

# Spectrophotometric Determination of Sodium Nitroprusside and Its Photodegradation Products

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**Abstract** □ A specific spectrophotometric method of analysis for sodium nitroprusside was developed utilizing the molar absorptivity values at the maxima appearing in the electronic spectrum at 394 and 498 nm that may be attributed to metal  $d \rightarrow \pi^*$  NO transitions. These measurements appear to be indicative of the unaltered nitroferricyanide complex. A reaction sequence is postulated for aqueous solutions of nitroprusside exposed to normal artificial light. Evidence suggests that one species in the sequence is nitroferricyanide in a higher energy state but with the nitrosyl moiety still present in the coordination sphere, which exhibits an increased molar absorptivity at 394 nm. The molar absorptivity at the 498-nm maximum remains unchanged. Corroborating polarographic data are presented.

**Keyphrases** □ Sodium nitroprusside—spectrophotometric determination, photodegradation products, compared to polarographic data □ Photoirradiation—spectrophotometric determination of sodium nitroprusside and degradation products, compared to polarographic data

Sodium nitroprusside (sodium nitroferricyanide), a potent, rapid acting hypotensive agent when administered intravenously, has been known for many years but has not been used extensively in clinical practice until recently. The chemical and physical properties of the nitroferricyanide ion,  $[\text{Fe}(\text{CN})_5\text{NO}]^{-2}$ , have been investigated (1). The chemistry of the nitroferricyanide ion is dominated by the nitrosyl moiety; virtually all studies during the past 2 decades have centered on the reactivity and physicochemical properties of this ligand.

## BACKGROUND

The crystal structure of sodium nitroprusside has been determined by X-ray diffraction; the nitroferricyanide ion possesses approximate  $C_{4v}$  symmetry (2). A complete interpretation of the electronic spectrum of nitroferricyanide was carried out (3) using extensive self-consistent charge and configuration molecular orbital calculations. Studies of the IR (4) and Mössbauer (5) spectra indicate a large amount of back-bonding between the metal and the nitrosyl ligand. There has been considerable controversy as to the formal charge of iron and nitrosyl in the complex; although no unambiguous assignment has been possible, the consensus is that iron and nitrosyl possess formal charges of +2 and +1, respectively (3, 6, 7).

The nitrosyl moiety can undergo numerous substitution and addition reactions with various reagents, and numerous transformations have been described (1). Polarographic studies also have been conducted (6, 8); three reduction waves, occurring at -0.4, -0.6, and -1.2 *v* versus a saturated calomel electrode, were observed. The first two waves involve one electron each, as calculated from the *n* in Ilkovic's equation, and are reversible; the third wave is irreversible and the value of *n* is 2.

In the presence of light, sodium nitroprusside undergoes numerous reactions, many of which are undefined. Most literature reports are vague and often contradictory when describing the characteristics and properties of its photodecomposition products. In direct sunlight, sodium nitroprusside ultimately yields Prussian blue, cyanic acid, and nitric oxide (9), while the immediate products of the photodecomposition in light of low energy are appar-

Table I—Microanalysis of Sodium Nitroprusside

Determination	Theory, %	Found, %
C	20.16	19.99
H	1.35	1.29
N	28.20	28.28
Fe	18.74	18.52

ently nitric oxide and  $[\text{Fe}(\text{CN})_5(\text{H}_2\text{O})]^{-3}$  (10). It has also been reported that nitroferricyanide is photoreduced in aqueous solution to yield nitroferrocyanide,  $[\text{Fe}(\text{CN})_5\text{NO}]^{-3}$  (11).

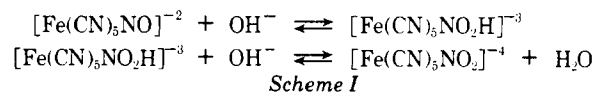
Photoirradiation of nitroferricyanide in dimethylformamide yields an electron spin resonance (ESR) spectrum, which is essentially identical to that obtained by electrolytic reduction of nitroferricyanide in dimethylformamide and is attributed to nitroferrocyanide (12-14). More recently (15), it has been argued that photoirradiation of nitroferricyanide facilitates the formation and stabilization of  $[\text{Fe}(\text{CN})_5\text{NO}_2\text{H}]^{-3}$ , which has been postulated as an intermediate (Scheme I) (16).

