EFFECTS OF ASCORBIC ACID AND DISODIUM EDETATE ON THE DEGRADATION OF ISOPRENALINE

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We have previously reported an ion-pair high-pressure liquid chromatographic method to determine isoprenaline in the presence of its known degradation products and of ascorbic acid, disodium edetate and sodium metabisulphite. The method was used to examine the effects of autoclaving isoprenaline injection (0.02%) in 2 ml neutral glass ampoules filled with nitrogen and showed that the stability of the injection to autoclaving could be enhanced by adjustment of the pH to 2.75 and by the addition of ascorbic acid 0.1%, disodium edetate 0.01% or both substances (Clements et al 1979,1980).

In the present work the influence of ascorbic acid and disodium edetate (EDTA) on the kinetics of oxidation of an aqueous solution of isoprenaline hydrochloride was investigated. Experiments were carried out, protected from light, at 90° and pH 2.8 (citrate buffer 0.04M) and at 60° and pH 7.0 (phosphate buffer 0.027M) with or without cupric or ferric ions (10 ppm at pH 2.8; 4 ppm at pH 7.0). In each experiment 5 ml of isoprenaline hydrochloride solution (0.4%) was added to 95 ml of buffer (previously heated to the required temperature) in a flask (500 ml) fitted with a condenser, gas tube and thermometer, and immersed in a water-bath; water-saturated oxygen was passed through the solution at 50 ml min^{-1}. Aliquots were removed at intervals and analysed for isoprenaline.

Table Effect of additives on loss of isoprenaline from light-protected oxygenated solution (0.02%). First-order rate constants (s^{-1}) x 10^5

Additive	pH 2.8 at 90°	pH 7.0 at 60°
None	1.08	32.5
0.1% ascorbic acid	0.82	— a,b
0.01% EDTA	~0	43.9
0.1% ascorbic acid + 0.01% EDTA	0.21	— a,c
Cu^{++}	8.5	169
Cu^{++} + 0.01% EDTA	~0	28.5
Fe^{+++}	2.93	77.1
Fe^{+++} + 0.01% EDTA	~0	98.3

a: degradation not first-order; 50% loss in 205 (b) or 250 (c) min.

Ascorbic acid had little or no protective action but the addition of EDTA enhanced the stability at both pH values (Table). EDTA alone was effective at pH 2.8 but not at pH 7.0. As expected, the addition of metal ions increased degradation. EDTA gave complete protection against added cupric ions at pH 2.8 but some degradation occurred at pH 7.0. In contrast, EDTA protected against ferric ions at pH 2.8 but enhanced the degradation at pH 7.0; a similar finding was reported by Green et al (1956) who showed that adrenaline degradation by ferric ions at pH 7.4 was increased by EDTA.

Clements, J.A. et al (1979) J. Pharm. Pharmac. 31: 24P
Clements, J.A. et al (1980) J. Chromatogr. 189: 272-275
Green, S. et al (1956) J. biol. Chem. 220: 237-255