DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY, 11(12), 2109-2125 (1985)

INFLUENCE OF DL-METHIONINE ON THE PHOTOSTABILITY OF ASCORBIC ACID SOLUTIONS

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ABSTRACT

The photostablizing effect of DL-methionine for various buffered solutions of ascrobic acid was investigated. DL-methionine in a concentration of 10 mg% was found to enhance the photostability of 40 mg% ascorbic acid in acetate and phosphate buffers, but not in citrate buffer of pH 4.5. The photoprotective action of DL-methionine appeared to be influenced by its concentration, the pH of the medium and its buffer species. DL-methionine was also found to demonstrate its photoprotective action in presence of glycerin, EDTA and Tween 80. PEG 300, however, appeared to have a detrimental effect on the photostabilizing action of DL-methionine for ascorbic acid in acetate buffer of pH 4.5

INTRODUCTION

Several factors have been considered in the preparation of stable solutions of ascorbic acid. These factors included excluscon of air and oxygen, pH adjustment, protection from light and the use of additives such as antioxidants and chelating agents (1).

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0363-9045/85/1112-2109$3.50/0

The photochemical oxidation of ascorbic acid has been reported to proceed under either aerobic or anaerobic conditions. X-rays and gamma irradiations have been found to be more effective than UV radiations in enhancing the decomposition of ascorbic acid (2). The stability of ascorbic acid was reported to be enhanced in aqueous solutions of sucrose, sorbitol, glycerin and propylene glycol (3-5). Low surfactant concentrations have been found by Nixon and Chawla (6) and Poust and Colaizzi (7) to enhance the rate of oxidation of ascorbic acid.

DL-methionine has been reported by Asker and his associates (8) to enhance the photostability of reserpine solutions exposed to UV light. Therefore, it appeared worthwhile to study the effect of DL-methionine as a photoprotective agent on the photostability of buffered solutions of ascorbic acid in absence and in presence of some additives of pharmaceutical importance.

EXPERIMENTAL

Materials: Ascorbic acid, DL-methionine, sodium hydroxide, citric acid, monobasic potassium phosphate, dibasic potassium phosphate, sodium acetate, glacial acetic acid, potassium hydroxide, sodium bicarbonate, glycerin, PEG 300, EDTA, Tween 80 and 2,6 dichlorophenol-indophenol sodium were obtained from commerical sources in pharmacetuical or reagent grade and were used without further purification.

Equipment: The following were used: a light-stability cabinet equipped with 18-inch, 15-watt Sylvania fluorescent lamps to serve as the light source; Orion digital pH meter.

Procedure: The typical experimental procedure was as follows: Solutions containing 40 mg % of ascorbic acid in the various buffers were prepared with and without DL-methionine. Volumes each of 6 ml were placed in 10 x 100 mm Spectronic 20

tubes, covered with parafilm and exposed to the light source. Solutions of DL-methionine in the various buffers were similarly exposed to the light source to serve as blanks. Analysis of ascorbic acid solutions was carried out on duplicate samples at definite time intervals using the official dichlorophenol-indophenol method (9). In all cases, the quantity of ascorbic acid found in analysis immediately after preparation of the solutions was considered as 100%.

In studying the effect of variation of DL-methionine concentration on the photostability of ascorbic acid, solutions containing 40 mg % of ascorbic acid and 10, 20 and 40 mg of DL-methionine in acetate buffer of pH 4.5 were exposed to the light source and analysed periodically.

The effect of buffer species on the photostabilizing action of DL-methionine was studied using solutions containing 40 mg % ascorbic acid and 10 mg % DL-methionine in acetate, phosphate and citrate buffers of pH 4.5.

The effect of pH was determined for solutions containing 40 mg % ascorbic acid and 10 mg % of DL-methionine in phosphate buffers of pH values of 4.5, 7.0 and 7.9.

The influence of additives was investigated in presence and in absence of 10 mg % of DL-methionine using ascorbic acid solutions in acetate buffer of pH 4.5 and containing 40 mg % ascorbic acid and each of the following additives: 30% w/v glycerin, 30% w/v PEG 300, 0.5% w/v Tween 80 and 0.2% EDTA. Appropriate blanks were also prepared and exposed to the light source.

DISCUSSION OF RESULTS

Influence of DL-Methionine on the Photostability of Ascorbic Acid:

Figure 1 shows that the incorporation of 10 mg % of DL-methionine into 40 mg % ascorbic acid in acetate buffer of pH

