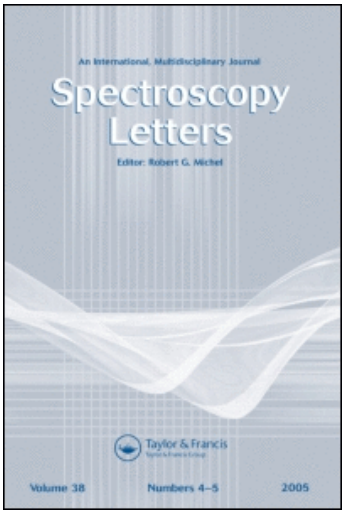

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A Simple Purity Test of p-Aminosalicylic Acid, Advantageously Alternative to USP Method, by UV Spectrophotometry

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A SIMPLE PURITY TEST OF p-AMINOSALICYLIC ACID, ADVANTAGEOUSLY ALTERNATIVE TO USP METHOD, BY UV SPECTROPHOTOMETRY

Key words: p-Aminosalicylic acid; m-Aminophenol;PAS degradation.

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ABSTRACT

A very simple and fast analytical method to determine the degradation level of p-Aminosalicylic acid by UV spectrophotometry was described. The method allows also the simultaneous determination of the drug and its major degradation product, m-Aminophenol.

Relationships of two UV maxima, one due to PAS only, the other one due to both substances, versus PAS and MAP mixture composition was defined by multiple linear regression analysis (MLRA) utilising data for a high number of standard solutions.

The method was compared with official procedure described in USP XX. It proved sensitive over a range of 2.5 - 30 and 0.2 - 20 mcg·mL^{-1} for PAS and MAP respectively, yielding highly accurate and precise results.

INTRODUCTION

p-Aminosalicylic acid (PAS) is a bacteriostatic agent used in the treatment of pulmonary and extrapulmonary tubercolosis; in spite of its partial remplacement with recent drugs, it is still used, particurarly administered with antibiotics and other drugs (1-2).

In view of the appreciable instability of pure PAS and its salts, the quality of PAS preparations is a very important problem for

technology of pharmaceutical forms preparations. In particular, the toxicity of PAS is due to m-Aminophenol (MAP), its decarboxylation product.

Many analytical procedures (3-7) have been reported to evaluate PAS purity and to determine MAP concentration in PAS formulations but these methods were not reliable because of poor specificity; the USP, BP and EU.Ph. require a colorimetric limit test to determine MAP, based on the diazotization reaction with sodium nitrite (8-10).

Recently, Vetuschi et al. (11-12), while studying the effects caused by medium modifications on absorbance spectra of both compounds, verified that in ethanol and in citrate buffer pH3 the mixture solutions of two compounds exhibited two maxima, one almost exclusively due to p-Aminosalicylic acid and the other one due to both substances. The present paper, starting from these studies proposes the use of simple relationships, obtained by multiple linear regression analysis (13) for data from a high number of standard mixtures, between percentage of PAS purity, or PAS and MAP concentrations, versus absorbance levels at two maxima.

EXPERIMENTAL

Materials and methods

p-Aminosalicylic acid, analytical grade: was obtained from commercial sample by several recrystallizations from ethanol without heating or exposing to light.

m-Aminophenol was recrystallized from 70% hot ethanol.

Commercial forms:

-Eupasal sodico (Stholl). Tablets, five years old.

-Eupasal calcico (Stholl). Tablets, three years old.

-Pasmicina (Morgan) . Tablets.

-Salf PAS (S.A.L.F. S.p.A. Bergamo, Italy). Perfusion solution.

Standard solutions of PAS and MAP were freshly prepared to use.

Ethanol was analytical grade (C. ERBA).

Buffer pH3: citrate/citric acid (Normex C. ERBA).

Spectrophotometric measurements were recorded in 10 mm silica quartz cell, at 26-28 °C, using a Perkin-Elmer 320 UV-Vis spectrophotometer.
Data elaboration was by PS System/2 IBM Mod 50.
Spectral bandwidth was 1 nm, the scan rate 1 $mm \cdot s^{-1}$ and the response (time constant) 1 sec.