This hypothesis is supported by the report that irradiation of a neutral solution of nitroferricyanide results in a pH decrease, which increases to nearly the original value when irradiation ceases (17). 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.

Relatively few literature references describe analytical methods for the determination of sodium nitroprusside. It has been assayed colorimetrically as the isophorone complex (18), and the potentiometric titration with silver nitrate using a saturated calomel-silver-specific ion electrode system is well known. Although polarographic investigations (6, 8) have been conducted to evaluate equilibrium constants between the various reduced species in solution, polarography also can be applied to the quantitative determination of nitroprusside. Martin and Patel (19) analyzed aqueous solutions of sodium nitroprusside spectrophotometrically by determining the absorbance at 390 nm. Upon exposure to light and elevated temperatures, a pronounced increase in the absorbance was observed. However, no attempt was made to correlate the increase in absorbance to the amount of sodium nitroprusside degraded.

The introduction of sodium nitroprusside as a therapeutic agent for the treatment of hypertensive emergencies led to the present investigation to develop an analytical method for determining the purity and stability of crystalline and lyophilized powders of the material. Since the drug is often administered in 5% dextrose infusion solutions stored in clear glass or plastic containers, a study was initiated to determine its light stability when dissolved in an aqueous medium. The present investigation correlates absorbance changes upon photoirradiation with the amount of sodium nitroprusside degraded by utilizing the molar absorptivity values at the maxima appearing in the electronic spectrum at 394 and 498 nm that may be attributed to metal  $d \rightarrow \pi^*$  NO transitions (3).

Since the nitrosyl moiety is the therapeutically active portion of the molecule (20), it was desirable to develop an analytical method that would be specific for the intact coordination sphere of iron and particularly for the nitrosyl substituent. The spectrophotometric method should provide this specificity, since the molar absorptivity values at 394 and 498 nm appear to be indicative of unaltered sodium nitroprusside.



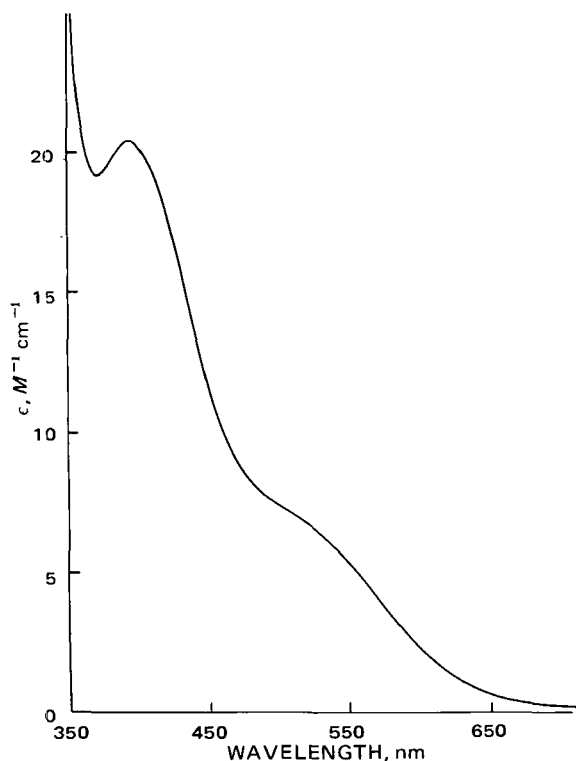


Figure 1—Spectrum of sodium nitroprusside in aqueous solution.

Polarographic studies also were conducted to compare the sensitivity and specificity of the polarographic and spectrophotometric techniques as applied to the photodegraded material. The thermal stability of aqueous solutions was investigated, and the rates of photodegradation *versus* thermal decomposition were determined.

