourimetric method was suggested for the determination of flurbiprofen and tiaprofenic acid and A.A.S technique for determination of flurbiprofen.

EXPERIMENTAL

Apparatus

Shimadzue atomic absorption flame spectrophotometer. Model AA 460-13. Shimadzue UV-visible recording spectrophotometer UV-260.

MATERIALS AND REAGENTS

Materials used in this work were obtained from the following soureces :

1. Pure flurbiprofen (Kahira-Boots).
2. Froben tablets (Kahira-Boots), labelled to contain 100 mg flurbiprofen per tablet.
3. Froben suppositories (Kahira-Boots), labelled to contain 100 mg flurbiprofen per suppository.
4. Pure tiaprofenic acid (Roussel uclaf Co.).
5. Surgam tablets (Roussel Co., Egypt), labelled to contain 100 mg tiaprofenic acid per tablet.
6. Surgam suppositories (Roussel Co., Egypt), labelled to contain 300 mg tiaprofenic acid per suppository.
7. Copper acetate (Prolabo), 0.5% W/V aqueous solution.
8. Sodium diethyldithiocarbamate (BDH), 0.1% W/V aqueous solution.
9. Ammonium hydroxide 50% (May & Baker).
10. Ethyl alcohol (Merck).
11. Chloroform (Prolabo).
12. Standard solution with concentration 2.5 mg ml^{-1} of fluriprofen and tiaprofenic acid were prepared by dissolving 250 mg of each drug separately in about 50 ml alcohol, the solution rendered neutral to phenol red with 0.1 N sodium hydroxide and completed to 100 ml in volumetric flask with deionized water.

Preparation of tablet solutions

Twenty tablets were weighed and finely powdered. A quantity of the powdered tablets equivalent to 250 mg of flurbiprofen or tiaprofenic acid was transferred to 100 ml volumetric flask and shaken with 50 ml ethanol, the solution rendered neutral to phenol red with 0.1 N sodium hydroxide filtration was carried out and volume completed using deionized water.

Preparation of suppository solutions

Ten suppositories were weighed, placed in small dish, melted on steam bath and mixed by stirring. The melted suppositories were cooled. A portion of the mass equivalent to 250 mg of flurbiprofen or tiaprofenic acid was transferred to a beaker extracted with three portion of warming ethanol (20, 20, 10 ml), the extract was collected in 100 ml volumetric flask, neutralized to pH (7.1 - 8.1) with 0.1 N sodium hydroxide filtered and the volume completed with deionized water.

PROCEDURES

A. Direct colourimetric method

To different aliquots of the standard solutions or dosage forms equivalent to (5 - 35 mg flurbiprofen) and (4 - 24 mg tiaprofenic acid), 10 ml of copper acetate solution was added, shaken in separating funnel, then extracted with two portions of chloroform (2 x 5 ml). The extracts were collected and shaken with anhydrous sodium sulphate then filtered into 10 ml volumetric flask, the volume completed and the absorbance was measured at 686 nm for flurbiprofen and 696 nm for tiaprofenic acid against a blank carried out similarly omitting the drug addition.

B. Indirect colourimetric method

To different aliquots of the standard solutions or dosage forms equivalent to (3 - 13 mg flurbiprofen or tiaprofenic acid) 5 ml of copper acetate solution was added, shaken well and filtered. The precipitate was washed with deionized water till copper free. The obtained precipitate was dissolved in 5 ml of dilute ammonia solution, transferred into 25 ml volumetric flask, the volume was completed with deionized water. Two ml of the above solution were transferred into 10 ml volumetric flask, then 5 ml of sodium diethyldithiocarbamate solution were added. The volume was completed to the mark with deionized water and the absorbance of the solution was measured at 447 nm against blank.

C. The atomic absorption method

The same procedure mentioned under (B) for flurbiprofen only was carried out using the same concentration (3 - 13 mg) for both the pure and dosage forms. The collected precipitate dissolved in 5 ml of ammonia solution and volume completed to 50 ml in volumetric flask with deionized water. The absorbance was measured at the following conditions: wave length 327.7 nm, lamp current 7 mA, slit width 3.8 A, air pressure 10 L /min, and acetylene pressure 2.3 L /min.

RESULTS AND DISCUSSION

The procedure described in this work for the determination of flurbiprofen and tiaprofenic acid based upon their precipitation as copper salt and subsequent determination of the copper content by A.A.S for flurbiprofen or extracting the formed precipitate with chloroform, then measuring the absorbance at 686 nm for flurbiprofen and 696 nm for tiaprofenic acid. Moreover, these drugs could be determined by indirect method through reacting the formed copper salt with sodium diethyl dithiocarbamate and measuring the obtained colour at 447 nm.

