IRONMAN WORLD CHAMPIONSHIP MEDICAL SYMPOSIUM

Nitrate and Ketone Supplements: Do They Work?

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Disclosures

None

Learning Objectives

1) To explain the physiological basis of nitrate and ketone supplementation on exercise responses.

2) To interpret evidence regarding the effect of nitrate and ketone supplementation on endurance performance.

Nitrate and Performance: Potential Mechanisms

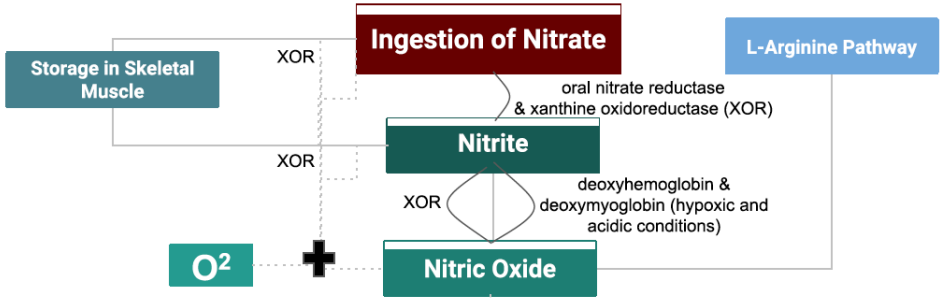


Fig. 1 Possible mechanisms of effect of nitrate on athletic performance

Gao et al. J Int Soc Sport Nutr 2021. doi: 10.1186/s12970-021-00450-4.

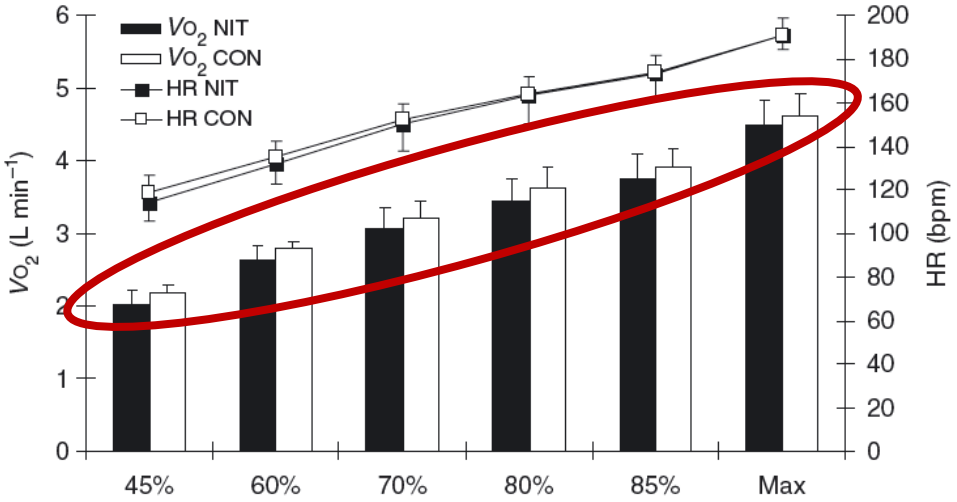
Nitrate Content in Common Vegetables

Nitrate content (mg/100 g fresh weight)	Vegetable varieties
Very low, <20	Artichoke, asparagus, broad bean, eggplant, garlic, onion, green bean, mushroom, pea, pepper, potato, summer squash, sweet potato, tomato, watermelon
Low, 20 to <50	Broccoli, carrot, cauliflower, cucumber, pumpkin, chicory
Middle, 50 to <100	Cabbage, dill, turnip, savoy cabbage
High, 100 to <250	Celeriac, Chinese cabbage, endive, fennel, kohlrabi, leek, parsley
Very high, >250	Celery, cress, chervil, lettuce, red beetroot, spinach, rocket (rucola)

Hord et al. Am J Clin Nutr 2009. doi: 10.3945/ajcn.2008.27131 (Image: Pixabay)

Effects of dietary nitrate on oxygen cost during exercise

N **= 9 trained men ingested a placebo or 0.1 mmol/kg/d of sodium nitrate for 3 d (equivalent to amount found in 150-250 g of nitrate-rich vegetables)**



