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## Supplementation with nitrate and nitrite salts in exercise: a word of caution

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TO THE EDITOR: Recent studies show that dietary supplementation with inorganic nitrate ( $\text{NO}_3^-$ ) reduces whole body oxygen cost during physical exercise, an effect that might be used by endurance athletes in an attempt to increase stamina (1–3, 6, 7, 9–11). In the cited exercise studies, nitrate was taken in the form of a salt (e.g., sodium nitrate) or from a food source such as beetroot juice, which naturally contains high amounts of nitrate. Although the true performance-enhancing effects of nitrate are yet to be proven under actual competitive conditions, it is clear from internet forums, articles, and discussions within the sports community that the use of nitrate supplementation currently is spreading rapidly among athletes. Bioactivation of nitrate involves its initial metabolism to form the more reactive nitrite anion ( $\text{NO}_2^-$ ), which may be further reduced to nitric oxide (NO) and other bioactive nitrogen species. Importantly, the dose of nitrate that reduces oxygen cost efficiently is in the range 300–500 mg and there is no evidence that higher doses would increase the effects further.

We wish to raise a word of caution regarding the uncontrolled use of nitrate and nitrite salts for performance-enhancing purposes. In particular, this warning relates to the intentional or unintentional use of nitrite. While nitrate is nontoxic even in higher doses, nitrite can cause serious harm already at considerably lower levels. In fact the reported  $\text{LD}_{50}$  for oral nitrite (~100–200 mg/kg) is comparable to that of cyanide. Acute nitrite toxicity is a result of its rapid reaction with hemoglobin in blood, which may cause methemoglobinemia, a potentially life-threatening condition. In addition, nitrite in higher doses may cause hypotension, especially if combined with other vasodilatory drugs. A case of unintentional ingestion of nitrite by an athlete was recently reported on a runners' internet forum. The subject had taken a nitrite salt before exercise in the belief that it was nitrate, and he developed symptoms suggestive of methemoglobinemia. Nitrate salt (saltpeter) is used for food conservation purposes and is commonly sold in regular grocery stores, while nitrite salts are available from various internet sites. While direct ingestion of a nitrite salt is potentially hazardous, the use of nitrate from natural vegetable sources is clearly of much less concern in terms of acute toxicity. This is because only a minor part of the nitrate is converted to nitrite in vivo. In fact, this slow controlled release of nitrite from dietary nitrate may have desirable health effects, including a lowering of blood pressure (8, 12, 14). Also, the reduction in oxygen cost obtained by nitrate may be used in the future in treatment and prevention of ischemic conditions such as myocardial infarction (4, 13) and peripheral artery disease (5). These medical implications of nitrate and nitrite are in fact the long-term ultimate goal with the ongoing

research in this field. Still, a potential risk exists also with a nitrate-containing vegetable juice if stored inappropriately. Contamination of food or beverage by nitrate-reducing bacteria may then occur, leading to substantial nitrite accumulation over time. In addition, there is also a considerable confusion related to organic nitrates and nitrites, for example nitroglycerine and amyl nitrite. These drugs are extremely potent vasodilators and unintentional overdosing may lead to fatal vascular collapse.

In summary, at this time we advise athletes to refrain from the uncontrolled use nitrate and nitrite salts as dietary supplements. While the acute toxicity of nitrate is very low or absent, any confusion leading to a large unintentional intake of nitrite or organic nitrates and nitrites is potentially life threatening. In contrast, with natural sources of nitrate such as whole vegetables or vegetable juices, we do not foresee any acute risks.

