DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY, 9(5), 837-848 (1983)

DIMETHYL SULFOXIDE AS A PHOTOPROTECTIVE AGENT FOR SODIUM NITROPRUSSIDE SOLUTIONS

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ABSTRACT

The effect of dimethyl sulfoxide (DMSO) as a photoprotective agent for various buffered solutions of sodium nitroprusside was investigated. DMSO was found to enhance the photostability of 50 mg% solutions of sodium nitroprusside. In general, the higher the concentration of DMSO, the greater was its photostabilizing effect. However, a 10% v/v of DMSO appeared to be an optimum concentration when acetate buffer of pH 4.65 was used as the solvent medium. The photoprotective action of dimethyl sulfoxide was found to be influenced by the pH of the medium and its buffer species.

INTRODUCTION

Sodium nitroprusside (sodium nitroferricyanide), a potent, rapid-acting hypotensive agent when administered

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0363-9045/83/0905-0837$3.50/0

intravenously, has been known for many years, but has been receiving increased attention only recently.

Sodium nitroprusside is very soluble in water, less soluble in alcohol, forming an orange colored solution of pH 4.5-5 which is sensitive to light and heat.

In the presence of light, sodium nitroprusside undergoes numerous reactions many of which are reported to be undefined (1). In direct sunlight, sodium nitroprusside eventually yields Prussian blue, cyanic acid and nitric oxide (2). Immediate products of the photodecomposition in light of low energy appear to be nitric oxide and $[Fe(CN)_5(H_2O)]^{-3}$ (3). It has also been reported that nitroferricyanide is photoreduced in aqueous solution to yield nitroferrocyanide (4). Depending on the intensity and energy of the incident light, aqueous solutions of nitroferricyanide eventually develop a blue color; no blue color is observed when nitroferricyanide is irradiated in water with light of moderate intensity over long periods (1).

"Solutions of sodium nitroprusside must be protected from light during infusion by wrapping the container with aluminum foil or some other opaque material. Solutions discolored by reaction of nitroprusside with organic and inorganic materials should be discarded", (5). Hargrave (6) has reported that the appearance of a blue coloration should be taken to indicate that injections are unfit for use. Patel (7) studied the effect of light and heat on the stability of aqueous solutions of sodium nitroprus-

side. He analyzed the solutions spectrophotometrically by determing the absorbance at 390 nm. Upon exposure to light and elevated temperatues, a pronounced increase in absorbance was observed.

Dimethyl sulfoxide (DMSO) has been reported by Ashwood-Smith (8) to be a radioprotective agent in mice. Therefore, in view of the susceptibility of sodium nitroprusside solutions to photodegradation, it appeared worthwhile to investigate the potential use of DMSO as a photoprotective agent for sodium nitroprusside solutions.

EXPERIMENTAL

Materials: Sodium nitroprusside, dimethyl sulfoxide, sodium hydroxide, citric acid, monobasic potassium phosphate, dibasic potassium phosphate, sodium acetate and potassium hydroxide were obtained from commercial sources in pharmaceutical or reagent grade and were used without further purification.

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

Procedure: The typical experimental procedure was as follows: Volumes of solutions prepared with and without DMSO, each of 6 ml were placed in 10x100 mm spectrophotometer tubes covered with parafilm and exposed to the fluorescent light. Solutions consisting of DMSO in the various buffers were similarly exposed to light to serve as blanks.

Absorbance readings were made on duplicate samples at various time intervals on the Spectronic 20 at 395 nm using appropriate blanks. Samples of sodium nitroprusside solutions containing no DMSO were stored in the dark to serve as controls.

In studying the effect of variation of dimethyl sulfoxide concentration on the photostability of sodium nitroprusside, solutions containing 50 mg% of sodium nitroprusside and 3%, 5%, 10% and 20% v/v of DMSO in acetate buffer of pH 4.65 were exposed to the light source.

The effect of buffer species on the photoprotective action of DMSO for sodium nitroprusside solutions was studied using solutions containing 50 mg% sodium nitroprusside and 10%v/v DMSO in acetate, phosphate and citrate buffers of pH 4.65.

The pH effect was determined for solutions containing 50 mg% of sodium nitroprusside and 10%v/v DMSO in phosphate buffers with the following pH values: 4.65, 7.0 and 7.9.