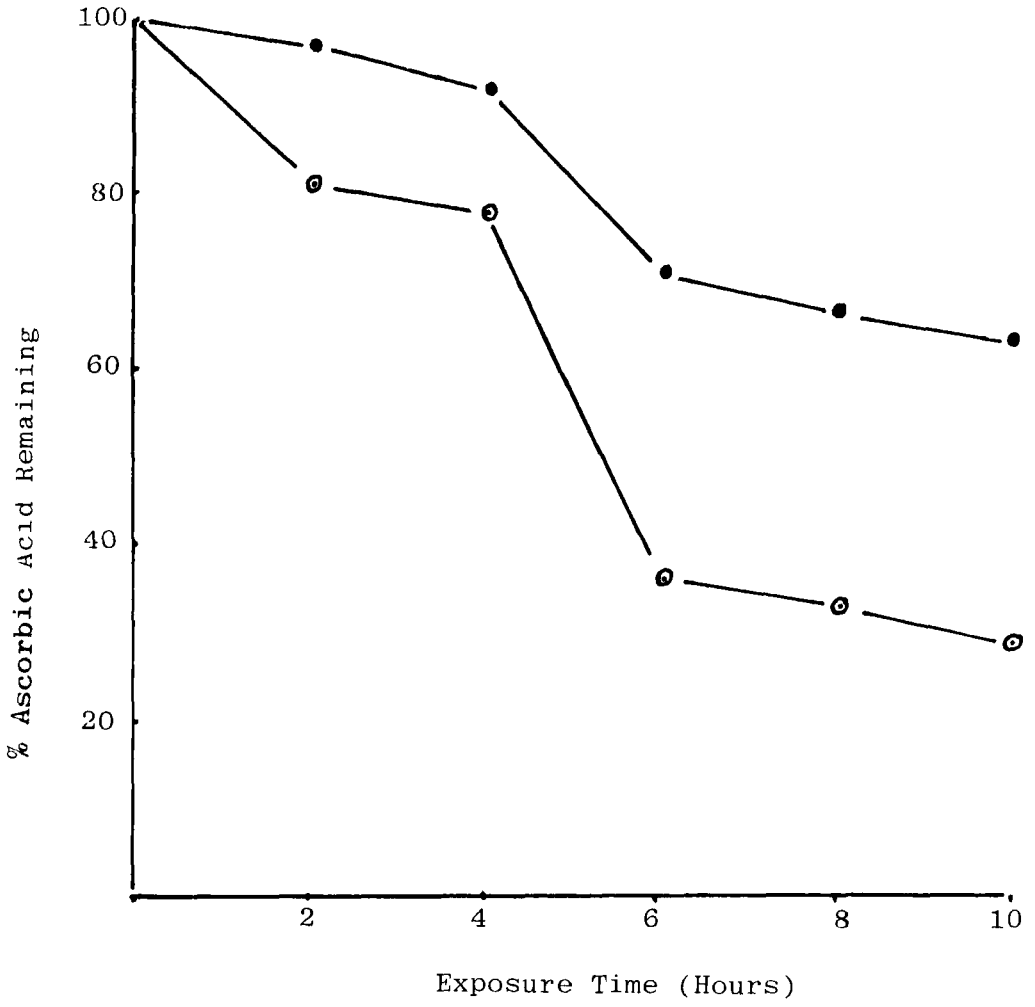

FIGURE 1. Photostabilizing Effect of DL-Methionine for Ascorbic Acid in Acetate Buffer of pH 4.5

○ Solution without DL-Methionine

● Solution with Dl-Methionine

4.5, produced a measurable protection against phtodegradation of ascorbic acid. It appears also from Figure 2 that the higher the concentration of DL-methionine, the better was its photoprotective action within the concentration range studied.

Effect of Buffer Species:

It can be seen from Figures 1 and 3 that DL-methionine demonstrated its phtoprotective action in acetate and in phosphate

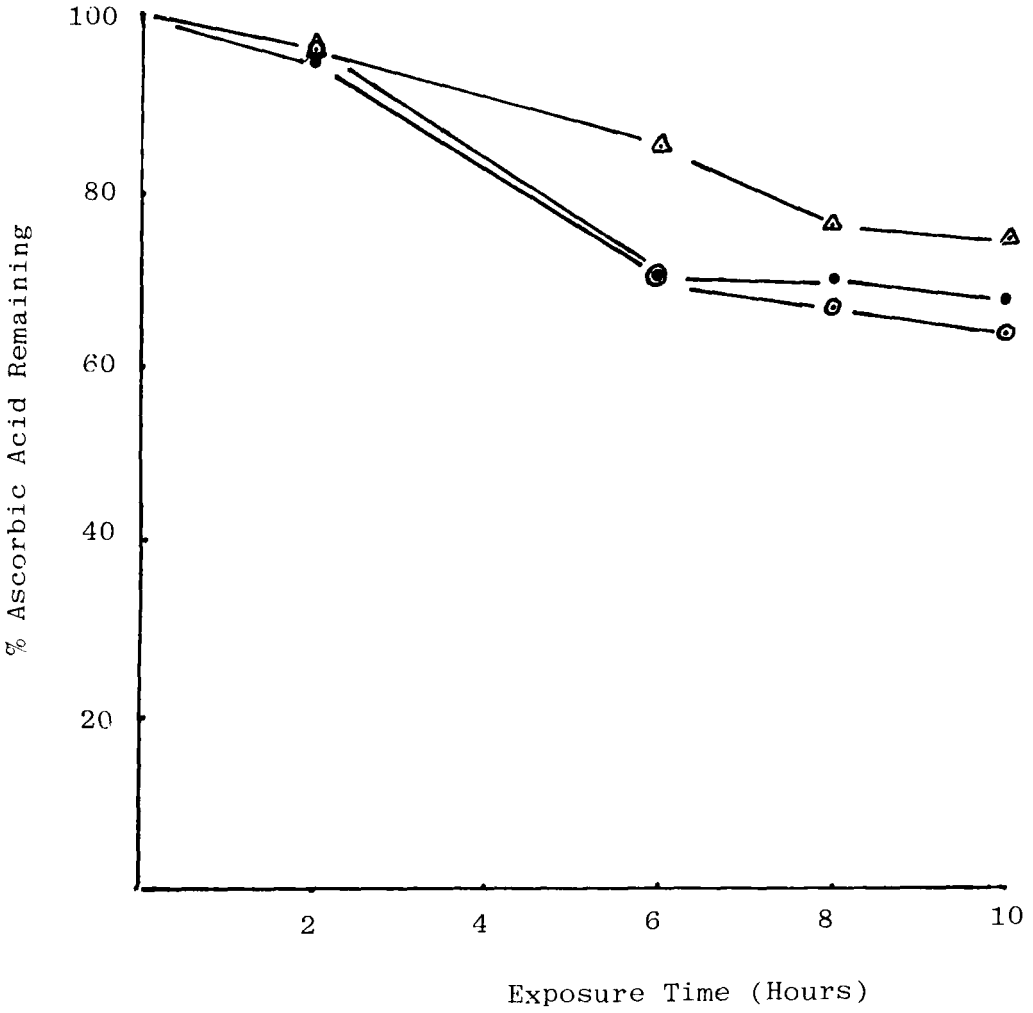

FIGURE 2. Effect of Dl-Methionine Concentration on the Photostability of Ascorbic Acid in Acetate Buffer of pH 4.5

- ⊙ 10 mg %
- ● 20 mg %
- ▲ 40 mg %

buffers of pH 4.5. On the other hand, the photoprotective action of DL-methionine appeared to be impaired in citrate buffer of pH 4.5 as shown in Figure 4. DL-methionine demonstrated a slightly better photoprotective action in the acetate buffer than in the phosphate buffer as shown in Figure 5. The detrimental effect

