J. Pharm. Pharmac. 1971, **23**, 214

LETTERS TO THE EDITOR

A note on the assay of atropine sulphate injections

During a study on the stability of some batches of atropine sulphate injections, the U.S.P. XVII and B.P. 68 methods of assay were compared. Samples of three commercial batches of atropine sulphate injections (U.S.P. XVII), having pH values between 5·2 and 6·0, were subjected to autoclaving for 1 to 6 h. These injections were then assayed by the two methods (Table 1). The B.P. method gave, for all the samples examined, higher results compared with the U.S.P. method. Batch C, which showed by the U.S.P. method about 50% decomposition, gave about 36% decomposition by the B.P. method (Table 1). This particular batch revealed, on using a thin-layer chromatography system,* two spots corresponding to atropine and tropine; the former gave an orange colour and the latter a deep violet colour with dilute potassium iodobismuthate solution. It was concluded, therefore, that the hydrolytic product tropine may interfere in the B.P. method. Tropine, chromatographically pure, was analysed following the U.S.P. and B.P. methods of assay of atropine sulphate injections. The results (Table 2) showed that tropine interferes in the B.P. method; the plot is linear and has a slope of 1·52 indicating the constant contribution due to tropine. The latter in a concentration of 20·3 mg% (corresponding to 100% hydrolysis of atropine sulphate) gave by the B.P. method the equivalent of 30·6 mg% of atropine sulphate. In the U.S.P. method, however, the effect due to

Table 1. *Results of assay of atropine sulphate injections, autoclaved for various time intervals, by the U.S.P. XVII, B.P. 68 and the modified B.P. methods.*

Batch No.	Autoclaving time (h)	Results of assay*		
		U.S.P.	B.P.	Modified B.P.
A	1	101·76	106·02	100·80
B	4	92·64	94·36	91·41
C	6	50·06	63·91	48·88

* Average of four replicates (±1·5%).

Table 2. *Results of assay of tropine by the U.S.P. XVII and B.P. 68 methods of assay of atropine sulphate injections and by the modified B.P. method.*

Tropine added mg%	Corresponding % hydrolysis*	Results of assay in terms of mg% atropine sulphate†		
		U.S.P.	B.P.	Modified B.P.
2·03	10	3·01	3·20	
4·06	20	3·63	6·70	The results
8·12	40	3·88	11·45	obtained ranged
12·18	60	4·01	21·55	between 1 and
16·24	80	4·95	24·65	1·8%
20·30	100	5·83	30·61	

* Calculated on the basis that 1 mg atropine sulphate yields on complete hydrolysis 0·203 mg tropine.

† Average of four replicates (±1·5%).

* Dimethylformamide–ammonia–ethanol–ethyl acetate(1:1:6:12) using Silica Gel G as the adsorbent.

Table 3. *Analyses of mixtures of atropine sulphate and tropine, corresponding to various degrees of hydrolysis, by the U.S.P. XVII, B.P. 68 and modified B.P. methods.*

Mixture No.	Composition (mg%) Atropine sulphate	Tropine	Hydrolysis %	Results of assay* U.S.P.	B.P.	Modified B.P.
1	5·0	19·29	95	9·93	33·82	5·07
2	20·0	16·24	80	22·75	44·50	20·20
3	50·0	10·15	50	52·01	64·34	50·91
4	70·0	6·09	30	74·74	79·11	71·03
5	80·0	4·06	20	83·80	84·00	79·71
6	85·0	3·05	15	88·06	86·91	84·54
7	90·0	2·03	10	92·77	91·83	90·31
8	100·0	0	0	99·10	100·64	100·30

* Average of four replicates (±1·5%).

tropine was less pronounced being between 3·01 and 5·83% for 10 and 100% hydrolysis respectively (Table 2). Mixtures containing varying amounts of atropine sulphate and tropine, corresponding to different degrees of hydrolysis, were prepared and assayed by the two methods. The results obtained (Table 3) showed the non-selectivity of the B.P. method due to tropine interference. In mixtures showing 30 to 95% hydrolysis the contribution due to tropine was similar to that found in Table 2 for tropine solutions. In other mixtures, with lower percentages of hydrolysis, the effect of tropine was less pronounced (Table 3). Analysis of the mixtures by the U.S.P. method revealed that the method is more selective especially for mixtures of low percentages of hydrolysis (Table 3). The low contribution of tropine in the U.S.P. method is probably due to its loss during extraction as the result of partitioning (being more water soluble). Partial volatilization of tropine also occurs during the evaporation of the chloroform–ethanol mixture. The percentage loss of tropine during the U.S.P. assay was estimated to be 92·3%.

Trials were made to improve the B.P. method. We found that tropine did not interfere when dilute sulphuric acid was substituted for the acetate buffer of pH 2·8. This was shown in Tables 2 and 3, where no interference due to tropine was observed in mixtures showing up to 95% hydrolysis.

It should be pointed out that both official methods are satisfactory for the control analysis of the injections since the interference due to tropine lies within the official limits specified in the monographs. However, for stability studies the suggested modified B.P. method is more selective than both official methods beside being simpler and less time consuming than the U.S.P. procedure.

Faculty of Pharmacy,
University of Alexandria,
Alexandria, U.A.R.

SALEH A. H. KHALIL
YOUSSEF EL-BELTAGY
SAWSAN EL-MASRY

November 9, 1970

REFERENCES

British Pharmacopoeia (1968). pp. 75, London: The Pharmaceutical Press.
United States Pharmacopeia XVII (1965). pp. 53, Mack Co., Easton, Pa.