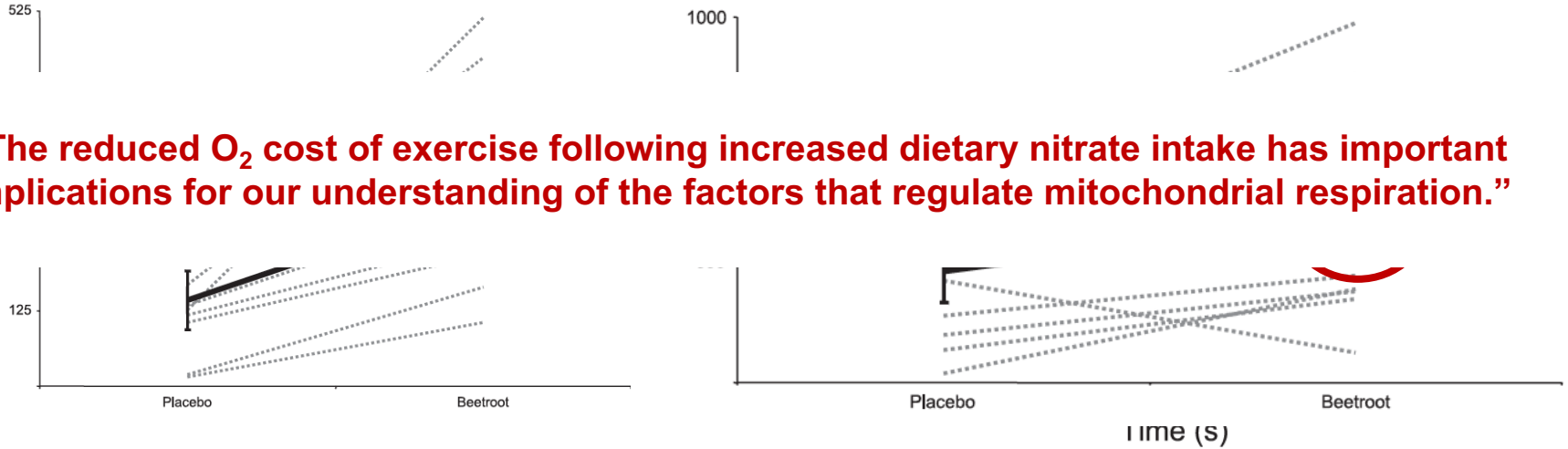
"our findings show a lower oxygen cost during submaximal work after dietary supplementation with nitrate…

(suggesting) energy production had become more efficient."

Larsen et al. Acta Physiol 2007. doi: 10.1111/j.1748-1716.2007.01713.x.

Dietary nitrate supplementation reduces the O_2 cost of low-intensity exercise and enhances tolerance to high-intensity exercise in humans

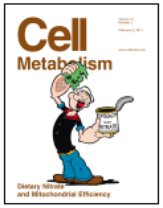
***N* = 8 active men ingested 500 ml/d of beetroot juice or blackcurrent as placebo for 6 d**



"The reduced O_2 cost of exercise following increased dietary nitrate intake has important implications for our understanding of the factors that regulate mitochondrial respiration."

Bailey et al. J Appl Physiol 2009. doi:10.1152/japplphysiol.00722.2009.

Dietary Inorganic Nitrate Improves Mitochondrial Efficiency in Humans



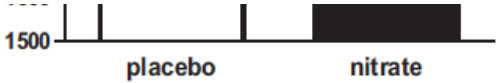
***N* = 14 young adults ingested sodium nitrate (0.1 mmol/kg/d) or placebo for 3 d**

P/O ratio

Whole body VO_2

Watt / VO_2

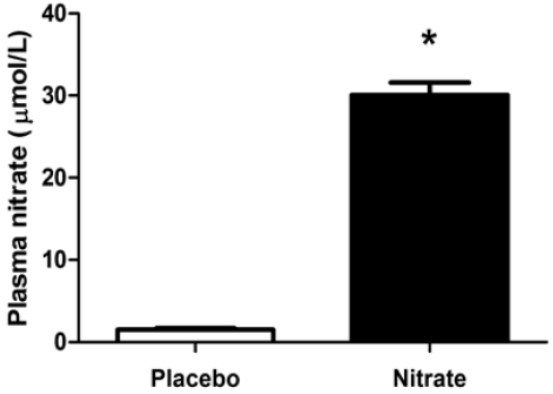
"Dietary nitrate has profound effects on basal human mitochondrial function (and) whole-body oxygen consumption during exercise."