DISCUSSION OF RESULTS

Influence of DMSO on the Photostability of Sodium Nitroprusside:

Figure 1 shows that the incorporation of 10%v/v of DMSO into 50 mg% of sodium nitroprusside solution in acetate buffer of pH 4.65, produced a measureable protective action against photodegradation of sodium nitroprusside. It would also appear from Table 1, that there is an optimum concentration of DMSO that would produce the maximum

TABLE 1: Effect of Light on the Absorbance Values of Sodium Nitroprusside Solutions in Acetate Buffer of pH 4.65

Solutions	Absorbance Values at				
	0hr	3hr	6hr	9hr	12hr
50mg% Sodium Nitroprusside	0.034	0.231	0.389	0.493	0.570
50mg% Sodium Nitroprusside plus:					
3%v/v DMSO	0.036	0.141	0.171	0.171	0.180
5%v/v DMSO	0.035	0.142	0.151	0.151	0.163
10%v/v DMSO	0.040	0.105	0.131	0.143	0.155
20%v/v DMSO	0.039	0.122	0.132	0.161	0.180

stabilizing effect. This concentration was found to be 10% v/v when acetate buffer of pH 4.65 was used as the solvent medium. The reason for the relative decrease in photostability of sodium nitroprusside with higher concentrations of DMSO could be attributed to reduction of the dielectric constant of the solvent system. The dielectric constant of DMSO lies near that of glycerin which was found in a previous report (9) to enhance the photodecomposition of FD&C Blue No.2. However, further studies are needed to fully understand the role of higher concentration of DMSO in the photostabilization of sodium nitroprusside solutions.

Effect of Buffer Species:

It can be seen from Figures 1-3 that DMSO exercised its photoprotective action in acetate, citrate and phos-

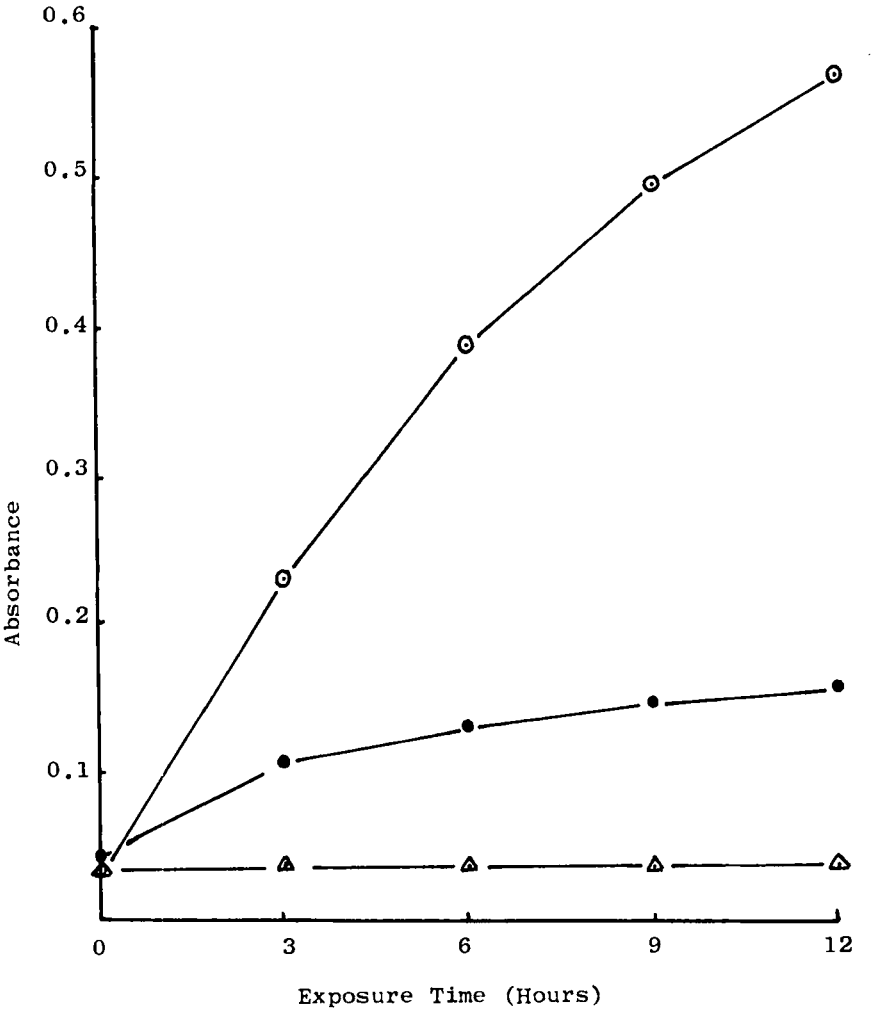

FIGURE 1. Photostabilizing Effect of DMSO for Sodium Nitroprusside in Acetate Buffer of pH 4.65