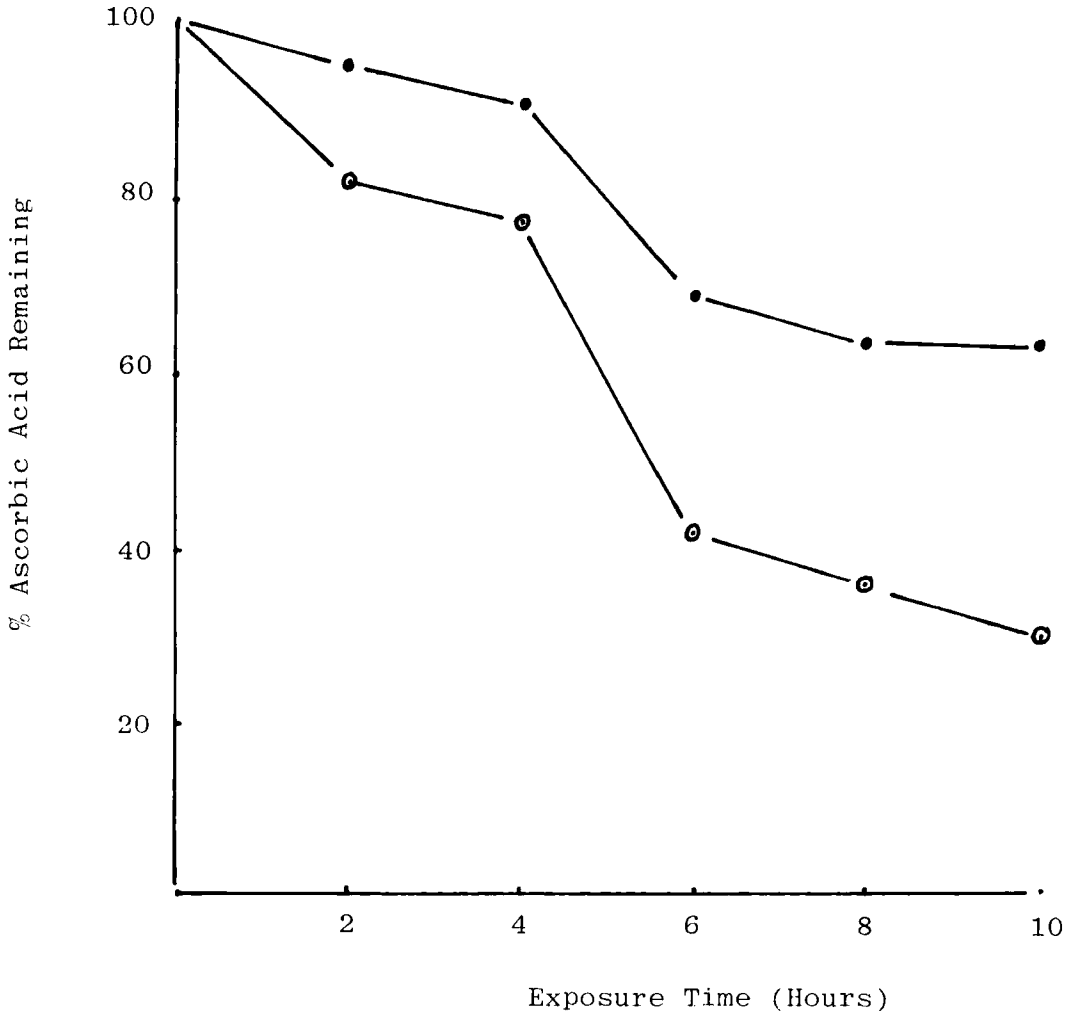

FIGURE 3. Photostabilizing Effect of DL-Methionine for Ascorbic Acid in Phosphate Buffer of pH 4.5

⊙ Solution without DL-Methionine

● Solution with Dl-Methionine

of the citrate ions on the photoprotective action of DL-methionine requries further investigation. In a previous report by Asker and Collier (10), the citrate ions were found to significantly decrease the photostabilizing effect of uric acid for solution of FD&C Blue No. 2. It can be concluded therefore, that buffer species would influence the photostabilizing effect of DL-methionine for ascorbic acid solutions.

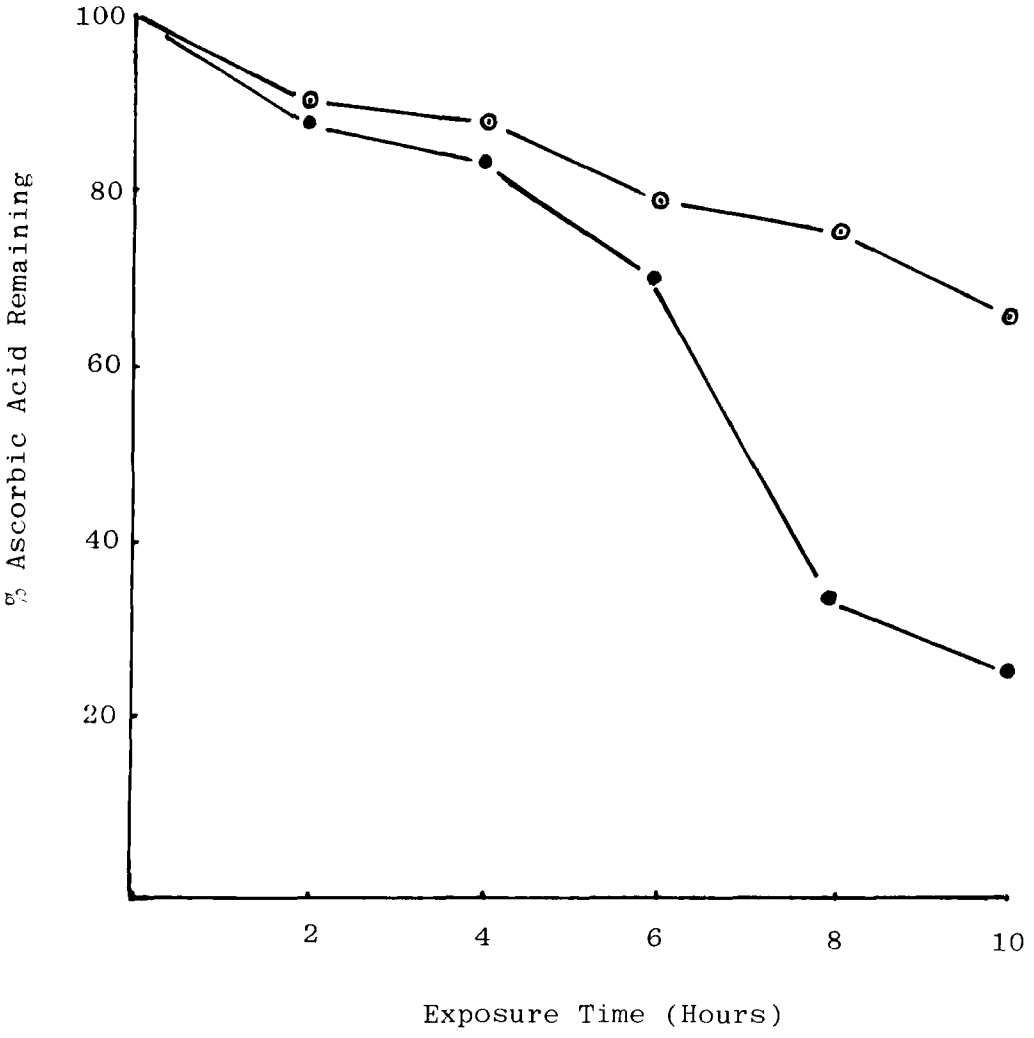

FIGURE 4. Effect of DL-Methionine on the Photostability of Ascorbic Acid in Citrate Buffer of pH 4.5