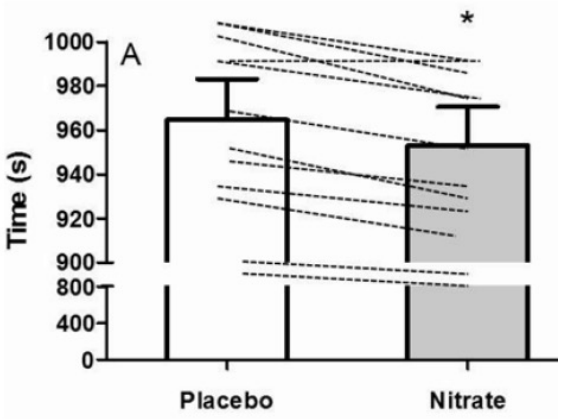


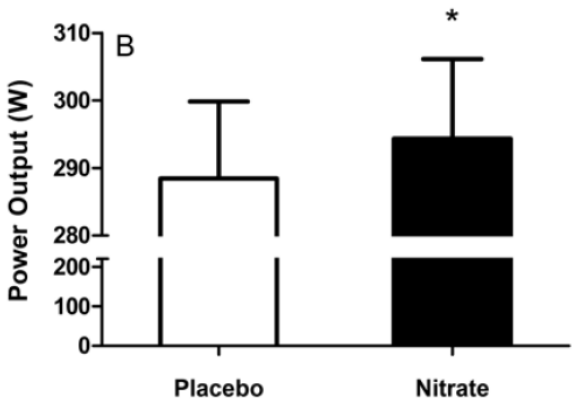
Larsen et al. Cell Metab 2011. doi: 10.1016/j.cmet.2011.01.004.

Nitrate Supplementation's Improvement of 10-km Time-Trial Performance in Trained Cyclists

N **= 12 male cyclists (~58 ml/kg/min) ingested concentrated beetroot juice ("Beet It") or a depleted placebo for 6 d in a double-blind, crossover design 14-d washout)**







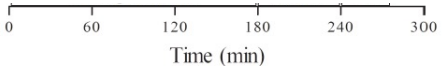
"Six days of nitrate supplementation reduced VO_2 during submaximal exercise and improved time-trial performance in trained cyclists."

Cermak et al. Int J Sport Nutr Exerc Metab. 2012. doi: 10.1123/ijsnem.22.1.64.

No Effect of Acute and 6-Day Nitrate Supplementation on VO_2 and Time-Trial Performance in Highly Trained Cyclists

***N* = 17 highly trained men (~65 ml/kg/min) ingested ~1 g/d of sodium nitrate for 1 or 6 d or a placebo in a double-blind, crossover design**

"Physiological changes (in highly-trained individuals) are believed to account for the attenuated response to elevations in NO-bioavailability in elite athletes."



Nyakayiru et al. Int J Sport Nutr Exerc Metab. 2017. doi: 10.1123/ijsnem.2016-0034.

The effects of dietary nitrate supplementation on endurance exercise performance and cardiorespiratory measures in healthy adults: a systematic review and meta-analysis

