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A rapid gas chromatographic method for the determination of benzhexol hydrochloride

Benzhexol hydrochloride, also known as trihexyphenidyl hydrochloride, is a spasmolytic which is commonly formulated as tablets to give daily dose levels from 2 to 20 mg*.

The B.P. method of analysis for this compound in dosage form is specific only for tertiary amines. The complex with Bromocresol Purple is examined spectrophotometrically. Gravimetric[1] and volumetric[2] procedures have been reported and polarography[3,4] has been used. Potentiometric titration[5–7] is widely reported and a diphasic titration has been described[8]. The preparation of derivatives for identification has been reported[9] and a spectrophotometric method for benzhexol hydrochloride as the ammonium reineckate[10] has recently been described.

Of these reported methods polarography is potentially the most sensitive. However, the polarographic methods described[3,4] involve the preparation of derivatives prior to the actual determination. It was found necessary to determine benzhexol hydrochloride in very low concentrations in the order of 0.025 mg/ml. In these circumstances none of the reported methods was likely to have sufficient sensitivity. A gas chromatographic method has been developed and successfully applied to this determination.

Experimental

Apparatus. A Pye 104 gas chromatograph fitted with a flame ionisation detector with nitrogen carrier gas at 75 ml/min was used.

Chromatographic conditions. A glass column 150 cm long and of 3 mm I.D. was packed with 10 % of silicone gum E301 on Gas-Chrom Q of 60–80 mesh. This column was preconditioned at 280° for 48 h. In operation the injector port temperature was 270°, the column oven at 245° and the detector at 290°. The column was used isothermally.

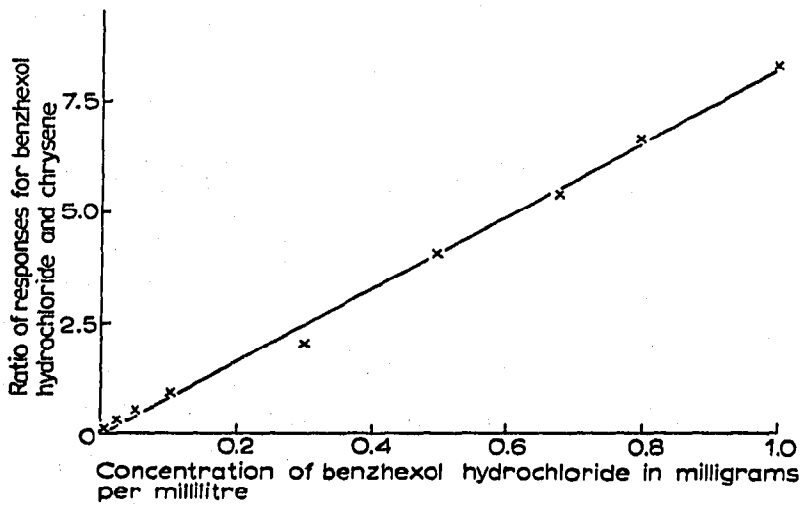
Solutions. Solutions of benzhexol hydrochloride were prepared in suitable concentrations in chloroform. Chrysene was used as an internal standard. The ratio of the concentrations of chrysene to benzhexol hydrochloride in the injected solutions was 0.7.

Results

The method has been tested between concentrations of 0.025 and 1.0 % w/v of benzhexol hydrochloride in chloroform. The graph (Fig. 1) illustrates the linear response with concentration across this range. Fig. 2 is a typical chromatogram indicating the convenient ratio of the retention times of benzhexol hydrochloride and chrysene under the conditions described above. Standard variations of 0.61 and 0.50 respectively were found in determinations of solutions of 0.06 and 0.04 % w/v benzhexol hydrochloride in chloroform.

This method has been applied successfully to the determination of the benzhexol hydrochloride in single tablets of 2 and 5 mg label strength after suitable extractions.

* Lederle market the compound in Artane® 2 and 5 mg tablets.



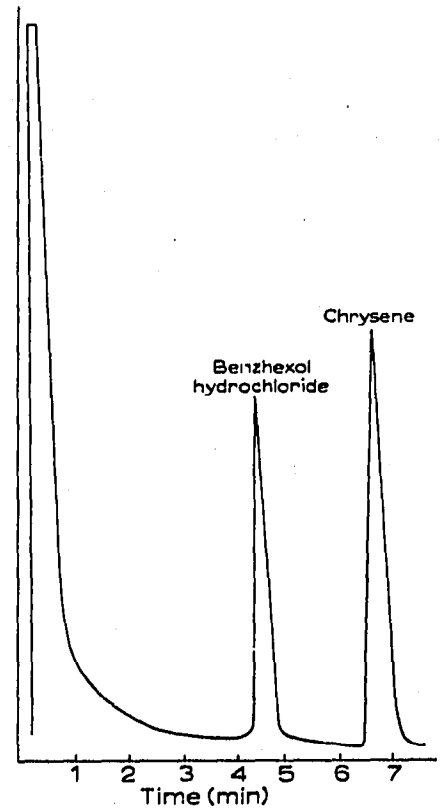


Fig. 1. Linearity of response.

Fig. 2. Isothermal chromatogram of a solution of 0.05% benzhexol hydrochloride and 0.07% chrysene in chloroform at 245°.

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