EPA/600/8-88/081
June 1988

Summary Review of Health Effects Associated with Sodium Hydroxide

Health Issue Assessment

Environmental Criteria and Assessment Office
Office of Health and Environmental Assessment
Office of Research and Development
U.S. Environmental Protection Agency
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Preface

The Office of Health and Environmental Assessment has prepared this summary health assessment for use by the Office of Air Quality Planning and Standards to support decision making regarding possible regulation of sodium hydroxide as a hazardous air pollutant.

In the development of this document, the scientific literature has been inventoried, key studies have been valuated, and the summary and conclusions have been prepared so that the chemical's toxicity and related characteristics are qualitatively identified. Observed-effect levels and other measures of dose-response relationships are discussed, where appropriate, so that the nature of the adverse health responses is placed in perspective with observed environmental levels. The relevant literature for this document has been reviewed through June 1986.

Any information regarding sources, emissions, ambient air concentrations, and public exposure has been included only to give the reader a preliminary indication of the potential presence of this substance in the ambient air. While the available information is presented as accurately as possible, it is acknowledged to be limited and dependent in many instances on assumption rather than specific data. This information is not intended, nor should it be used, to support any conclusions regarding risk to public health.

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1. Summary and Conclusions

Sodium hydroxide (NaOH), or caustic soda, is a strongly alkaline substance, which is soapy to the touch, dissolves in water with the liberation of heat, and rapidly absorbs carbon dioxide and water from the air. Sodium hydroxide will neither burn nor support combustion, but it reacts with amphoteric metals, such as aluminum, tin, and zinc, generating hydrogen which may form an explosive mixture. NaOH reacts with all the mineral acids to form the corresponding salts and also reacts with weak-acid gases, such as hydrogen sulfide, carbon dioxide, and sulfur dioxide.

Sodium hydroxide is produced in large quantities in the United States; in 1985, 13,117,000 tons were produced. The primary method for the production of NaOH is the electrolysis of sodium chloride. In this electrolytic production, diaphragm cells are most commonly used in the United States, whereas mercury cells are prevalent in Europe and the Far East. Sodium hydroxide is widely used in the manufacture of other chemicals, and in the pulp and paper industry.

Because of its use in many industries, there are many opportunities for human exposure to NaOH. NIOSH gives an estimate of 150,000 workers who are potentially exposed to NaOH. With the high production (10,959,000 tons in 1985), the number of exposed workers in the United States is likely to continue to be high. The Threshold Limit Value-Ceiling for NaOH (the concentration that should not be exceeded at any time in workplace air) is 2 mg/m^3.

Since NaOH is used in so many industries, the atmosphere may be subjected to pollution from industrial plants. In detergent manufacture, the spray drying procedure is the main source of particulate emissions. The fate of the NaOH aerosol in air depends on its reactions with carbon dioxide and on its equilibrium with the ambient humidity. It was shown that the particles were predominantly sodium carbonate at 30 times the atmospheric CO_2 level and between 70 and 90 percent relative humidity. In normal situations the atmospheric concentration of CO_2 is fairly constant, (0.03 percent), thus the atmospheric fate and form of NaOH would depend on the relative humidity and time exposed.

From the dissociation constant of NaOH, it is noted that the compound is fully ionized; no data could be found on the metabolism of NaOH itself. Radiosodium appears in the circulation of man 3 min. after ingestion. It also appears promptly in the bloodstream after application to intact skin, and after subcutaneous, intramuscular, and intrasynovial injection. The urine is the main avenue for excretion of Na, but small amounts are lost in the stool, in sweat, tears, nasal mucus, saliva, and vaginal and urethral discharges.

Sodium hydroxide was assayed for genotoxicity by the Ames reversion test using *Salmonella typhimurium* strains TA1535, TA1537, TA1538, TA98, and TA100, and in a DNA-repair test with *Escherichia coli* strains, WP2, WP67, and CM871. Both tests showed that NaOH was not genotoxic. A microsuspension assay designed for the detection of DNA damage, using

Escherichia coli strains WP2, WP2 uvr A, WP67, CM611, WP100, W3110 pol A^+, and p3478 pol A^-, also gave a negative response for NaOH.

The incidence of carcinoma of the esophagus among patients with chronic esophageal stricture due to the ingestion of lye is at least a thousandfold greater than in the general population. Although the cases of cancer were causally related to NaOH ingestion, it may be possible that the cancers were the direct result of tissue destruction and possibly scar formation, although it has not been disproven that NaOH may have a direct carcinogenic potential itself. NaOH is classified in Group D as to carcinogenicity.

In the only teratology study reported, NaOH was found to be not teratogenic in mice, but caused significant embryo mortality. In this study, 0.001 M NaOH solution administered intraamniotically to fetuses on the 13th day of gestation gave negative results for teratogenicity, but had a pronounced lethal effect (45.8 percent mortality).

Regarding the effects of NaOH on man, the main deleterious effects were noted on the eyes, the skin, and the alimentary and the respiratory tracts. Several cases of eye damage by NaOH have been reported, most caused by the liquid or dust. The damage can be very severe, with many cases resulting in blindness.

NaOH of sufficient concentration causes damage to skin if it remains in contact with the skin for a long enough time. An example of skin damage was seen in a 42-year old man who developed alopecia following the accidental dripping of NaOH on his scalp.

Inhalation of NaOH dust or concentrated mist can cause damage to the upper respiratory tract and to lung tissue, depending on the extent of the exposure. The effects of inhalation may range from mild irritation of the mucous membranes to a severe pneumonitis. In workers exposed chronically to NaOH dust (0.5 to 2.0 mg/m^3) for up to 30 years there was no significant increase in mortality in relation to duration or intensity of exposure. Observed deaths due to malignant neoplasms were less than expected, except for neoplasms of the digestive organs and peritoneum. Only 2 respiratory malignancy deaths were found compared to 3.9 that were expected. In another study on 500 workers at a Soviet plant, where the concentrations of caustic substances in the air ranged from 0 to 9 mg/m^3, examinations of the effects of aerosols on the upper respiratory tract showed that there was a related health hazard.

The form in which NaOH is ingested determines the location of mucosal damage. The injury from ingestion of NaOH may be quite severe, as in a patient who ingested 20 g Drano in water and died of esophageal, gastric and duodenal injury. Lye ingestion often leads to complications with a risk for early death. Some of these complications are shock, laryngeal edema, esophageal or ventricular perforation, pneumonia, hemorrhage, mediastinitis, pericarditis, pleuritis, and peritonitis.

Several studies of the effects of NaOH on animals have been reported. NaOH would be considered as very toxic since the LD_{50} in mice by the intraperitoneal route is 40 mg/kg. In an experiment on the effects of NaOH on the eyes of rabbits, devastating lesions were produced by irrigation of the entire cornea of a proptosed eye for over 3 min. with a 0.2 percent solution of NaOH.

The effects of NaOH on the skin of mice, as well as the effectiveness of immediate treatment were reported. When 50 percent NaOH was applied to the clipped backs of A/He and C57 black mice extensive burns were produced. In groups immediately irrigated with water, no deaths occurred,

but as the time lapse between burning and treatment increased, so did the mortality. Biopsies of treated mice showed severe necrosis.

Ingestion of NaOH in animals leads to damage to the gastric mucosa. In one study, where 0.2 N NaOH was administered orally to fasted rats there was necrosis extending down through about two-thirds of the mucosa.

NaOH has been shown to affect the cardiovascular system of rats. When 0.5 percent NaOH was applied to the gastrointestinal serosa of rats it caused a fall in blood pressure and also inhibited respiration.

In a study of the effects of NaOH on the respiratory system, rats were exposed to finely dispersed aerosols of 40 percent NaOH for 20 minutes twice weekly for two and a half months. This treatment resulted in the bronchial epithelium becoming ulcerated and necrotic in places. In another study where rats were exposed to aerosols generated from a 20 percent NaOH solution, it was found that the bronchi were dilated and their epithelial cover was thin and frequently desquamated, and there was a light round-cell infiltration of the submucous membrane tissue.

