The Safety of Inorganic Nitrates

Nitrates have received some bad press in the past, but the truth is that more and more research is showing that they are a safe and healthy part of your diet. For instance, some of the healthiest foods, including spinach, kale and beetroot, contain very high levels of nitrates. Recent population and toxicological studies have also shown that nitrates are important nutrients with significant health benefits and without negative effects.

Despite the use of nitrates for centuries, there are two major areas of concern which are often brought up regarding their safety. These are the possibility of methemoglobinemia and the potential to cause cancer through the formation of nitrosamines. These two issues are addressed below.

Do Nitrates cause Methemoglobinemia?

Methemoglobinemia is a condition that occurs when nitrite binds to the iron in the hemoglobin molecule in red blood cells. Hemoglobin is an essential protein that binds to oxygen and then transports the oxygen to cells all over the body. In the 1950's, a few cases of cyanosis or blue-baby syndrome caused by a reduced ability of oxygen to bind with hemoglobin were documented in infants. These occurrences were immediately attributed with nitrites and diagnosed as methemoglobinemia. The infants were found to live in an area that had high levels of nitrite in the well water, and therefore it was thought that this was the cause of the reduced oxygen binding capacity of the babies' hemoglobin. While it is possible that this was the case, other factors were not taken into account. For instance, the possible contamination of the drinking water with bacteria was not investigated.

As a consequence of this diagnosis, governments around the world quickly implemented strict regulations regarding the nitrate and nitrite content of drinking water, and took very expensive measures (hundreds of millions of dollars per year) to remove nitrate from the water supply. The current limit imposed in the US, Canada and the UK is 50 mg or 1 millimole per litre.

However, careful evaluation of the data does not support such rigid limitations. For example, commercial beetroot juice contains close to 20-45 millimoles per litre of nitrate and measurements of plasma levels following consumption of such high doses show that levels remain within the physiological limit of 1 micromole per litre. It seems that the body is able to rapidly regulate nitrate levels and excess intake does not equate to dramatically elevated plasma levels.

Glass of Water: Limited to less than 1 millimole per litre of nitrates

Beetroot Juice: Up to 45 millimoles per litre of nitrates; associated with numerous health benefits!

Figure 14. The limit of nitrate allowed in drinking water in Canada and the US is 1 millimole per litre, however, a healthy glass of beetroot juice can contain up to 45 millimoles per litre!

Secondly, the research of Dr. Mark Gladwin in the US has shown that when very high doses of nitrite are given intravenously to patients to prevent damage to the heart, plasma levels increased to 16 times normal physiological levels, yet the percentage of hemoglobinemia was less than 1 percent! It seems that the body has various homeostatic mechanisms to maintain physiological levels of nitrite. While caution should be exercised in not administering nitrates and/or nitrites to infants and/or children, research indicates that in adults methemoglobinemia may not be as serious as originally thought, especially when the doses consumed are similar or less than those that would be found in a plate of salad or a glass of beetroot juice.

Do Nitrates form Carcinogenic Nitrosamines?

The second potential cause for concern is the formation of nitrosamines. Nitrosamines are chemicals that can form between secondary amines present in foods and nitrite. Nitrosamines have long been associated with cancer formation in the liver. However, there are several shortcomings to the theory that dietary nitrates can form nitrosamines in humans.

First, the extrapolation of animal data to humans is questionable when it comes to nitrates. Humans, unlike rats, have evolved mechanisms of concentrating nitrate in the salivary glands much we concentrate iodide ions in the thyroid gland. Second, nitrate is actively reabsorbed in the kidneys, suggesting an evolutionary advantage of concentrating this ion. Why else would evolution design such a conservation mechanism if such an ion was toxic? Third, a very comprehensive 2003 WHO (world health organization) and joint expert committee on food additives concluded that: "overall the epidemiological studies showed no consistently increased risk for cancers with increasing consumption of nitrate". Further epidemiological and animal studies have failed to find any conclusive correlation. Fourth, certain populations, for instance Tibetans living at high altitude, have a hundred-fold greater plasma levels of nitrates than those living at sea level without any concomitant increase in cancer rate.

In conclusion nitrate has been used in food and nutrition for centuries without evidence of negative health effects. It is especially telling that some of the healthiest foods (like green, leafy vegetables) contain very high levels of nitrates, and that the high nitrate content of these foods has been linked to their health benefits. As mentioned previously, researchers have suggested that nitrates are probably responsible for the health benefits associated Mediterranean and Japanese diets. Studies showing beneficial effects of these important molecules are extensive, and provide strong support for their benefits to health (see Table 3).

The ability of nitrate to increase NO levels quickly and easily through the NOx3,2,1 pathway offers a novel approach for maintaining optimal health. Nitric oxide is an important molecule that plays a key role in numerous and diverse physiological mechanisms. Furthermore, nitrate is an important nutritional therapeutic approach in preventing numerous diseases by playing a key role in NO homeostasis.

