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INFLUENCE OF URIC ACID ON PHOTOSTABILITY OF SULFATHIAZOLE SODIUM SOLUTIONS

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ABSTRACT

The effect of uric acid as a photoprotective agent for buffered and unbuffered solutions of sulfathiazole sodium was investigated. Uric acid solution in glycerin was found to enhance the photostability of sulfathiazole sodium solutions. The higher the concentration of uric acid used, the greater was its photoprotective action within the concentration range studied. Uric acid was also found to demonstrate its photoprotective effect in the presence of either sodium sulfite or EDTA. Sodium sulfite alone in a concentration of 0.1% produced a detrimental effect on the photostability of sulfathiazole sodium in either borate or phosphate buffer of pH 9 ± 0.2. From the standpoint of the overall chemical stability of sodium sulfathiazole, uric acid appeared to be most effective when used alone in the borate buffer. However, the incorporation of 0.1% sodium sulfite in addition to uric acid contributed to the prevention of discoloration in either the borate or the phosphate buffer.

INTRODUCTION

Sulfathiozole sodium solutions have been reported to undergo discoloration on exposure to light and gamma-irradiation (1). Although Whittet (2) has stated that discoloration does not increase toxicity nor alter therapeutic activity, it is nonetheless undesirable. Kostenbauder et al. (3), reported

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that 0.1% sodium sulfite retarded discoloration of a 5% sulfathiazole sodium solution. They also recommended a buffer of pH9 to ensure complete solubility of sulfathiazole. Several workers (4,5,6) have shown that sulfonamides undergo oxidative decomposition to form colored solutions. Direct oxidation of sulfacetamide has been shown to result in the formation of azobenzene-4, 4'-disulfonamide and azoxybenzene-4, 4'-disulfonamide (6). In previous reports by Asker and Collier (7,8), uric acid was found to be an effective photoprotective agent for solutions of FD&C Blue No. 2. Therefore, it appeared worthwhile to study the photoprotective action of uric acid for sodium sulfathiazole solutions.

EXPERIMENTAL

Materials: Sulfathiazole sodium, uric acid, glycerin, boric acid, sodium hydroxide, dibasic potassium phosphate, hydrochloric acid, sodium nitrite, ammonium sulfamate and N-(1-naphtyl) ethylene diamine dihydrochloride were obtained from commercial sources in reagent or pharmaceutical grade and were used without further purification.

Equipment: The following were used: a light-stability cabinet equipped with two 30-inch, 30-watt Philips fluorescent tubes; Orion digital pH meter; a spectronic 20 spectophotometer.

Exposure to Light: The spectrophotometer tubes containing the solutions to be exposed to light were kept 7 cm from the light source in the light-stability cabinet. The light intensity was maintained at 1600 foot-candles.

Procedure: Because of the poor solubility of uric acid in water, a solution in glycerin was prepared by dissolving 50 mg of uric acid in 200 g of glycerin at a temperature not exceeding 100°C.

The typical experimental procedure was as follows: Volumes of sulfathiazole sodium solutions prepared with and without uric acid were placed in 10 x 100mm spectrophotometer tubes, covered with parafilm and exposed to the light source. Solutions free of sodium sulfathiazole were also prepared and exposed to the light source to serve as blanks. Samples were withdrawn at designated time intervals and assayed for sulfathiazole content by the Bratton-Marshall (9) techniques. Each determination was in duplicate, the results

averaged and used to calculate the percentage of sodium sulfathiazole in the sample by reference to a Beer-Lambert plot. The difference between duplicates was usually 0-1.3%.

The photoprotective effect of uric acid was first studied in an unbuffered aqueous solution containing 10mg% of sodium sulfathiazole in the presence of 10%, 20% and 30% w/v of the uric acid solution in glycerin. The photodegradation of sodium sulfathiazole solution in the presence of 10% w/v of glycerin was evaluated. Photodegradation of sulfathiazole sodium in borate and phosphate buffers of pH 9 ± 0.2 was also studied in the presence and absence of 7.5mg% uric acid, 0.1% sodium sulfite and 0.1% EDTA.