Variable parameters affecting the precipitation process were optimized. Alcohol was added to solubilize the drugs and to help the coagulation of the precipitate. The medium was neutralized to pH (7.1-8.1). In acidic medium the formed precipitate was dissolved, while the alkaline medium precipitate the copper as hydroxide.

Many solvent (benzene, n -hexane, carbon tetrachloride and chloroform) were tried to extract, the formed salt, only chloroform proved to be the most suitable. The amount of copper (II) concentration was also studied and found that 10 ml of 0.5% of copper acetate solution were sufficient for complete precipitation in the direct colourimetric method while 5 ml of the same reagent were sufficient for the A.A.S procedure and the indirct method due to the lower concentration of the drugs used.

For further study of the reaction the molar ratio of flurbiprofen and tiaprofenic acid to the copper (II) were determined by Job's method [12]. The exact results were obtained by performing C,H, Cu microelemental analysis and found to be 2 : 1 (drug : Cu) Fig.(1,2).

On studying the absorption concentration relationship the range was found to be 0.5 - 3.5 mg ml^{-1} for flurbiprofen and 0.2 - 2.4 mg ml^{-1} tiaprofenic acid in case of the direct colourimetric method with regression equations.

Conc = 26.901. Abs + 0.3467 for flurbiprofen

Conc = 26.507. Abs + (-0.398) for tiaprofenic acid.

Great improvement in the sensitivity was obtained upon applying the indirect colourimetric procedure.

Bear's Law was obeyed at the concentration ranges 24-104 μgm^{-1} for both flurbiprofen and tiaprofenic acid by the indirect procedure with regression equations.

Conc = 9.6951. Abs + 0.1921 for flurbiprofen.

Conc = 14.829. Abs + (-2.3951) for tiaprofenic acid.

In applying the atomic absorption method for determination of flurbiprofen, the absorption concentration relationship was found to be 60-260 mg ml^{-1} with the following regression equation.

Conc = 0.0124. Abs + (-2.0224).

The proposed methods were successfully applied for the determination of pure flurbiprofen and tiaprofenic acid, the results obtained were compared with the official methods. Statistical analysis of the results revealed that there is no significant difference between them (Tables 1).

Zagazig J. Pharm. Sci. December, 1996
Vol. 5, No. 2, pp.138-142

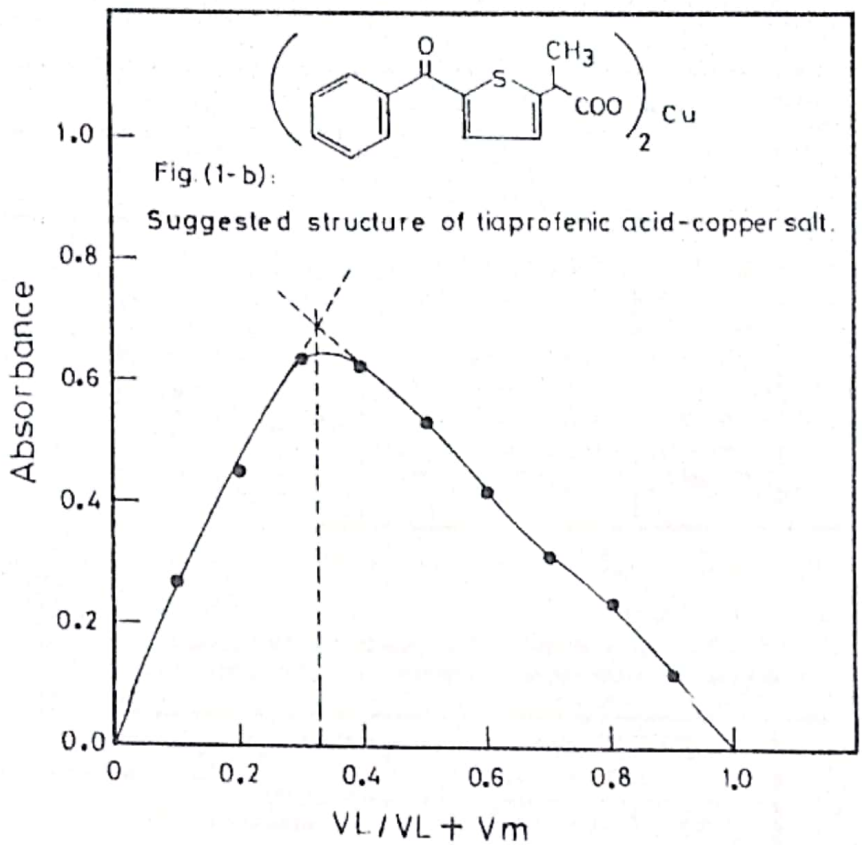

Fig. (1-b):
Suggested structure of tiaprofenic acid-copper salt.

