DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY, 10(7), 1025-1039 (1984)

INFLUENCE OF CERTAIN ADDITIVES ON THE PHOTOSTABILIZING EFFECT OF DIMETHYL SULFOXIDE FOR SODIUM NITROPRUSSIDE SOLUTIONS

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ABSTRACT

The influence of certain pharmaceutical adjuvants on the photostabilizing effect of dimethyl sulfoxide for a buffered solution of sodium nitroprusside was investigated. Dimethyl sulfoxide in a concentration of 10% v/v was found to exercise its effect as a photoprotective agent in the presence of methylparaben, sodium sulfite, sodium chloride, destrose, PEG 300, Tween 80, citric acid and sodium edetate. In the absence of dimethyl sulfoxide, sodium sulfite produced the most deleterious effect on the photostability of sodium nitroprusside solution. The photoprotective action of dimethyl sulfoxide appeared to be slightly enhanced by the presence of sodium edetate, methylparaben, sodium chloride or citric acid.

INTRODUCTION

In a previous report by Asker and Gragg (1), dimethyl sulfoxide (DMSO) was found to be an effective photoprotective agent for various buffered solutions of sodium nitroprusside.

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0363-9045/84/1007-1025$3.50/0

The photoprotective action of DMSO was reported to be influenced by the pH of the medium and its buffer species.

Since organic and inorganic pharmaceutical adjuvants may be involved in bulk compounding of sodium nitroprusside solutions to be administered by intravenous infusion, it appeared desirable to investigate the photostabilizing effect of DMSO in presence of some pharmaceutical adjuvants. The materials selected belong to various classes of pharmaceutical adjuvants such as antioxidants, preservatives, chelating agents, surfactants, sugars, tonicity-adjusting solutes and non-aqueous solvents.

EXPERIMENTAL

Materials: Sodium nitroprusside, dimethyl sulfoxide, sodium acetate, glacial acetic acid, sodium hydroxide, citric acid, Tween 80, methylparaben, sodium sulfite, dextrose, sodium edetate, sodium chloride and PEG 300 were obtained from commercial sources in pharmaceutical or reagent grade and were used without further pruification.

Equipment: The following equipment were used: a light-stability cabinet equipped with an 18-inch, 15-watt Sylvania fluorescent lamp to serve as the light source; Spectronic 20 spectrophotometer; Orion digital pH meter.

Procedure: The solutions investigated were made to contain 50 mg% of sodium nitroprusside, 10% v/v of DMSO and the following concentrations of the various adjuvants: 0.9% sodium chloride, 5% dextrose, 0.2% sodium edetate, 0.2% citric acid, 0.01% methylparaben, 0.1% sodium sulfite, 30% w/v PEG 300 and 0.5% w/v Tween 80.

The typical experimental procedure was as follows: Volumes of sodium nitroprosside solutions each of 6 ml con-

taining the adjuvants in question, with and without DMSO, were placed in 10 x 100 mm spectrophotometer tubes covered with parafilm and exposed to the fluorescent light. Appropriate blank solutions were similarly prepared and exposed to light. Duplicate samples were withdrawn every 2 hours and their absorbance values were determined on the Spectronic 20 spectrophotometer at 395 nm using appropriate blanks.

DISCUSSION OF RESULTS

Effect of Methylparaben:

Figure 1 illustrates the effect of methylparaben on the photodegradation of sodium nitroprusside solution in presence and absence of DMSO. It appears that methylparaben enhanced to some extent the photodegradation of sodium nitroprusside. The solution developed a green color after exposure to light for 8 hours. Schumacher (2) in his study on the stability of sodium nitroprusside in some vehicles reported that parabens decreased the shelf-life stability of sodium nitroprusside solution. Similar results were obtained by Asker and Colbert (3) who reported that methylparaben enhanced the rate of fading of FD & C Blue No. 2 solution when exposed to light.

The incorporation of DMSO into sodium nitroprusside solution containing methylparaben resulted in a substantial photoprotective action for the drug whose solution remained almost colorless after exposure to light for 10 hours. Methylparaben appeared to slightly enhance the photoprotective action of DMSO.

Effect of Dextrose:

It can be seen from Figure 2 that dextrose enhanced the photodegradation of sodium nitroprusside although the drug is