### EXPERIMENTAL

**Spectrophotometry**—Spectra and spectrophotometric assays were determined with a double-beam UV-visible recording spectrophotometer<sup>1</sup> using matched 1- or 10-cm quartz cells. All absorbance measurements were made at 25°.

**Polarography**—The polarographic studies were performed on a recording polarograph<sup>2</sup> at 25°. All potentials were measured *versus* a silver-silver chloride reference electrode in a saturated potassium chloride salt bridge containing 3% agar. The polarograms were run in pH 7.2 Britton-Robinson buffer prepared by combining 100 ml of a solution which is 0.04 M in phosphoric acid, acetic acid, or boric acid with 55 ml of 0.2 N sodium hydroxide. All test solutions were deoxygenated with nitrogen for at least 10 min and were maintained in a nitrogen atmosphere throughout the analysis. The polarographic cell was covered with aluminum foil to prevent exposure to light during the analysis.

**Photoirradiation Studies**—Solutions of sodium nitroprusside were photoirradiated in a Cooper-Lachman light chamber (21) or under normal laboratory fluorescent lighting. The solutions were stored in clear Pyrex flasks or in plastic containers<sup>3</sup> during the irradiation process.

**Thermal Stability Studies**—Solutions of sodium nitroprusside were sealed in 5-ml amber ampuls and stored in an oven thermostated at the desired temperature. Samples were withdrawn at appropriate time intervals and analyzed spectrophotometrically.

**Reagents**—The microanalysis of sodium nitroprusside<sup>4</sup> is presented in Table I. The microanalytical data indicate that the substance was essentially pure. The 5% dextrose injection USP solution was purchased in glass<sup>5</sup> or plastic<sup>3</sup> containers.

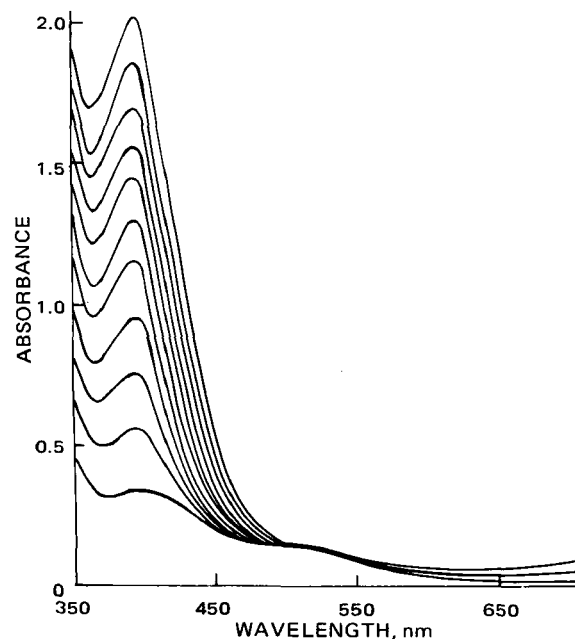


Figure 2—Spectral changes observed on irradiation of a 0.5% aqueous solution of sodium nitroprusside in a Cooper-Lachman light chamber. Spectra were recorded at 1-hr time intervals.

All other common reagents were ACS certified grade. Distilled, deionized water was used for the preparation and dilution of all solutions unless otherwise described.

### RESULTS AND DISCUSSION

The spectrum of sodium nitroprusside in aqueous solution in the 350–700-nm region is shown in Fig. 1. There are two maxima in the spectrum at 394 and 498 nm, having molar absorptivity values of 20.4 and 7.4, respectively. These molar absorptivity values are in good agreement with those reported previously (3, 16).

Although the 498-nm transition appears only as a shoulder in the spectrum, its existence as a distinct absorption band was confirmed by the determination of the polarized crystal spectrum of a single crystal of sodium nitroprusside (3).