DISCUSSION OF RESULTS

Photodegradation in Unbuffered Solutions:

Figure 1 shows that the incorporation of 2.5mg%, 5mg% and 7.5mg% of uric acid dissolved in glycerin into a 10mg% of aqueous solutions of sulfathiazole sodium, produced a measurable protective action against photodegradation of the drug. It is evident from the figure that as the concentration of uric acid increased the photostability of the drug increased.

In order to eliminate the possibility that photostabilizing effect of uric acid solution in glycerin was due to the glycerin and not to the uric acid, photodegradation of sulfathiazole sodium solution was studied in the presence of 10% w/v of glycerin. The data were compared with those obtained by solution containing 10% w/v glycerin and 2.5mg% uric acid. The results indicated that glycerin alone demonstrated a photostabilizing effect but to a lesser extent than that produced by uric acid dissolved in glycerin as can be seen from Figure 1.

Photodegradation in Buffered Solutions:

Borate Buffer

Figure 2 shows that uric acid in glycerin substantially enhanced the photostability of sulfathiazole sodium solutions in the presence or absence of 0.1% sodium sulfite. It is evident from the figure that sodium sulfite alone enhanced the chemical degradation of sulfathiazole sodium solution on exposure to light. From the standpoint of the overall chemical stability of the drug,