⊙ Solution without DL-Methionine

● Solution with DL-Methionine

Effect of pH:

The effect of pH on the photostabilizing action of DL-methionine for ascorbic acid was carried out in phosphate buffers having the following pH values: 4.5, 7.0 and 7.9. The data are represented by Figures 3, 6 and 7 respectively. The results indicate that DL-methionine demonstrated its greatest photopro-

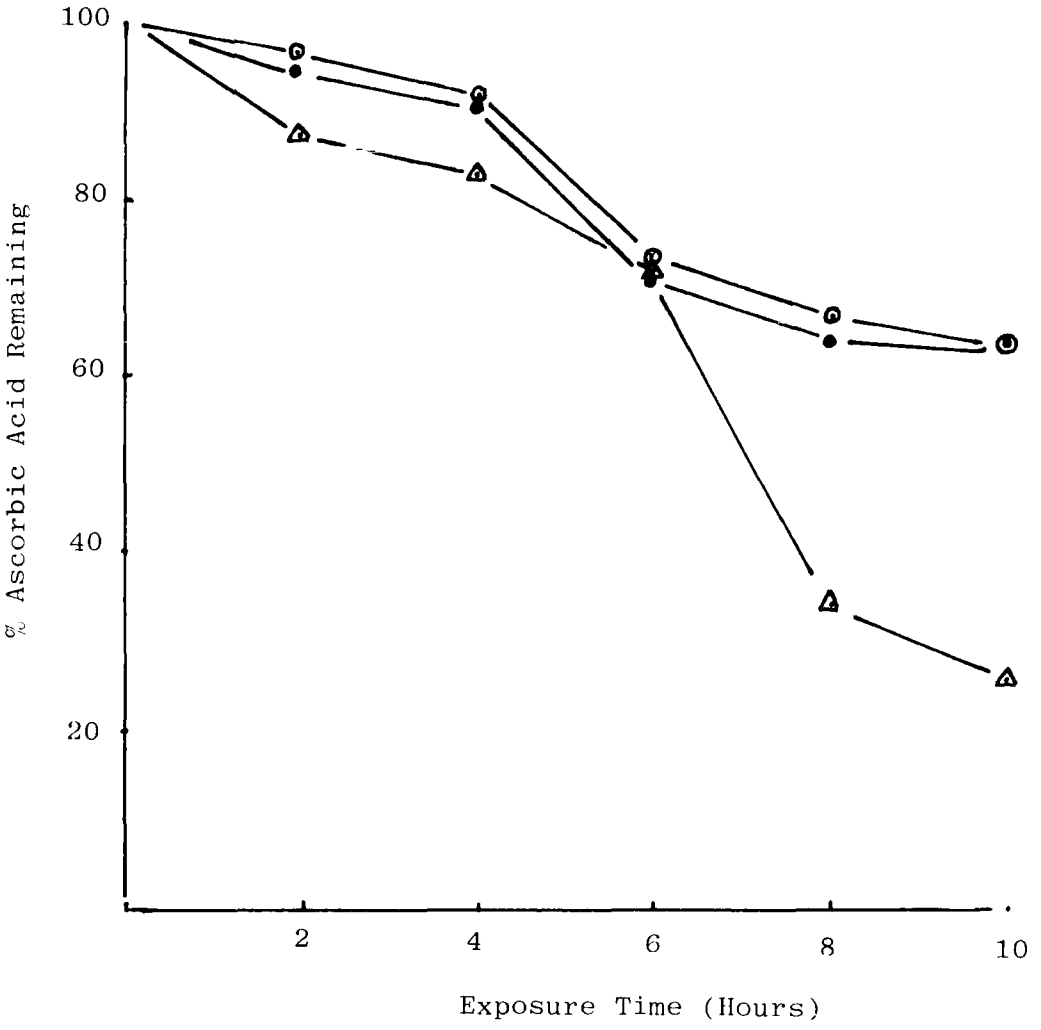

FIGURE 5. Effect of Buffer Species on the Photostabilizing Action of DL-Methionine for Ascorbic Acid Solutions

- Acetate Buffer, pH 4.5
- Phosphate Buffer, pH 4.5
- Citrate Buffer, pH 4.5

tctive action at pH 7 followed by pH 4.5, and then pH 7.9 as shown in Figure 8.

Effect of Glycerin:

The presence of 30% w/v of glycerin in ascorbic acid solution prepared in acetate buffer of pH 4.5 enhanced the photostabi-