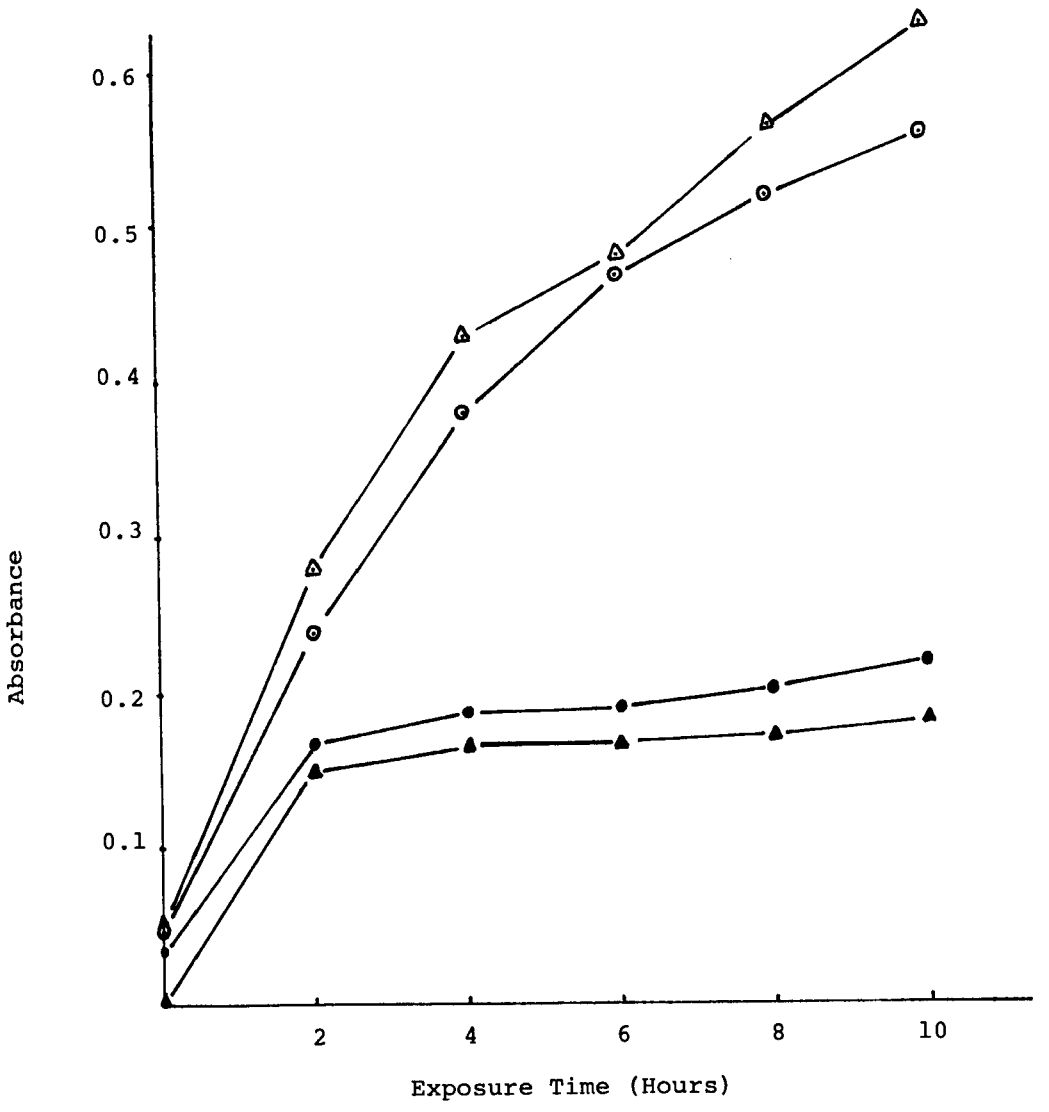

FIGURE 1. Photostabilizing Effect of DMSO for Sodium Nitroprusside Solution Containing Methylparaben

- ⊙ Sodium Nitroprusside Solution without DMSO
- ● Sodium Nitroprusside Solution + DMSO
- △ Sodium Nitroprusside Solution + Methylparaben
- ▲ Sodium Nitroprusside Solution + Methylparaben + DMSO