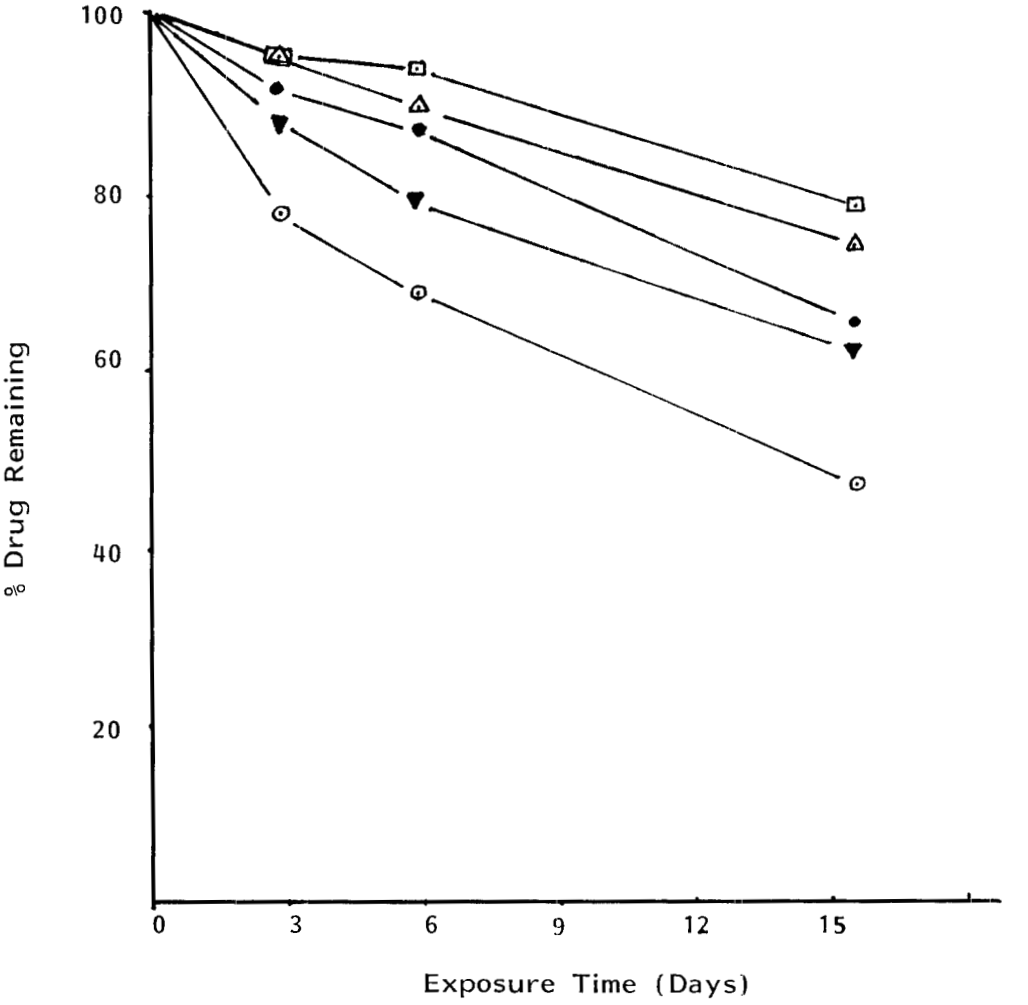

FIGURE 1. Photostabilizing Effect of Uric Acid For Aqueous Solutions of Sulfathiazole Sodium

- ⊙ Solution without Uric acid or Glycerin
- ● Solution with 2.5mg% Uric Acid + 10% w/v Glycerin
- △ Solution with 5 mg% Uric Acid + 20% w/v Glycerin
- ⊡ Solution with 7.5 mg% Uric Acid + 30% w/v of Glycerin
- ▼ Solution with 10% w/v Glycerin

