

## Nitrate and Nitrite

**What Are They?** Nitrate and nitrite are compounds that contain a nitrogen atom joined to oxygen atoms, with nitrate containing three oxygen atoms and nitrite containing two. In nature, nitrates are readily converted to nitrites and vice versa. Both are anions, or ions with a negative charge. They tend to associate with cations, or ions with a positive charge, to achieve a neutral charge balance.

<b>Symbol:</b>	<b>NO<sub>3</sub> / NO<sub>2</sub></b>
<b>Molecular Weight:</b>	<b>62 / 46</b>

**How Are They Used?** Nitrates are used primarily to make fertilizer, but they are also used to make glass and explosives. These compounds also are used in various chemical production and separation processes. Nitrites are manufactured mainly for use as a food preservative, and both nitrates and nitrites are used extensively to enhance the color and extend the shelf life of processed meats.

**What's in the Environment?** Nitrates are naturally present in soil, water, and food. In the natural nitrogen cycle, bacteria convert nitrogen to nitrate, which is taken up by plants and incorporated into tissues. Animals that eat plants use the nitrate to produce proteins. Nitrate is returned to the environment in animal feces, as well as through microbial degradation of plants and animals after they die.

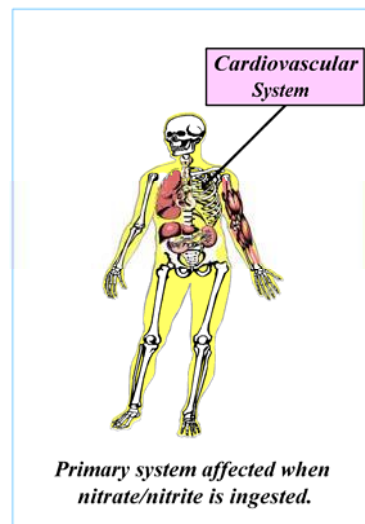


Microorganisms can convert nitrate or the ammonium ion (which is a nitrogen atom combined with four hydrogen atoms) to nitrite; this reaction occurs in the environment as well as within the digestive tract of humans and other animals. After bacteria convert (reduce) nitrate to nitrite in the environment, the nitrogen cycle is completed when they then convert the nitrite to nitrogen. Normally, this natural cycling process does not allow excessive amounts of nitrates or nitrites to accumulate in the environment. However, human activities have increased environmental nitrate concentrations, with agriculture being the major source. This includes increased use of nitrogen-containing fertilizers as well as concentrated livestock and poultry farming; the latter two produce millions of tons of nitrate-containing manure each year. Nitrate and nitrite compounds are very soluble in water and quite mobile in the environment. They have a high potential for entering surface water when it rains, as nitrates in applied fertilizers can dissolve in runoff that flows into streams or lakes; they also have a high potential for entering groundwater through leaching. The concentration associated with soil particles has been estimated to be about half the concentration in interstitial water (the water in the pore spaces between the soil particles).

**What Happens to It in the Body?** Nitrate is a normal component of the human diet, with the average daily intake from all sources estimated at 75 milligrams (mg), or about 0.0026 ounce. Upon ingestion, about 5% of the nitrate taken in by healthy adults is converted (reduced) to nitrite by bacteria in saliva. Further nitrate is converted by bacteria inside the alimentary tract. Certain conditions in the stomach can increase the conversion of nitrate to nitrite, specifically when the pH of the gastric fluid is high enough (above 5) to favor the growth of nitrate-reducing bacteria. This process is of major concern for infants, whose gastrointestinal systems normally have a higher pH than those of adults. Nitrites in the stomach can react with food proteins to form N-nitroso compounds; these compounds can also be produced when meat containing nitrites or nitrates is cooked, particularly using high heat. While these compounds are carcinogenic in test animals, evidence is inconclusive regarding their potential to cause cancer (such as stomach cancer) in humans.