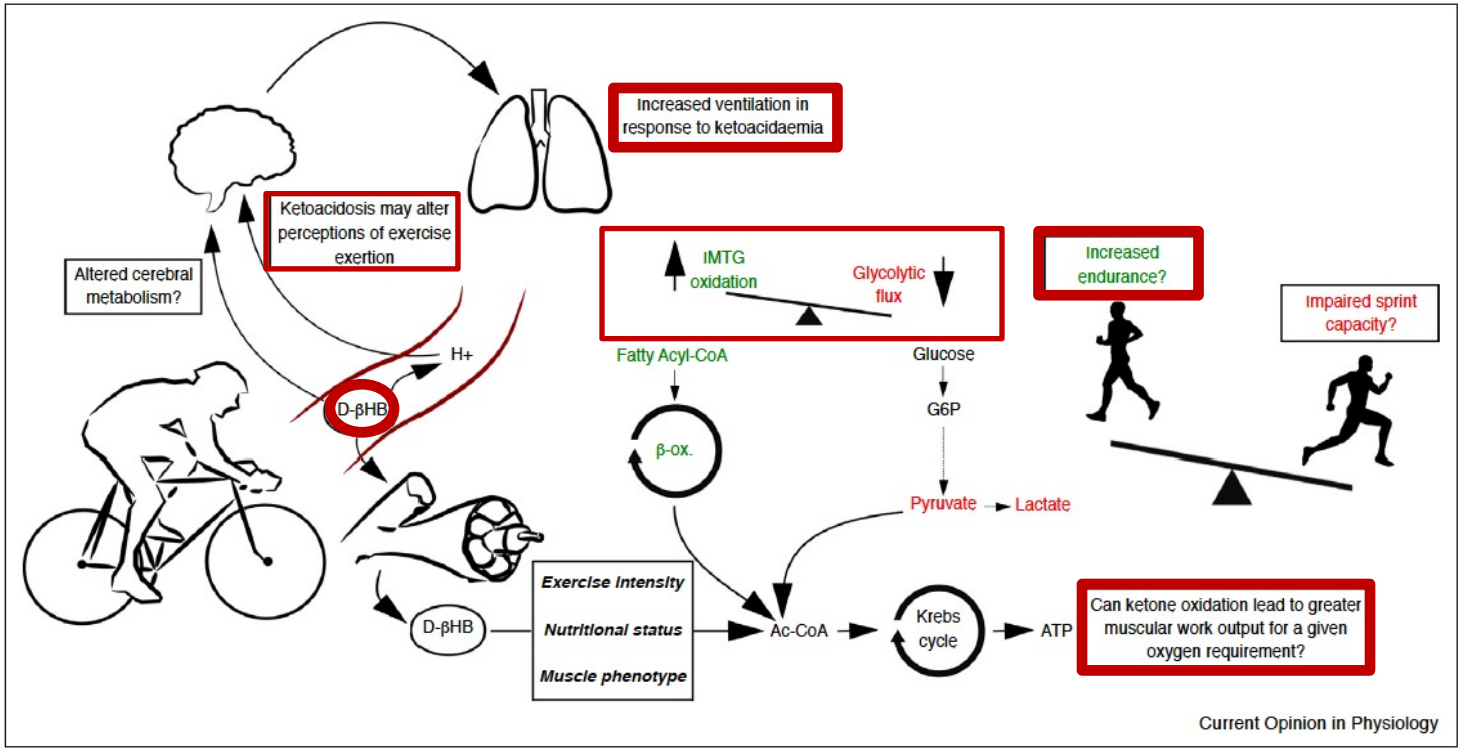
"Dietary nitrate supplementation improves performance during endurance sports (and) outcomes, such as power output, time to exhaustion, and distance travelled."

Effect of dietary nitrate on human muscle power: a systematic review and individual participant data meta-analysis

"Acute or chronic dietary NO_3^- intake significantly increases maximal muscle power in humans (which) is sufficient to have important practical and clinical implications."

