Journal of Chromatography, 329 (1985) 434–437
Elsevier Science Publishers B.V., Amsterdam — Printed in The Netherlands

CHROM. 17 830

Note

Determination of glycerol in pharmaceutical preparations by reversed-phase high-performance liquid chromatography using a refractive index detector

F. BRESLIN* and G. P. STEPHENSON
Medicines Testing Laboratory, Pharmaceutical Society of Great Britain, 36 York Place, Edinburgh EH1 3HU (U.K.)
(Received April 22nd, 1985)

Glycerol (propan-1,2,3-triol) is of importance in the pharmaceutical industry; among its uses are as a sweetener in elixirs and syrups; as an hygroscopic agent in pastes and poultices and as a solvent in ear drops. Several glycerol-containing formulations are described in the British Pharmacopoeia (BP)[1], but for only a few of those preparations (*e.g.* compound cardamom tincture, compound rhubarb tincture and glycerol suppositories) is a periodate method of assay specified, for the determination of glycerol. The periodate method is limited in its application to pharmaceutical products because sucrose, an excipient often used in liquid preparations, interferes. In recent years, high-performance liquid chromatography (HPLC) has been employed in the identification and quantification of polyhydric alcohols in domestic products such as soap, apple juice, tobacco and toothpaste[2–5]. The determination of glycerol in pharmaceutical preparations by HPLC has not, as far as we are aware, been previously described. This paper describes a precise and specific HPLC procedure, using a refractive index detector, for the determination of glycerol in a variety of pharmaceutical preparations.

EXPERIMENTAL

Apparatus

An Altex Model 110A pump was used in conjunction with an Altex Model 500 automated injection system provided with a 20-μl loop. The analytical column (200 × 5 mm I.D.) was packed with Spherisorb S5-NH2 (particle size 5 μm) and used in line with an eluent saturation column (250 × 4.6 mm I.D.) containing Partisil silica gel (particle size 20 μm) prior to the injection valve. Monitoring was by a refractive index detector (Refractomonitor III from LDC) operating at ambient temperature. Chromatograms and integrations were recorded using a Shimadzu C-R1B Chromatopac. Throughout the experiments the flow-rate of the mobile phase was 1.0 ml/min.

Reagents

Acetonitrile (HPLC/Spectroscopy grade) was purchased from Glenrothes

0021-9673/85/$03.30

Chemicals, U.K. The water used was that obtained from the Milli R/Q water purifier (Millipore U.K., Middlesex, U.K.). Glycerol (SLR grade) was used as received from Fisons, Leicestershire, U.K. The mobile phase consisted of a mixture of acetonitrile–water (80:20, v/v) degassed by vacuum filtration using Whatman GF/C filters. Samples of pharmaceutical products were obtained from commercial sources and used as received; for details see Table II.

Standard preparation

Glycerol, 40.00 g, was accurately weighed into a 200-ml volumetric flask and diluted to volume with water; this was the stock standard solution. Aliquots of stock standard solution (1.0, 2.0, 3.0, 4.0 and 5.0 ml, respectively) were pipetted into separate 200-ml volumetric flasks. Mobile phase (100 ml) was added to each flask and the contents were diluted to volume with water.

Sample preparation

The products were accurately weighed, dispersed and diluted with mobile phase and water to yield a final solution containing 40% (v/v) acetonitrile and approximately 0.25% (w/v) glycerol. The sample solutions were passed through a 0.45 μm ARCO LC13 filter (Gelman Sciences, Northampton, U.K.) prior to injection.

RESULTS AND DISCUSSION

Linearity, precision and recovery of the described procedure were investigated and the applicability assessed by determining the glycerol content in a variety of pharmaceutical products.The linearity of response of the detector was established for glycerol concentrations over the range 0–5.0% (w/v); a rectilinear relationship between concentration and peak areas was obtained with a coefficient of correlation of better than 0.999. However, in order to reduce the risk of overloading or contaminating the column with high concentrations of excipient material, the lower concentration range of 0–0.5% (w/v) was adopted for assays.

The precision of the method was studied using a sample of compound cardamon tincture BP. Ten separate assays of the preparation were performed by the described method; the coefficient of variation was 0.88%.