The molecular orbital energy level diagram for nitroferricyanide was derived previously (3). The two highest filled molecular orbitals in the ground state of the ion are designated  $6e$  and  $2b_2$ ; thus, the ground state is  $(6e)^4(2b_2)^2$ . The effective electronic configuration of iron is  $3d^6$ , and nitroferricyanide formally contains Fe (II) and  $\text{NO}^+$ , consistent with the observation that the ion is diamagnetic (22). The  $6e$  level is mainly  $dxz$  and  $dyz$  but contains 24.8%  $\pi^*$  NO character, indicating substantial  $\text{FE} \rightarrow \text{NO}$  back-bonding. The  $2b_2$  level consists of 84.5%  $dxy$ , 13.9%  $\pi$  CN, and 1.6%  $\pi^*$  CN, suggesting that the degree of  $\text{FE} \rightarrow \text{NO}$  back-bonding is relatively slight.

The lowest unfilled molecular orbital, represented by the symbol  $7e$ , contains 72.5%  $\pi^*$  NO and some contributions from  $d\pi$ ,  $\sigma$  CN,  $\pi$  CN, and  $\pi^*$  CN. The low energy transitions appearing at 394 and 498 nm were given the following band assignments: 394 nm,  $6e \rightarrow 7e$ ; and 498 nm,  $2b_2 \rightarrow 7e$  (3). These long wavelength absorption bands involve transitions from essentially metal  $d$  orbitals to a molecular orbital containing primarily the antibonding  $\pi^*$  NO orbital on the nitrosyl moiety. Since the other absorption bands of nitroferricyanide appear in the UV region of the spectrum, irradiation of solutions of the ion with low energy light should have important consequences on the 394- and 498-nm transitions. Moreover, since there is no transmission through Pyrex below 360 nm, the course of the photochemical reactions should be intimately involved with the electronic transitions in the visible region of the electronic spectrum of nitroferricyanide.

The spectral changes observed on irradiation of a 0.5% aqueous solution of sodium nitroprusside in a Cooper-Lachman light chamber are illustrated in Fig. 2. The increase in absorbance at 394 nm as a function of irradiation time is shown in Fig. 3. The sam-

<sup>1</sup> Beckman Acta C III.

<sup>2</sup> Model EUW-401, Heath Co.

<sup>3</sup> Vialflex, Travenol Laboratories, Deerfield, Ill.

<sup>4</sup> Mallinckrodt reagent grade.

<sup>5</sup> Saftiflask, Cutter Laboratories, Berkeley, Calif.

Table II—Light Stability Data (Absorbance) for Sodium Nitroprusside 0.01% Solutions

Hours	Crystalline Powder in Dextrose Infusion Solution				Lyophilized Material							
					Water				Dextrose Infusion Solution			
	394 nm	498 nm	700 nm	% Degraded	394 nm	498 nm	700 nm	% Degraded	394 nm	498 nm	700 nm	% Degraded
0	0.104	0.042	0.009	—	0.092	0.040	0.009	—	0.090	0.039	0.009	—
1	0.125	0.041	0.008	5.1	0.108	0.040	0.009	4.4	0.106	0.038	0.009	4.5
2	0.148	0.042	0.008	10.6	0.125	0.040	0.009	9.1	0.123	0.038	0.009	9.2
3	0.170	0.043	0.009	15.9	0.142	0.040	0.009	13.8	0.140	0.038	0.009	13.9
4	0.191	0.042	0.009	20.9	0.159	0.040	0.009	18.2	0.156	0.038	0.009	18.3
5	0.212	0.042	0.008	26.0	0.175	0.040	0.009	22.6	0.172	0.038	0.009	22.8
6	0.230	0.042	0.008	30.8	0.191	0.039	0.009	26.9	0.189	0.038	0.009	27.5
7	0.253	0.041	0.008	35.8	0.208	0.040	0.009	31.5	0.205	0.038	0.009	31.9
8	0.273	0.041	0.008	40.4	0.226	0.039	0.009	36.4	0.220	0.038	0.009	36.1
Control Sample Stored in Dark												
0	0.104	0.042	0.009	—	0.092	0.040	0.009	—	0.090	0.039	0.009	—
24	0.105	0.042	0.008	None detected	0.094	0.041	0.008	None detected	0.091	0.039	0.009	None detected

ples were withdrawn at 1-hr intervals, and the spectrum was recorded. Irradiation for up to 8 hr produced an absorbance increase only at 394 nm while the absorbance at 498 nm remained constant. After 9 hr of exposure to light, an absorbance increase was observed not only at 394 but also at 498 and 700 nm, suggesting that another reaction was occurring subsequent to, or simultaneous with, the primary photodegradation reaction. That is, a process other than the one exhibiting an absorbance increase at only 394 nm became operative.