In conclusion, the features of NaOH that are remarkable are its extreme corrosive effects on eye, skin, or mucous membranes. In the case of the skin, it was shown that solutions as weak as 0.03 N (0.12 percent) NaOH have caused damage to healthy human skin. There are, however, very few reports in the literature on the effects of airborne NaOH. The report by Lewis (written communication to NIOSH, 1975) suggests that irritation from NaOH aerosols may occur at concentrations below 2 mg/m^3, but there were a number of uncontrolled variables in the study, including questions of the reliability of the estimates of airborne NaOH, and the fact that there were other undescribed ingredients in the oven cleaner to which the subjects were exposed. Better controlled studies should be carried out before one can arrive at the No-Observed-Effect Level (NOEL) or No-Observed-Adverse-Effect-Level (NOAEL) for NaOH via the inhalation route.

2. Introduction

The purpose of this overview is to provide a brief summary of the data currently available concerning the health effects associated with exposure to sodium hydroxide. Primary consideration is given to determining whether or not evidence exists which suggests that sodium hydroxide exerts effects on human health at concentrations commonly encountered by the general public under ambient air exposure conditions. Acute and chronic health effects are addressed, including systemic toxicity, genotoxicity, carcinogenicity, and reproductive and developmental effects. This report also reviews sources, environmental fate, and concentrations found in air, as background for placing the health effects discussion in perspective.

Sodium hydroxide, or caustic soda, is a strongly alkaline substance, which is soapy to the touch, dissolves in water with the liberation of much heat, and rapidly absorbs carbon dioxide and water from the air (NIOSH, 1975; Weiss, 1980; Windholz et al., 1983).

The CAS Registry No. for sodium hydroxide is 1310-73-2, and the synonyms listed in MEDLARS(CHEMLINE) (1986), are as follows: aetznatron; ascarite; caustic soda; caustic soda, bead; caustic soda, dry; caustic soda, flake; caustic soda, granular; caustic soda, liquid; caustic soda, solid; caustic soda, solution; collo-grillrein; collo-tapetta; HSDB 229; hydroxyde de sodium; Lewis-red devil lye; lye; natriumhydroxid; natriumhydroxyde; soda lye; soda, caustic; sodio(idrossido di); sodium hydrate; sodium hydroxide, bead; sodium hydroxide, dry; sodium hydroxide, flake; sodium hydroxide, granular; sodium hydroxide, liquid; sodium hydroxide, solid; sodium hydroxide, solution; sodium(hydroxyde de); UN 1823; UN 1824; and white caustic.

2.1 Physical and Chemical Properties

NaOH is a white, deliquescent material and may be encountered as pellets, flakes, lumps or sticks (Sittig, 1985) and as solutions, usually 45 to 75 percent in water (Wands, 1981). Some physical and chemical properties of Na0H are shown in Table 2-1. Sodium hydroxide will neither burn or support combustion, but it reacts with amphoteric metals, such as aluminum, tin, and zinc, generating hydrogen which may form an explosive mixture. NaOH reacts with all the mineral acids to form the corresponding salts. It also reacts with weak-acid gases, such as hydrogen sulfide, carbon dioxide, and sulfur dioxide (Leddy et al., 1978).

NaOH will react with all organic acids to form soluble salts. Of great industrial importance is the saponification of esters to form the corresponding salt of the organic acid and an alcohol. For example, in the reaction of NaOH with fatty acid triglycerides the products are soap and glycerol.

Table 2-1. Physical and Chemical Properties of Sodium Hydroxide

Parameter	Data	Reference
Molecular Wt.	40.01	ACGIH, 1980
Specific Gravity (20°/4°C)	2.130	Leddy et al., 1978
Melting Point (°C)	318.4	ACGIH, 1980
Boiling Point (°C)	1390	ACGIH, 1980
Freezing Point (°C)	318	Weiss, 1980
Index of Refraction	1.3576	Leddy et al., 1978
Vapor Pressure (mm Hg at 739°C)	1	Wands, 1981
Dissociation Const., pKa	Fully ionized, not easily measurable	Albert and Serjeant, 1971
Latent Heat of Fusion (J/g)	167.4	Leddy et al., 1978
Transition Temperature (°C)	299.6	Leddy et al., 1978
Heat of Transition,Alpha to Beta (J/g)	103.3	Leddy et al., 1978
Solubility	42 g in 100 mL H_2O at 0°C	Wands, 1981
	347 g in 100 mL H_2O at 100°C	Wands, 1981
	Soluble in aliphatic alcohols	Wands, 1981
pH of 0.05% solution	~12	Windholz et al., 1983
pH of 0.5% solution	~13	Windholz et al., 1983
pH of 5% solution	~14	Windholz et al., 1983

2.2 Production and Use

Sodium hydroxide is produced in large quantities in the United States. The primary method for its production is the electrolysis of sodium chloride. In this electrolytic production, diaphragm cells are most commonly used in the United States, whereas mercury cells are prevalent in Europe and the Far East (Leddy et al., 1978). In 1985, 11 x 10^6 tons of NaOH were produced (Reisch, 1987). The major U.S. companies producing NaOH in 1985 are listed in Table 2-2 and the total annual capacity for these companies plus several others listed in the directory of chemical producers is 13,510,000 metric tons (SRI International, 1985).

Table 2-2. Principal U.S. Companies Producing Sodium Hydroxide as of 1985[a]

Company	Annual Capacity (Thousands of Metric Tons)
Dow Chem. U.S.A. Freeport, Tex. Plaquemine, La.	2560 1155
PPG Indust., Inc. Lake Charles, La.	1146
Occidental Petroleum Corp. Taft, La.	578
Diamond Shamrock Corp. La Porte, Tex.	511
Olin Corp. McIntosh, Ala	508
Georgia-Pacific Corp. Plaquemine, La	451
Diamond Shamrock Corp. Deer Park, Tex.	396
Occidental Petroleum Corp. Niagara Falls, N.Y.	357
Dow Chem. U.S.A. Oyster Creek, Tex.	352
E.I. du Pont de Nemours and Co., Inc. Corpus Christi, Tex.	326

[a] >300,000 MT capacity. The national total is 13,117 thousand MT Source: SRI International, 1985.

Sodium hydroxide is one of the most widely used chemicals. In 1982, the total U.S. consumption of NaOH was slightly greater than 8 million metric tons (See Table 2-3) which was 20 percent below the record consumption of 10.1 million metric tons in 1979 (Ferguson et al., 1984). The largest market for NaOH is in the chemical industry (48 percent of total demand) where it is used in the production of alumina from bauxite, and also used for pH control and in the neutralization of waste acids. The next major market is the pulp and paper industry with 26 percent of total demand (Ferguson et al., 1984).

2.3 Occupational Exposure Limits in Air

The Threshold Limit Value-Ceiling for NaOH, that is the concentration that should not be exceeded during any part of the working exposure, is 2 mg/m^3 (American Conference of Governmental Industrial Hygienists, 1986). The National Institute for Occupational Safety and Health (NIOSH) recommendation for a workplace environmental standard, as determined by a ceiling concentra-tion of 15 min, is 2 mg/m^3 (NIOSH, 1975). There is no short-term exposure limit (STEL) value set (Sittig, 1985).

Table 2-3. Total U.S. Consumption of Sodium Hydroxide: 1982

	Thousands of Metric Tons
Chemical Manufacturing	
Inorganic Chemicals	950
Organic Intermediates and Polymers	2,200
Other and Unidentified	750
Subtotal	3,900
Pulp and Paper Manufacturing	2,07
Cleaning Products	
Soap and Other Detergents	300-360
Bleaches, Polishes, and other Cleaning Goods	82-87
Miscellaneous Surface-Active Agents	30
Subtotal	412-477
Petroleum and Natural Gas	
Oil and Gas Production	123-133
Oil and Gas Processing	360
Subtotal	483-493
Cellulosics	
Rayon	112
Other	73
Subtotal	185
Cotton Mercerizing	109
Other	887-812
Total	8,046

Source: Ferguson et al., 1984.

Other recommendations are: East Germany (1973) and West Germany (1974), 2 mg/m^3; Sweden (1975), Ceiling Limit, 2 mg/m^3; USSR (1972), 0.5 mg/m^3 (American Conference of Governmental Industrial Hygienists, 1980).