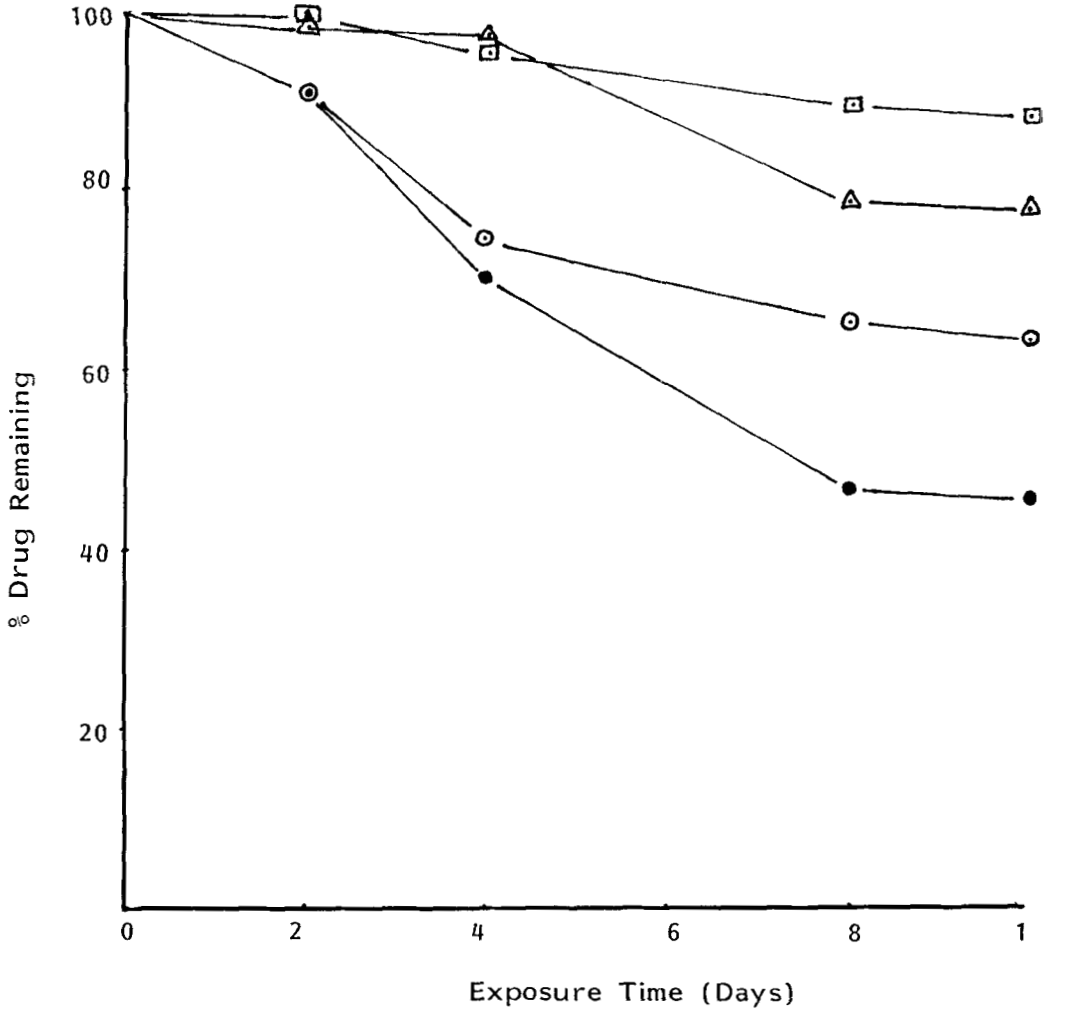

FIGURE 2. Photostabilizing Effect of Uric Acid for Sulfathiazole Sodium in Borate Buffer, pH 9±0.2 in Presence of Sodium Sulfite

- ⊙ Solution without Uric Acid or Sodium Sulfite
- ● Solution with Sodium Sulfite
- △ Solution with Uric Acid + Sodium Sulfite
- ⊡ Solution with Uric Acid

TABLE 1

Solutions	% Drug Remaining after Exposure to light for 10 Hours in		Color of Solutions after Exposure to light for 10 Hours in
	Borate Buffer	Phosphate Buffer	Borate & Phosphate Buffers
Solution without Additives	63.7	61.8	Yellow
Solution + Uric Acid	89.2	69.3	Very Slightly Yellow
Solution + Sodium Sulfite	46.0	55.6	Slightly Yellow
Solution + Uric Acid + Sodium Sulfite	79.3	62.6	Colorless
Solution + EDTA	68.2	72.9	Yellow
Solution + Uric Acid + EDTA	84.0	70.6	Very Slightly Yellow

uric acid appeared to be most effective when used alone in the borate buffer. However, the incorporation of 0.1% sodium sulfite in addition to uric acid contributed to the prevention of discoloration of the solution in either the borate or the phosphate buffer as shown in Table 1.

Kostenbauder et al. (3) recommended 0.1% sodium sulfite to retard discoloration of sulfathiazole sodium solution in borate buffer of pH 9 ± 0.2, but no data were given on the effect of sodium sulfite on drug degradation. It appears therefore, that the extent of discoloration is not always indicative of the overall drug degradation.

Figure 3 shows that EDTA alone slightly improved the photostability of sulfathiazole sodium solution. However, a combination of 7.5mg% uric acid dissolved in glycerin and 0.1% EDTA demonstrated a slightly less photoprotective action than that produced by uric acid alone.

Phosphate Buffer:

It can be seen from Fig. 4 that uric acid enhanced the photostability of sulfathiazole sodium solution in the presence or absence of 0.1% sodium sulfite. As with the borate buffer, sodium sulfite demonstrated a detrimental effect on the