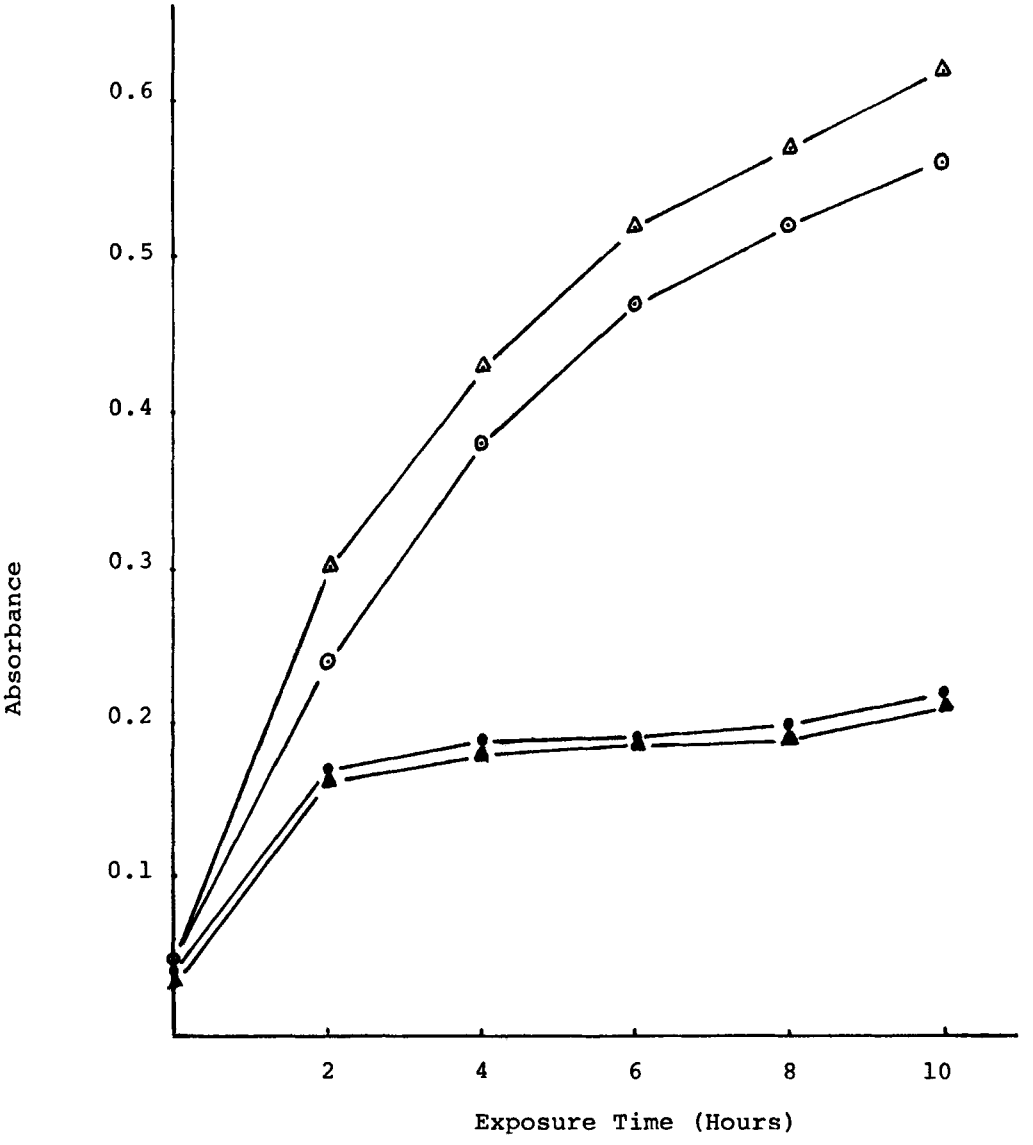

FIGURE 2. Photostabilizing Effect of DMSO for Sodium Nitroprusside Solution Containing Dextrose

- Sodium Nitroprusside Solution without DMSO
- Sodium Nitroprusside Solution + DMSO
- Sodium Nitroprusside Solution + Dextrose
- Sodium Nitroprusside Solution + Dextrose + DMSO

often administered in 5% dextrose infusion solution (4). Solution of sodium nitroprusside 100 mg in 250 ml of 5% dextrose solution was found by Challen (5) to decompose with the formation of a pale blue-green precipitate when autoclaved at 115°for 30 minutes. Sodium nitroprusside has been reported (6) to be photoreduced in aqueous solution. Therefore, it appears that dextrose, being a reducing agent, had enhanced the photoreduction of the ferricyanide to the ferrocyanide.

Sodium nitroprosside solution developed a light green color after exposure to light for 6 hours. The color changed to dark green after exposure for 10 hours. However, the incorporation of DMSO into sodium nitroprusside solution containing dextrose produced a more stable solution which remained almost colorless after exposure to light for 10 hours. Dextrose appeared to have little or no effect on the photostabilizing action of DMSO for sodium nitroprusside solution

Effect of Sodium Chloride:

It appears from Figure 3 that sodium chloride had no effect on the photostability of sodium nitroprusside solution. Based on this finding, it would seem advisable to administer sodium nitroprusside in 0.9% sodium chloride infusion solution rather than in 5% dextrose solution.

The incorporation of sodium chloride into sodium nitroprusside solution appeared to slightly enhance the photoprotective action of DMSO. Solution of sodium nitroprusside containing DMSO and sodium chloride assumed a very faint yellow color after storage for 8 hours, whereas solution free of DMSO developed a darker yellow color.

Effect of PEG 300:

