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The determination of sodium aminosalicylate in cachets of sodium aminosalicylate and isoniazid by ultraviolet absorption

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Sodium aminosalicylate can be determined in the presence of isoniazid by its ultraviolet absorption at 299 nm. The method is at least as accurate as the B.P.C. 1968 bromination method for cachets of sodium aminosalicylate and isoniazid. Analysis of a powder mix containing sodium aminosalicylate (2 g) and isoniazid (50 mg) gave a mean value of 2·02 ± 0·01 (s.d.) for ten determinations using the proposed method. The B.P.C. method gave a mean value of 2·03 ± 0·33 (s.d.). The proposed method has the advantage that the determination is independent of the isoniazid content and is more rapid than the official method. It can be easily adapted for automatic analysis.

The British Pharmaceutical Codex (1968) method for the determination of sodium aminosalicylate (NaPAS) in cachets of sodium aminosalicylate and isoniazid has the disadvantages that it is not independent of the isoniazid content, breakdown products interfere and it is not easily adapted to automatic methods of analysis.

The method is based on the bromination techniques of Simmonite (1949). As isoniazid also absorbs bromine, a correction factor must be applied after the isoniazid content has been determined by the method of Elliston & Hammond (1965). 3-Aminophenol, a breakdown product of NaPAS also absorbs bromine, but no correction for this is applied in the B.P.C. method.

Several methods have been described where NaPAS and isoniazid are separated on ion-exchange columns and determined independently (Fan & Wald, 1965; van Pinxteren & Verloop, 1965). Colorimetric methods have also been proposed for the determination of NaPAS in the presence of isoniazid (Fried, 1962). Wray, Smith & others (1948) found NaPAS at pH 7 to give two ultraviolet absorption peaks, one at 299 nm and a larger one at 265 nm. An assay method, based on the absorption at 265 nm was used in New and Non-official Remedies (1951) for the assay of aminosalicylic acid tablets. A spectrometric method for the determination of aminosalicylic acid (PAS) in the presence of isoniazid was reported by Welsh (1957, 1958). He found that although interference due to isoniazid at 265 nm was small in the ratios of PAS : isoniazid normally found in tablets, the interference could be reduced further by using the peak at 299 nm. Absorption of PAS (pH 7) at 299 nm was only two-thirds that at 265 nm, but interference due to isoniazid was cut to one tenth at 299 nm and could be discounted.

This paper describes the adaptation of the method of Welsh (1957) to the determination of sodium aminosalicylate in cachets of sodium aminosalicylate and isoniazid B.P.C., and a comparison with the official method.

EXPERIMENTAL AND RESULTS

The NaPAS and isoniazid were to British Pharmacopoeia (1968) specification. 3-Aminophenol was obtained commercially and was further purified by sublimation.

The method of Welsh (1957) for PAS necessitated an initial extraction with sodium bicarbonate solution with a final adjustment of the solution to pH 7. As NaPAS is essentially neutral, it was found that direct solution into distilled water was sufficient. Preliminary studies indicated that the ultraviolet absorption of NaPAS was independent of pH between pH 5–9 and that Beer's law was observed at 265 nm and 299 nm in solutions containing 5–40 μg/ml NaPAS.

Interference from isoniazid and 3-aminophenol

Solutions of NaPAS, isoniazid and 3-aminophenol (20 μg/ml) were prepared and the ultraviolet absorption curve for each compound was determined on a Unicam SP800 spectrophotometer using 1 cm cells. Isoniazid interference is markedly reduced at 299 nm compared to that at 265 nm. At the lowest NaPAS : isoniazid ratio in the B.P.C. cachets (30 : 1) absorption due to isoniazid at 299 nm produces an overestimate of 0·1% in the NaPAS content and can be neglected for all practical purposes. Interference from 3-aminophenol is negligible.

Determination of E (1%, 1 cm) for NaPAS at 299 nm

Approximately 200 mg NaPAS were weighed accurately and made up to 1 litre with distilled water. 5 ml of this solution was diluted to 100 ml with distilled water and the extinction at 299 nm measured on a Unicam SP500 spectrophotometer using 1 cm cells. The experiment was repeated ten times, a mean value of 407·2 $\pm$ 2·85 (s.d.) was obtained for E (1%, 1 cm).

Assay of a known NaPAS: isoniazid powder mix

The mix was prepared by diluting isoniazid (1 g) with NaPAS (40 g). The mix was blended for 2 h in a cube mixer after a preliminary mix with a mortar and pestle. The powder is equivalent to that found in NaPAS (2 g) isoniazid (50 mg) cachets of the B.P.C.

Proposed method. Approximately 200 mg of powder mix were weighed accurately and made up to 1 litre with distilled water. 5 ml of this solution was diluted to 100 ml with distilled water, and the extinction at 299 nm measured as before. By using an E (1%, 1 cm) of 407, the amount of NaPAS in 2·05 g powder mix was determined. Ten such determinations were made, a mean value of 2·02 g $\pm$ 0·01 (s.d.) was obtained.

B.P.C. method. Approximately 200 mg of powder mix were weighed accurately and made to 100 ml with distilled water. 25 ml of this solution was used for the bromination part of the assay and 5 ml solution for the isoniazid determination. 5 ml quantities of the other reagents were also used and the final volume made to 25 ml. Ten determinations were made, a mean value of 2·03 g $\pm$ 0·03 (s.d.) was obtained for NaPAS content and 49·38 mg $\pm$ 0·70 (s.d.) for isoniazid content.

DISCUSSION

The direct ultraviolet absorption method of analysis for NaPAS in the presence of isoniazid is at least as accurate as the B.P.C. bromination method described under

cachets of sodium aminosalicylate and isoniazid. The ultraviolet method has the advantages that it is independent of the isoniazid content normally found in pharmaceuticals, it is more rapid and can be easily automated.

It is recommended that the ultraviolet method of analysis should be considered as a replacement for the B.P.C. bromination method in official standards for the estimation of sodium aminosalicylate in cachets of sodium aminosalicylate and isoniazid.

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