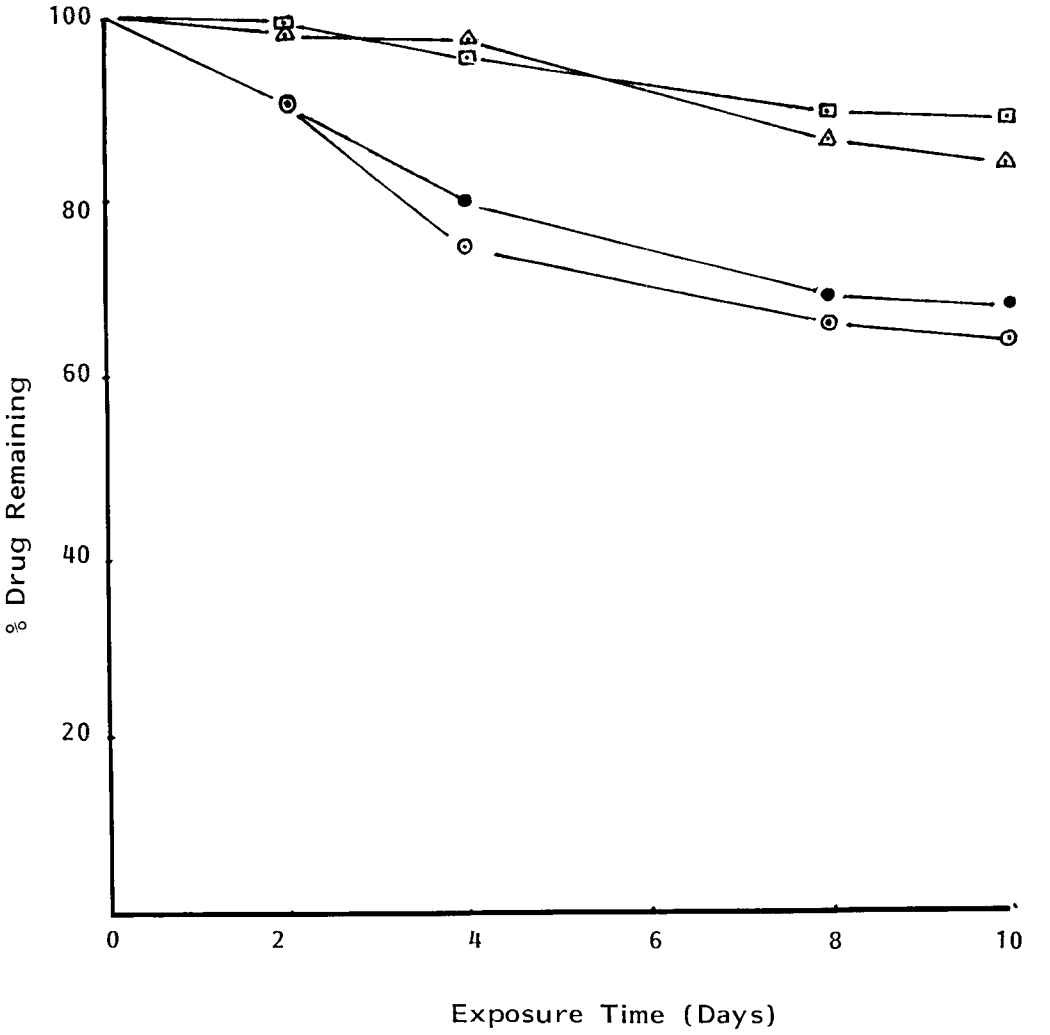

FIGURE 3. Photostabilizing Effect of Uric Acid for Sulfathiazole Sodium in Borate Buffer, pH 9±0.2 in Presence of EDTA