Figure 4 shows that PEG 300 enhanced to some extent the

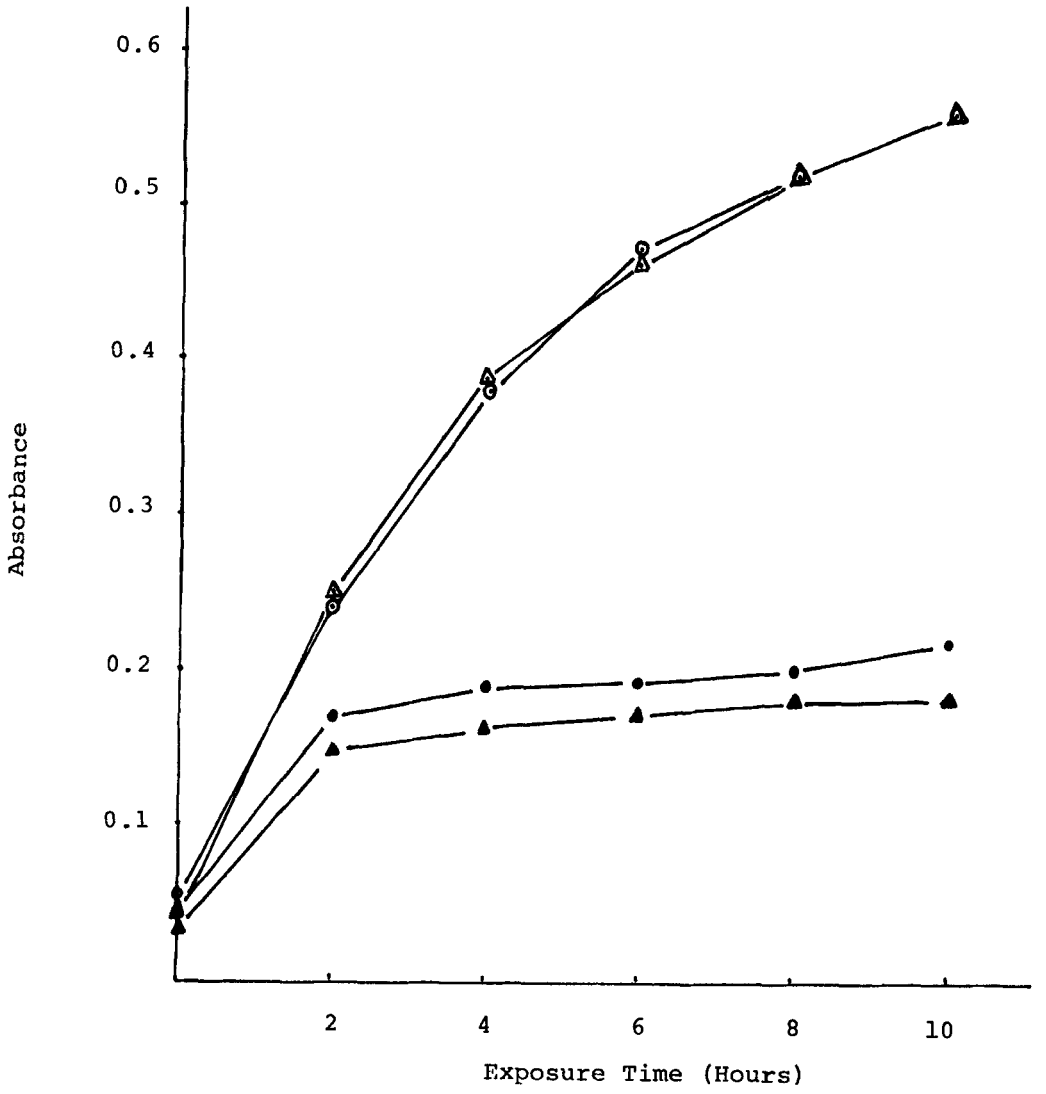

FIGURE 3. Photostabilizing Effect of DMSO for Sodium Nitroprusside Solution Containing Sodium Chloride

- ⊙ Sodium Nitroprusside Solution without DMSO
- ● Sodium Nitroprusside Solution + DMSO
- △ Sodium Nitroprusside Solution + NaCl
- ▲ Sodium Nitroprusside Solution + NaCl + DMSO