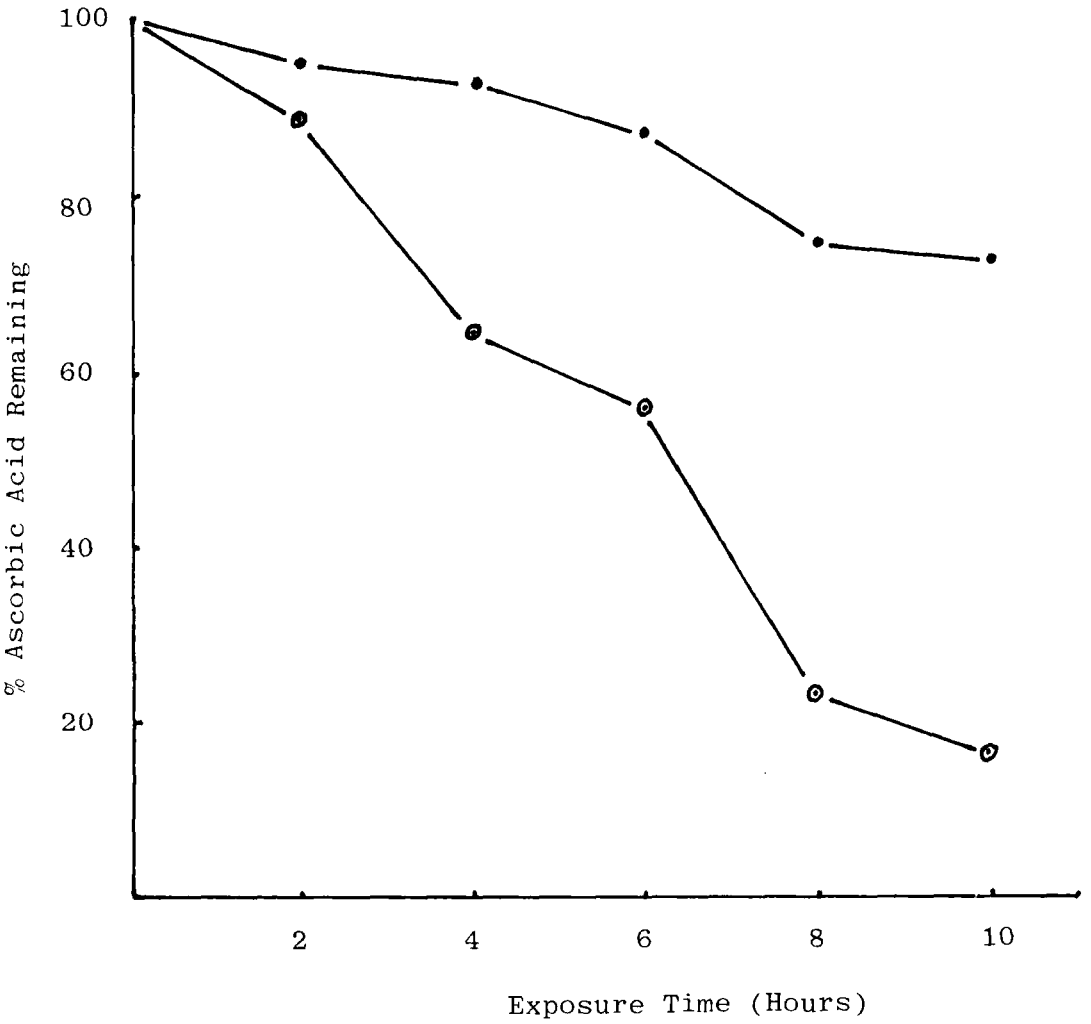

FIGURE 6. Photostabilizing Effect of DL-Methionine for Ascorbic Acid in Phosphate Buffer of pH 7.0

● Solution without DL-Methionine
● Solution with DL-Methionine

lity of ascrobic acid as shown in Figure 9. The results are in acordance with those published by Bandelin and Tuschhoff (3) who found that glycerin retarded the destruction of ascorbic acid solutions on aging. It can be also seen from Figure 9 that DL-methionine demonstrated its photoprotective action in presence of glycerin.

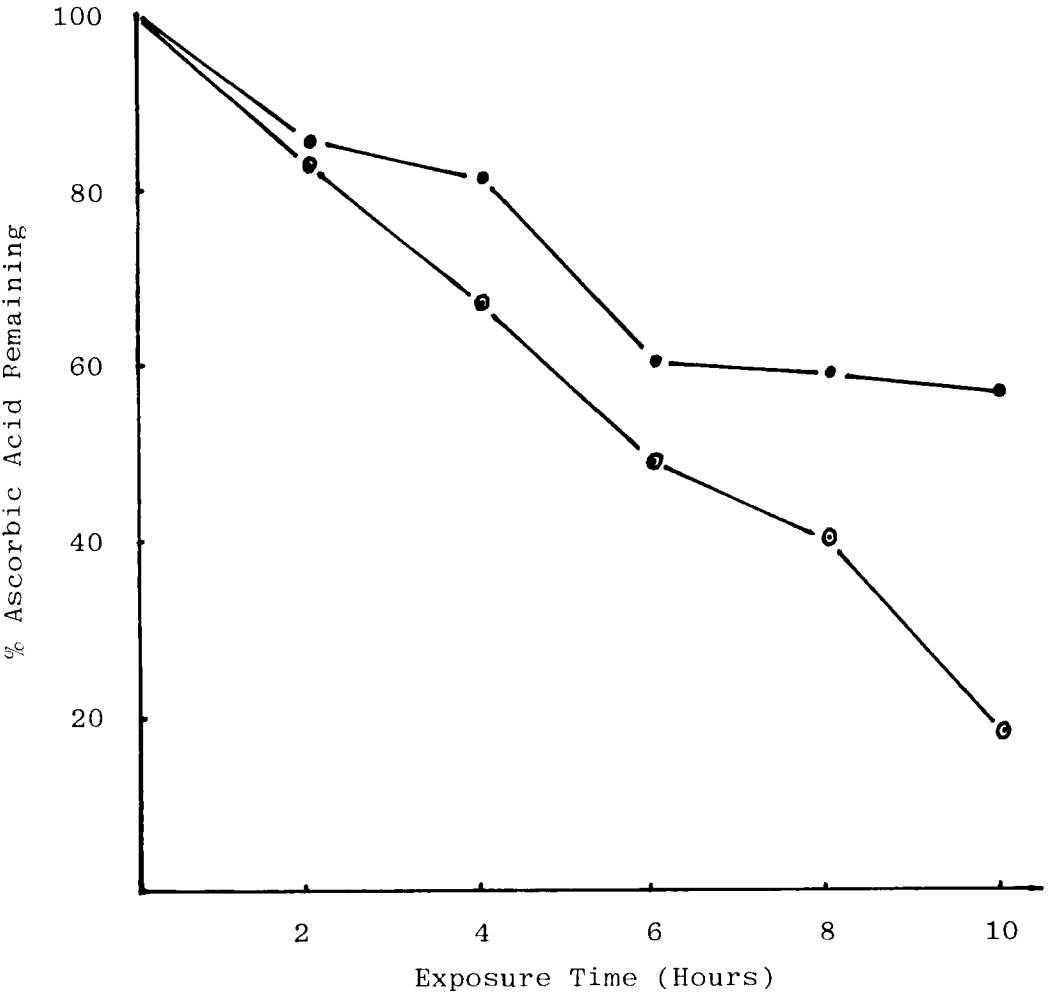

FIGURE 7. Photostabilizing Effect of DL-Methionine for Ascorbic Acid in Phosphate Buffer of pH 7.9

⊙ Solution Without DL-Methionine

● Solution With DL-Methionine

Effect of EDTA:

The incorporation of 0.2% EDTA into ascrobic acid solutions prepared in acetate buffer of pH 4.5 substantially enhanced the photostability of ascrobic acid as shown in Figure 10. The increase in stability resulted from chelation from solution of the heavy metal ions which cause decomposition of ascorbic acid. The