⊙ Solution without Uric Acid or EDTA

● Solution with EDTA

△ Solution with Uric Acid + EDTA

▣ Solution with Uric Acid

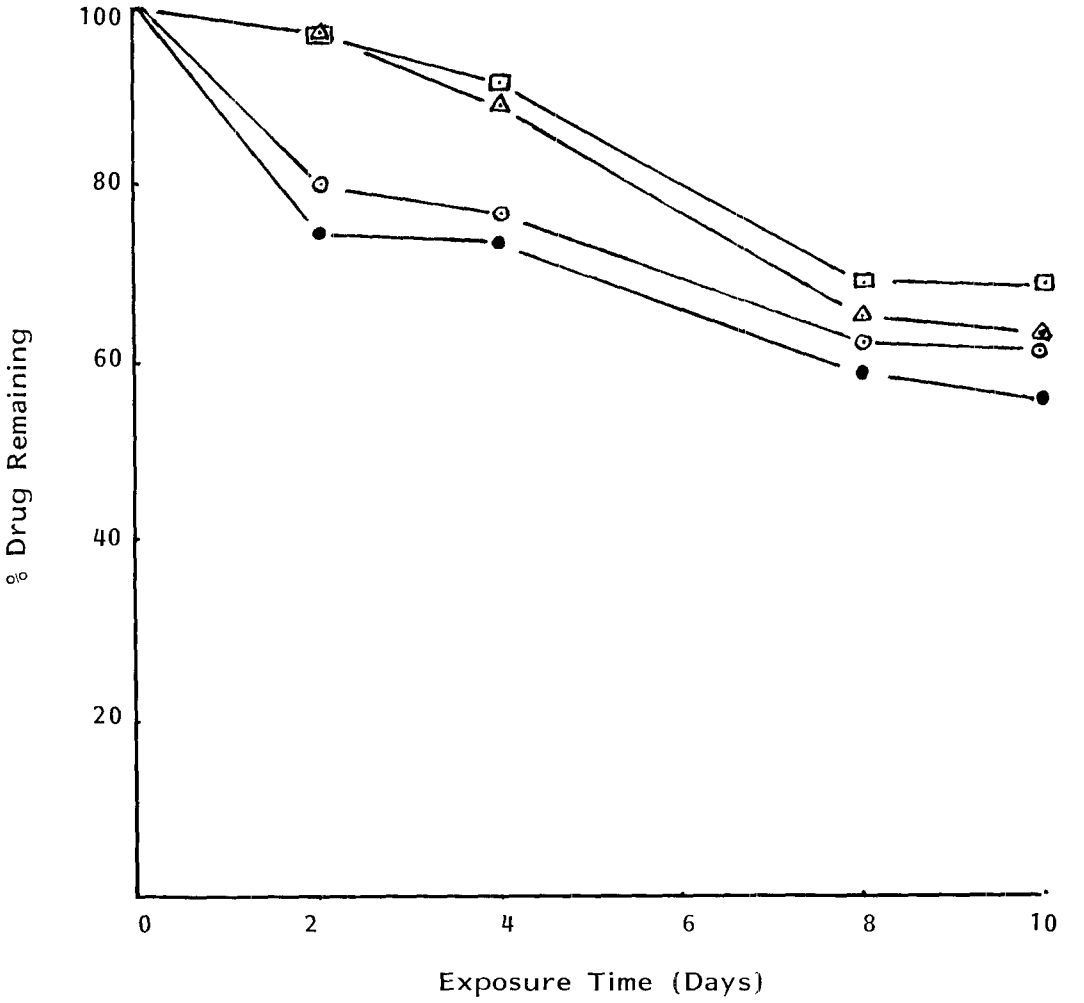

FIGURE 4. Photostabilizing Effect of Uric Acid for Sulfathiazole Sodium in Phosphate Buffer pH 9±0.2 in Presence of Sodium Sulfite

- ⊙ Solution without Uric Acid or Sodium Sulfite
- ● Solution with Sodium Sulfite
- △ Solution with Uric Acid + Sodium Sulfite
- ⊡ Solution with Uric Acid