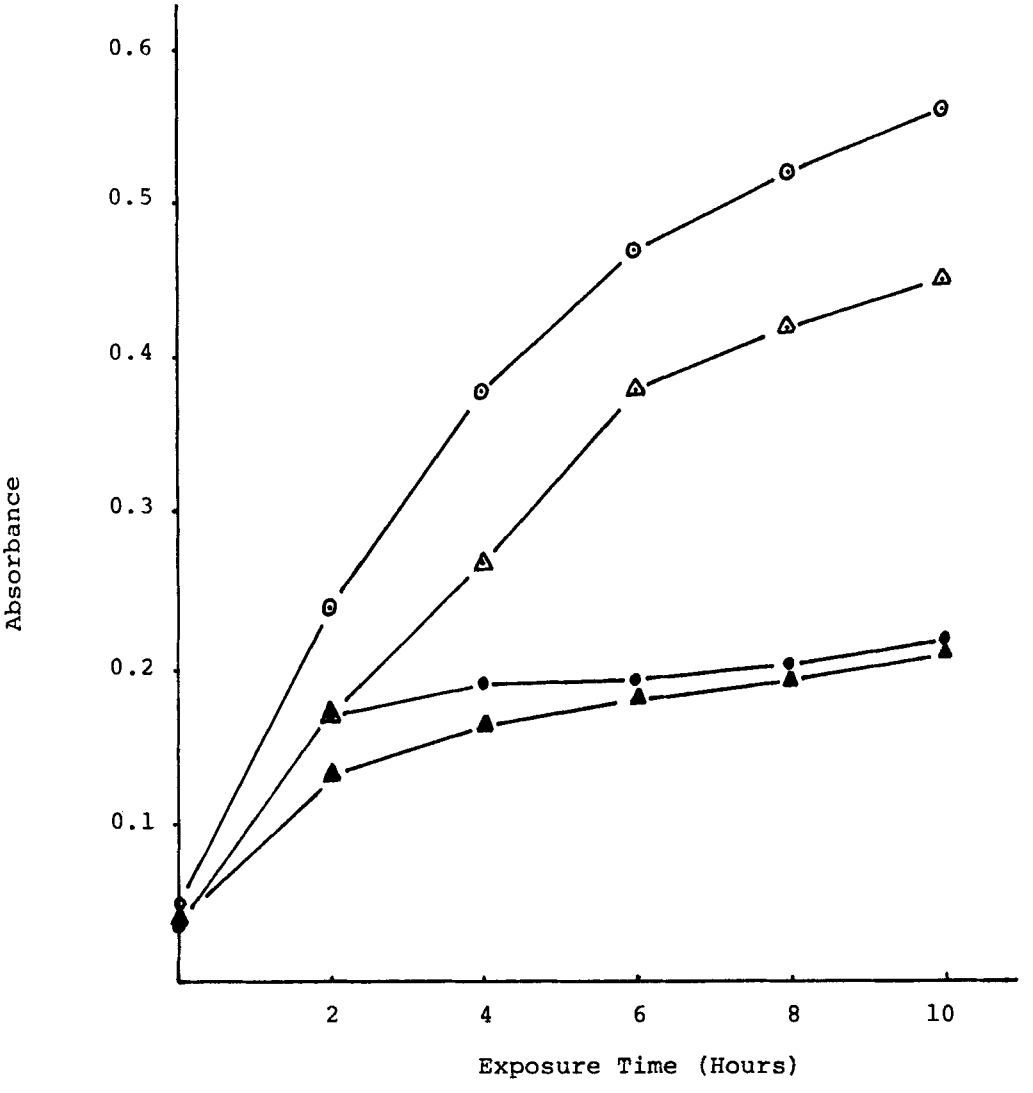

FIGURE 4. Photostabilizing Effect of DMSO for Sodium Nitroprusside Solution Containing PEG 300

⊙ Sodium Nitroprusside Solution without DMSO

● Sodium Nitroprusside Solution + DMSO

△ Sodium Nitroprusside Solution + PEG 300

▲ Sodium Nitroprusside Solution + PEG 300 + DMSO

photostability of sodium nitroprusside solution. Schumacher (2) found that the use of 20% and 50% aqueous solutions of PEG 300 as vehicles for sodium nitroprusside, significantly enhanced its stability. He atrributed this effect to the chelating potential of PEG 300 rather than the decreased polarity of the vehicle, thus maintaining the iron complex in the ferric rather than the ferrous form.

It appears also from Figure 4 that PEG 300 had little or no effect on the photostabilizing action of DMSO. Sodium nitroprusside solution containing PEG 300 and no DMSO developed a yellow color after exposure to light for 8 hours, whereas the solution with DMSO remained almost colorless.

Effect of Citric Acid:

Figure 5 indicates that citric acid enhanced the photostability of sodium nitroprusside solution. This finding is in accordance with that published by Anderson and Rae (7). They found negligible changes in absorbance of solutions of sodium nitroprusside for up to 6 months, when solutions were stored in the dark in aqueous solution, or in the presence of sodium citrate, citric acid, acetic acid or acetate buffer of pH 4.65. Schumacher (2) reported that 5% sodium citrate solution increased the shelf life of sodium nitroprusside solution from 13 days to over 800 days. It appears, therefore, that the citrate ions enhanced the stability of sodium nitropursside. Such a conclusion has been confirmed in a recent report by Asker and Gragg (1) who indicated that DMSO demonstrated its greatest stabilizing effect in citrate buffer, followed by acetate buffer and then phosphate buffer.

It appears also that citric acid has a slight potentiating effect on the photoprotective action of DMSO. Sodium nitro-