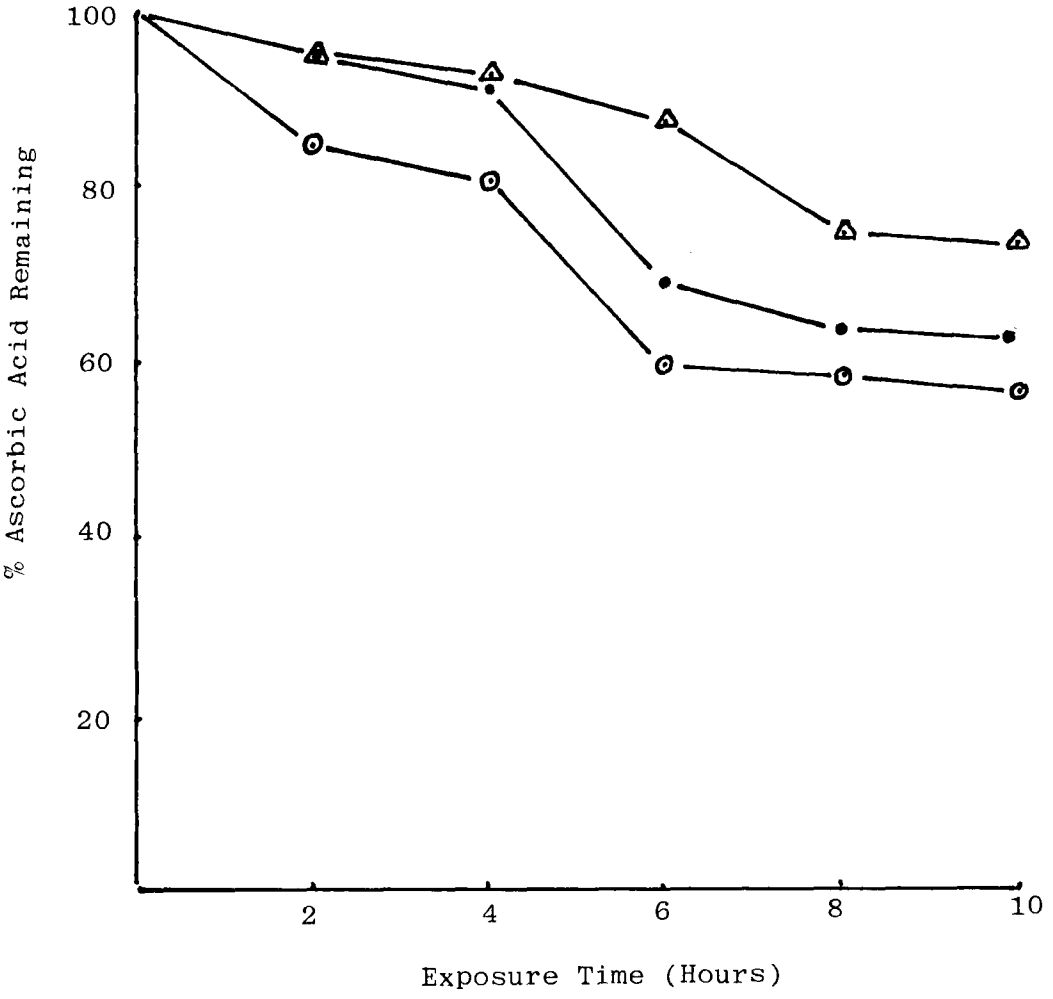

FIGURE 8. Effect of pH on the Photostabilizing Action of DL-Methionine for Ascorbic Acid in Phosphate Buffers

● pH 4.5
▲ pH 7.0
⊙ pH 7.9

photoprotective action of DL-methionine appeared not to be influenced by the presence of EDTA as shown in Figure 10.

Effect of Tween 80:

The incorporation of 0.5 % w/v of Tween 80 into ascrobic acid solution prepared in acetate buffer of pH 4.5, appeared to

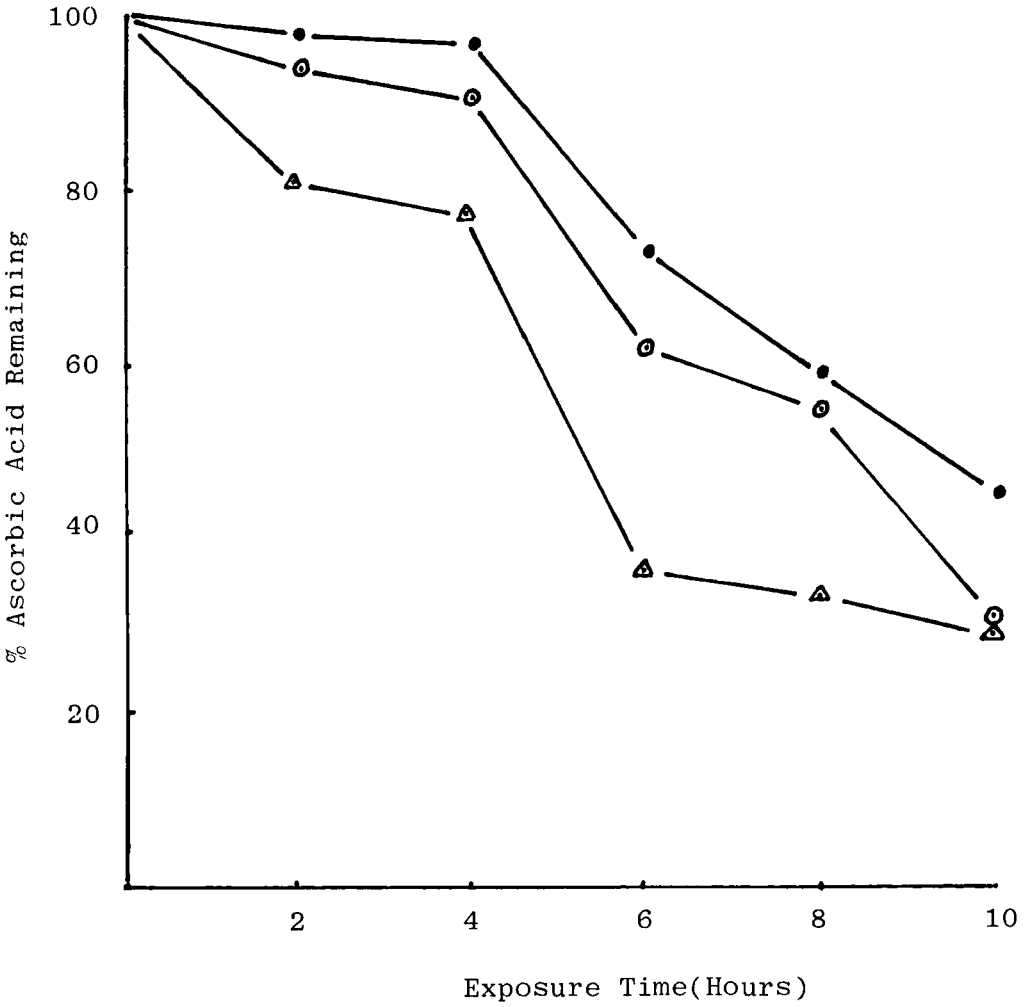

FIGURE 9. Photostabilizing Effect of DL-Methionine for Ascorbic Acid Solution Contaning Glycerin

