

MICRODETERMINATION OF SOME ANALGESICS AND ANTI-INFLAMMATORY DRUGS USING SILVER NITRATE

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ABSTRACT

A simple and accurate method is described for the microquantitative determination of mefenamic acid, flufenamic acid and flurbiprofen. The method is based on the reaction of the above cited drugs with a silver nitrate solution in a neutral alcoholic medium. The formed precipitate is quantitatively determined directly or indirectly through the silver content of the precipitate formed or the residual unreacted silver ions in the filtrate by atomic absorption spectrophotometry. The results obtained in both procedures either in their pure form or in their pharmaceutical formulations are accurate and precise. The stoichiometric relationship of the reaction was studied using Job's continuous variation method, it was found to be (1:1) drug: Ag^+ for the above drugs.

INTRODUCTION

Mefenamic acid, flufenamic acid and flurbiprofen are currently used as analgesic and anti-inflammatory drugs. Several methods were reported for the determination of the above three drugs including alkalimetry^(1,2), colourimetric methods⁽³⁾ and HPLC experiments⁽⁴⁻⁸⁾, spectrophotometry^(2,4,9-11) as well as fluorometry⁽¹²⁾, titrimetry⁽¹³⁾, atomic absorption spectrophotometry⁽¹⁴⁾ and diverse chromatographic techniques^(12,15-17).

The present work describes the use of silver nitrate for atomic absorption determination of mefenamic acid, flufenamic acid and flurbiprofen directly and indirectly in pharmaceutical preparations or in pure state. The proposed method proved to be simple and accurate.

EXPERIMENTAL

Apparatus:

Shimadzu atomic absorption flame spectrophotometer, Model AA-640-13.

Materials and Reagents:

All the reagents were analytical grade. Double distilled, deionized water was used:

1. Mefenamic acid (Parke-Davis).
2. Ponstan capsules (Parke-Davis), labelled to contain 250 mg mefenamic acid per capsule.
3. Flufenamic acid (Alexandria Co., Egypt).

4. Pinoc capsules (Alexandria Co. Egypt), labelled to contain 100 mg flufenamic acid per capsule.
5. Flurbiprofen (Kahira-Boots).
6. Froben tablets (Kahira-Boots), labelled to contain 100 mg flurbiprofen per tablet.
7. Stock solution with concentration of 1 mg / ml of mefenamic acid, flufenamic acid, and flurbiprofen were prepared by dissolving 100 mg of each in 50 ml ethanol, The solutions were rendered neutral to phenol red with 0.1 N NaOH and then completed to 100 ml with bidistilled deionized water.
8. Mefenamic acid flufenamic acid and flurbiprofen (0.005 M) for Job's method of continuous variation were prepared as before.
9. Silver nitrate 0.005 M solution.

Procedures:

Authentic Sample:

To different aliquots of stock solution (equivalent to 1.2-7.3 mg flurbiprofen, 1.4-7.0 mg of flufenamic acid and 2.4-9.6 mg of mefenamic acid) 25 ml of 0.005 M silver nitrate solution was added and the mixture was protected from light.

The mixture was shaken, then filtered using paper previously wet with bidistilled water. The precipitate was washed with the same water.

A. Direct method:

The formed precipitate was dissolved in 5 ml diluted ammonia solution and completed to 25 ml, with deionized bidistilled water (solution 1).

B. Indirect method:

The filtrate and washing in each experiment were collected in 50 ml measuring flasks and completed to the volume with deionized bidistilled water (solution 2).

A blank (omitting addition of the drug) was performed and absorbance for solution 1 and 2 was measured under these conditions: wave length 328.1 nm, lamp current 7, slit width 3.8 A, burnex height 5 mm, burnex slot/flame 10cm, air pressure 10 i/min; acetylene pressure 2.6 i/min.

The concentration of the consumed and the residual silver were calculated from the calibration graph of standard Ag NO₃ solution.

II. Application for pharmaceutical preparations:

A. Ponstan capsule:

The content of 20 capsules was mixed, on amount equivalent to 100mg mefenamic acid was added to 20ml water and shaken frequently for 10 minutes in 100 ml volumetric flask, 50ml alcohol were added mixed and filtered if necessary.

The solution was rendered neutral to phenol red with 0.1N NaOH and completed to volume with deionized bidistilled water. To different aliquots of this solution (2.5-8.75mg) was added the specified volume of AgNO₃.

The procedure was completed as mentioned under (I), the concentration of mefenamic acid was calculated by A.A.S method described above.

B. Pinox capsule.

The contents of 20 capsule was thoroughly mixed, an amount equivalent to 100mg mefenamic acid was taken and solution was prepared as mentioned under ponstan capsule, an aliquot equivalent to (1.6-6.4mg) flufenamic acid was taken and the procedure was completed as mentioned under (I).

C. Froben tablets.

Twenty tablets were weighted and finely powdered. An amount equivalent to 100mg flurbiprofen was taken, and solution was prepared as mentioned under ponstan capsule, an aliquot equivalent to (1.6-7.0mg) flurbiprofen was taken, and the procedure was completed as mentioned under (I).

