

The Eurasia Proceedings of Health, Environment and Life Sciences (EPHELs), 2023

Volume 12, Pages 22-26

ICMeHeS 2023: International Conference on Medical and Health Sciences

The Effect of Nitrate Supplementation on Sportive Performance

Cemre Didem Eyipinar
Gaziantep University

Abstract: Beetroot juice is typically used as a source of dietary nitrate supplementation, which has been hailed as a potential new ergogenic aid for athletic and exercise performance. A 0.6% performance boost is now deemed adequate to make a difference due to the rise in competitive equality in top-level sport especially. The aim of this study is to examine the effects of nitrate supplementation on sports performance and to reveal the mechanisms of action. For that, information from the publications evaluated throughout the scope of SCI, SCI-Expanded, and ESCI were collected by scanning the literature in the SportDiscus, EMBASE, PubMed, and Google Scholar databases over a 10-year period. According to literature, it has been stated that nitrate supplementation provides vasodilation, triggers mitochondrial biogenesis, glucose uptake, and calcium transport from the sarcoplasmic reticulum. Nitrate supplementation has been demonstrated to have physiological effects that may be advantageous for improving exercise performance, at least in recreationally active or sub-elite athletes.

Keywords: Beetroot, Nitric oxide, Phytochemicals

Introduction

Numerous vascular and cellular processes, such as cellular respiration, vasodilation, and angiogenesis, depend on the signaling molecule nitric oxide (NO). Through both endogenous and exogenous mechanisms, dietary nitrate (NO_3^-) consumption causes the production of NO (Clements et al., 2014). Nitric oxide, which is known to play a number of significant roles in vascular and metabolic control, can be produced from nitrite under situations of insufficient oxygen accessibility. In addition to this, plasma nitrite levels is raised by dietary nitrate intake (Jones, 2014). Nitric oxide is a substance produced from L-arginine by the enzyme nitric oxide synthetase, and since its half-life is very short, it turns into inactive nitrite (NO_2^-) and nitrate (NO_3^-). In addition to its production in the body, it can also be taken externally through diet (Maughan, 2018). Some veggies contain an active substance called NO_3^- that may have ergogenic and health-improving benefits. Therefore, NO_3^- appears as an intriguing substance from the perspectives of both sports as an ergogenic aid and as a possibly affordable strategy for lowering the likelihood of cardiovascular events (Clements et al., 2014). All the same, for the past ten years, dietary nitrate (NO_3^-) supplementation has been studied for its potential ergogenic effects (Senefeld et al., 2020). This review's goal is to clarify the mechanisms by which nitrate supplementation improves athletic performance. Promoting the nitrate-nitrite-NO pathway's bioavailable of NO may have an impact on how well muscles work during exercise. By controlling blood flow, contractility, glucose and calcium homeostasis, as well as mitochondrial respiration and biogenesis, NO plays a role in the controlling of the functioning of skeletal muscles.

Shortly, nitrate supplementation affects sportive performance in a number of ways: provides vasodilation, triggers mitochondrial biogenesis, glucose uptake, and calcium transport from the sarcoplasmic reticulum (Jones, 2014). All these pathways will be examined from a biochemical perspective in this review.

Vasodilatation Effect

- This is an Open Access article distributed under the terms of the Creative Commons Attribution-Noncommercial 4.0 Unported License, permitting all non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

- Selection and peer-review under responsibility of the Organizing Committee of the Conference

©2023 Published by ISRES Publishing: www.isres.org

Nitrate needs some enzymatic processes to turn into nitric oxide. Nitrate groups interact with enzymes and sulfhydryl groups that remove nitrate groups. By this way, nitric oxide converts Guanylyl Cyclase (GC) to 3'-5'-cyclic guanosine monophosphate (cGMP). cGMP reduces the strength of cardiac contractions in cardiac cells by stimulating the ion pumps that enable Ca^{2+} to be removed from the cytoplasm and by reducing the Ca^{2+} sensitivity of the contractile apparatus. Increasing intracellular cGMP concentration inhibits the entry of Ca^{2+} into the cell, thus decreasing the intracellular Ca^{2+} concentration. Veins expand. Additionally, nitric oxide opens K^+ channels, causing hyperpolarization and relaxation. Finally, NO can activate myosin light chain phosphatase, an enzyme that dephosphorylates myosin light chains and causes relaxation, by stimulating a cGMP-dependent protein kinase (Gormus & Ozmen, 2005). Enhancing the $\text{NO}_3^- / \text{NO}_2^- / \text{NO}$ pathway may have an impact on how well muscles work during exercise. NO's function in skeletal muscle contractility can modify that muscle's activity (Stamler & Meissner, 2001).