Standard solutions

Standard solutions in ethanol and buffer solution were prepared with PAS concentration ranged from 5 to 40 $mcg \cdot mL^{-1}$. Corresponding mixture solutions were prepared with MAP concentration ranged from 0.5 to 20 $mcg \cdot mL^{-1}$.
In all cases PAS/MAP ratio from 1 to 100 were performed.
Spectrophotometric analysis were measured against relative solvents as blanks.

Sample solutions

Solid forms: an accurately weighed portion of finely-powdered tablets or bulk material was treated with ethanol; the solution was filtered (if necessary) through dry filter paper. An aliquot of this solution was transferred in a volumetric flask and then brought to volume to yield a solution with a PAS concentration within the range 5 - 40 $mcg \cdot mL^{-1}$. The solution was analyzed against ethanol as a blank.

Perfusion solutions: an aliquot of aqueous perfusion solution was properly diluted with acid buffer pH3 in such a way as to obtain a PAS concentration in the range above indicated.
The solution absorbance was measured against buffer solution as a blank.

RESULTS AND DISCUSSION

The UV scanning of ethanol solutions of PAS exhibited three maxima at 304, 285 and 238 nm whereas MAP solutions

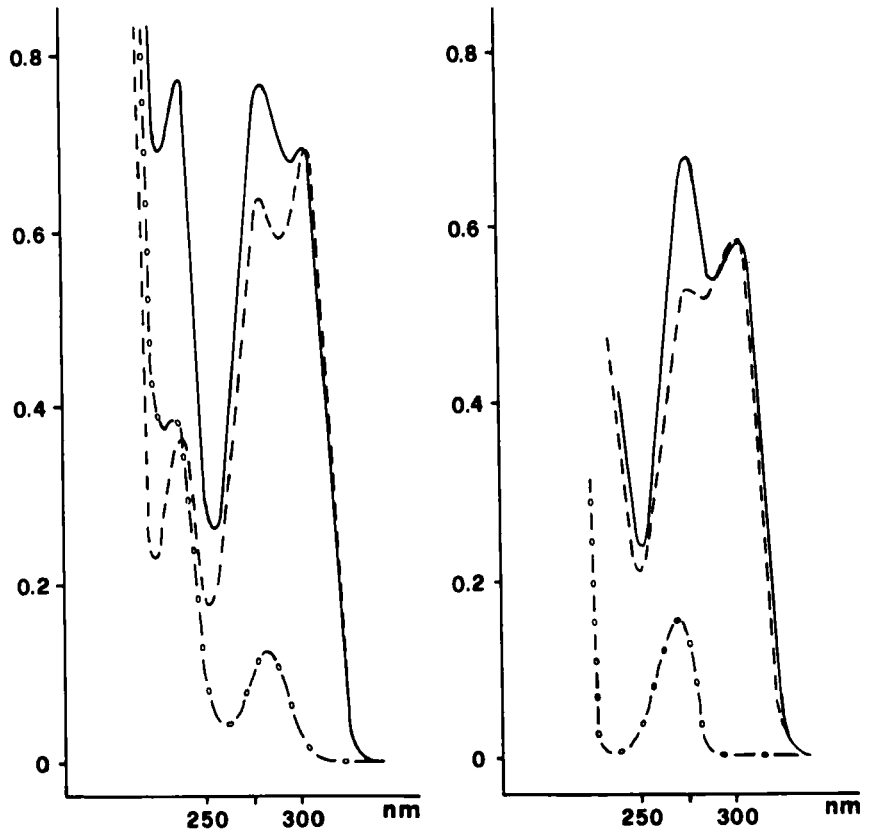

FIGURE 1

exhibited two maxima at 237 and 286 nm . In citrate buffer pH3 PAS presents two maxima at 300 and 275 nm, MAP a maximum only at 275 nm (see fig.). Standard curves were made separately at each of the maxima for PAS and MAP solutions and are found to obey the Beer - Lambert's law for concentration ranging between 2.5 and 30 mcg·mL^{-1} for PAS and 0.2 - 20 mcg·mL^{-1} for MAP.