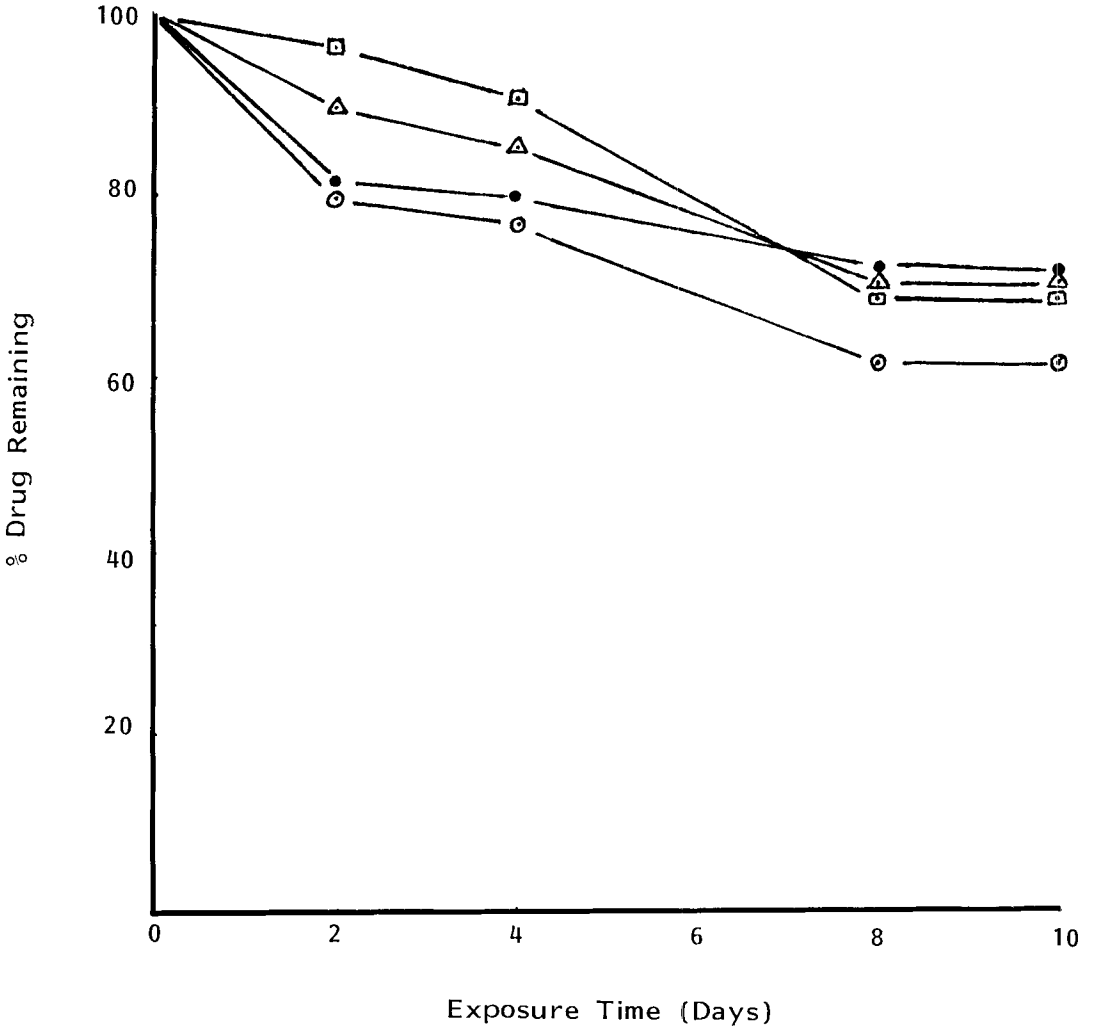

FIGURE 5. Photostabilizing Effect of Uric Acid for Sulfathiazole Sodium in Phosphate Buffer pH 9±0.2 i Presence of EDTA

- ⊙ Solution without Uric Acid or EDTA
- ● Solution with EDTA
- ◬ Solution with Uric Acid + EDTA
- ⊡ Solution with Uric Acid

photostability of the drug. Uric acid appeared to be less effective when used with sodium sulfite than when used alone as far as the overall chemical stability is concerned. However, the incorporation of 0.1% sodium sulfite in addition to uric acid prevented discoloration of the solution during storage.

Figure 5 shows that uric acid improved the photostability of sulfathiazole sodium solution in presence or absence of 0.1% EDTA. EDTA alone demonstrated a stabilizing effect for sulfathiazole sodium solution. However, after 8 hours of exposure to light, there was practically no difference in the photostabilizing effect amont the solutions containing EDTA, uric acid or a combination of both.

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