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INFLUENCE OF CERTAIN ADDITIVES ON THE PHOTOSTABILITY OF COLCHICINE SOLUTIONS+

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ABSTRACT

The photostability of colchicine solutions in the presence of selected additives under shortwave ultraviolet light was investigated. P-aminobenzoic acid (PABA) and uric acid solubilized by lithium carbonate enhanced the photostability of colchicine. Glycerin on the other hand demonstrated a detrimental effect. Buffer species and pH of the vehicle were found to influence the apparent zero-order rate of degradation of colchicine solutions.

INTRODUCTION

Colchicine is used for the relief of pain in acute gout. It is usually administered in tablets, but where a rapid response is required or where oral administration causes gastrointestinal disturbance, it may be given by intravenous injection. Several papers (1-3) reported on the photodegradation of colchicine and its mechanism. However, it appears from the survey of literature that no work has been published on the effect of formulation factors on the photostability of this drug. Previous reports (4-8) from our laboratory have shown that certain additives could influence the photostability of light-sensitive pharmaceuticals. Therefore, it appeared worthwhile to investigate the effects of certain additives on the photostability of colchicine solutions.

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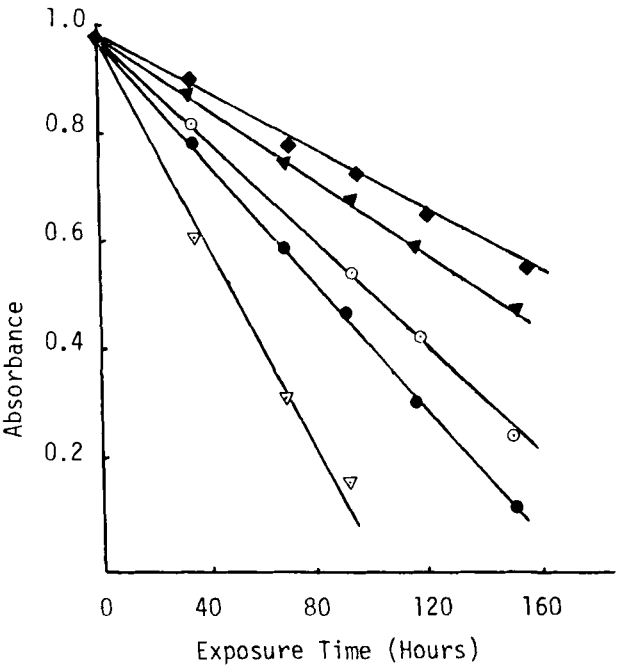

FIGURE 1

Photodegradation of Colchicine Solutions in Acetate Buffer of pH 4.5. Key: ⊙ Colchicine; △with 50% v/v glycerin; ▲ with 0.1% PABA; ● with 0.05% Uric Acid Solubilized by Glycerin; ◆ with 0.1% Uric Acid Solubilized by Lithium Carbonate

EXPERIMENTAL

Materials: Colchicine was obtained from Sigma Chemical Company. Other chemicals were purchased from commercial sources in pharmaceutical or reagent grade and were used without further purification.

Procedure: Volumes of 0.25% colchicine solutions with and without the additives were exposed to the light source as previously described (4-8). At appropriate time intervals, 0.3 ml of the solution was diluted with 3 ml of the buffer solution and assayed spectrophotometrically (Hitachi UV-Visible Spectrophotometer, Model 100-60) at 353 nm against the appropriate blank. At this wavelength, there was no interference by the degradation products (1). The analysis was done on duplicate samples and the difference between duplicates was usually 0 - 1.2%

TABLE 1

Effect of Certain Additives on the Photostability of Colchicine Solutions in Acetate Buffer of pH 4.5

Additives	Rate Constant $K \times 10^3\ hr^{-1}$	% Increase/Decrease in K $\frac{K_o - K_s}{K_o} \times 100$
None	$4.90 = K_o$	----
PABA 0.1%	3.60	26.5
Uric Acid 0.1% in Lithium Carbonate	2.75	43.9
Uric Acid 0.1 % in Glycerin	5.6	-14.3
Glycerin 50% v/v	8.5	-73.5