2.4 Recommended Concentration in Water

There are no criteria for NaOH as such. However, the EPA has recommended criteria for pH as follows (Sittig, 1985):

- To protect freshwater aquatic life - pH 6.5 to 9.0
- To protect saltwater aquatic life - pH 6.5 to 8.5
- To protect humans' drinking water - pH 5 to 9

2.5 Potential Exposure

A separate source assessment is being prepared by the Office of Air Quality Planning and Standards, which will provide a more detailed discussion of potential exposure, sources, fate and ambient levels. The following is provided for the information of the reader of the Health Assessment Summary.

Sodium hydroxide is used in a wide variety of industries as shown in Table 2-3. Thus there are many opportunities for human exposure. NaOH is used to neutralize acids and make sodium salts in petroleum refining, in the production of viscose rayon, cellophane, and plastics, and in the reclamation of rubber. It is also used in the manufacture of soaps, mercerized cotton, paper, explosives, and dyestuffs, in metal cleaning, electrolytic extraction of zinc, tin plating, oxide coating, laundering, bleaching, and dishwashing, and in the chemical industries (Sittig, 1985). Sodium hydroxide is a general food additive, and can also migrate to food from packaging materials (Sax, 1984). NIOSH (1975) gives an estimate of 150,000 workers who are potentially exposed to NaOH. An example of exposure from consumer products, described by Vilogi et al. (1985) is the injuries to the oral cavity and eyes from oven cleaner pads which contain lye in excess of 5 percent. Also there has been exposure to children from calculator, hearing aid, and camera batteries, whose alkaline solutions may contain as much as 45 percent NaOH (Krenzelok, 1982).

Renewed interest in human exposure to NaOH aerosols developed as part of the safety evaluation of the Liquid Metal Fast Breeder Reactor; if leakage of the liquid sodium occurred, sodium oxide aerosols could be produced and reactor personnel and neighboring populations could be exposed (Cooper et al., 1979).

3. Air Quality: Sources, Fate, and Ambient Levels

3.1 Sources

One source of atmospheric pollution from sodium hydroxide is the manufacture of soap. Odors from the process may be controlled by scrubbing all exhaust fumes. If a spray dryer is used, a particulate problem may also occur (Sittig, 1975).

In detergent manufacture, a fatty alcohol is sulfurated then neutralized with NaOH. The resulting paste or slurry is then sprayed under pressure into a vertical drying tower where it is dried with hot air. This spray drying tower is the main source of particulate emissions leading to atmospheric pollution. When no control devices are present in the spray drying process, the particulate emissions may be as much as 90 lb/ton of product Odors may also be emitted from the spray drying operation and from storage and mixing tanks (Sittig, 1975).

Besides the soap and detergent manufacturing processes, NaOH is used in several other industries and these undoubtably could provide some emissions to the atmosphere. These industries include the pulp and paper industry, food processing, petroleum, and textile industry (Leddy et al., 1978).

No data could be found on the contamination of the atmosphere from NaOH manufacture. Leddy et al. (1978) states that in 1975 all the NaOH produced in the United States was made by the electrolysis of sodium chloride, and also that most of this NaOH is produced as the 50 percent water solution. In the use of chlor-alkali diaphragm cells for NaOH production, some of the processes involve caustic evaporation and caustic concentration (Leddy et al., 1978; Faith et al., 1965), and it is likely that some NaOH may be lost to the atmosphere during these production steps.

3.2 Environmental Fate

NaOH is very reactive in the atmosphere, and both it and its reaction products are hygroscopic (Cooper et al., 1979). The fate of the NaOH aerosol depends on its reactions with carbon dioxide and on its equilibrium with the ambient humidity (Cooper et al., 1979). Interactions between the NaOH aerosol and the ambient CO_2 and water vapor produce solid or liquid particles which may be wholly one species or may contain several compounds. Both in the solid or liquid state, NaOH undergoes the reaction:

$$2\ NaOH + CO_2 = Na_2CO_3 + H_2O$$

forming the less alkaline carbonate. As a NaOH particle undergoes this reaction, it tends to become solid (if not already in that state), unless the relative humidity is above 95 percent (Clough and Garland, 1971). The saturated solution droplet would have various hydrated forms of Na_2CO_3

depending on the ratios of hydroxide to carbonate. Various factors govern the transformation, for example, the rate of diffusion of CO_2 through the NaOH particle. Thus for solid NaOH particles of 20 μm diameter or smaller, enough CO_2 could diffuse to the surface within 10 seconds to convert the hydroxide to carbonate. However, when the relative humidity is low, respirable, solid NaOH particles may require minutes to be converted to sodium carbonate (Cooper et al., 1979). Murata et al. (1974) studied the chemical transformation of NaOH aerosols, and they found that the particles were predominantly carbonate at 30 times the atmospheric CO_2 level and between 70 and 90 percent relative humidity.

In normal situations the atmospheric concentration of CO_2 is fairly constant, (0.03 percent), thus the atmospheric fate and form of NaOH would depend on the relative humidity and time exposed (See Table 3-1).

3.3 Ambient Levels

No data were found on ambient levels of NaOH in the atmosphere.

Table 3-1. Species Expected from NaOH (2 μm Diameter Particles) in Atmosphere at 20°C

Atmospheric Relative Humidity	<3.5 Percent	35-95 Percent	>95 Percent
Seconds	NaOH(s)*	NaOH(l)	NaOH(l)
Minutes	Na_2CO_3(s)**	Na_2CO_3(s)**	Na_2CO_3(l)
Hours	Na_2CO_3(s)**	Na_2CO_3(s)**	Na_2CO_3(l)
Days	Na_2CO_3(s)**	Na_2CO_3(s)**	Na_2HCO_3(l)

*Probably as $NaOH \cdot H_2O$
**Probably as $Na_2CO_3 \cdot 10\ H_2O$
s = solid
l = liquid
Source: Cooper et al., 1979.

4. Pharmacokinetics

No data on metabolism of NaOH were found in the literature. From the known reactivity of NaOH one can surmise that some would react with the stomach contents and the stomach wall itself when ingested. Ottosson (1981) mentions that the strongly corrosive effect of lye is caused by dissociation and saponification of fatty acids, together with denaturation and coagulation of proteins to form albuminates. This results in a continuous disintegration of the attached tissues. In considering the dissociation constant (pKa) of NaOH, it is noted that NaOH is fully ionized (Albert and Serjeant, 1971) and since Na is essential to higher animals and is the principal cation of extracellular fluids (Considine, 1976) the metabolism of Na in the animal system will be mentioned briefly.

4.1 Absorption and Distribution

Radiosodium appears in the circulation of man 3 min. after ingestion. It also appears promptly in the bloodstream after application to intact skin, the vagina, and after subcutaneous, intramuscular and intrasynovial injection (Forbes, 1962).

Most of the Na and K in the animal is in a dynamic state, being exchanged between different parts of the cell, between the cell and the extracellular fluid, and intermixing with ingested Na and K in body fluids (Considine, 1976). In Forbes (1962) an internal circulation for Na is described, which consists of the outpouring of the various Na-containing secretions into the gastrointestinal tract and their subsequent reabsorption.

For the turnover of sodium in the body, it is estimated that the daily intake (and excretion) amounts to about 4 percent of total body content in an adult and about 5 percent for the young infant taking cow's milk. One study on the biological half-life of injected Na-22 in man shows a three-compartment curve; 49 percent of the injected dose is eliminated with t1/2 of 8.5 days; 51 percent with t1/2 of 13.5 days; and 0.37 percent with t1/2 of 460 days (Forbes, 1962).

4.2 Excretion

A key regulator of the sodium content of higher animals is the kidney. An ultrafiltrate containing the smaller molecules of the plasma is normally produced in the glomerulus of the kidney nephron, and as this ultrafiltrate passes down the kidney tubule, 97.5 percent or more of the Na is reabsorbed. When there is low intake of sodium, excretion is reduced to a low level in order to conserve the supply in the body (Considine, 1976). Although the urine is the main avenue for excretion of Na, small amounts are lost in the stool, in sweat, tears, nasal mucus, saliva, and vaginal and urethral discharges (Forbes, 1962).