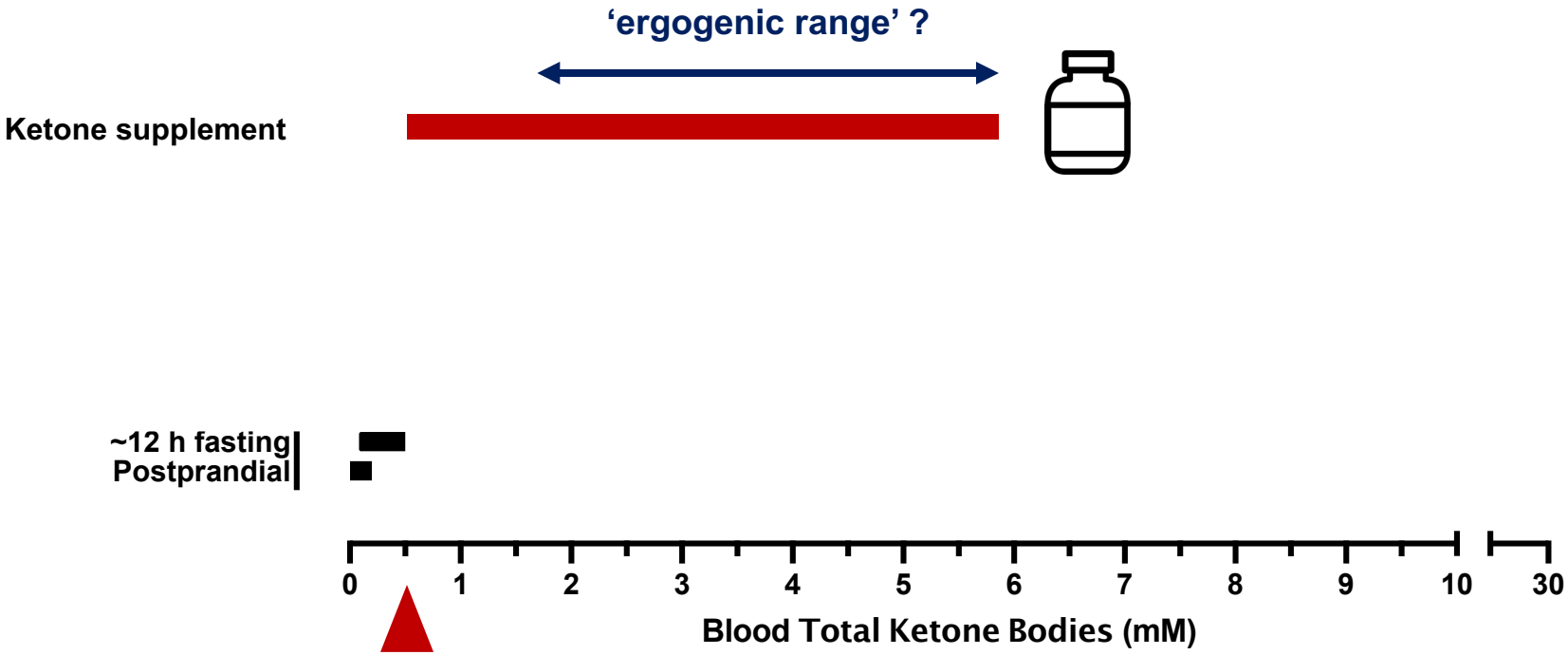
Gao et al. J Int Soc Sport Nutr 2021. doi: 10.1186/s12970-021-00450-4 (top);
Coggan et al. J Int Soc Sport Nutr 2021. doi: 10.1186/s12970-021-00463-z (bottom).