TABLE I

GLYCEROL RECOVERY IN SODIUM BICARBONATE EAR DROPS

Glycerol added (%, v/v)	*% BPC formulation*	*Glycerol found (%, v/v)*	*Recovery (%)*
15.03	50	15.02	99.9
22.53	75	22.25	98.8
30.00	100	30.16	100.5
37.53	125	37.36	99.5
45.01	150	44.92	99.8
Mean			99.7
Standard deviation			0.63
Coefficient of variation			0.63%

TABLE II

HPLC AND PERIODATE ASSAY OF GLYCEROL IN PHARMACEUTICAL PRODUCTS

N.A. = Not applicable.

Product	*% of theory found by*	
	HPLC	*Periodate method*
Cascara elixir BP	97.2	97.1
Compound cardamom tincture BP	100.6	96.4
Compound rhubarb tincture BP	96.5	93.9
Phenobarbitone elixir BP	101.3	97.4
Ipecacuanha tincture BP	91.0	89.3
Titanium dioxide paste BP	98.7	95.8
Compound thymol glycerin BP	102.2	N.A.
Ephedrine elixir BP	102.4	N.A.
Paediatric opiate squill linctus BP	96.0	N.A.
Paracetamol paediatric elixir BP	98.4	N.A.
Sodium bicarbonate ear drops BPC	97.1	N.A.
Cough mixture 1	109.3	N.A.
Cough mixture 2	101.3	N.A.
Cough mixture 3	105.2	N.A.
Cough mixture 4	87.5	N.A.

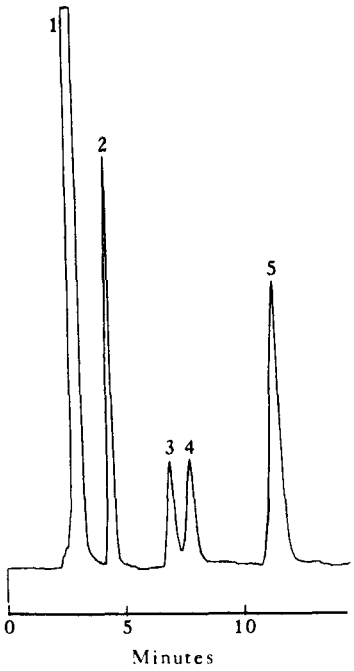

Fig. 1. Typical chromatogram of an assay for glycerol in ephedrine elixir BP. Peaks: 1 = non-retained including water; 2 = glycerol; 3 = D-fructose; 4 = D-glucose; 5 = sucrose. Conditions were as described with detector sensitivity of $50 \cdot 10^{-6}$ refractive index units.

Recovery experiments were carried out on samples of sodium bicarbonate ear drops prepared in the laboratory. Glycerol was added at levels of between 50 and 150% of the concentration described in the British Pharmaceutical Codex (BPC)[6] for this formulation. Table I illustrates the excellent recoveries obtained.

To examine the versatility of the procedure fifteen formulations were analysed by the HPLC method. Fig. 1 illustrates the separation of glycerol from the components of ephedrine elixir BP. Sucrose, the principal ingredient of syrup BP and D-fructose and D-glucose, components of invert syrup BP, do not interfere in the determination of glycerol. For comparison, the periodate oxidation method, described under compound cardamon tincture in the British Pharmacopoeia, was applied to those products that were amenable to this type of assay. The figures obtained by both methods are summarised in Table II.

These results confirm the validity of the described HPLC procedure and its applicability to the determination of glycerol in a range of pharmaceutical products.

REFERENCES

1 *British Pharmacopoeia*, HMSO, London, 1980.
2 R. Schwarzenbach, *J. Chromatogr.*, 140 (1977) 304.
3 K. Aitzetmüller, *J. Chromatogr.*, 156 (1978) 354.
4 D. L. Hendrix, R. E. Lee, Jr., J. G. Baust and H. James, *J. Chromatogr.*, 210 (1981) 45.
5 E. D. George and J. A. Acquaro, *J. Liquid Chromatogr.*, 5 (1982) 927.
6 *British Pharmaceutical Codex*, The Pharmaceutical Press, London, 1973, p. 665.