5. Mutagenicity

Sodium hydroxide was assayed for genotoxicity by the Ames reversion test using *Salmonella typhimurium* strains TA1535, TA1537, TA1538, TA98, and TA100, and in a DNA-repair test with *Escherichia coli* strains, WP2, WP67, and CM871. Both tests showed that NaOH was not genotoxic (De Flora et al., 1984). McCarroll et al. (1981) tested NaOH in a microsuspension assay designed for the detection of DNA damage, using *Escherichia coli* strains WP2, WP2 uvr A, WP67, CM611, WP100, W3110 pol A^+, and p3478 pol A^-. NaOH gave a negative response in this test.

Manna and Mukherjee (1966) studied the effects of NaOH on the chromosomes of the grasshopper, *Spathosternum prasiniferum*. The grasshoppers were injected abdominally with 0.02 mL of a pH 9 NaOH solution and the testes were fixed after intervals of 4, 18, and 24 hrs. Marked changes were observed in the spermatocyte chromosomes of the 24-hr specimens. The frequency of chromatid and chromosome type breaks was 3.2 percent (18 out of 564 cells examined). Other abnormalities included multipolar spindles, asynchronous separation of chromosomes, distribution of chromosomes in small groups, extreme stickiness and clumping of chromosomes, and sticky bridges.

6. Carcinogenicity

No *in vivo* animal studies of NaOH carcinogenicity were found in the literature. It was pointed out that the incidence of carcinoma of the esophagus among patients with chronic esophageal stricture due to the ingestion of lye is significantly higher than in the general population (Lansing et al., 1969). Indeed, Kiviranta (1952) estimated that the incidence of esophageal carcinoma in these patients was at least a thousandfold greater than in the general population. Lansing et al. (1969) presented a case report of a 54-year old woman, who had swallowed a lye solution 22 years previously, and later developed carcinoma of the esophagus. Similar case histories have been reported in the literature; Parkinson et al. (1970) reported on a 76-year old man who ingested a large quantity of lye at the age of 45 years and later developed squamous carcinoma at the site of obliteration of the esophagus; Benedict (1941) reported on a 35-year-old man with a history of the ingestion of lye at the age of 15 months followed by multiple strictures of the esophagus, with development of epidermoid carcinoma; Bigelow (1953) presented the case of a 43-year old woman, who had swallowed lye at the age of one year, then later developed infiltrating squamous cell carcinoma in the region of the old lye stricture; Gerami et al. (1971) described the case of a 34-year-old woman who developed extensive carcinoma in the lower third of the esophagus 12 years after the ingestion of lye. Bigelow (1953) also tabulated 9 other cases where the average age of the patients was 35 years, the average age that the lye was swallowed was 3.5 years, and the average interval until the cancer developed was 31.2 years.

A number of case studies have shown that patients with chronic esophageal stricture due to the ingestion of lye develop esophageal carcinomas. Kiviranta (1952) suggested that these carcinomas may be the result of the tissue destruction and scar formation brought on by exposure to the caustic effects of NaOH itself rather than a carcinogenic potential of NaOH.

The epidemiological study of Ott et al. (1977) is described in Section 8.1.2. These investigators studied the mortality among workers who had been exposed chronically to NaOH dust for up to 30 years. No significant increased mortality in relation to duration or intensity of exposure were found. Observed deaths due to malignant neoplasms were less than expected, except for neoplasms of the digestive organs and peritoneum. With respect to digestive duration cancer, no relationship to duration or intensity was found. However, the power to detect a carcinogenic excess as significant is extremely poor due to the small sample size of the cohort.

Exposure to concentrations of NaOH that do not result in tissue destruction and scarring have not been shown to cause cancer in humans. However, the few studies cited by the authors have several limitations that preclude their use as evidence of a non-carcinogenic effect.

7. Development and Reproductive Toxicity

Dostal (1973) administered 2 µL of 0.001 M NaOH solution intraamniotically to groups of fetuses of 7 mice on the 13th day of gestation. The fetuses in the right uterine horn were treated, and the untreated fetuses in the contralateral horns served as controls. Fetal mortality and the incidence of cleft palate were studied in the surviving embryos. It was shown that 0.001 M NaOH had a pronounced lethal effect (45.8 percent mortality, 11/24 fetuses) and no cleft palates were observed in the remaining fetuses. Only 1/33 control fetuses died.

8. Other Toxic Effects

8.1 Human

Contact with NaOH has resulted in severe eye injury, damage to the skin, loss of hair, and injury of mucous membranes. Ingestion of NaOH, though infrequent, also causes severe damage. There are only a few cases of effects of airborne NaOH reported in the literature (NIOSH, 1975). The effects of NaOH on humans are summarized in Table 8-1 and discussed in the following sections.

8.1.1 Effects on Eyes

The pH of the NaOH solution is important in considering the effect on the eye, since substances with pH higher than 11 are very hazardous to eyes (Fox, 1973, as reported in Cooper et al., 1979). The pH is equal to 11 at NaOH concentrations of 0.001 N and at Na_2CO_3 concentrations of 0.02 N (20 times the NaOH normality) (Kotowski, 1966). Thus it is important to know the chemical composition of the aerosol when considering its toxicity.

Most cases of eye damage by NaOH have been caused by the liquid or dust. Terry (1943, as reported in NIOSH, 1975) and Hughes (1946a, 1946b) describe the severe damage to the eye as a result of contact with NaOH, with many cases resulting in blindness. Terry (1943, as reported in NIOSH, 1975) described some of the long-term sequelae following contact with NaOH. These included formation of granulation tissue over the sclerotic and inner surfaces of the eyelids, sticking of the eyelids to the eyeball, tough bands of adhesion between eyelids and eyeball, and severe corneal burns.

Hughes (1946b) compiled a general chronology of events following contact of the eye with NaOH. He described the acute stage, the stage of reparation, and the stage of late complications and concluded (Hughes, 1946a) that the concentration of the alkali, duration of exposure, and alkalinity were responsible for the severity of the eye burn, rather than the speciation itself.

8.1.2 Effects on Respiratory Tract

Several factors determine the region of the respiratory tract where NaOH aerosols are deposited upon inhalation, as well as the form of the particles. The high CO_2 concentrations in the upper respiratory tract will favor the formation of carbonate (Cooper et al., 1979). When a dry NaOH particle is transformed to a dry $Na_2CO_3 \cdot 10\ H_2O$ particle, the aerodynamic diameter is increased by about 40 percent, resulting in more deposition from gravitational settling and impaction (Fuchs, 1964, as reported in Cooper et al., 1979). In addition, the 100 percent relative humidity in the respiratory tract will cause a substantial growth in the particle size, increasing the amount deposited in the nasal passages and upper respiratory tract.

Table 8-1. Effects of Sodium Hydroxide on Man

Organ or System	Route or Source	Dose	Effect	Reference
Eye	Contact	Not given	Formation of granulation tissue over eyelids; sticking of eyelids to the eyeball; bands of adhesion between eyelids and eyeball; severe corneal burns	Terry, 1943, as reported in NIOSH, 1975
Respiratory System	Aerosols from oven cleaner	0.24-1.13 mg/m^3	Respiratory tract irritation in 2-15 min	Lewis, 1974 (written communication to NIOSH, 1975)
Respiratory System	Dust	0.5-2.0 mg/m^3 (up to 30 yr)	2 respiratory malignancy deaths compared to 3.9 expected	Ott et al., 1977
Respiratory System	Aerosols	0-9 mg/m^3	Effect on upper respiratory tract	Gavrilova, 1958, as reported in Cooper et al., 1979
Skin	Contact - solution applied to forearm	0.03 N (0.12%) for 1 hr	Damage, represented by increase of water vapor loss	Malten and Spruit, 1966

Table 8-1. Continued

Organ or System	Route or Source	Dose	Effect	Reference
Skin	Contact - solution applied to forearm	1 N, for 15-180 min	Swelling of the horny layer, pyknotic nuclei in prickle-cell layer, edema, destruction of entire dermis in 60 min	Nagao et al., 1972
Skin (scalp)	Solution - dripping on scalp	Not given - (pH 13.5), cleaning solution	Alopecia (irregular patches of complete baldness), minute pustules, underlying skin erythematous	Morris, 1952
Alimentary Tract	Solution - oral	50% wt; 9.5% solution	Damage to esophagus and stomach. Death in patient who ingested 20 g Drano in water - had extensive esophageal, gastric and duodenal injuries; 3 patients developed esophageal stricutres	Cello et al., 1980
Aorta	Solution - oral	30%	Aortic rupture, tissue damage	Ottosson, 1981
Renal, vascular	Injection in basilic vein	10 mL conc. NaOH	Local Necrosis, hemolysis, acute renal failure, intravascular coagulation, cyanosis	Blin et al., 1983

Several factors determine the region of the respiratory tract the aerosols will be deposited upon inhalation, and whether they will be in the form of the hydroxide or carbonate.