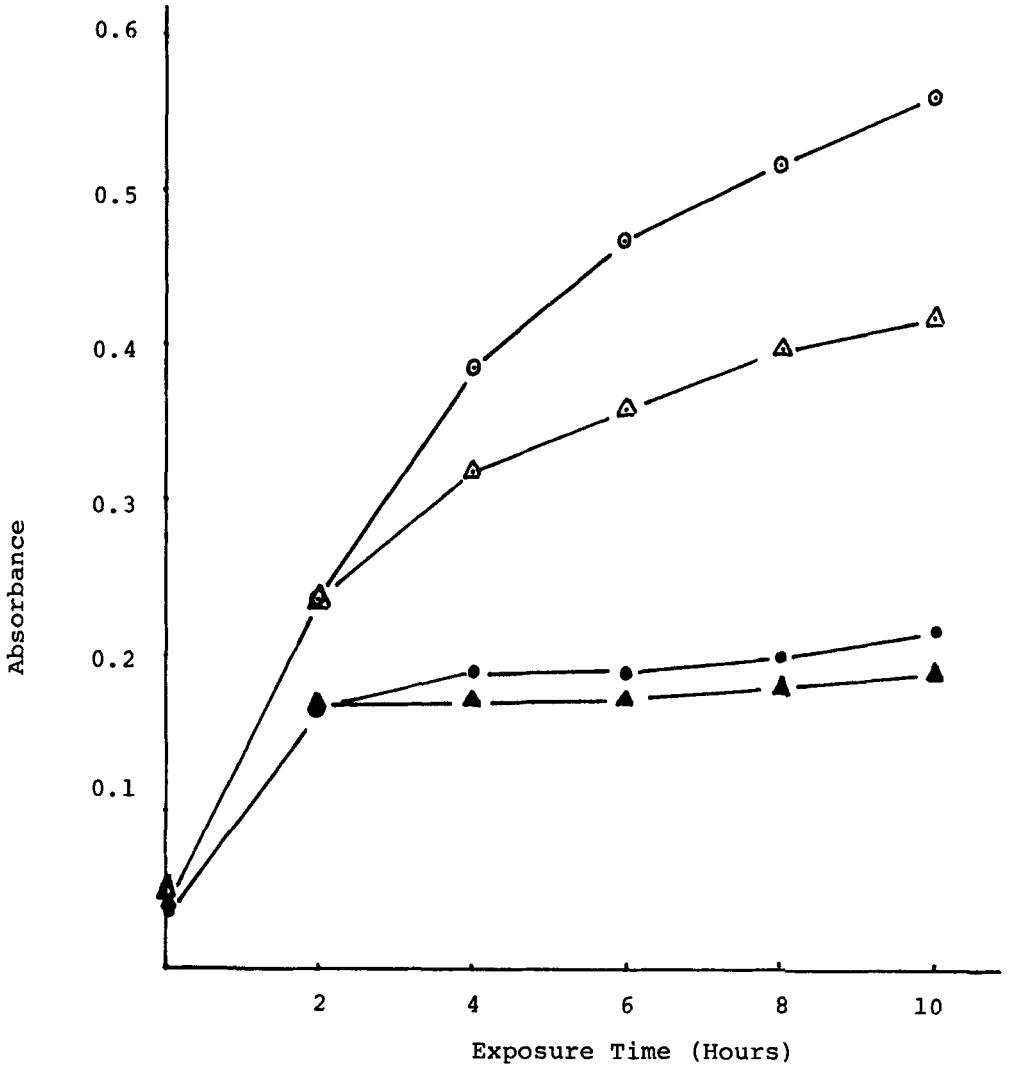

FIGURE 5. Photostabilizing Effect of DMSO for Sodium Nitroprusside Solution Containing Citric Acid

⊙ Sodium Nitroprusside Solution without DMSO

● Sodium Nitroprusside Solution + DMSO

△ Sodium Nitroprusside Solution + Citric Acid

▲ Sodium Nitroprusside Solution + Citric Acid + DMSO

prusside solution containing citric acid and no DMSO, developed a yellow color after exposure to light for 8 hours, whereas solution containing DMSO developed only a faint yellow color.

Effect of Sodium Edetate:

It can be seen from Figure 6 that sodium edetate had an enhancing effect on the photostability of sodium nitroprusside solution. This finding is an accordance of that reported by Schumacher (2) who noted that sodium edetate in 0.01% concentration increased the shelf life of sodium nitroprusside solution from 13 days to over 39 days. This effect can be attributed to the chelating action of sodium edetate, therefore maintaining the iron complex in the ferric rather than the ferrous form.

Sodium edetate appeared to potentiate the photostabilizing effect of DMSO for sodium nitroprusside solution. Solutions of sodium nitroprusside containing sodium edetate without DMSO developed a yellow color after exposure to light for 8 hours. However, the solution containing DMSO devleoped only a very faint yellow color.

Effect of Tween 80:

It appears from Figure 7 that Tween 80 had little or no effect on the photostability of sodium nitroprusside solution. The photoprotective action of DMSO was not influenced by the presence of Tween 80.

Sodium nitroprusside solution containing Tween 80 and no DMSO developed a light green color after exposure to light for 8 hours. However, the solution containing DMSO remained almost colorless.