Fig.(1-a) Continuous variation plot obtained from tiaprofenic acid ($5x10^{-2}$M) and copper acetate ($5x10^{-2}$M) in chloroform.

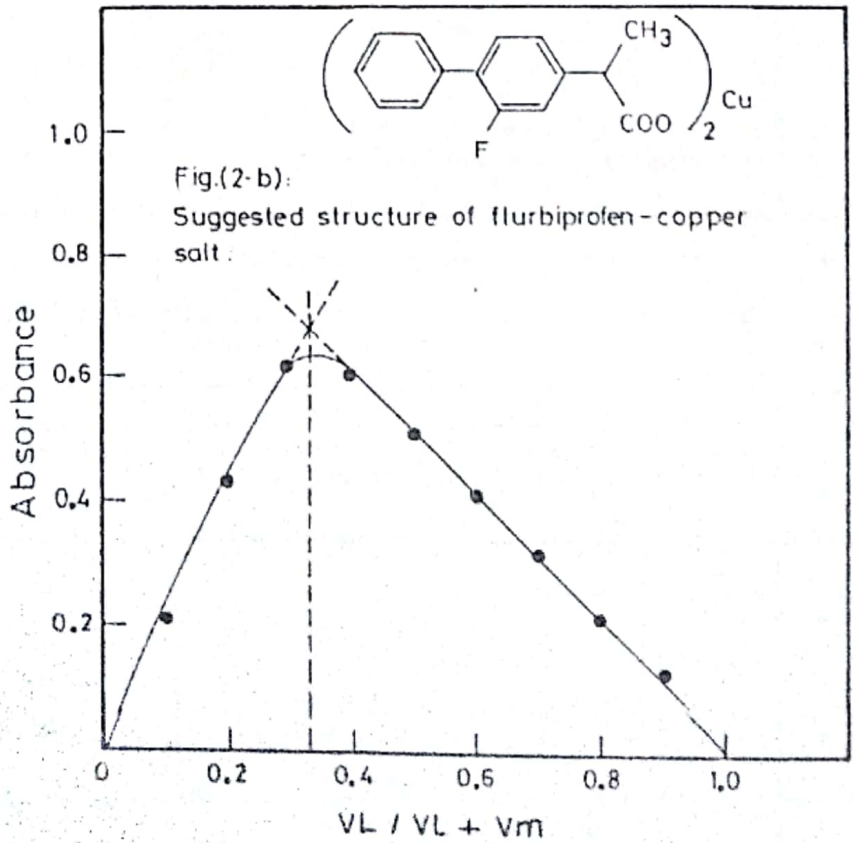

Fig.(2-b):
Suggested structure of flurbiprofen-copper salt.

Fig.(2-a) Continous variation plot obtained from flurbiprofen ($5x10^{-2}$M) and copper acetate ($5x10^{-2}$M) in chloroform.

Table (1) : Statistical analysis of results obtained using the proposed methods compared with the reference methods for the analysis of authentic drugs.

Statistic	FLURBIPROFEN				TIAPROFENIC ACID		
	Proposed methods			B.P (1993)[12] method	Proposed methods		Amax method[3]
	Direct	Indirect	A.A.S method		Direct	Indirect	
Mean recovery*% ±S.D (P=0.05)	100.02± 0.576	100.17 ±0.516	99.41 ±0.346	100.01± 0.425	100.02 ±0.628	99.94±0.560	99.98±0.519
N	7	6	6	6	6	6	6
V	0.332	0.266	0.120	0.181	0.395	0.314	0.269
t	0.034 (2.201)	0.584 (2.23)	2.679 (2.23	-	0.120 (2.23)	0.129 (2.23)	-
F	1.83 (4.95)	1.47 (5.05)	1.51 (5.05)	-	1.47 (5.05)	1.17 (5.05)	-

* Average of three experiments

Table (2) : Statistical analysis of results obtained using the proposed methods compared with the reference methods for the analysis of flurbiprofen and tiaprofenic acid in the tablets form.

Statistic	FLURBIPROFEN (Froben tablets)				TIAPROFENIC ACID (Surgam tablets)		
	Proposed methods			B.P (1993)[13] method	Proposed methods		Amax method[3]
	Direct	Indirect	A.A.S method		Direct	Indirect	
Mean recovery*% ±S.D (P=0.05)	98.86±0.496	99.35±0.360	98.77±0.318	99.14±0.468	99.13±0.313	99.26±0.454	99.16±0.439
N	5	5	5	5	5	5	5
V	0.246	0.130	0.101	0.219	0.098	0.206	0.193
t	0.918 (2.31)	0.792 (2.31)	1.462 (2.31)	-	0.124 (2.31)	0.356 (2.31)	-
F	1.123 (5.19)	0.185 (5.19)	2.168 (5.19)	-	1.97 (5.19)	1.07 (5.19)	-

* Average of three experiments

Table (3) : Statistical analysis of results obtained using the proposed methods compared with the reference methods for the analysis of flurbiprofen and tiaprofenic acid in the suppositories form.