In Patty (1963), it is noted that exposure to NaOH results in characteristic irritation of nasal tissue frequently causing sneezing. He points out that the greatest hazard from NaOH is the rapid destruction of tissue that comes in contact with the solid or concentrated solution, whereas the inhalation of dust or mist is of secondary industrial importance. However, with regard to sodium carbonate, it is recommended that the maximum permissible standard should be higher than that allowed for NaOH, thus reinforcing the importance of determining whether the hydroxide has had time to become carbonate before humans are exposed to the aerosol.

Sax (1984) reports that inhalation of NaOH dust or concentrated mist can cause damage to the upper respiratory tract and to lung tissue, depending on the extent of the exposure. The effects of inhalation may thus range from mild irritation of the mucous membranes to a severe pneumonitis.

In a report by Lewis (1974, written communication to NIOSH, 1975) the effects of aerosols of NaOH on healthy volunteers was described. The volunteers sprayed oven cleaner (containing NaOH among its other ingredients) and developed respiratory tract irritation in 2 to 15 minutes. The concentration of airborne NaOH, the only ingredient of the spray cleaner that was analyzed for, was 0.24 to 1.18 mg/m^3.

Many of the effects of NaOH on the respiratory tract can be discovered by reviewing investigations of occupational exposure. For example, Ott et al. (1977) studied the mortality among 291 workers who had been exposed chronically to NaOH dust for up to 30 years at a Dow Chemical plant in Midland, Michigan. The time-weighted average concentrations of caustic dust ranged from 0.5 to 2.0 mg/m^3 for the different categories of workers. The findings showed no significant increased mortality in relation to duration or intensity of exposure. Observed deaths due to malignant neoplasms were less than expected, except for neoplasms of the digestive organs and peritoneum. With respect to digestive cancer, no relationship to length or intensity was found. Only 2 respiratory malignancy deaths were found compared to 3.9 that were expected. The study also reviewed records of acute exposure episodes reported to the medical department from 1954 to 1972. These records showed that medical aid was sought more for skin contact than for eye contact, and more for eye contact than for inhalation.

Investigations were carried out on 500 workers at a Soviet plant that produced alumina by a wet caustic process (Gavrilova, 1958, as reported in Cooper et al., 1979). The concentrations of caustic substances in the air were found to range from 0 to 9 mg/m^3. Examinations of the effects of aerosols on the upper respiratory tract showed that there was a related health hazard, and a concentration of 0.5 mg/m^3 (as NaOH) was recommended as a limiting permissible value for caustic aerosols. [The U.S. standard is 2 mg/m^3, (ACGIH, 1986)].

Another study of occupational exposure of workers near an open vat, in a chemical degreasing operation, was reported by Hervin and Cohen, 1973. In the process, the solvent, contained primarily NaOH (but also other substances such as sodium gluconate), the pH was 12.5 to 13.5, and the caustic solution in the vat was maintained at 93°C by steam bubbling through it. Operations adjacent to the vat involved the use of other substances such as Stoddard solvent. Symptoms of upper respiratory tract irritation were found in about half the 15 workers in the vicinity of the vat.

Ten workers from another area of the plant served as controls, and all participants in the study had worked at the plant for at least 16 months. NIOSH points out that some other observations were are not entirely consistent with the conclusions that the mist from the vat produced the symptoms. Also, some of the effects may have been caused by the Stoddard solvent.

8.1.3 Effects on Skin

NaOH of sufficient concentration causes damage if it remains in contact with the skin for a long enough time (NIOSH, 1975). Malten and Spruit (1966) report damage to healthy skin following contact with NaOH solutions as weak as 0.03 N (0.12 percent) for 1 hr. The severity of the damage and the extent of its reversibility increases with increasing contact time, regardless of the concentration (NIOSH, 1975).

Nagao et al. (1972) examined skin biopsies from volunteers who had 1.0 N NaOH applied to their arms for 15 to 180 min. Progressive changes were seen, beginning with swelling of the horny layer and a few pyknotic nuclei in the prickle-cell layer, progressing through edema to destruction of the entire epidermis in 60 min.

NaOH was found to cause alopecia in a 42-year old man employed in a candy factory (Morris, 1952). A compound containing NaOH, (with a pH of 13.5), was used to flush out drain pipes at the factory and some of this liquid had apparently eaten its way through the pipe and dripped onto the head of the worker. This caused irregular patches of complete baldness, with minute pustules and with the underlying skin erythematous. However, after washing frequently with cold water the dermatitis subsided and the hair grew back.

8.1.4 Effects on Alimentary Tract

Palmer (1971) reported on injuries to the Allied soldiers in France and Germany toward the end of World War II that resulted from drinking schnapps that had been adulterated with lye. There were about 1500 serious casualties. In most cases, by the time the patient reached the medical officer, the only serious sequel was esophageal stenosis.

Several other reports involving the ingestion of NaOH are described in the section on carcinogenicity where esophageal carcinoma has been a late sequel to lye injury.

Cello et al. (1980) reported on patients at the San Francisco General Hospital admitted after ingesting caustic substances. Nine of 17 cases examined had ingested Drano. Drano, which contains 50 percent/weight NaOH was prepared by 5 of the patients themselves, by dissolving 20 to 30 g of the crystalline material in a glass of water. The actual amounts ingested ranged from 200 to 300 ml of a 5 to 15 percent solution. The other 4 patients drank varying amounts of commercially prepared Liquid Drano, which contains 9.5 percent NaOH. Cello et al. (1980) mention that the form in which NaOH is ingested determines the location of mucosal damage. The solid form tends to adhere to the glossopharyngeal, palatal, and proximal esophageal mucosa, and produces deep, irregularly arranged burns. The liquid form causes diffuse damage to the esophagus and stomach. One of the above-mentioned patients, who ingested 20 g Drano in water, died of extensive esophageal, gastric and duodenal injury, and three other patients developed esophageal strictures.

A case of aortic rupture following the ingestion of lye was described by Ottosson (1981). The patient was a 14 year-old boy who drank liquid detergent containing 30 percent NaOH. The rupture occurred on the 44th day after the lye ingestion, and this was considered unusually late. Not only the lye-induced tissue damage, but also an esophageal perforation resulting from the dilatation of a stricture, may have contributed to the aortic rupture.

Lye ingestion often leads to complications with a risk for early death. Some of these complications are shock, laryngeal edema, esophageal or ventricular perforation, pneumonia, hemorrhage, mediastinitis, pericarditis, pleuritis, and peritonitis (Ottosson, 1981).

8.2 Animals

Several studies of the effects of NaOH on animals have been reported. The more significant effects of NaOH on animals are summarized in Table 8-2 and discussed in the following sections. NaOH would be considered as very toxic since the LD_{50} of NaOH in mice by the intraperitoneal route is 40 mg/kg (Sax, 1984).

8.2.1 Effects on Eyes

Hughes (1946b) gives a detailed description of the effects of NaOH on the eyes of rabbits. First he presents a chronological account (with illustrations) of the moderately severe burn resulting from irrigation of one-half the rabbit cornea with 0.2 percent NaOH for 3 min. He next describes the mild burn that results from the irrigation of the rabbit eye with 0.25 percent NaOH for 30 sec. or less without subsequent lavage. Finally, he describes the devastating lesions produced by irrigation of the entire cornea of a proptosed eye for over 3 min. with a 0.2 percent solution of NaOH. With these last mentioned burns, the most remarkable features were: necrosis of the conjunctiva, ischemic necrosis of the limbal blood vessels, opacification of the cornea, and extreme congestion and thickening of the iris.