⊙ Solution without DMSO Exposed to Light

● Solution with 10%v/v DMSO Exposed to Light

△ Solution without DMSO Stored in the Dark

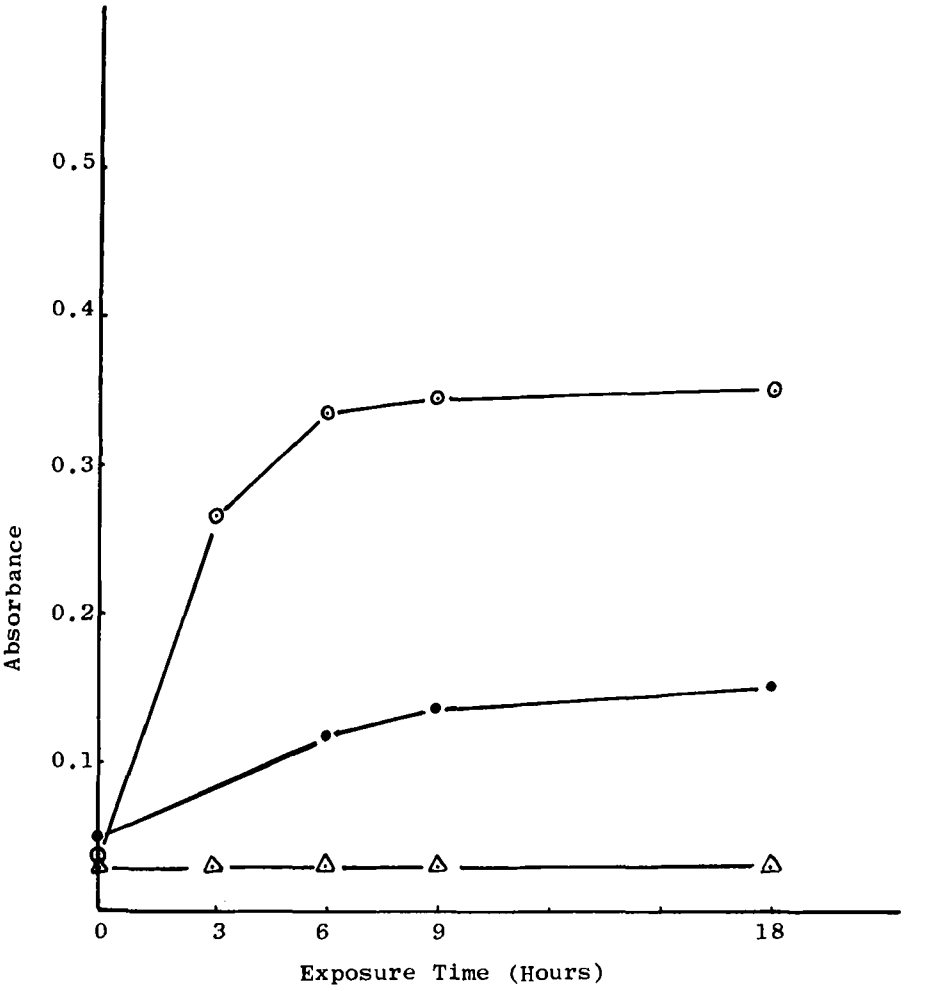

FIGURE 2. Photostabilizing Effect of DMSO for Sodium Nitroprusside in Citrate Buffer of pH 4.65

