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SHORT COMMUNICATION

A direct non-aqueous titration procedure for determining barbiturates in different pharmaceutical forms

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Non-aqueous titration methods for the analysis of barbiturates all involve titration of the barbiturate itself with a basic reagent (Heiz, 1952; Vespe & Fritz, 1952; Pifer, Wollish & Schmall, 1953; Swartz & Foss, 1955; Vincent & Blake, 1959; Chatten, Mainville & Pernarowski, 1961). Difficulties are caused in all those methods especially with the sodium salts by the need to liberate the barbiturate itself, and to extract it into an organic solvent. The use of an acidic reagent directly applicable to sodium salts was therefore examined.

Apparatus and reagents

Pye-titrimeter model 79 equipped with a combination electrode. A 10 ml burette graduated to read in 0·01 ml. 0·02N solution of perchloric acid in dioxane. 0·1% tropeolin OO in absolute ethanol. Chloroform–acetic anhydride mixture (3:2).

Procedure

Pure barbiturates. About 50 mg, accurately weighed, was dissolved in about 25·0 ml of chloroform–acetic anhydride mixture using a magnetic stirrer and warming if necessary. Ethanolic solution of tropeolin OO (3 drops) was added and the solution titrated with 0·02N perchloric acid in dioxan to the first permanent red colour.

Titrations were also followed potentiometrically when it was found that the appearance of a permanent red colour coincided with the point of maximum change in mV reading.

Tablets and capsules. A quantity of powdered tablets or mixed contents of capsules equivalent to 50 mg was dissolved in chloroform–acetic anhydride mixture. The titration was carried out as described above.

Injections. A volume of the mixed contents of ampoules equivalent to 50 mg of barbiturate was evaporated to dryness, and the residue titrated in chloroform–acetic anhydride mixture as described above.

The barbiturates, in pure form and in different pharmaceutical forms such as tablets, capsules and ampoules, were assayed by the gravimetric procedures described in the U.S.P. XVII and B.P. 1968.

The same barbiturates were also assayed using the proposed non-aqueous titration procedure. The results (Table 1) show that this method is equivalent to the official methods in accuracy and precision. The method does not involve the conversion of salts to free acid before titration. It is more rapid, and eliminates processes of extraction.

Table 1. *Analysis of barbiturates* (*mean* ± s.d. *of eight experiments*)

Compound	Non-aqueous titration recovery %	U.S.P. XVII recovery %	B.P. 1968 recovery %
Pure compounds			
Phenobarbitone sodium	100·2 ± 0·10	99·0 ± 0·15	98·6 ± 0·18
Barbitone sodium	100·2 ± 0·27	—	98·9 ± 0·22
Amylobarbitone sodium	100·1 ± 0·21	98·8 ± 0·14	98·5 ± 0·15
Pentobarbitone sodium	100·2 ± 0·18	98·9 ± 0·25	98·6 ± 0·25
Quinalbarbitone sodium	100·0 ± 0·23	99·1 ± 0·13	98·9 ± 0·19
Tablets			
Phenobarbitone sodium	99·3 ± 0·42	—	98·4 ± 0·19
Barbitone sodium	99·4 ± 0·22	—	98·4 ± 0·24
Amylobarbitone sodium	99·3 ± 0·17	—	98·7 ± 0·14
Pentobarbitone sodium	99·4 ± 0·22	—	98·0 ± 0·26
Quinalbarbitone sodium	99·3 ± 0·33	—	98·5 ± 0·29
Capsules			
Phenobarbitone sodium	99·0 ± 0·42	—	—
Barbitone sodium	98·9 ± 0·22	—	—
Amylobarbitone sodium	98·9 ± 0·22	98·8 ± 0·13	98·7 ± 0·14
Pentobarbitone sodium	99·0 ± 0·29	98·6 ± 0·17	98·5 ± 0·11
Quinalbarbitone sodium	98·9 ± 0·21	98·9 ± 0·24	—
Injections			
Phenobarbitone sodium	99·9 ± 0·21	—	98·8 ± 0·17
Barbitone sodium	99·2 ± 0·32	—	—
Amylobarbitone sodium	99·6 ± 0·22	—	—
Pentobarbitone sodium	99·3 ± 0·33	98·9 ± 0·25	—
Quinalbarbitone sodium	99·5 ± 0·21	—	—

Blank determinations showed that the colour change of the indicator, tropeolin OO, took place with a negligible volume of titrant. Tablet excipients such as lactose, glucose, starch, stearic acid and gelatin did not interfere with the determination.

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