Bolkova and Cejkova (1984) studied both the biochemical and histochemical effects of various concentrations of NaOH on the rabbit cornea. The concentrations tested were 0.5, 0.25, 0.1, 0.05, and 0.01 N, and the activities of alkaline and acid phosphatases were examined on days 1, 4, and 7 after injury. At all time intervals there was a dramatic decrease in enzyme activity by 0.5 and 0.25 N NaOH. These highest concentrations also caused the cornea to become grey-white and edematous. It was concluded that both histologic and metabolic patterns, as well as re-epithelization, of the experimentally burned cornea were a function of the NaOH concentration and of the duration of contact.

Another study of eye irritancy by NaOH was conducted by Griffith et al. (1980). A system for classification of eye irritancy is described, and the work focuses on eye irritancy procedures in animals as a means for predicting ocular responses in man. In the system of Griffith et al. (1980), the test material was placed directly on the cornea of albino rabbits, and the eyes were later examined and scored. In the system of classification used, 0.5 percent NaOH was classified as an innocuous or slight irritant, that is, causing transient effects, while 10 percent NaOH was classified as a severe irritant or corrosive, that is, causing very severe or permanent injury.

Table 8-2. Effects of Sodium Hydroxide on Animals

Organ or System	Speciess	Route or Source	Dose	Effect	Reference
Eyes	Rabbits	Irrigation (solution)	0.2% for 3 min	Moderately severe burns	Hughes, 1946b
Eyes	Rabbits	rrigation (solution)	0.25% for 30 sec or less	Mild burn	Hughes, 1946b
Eyes	Rabbits	rrigation (solution)	0.2% for over 3 min	Devasting lesions	Hughes, 1946b
Eyes	Rabbits	Solution	0.5, 0.25, 0.1, 0.05 and 0.01 N	0.5 and 0.25 N caused descrease in alkaline and acid phosphatase activity, cornea became grey-white and edematous	Bolkova and Cejkova, 1984
Eyes	Rabbits	Solution, placed on cornea	0.5%; 10%	0.5% caused slight irritation, 10% caused severe irritation and corrosion	Griffith et al., 1980
Skin	Mice	Solution to clipped backs	50%	Burns. No deaths if treated immediately by irrigation, but increased mortality with increased time between burn and treatment. Necrosis	Bromberg et al., 1965

Table 8-2. Continued

Organ or System	Speciess	Route or Source	Dose	Effect	Reference
Esophagus	Cats	Application to exposed esophagus	8.3%	Destruction of superficial layer of squamous mucosa; submucosal and transmural thrombosis in blood vessels	Ashcraft and Padula, 1974
Stomach	Rats	Oral	0.2 N	Necrosis of gastric mucosa	Robert et al., 1979
Stomach	Rats	Infusion	0.5 N (1 day to 10 months)	Falling off of entire gastric mucosa. Intestinal metaplasia in 18 of 26 rats	Oohara et al., 1982
Respiratory System	Rats	Aerosols	40% NaOH 20 min, 2x weekly for 2.5 mos	Bronchial epithelium wrinkled or flattened, ulcerated, necrotic. Hypertrophy or peribronchial lymphadenoid tissue	Dluhos et al., 1969

Table 8-2. Continued

Organ or System	Speciess	Route or Source	Dose	Effect	Reference
Respiratory System	Rats	Aerosols	40% 2x weekly; 20%	Death from bronchopneumonia with 40%. With 20% NaOH; bronchi dilated, epithelium thin and desquamated, round-cell infiltration of submucous membranes	Vyskocil et al., 1966, as reported in NIOSH, 1975
Cardiovasvular System	Dogs	Injection into pericardium	0.5%	S-T changes consistent with pericarditis, prolonged episodes of supraventricular and ventricular tachycardia	Srinivasan et al., 1984
Cardiovasvular System	Rats	Solution applied to gastrointestinal serosa	0.5%	Fall in blood pressure, inhibition of respiration; fall in heart rate in 8% of animals	Radhakrishan et al., 1985
Pancreas	Rats	Instillation into duodenum	0.1 M	Increase in pancreatic juice secretion	Kato, 1985

In conclusion, NaOH is irritating to the eye of animals, and the severity of the irritation depends on the concentration of NaOH and on the duration of contact.

8.2.2 Effects on Skin

Bromberg et al. (1965) evaluated the effects of NaOH on the skin of mice, and also the effectiveness of treatments. They applied 50 percent NaOH to the clipped backs of A/He and C57 black mice and treated them with water irrigation for various time periods. All mice except those treated immediately developed a rapidly progressive burn in both depth and extent. There were no deaths in the group immediately irrigated, but as the time lapse between burning and treatment increased, so did the mortality. Biopsies of treated mice showed severe necrosis.

Bucher et al. (1981) in testing the irritative potentiality of various chemicals, applied solutions of NaOH to the soft and tender abdominal skin of juvenile white mice, measured the intensity of the edematous reaction, and proposed a scoring system to estimate the risks to man. In their system of classification both 0.5 and 2.5 percent NaOH were put in Class d, and members of this class were predicted to be strongly irritating when brought in contact with human mucous membranes. Seven and one-half percent NaOH was placed in Class e, and was predicted to be very strongly irritating to mucous membranes of man.

8.2.3 Effects on Alimentary Tract

In the study of Ashcraft and Padula (1974) the effects of 8.3 percent NaOH on the esophagus of cats were investigated. It was found that NaOH destroyed the superficial layer of squamous mucosa, and caused submucosal and transmural thrombosis in the blood vessels.

Robert et al. (1979) found that when 0.2 N NaOH was administered orally to fasted rats there was extensive damage to the gastric mucosa. On opening the stomach, the lesions found in the mucosa consisted of black elongated bands, usually located in the corpus (the portion of the stomach secreting acid and pepsinogen). Histologically, the lesions consisted of necrosis usually extending down through about two-thirds of the mucosa. One interesting finding was that pretreatment of the rats, either orally or subcutaneously, with several prostaglandins of the A, E, or F type prevented gastric necrosis; the protective effect was dose-dependent. The most potent of the prostaglandins was 16,16- dimethyl PGE_2.

In the experiments of Oohara et al. (1982) approximately 7 mL of 0.5 N NaOH were infused into the stomach of Wistar rats and at intervals of 1 day to 10 months the stomach was examined histologically. The alkaline treatment resulted in the falling-off of the entire gastric mucosa, thus facilitating study of regenerative epithelialization. It was shown that in 18 of 26 rats there was intestinal metaplasia associated with goblet cells in the regenerative epithelium. The authors point out that although intestinal metaplasia is known to be induced by weak carcinogenic agents, in this case it was induced by a benign process of regeneration, thus intestinal metaplasia itself does not represent a precancerous state.

8.2.4 Effects on Respiratory System

In a study of the effects of NaOH on the respiratory system, Dluhos et al. (1969) exposed 20 rats to finely dispersed aerosols of 40 percent NaOH. The rats inhaled the aerosols for 20 minutes twice weekly for two and a half months. The authors observed that in the treated animals the bronchial epithelium was sometimes wrinkled and sometimes flattened, and in places it was ulcerated and necrotic. They also noted that the peribronchial lymphadenoid tissue was hypertrophic and extruded cushion-like into the bronchial lumen, causing slit-like deformities.

Vyskocil et al. (1966) reported on the effects on rats of exposure to aerosols generated from 5 percent, 10 percent, 20 percent, and 40 percent solutions of NaOH. The aerosol inhalation apparatus produced 80 percent of particles under 1.4 μ in size, and the rats were exposed 2x/week for 30 minutes. All 27 rats exposed to aerosols from the 40 percent solution perished within a month, mostly from bronchopneumonia. When the rats were exposed to aerosols generated from a 20 percent NaOH solution, it was found that the septa were dilated and cracked, the bronchi were dilated and their epithelial cover was thin and frequently desquamated, and there was a light round-cell infiltration of the submucous membrane tissue of the trachea. The rats in these experiments were also exposed to quartz dust at a concentration of 10 g/m^3, but the effects of this exposure on the results is unclear (Vyskocil et al., 1966).

