Journal of Chromatography, 322 (1985) 246–247
Elsevier Science Publishers B.V., Amsterdam — Printed in The Netherlands

CHROM. 17,547

Note

Determination of emepronium bromide in tablets by reversed-phase high-performance liquid chromatography

SALLY MARGARET GORDON*, LESLEY K. FREESTON, ANTONY J. COLLINS and ROGER BAIN

Wessex Regional Pharmaceutical Quality Control Laboratory, Queen Alexandra Hospital, Cosham, Portsmouth PO6 3LY (U.K.)

(Received January 10th, 1985)

Emepronium bromide (N-ethyl-N,N,α-trimethyl-γ-phenylbenzenepropanaminium bromide) is a quaternary ammonium compound with anticholinergic effects similar to those of atropine. It is used in the treatment of urinary frequency and severe incontinence in geriatric patients, in nocturnal frequency, and after bladder surgery, prostatectomy or bladder radiotherapy[1]. The drug is usually administered as tablets, each containing 100 mg emepronium bromide ("Cetiprin", KabiVitrum, Middlesex, U.K.).

There is little published work concerning the quantification of emepronium bromide. Hartvig *et al.*[2] have developed an electron-capture gas chromatographic method for the measurement of subnanogram amounts of this drug in human serum. High-performance liquid chromatography (HPLC) does not appear to have been used for the determination of this compound, although the technique has been applied to similar quaternary ammonium drugs, such as lachesine[3].

Within this laboratory, we are developing HPLC methods for assaying the active ingredients in bulk-purchased tablets and capsules. In this communication, we present a method for the analysis of emepronium bromide tablets.

EXPERIMENTAL

The chromatography system consisted of an Applied Chromatography Systems 750-03 pump, a Rheodyne 7125 injection valve fitted with a 20-μl sample loop, a Cecil 2112 variable-wavelength absorbance detector operated at 258 nm, and a Phillips PM 8251 recorder (chart speed 300 mm h^{-1}, with an operating voltage of 10 mV). The assay was carried out using a 250 × 4.6 mm I.D. stainless-steel column packed with LiChrosorb 10 RP-8 (Chrompack, London, U.K.), and the mobile phase was acetonitrile–water (90:10) containing 0.005 *M* 1-heptanesulphonic acid (sodium salt). The pH of this solution was adjusted to 4.1 using glacial acetic acid. A flow-rate of 2 ml min^{-1} was found to give an acceptable retention time. All solvents and reagents were of chromatographic grade (Fisons, Loughborough, U.K.).

Standard solutions were prepared by dissolving emepronium bromide (KabiVitrum) in distilled water. Test solutions were made either by dispersing a single

0021-9673/85/$03.30

tablet in water using an ultrasonic bath, or by dispersing finely ground tablet powder equivalent to 100 mg of drug in water. The volumes of the test solutions were adjusted to give a final nominal concentration of 1 mg ml^{-1}. All solutions were filtered using 0.45-μm filters (Acrodisc CR, Gelman Sciences, MI, U.S.A.) before use. Injections were made using the loop-filling technique.

RESULTS AND DISCUSSION

The peak height was found to be linearly related to the amount of emepronium bromide injected over the range 10 to 200 μg. The best-fit straight line was calculated, and the regression coefficient (r) found to be 0.9975. The relationship between peak height and amount of drug injected is given by the expression:

$$\text{Amount of drug injected } (\mu g) = \frac{\text{Peak height (mm)} - 18.62}{4.11}$$

Ten consecutive injections of 20 μg emepronium bromide gave a mean peak height of 103.1 mm, and the limits of error ($p = 0.95$, degrees of freedom = 9) were calculated as $\pm 0.4\%$. The minimum detectable quantity of emepronium bromide was found to be 4 μg, using an absorbance of 0.05 a.u.f.s. Using a higher sensitivity produced an unacceptable level of baseline noise.

Injection of the test solution (one tablet to 100 ml of solution) indicated that the tablet excipients did not interfere with the assay. A single, sharp peak with a retention time of about 4 min was obtained for both test and standard solutions.

From these results, it would seem that HPLC is a suitable method for the determination of emepronium bromide in tablets. For routine assays, it should be possible to use only two or three standard solutions (for example, 0.9 mg ml^{-1}, 1.0 mg ml^{-1} and 1.1 mg ml^{-1}), since the linearity of response has been established, and the limits set within this laboratory are 92.5 to 107.5 mg of emepronium bromide per tablet. These tablets are not the subject of a British Pharmacopoeia monograph, and there are no official limits for related substances or other impurities.

REFERENCES

1 J. E. F. Reynolds (Editor), *Martindale: The Extra Pharmacopoeia*, The Pharmaceutical Press, London, 28th ed., 1982, p. 299.
2 P. Hartvig, B. Naslund and J. Vessnas, *J. Pharm. Sci.*, 65 (1976) 1707.
3 A. J. Collins, T. A. Burbridge and R. Bain, *J. Clin. Hosp. Pharm.*, 5 (1980) 217–223.