Beetroot juice & nitrate health benefits: clinical trials scientific review

1 BLOOD PRESSURE

More than 10 clinical studies have been carried out on nitrate and blood pressure since 2006. Most of them concern nitrates naturally contained in beetroot juice. These studies have provided some evidence for a 'nitrate-nitrite-NO' pathway.
Kapil *et al*. in 2010 demonstrated a dose dependent reduction in BP (with 4, 12 and 24 mmol nitrate) equivalent to beetroot juice nitrate [34]. This study also demonstrated that the peak increase in plasma nitrite at ~3 h was associated with a significant increase in cGMP, the most sensitive indicator of NO bioactivity [35], thus providing evidence of bioactive NO generation from nitrite.
The Kapil *et al*. study also provided a clue to the heterogeneity of blood pressure responses to dietary nitrate: strong inverse correlations were demonstrated between the peak decrease in BP and the baseline BP (both systolic and diastolic). This therefore holds promise that dietary nitrate should be more effective in reducing blood pressure when it is needed, i.e. in people with high normal BP or hypertension. Similarly, dietary nitrate would appear not to induce unwanted hypotension in people with low normal BP.

Nitrate clinical studies have been designed with one acute daily dose or have been prolonged during several days: Cf Sobko *et al*. which showed a sustained reduction in diastolic BP of ~4.5 mmHg over 10 days [36], and the study of Vanhatalo *et al*., which showed a reduction in BP of ~7/5 mmHg following 15 days' supplementation with 500 ml beetroot juice [37].
Studies showing effects of dietary nitrate include other forms such as spinach [38,39], and very recently with red and white beetroot-enriched bread [40].

In 2013 and 2014, new studies on hypertensive people have been carried out and has confirmed the hypothesis that dietary nitrate are more effective when it is needed:

- Ghosh and colleagues [41] studied the effects of increased systemic plasma NO_2^- levels in 15 drug naïve grade 1 hypertensives. Using dietary NO_3^- doses of approximately 3.5 mmol, the group found that NO_2^- levels were elevated by ~1.5 fold. The dose caused substantial reduction to SBP (~12 mmHg). They effectively demonstrated that NO_3^- supplementation was indeed an effective, low-cost approach to the treatment of hypertension. [42]
- In 2014, Pr Ahluwalia launched a double-blind phase 2 clinical trial with a daily beetroot juice dose of 250 ml during 4 weeks on 64 patients: average decrease in blood pressure of about 8/4 mm Hg. Considering that the average reduction in blood pressure through a single hypertensive drug is 9/5 mmHg, these findings suggest a role for dietary nitrate as an effective, easy and affordable treatment in managing blood pressure with similar results to drug treatment. [43]

Of note, 5 mm Hg decrease is significantly associated with decreased cardiovascular morbidity and mortality, whereas a comparable increase was associated with the opposite effect. [11]

Summary of main clinical trials on Blood Pressure are summarized in Table 4.

Table 4: Effect of dietary nitrate on BP in humans studies (completed from Lidder 2013) [30]:

Study	population	Source	Nitrate dose (mmol)	Nitrate dose (mg)	Peak SBP (mm Hg) (time)	Peak (mm Hg) (time)
Larsen *et al.* (2006) [44]	healthy	Sodium nitrate **3 days**	~7	434		– -3.7
Webb *et al.* (2008) [45]	healthy	Beetroot juice 500 ml x 1	22.5	1395	-10.4 (2.5–3 h)	-8
Kapil *et al.* (2010) [34]	healthy	Potassium nitrate	24 12 4	1488 744 248	-9.4 (6 h) -6 (2,25 h) -2.5 (1,75 h)	- 6 (2,75 h) - 4,5 (3 h) - 4,5 (2,25 h)
Kapil *et al.* (2010) [34]	healthy	Beetroot juice 250 ml x 1	5.5	341	-5.4	
Sobko *et al.* (2010) [36]	healthy	Japanese Traditional Diet **10 days**	~18	1116		-4.5
Vanhatalo *et al.* (2010) [37]	healthy	Beetroot juice (500 ml) **15 days**	5.2	322	-7	-5
Bahra *et al.* (2012) [46]	healthy	Potassium nitrate x 1	8	496	-5	
Bondonno *et al.* (2012) [38]	healthy	Spinach (200 g)	3	186	-2.7	
Hobbs *et al.* (2012) [40]	healthy	Beetroot juice (100, 250, 500 ml)	2.3 5.7 11.4	143 353 707	-13.1 (2–3 h) -20.5 (2–3 h) -22.2 (2–3 h)	-16.6 (2–3 h) -14.6 (2–3 h) -18.3 (2–3 h)
Hobbs *et al.* (2012) [40]	healthy	Beetroot-enriched bread (100 g)	1.8 1.6	112 99	-16.5 (2–3 h) -19.3 (2–3 h)	-23.2 (2–3 h) -23.6 (2–3 h)
Wylie *et al.* (2013) [52]	healthy	Beetroot juice (70,140,280 ml)	4.2 8.4 16.8		-4 (1 h) -8 (4 h) -9 (2 h)	-1.5 (1 h) - 3 (4 h) -4 (2 h)
Ghosh et al (2013) [41]	Hypertensive people	Beetroot juice 250 ml	3.5	217	-12	
Kapil et al, 2015 [43]	64 Hypertensive people	Beetroot juice 250 ml **4 weeks**	5.5	396	-8	-4

