

EFFECT OF pH ON THE PHOTOSTABILITY OF SULPHACETAMIDE EYE-DROP SOLUTIONS

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ABSTRACT

The photolysis of aqueous solutions of sulphacetamide and sulphanilamide has been studied at pH 3-11. The rate of photolysis appears to be the highest around pH 5.0 and 3.0 for sulphacetamide and sulphanilamide respectively. The log k-pH profiles of both compounds in the buffered and unbuffered solutions are presented. Various buffer ions e.g. citrate and phosphate catalyse the photodegradation reactions. Sulphacetamide eye-drop solutions prepared at pH 7 to 9 have ideal stability and clinical efficacy.

Introduction

Sulphacetamide sodium eye-drops are widely prescribed in 5-30% concentrations for acute conjunctivitis and prophylaxis of ocular infections after injury or burns. Special attention is required for more effective penetration of solutions into eye tissues and isotonicity with natural lacrymal secretions and tears (Grove-Rasmussen, 1953). The eye can tolerate solutions of a moderate range of pH 4.0 to 8.0. Ideally, the solutions should, therefore, be buffered to specific pH values to ensure optimum photostability, comfort to patient and enhanced therapeutic activity of the drug (Smith, 1967).

The present study has been carried out to investigate the effect of pH on the rates of photodegradation of sulphacetamide in the buffered and unbuffered solutions of pH 3-11.

Materials and Method

Sulphacetamide (Sigma) and sulphanilamide (BDH) were found to be chromatographically pure. Azobenzene-4, 4'-disulphonamide and azoxybenzene-4, 4'-disulphonamide were prepared using the method of Seikel, 1940.

Sulphacetamide and sulphanilamide solutions (10^{-3} M) at pH 3-11 were photolysed using a Philips 30W mercury discharge UV tube according to the method previously reported by Ahmad and Ahmad, 1981 and the concentrations of sulphacetamide and photoproducts were determined by a multicomponent spectrophotometric method (Ahmad and Ahmad, 1983).

Result and Discussion

Colour changes: The nature of colour changes observed during the photolysis of sulphacetamide solution appears to be a function of the effective wavelength and its intensity, amount of available oxygen drug concentration and pH of the solution. The fact that the nature and intensity of the colour noticed during the photolysis of sulphacetamide solutions varies from violet pink (pH 3), pink brown (pH 5) and dark brown (pH 7-9) to red pink (pH 11) suggests that a number of intermediate compounds are involved in the reaction (Ahmad and Ahmad, 1981). The intensity of the colour changes and hence the rate of photolysis is affected by the presence of antioxidants which may control the extent of degradation processes (Ahmad and Ahmad, 1983).

Sulphanilamide an intermediate in the photolysis of sulphacetamide, on subsequent UV irradiation in aqueous solutions (pH 3-11) undergoes oxidation accompanied by colour changes ranging from yellow brown (pH 3) and pale blue (pH 5) to red violet (pH 7-11) which are concentration dependent (Ahmad, et al. 1972). In these reactions a number of photoproducts are formed probably as a result of the fission/condensation of sulphanilamide molecule via radical mechanism (Ahmad and Ahmad, 1981; Chignell et al. 1981).

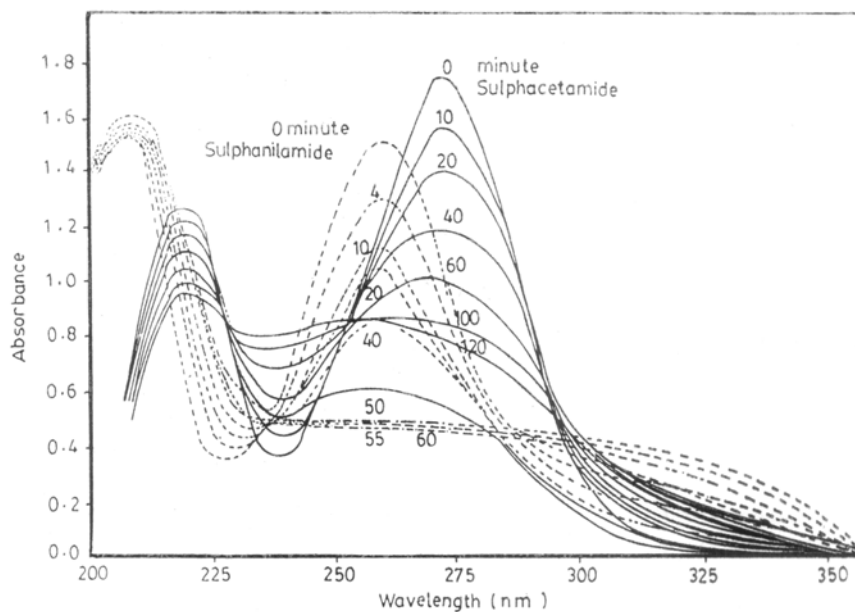


Fig. 1. Spectral variations during photolysis of 10^{-4} M sulphacetamide and sulphanilamide at pH 4.0 (Buffered).