The literature (1) is ambiguous and inconclusive concerning the photochemical course of the reactions undergone by nitroferrocyanide on photoirradiation. Photoaquation to yield nitric oxide and  $[\text{Fe}(\text{CN})_5(\text{H}_2\text{O})]^{-3}$  (10) and photoreduction to produce nitroferrocyanide (11) have been described most frequently as the immediate photodecomposition products of nitroprusside. The difficulty in determining the reaction sequence of photochemical processes lies in the fact that usually a series of undefined, metastable intermediates are formed prior to the final product. Sometimes it is possible to detect these transitory intermediates by a variety of spectroscopic techniques such as electron spin resonance, NMR, and Mössbauer spectroscopy.

When the nature of electronic transitions is well understood, UV and visible spectrophotometry are applied routinely to elucidate the photochemical reactions. The two visible absorption bands of nitroferrocyanide have been assigned on a theoretical basis (3), and these assignments receive substantial support from the measured

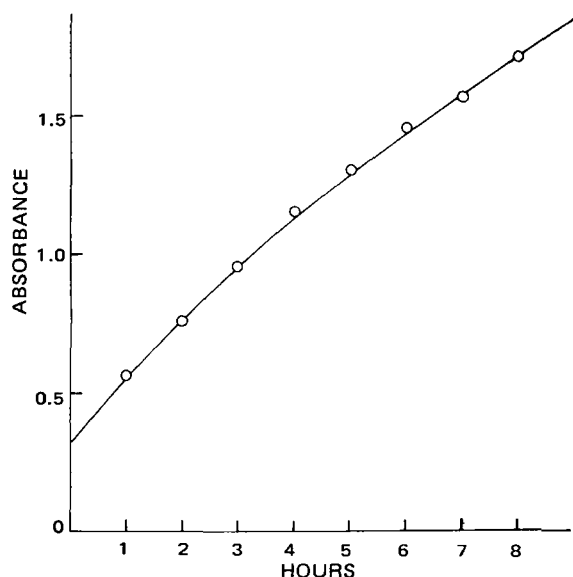


Figure 3—Change in absorbance at 394 nm versus time on irradiation of a 0.5% sodium nitroprusside aqueous solution in a Cooper-Lachman light chamber.

spectra of a single crystal of sodium nitroprusside using polarized light. In the present study, absorption bands at 394 and 498 nm, attributed to metal  $d \rightarrow \pi^*$  NO transitions, were followed to determine the course of the photodecomposition and the amount of sodium nitroprusside degraded on photoirradiation.

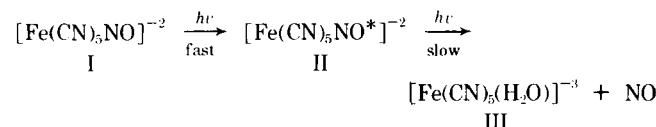
The fact that initially only the absorbance at 394 nm increased while no absorbance change was observed at 498 nm suggests that the nitrosyl moiety remains intact and that initial irradiation results in a photoexcited nitroferrocyanide species accompanied by electronic rearrangement, most likely involving the  $\pi^*$  NO molecular orbital. If the effects of long wavelength irradiation of nitroferrocyanide are essentially confined to the  $\pi^*$  NO molecular orbital, only the 394-nm band attributed to the  $6e \rightarrow 7e$  transition is expected to reflect this transformation, since the 6e level contains approximately 24.8%  $\pi^*$  NO character. The 498-nm band assigned the  $2b_2 \rightarrow 7e$  transition is not expected to be affected as markedly, since the  $2b_2$  state possess no  $\pi^*$  NO character.

