A NOTE ON THE STABILITY OF SOLUTIONS OF ISOPRENALINE

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ISOPRENALINE Spray Solution (B.P.C.) contains sodium metabisulphite (0·1 per cent) and must be recently prepared or stored protected from light in small well-filled containers. Since metallic ions catalyse the decomposition of isoprenaline (B.P.C. 1958) and since disodium edetate is a better preservative than sodium metabisulphite for solutions of the related phenylephrine (West and Whittet, 1960) comparison of the stabilising power of these two agents has been extended to the Spray Solution of Isoprenaline. Four solutions were prepared: (1) Isoprenaline Spray, B.P.C., (2) Isoprenaline Spray, B.P.C. omitting sodium metabisulphite, (3) Isoprenaline Spray, B.P.C. omitting metabisulphite but containing disodium edetate (0·1 per cent) and (4) Isoprenaline Spray, B.P.C. containing added disodium edetate. Ampoules (5 ml.) of each of these were sealed under air and stored at 15–20° for 16 months. They were then assayed for biological activity using the blood pressure of the anaesthetised cat (depressor action) and the isolated rabbit ileum (inhibitory action). Only solution 3 differed significantly in activity from the standard solution 1: the loss in activity, however, was slight. Both solutions not containing metabisulphite turned light brown in colour.

Although intravenous infusion of isoprenaline has been recommended (Segal, 1960; Hellerstein, 1960) no information is available as to how the solutions are sterilised and the effect of various methods on the stability of isoprenaline has been examined. A solution of isoprenaline sulphate (1 in 10,000) in water for injection containing sodium metabisulphite (1 in 1,000) was prepared. Part of this was sterilised by filtration through a bacteria-proof sintered glass funnel and sealed in sterile 2 ml. ampoules, half of these under air and half under nitrogen. The remaining solution was placed in 2 ml. ampoules, half of which were sealed under air and half under nitrogen; ampoules from both of these two groups were autoclaved at 115° for 30 min., the rest were steamed at 100° for 30 min. Samples from each of the 6 batches were assayed on the isolated guinea-pig heart (cardiac stimulant action) and on the rabbit ileum (inhibitory action). There was no loss of biological activity in any of the solutions. Even after storage at 15–20° for 16 months, there was no significant loss of activity and all solutions remained colourless.

Isoprenaline solutions of this composition showed no incompatibility with chlorocresol 0·2 per cent or phenylmercuric nitrate 0·002 per cent.

Thus, in the Spray Solution of Isoprenaline, disodium edetate does not prevent deterioration; it is not recommended as a preservative for this

solution. For isoprenaline solutions for injection, any one of the B.P. sterilisation methods is satisfactory when sodium metabisulphite is present as an antoxidant.

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