From using the A_{304}/A_{238} ratio in ethanol and A_{300}/A_{275} ratio in buffer pH3 it is possible to derive the PAS purity in the

TABLE 1

Sample	Ethanol %	Ethanol RSD	Buffer pH3 %	Buffer pH3 RSD	USP XX %	USP XX RSD
Laboratory mixtures						
PAS 78.3 MAP 21.7	79.6	0.74	78.1	1.02	81.2	1.45
PAS 93.5 MAP 6.5	92.1	0.62	93.0	0.91	91.4	1.89
Commercial forms						
Eupasal Na	90.1	0.92			89.3	3.52
Eupasal Ca	94.3	0.84			92.4	2.69
Pasmicina	92.6	0.90			86.1	2.95
Salf PAS			85.8	0.87	89.0	3.15

All values are means of 5 determinations for each sample.

sample by using the following equations:

Ethanol : $$\% \text{ PAS} = 54.129 \left(\frac{A_{304}}{A_{238}}\right) + 1.266 \qquad r = 0.9998$$

Buffer pH3 : $$\% \text{ PAS} = 77.235 \left(\frac{A_{300}}{A_{275}}\right)^{2.806} \qquad r = 0.9989$$

The following equations to evaluate concentration of the two products also have been defined:

$$y = a\, A\lambda_1 + b\, A\lambda_2 + c$$

medium	y	λ_1	λ_2	a	b	c	r
ethanol	PAS	304	238	9.624	-0.422	0.440	0.9994
	MAP			-9.059	16.937	-0.538	0.9999
buffer	PAS	300	275	16.298	0.450	0.040	0.9998
	MAP			-59.659	64.880	0.046	0.9997

Validation of the present method was effected by a recovery assay on standard laboratory mixtures. Results obtained from analysis of laboratory mixtures and commercial forms, compared with those obtained with the USP XX procedure, are reported in Table 1.

Unlike the official methods which are tedious and time-consuming, the use of these equations is very rapid and simple. The results reported in table show that the proposed method is precise and accurate.

REFERENCES

1) Wesolowsky M. Pharmacotherapeutic Combinations of p-Aminosalicylic Acid. Pharm. Acta Helv. 1977; 52: 239-46.

2) Wesolowsky M. Forms of p-Aminosalicylic Acid and its Salts in Pharmaceutical Practice. Pharm. Ind. 1979; 41: 990-5.

3) Blake M.I., Makris K., Hunt J. Determination of Sodium p-Aminosalicylate in the Presence of m-Aminophenol. J. Pharm. Sci. 1971; 60: 1694-5.

4) Shih I.K., Analytical Applications of p-Nitrosobenzoic Acid I: Specific Colorimetric Determinations of m-Aminophenol in p-Aminosalicylic Acid and Sodium p-Aminosalicylate. J. Pharm. Sci. 1971; 60: 1853-6.

5) Moussa A.F. Spectrophotometric Determination of PAS in presence of its Degradation Product m-Aminophenol. Pharmazie 1978; 33: 460.

6) Butterfield A.C., Curran N.M.,Matsui F.F., Sears R.W. Isoniazid and 1-Glucopyranosyl-isonicotinylhidrazines in Isoniazide Liquid Oral Formulations by HPLC. Can. J. Pharm. Sci. 1980; 15: 94-7.

7) Goto M., Koyanagi Y., Ishii D. Electrochemical Detector for Micro High Performance Liquid Chromatography and its Application to the Determination of Aminophenol Isomers. J. Chromatogr. 1981; 208: 261-8.

8) The United States Pharmacopœia, 20 th rev., p. 36. Mack Printing Company, Easton Pa. 18042, 1980.

9) The British Pharmacopœia, vol. 1, p. 405. London Her Majesty's Stationery Office, 1980.

10) The European Pharmacopœia, vol. 1, p. 329. Maisonneuve S.A.; Sainte Ruffine, France, 1969.

11) Vetuschi C., Ragno G., Mazzeo P. Determination of p-Aminosalicylic Acid and m-Aminophenol by Derivative UV Spectrophotometry. J. Pharm. Biom. Anal.1988; 6:383-91

12) Vetuschi C., Ragno G. Simultaneous Spectrophotometric Determination of PAS and its Degradation Product, m-Aminophenol. Pharm. Acta. Helv. (in press).

13) Spiegel M.R. Theory and Problems of Probability and Statistics, Mc. Graw Hill, New York, 1975.

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