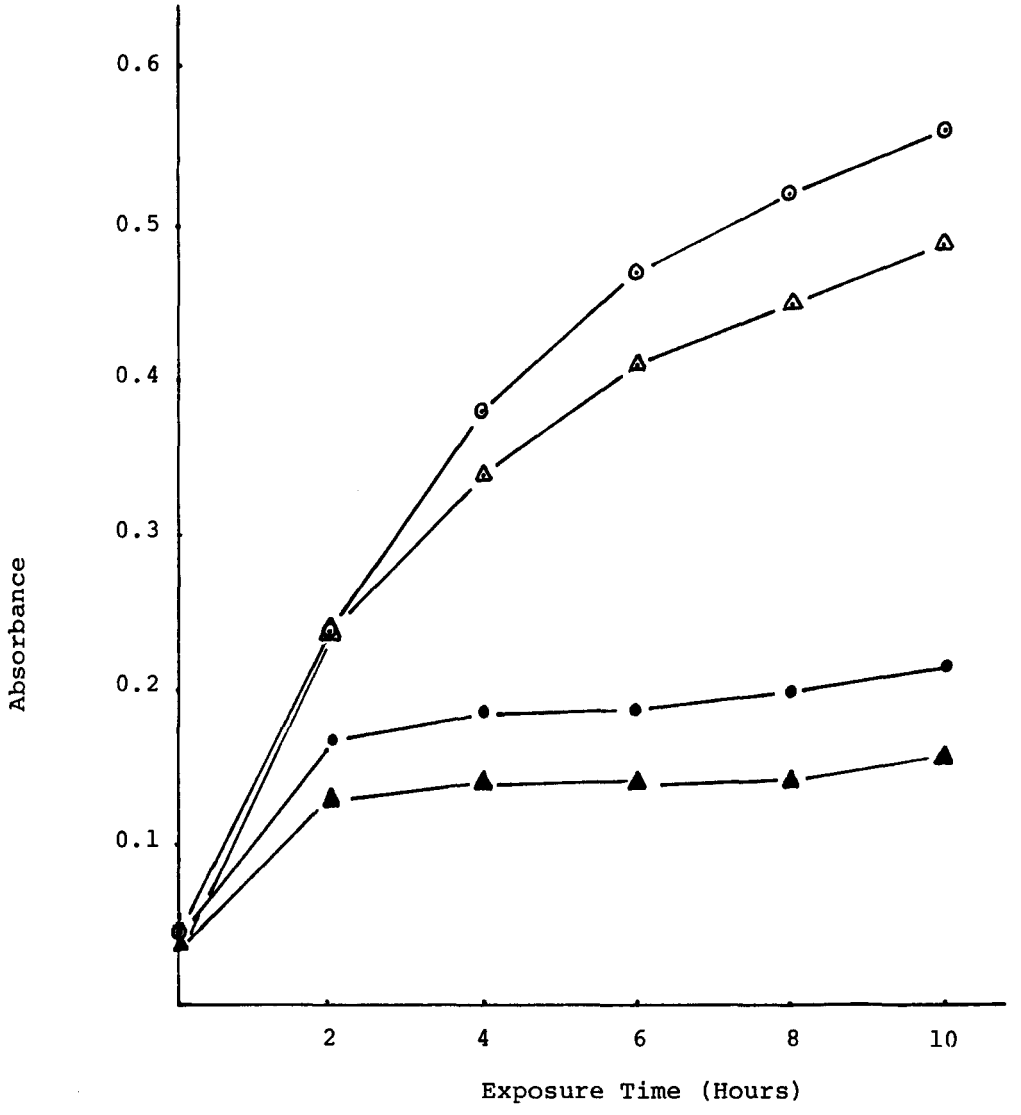

FIGURE 6. Photostabilizing Effect of DMSO for Sodium Nitropursside Solution Containing Sodium Edetate

⊙ Sodium Nitroprusside Solution without DMSO

● Sodium Nitroprusside Solution + DMSO

△ Sodium Nitroprusside Solution + Sodium Edetate

▲ Sodium Nitroprusside Solution + Sodium Edetate + DMSO

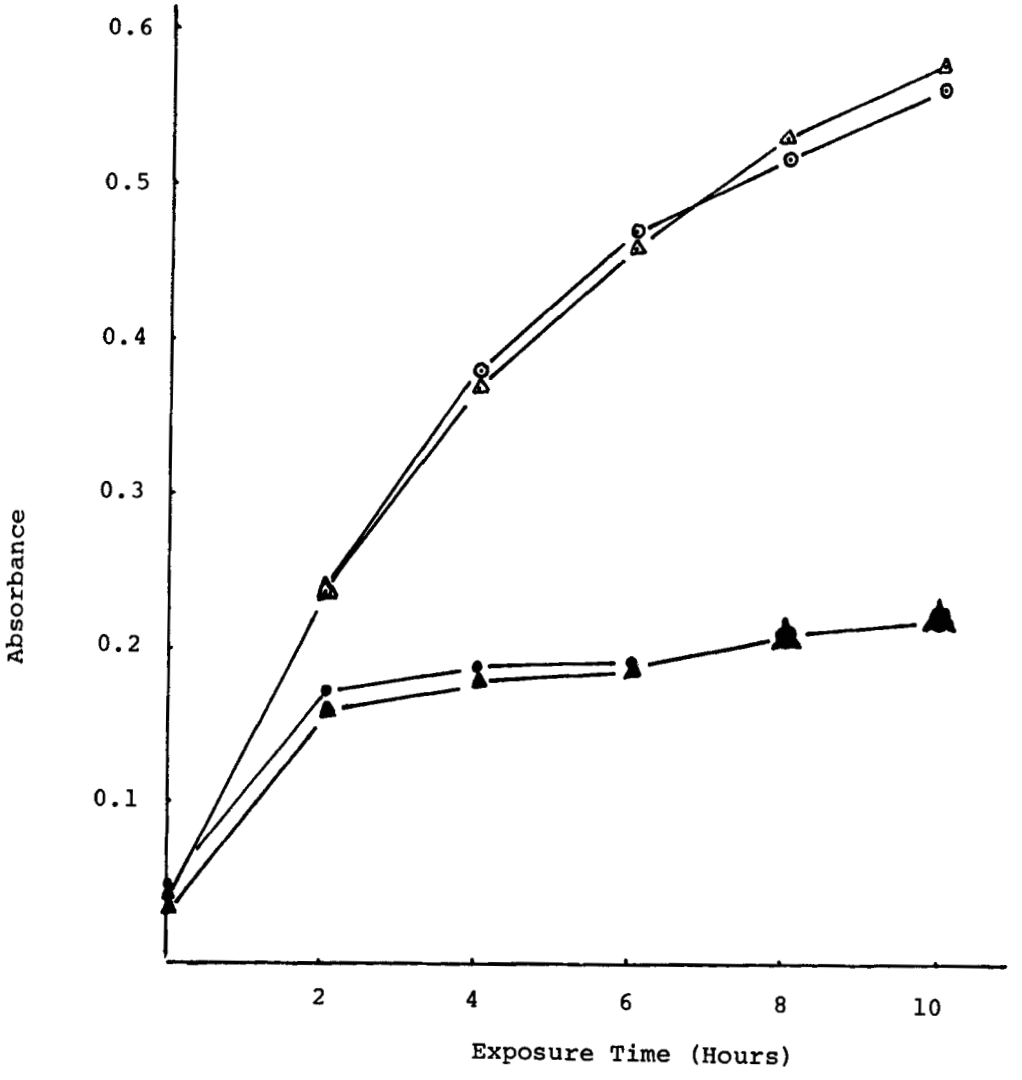

FIGURE 7. Photostabilizing Effect of DMSO for Sodium Nitroprusside Solution Containing Tween 80