Mitochondrial Biogenesis

The genomic process that produces new mitochondria, known as mitochondrial biogenesis, is essential for preserving an adequate amount of mitochondria and is the basis for adaptations that are triggered by external stimuli like exercising (Hollooszy, 1967). Nitrate, is a well-known mediator of mitochondrial activity that promotes the synthesis of cyclic guanosine monophosphate (cGMP) and soluble guanylate cyclase (sGC) to promote mitochondrial biogenesis (Nisoli et al., 2005).

The relationships between nitrate, nitrite, NO, and the mitochondria are many. The effect of NO that has been studied the most may be its binding to cytochrome oxidase (COX), the electron transport system's (ETS) terminal electron acceptor, which partially inhibits the respiration of mitochondria (Brown & Cooper, 1994). Dynamic and oxygen-regulated, this binding may also be involved in tissue oxygen gradient regulation and reactive oxygen species (ROS) signaling regulation. Furthermore, NO promotes mitochondrial biogenesis via a process that is dependent on cGMP. Because proteins in the ETS can convert nitrite to NO, the effects of nitrite may resemble those of NO. Lastly, nitrite may signal to control tissue protein expression and activation without the need for NO synthesis (Nisoli et al., 2003).

The traditional method of measuring mitochondrial oxidative phosphorylation efficiency is the P/O ratio, which is the quantity of oxygen used for every ATP generated. After receiving nitrate supplementation, muscle tissue mitochondria were extracted and showed improved oxidative phosphorylation efficiency (P/O ratio). There was a correlation between the decrease in oxygen cost during exercise and the enhanced mitochondrial P/O ratio. Nitrate lowered the expression of ATP/ADP translocase, a proton conductance-related protein, mechanistically (Larsen et al., 2011).

Glucose Uptake

Throughout physical activity, glucose is a key fuel source, and during activity bouts, skeletal muscle can absorb glucose up to 50 times more efficiently. Exercise length and intensity are important factors that affect how well skeletal muscle absorbs glucose. The intracellular metabolic state controls the glucose transport triggered by exercise (controlled by AMPK) (Sylov et al., 2007). The protein kinase needed for glucose-repressed transcription is called AMPK (Chen et al., 1999).

The translocation of GLUT4 to the cell surface is enhanced by contraction and exercise, which facilitates the transport of glucose into muscle cells. Though the exact mechanisms by which contraction boosts GLUT4 translocation and muscle glucose uptake remain unclear, it is generally agreed that the signals controlling this process are distinct from those governing the insulin-signaling system. Many mechanisms have been proposed to control contraction-stimulated glucose absorption, with AMP-activated protein kinase (AMPK) being one of the more appealing and thoroughly researched possibilities (Lira et al., 2007). The translocation of GLUT4 and other catabolic activities are increased when AMPK is pharmacologically activated (Lee-Young et al., 2009).

It has been suggested that NO regulates contraction and NO-mediated glucose absorption by acting both upstream and downstream of AMPK. On the other hand, it has been demonstrated that NOS inhibition minimizes glucose absorption without altering AMPK signaling during contractions. In muscles with a higher percentage of glycolytic fibers, NO has a role in controlling glucose absorption during contraction independently of AMPK (Lee-Young et al., 2009). The phosphorylation of NOS by AMPK results in a rise in

NOS activation (Chen et al., 1999). Briefly, nitrate controls the uptake of glucose by muscles in the skeleton during exercise in a manner that is independent of AMPK.

Calcium Transport to Sarcoplasmic Reticulum

Sarcoplasmic reticulum (SR), Ca^{2+} release in isolated skeletal muscle fibers decreases significantly in the later phases of exhaustion (Westerblad et al., 1998). By modifying Ca^{2+} release and absorption by the sarcoplasmic reticulum, NO controls muscle contraction. After nitrate supplementation, the impact of NO on these systems may enhance exercise efficiency (Hoon et al., 2015).