- △ Ascorbic Acid Solution
- ⊙ Ascorbic Acid Solution with Glycerin
- ● Ascorbic Acid Solution with Glycerin and DL-Methionine

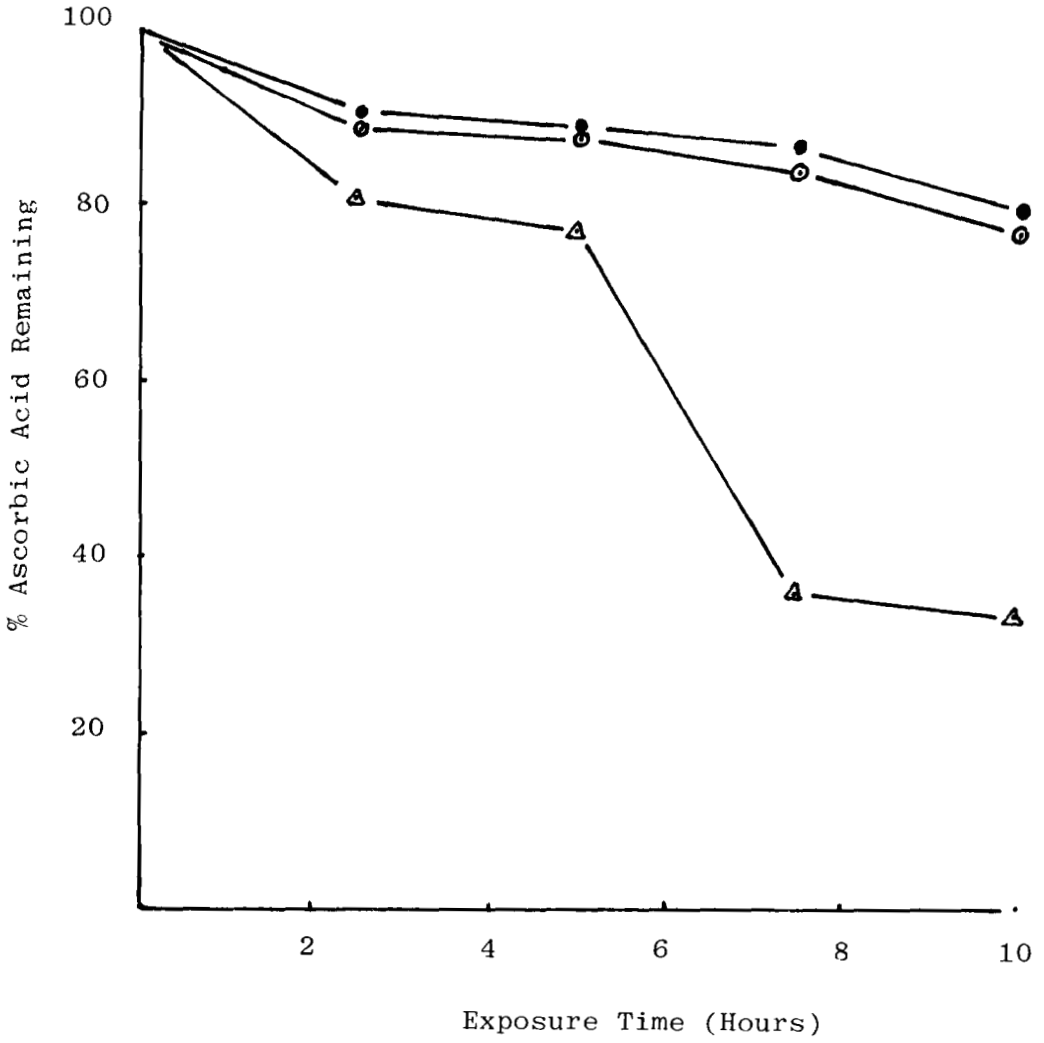

FIGURE 10. Photostabilizing Effect of DL-Methionine for Ascorbic Acid Solution Containing EDTA