The facts that the energy of the absorption bands is constant and that no new bands appear in the visible region of the spectrum support the theory that initial irradiation chiefly involves the  $\pi^*$  NO molecular orbital. Irradiation apparently does not alter the relative energies of the 6e,  $2b_2$ , and 7e levels, and photoexcitation results only in increased orbital overlap between the 6e and 7e orbitals, which is a powerful mechanism for enhancing absorbance.

The spectral data from the present study indicate that initial photoirradiation results in the formation of a relatively long-lived species, as evidenced by the constancy of the absorbance at 498 nm and the lack of any new absorption bands. This rationale is supported by the fact that a blue-green species and nitric oxide, whose distinct odor can easily be detected, are observed only on prolonged irradiation—greater than 8 hr in a Cooper-Lachman light chamber.

Although the course of the photochemical reaction has not been established conclusively, Scheme II is proposed. Species II is photoexcited nitroferrocyanide, and III is the photoreduced aquation product. The transformation of II to III probably involves a series of complex intermediates whose identities are not well defined (1). Possible intermediates include  $[\text{Fe}(\text{CN})_5\text{NO}(\text{OH})]^{-3}$ ,  $[\text{Fe}(\text{CN})_5\text{NO}_2]^{-4}$ , and  $[\text{Fe}(\text{CN})_5\text{NO}]^{-3}$ , but the true nature of these species cannot be ascertained.

If it is assumed that essentially all of I is converted to II prior to the appearance of spectral changes at 498 and 700 nm, a fivefold increase in the initial absorbance at 394 nm may be equated to a 100% conversion of I to II. Based on this assumption, the molar absorptivity of II may be approximated at  $102 M^{-1} \text{ cm}^{-1}$ . Since the molar absorptivity of sodium nitroprusside at 394 nm is 20.4, an increase of 0.8 in this value represents a 1% loss. The amount of



Scheme II

**Table III—Spectrophotometric and Polarographic Changes Observed on Irradiation of Aqueous Sodium Nitroprusside Solution**

Hours	Absorbance (10-cm Cell)			Polarographic Response (Relative Units)	
	394 nm	498 nm	700 nm	Wave I	Wave II
0	0.214	0.079	0.006	46	91
1	0.608	0.080	0.007	43	85
2	0.925	0.080	0.007	41	82
4	1.410	0.085	0.008	40	80
6	1.761	0.093	0.010	40	80

degraded nitroprusside can be calculated from the following relationship:

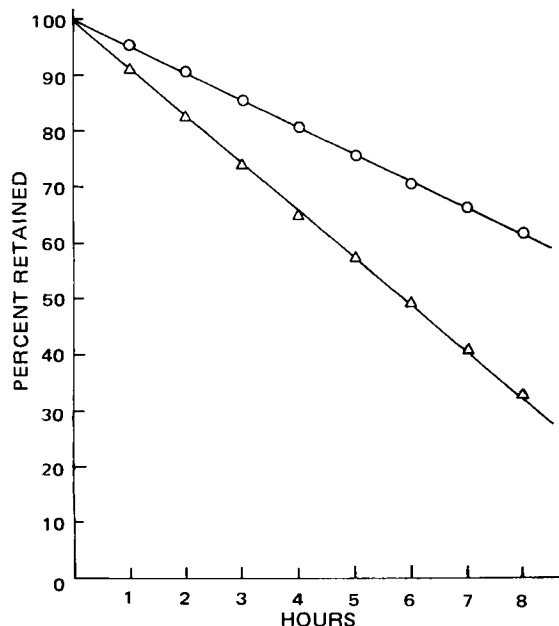
$$\frac{\text{molar absorptivity} - 20.4}{0.8} = \% \text{ degraded nitroprusside (Eq. 1)}$$

The concentration of sodium nitroprusside in a dry filled vial can be determined spectrophotometrically by using the standard molar absorptivity value at 394 nm and inserting the appropriate dilutions into the equation relating absorbance and concentration:

$$\frac{\text{absorbance/cm} \times \text{dilution (ml)}}{\frac{1000 \text{ ml}}{297,970 \text{ mg/M}} \times \epsilon M^{-1} \text{ cm}^{-1}} = \text{mg/vial (Eq. 2)}$$

In the case of lyophilized material in the anhydrous form, a milliequivalent weight of 261,970 mg must be used in the calculation.