Dihydropyridine receptor (DHPR) and calsequestrin 1 (CASQ1) are two proteins that bind Ca^{2+} . A rise in DHPR would facilitate the release of Ca^{2+} more easily throughout contraction, whereas higher CASQ1 expression and intracellular $[\text{Ca}^{2+}]$ probably increase the quantity of releasable Ca^{2+} from the sarcoplasmic reticulum during excitation–contraction coupling (creating extra actin–myosin binding sites) (Hernández et al., 2012). Furthermore, after supplementation, there was a stated rise in metabolic efficiency, which decreased the accumulation of intracellular phosphate ([Pi]) throughout contraction. Considering that raised [Pi] has been shown to reduce Ca^{2+} sensitivity and sarcoplasmic reticulum Ca^{2+} release to sarcoplazma, this may further help to preserve the muscle force found throughout exhaustive exercise (Duke & Steele, 2001). Shortly, since nitrate supplementation increased NO generation, there may have been a decrease in skeletal muscle ATP turnover through a decrease in actomyosin ATPase and/or Ca^{2+} -ATPase activity (Bailey et al., 2010).

Method

In order to gather information from publications that were reviewed within the scope of SCI, SCI-Expanded, and ESCI for this review, the literature in the SportDiscus, EMBASE, PubMed, and Google Scholar databases was scanned over a ten-year period using the keywords "nitrate" AND "sportive performance supplements" AND "nitric oxide." A thorough analysis of the chosen studies was done in an effort to describe how nitrate has ergogenic effects.

Conclusion

According to recent research, NO_3^- is a helpful ergogenic aid that can be used in a range of sports and exercise scenarios to enhance performance through a variety of processes (Macuh & Knap, 2021). Nitrate supplementation has been reported in studies to promote vasodilation, mitochondrial biogenesis, glucose uptake, and sarcoplasmic reticulum calcium transfer. At least in recreationally active or sub-elite athletes, nitrate supplementation has been shown to produce physiological responses that may be beneficial for enhancing athletic performance.

Recommendations

When given acutely or chronically in the range of 300–1041 mg NO_3^- , 2-3 hours before to exercise, and mainly in the case of exercise duration of 10–17 min, the effect of NO_3^- is most noticeable in less-trained individuals (Macuh & Knap, 2021). That is the case with any sports supplements, one must evaluate the risk against the potential benefits. Since nitrate can be consumed in naturally occurring forms like vegetables and beetroot juice, this may reduce the chance of consuming illegal substances and provide additional health advantages linked to higher dietary nitrate intake. In addition to the small number of research findings indicating adverse effects, nitrate supplements appear to be a low risk intervention that could improve performance during exercises (Hoon et al., 2013).

Scientific Ethics Declaration

The author declares that the scientific ethical and legal responsibility of this article published in EPHELS journal belongs to the author.

Acknowledgements

This article was presented as an oral presentation at the International Conference on Science and Education (www.iconse.net) conference held in Antalya/Turkey on November 16-19, 2023.