Table 3: Therapeutic Effects of Inorganic Nitrate or Natural Sources Containing Nitrate. MAP = Mean artial pressure, DBP = Diastolic Blood Pressure, SBP = Systolic Blood Pressure. (From Weitzberg et al. 2010)

Organ System	Nitrate Source	Species	Effect	Reference
Cardiovascular, Kidney	Sodium Nitrate	Rat	Increased post-ischemic blood flow	Jansson et al., 2008
Cardiovascular, Stomach	Sodium Nitrate		Decreased MAP, decreased DBP, increased NO formation in the stomach, increased blood flow to the stomach	Petersson et al., 2009
StomachPotassium Nitrate		Rat	Decreased ulcer formation, increased NO formation in the stomach, increased blood flow to the stomach	Miyoshi et al., 2003
StomachSodium Nitrate		Rat	Decreased ulcer formation, increased gastric mucus production	Jansson et al., 2007
Cardiovascular	Potassium Nitrate	Human	Decreased platelet aggregation	Richardson et al., 2002
Cardiovascular	Sodium Nitrate	Human	Decreased DBP, decreased MAP	Larsen et al., 2006
Cardiovascular	Beetroot Juice	Human	Decreased SBP, DBP and MAP, reduced platelet aggregation, decreased endothelial function	Webb et al., 2008
Cardiovascular	Potassium Nitrate, Beetroot Juice	Human	Decreased SBP and DBP	Kapil et al., 2010
Cardiovascular	Traditional Japanese Diet	Human	Decreased DBP	Sobko et al., 2010
Cardiovascular, Musculoskeletal	Sodium Nitrate	Human	Decreased DBP and SBP, decreased oxygen consumption during moderate exercise	Larsen et al., 2007
Cardiovascular, Musculoskeletal	Beetroot Juice	Human	Decreased SBP, decreased oxygen consumption during moderate exercise, increased time to exhaustion during exercise	Bailey et al., 2009
Cardiovascular, Musculoskeletal	Beetroot Juice	Human	Decreased DBP and SBP, decreased oxygen consumption during low intensity exercise, decreased muscle phosphocreatine, increased muscle efficiency	Bailey et al., 2010
Cardiovascular, Musculoskeletal	Beetroot Juice	Human	Decreased DBP, SBP and MAP, decreased oxygen consumption during exercise	Vanhatalo et al., 2010
Musculoskeletal	Sodium Nitrate	Human	Decreased oxygen consumption during maximal exercise	Larsen et al., 2010
Sickle Cell Disease	Sodium Nitrate	Human	Increased regional blood flow	Mack et al., 2008

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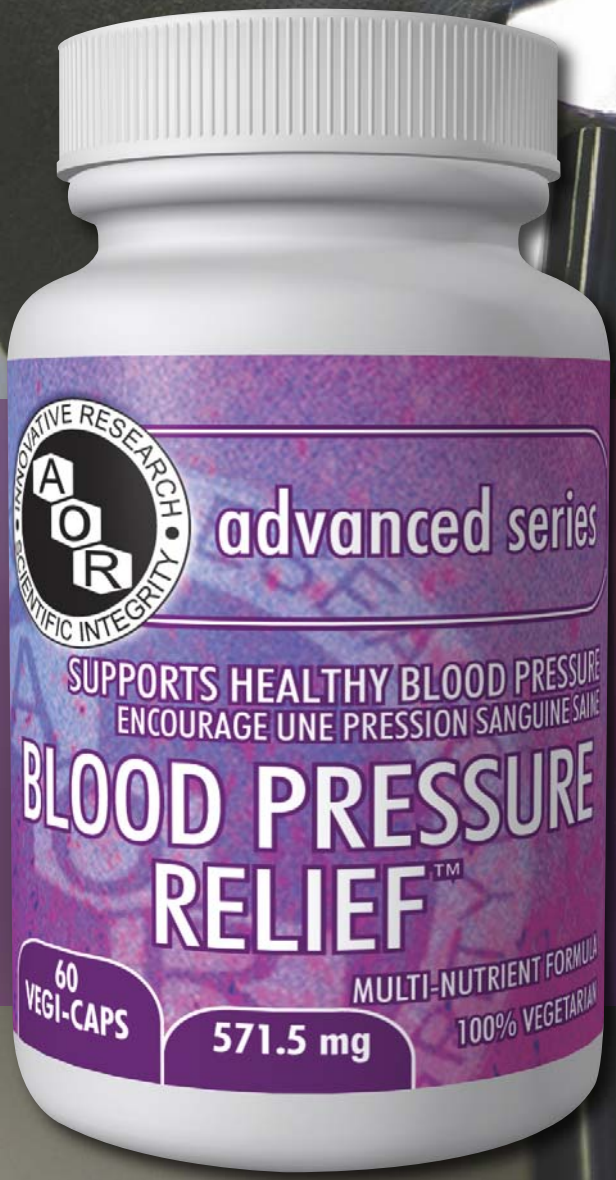

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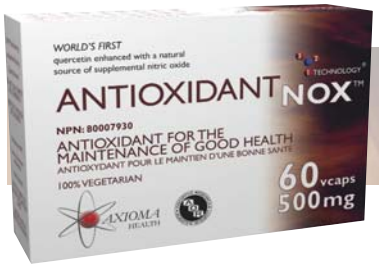

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