SODIUM NITROPRUSSIDE DIHYDRATE
Sigma Prod. No. S0501

CAS NUMBER: 13755-38-9
SYNONYMS: Sodium Nitroferricyanide Dihydrate; Nipride Dihydrate; Sodium Nitroprussiate Dihydrate; Sodium Nitrosylpentacyanoferrate Sodium[1]

PHYSICAL DESCRIPTION

Appearance: brown-red powder
Molecular Formula: $Na_2Fe(CN)_5NO.2H_2O$
Molecular Weight: 298.0
E_M (390-395 nm) = approx. 20.4 (water); shoulder at 500 nm[2,3;]
E_M (396 nm) = approx. 25 (water)[4]

The IR and UV/VIS spectra were reported.[2] Methods of analysis including High Performance Liquid Chromatography (HPLC), Identification tests, Thin-Layer Chromatography (TLC), Colorimetry, and Titrimetry have been reported.[2,4-7] Methods for the determination of low concentrations of SNP, its degradation products and SNP levels in plasma were described.[4,8,9]

METHOD OF PREPARATION:

The product is synthetically prepared.[10] A synthetic method of preparation has been reported.[2]

STABILITY / STORAGE AS SUPPLIED:

Sodium Nitroprusside (SNP) should be stable for at least one year when stored desiccated at room temperature in the dark.[11] The absorbance of a small amount of moisture may facilitate the photodegradation of SNP.[2]

SOLUBILITY / SOLUTION STABILITY:

Solubilities (mg/ml, 25°C) of SNP in various solvents are: water, >200; normal saline, >200; 95% ethanol, 1.1; absolute ethanol, 5.0; methanol, 100-200; and isopropyl alcohol, 0.1. SNP is virtually insoluble in acetone, ether and chloroform.[2] Approximately a 200 mg/ml solution in deionized water was prepared forming a clear red-brown color.[11] SNP solutions degraded when exposed to white or blue light (releasing nitrosyl ligand and cyanide ion) but not to red light.[12] The rate of photodegradation upon exposure to daylight and to light of 350 nm is the same in water, in 0.9% saline and in 5% glucose solutions.
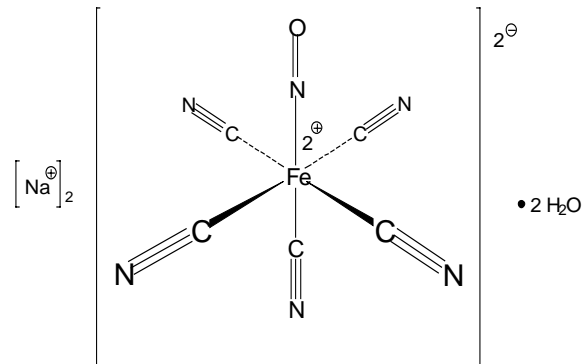
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SOLUBILITY / SOLUTION STABILITY: (continue)

The photochemical degradation is a non-linear process; the relevant chemical reactions for the mechanism have been reported.[2,4] The effect of natural light on the rate of photodegradation of unprotected SNP solutions is more deleterious than that of fluorescent light. It was reported that after 24 hours of storage of SNP solutions (0.1% w/w) in aluminum foil-wrapped bottles under fluorescent light, about 3.4% decomposition was observed (more concentrated solutions would undergo less degradation). The identity of the breakdown products was reported.[13] SNP solutions in physiological saline, stored in foil-wrapped glass containers at 4°C in the dark are reportedly stable (no storage time given).[8] Mahoney et al. reported that SNP solutions (50 µg/ml, 100 µg/ml) are stable in 5% dextrose, lactated Ringer's and normal saline when stored in glass (silanized) and plastic containers (both wrapped in aluminum foil), and the covered vials left exposed to fluorescent light for 48 hours.[5] Aqueous solutions of SNP, which are both temperature (under certain conditions) and light sensitive may release cyanide ion during decomposition.[6,13,14] It is recommended to prepare fresh solutions, preferably or store SNP solutions (>0.1% w/v) for no more than 24 hours after preparation in the dark at 4°C.[13,15]

Since SNP (30 µM, 37°C) releases NO in a pH dependent manner (the greatest quantity being released at pH 5.0 with decreasing amounts of NO released up to pH 7.2), stock solutions at pH 7.4 were prepared immediately prior to use.[16] Acidic solutions of SNP exposed to a light source for only a few hours decompose producing a blue haze and an odor of cyanide.[17] SNP will react with minute amounts of organic and inorganic substances forming highly colored products; these solutions should be discarded.[15]

Substances which increase the stability of SNP solutions are: dimethyl sulfoxide (10% v/v)[18], glycerol, cyanocobalamin (10 mg/L) and other components with anionic chelating potential, i.e., sodium acetate or phosphate.[4,6,15] Substances which reduce the stability of SNP solutions are sodium bisulfate and hydroxybenzoates.[15] Addition of citric acid or sodium EDTA (both at 0.5 mg/100 ml) to 5% dextrose solution of SNP (50 mg/L) does not improve the stability.[4,6] SNP solutions in water and in 0.9% saline (50 mg/ml) are stable to autoclaving (15 min., 121°C) but sterilization of SNP solutions in a 5% glucose solution resulted in a 40% loss of nitroprusside.[6]

