EFFECTS OF AUTOCLAVING ISOPRENALINE HYDROCHLORIDE INJECTIONS

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Investigations of the stability of isoprenaline have been hampered by the lack of a specific assay. The method of Kaistha (1970), based on the formation of an ether-soluble ion-pair of isoprenaline with di-(2-ethylhexyl) phosphoric acid, was tedious and imprecise (Stevenson, 1973). A spectrofluorimetric assay (Prasad et al, 1973) was unreliable in the presence of ascorbic acid and sodium edetate (Lund, 1976). The present work describes an assay for isoprenaline in degraded solutions and with ascorbic acid and sodium edetate, and its use to examine the effects of autoclaving injections of isoprenaline.

Samples containing isoprenaline hydrochloride were analysed by ion-pair reversed-phase high-pressure liquid chromatography on a column (100 mm x 4.5 mm id) of ODS-Hypersil (5 μm) with ultraviolet detection (Cecil 212) at 280 nm. The mobile phase (pH* = 2.8) was aqueous methanol (30%) containing acetic acid (2%) and sodium lauryl sulphate (0.002%) at a flow rate of 1.4 ml min^{-1} (pressure 1100 psig). Syringe injection (5 to 20 μl) gave peaks for isoprenaline hydrochloride (capacity factor, k' = 14.3) and adrenaline acid tartrate as internal standard (k' = 8.7); analysis time was 10 min. There was no interference from degradation products or from ascorbic acid or sodium edetate (fresh and after autoclaving). Peak area ratio was proportional to concentration in the range 0.1 to 0.8 mg ml^{-1} and 95% confidence limits at 0.5 mg ml^{-1} were ± 2% (n = 24). The coefficient of variation of replicate solutions (n = 5) was 1.7% (triangulation). Concentrations of isoprenaline hydrochloride in samples were calculated from peak area ratios with reference to standard solutions run concurrently.

The procedure was applied to a solution of isoprenaline hydrochloride (0.02%) in water for injections alone, and with ascorbic acid (0.1%) or sodium edetate (0.01%) or both antioxidants, in 2 ml neutral glass ampoules filled with nitrogen and sterilised by autoclaving at 116° for 30 min. When the experiment was repeated on solutions adjusted to pH 2.75 before autoclaving, degradation was reduced (Tables 1 and 2).

Table 1 Effects of autoclaving isoprenaline hydrochloride (0.02%)

Antioxidant	Initial pH	pH After Autoclaving	% Residual Concentration	Appearance
none	4.80	4.80	72.2	pinkish brown
ascorbic acid 0.1%	2.95	2.90	98.1	colourless
sodium edetate 0.01%	4.30	5.00	90.0	pinkish brown
ascorbic acid 0.1% + sodium edetate 0.01%	2.70	2.70	100.1	colourless

Table 2 Effects of autoclaving isoprenaline hydrochloride (0.02%) at pH 2.75

Antioxidant	pH After Autoclaving	% Residual Concentration	Appearance
none	3.20	91.9	pinkish brown
ascorbic acid 0.1%	2.90	100.0	colourless
sodium edetate 0.01%	3.00	100.2	colourless
ascorbic acid 0.1% + sodium edetate 0.01%	2.80	99.1	colourless

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