Ketones and Performance: Potential Mechanisms



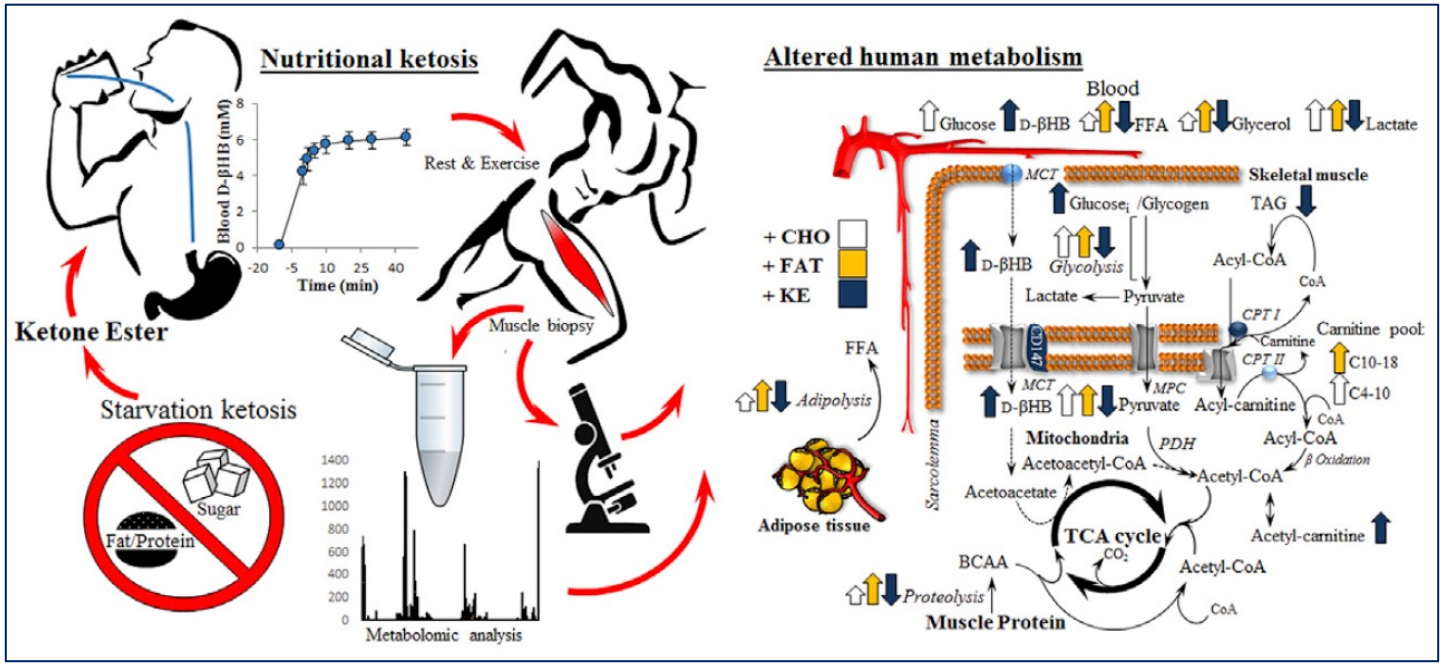
Dearlove et al. 2019. doi: 10.1016/j.cophys.2019.04.010.

Nutritional Ketosis: Dietary Strategies



Modified from: Evans et al. 2017. doi: 10.1113/JP273185; Stubbs et al. 2018 doi: 10.3389/fphys.2018.00279.

Nutritional Ketosis Alters Fuel Preference and Thereby Endurance Performance in Athletes

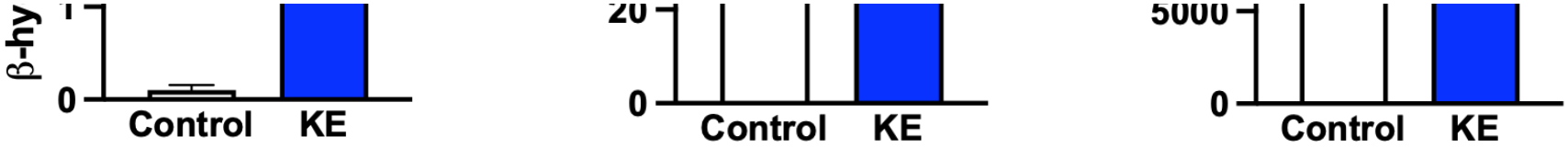


Cox et al. Cell Metab. 2016. doi: 10.1016/j.cmet.2016.07.010.

Nutritional Ketosis Alters Fuel Preference and Thereby Endurance Performance in Athletes

Endurance trained adults ingested ~0.6 g/kg ketone monoester or placebo (*N* = 6-10)