References

- Bailey, S. J., Fulford, J., Vanhatalo, A., Winyard, P. G., Blackwell, J. R., DiMenna, F. J., ... & Jones, A. M. (2010). Dietary nitrate supplementation enhances muscle contractile efficiency during knee-extensor exercise in humans. *Journal of Applied Physiology*, 109(1), 135-148.
- Brown, G. C., & Cooper, C. E. (1994). Nanomolar concentrations of nitric oxide reversibly inhibit synaptosomal respiration by competing with oxygen at cytochrome oxidase. *FEBS Letters*, 356(2-3), 295-298.
- Chen, Z. P., Mitchelhill, K. I., Michell, B. J., Stapleton, D., Rodriguez-Crespo, I., Witters, L. A., ... & Kemp, B. E. (1999). AMP-activated protein kinase phosphorylation of endothelial NO synthase. *FEBS letters*, 443(3), 285-289.
- Clements, W. T., Lee, S. R., & Bloomer, R. J. (2014). Nitrate ingestion: a review of the health and physical performance effects. *Nutrients*, 6(11), 5224-5264.
- Duke, A. M., & Steele, D. S. (2001). Mechanisms of reduced SR Ca²⁺ release induced by inorganic phosphate in rat skeletal muscle fibers. *American Journal of Physiology-Cell Physiology*, 281(2), 418-29.
- Gormus, U., & Ozmen, D. (2005). cGMP ve klinik önemi. *Türkiye Klinikleri Tıp Bilimleri Dergisi*, 25(5), 678-87.
- Hernández, A., Schiffer, T. A., Ivarsson, N., Cheng, A. J., Bruton, J. D., Lundberg, J. O., ... & Westerblad, H. (2012). Dietary nitrate increases tetanic [Ca²⁺] and contractile force in mouse fast-twitch muscle. *The Journal of Physiology*, 590(15), 3575-3583.
- Holloszy, J. O. (1967). Biochemical adaptations in muscle: effects of exercise on mitochondrial oxygen uptake and respiratory enzyme activity in skeletal muscle. *Journal of Biological Chemistry*, 242(9), 2278-2282.
- Hoon, M. W., Johnson, N. A., Chapman, P. G., & Burke, L. M. (2013). The effect of nitrate supplementation on exercise performance in healthy individuals: A systematic review and meta-analysis. *International Journal of Sport Nutrition and Exercise Metabolism*, 23(5), 522-532.
- Hoon, M. W., Fornusek, C., Chapman, P. G., & Johnson, N. A. (2015). The effect of nitrate supplementation on muscle contraction in healthy adults. *European Journal of Sport Science*, 15(8), 712-719.
- Jones, A. M. (2014). Dietary nitrate supplementation and exercise performance. *Sports Medicine*, 44 (1), 35-45.
- Larsen, F. J., Schiffer, T. A., Borniquel, S., Sahlin, K., Ekblom, B., Lundberg, J. O., & Weitzberg, E. (2011). Dietary inorganic nitrate improves mitochondrial efficiency in humans. *Cell Metabolism*, 13(2), 149-159.
- Lee-Young, R. S., Griffiee, S. R., Lynes, S. E., Bracy, D. P., Ayala, J. E., McGuinness, O. P., & Wasserman, D. H. (2009). Skeletal muscle AMP-activated protein kinase is essential for the metabolic response to exercise in vivo. *Journal of Biological Chemistry*, 284(36), 23925-23934.
- Lira, V. A., Soltow, Q. A., Long, J. H., Betters, J. L., Sellman, J. E., & Criswell, D. S. (2007). Nitric oxide increases GLUT4 expression and regulates AMPK signaling in skeletal muscle. *American Journal of Physiology-Endocrinology and Metabolism*, 293(4), 1062-68.
- Macuh, M., & Knap, B. (2021). Effects of nitrate supplementation on exercise performance in humans: A narrative review. *Nutrients*, 13(9), 3183.
- Maughan, R.J. (2018). IOC medical and scientific commission reviews its position on the use of dietary supplements by elite athletes. *British Journal of Sports Medicine*, 52(7), 418-419.
- Nisoli, E., Clementi, E., Paolucci, C., Cozzi, V., Tonello, C., Sciorati, C., Bracale, R., Valerio, A., Francolini, M., Moncada, S., & Carruba, M. O. (2003). Mitochondrial biogenesis in mammals: the role of endogenous nitric oxide. *Science*, 299(5608), 896-899.
- Nisoli, E., Tonello, C., Cardile, A., Cozzi, V., Bracale, R., Tedesco, L., ... & Carruba, M. O. (2005). Calorie restriction promotes mitochondrial biogenesis by inducing the expression of eNOS. *Science*, 310(5746), 314-317.
- Senefeld, J. W., Wiggins, C. C., Regimbal, R. J., Dominelli, P. B., Baker, S. E., & Joyner, M. J. (2020). Ergogenic effect of nitrate supplementation: A systematic review and meta-analysis. *Medicine and Science in Sports and Exercise*, 52(10), 2250-2261.
- Stamler, J. S., & Meissner, G. (2001). Physiology of nitric oxide in skeletal muscle. *Physiological Reviews*, 81(1), 209-237.

- Sylow, L., Kleinert, M., Richter, E. A., & Jensen, T. E. (2017). Exercise-stimulated glucose uptake - regulation and implications for glycaemic control. *Nature reviews. Endocrinology*, *13*(3), 133–148.
- Westerblad, H., Allen, D. G., Bruton, J. D., Andrade, F. H., & Lännergren, J. (1998). Mechanisms underlying the reduction of isometric force in skeletal muscle fatigue. *Acta Physiologica Scandinavica*, *162*(3), 253-260.

Author Information

Cemre Didem Eyipinar
Gaziantep University
Gaziantep University Sport Sciences Faculty Şehitkamil/
Gaziantep/Türkiye
Contact e-mail: cemreeyipinar@gantep.edu.tr

To cite this article:

Eyipinar, C. D. (2023). The effect of nitrate supplementation on sportive performance. *The Eurasia Proceedings of Health, Environment and Life Sciences (EPHELS)*, *12*, 22-26.