## DISCLOSURES

J. O. Lundberg and E. Weitzberg have filed patents relating to the medical use of inorganic nitrate and nitrite.

## REFERENCES

1. Bailey SJ, Fulford J, Vanhatalo A, Winyard PG, Blackwell JR, DiMenna FJ, Wilkerson DP, Benjamin N, Jones AM. Dietary nitrate supplementation enhances muscle contractile efficiency during knee-extension exercise in humans. *J Appl Physiol* 109: 135–148, 2010.
2. Bailey SJ, Winyard P, Vanhatalo A, Blackwell JR, DiMenna FJ, Wilkerson DP, Tarr J, Benjamin N, Jones AM. Dietary nitrate supplementation reduces the O<sub>2</sub> cost of low-intensity exercise and enhances tolerance to high-intensity exercise in humans. *J Appl Physiol* 107: 1144–1155, 2009.
3. Bescos R, Rodriguez FA, Iglesias X, Ferrer MD, Iborra E, Pons A. Acute administration of inorganic nitrate reduces  $\text{VO}_{2\text{peak}}$  in endurance athletes. *Med Sci Sports Exerc* Mar 10, 2011 (Epub ahead of print).
4. Gladwin MT, Schechter AN, Kim-Shapiro DB, Patel RP, Hogg N, Shiva S, Cannon RO 3rd, Kelm M, Wink DA, Espey MG, Oldfield EH, Pluta RM, Freeman BA, Lancaster JR Jr, Feelisch M, Lundberg JO. The emerging biology of the nitrite anion. *Nat Chem Biol* 1: 308–314, 2005.
5. Kenjale AA, Ham KL, Stabler T, Robbins JL, Johnson JL, Vanbruggen M, Privette G, Yim E, Kraus WE, Allen JD. Dietary nitrate supplementation enhances exercise performance in peripheral arterial disease. *J Appl Physiol* 110: 1582–1591, 2011.
6. Lansley KE, Winyard PG, Bailey SJ, Vanhatalo A, Wilkerson DP, Blackwell JR, Gilchrist M, Benjamin N, Jones AM. Acute dietary nitrate supplementation improves cycling time trial performance. *Med Sci Sports Exerc* 43: 1125–1131, 2011.
7. Lansley KE, Winyard PG, Fulford J, Vanhatalo A, Bailey SJ, Blackwell JR, DiMenna FJ, Gilchrist M, Benjamin N, Jones AM. Dietary nitrate supplementation reduces the O<sub>2</sub> cost of walking and running: a placebo-controlled study. *J Appl Physiol* 110: 591–600, 2011.
8. Larsen FJ, Ekblom B, Sahlin K, Lundberg JO, Weitzberg E. Effects of dietary nitrate on blood pressure in healthy volunteers. *N Engl J Med* 355: 2792–2793, 2006.
9. Larsen FJ, Schiffer TA, Borniquel S, Sahlin K, Ekblom B, Lundberg JO, Weitzberg E. Dietary inorganic nitrate improves mitochondrial efficiency in humans. *Cell Metab* 13: 149–159, 2011.

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10. **Larsen FJ, Weitzberg E, Lundberg JO, Ekblom B.** Dietary nitrate reduces maximal oxygen consumption while maintaining work performance in maximal exercise. *Free Radic Biol Med* 48: 342–347, 2010.
11. **Larsen FJ, Weitzberg E, Lundberg JO, Ekblom B.** Effects of dietary nitrate on oxygen cost during exercise. *Acta Physiol (Oxf)* 191: 59–66, 2007.
12. **Lundberg JO, Weitzberg E, Gladwin MT.** The nitrate-nitrite-nitric oxide pathway in physiology and therapeutics. *Nat Rev Drug Discov* 7: 156–167, 2008.
13. **Webb A, Bond R, McLean P, Uppal R, Benjamin N, Ahluwalia A.** Reduction of nitrite to nitric oxide during ischemia protects against myocardial ischemia-reperfusion damage. *Proc Natl Acad Sci USA* 101: 13683–13688, 2004.
14. **Webb AJ, Patel N, Loukogeorgakis S, Okorie M, Aboud Z, Misra S, Rashid R, Miall P, Deanfield J, Benjamin N, MacAllister R, Hobbs AJ, Ahluwalia A.** Acute blood pressure lowering, vasoprotective, and anti-platelet properties of dietary nitrate via bioconversion to nitrite. *Hypertension* 51: 784–790, 2008.

