



## Understanding Nitrite and Nitrate in Human Health

- Around 85% of the nitrate in the diet comes from vegetables, notably red beets, spinach, radishes, celery, lettuce, cabbage, fennel, broccoli, cucumbers and leeks; the remainder is from cured meat, fish, dairy products and drinking water.
- Nitrite is an essential ingredient required by the Government of Canada to be added to some prepared meat products to prevent spoilage and protect against listeriosis and botulism. Nitrite can be added to meat products in two ways: either through sodium nitrite, which is synthetically produced, or through a natural source like cultured celery extract. Either way, they provide the same important food safety benefits.
- Emerging research suggests nitrite from dietary sources can form nitric oxide. Identified as one of the most important cellular signalling mechanisms in the body, maintaining nitric oxide balance is critical for optimal health, such as improved energy, memory, stamina, and sexual function, and disease prevention. The lack of nitric oxide production can lead to hypertension, atherosclerosis, peripheral artery disease, heart failure, and thrombosis resulting in heart attack and stroke; all of which have been treated by dietary nitrite interventions.

### Chemical Formula

Nitrite ( $\text{NO}_2^-$ ) and nitrate ( $\text{NO}_3^-$ ) are naturally occurring ions found in the environment and in some foods. Nitrate is naturally converted into nitrite predominately by saliva in the mouth.<sup>1</sup>

### Dietary Sources

Vegetables are the major dietary source of nitrate, providing over 85% of daily intake.<sup>2</sup> Other sources are cured meat, fish, dairy products and drinking water.

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**MEAT...**  
GOOD FOR YOU.  
GOOD FOR CANADA.

**LA VIANDE...**  
BONNE POUR VOUS.  
BONNE POUR LE CANADA.

Vegetables containing the highest levels of nitrate include red beets, spinach, radishes, celery, lettuce, cabbage, fennel, broccoli, cucumbers and leeks.<sup>3</sup> Cured meat products are required by federal food safety regulations to have the addition of at least 100 mg/kg of nitrate and nitrite, during the preparation process. Prepared meat products use natural nitrites, such as celery extract, or traditional sodium nitrite.

Nitrate and Nitrite Levels in Foods <sup>1</sup>		
	Nitrate (mg/100g)	Nitrite (mg/100g)
<b>Vegetables</b>		
Spinach	741.0	0.02
Mustard greens	116.0	0.003
Salad mix	82.1	0.13
Cole slaw	55.9	0.07
Broccoli	39.5	0.07
Tomato	39.2	0.03
Carrots	0.1	0.006
<b>Fruit</b>		
Banana	4.5	0.009
Fruit mix	0.9	0.08
Orange	0.8	0.02
<b>Meats/prepared meats</b>		
Hot dog	9.0	0.05
Bacon	5.5	0.38
Pork tenderloin	3.3	0
Ham	0.90	0.89

<sup>1</sup> The Nitric Oxide (NO) Solution: How to Boost the Body's Miracle Molecule to Prevent and Reverse Chronic Disease by Nathan S. Bryan, PhD and Janet Zand, OMD with Bill Gottlieb. Published in 2010 by Neogenis.

## Nitrite is Essential

Nitrite is an essential ingredient in cured meat products. It is used as a preservative and an antibacterial agent; it also gives cured meat their characteristic colour and flavour. Nitrite minimizes waste by preventing spoilage and enhances food safety by blocking the growth of *Clostridium botulinum* and *Listeria monocytogenes*.

## The Nitrite Debate

During the 1950s and 1960s, some animal studies indicated the potential for nitrite to form carcinogenic *N-nitrosamines*.<sup>4,5</sup> In the case of cured meats, *N-nitrosamine* formation may occur when secondary amines react with nitrous acid produced from nitrite at very high temperatures, for example, when bacon is fried at 170°C.

As potential public health concerns were related to the formation of *N-nitrosamines* rather than to the nitrite itself, government regulations were introduced in the 1970s that both limited the addition of nitrite to cured meat products and required the inclusion of *N-nitrosamine* formation inhibitors in bacon, such as ascorbic acid (vitamin C), erythorbic acid and alpha-tocopherol (vitamin E).<sup>6</sup>

From the 1980s to 2000s, the U.S. Food and Drug Agency and the U.S. National Toxicology Program, conducted numerous assessments and studies which consistently found that nitrite is safe at the levels consumed through the diet.<sup>7,8,9</sup>

In 2006, a review of various epidemiological investigations that endeavoured to assess the potential carcinogenicity of nitrate and nitrite was conducted by the International Agency for Research on Cancer (IARC). The report concluded that under certain conditions the nitrate we consume could be altered to form carcinogenic nitrosamines.<sup>10</sup> However, newly published cohort studies did not support this conclusion.<sup>11</sup>

## Health Benefits

Recent research is demonstrating health benefits of nitric oxide (NO), including improved energy, memory, stamina, and sexual function.<sup>12</sup> Nitric oxide is a signaling molecule. It signals arteries to relax and expand, immune cells to kill bacteria, and brain cells to communicate with each other.<sup>13,14</sup>