**What Are the Primary Health Effects?** Nitrates themselves are relatively nontoxic. However, when swallowed, they are converted to nitrites that can react with hemoglobin in the blood, oxidizing its divalent iron to the trivalent form and creating methemoglobin. This methemoglobin cannot bind oxygen, which decreases the capacity of the blood to transport oxygen so less oxygen is transported from the lungs to the body tissues, thus causing a condition known as methemoglobinemia.

Normal individuals have low levels (0.5 to 2%) of methemoglobin in their blood. When this level increases to 10%, the skin and lips can take on a bluish tinge (cyanosis), and levels above 25% can cause weakness and a rapid pulse. At levels above 50 to 60%, a person can lose consciousness, go into a coma, and die. Infants are much more sensitive than adults to nitrates/nitrites, and essentially all deaths from nitrate/nitrite poisoning have been in infants. Long-term exposure to lower levels of nitrates and nitrites can cause diuresis (an increase in the amount of urine, and starchy deposits and hemorrhaging of the spleen).



**What Are the Risks?** The U.S. Environmental Protection Agency (EPA) has developed toxicity values to estimate the risk of non-cancer health effects from ingesting nitrates and nitrites. The toxicity value used to estimate a non-cancer effect following ingestion is called a reference dose (RfD). An RfD is an estimate of the highest dose that can be taken in every day without causing an adverse effect.

The RfD for nitrate was developed considering the concentration at which methemoglobinemia was indicated at levels above 10% for 0- to 3-month-old infants. This was based on a daily intake of formula made with water containing 10 mg per liter (mg/L) of nitrate as nitrogen. (This reflects the amount of nitrogen within a nitrate molecule, where 1 mg nitrate as nitrogen = 4.4 mg nitrate as measured in the water.) Most cases of infant methemoglobinemia are associated with exposure to formula prepared with drinking water at nitrate-nitrogen levels at least two times higher, or exceeding 20 mg/L nitrate-nitrogen. For nitrite, the RfD is based on a 10-kg (22-pound [lb]) child drinking 1 liter, or about 1 quart, of water every day. The RfD represents a “safe daily dose” and so is compared to the amount an individual is estimated to take in every day, as a ratio. No adverse effects have been linked with inhaling nitrates or nitrites, so reference concentrations (RfCs), which are used to assess inhalation toxicity, have not been developed. The contribution of nitrites, and indirectly nitrates, to potential human carcinogenicity and the magnitude of the associated risk are unclear. Nitrites react with secondary amines in food to form nitrosamines, many of which are carcinogenic in experimental animals and exert other toxic effects. While the EPA has not developed slope factors (toxicity values used to estimate cancer risk) for nitrates or nitrites, some are available for nitrosamines.

<i>Chemical Toxicity Values</i>	
<b>Non-Cancer Effect</b>	
<i>Oral RfD: NO<sub>3</sub></i>	<i>Oral RfD: NO<sub>2</sub></i>
1.6 mg/kg-day	0.1 mg/kg-day

**What Are Current Limits for Environmental Releases and Human Exposure?** The EPA requires that sodium nitrite releases of more than 100 lb (45.4 kg) and nitrate releases of more than 10,000 lb (4,540 kg) be reported immediately and that normal releases be reported annually for inclusion in the nationwide Toxics Release Inventory. The limits for nitrosamines range from 1 to 10 pounds. The EPA primary drinking water standards for nitrate and nitrite are 10 and 1 parts per million (ppm), respectively. The Food and Drug Administration allows these compounds to be used as food additives as long as they are of food grade and are added only in the amount needed. The maximum amount of nitrite allowed in smoked and cured fish and meat is 200 ppm.

**Where Can I Find More Information?** More information on nitrates and nitrites can be found in the primary information sources used to prepare this overview: (1) Consumer Fact Sheet on Nitrates/Nitrites, EPA Office of Groundwater and Drinking Water, available through <http://www.epa.gov/OGWDW/dwh/c-ioc/nitrates.html>; (2) the EPA’s Integrated Risk Information System, <http://www.epa.gov/iris/subst/0076.htm> (nitrate) and [/0078.htm](http://www.epa.gov/iris/subst/0078.htm) (nitrite); and (3) the National Library of Medicine Hazardous Substances Data Bank (<http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB>).