Studies have shown that cyanide is released from SNP incubated with serum, plasma, whole blood, liver homogenate, hemoglobin and erthyrocytes[8,19]. Incubation of SNP with blood releases 50% of the total amount of cyanide within approximately 30 minutes and more than 90% in two hours.[8]

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USAGE/APPLICATIONS:

By the release of nitric oxide (NO), SNP increases the amount of 6-keto-prostaglandin $F_{1\alpha}$ (6-keto-$PGF_{1\alpha}$) both in vitro (through cyclooxygenase activation) and in vivo. The released NO in concert with 6-keto-$PGF_{1\alpha}$ contributed to the inhibition of thrombin-induced human platelet aggregation.[20] Azula, F.J. et al. reported that thrombin-stimulated phospholipase C activity is quickly inhibited by a rapid increase in cyclic GMP levels induced by SNP.[21] SNP infusion (10 μg/kg/hr) significantly inhibited thrombus formation, increased vessel diameter and enhanced mean red cell velocity in rat cerebral arterioles and venules without affecting wall shear rates.[22] SNP ($10^{-4}M$-$10^{-7}M$) stimulated human colonic ion transport, i.e., electrogenic chloride secretion and possibly bicarbonate secretion.[23] SNP, through released nitric oxide (NO), produced reversible vasodilation and tachycardia in rainbow trout probably through NO-mediated stimulation of soluble guanylyl cyclase (SGC).[24] Treatment of a human glioblastoma cell line, T98G, with 0.1 mM and 1 mM SNP solutions caused a significant increase in the levels of heme oxygenase-1 (stress protein) mRNA in human brain tissues which suggests a possible relationship between the CO/heme oxygenase system with the NO/NO synthase system in the brain.[25] NO release from SNP (20 mM) was enhanced under hypoxic conditions (relative to aerobic conditions) in leading to a greater cytoxicity of SNP of cultivated endothelial cells.[26] Under intense light exposure large amounts of NO were released from SNP (1 mM) which induced an inhibition of the respiratory rate in a glioma cell line.[27] SNP inhibited the dioxygenase activity of lipoxygenase (LOX-2), a key enzyme for arachidonic acid metabolism in human cells, in human platelets and human CHP100 neuroblastoma cells. SNP was shown to be a competitive inhibitor of LOX-2 (inhibition constant, 525 μM).[28]

SNP inhibited the non-selective cation conductance activated as a result of intracellular calcium store depletion in mouse cells and this inhibition is probably mediated by the guanylyl cyclase/cyclic GMP pathway.[29] SNP (50 nM) and other nitrovasodilators induced relaxation of the endothelium of the rat thoracic aorta probably through cyclic GMP-dependent protein phosphorylation and dephosphorylation of myosin light chain.[30] SNP (5-200 μM) has also been shown to stimulate a cytosolic ADP-ribosyltransferase (in human platelets). The effect was reportedly not related to stimulation of soluble guanylate cyclase nor the production of cyclic GMP.[31] Kiedrowski, L. et al. reported that the SNP protection of cerebellar granule cells from glutamate and N-methyl-D-aspartate (NMDA) may be mediated by the ferrocyanide moiety (rather than NO) of SNP which may inhibit NMDA receptors.[32]

SNP has been used for the detection of many organic compounds including aldehydes, ketones, alkali sulfides, unsubstituted dithiocarbamates, zinc, sulfur dioxide, secondary amines, sulfur-containing amino acids and others.[4,33-35]

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GENERAL NOTES:

SNP is an iron-nitrosyl short-acting hypotensive agent. It produces peripheral vasodilation and reduces peripheral resistance by directly acting on both veins and arteries.[15] SNP rapidly lowers blood pressure and causes endothelium-independent vascular smooth muscle relaxation. Both effects are attributable, at least in part, to the released NO free radical.[2,36] NO is released from SNP mainly by the decomposition of pure solutions due to photochemical reactions or by the various reducing metabolites, including thiols, in biological organelles such as microsomes.[26,37,38] NO is responsible for some biological responses such as relaxation of smooth muscle, inhibition of platelet activation, modulation of neurotransmission and non-specific cell-bound cytotoxicity. The physiology, chemistry, pathophysiology and pharmacology of NO have been discussed.[14,39-42] The pharmacodynamic action of SNP and other nitrovasodilators is probably mediated by the second messenger, cyclic GMP. The principal activators of guanylate cyclase derived from nitrovasodilators may be NO but may also be S-nitrosothiol or nitrite itself produced through chemical reactions with cellular components.[43-46] Other mechanisms not mediated by cyclic GMP and NO[45] may be involved in the control of regulatory systems[14,31,32] i.e., in SNP-induced tracheal relaxations. Erythrocytes convert SNP to cyanide which is further metabolized in the liver to thiocyanate by the enzyme rhodanase.[2,15] The metabolism, proposed mechanism of vasodilation, pharmacology, and toxicology of SNP have been reported.[2,19,37,46-50]

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