Since sodium nitroprusside is administered at concentrations of approximately 0.01%, the light stability of crystalline powder and lyophilized material in water and in 5% dextrose solution under normal laboratory fluorescent lighting conditions was investigated. All absorbances were determined with 10-cm quartz cells. The results (Table II) indicate that the rate of degradation is linear over the 8-hr period. The rate of degradation is lower than that encountered in a Cooper-Lachman light chamber because the light intensity is much less in the normal laboratory situation. Since sodium nitroprusside may also be dispensed in a 5% dextrose solution from polyvinyl chloride containers, the light stability of a 0.01% solution on exposure to laboratory fluorescent lighting also was determined. A comparison of the rate of photodecomposition of clear Pyrex and polyvinyl chloride containers is shown in Fig. 4. The increased rate of sodium nitroprusside degradation in the plastic



**Figure 4—Sodium nitroprusside stability in 5% dextrose infusion solution on photoirradiation. Key: O, Pyrex container; and Δ, plastic container.**

**Table IV—Effect of Temperature on the Molar Absorptivity of Sodium Nitroprusside Solutions**

Hours	Molar Absorptivity								
	394 nm			498 nm			700 nm		
	25°	55°	65°	25°	55°	65°	25°	55°	65°
0	20.4	—	—	7.4	—	—	0.18	—	—
24	—	20.4	20.5	—	7.4	7.4	—	0.18	0.18
96	—	20.4	20.6	—	7.5	7.5	—	0.18	0.18
192	20.3	20.6	20.8	7.4	7.5	7.5	0.18	0.18	0.18
472	20.4	20.6	21.2	7.5	7.5	7.5	0.18	0.18	0.18

unit is due to the greater transparency of polyvinyl chloride to higher energy UV radiation as compared to glass.

Several reports (12, 14) indicate that electrolytic reduction and photoirradiation of nitroprusside in dimethylformamide yield the same species,  $[\text{Fe}(\text{CN})_5\text{NO}]^{-3}$ . To establish a similar correlation in aqueous media, an investigation was conducted to determine the effect of photoirradiation on polarographic response, i.e., wave height and half-wave potential. The solutions contained 0.3 mg/ml of sodium nitroprusside, and the absorbances and polarograms were determined initially and after irradiation in a Cooper-Lachman light chamber. The polarogram of the original solution showed two reduction waves of equal size at  $-0.31$  and  $-0.58$  v versus the silver-silver chloride reference electrode, and no new reduction waves appeared on photoirradiation. The results of the study are summarized in Table III.

The data show that the decrease in polarographic response levels off after 4 hr of light exposure, suggesting that photoreduction is not an initial primary photodegradation route of sodium nitroprusside. The results do indicate, however, that spectrophotometry is a much more sensitive method for detecting photodegradation than polarography. In addition, the fact that the polarographic response plateaued after approximately a fivefold increase in the absorbance at 394 nm supports the hypothesis that, on irradiation, nitroferriyanide is initially converted to III, which then slowly degrades to form IV.

A solution study of the thermal stability of sodium nitroprusside was reported previously (19). The stability relative to a sample stored at 25° was determined by measuring the increase in absorbance at 390 nm at selected time intervals. The data show that storage of a solution at 65° for 96 hr results in a threefold absorbance increase at 390 nm. Since preliminary results of experiments designed to ascertain the thermal stability of sodium nitroprusside solutions did not agree with the literature findings, a detailed study was conducted (Table IV).