8.2.5 Effects on Other Organ Systems

The sclerosing potential and cardiac effects of NaOH were investigated in dogs by Srinivasan et al. (1984). They instilled 0.5 percent NaOH into the pericardium of 4 dogs and normal saline into one control. One animal was sacrificed at the end of 24 hrs, 1 at 7 days, and 3 at 28 days. All 4 treated dogs developed S-T changes consistent with pericarditis and prolonged episodes of supraventricular and ventricular tachycardia during the instillation of the NaOH into the pericardium. In none of the dogs was there evidence of pericardial symphysis.

Radhakrishnan et al. (1985) also found that 0.5 percent NaOH had effects on the cardiovascular system. When the NaOH was applied to the gastrointestinal serosa of rats it caused a fall in blood pressure and also inhibited respiration in both hypertensive and normotensive rats. In 8 percent of the animals studied, a fall in heart rate was seen.

Pehrson and Jonsson (1981) describe a study where 6 bulls were fed for 5 to 7 months with 86 to 126 g Na/day, by means of alkali-treated straw. The controls were fed 10 to 15 g/day. It was found that there was an average increase in body weight of 1649 g/day compared with 1561 g/day in the controls. The size of the kidneys did not increase and no histopathological abnormalities were found which could be attributed to the overfeeding with Na.

The effects of NaOH on pancreatic exocrine secretion in rats was studied by Kato (1985). When 0.1 M NaOH (pH 12.9) was instilled into the duodenum of anesthetized rats, it caused an increase in pancreatic juice flow that was 19 times the control flow rate ($p < 0.01$). The protein concentration in the pancreatic juice also increased significantly ($p < 0.05$) to 71.4 ± 4.6 μg/L after 40 min., compared with 50 μg/L in the controls, and there was a similar increase in amylase activity after NaOH injection.

9. References

Albert, A.; Serjeant, E. P. (1971) The determination of ionization constants: a laboratory manual. London, United Kingdom: Chapman and Hall Ltd.; p. 3.

American Conference of Governmental and Industrial Hygienists. (1980) Sodium hydroxide. In: Documentation of the threshold limit values. 4th ed. Cincinnati, OH: American Conference of Governmental and Industrial Hygienists Inc.; pp. 370-371.

American Conference of Governmental and Industrial Hygienists. (1986) Adopted values. In: TLVs: threshold limit values for chemical substances in the work environment adopted by ACGIH, with intended changes for 1986-87. Cincinnati, OH: American Conference of Governmental and Industrial Hygienists; p. 29.

Ashcraft, K. W.; Padula, R. T. (1974) The effect of dilute corrosives on the esophagus. Pediatrics 53:226-232.

Austin, S. G.; Schnatter, A. R. (1983) A case-control study of chemical exposures and brain tumors in petrochemical workers. JOM J. Occup. Med. 25:313-320.

Benedict, E. B. (1941) Carcinoma of the esophagus developing in benign stricture. N. Engl. J. Med. 224:408-412.

Bigelow, N. H. (1953) Carcinoma of the esophagus developing at the site of lye stricture. Cancer 6:1159-1164.

Blin, F.; Rochette, J.; Taulet, G.; Pellerin, M.; Marsepoil, T.; Starkman, M. (1983) Intoxication volontaire par injection intraveineuse de soude caustique [Voluntary intoxication by intravenous injection of caustic soda]. Ann. Fr. Anesth. Reanim. 2:97-99.

Bolkova, A.; Cejkova, J. (1984) Relationship between various concentrations of NaOH and metabolic effects in experimentally burned rabbit cornea. A biochemical and histochemical study. Graefe's Arch. Clin. Exp. Ophthalmol. 222:86-89.

Bromberg, B. E.; Song, I. C.; Walden, R. H. (1965) Hydrotherapy of chemical burns. Plast. Reconstr. Surg. 35:85-95.

Bucher, K.; Bucher, K. E.; Walz, D. (1981) The topically irritant substance: essetials -- bio-tests -- predictions. Agents Actions 11:515-519.

Cello, J. P.; Fogel, R. P.; Boland, C. R. (1980) Liquid caustic ingestion: spectrum of injury. Arch. Intern. Med. 140:501-504.

Clough, W. S.; Garland, J. A. (1971) The behaviour in the atmosphere of the aerosol from a sodium fire. J. Nucl. Energy 25:425-435.

Considine, D. M., ed. (1976) Potassium and sodium in biological systems. In: Van Nostrand's scientific encyclopedia. 5th ed. New York, NY: Van Nostrand Reinhold Co.; pp. 1821-1822.

Cooper, D. W.; Underhill, D. W.; Ellenbecker, M. J. (1979) A critique of the U. S. standard for industrial exposure to sodium hydroxide aerosols. Am. Ind. Hyg. Assoc. J. 40:365-371.

De Flora, S.; Zanacchi, P.; Camoirano, A.; Bennicelli, C.; Badolati, G. S. (1984) Genotoxic activity and potency of 135 compounds in the Ames reversion test and in a bacterial DNA-repair test. Mutat. Res. 133:161-198.

Dluhos, M.; Sklensky, B.; Vyskocil, J. (1969) Pokusna studie o pusobeni aerosolovych inhalaci roztoku louhu sodneho na dychaci ustroji krys [Experimental study of the effect of aerosol inhalations of sodium hydroxide on the respiratory system of rats]. Vnitr. Lek. 15:38-42.

Dostal, M. (1973) Effect of some nonspecific factors accompanying intraamniotic injection in mouse foetus. Folia Morphol. 21:97-101.

Faith, W. L.; Keyes, D. B.; Clark, R. L. (1965) Sodium hydroxide (caustic soda): NaOH. In: Industrial chemicals. 3rd ed. New York, NY: John Wiley & Sons, Inc.; pp. 690-698.

Ferguson, F. A.; Callison, S. L.; Heydorn, B.; Suzuki, H.; Garnett, A. (1984) CEH marketing research report: chlorine/sodium hydroxide. In: Chemical economic handbook. Menlo Park, CA: SRI International; pp. 733.1000 A-733.1003V.

Forbes, G. B. (1962) Sodium. In: Comar, C. L.; Bronner, F., eds. Mineral metabloism: an advanced treatise, v. II, the elements, pt. B. New York, NY:Academic Press.; pp. 23-27.

Fox, S. L. (1973) Industrial and occupational ophthalmology. Springfield, IL: C. C. Thomas; p. 121.

Fuchs, N. A. (1964) The mechanics of aerosols. New York, NY: The Macmillan Co.; pp. 233-240. [As cited in: Cooper et al., 1979].

Gavrilova, V. A. (1958) Caustic aerosols occurring during the wet caustic process of alumina production and their evaluation in regard to occupational health. Trudy Sverdlovsk. Gosudarst. Med. Inst. 21:269-276. [As cited in: Cooper et al., 1979].

Gerami, S.; Booth, A.; Pate, J. W. (1971) Carcinoma of the esophagus engrafted on lye stricture. Chest 59:226-227.

Griffith, J. F.; Nixon, G. A.; Bruce, R. D.; Reer, P. J.; Bannan, E. A. (1980) Dose-response studies with chemical irritants in the albino rabbit eye as a basis for selecting optimum testing conditions for predicting hazard to the human eye. Toxicol. Appl. Pharmacol. 55:501-513.

Hervin, R. L.; Cohen, S. R. (1973) Health hazard evaluation determination--report no. 72-97-135. Cincinnati, OH: U. S. Department of Health, Education and Welfare, National Institute for Occupational Safety and Health.

Hughes, W. F., Jr. (1946a) Alkali burns of the eye: I. review of the literature and summary of present knowledge. Arch. Ophthalmol. 35:423-449.

Hughes, W. F., Jr. (1946b) Alkali burns of the eye: II. clinical and pathologic course. Arch. Ophthalmol. 36:189-214.

