*Arab Gulf J. Scient. Res., Math. Phys. Sci.*, **A5** (2), pp. 185-190 (1987)

# Microdetermination of Some Antipyrines with Iodine

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ABSTRACT. A new simple, accurate, and sensitive titrimetric method has been developed for the determination of antipyrine, 4-aminoantipyrine and dipyrone. The method is based on the oxidation of the entitled compounds with an excess of a chloroform solution of iodine, removal of its excess and determination of the resulting ioddide by the "so-called" Leipert procedure after 6-fold amplification. Antipyrine and 4-aminoantipyrine undergo quantitative oxidation in a media ranging from 0.1 M hydrochloric acid to 0.1 M sodium acetate solution with a consumption of 2 and 3 moles of iodine per mole of antipyrine and 4-aminoantipyrine, respectivcly. However, dipyrone consumes 3 moles of iodine in 0.1 M hydrochloric acid solution. The present method enables analysis of amounts as low as 30,10 and 20 μg of antipyrine, 4-aminoantipyrine and dipyrene, respectively. The recoveries ranging from 98.1-102.2%, and standard deviatious from 0.1-1.6%, depending on the concentration level.

Antipyrine (AP), 4-aminoantipyrine (4-AAP) and dipyrone (DP) are important organic compounds widely used as pain relieving drugs by lowering the increased body temperature and have been used successfully in rheumatic diseases. Several titrimetric methods have been reported for the determination of antipyrine (Walash *et al.* 1979, Popper *et al.* 1972, Saxena and Pandey 1972), 4-aminoantipyrine (Walash *et al.* 1979, Popper *et al.* 1972, Botev 1981, Subert *et al.* 1981, Subert *et al.* 1975) and dipyrone (Walash *et al.* 1979, Botev 1981, Mamatalieva 1981, Gachon *et al.* 1974). However, some of these methods are not sensitive, whilst others are tedious and time consuming.

In order to develop a reliable and sensitive method we have investigated the combination of a titrimetric procedure with an amplification reaction for determination of AP, 4-AAP and DP, based on the oxidation of these compounds

with an excess of a chloroform solution of iodine, removal of its excess, and determination of the resulting iodide by the Leipert amplification procedure. The liberated iodine is titrated with standard thiosulphate solution, using starch as indicator.

## Experimental

*Reagents*

All chemicals used were of A.R. grade and all preparations were made in distilled water.

Standard solutions of AP, 4-AAP and DP (1 mg/ml of each) were prepared in water. Less concentrated solutions were made by dilution. The solid samples, such as tablets were first weighed, powdered, dissolved in water, filtered and then diluted to the required volume with water.

Iodine solution (0.12%). Dissolve 0.3 g of pure iodine in 250 ml of pure dry chloroform.

Sodium thiosulphate solutions (0.01 and 0.001 N). Standardized against potassium iodate solutions of similar normality.

Solutions of bromine water (saturated) formic acid (90%), starch (1%), hydrochloric acid (0.1 M) and sodium acetate (0.1 M), were also used.

*Procedure*

In a 100-ml separating funnel, introduce a suitable volume (1-2 ml) of sample solution containing 40-5000 μg of AP, 10-5000 μg of 4-AAP or 20-5000 μg of DP.

Add 10 ml of 0.1 M hydrochloric acid (for AP and 4-AAP, 10 ml of water or 10 ml of 0.1 M sodium acetate could be used) and 10 ml of iodine solution. Stopper the funnel and shake for 5 min, using the electric shaker. Separate the organic (lower) layer, and remove the last traces of iodine from the aqueous layer by extraction with 10 ml of chloroform. Transfer the aqueous phase (containing iodide) quantitatively into a 100-ml conical flask, add 3 ml of bromine water, stopper the flask and stir for 2 min. Destroy the excess of bromine with 2 ml of formic acid. Add about 0.5 g of potassium iodide and titrate the liberated iodine with 0.01 N thiosulphate solution, using starch as indicator (for less than 500 μg of AP, 4-APP or DP use 0.001 N thiosulphate solution). Run a blank determination following the above procedure but without the intended compounds. The blank value was 0.05 ml of 0.01 N thiosulphate. Calculate the amount of each compound as follows:

1 ml of 0.01 N thiosulphate ≡ 313.72 μg of AP, 112.92 μg of 4-AAP or 195.00 μg of DP monohydrate.