The present results, as opposed to the earlier report (19), indicate that sodium nitroprusside solutions are stable for long periods even at elevated temperatures. The apparent discrepancies may arise from the previous study being carried out with sodium nitroprusside material containing impurities or with contaminated solutions, thereby accelerating the thermal degradation process.

The present results clearly demonstrate that sodium nitroprusside is extremely photosensitive. Although complex, the theory presented to explain photochemical phenomena provides a method for the simultaneous determination of the purity, stability, and concentration of sodium nitroprusside in the solid state and in solution.

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## Effect of Solvent Flow Reynolds Number on Dissolution Rate of a Nondisintegrating Solid (Potassium Chloride)

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**Abstract** □ An apparatus for measuring dissolution rates of solids in the form of disks was designed to possess the following features. The solvent flowed continuously and reproducibly past the disk at various rates associated with calculable Reynolds numbers, *Re*. The effluent solution was adequately mixed before analysis. The concentration of dissolved solute was much less than the solubility. The surface area of the disk in contact with the solvent was constant during measurements. The dissolution rate of the disk was reproducible, and the disk and its surface could be readily characterized. The apparatus was tested at 37° with compressed potassium chloride and water. The intrinsic dissolution rate, *G*, was a linear function of *Re* from *Re* = 360 to >6000. This relationship enabled one unknown constant in each dissolution theory to be expressed in terms of *Re*. For the diffusion layer model, the thickness of this layer, calculated from the experimental value of *G*, agreed well with that calculated from the various physical properties, provided that natural convection did not predominate. The dissolution of potassium chloride in this system was, therefore, controlled by diffusion.

**Keyphrases** □ Dissolution rates—solid nondisintegrating disk (potassium chloride), apparatus described, effect of solvent flow Reynolds number □ Solvent flow—Reynolds number, effect on dissolution rate of nondisintegrating solid disk (potassium chloride) □ Reynolds number—effect on dissolution rate of nondisintegrating potassium chloride solid disk, apparatus described and evaluated

The first major objective of this work was to design, construct, and test an apparatus with the following features for determining the dissolution rate of solids.

(a) The solvent flow in the apparatus should be controlled and characterized by a calculable value of the Reynolds number, *Re*.

(b) The effluent solution from the apparatus should be adequately mixed before analysis.

(c) The concentration, *c*, of dissolved solute must

be much less than the solubility, *c<sub>s</sub>*, i.e., (*c<sub>s</sub>* - *c*) ≈ *c<sub>s</sub>*, or, in other words, sink conditions must apply.

(d) The surface area of the solid disk in contact with the dissolution medium must be constant.

(e) The dissolution rate of the solid must be reproducible.

(f) The solid disk and its surface must have reproducible properties that can readily be characterized.

(g) The solid surface should be positioned in the solvent stream so that the flow over the solid is reproducible.

The second major objective was to study how the intrinsic dissolution rate, *G*, of a solid substrate depends on the flow rate of the solvent and, therefore, on *Re*. The third major objective was to deduce which dissolution theory or model best fits the results and describes the dissolution process.

#### EXPERIMENTAL

**Materials**—The potassium chloride was spectroscopic grade<sup>1</sup>, and the solvent in the dissolution experiments was glass-distilled water of very low potassium content (<0.01 mg/liter).

**Preparation of Solid Disks**—Transparent disks, 13 mm in diameter, 2 mm thick, and encircled by a 21-mm external diameter Nimonic<sup>2</sup> creep-resistant alloy ring (disk holder K), were prepared by compressing 315 mg of finely powdered potassium chloride at 10 tons load for 5 min under vacuum in a die and punch assembly (Fig. 1). The upper surface of the finished disk to be exposed to the solvent was level with the rim of the holder while the lower surface was recessed to enable it to fit on the raised knob on stub D in dissolution chamber C (Fig. 2).

Petroleum jelly was used for adhesion and ensured that the sol-

<sup>1</sup> B.D.H. Chemicals Ltd., Poole, Dorset, BH12 4NN, England.

<sup>2</sup> Henry Wiggin and Co. Ltd., Wiggin Street, Birmingham, England.