⊙ Solution without DMSO Exposed to Light

● Solution with 10%v/v DMSO Exposed to Light

△ Solution without DMSO Stored in the Dark

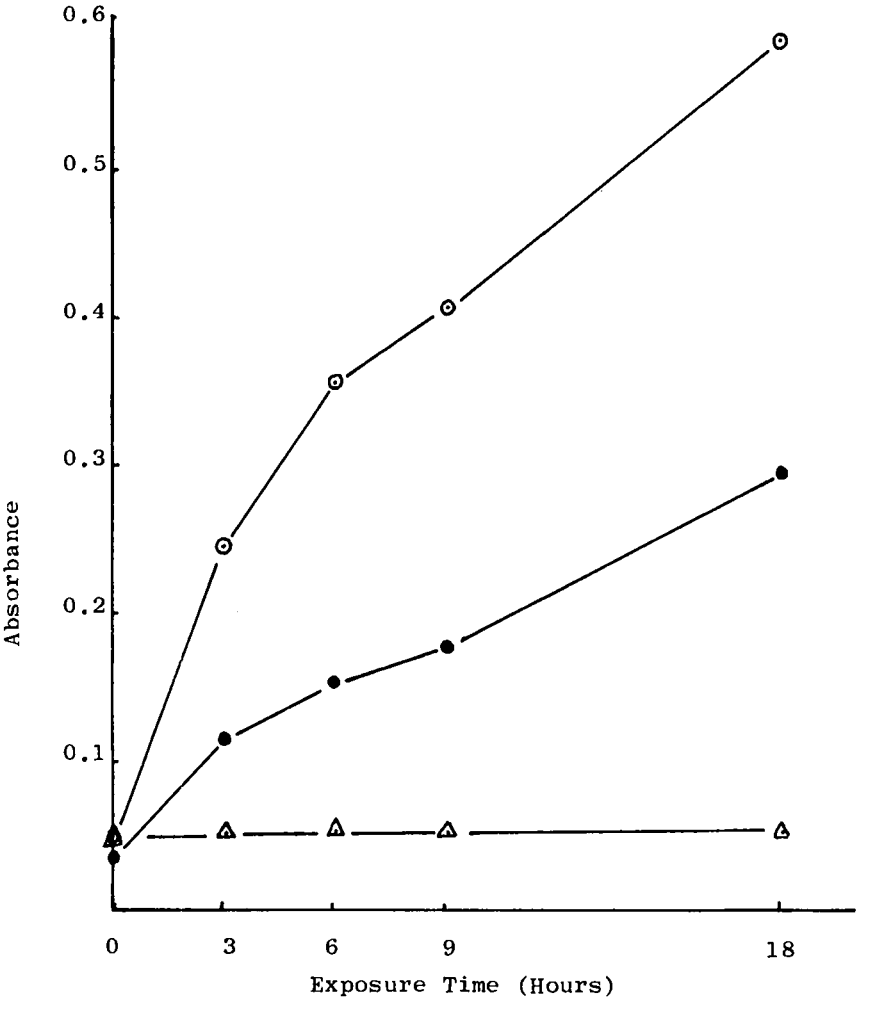

FIGURE 3. Photostabilizing Effect of DMSO for Sodium Nitroprusside in Phosphate Buffer of pH 4.65

⊙ Solution without DMSO Exposed to Light

● Solution with 10% v/v DMSO Exposed to Light

△ Solution without DMSO Stored in the Dark

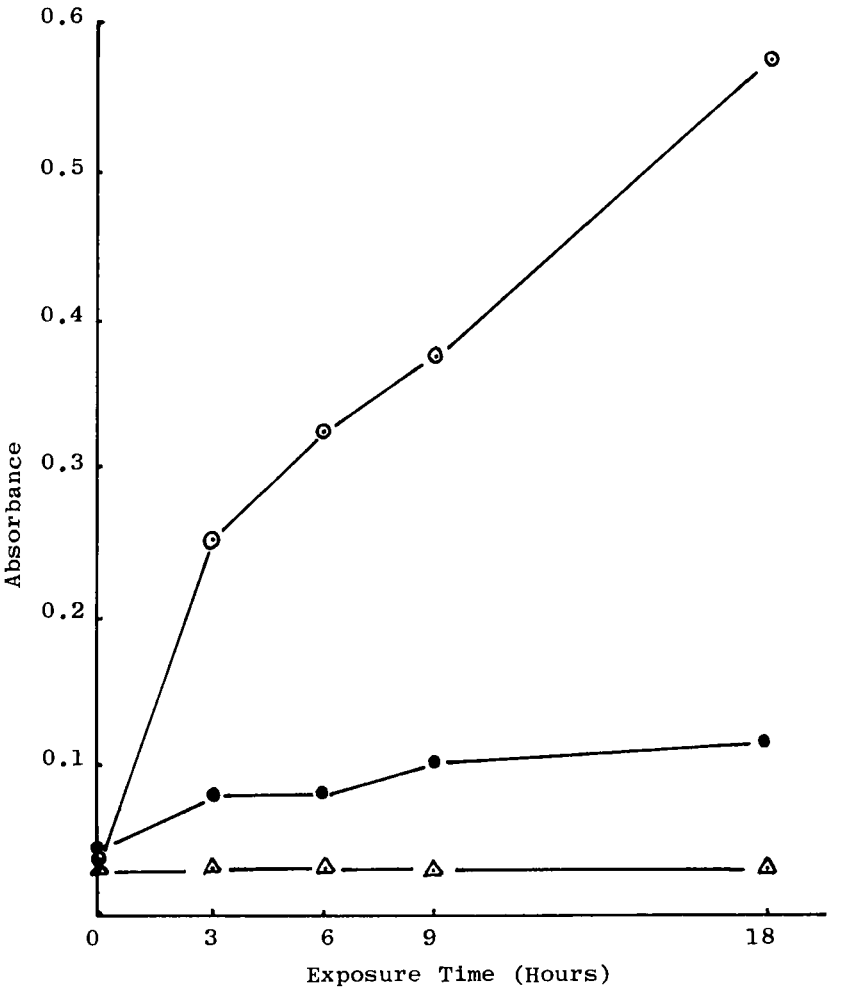

FIGURE 4. Photostabilizing Effect of DMSO for Sodium Nitroprusside in Phosphate Buffer of pH 7.0