Nitrite from dietary sources can form nitric oxide within the human body. Identified as one of the most important cellular signalling mechanisms in the body, maintaining nitric oxide balance is critical for optimal health and disease prevention.<sup>12</sup>

The lack of nitric oxide production can lead to hypertension, atherosclerosis, peripheral artery disease, heart failure, and thrombosis resulting in heart attack and stroke.<sup>15,16,17,18</sup> All of these conditions have been shown to be affected positively by dietary nitrite interventions.<sup>19, 20</sup>

The profound and far-reaching significance of this revelation was of such importance that, in 1998, the Nobel Prize in Physiology or Medicine was awarded for its discovery.<sup>21</sup>

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### References

1. Eisenbrand, G., Spiegelhalder, B. and Preussmann, R. (1980). Nitrate and nitrite in saliva. *Oncology*, 37(4): 227-231.
2. Gangolli, S.D., Van Den Brandt, P.A., Feron, V.J., Janzowsky, C., Koeman, J.H., Speijers, G.J.A., Spiegelhalder, B., Walker, R. and Wishnok, J.S. (1994). Nitrate, nitrite and *N*-nitroso compounds. *Eur. J. Pharmacol.*, 292(1): 1-38.
3. Pennington, J.A.T. (1998). Dietary exposure models for nitrates and nitrites. *Food Control*, 9(6): 385-395.
4. Barnes, J.M. and Magee, P.N. (1954). Some toxic properties of dimethylnitrosamine, *Br J. Ind. Med.* 11:167.
5. Challis, B.C. and Butler, A.R. (1968). Substitution in an amino nitrogen, *The Chemistry of the Amino Group*, P. Patai (ed). Interscience Publishers, New York.
6. Jeffrey J. Sindelar, A. L. Milkowski. (2012) Human safety controversies surrounding nitrate and nitrite in the diet, *Nitric Oxide*. ELSEVIER Inc.
7. FDA (1980a). Evaluation of the MIT nitrite feeding study to rats. Report by the Interagency Working Group on Nitrite Research. Food and Drug Administration, Public Health Service, U.S. Department of Health and Human Services, Washington, DC.
8. FDA (1980b). Re-evaluation of the pathology findings of studies on nitrite and cancer: histologic lesions in Sprague-Dawley rats. Final report submitted by the Universities Associated for Research and Education in Pathology to the Food and Drug Administration, Public Health Service, U.S. Department of Health and Human Services, Washington, DC.
9. NTP (2001). Toxicology and carcinogenesis studies of sodium nitrite (CAS No. 7632-00-0) in F344/N rats and B6C3F1 mice (drinking water studies). National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC. pp. 7-273 (Technical Report Series TR-495). For U.S. National Toxicology Program.
10. IARC (2010). Ingested nitrate and nitrite and cyanobacterial peptide toxins. International Agency for Research on Cancer, Lyon. 464 pp. (IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Volume 94).
11. Bryan, N.S., Alexander, D.D., Coughlin, J.R., Milkowski, A.L., Boffetta, P. (2012). Ingested nitrate and nitrite and stomach cancer risk: An updated review. *Food Chem Toxicol.* 50, 3646-3665.
12. Parthasarathy, D.K., Bryan, N.S. (2012). Sodium nitrite: The "cure" for nitric oxide insufficiency. *Meat Science*, Volume 92, Issue 3.
13. Bryan, N.S. (2011). Application of nitric oxide in drug discovery and development. *Expert Opin Drug Discov.* Nov;6(11):1139-54.
14. Moncada, S., Palmer, R.M., Higgs E.A. (1991). Nitric oxide: physiology, pathophysiology, and pharmacology. *Pharmacol Rev.* Jun;43(2):109-42. Review.
15. Schachinger, V., M.B. Britten, and A.M. Zeiher. (2000). Prognostic impact of coronary vasodilator dysfunction on adverse long-term outcome of coronary heart disease. *Circulation*, 101(16): p. 1899-906.
16. Halcox, J.P., et al. (2002). Prognostic value of coronary vascular endothelial dysfunction. *Circulation*, 106(6): p. 653-8.
17. Bugiardini, R., et al. (2004). Endothelial function predicts future development of coronary artery disease: a study of women with chest pain and normal coronary angiograms. *Circulation*, 109(21): p. 2518-23.
18. Lerman, A. and A.M. Zeiher. (2005) Endothelial function: cardiac events. *Circulation*, 111(3): p. 363-8.
19. Bryan, N.S. (2009). Cardioprotective actions of nitrite therapy and dietary considerations. *Front Biosci*, Jan 1;14:4793-808. Review.
20. Lundberg, J.O., Weitzberg, E., Gladwin, M.T. (2008) The nitrate-nitrite-nitric oxide pathway in physiology and therapeutics. *Nat Rev Drug Discov.* Feb;7(2):156-67.
21. The Nobel Prize in Physiology or Medicine 1998. Nobelprize.org. 30 May 2013  
[http://www.nobelprize.org/nobel\\_prizes/medicine/laureates/1998](http://www.nobelprize.org/nobel_prizes/medicine/laureates/1998).