Statistic	FLURBIPROFEN (Froben suppositories)			reference method	TIAPROFENIC ACID (Surgam suppositories)		
	Proposed methods				Proposed method		Amax method[3]
	Direct	Indirect	A.A.S method		Direct	Indirect	
Mean recovery*% ±S.D (P=0.05)	99.19±0.274	99.45±0.197	99.28±0.425	99.31±0.346	98.94±0.431	98.97±0.423	99.00±0.315
N	5	5	5	5	5	5	5
V	0.075	0.039	0.181	0.119	0.186	0.179	0.099
t	0.619 (2.31)	0.78 (2.31)	1.22 (2.31)	-	0.126 (2.31)	0.127 (2.31)	-
F	1.59 (5.19)	3.05 (5.19)	1.52 (5.19)	-	1.88 (5.19)	1.81 (5.19)	-

* Average of three experiments

Zagazig J. Pharm. Sci. December. 1996
Vol. 5, No. 2, pp 138-142

Different pharmaceutical preparations containing flurbiprofen and tiaprofenic acid were analysed by the proposed methods (Tables, 2, 3) and compared with the reference methods, statistical analysis of the results revealed that the proposed methods were equally precise and accurate as the official ones.

REFERENCES

1. Alfred, G.G.; Theodore, W.R., Alan, S.N. and Plamer, T.; The Pharmacological Basis of Therapeutics, 8th ed., Vol. 1, **Pergamon Press, New York** (1991).
2. Clohs, L. and Korolkovas, A.; **Rev. Farm. Bioquim.**, 24 (2), 81- 86 (1988). Through Anl. A. 52 (2) 1990.
3. Clark, S.; Isolation and Identification of Drugs, Moffat, A. C.; Jeckson, J. V.; Moss, M. S.; Widdop, B. and Greenfield, E. S. The pharmaceutical press, London, 2 ed. (1986).
4. Udupa, N. and Seetharaju, G.; Indian Drugs, 26 (10), 585 - 587 (1989).
5. Ali, A. M. M.; Emara, K. M. and Khodari, M.; **Analyst** (London), 119 (5), 1071 - 1074 (1994).
6. Berry, B.W. and Jamali, F.; **Pharm. Res.**, 5 (2), 123 - 125 (1988).
7. Mehvar, R., Jamali, F. and Pasutto, F.M.; **J. Chromatogr., Biomed. Appl.**, 69, 135 - 142 (1988). Through Anl. A. 50 (9) 1988.
8. Rieck, W. and Platt, D.; **J. Chromatogr., Biomed. Appl.**, 65, 206 -210 (1987). Through Anl. A. 50 (4) 1988.
9. Muller, N., Lapicque, F., Drelon, E., Gillet, P., Monot, C., Poletto, B. and Netter, P.; **J. Chromatogr. Biomed. Apple.**, 127, 261 - 270 (1993). Through Anl. A. 56 (3) 1994.
10. Salem, H. and Aboul Kheir, A.; Zagazig **J. Pharm. Sci.** Vol., 4. No. 1., 141- 149 (1995).
11. El-Kousy, N.; **Egypt J. Pharm. Sci.** Vol., 34, No. 1-3, 81 - 90 (1993).
12. Rose, J.; Advanced Physico-Chemical Experiments, Pitman, London, P. 54 (1964).
13. British Pharmacopoeia Her Majesty's Stationery Office London. Vol. I, 292 - 293 & Vol. II, 922 (1993).

استخدام الطرق الطيفيضوئية لتقدير الفلورباييروفين وحامض التيابروفنيك

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في هذا البحث تم استخدام طريقةدقيقة لتقدير الفلورباييروفن وحامض التيابروفنيك بعدتكوين املاح ملونة لكل منهما مع أيون النحاس الذى يضاف على هيئة محلول عيارى من خلات النحاس الى محلول متعادل من الفلورباييروفين وحامض التيابروفنيك ويستخلص الناتج فى الكلوروفورم ويقاس بالطريقة الطيفية وزيادة حساسية الطريقة يضاف (داى ايثيل داى ثيوكربامات الصوديوم) .

كما تمت دراسة العوامل المختلفة والنسب والنسب المولارية بين المواد المتفاعلة وتم لتقدير البايبروفين وحيده عن طريق الإستخلاص الطيفى الذرى عن طريق ترسيبه بمحلول عيارى من خلات النحاس . هذا وتم تطبيق الطرق المقترحه على المستحضرات الصيدلية فى أشكالها المختلفة وتمت مقارنتها بالطرق المنشوره وأعطت نتائج متماثلة فى الدقه والتكرار .