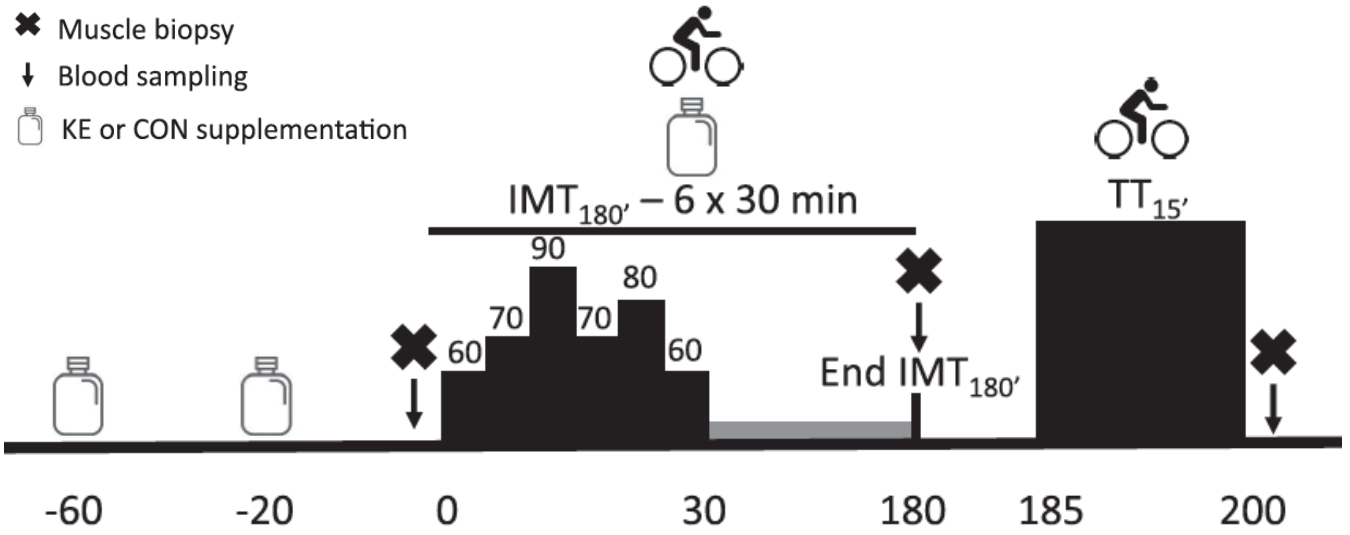
"we show how a nutritional source of ketone bodies alters conventional muscle fuel metabolism and physical performance (during) endurance exercise."



Cox et al. Cell Metab. 2016. doi: 10.1016/j.cmet.2016.07.010.

Exogenous ketosis impacts neither performance nor muscle glycogen breakdown in prolonged endurance exercise

***N* = 12 male cyclists ingested carbohydrate + ~60 g of ketone monoester or placebo**



Poffé et al. J Appl Physiol. 2020. doi: 10.1152/japplphysiol.00092.2020.

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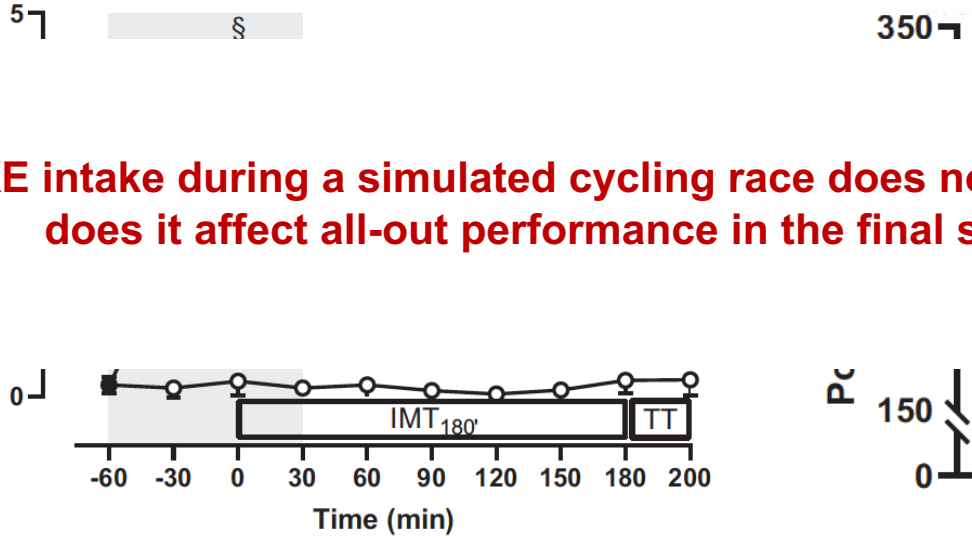


"KE intake during a simulated cycling race does not cause glycogen sparing, nor does it affect all-out performance in the final stage of a simulated race."

Poffé et al. J Appl Physiol. 2020. doi: 10.1152/japplphysiol.00092.2020.