Spectral Changes: Sulphacetamide solutions exhibit absorption maxima at 258-259 nm at pH 1-9. The photolysis of sulphacetamide and sulphanilamide solutions is accompanied by a modification of the spectral characteristics of these compounds. The major spectral variations (pH 4.0) result from the hydrolysis of sulphacetamide to sulphanilamide and its subsequent photooxidation to coloured compounds absorbing in the near UV region. The gradual decrease in the absorption of sulphacetamide at 268 nm and of sulphanilamide at 258 nm (Fig. 1) and simultaneous increase in absorption in the 280-380 nm region is in accordance with the absorption characteristics of the azo and azoxy derivatives which exhibit absorption maxima at 320 nm.

The UV irradiation of a 0.1% aqueous sulphacetamide solution (pH 9.0) was found to result in complete disappearance of the 268-258 nm peaks at 250 hours. The solution became light brown with deposition of coloured material. This is in agreement with the observations of Schwarz et al, 1968; who reported the loss of absorption maximum of sulphanilamide and an increase in absorption at 310 nm. This may be due to the formation of azo derivative.

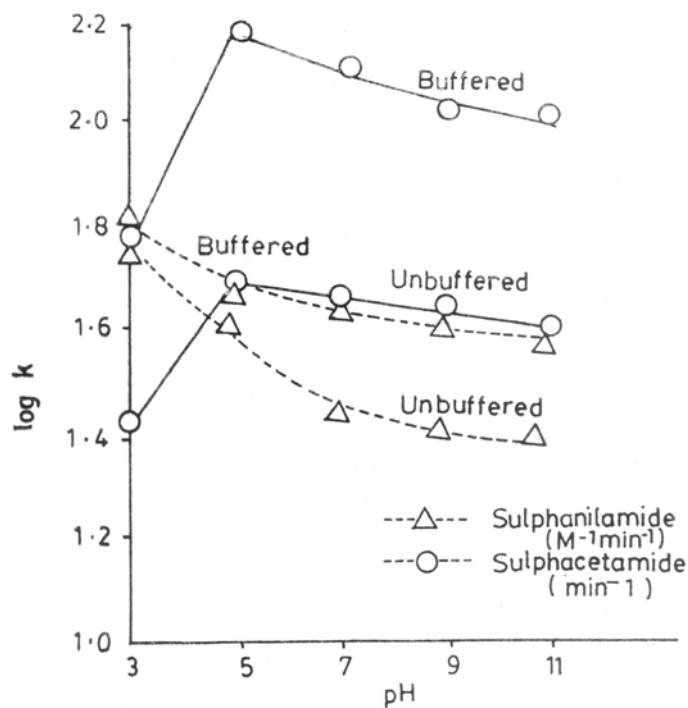


Fig. 2, log k-pH profile for the photolysis of sulphacetamide and sulphanilamide.

Rate of hydrolysis. The fate of photolysis appears to depend upon the state of ionization of sulphacetamide, pKa 5.4 (Yamazaki et al 1970) and of sulphanilamide, pKa 10.4 (Northey, 1948). The log k-pH profiles for the photolysis of both the compounds in buffered and unbuffered solutions (Fig. 2) are nonlinear, which is probably due to a difference in the ionic character of the molecules with a change in pH. The kinetic data suggest that the unionised form of sulphanilamide is more susceptible to photolysis than the ionised form whereas in the case of sulphacetamide it is vice versa. The rate of photolysis (hydrolysis) of sulphacetamide appears to be the highest around pH 5 (72% anion form) and is almost pH-independent in the region of 7 to 11. Sulphanilamide exhibits maximum photodegradation (oxidation) around pH 3 (0% anion form) and the rate is almost independent of pH over the range of 5 to 11. Below pH 5 (sulphacetamide) and pH 3 (sulphanilamide) the decrease in rate of photolysis appears to be due to protonation of the aromatic primary amino group in the molecule. In the pharmaceutically useful pH range of 7 to 9, the sulphacetamide solutions are more stable than that of pH 3-6.

Buffer effect: The buffer agents used to maintain the pH appear to influence the rate of photolysis of both sulphacetamide and sulphanilamide. The citrate ion (pH 3.5) in particular, exerts a catalytic effect on the rate of reaction. A comparison of the log k-pH profiles in the buffered and unbuffered solutions suggests that the shape of both curves in each case is almost same with an upward displacement in the buffered solutions. This behaviour indicates the magnitude of the overall catalytic effect of the various buffer ions e.g., citrate phosphate and borate present during the photolysis of these compounds at various pH values.

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