## Results and Discussion

The pain relieving drugs, AP (phenazone), 4-AAP (4-aminophenazone) and DP (sodium phenyldimethylpyrazolone-methansulphonate) were oxidized quantitatively by iodine. The conditions for the reactions were optimized as described below.

### *Effect of Reaction Medium*

Experimental results confirmed that the reaction of the intended compounds with iodine was quantitiative in 0.1 M hydrochloric acid solution. However, water and sodium acetate solutions could be used for the determination of AP and 4-AAP. Table 1 shows the effect of different media on the determination of the compounds under investigation.

**Table 1.** Effect of 10 ml of reaction medium on the determination of 2000 μg of AP, 4-AAP or DP.

| Medium | Recovery*,% | | |
|---|---|---|---|
| | AP | 4-AAP | DP |
| 0.5 M Hydrochloric acid | 90.6 | 85.8 | 92.6 |
| 0.1 M Hydrochloric acid | 99.8 | 99.9 | 100.2 |
| 0.05 M Hydrochloric acid | 99.3 | 99.2 | 94.8 |
| Water | 99.4 | 99.4 | 50.8 |
| 0.05 M Sodium acetate | 100.2 | 99.8 | 49.9 |
| 0.1 M Sodium acetate | 100.2 | 100.6 | 49.8 |
| 0.5 M Sodium acetate | 101.3 | 102.1 | 50.1 |

* Average of 5 determinations.

### *Effect of Iodine*

A 10-ml volume of 0.12% iodine solution was found essential for the rapid and quantitative oxidation of up to 500 μg of AP, 4-AAP or DP. Larger excesses of iodine should be avoided in order to decrease the number of exractions necessary. Any iodine left in suspension in the aqueous phase causes high results, and therefore, must be removed by extraction with cloroform. It should be noted that iodine in benzene or carbon tetrachloride can be used.

*Effect of Rdaction Time*

The reaction of AP, 4-AAP and DP with a chloroform solution of iodine goes to completion within 5 min. A reaction time of up to 20 min had no significant influence on the results.

*Accuracy and Precision*

Under the above optimized conditions, the accuracy and precision of the method were checked. The results (10 replicates) are given in Table 2 and indicate a reliable method.

**Table 2.** Accuracy and precision of the method

| Compound | Amount taken μg | Recovery % | Coefficient of variation % |
|---|---|---|---|
| Antipyrine | 30 | 98.5 | 1.3 |
| | 500 | 99.6 | 0.4 |
| | 5000 | 99.3 | 0.2 |
| 4-Aminotipyrine | 10 | 98.1 | 0.9 |
| | 500 | 100.0 | 0.1 |
| | 5000 | 99.0 | 0.2 |
| Dipyrone momohydrate | 20 | 102.2 | 1.6 |
| | 500 | 101.6 | 0.7 |
| | 5000 | 99.8 | 0.6 |
| Dyprone tablets[1] | 1000 | 103.3 | 0.8 |
| Samalgin[2] | 1000 | 101.7 | 1.4 |

(1) 500 mg dipyrone/tablet (Galenika, pharmaceutical and Chemical industry, Beograd-Yugoslavia).
(2) 500 mg dipyrone/tablet (SDI, Samarra, Iraq).

*Applications*

The present method was applied successfully to the analysis of dipyrone and samalgin tablets with an error of less than 2.7%. We always used at least five tablets for each sample preparation in order to obtain good sampling as individual tablets vary in weight by several percent.

*Proposed reactions*

$$C_{11}H_{12}N_2O + I_2 \longrightarrow C_{11}H_{11}N_2OI + HI \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (1)$$

AP

$$2C_{11}H_{13}N_3O + 3I_2 \longrightarrow 2C_{11}H_{10}N_3O + 6HI \quad \ldots\ldots (2)$$

4-AAP

$$2C_{13}H_{16}N_3O_4NaS + 3I_2 \longrightarrow 2C_{13}H_{13}N_3O_4NaS + 6HI \quad \ldots\ldots (3)$$

D P

$$I^- \xrightarrow[H_2O]{Br_2} IO_3^- \xrightarrow[6H^+]{5I^-} 3I_2 \quad \ldots\ldots (4)$$