⊙ Sodium Nitroprusside Solution without DMSO

● Sodium Nitroprusside Solution + DMSO

△ Sodium Nitroprusside Solution + Tween 80

▲ Sodium Nitroprusside Solution + Tween 80 + DMSO

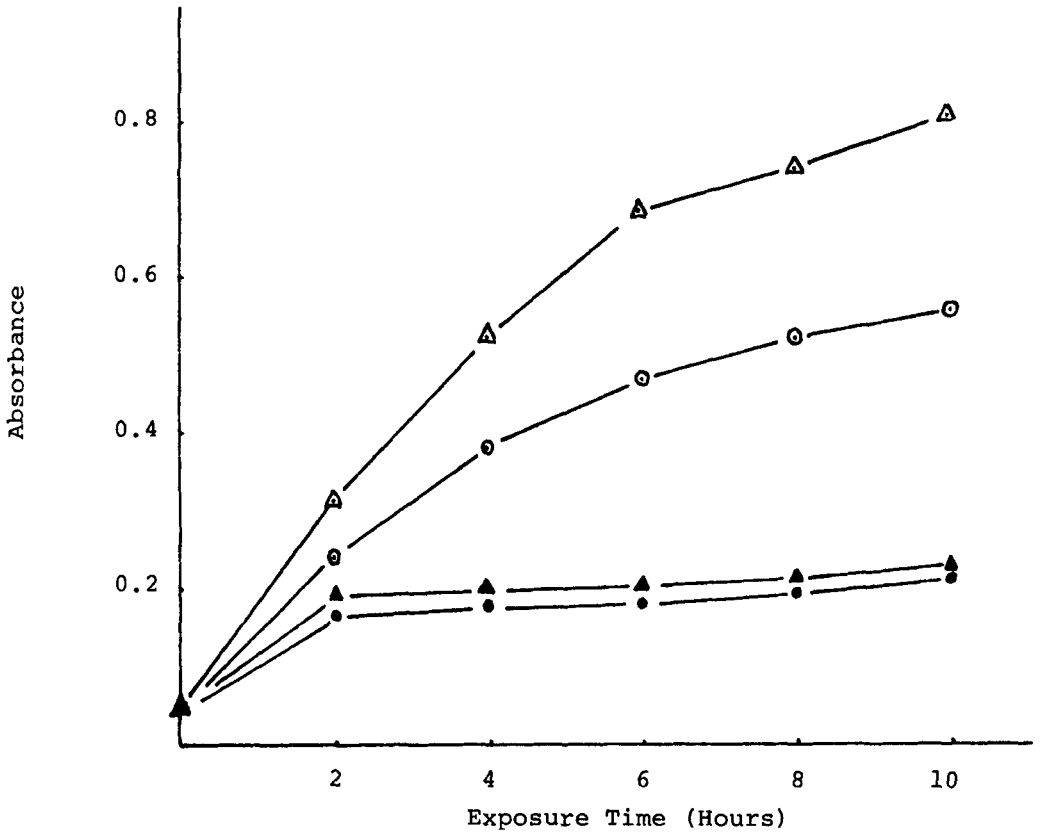

FIGURE 8. Photostabilizing Effect of DMSO for Sodium Nitroprusside Solution Containing Sodium Sulfite

⊙ Sodium Nitroprusside Solution without DMSO

● Sodium Nitroprusside Solution + DMSO

▲ Sodium Nitroprusside Solution + Sodium Sulfite

▲ Sodium Nitroprusside Solution + Sodium Sulfite + DMSO

Effect of Sodium Sulfite:

Sodium sulfite which is a strong reducing agent was found to substantially accelerate the photodegradation of sodium nitroprusside solution as can be seen from Figure 8. A green colored solution was obtained after exposure to light for 2 hours. This color changed to dark blue after 10 hours of exposure to light. This result is in accordance

with that obtained by Schumacher (2) who found that sodium bisulfite in a concentration of 0.05% greatly reduced the shelf-life stability of sodium nitroprusside solution from 13 days to only one day. It has been reported (6) that nitroferricyanide is photoreduced in aqueous solution to yield nitroferrocyanide $\left[Fe\ (CN)_5\ NO\right]^{-3}$ which explains the color change. Sodium sulfite appeared to potentiate the reduction of the ferricyanide to the ferrocyanide.

The incorporation of DMSO into sodium nitroprusside solution containing sodium sulfite resulted in a substantial protection against light as can be seen from Figure 8. The solution remained almost colorless after exposure to light for 10 hours.

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