Increased cardiorespiratory stress during submaximal cycling after ketone monoester ingestion in endurance-trained adults

***N* = 19 trained adults ingested 0.6 g/kg ketone monoester or placebo**

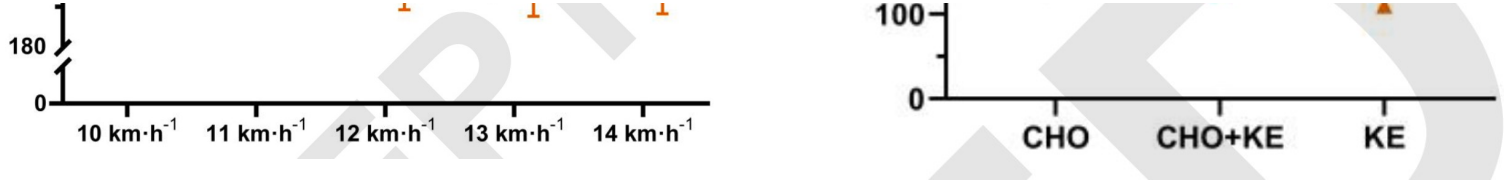
"These findings… may be related to the relatively large bolus dose of KE ingested and specific to the exercise conditions studied."

McCarthy et al. Appl Physiol Nutr Metab 2021. doi: 10.1139/apnm-2020-0999.

Acute Ingestion of a Ketone Monoester without Co-Ingestion of Carbohydrate Improves Running Economy in Male Endurance Runners

***N* = 11 male distance runners ingested 10% CHO and/or ~0.75 g/kg ketone monoester**

"Acute ingestion of a ketone monoester without carbohydrate, but not when co-ingested with carbohydrate, improved RE (but) did not alter TTE in a short duration ramp test."



Brady & Egan. Med Sci Sports Exerc 2023 (online ahead of print). doi: 10.1249/MSS.0000000000003278.

Utility of Ketone Supplementation to Enhance Physical Performance: A Systematic Review

"Heterogeneity across studies makes it difficult to conclude any benefit or detriment to consuming ketone supplements on physical performance."

Acute Ingestion of Ketone Monoesters and Precursors Do Not Enhance Endurance Exercise Performance: A Systematic Review and Meta-Analysis

"Acute ingestion of exogenous ketone precursors and monoesters do not significantly improve endurance exercise performance…

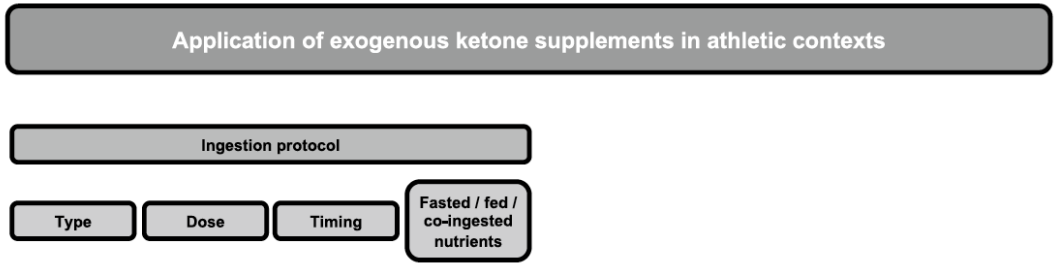
"Future studies may consider making trials more applicable to real-life competition."

Margolis & O'Fallon Adv Nutr 2020. doi: 10.1093/advances/nmz104 (top);
Brooks et al. Int J Sport Nutr Exerc Metab 2022. doi: 10.1123/ijsnem.2021-0280 (bottom).

Acute Ketone Monoester Supplementation Impairs 20-min Time-Trial Performance in Trained Cyclists: A Randomized, Crossover Trial

McCarthy et al. Int J Sports Nutr Exerc Metab 2023. doi: 10.1123/ijsnem.2022-0255.

Ketones and Performance: Relevant Considerations



Evans et al. Sports Med 2022. doi: 10.1007/s40279-022-01756-2.

Take Home Points

1) Dietary nitrate ingestion mainly as beetroot juice can enhance power output with practical relevance for endurance performance.

2) Nutritional ketosis elicited through acute ketone supplementation does not appear to enhance endurance performance.

3) Context is key when assessing supplement efficacy — including ingestion protocol, athlete profile, and event characteristics.

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Thank you!

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