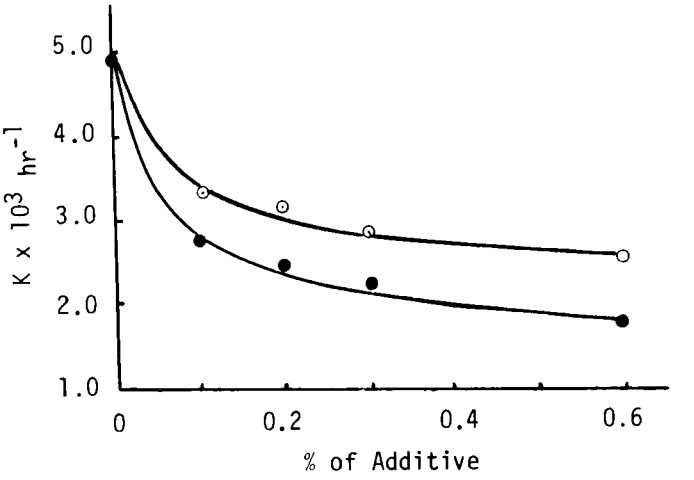

FIGURE 2

Effect of Concentration of PABA and Uric Acid Solubilized by Lithium Carbonate on the Photodegradation Rate Constant of Colchicine Solutions in Acetate Buffer of pH 4.5. Key: ⊙ with PABA; ● with Uric Acid Solubilized by Lithium Carbonate

TABLE 2

Effect of pH and Buffer Species on the Photostability of Colchicine Solutions

pH	Buffer	Degradation Rate Constant $K \times 10^3$ hr^{-1} Without PABA K_o	With PABA K_s	% Decrease in K $\frac{K_o - K_s}{K_o} \times 100$
2.0	HCl-KCl	4.60	3.3	28.3
4.5	Phosphate	4.90	3.6	26.5
4.5	Acetate	4.95	3.4	31.3
4.5	Citrate	4.80	3.8	20.8
7.0	Phosphate	4.90	4.5	8.1
8.0	Phosphate	4.90	4.6	6.1
10.5	Phosphate	5.30	4.8	7.7

DISCUSSION OF RESULTS

Photodegradation of Colchicine: The apparent zero-order rate of photodegradation of colchicine in the presence or absence of the additive can be seen from Fig. 1. The rate constants were calculated from this plot and are shown in Table 1.

Effect of Additives: Fig. 1 and Table 1 shows that PABA enhanced the photostability of colchicine solution in acetate buffer of pH 4.5 although color formation was not prevented. Uric acid solution in glycerin was found in previous reports (7,8) to enhance the photostability of some pharmaceuticals. However, with colchicine solutions it did not demonstrate this effect. This can be attributed to glycerin which was found in this study to enhance the photodegradation of colchicine as can be seen from Fig. 1. This was further confirmed by replacing glycerin by lithium carbonate solution to solubilize uric acid. Uric acid solubilized by lithium carbonate demonstrated a greater photostabilizing effect than that produced by PABA as shown in Fig. 1

and Table 1. Moreover, the solution did not show any color change after exposure to light for 40 hours.

Effect of Concentration of Additives: Fig. 2 shows that the higher the concentration of the additive, the greater was its photostabilizing effect within the concentration range studied.

Effect of pH and Buffer Species: Table 2 indicates that the rate of photodegradation of colchicine was influenced by the pH and the buffer species of the solutions. In the presence of PABA, the acetate ions demonstrated the greatest stabilizing effect, followed by the phosphate ions and then the citrate ions. Moreover, the stability of the solution decreased with increase of pH. However, in the absence of PABA, the effects of buffer species and pH within the range of 4.5 - 8.0, appeared to be less pronounced.

CONCLUSIONS

Photostability of colchicine solutions was enhanced by PABA and uric acid solubilized by lithium carbonate solution. Glycerin was most detrimental to the photostability of colchicine. Buffer species and pH of the solutions appeared to influence the rate of photodegradation of colchicine.

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