⊙ Solution without DMSO Exposed to Light

● Solution with 10%v/v DMSO Exposed to Light

△ Solution without DMSO Stored in the Dark

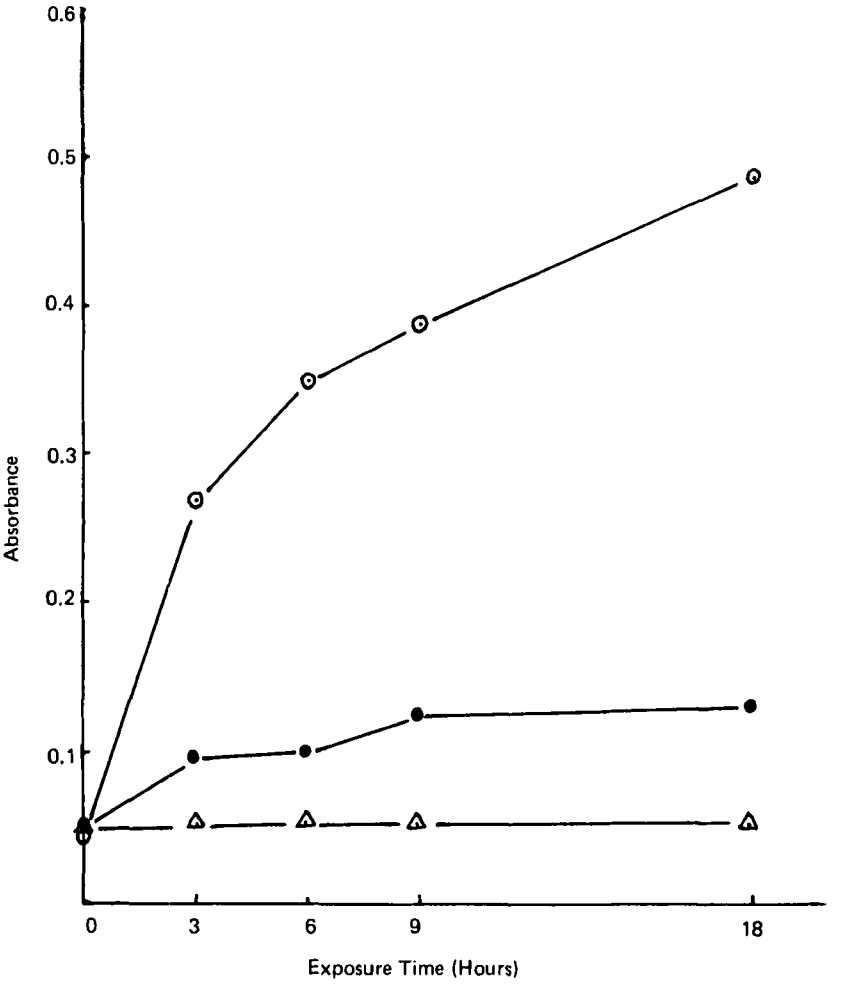

FIGURE 5. Photostabilizing Effect of DMSO for Sodium Nitroprusside in Phosphate Buffer of pH 7.9

⊙ Solution without DMSO Exposed to Light

● Solution with 10%v/v DMSO Exposed to Light

△ Solution without DMSO Stored in the Dark

phate buffers of pH 4.65. The absorbance values obtained after exposure of the various solutions to light for nine hours, were 0.143, o.133 and 0.175 for the acetate, citrate and phosphate buffers respectively. Such results indicated that DMSO demonstrated its greatest stabilizing effect in citrate buffer followed by acetate buffer and then phosphate buffer. The results are in agreement with those reported by Schumacher (10) who found that the use of a 5% solution of sodium citrate resulted in the most stable preparation.

Effect of pH:

The effect of pH on the photostabilizing action of DMSO was carried out in phosphate buffers having the following pH values: 4.65, 7.0 and 7.9. The data are represented by Figures 3-5. The results indicate that DMSO demonstrated its greatest photoprotective action at pH 7.0 followed by pH 7.9 and then pH 4.65.

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