RESULTS AND DISCUSSION

The procedure described in this work for the determination of the studied drugs was based upon precipitation of the silver salt and subsequent measurement of the combined and/or residual silver by A.A.S. Alcoholic neutral solutions to phenol red (6.8 -

8.4) of mefenamic acid, flufenamic acid and flurbiprofen were found to give coagulated precipitate when treated with AgNO₃ solution.

The precipitation in all case is quantitative. The excess metal ions could be determined indirectly by A.A.S.

The alcohol was carefully added to solubilize the drug and to help the coagulation of the precipitate. Excess alcohol was avoided due to its solubilizing effect upon the formed precipitate.

Complete precipitation was obtained at pH (6.8 - 8.4). Excess NaOH would precipitate the Ag⁺ as oxid or hydroxide, on the other hand, excess acid would dissolve the formed precipitate.

The linear relationship between absorbance and concentration of silver was found in the range of 5.4 - 135 µg Ag⁺ / ml. The correlation coefficient for the curve was found to be 0.9997.

Job's continuous variation method⁽¹⁸⁾ showed that, the above cited drugs react with silver ion by the ratio of 1: 1 (drug: Ag⁺). According to this ratio, it was found that:

$$\begin{aligned} 0.54 \text{ mg Ag}^+ &= 1.22 \text{ mg of flurbiprofen} \\ &= 1.20 \text{ mg of mefenamic acid} \\ &= 1.40 \text{ mg of flufenamic acid.} \end{aligned}$$

The proposed method was applied for the determination of different concentrations of the above mentioned drugs in their pure forms. The obtained results were compared with the official BP method^(1,2) for each drug.

Statistical analysis of the results revealed that the proposed method was as precise and accurate as the official one (Table 1).

The proposed method for the determination of flurbiprofen in froben tablets, mefenamic acid in ponston capsules and flufenamic acid in pinox capsules was applied, and the results were compared with the official methods.

Statistical analysis of the results showed that there is no significant difference in precision and accuracy (Table 2).

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Table (1): Statistical analysis of the results obtained using the proposed method compared with the official method for the analysis of authentic samples .

Statistic	Flurbiprofen			Mefenamic acid			Flufenamic acid		
	Proposed method		Official method	Proposed method		Official method	Proposed method		Official method
	Direct	Indirect		Direct	Indirect		Direct	Indirect	
Mean recovery* %	99.41	100.32	100.01	99.67	100.34	99.27	98.88	100.02	99.08
± S.D	±0.688	±0.232	± 0.425	±0.876	±0.947	±0.777	±0.763	±0.971	±0.410
(P = 0.05)									
N	6	6	6	5	5	5	5	5	5
V	0.474	0.052	0.181	0.767	0.898	0.604	0.852	0.943	0.168
t	1.82 (2.23)	1.57 (2.23)	-	0.765 (2.31)	1.953(2.31)	-	0.536(2.31)	1.992(2.31)	-
F	2.62 (5.05)	3.46 (5.05)	-	1.270 (6.39)	1.487(6.39)	-	3.464(6.39)	5.613 (6.39)	-

* Average of three experiments.

Table (2): Statistical analysis of the results obtained for pharmaceutical dosage form using the proposed method compared with the official method for the analysis.

Statistic	Froben tablets			Ponstan capsules			Pinox capsules		
	Proposed method		Official method	Proposed method		Official method	Proposed method		Official method
	Direct	Indirect		Direct	Indirect		Direct	Indirect	
Mean recovery* %	99.31	100.19	99.72	98.88	100.19	99.75	99.50	100.99	100.43
± S.D	±0.413	±0.561	±0.430	±0.520	±0.701	±0.744	±0.769	±0.517	±0.735
(P = 0.05)									
N	6	6	6	6	6	5	7	7	5
V	0.170	0.315	0.185	0.270	0.491	0.553	0.592	0.267	0.540
t	1.673 (2.23)	1.632(2.23)	-	2.203(2.26)	1.002(2.26)	-	2.70(2.23)	1.466(2.23)	-
F	1.088 (5.05)	1.703(5.05)	-	2.048(5.19)	1.126(5.05)	-	1.096(4.53)	2.022(6.16)	-

* Average of three experiments.

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التقدير الدقيق لبعض العقاقير المسكنة والمضادة للإلتهابات باستخدام نترات الفضة

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فى هذا البحث تم إستخدام طريقة الإمتصاص الذرى لعنصر الفضة لتقدير بعض العقاقير المسكنة والمضادة للإلتهابات مثل حامض الميفنمك وحامض الفلوفنيمك وكذلك الفلوربايبروفين.

وتم تطبيق هذه الطريقة على المستحضرات الصيدلية التى تحتوى على هذه العقاقير وأعطت نتائج دقيقة ومتفقة مع نتائج تقدير هذه المستحضرات بالطرق السابق نشرها.