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Catalytic degradation of hydrocortisone disodium phosphate solutions by copper(II) ions

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As part of a general study of the stability of hydrocortisone 21-phosphate (HDP) solutions, the effect of metal ions has been investigated. Traces of copper profoundly accelerate both the hydrolysis of the 21-phosphate ester linkage and the subsequent oxidative degradation of the dihydroxy-acetone side-chain with significant effects being observed at copper concentrations as low as 0.1 p.p.m. (w.r.t. HDP). The main degradation products are hydrocortisone, 11 β hydroxyandrost-4-ene-3,17-dione, 11 β ,17 α -dihydroxy-3,20-dione-4-pregnene-21-al, and 11 β , 17 α -dihydroxy-3-oxo-4-etiolic acid. The formation of the 21-aldehyde, a yellow, substituted glyoxal, is shown to be the cause of the undesirable yellowing of HDP solutions. The compound is known to be readily produced from the 20-keto-21-hydroxy steroid by catalytic concentrations of cupric ions (Lewbart & Mattox, 1963). The products were identified and measured by a combination of two or more of the methods of t.l.c., g.l.c., n.m.r., i.r. and u.v. spectroscopy together with elemental analysis. Copper was determined (at levels as low as 0.01 p.p.m.) by chelation and solvent extraction followed by atomic absorption spectrophotometry. Hydrolysis was measured by determining the inorganic phosphate formed, (Mokrasch, 1961) and the oxidative production of 21-aldehyde assessed from measurements of optical density at 450 nm. The copper-catalysed hydrolysis and oxidation processes are both pseudo-first order with respect to HDP concentration and the activation energy for hydrolysis (measured at 37°, 50°, 70°, 80° and 90°) is 107.0 KJ mol⁻¹. The order of both reactions with respect to copper concentration is 0.28, which strongly suggests that the hydrolysis, as the initial step in the degradation sequence, is rate-determining. No differences were shown between the degradation kinetics of sub-micellar and supra-micellar concentrations of HDP. The effect of antioxidants, buffers and EDTA will be briefly discussed and mechanisms proposed for the role of copper ions. Of nine ubiquitous metal ions examined, only copper, iron and nickel showed enhancement of degradation at catalytic concentrations. The effects shown by iron and nickel were only about 20 and 8%, respectively, of that produced by copper.

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Mechanism of degradation of 5-bromouracil in aqueous solutions of sodium bisulphite

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A kinetic study has been made of the reactions that occurred at 25° in solutions which contained 5-bromouracil (I) (initial concentration range 0.5-1.0 $\times 10^{-2}$ M) and sodium bisulphite (initial concentration range 0.5-6.0 $\times 10^{-1}$ M). Reactions were studied throughout the pH range 4.0-7.5 and ionic strength was maintained at 1.0 M with potassium chloride.

It has previously been reported (Sander & Deyrup, 1972) that uracil (II) was rapidly formed by reactions of I in aqueous sodium bisulphite and that II was slowly converted to