△ Ascorbic Acid Solution

⊙ Ascorbic Acid Solution with EDTA

● Ascrobic Acid Solution with EDTA and DL-Methionine

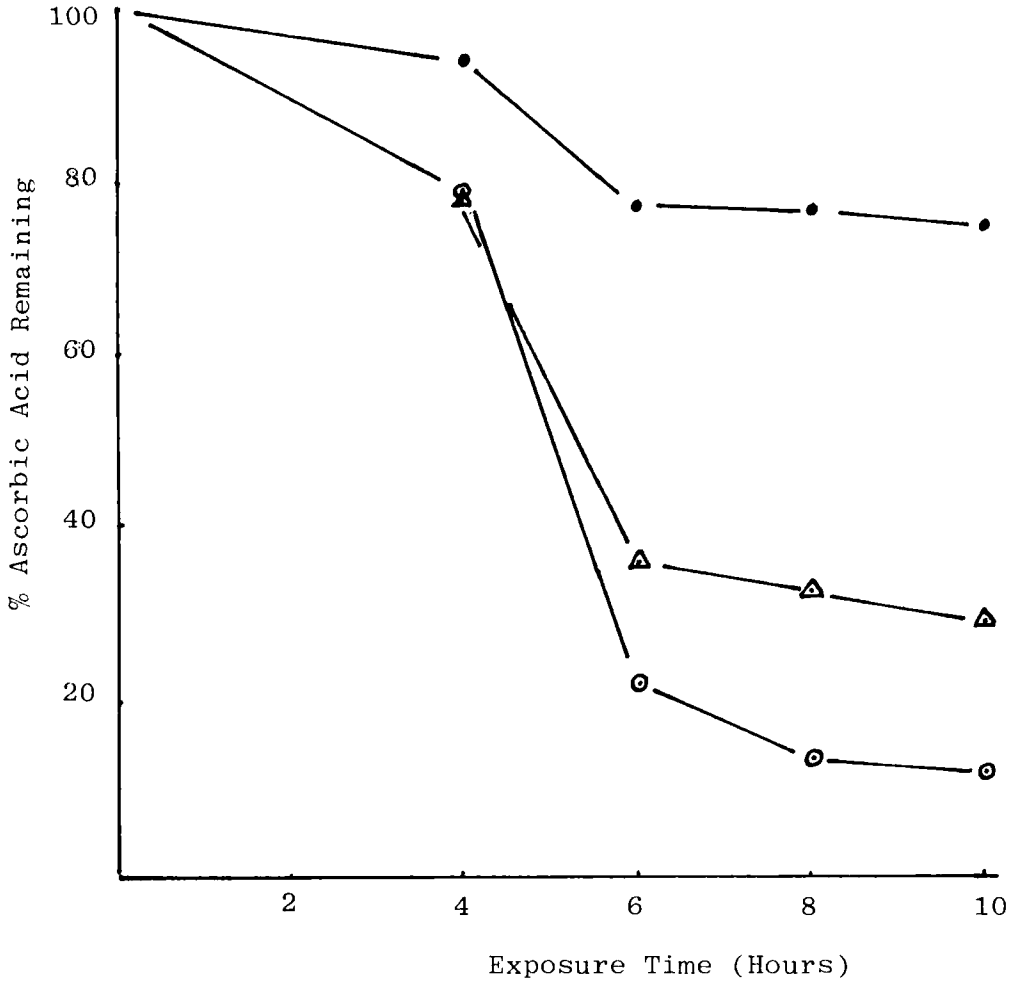

FIGURE 11. Photostabilizing Effect of DL-Methionine for Ascrobic Acid Solution Containing Tween 80

△ Ascorbic Acid Solution

⊙ Ascorbic Acid Solution with Tween 80

● Ascorbic Acid Solution with Tween 80 and DL-Methionine

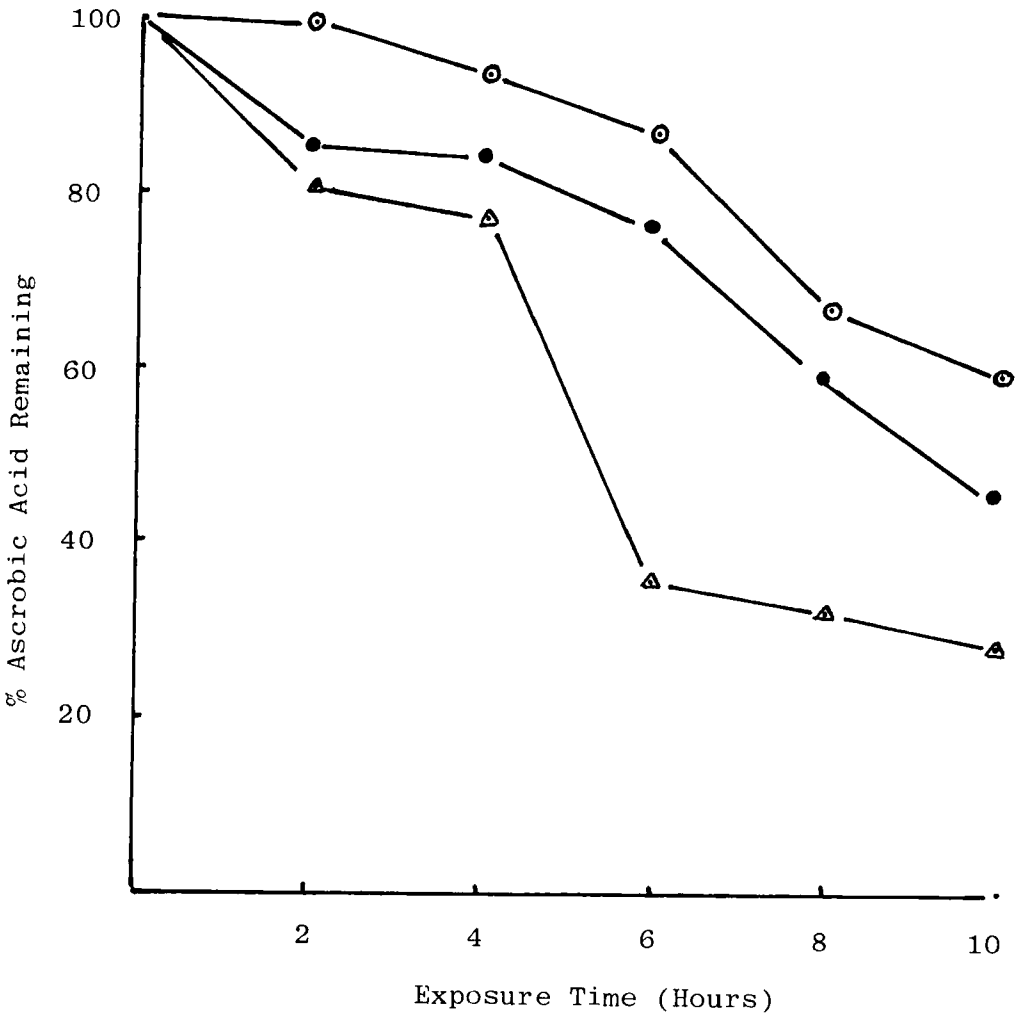

FIGURE 12. Photostabilizing Effect of DL-Methionine for Ascrobic Acid Solution Containing PEG 300

- ▲ Ascorbic Acid Solution
- ⊙ Ascorbic Acid Solution with PEG 300
- ● Ascorbic Acid Solution with PEG 300 and DL-Methionine

enhance the photodegradation of ascorbic acid (7) as shown in Figure 11. The results are in accordance with those reported by Nixon and Chawla (6) and Poust and Colaizzi (7) who found that low concentrations of Tween 80 enhanced the rate of oxidation of ascorbic acid. It can be also seen from Figure 11, that DL-methionine exercised its photoprotective action in presence of Tween 80.

Effect of PEG 300:

Figure 12 shows that the incorporation of 30% w/v of PEG 300 into ascorbic acid solution prepared in acetate buffer of pH 4.5 produced a stabilizing effect on ascorbic acid. However, PEG 300 appeared to have a detrimental effect on the photoprotective action of DL-methionine. PEG 300 was found by Boon and Mace (11) to enhance the decomposition of tripelennamine hydrochloride. This was attributed to the presence of ethylene oxide as an impurity in PEG 300. Moreover, the poor stability of a topical corticosteroid formulated in PEG 300 was found to be due to the high concentration of peroxides in the vehicle (12). Therefore, it appears that the reduction in the photoprotective action of DL-methionine can be attributed to the presence of ethylene oxide and peroxides in PEG 300 which would react with DL-methionine. However, further studies are needed before a final conclusion can be made.

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