The results showed that 1 mole of AP consumes 1 mole of iodine, while 3 moles of iodine were consumed per mole of 4-AAP or DP. This has been proved by testing the organic layer which shows the presence of one mole of iodide in the case of AP, and the absence of iodide in the case of 4-AAP and DP. The organic layer has been tested for the presence of iodide as follows: After the reaction of the entitled compounds with iodine has been completed, transfer the organic layer into another separating funnel, add 10 ml of water and 1 ml of 1% sodium sulphite solution to reduce the excess of iodine. Transfer the organic layer into another funnel, add 10 ml of water and 3 ml of bromine water and shake for 2 min. Drain the aqueous layer into a 100-ml conical flask, add 2 ml of formic acid and shake to a colorless solution. Add about 0.5 g of potassium iodide and titrate the liberated iodine (no iodine was liberated in the case of 4-AAP and DP) with 0.01 N thiosulphate solution.

## References

**Botev, B.** (1981) Quantitative analysis of a caffeine containing drug, *Probl. Farm.* **9:** 18-22.

**Gachon, M., Maire, G.** and **Eloy, F.** (1974) Determination of a mixture of sodium noramidopyrine methanesulphonate and sodium metabisulphite, *Annls pharm. Fr.* **32:** 697-700.

**Mamatalieva, K.A., Madraimov, A.** and **Usubbaev, M.** (1981) Iodimetric and complexometric methods for quantitative determination of analgin (dipyrone) in powders and tablets, *Med. Zh. Uzb.* **1:** 65-68.

**Popper, E., Galfalvi, E.** and **Kiss, V.** (1972) Determination of basic drugs by titration in non-aqueous media, *Farmacia Buc.* **20:** 469-473.

**Saxena, S.** and **Pandey, J.D.** (1972) Volumetric microdetermination of phenazone by oxidation with hexacyanoferrate (III), *Z. Analyt. Chem.* **262:** 368.

**Subert, J., Bachrata, M., Knazko, L.** and **Stemberova, A.** (1975) Acidimetric determination of some drugs of organic base type in concentrated aqueous solutions of neutral salts, *Cslka Farm.* **24:** 68-72.

**Walash, M.I., Rizk, M., Belal, F.** and **Abo-Ouf, A.** (1979) Evaluation of certain pharmaceuticals with 1-3,dibromodimethylhydration II. Determination of analgesics, *Pharmazie* **34:** 234-235.

*(Received 23/06/1986;*
*in revised form 15/11/1986)*

# التقدير الدقيق لبعض مضادات البايرين بواسطة الأيودين

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قسم الكيمياء ـ كلية العلوم ـ جامعة الموصل ـ الموصل ـ العراق

تم تطوير طريقة جديدة تتصف بالبساطة والدقة والحساسية لتقدير مضاد البايرين و٤ ـ مضاد البايرين الأميني والبايرين الثنائي، وقد بنيت هذه الطريقة على أكسدة هذه المركبات بزيادة في محلول الكلوروفورم للأيودين ثم إزالة هذه الزيادة وتقدير الأيوديد الناتج بالطريقة المسماة ليبرت وبعد ستة أضعاف من التكبير. ان مضاد البايرين و ٤ ـ مضاد البايرين الأميني خضعا إلى أكسدة كمية في وسط ممتد من ٠,١ M حامض الهيدروكلوريك إلى ٠,١ M من محلول أستيت الصوديوم مع صرف ٢ و٣ مول من الايودين لكل مول من مضاد البايرين و ٤ ـ مضاد البايرين الأميني على التوالي، وعلى كل حال فإن البايرين الثنائي يصرف ٣ مول من الأيودين في ٠,١ M محلول حامض الهيدروكلوريك. وقد وجد أن الطريقة هذه تستطيع تحليل كميات في حدود ٣٠ و١٠ و٢٠ مايكروجرام من مضاد البايرين و ٤ ـ مضاد البايرين الأميني والبايرين الثنائي على التوالي، وان نسبة الاسترجاع تتراوح من (٩٨,١ ـ ١٠٢,٢) ٪ وأن نسبة الانحرافات القياسية تتراوح من (٠,١ ـ ١,٦) ٪ معتمدةً على مستوى التركيز.