Kato, S. (1985) Stimulating effect of duodenal alkalinization on pancreatic exocrine secretion in rats. Jpn. J. Physiol. 35:159-161.

Kiviranta, U. K. (1952) Corrosion carcinoma of the eosphagus: 381 cases of corrosion and nine cases of corrosion carcinoma. Acta Oto-laryngol. 42:89-95.

Kotowski, A. (1965) Gmelins Handbuch der anorganischen Chemie: Natrium Ergaenzungsband, Lieferung 3. 8th rev. ed., Weinheim, Germany: Verlag Chemie-GmbH; pp. 860-861.

Kotowski, A. (1966) Gmelins Handbuch der anorganischen Chemie: Natrium Ergaenzungsband, Lieferung 3. Weinheim, Germany: Verlag Chemie GmbH; pp. 1344-1345.

Krenzelok, E. P. (1982) In vitro effects of HCl on calculator battery decomposition. In: proceedings of the 1982 international congress of clinical toxicology and the second world meeting of clinical toxicology; August; Snowmass, CO. Vet. Hum. Toxicol. 24(suppl.):99-100.

Lansing, P. B.; Ferrante, W. A.; Ochsner, J. L. (1969) Carcinoma of the esophagus at the site of lye stricture. Am. J. Surg. 118:108-111.

Leddy, J. J.; Jones, I. C., Jr.; Lowry, B. S.; Spillers, F. W.; Wing, R. E.; Binger, C. D. (1978) Chlorine and sodium hydroxide. In: Kirk-Othmer encyclopedia of chemical technology: v. 1, a to alkanolamines. 3rd ed. New York, NY: John Wiley & Sons; pp. 799-865.

Lewis, T. R. (1974) Written communication to NIOSH. [As cited in: NIOSH, 1975].

Malten, K. E.; Spruit, D. (1966) Injury to the skin by alkali and its regeneration. Dermatologica 132:124-130.

Manna, G. K.; Mukherjee, P. K. (1966) Spermatocyte chromosome aberrations in two species of grasshoppers at two different ionic activities. Nucleus (Calcutta) 9:119-131.

McCarroll, N. E.; Piper, C. E.; Keech, B. H. (1981) An E. coli microsuspension assay for the detection of DNA damage induced by direct-acting agents and promutagens. Environ. Mutagen. 3:429-444.

MEDLARS II, Medical Literature Analysis and Retrieval System [database]. (1986) [Printout of the CHEMLINE record on sodium hydroxide as of October]. Bethesda, MD: National Library of Medicine, MEDLARS Management Section. Disc. Available for inspection at: U. S. Environmental Protection Agency, Environmental Criteria and Assessment Office, Research Triangle Park, NC.

Morris, G. E. (1952) Chemical alopecia: a unique case. AMA Arch. Ind. Hyg. Occup. Med. 6 530-531.

Murata, M.; Naritomi, M.; Yoshida, Y.; Kokubu, M. (1974) Behavior of sodium aerosol in atmsophere. J. Nucl. Sci. Technol. 11:65-71.

Nagao, S.; Stroud, J. D.; Hamada, T.; Pinkus, H.; Birmingham, D. J. (1972) The effect of sodium hydroxide and hydrochloric acid on human epidermis -- an electron microscopic study. Acta Derm. Venereol. (Stockholm) 52:11-23.

National Institute for Occupational Safety and Health. (1975) Criteria for a recommended standard-occupational exposure to sodium hydroxide. Washington, DC: U. S. Department of Health, Education, and Welfare, Public Health Service, Center for Disease Control; DHEW (NIOSH) publication no. 76-105. Available from: NTIS, Springfield, VA; PB-246694.

Oohara, T.; Sadatsuki, H.; Kaminishi, M.; Mitarai, Y. (1982) Simple alkaline treatment induces intestinal metaplasia in the stomach of rats. Pathol. Res. Pract. 175:365-372.

Ott, M. G.; Gordon, H. L.; Schneider, E. J. (1977) Mortality among employees chronically exposed to caustic dust. JOM J. Occup. Med. 19 813-816.

Ottosson, A. (1981) Late aortic rupture after lye ingestion. Arch. Toxicol. 47:59-62.

Palmer, E. D. (1971) Corrosive adulterants as booby traps. Mil. Med. 136:814.

Parkinson, A. T.; Haidak, G. L.; McInerney, R. P. (1970) Verrucous squamous cell carcinoma of the esophagus following lye stricture. Chest 57:489-492.

Patty, F.A. (1963) Alkaline materials. In: Patty, F.A.: Fassett, D.W. Irish, D.D., eds. Industrial hygiene and toxicology: v. II, toxicology. New York, NY: John Wiley & Sons, Inc.; pp. 859-869.

Pehrson, B.; Jonsson, L. (1981) Effekten av utfodring av NaOH-lutad halm till notkreatur med speciell inriktning pa njurarnas reaktion [The effects of feeding NaOH treated straw to dairy cows with special reference to the reaction of the kidneys]. Nord. Veterinaermed. 33:231-235.

Radhakrishnan, V.; Shanker, N.; Gogia, M.; Sharma, K. N. (1985) Cardiorespiratory changes following chemical applications to gut serosa. J. Auton. Nerv. Syst. 14:363-375.

Reisch, M.S. (1987) Top 50 chemicals production steadied in 1986. Chem. Eng. News 65(15):20-23.

Robert, A.; Nezamis, J. E.; Lancaster, C.; Hanchar, A. J. (1979) Cytoprotection by prostaglandins in rats: prevention of gastric necrosis produced by alcohol, HCl, NaOH, hypertonic NaCl, and thermal injury. Gastroenterology 77:433-443.

Sax, N. I. (1984) Sodium hydroxide. In: Dangerous properties of industrial materials. 6th ed. New York, NY: Van Nostrand Reinhold Company; pp. 2434-2435.

Sirover, M. A.; Loeb, L. A. (1976) Infidelity of DNA synthesis in vitro: screening for potential metal mutagens or carcinogens. Science (Washington, DC) 194:1434-1436.

Sittig, M. (1975) Soap and detergent manufacture. In: Environmental sources and emissions handbook. Park Ridge, NJ: Noyes Data Corporation; pp. 466-471.

Sittig, M. (1985) Sodium hydroxide. In: Handbook of toxic and hazardous chemicals and carcinogens. Second edition. Park Ridge, NJ: Noyes Publications; pp. 797-798.

SRI International. (1985) Sodium hydroxide. In: 1984 directory of chemical producers: United States of America. Menlo Park, CA: SRI International; pp. 869-870.

Srinivasan, V.; Berdoff, R. L.; Goldberg, E.; Gallerstein, P. E.; Ehya, H.; Berger, M. (1984) Intrapericardial instillation of sodium hydroxide: failure to produce pericardial symphysis. Angiology 35:22-28.

Terry, H. (1943) Caustic burns--their prevention and treatment. Br. Med. J. 1:756-757. [As cited in: NIOSH, 1975].

Vilogi, J.; Whitehead, B.; Marcus, S. M. (1985) Oven-cleaner pads: new risk for corrosive injury. Am. J. Emerg. Med. 3:412-414.

Vyskocil, J.; Tuma, J.; Dluhos, M. (1966) The effect of aerosol inhalations of sodium hydroxide on the elimination of quartz dust from lungs of rats.

Scripta Med. 40: 25-29. [As cited in: NIOSH, 1975].

Wands, R. C. (1981) Alkaline materials: sodium hydroxide, NaOH (caustic soda, caustic flake, lye, liquid caustic). In: Clayton, G. D.; Clayton F. E., eds. Patty's industrial hygiene and toxicology: v. 2B, toxicology. 3rd rev. ed. New York, NY: John Wiley & Sons; pp. 3061-3062.

Weiss, G., ed. (1980) Sodium hydroxide. In: Hazardous chemicals data book. Park Ridge, NJ: Noyes Data Corporation.; p. 825.

Windholz, M.; Budavari, S.; Blumetti, R. F.; Otterbein, E. S., eds. (1983) Sodium hydroxide. In: The Merck index: an encyclopedia of chemicals, drugs and biologicals. 10th ed. Rahway, NJ: Merck & Co., Inc.; p. 1236.

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