On healthy people, a daily dose of beetroot juice (250-500 ml) containing 320-340 mg of nitrate allows a significant systolic blood pressure decrease (-5,4 to -7 mm Hg). Potassium nitrate seems to be less effective (around 500 mg of nitrate needed to reach a SBP decrease of – 5 mm Hg).

Hobbs study results are difficult to interpret because they don't fit with others studies.

Inconclusive clinical studies:

In opposition to the above findings, **Murphy** and colleagues failed to note a decrease in SBP or DBP in response to BR ingestion. However, the authors concluded that this was likely due to the blood pressure measurements taken **within 1 h of whole BR ingestion**. [48]

Is nitrate the unique compound of BRJ implicated in blood pressure decreasing?

We may hypothesize that other compounds like potassium and betaine have a synergistic role.

2 NITRATE & ENDOTHELIUM DYSFUNCTION

Hypertension, diabetes, dyslipidemia, smoking and ageing are strong risk factors contributing towards atherogenesis and are associated with impaired endothelial function, a key step in the pathogenesis of atherosclerosis and a surrogate marker. Such endothelial dysfunction usually results, at least in part, from decreased NO production from endothelial NOS and/or reduced NO bioavailability (as seen with ageing), which both result in, and are further diminished by inflammation.
Plasma nitrite concentration has been shown to reflect constitutive NOS activity in mammals and is inversely correlated with the number of cardiovascular risk factors, and positively correlated with endothelial function as assessed by flow mediated dilatation (FMD) in humans. Also, changes in nitrite (nitrite reserve) with reactive hyperaemia during FMD also reflected endothelial function. Hence, it may be anticipated that provision of dietary nitrate/nitrite may enhance endothelial function and suppress microvascular inflammation. Indeed, this was demonstrated in a hypercholesterolaemia model by Stokes *et al.*.
Whilst inorganic nitrate/nitrite has the potential to improve endothelial dysfunction in patients, Bahra *et al.* [46] found no effect in healthy volunteers with normal endothelial function. FMD was not altered at 3 h following the ingestion of dietary nitrate (8 mmol). However, a reduction in pulse wave velocity of ~0.3 m s-1 accompanied the reduction in SBP of ~5 mmHg. Bondonno *et al.*, (2012) found a small increase in mean FMD over 4 min of ~0.5% in 30 healthy volunteers following ingestion of 200 mg spinach, but this was not as great as flavanoid-rich apple (~1.1%) or apple and spinach (~0.9%) suggesting a potentially greater effect of flavanoids on eNOS function than nitrate in the context of normal endothelial function in healthy volunteers.
It is likely that provision of nitrate/nitrite enhances NO bioavailability predominantly by inhibiting inflammation and inactivating reactive oxygen species (ROS), in addition to providing a source of NO per se, rather than by enhancing eNOS.[39]

Endothelial dysfunction was earlier thought to be attributed mostly to decreased production of NO either due to decreased activity of eNOS or to a deficiency in the availability of L-arginine. However, recent evidence suggests that impaired endothelium-dependent relaxation is associated with increased rather than decreased expression of eNOS in vasculature. eNOS can also catalyse superoxide formation in a reaction which is primarily regulated by cofactor tetrahydrobiopterin rather than L-arginine. Thus, it seems that for normal endothelial function the balance between NO and superoxide anion is more important than the absolute levels of either alone. [49]

Is nitrate the unique compound of BRJ implicated in endothelium function?

Again, we can hypothesize than betaine, besides nitrate, through its role on homocysteine contribute to improvement of endothelium function.

3 NITRATE & EXERCISE PERFORMANCE

21 randomized double-blind crossover human clinical studies lend beetroot juice conclusive supports to sport performance since 2009. Only 4 on 25 have been inconclusive.

3.1 Mecanistic approach

The main implicated mechanisms are based on the physiological role of nitrates:

- NO is a powerful vasodilatator, which increases oxygen delivery to muscle
- a better mitochondrial efficiency, that means a reduction of O_2 cost of mitochondrial ATP re-synthesis: an elevation in NO_2/NO may increase the P/O ratio through the potential role for NO_2 as an alternative electron acceptor of the mitochondrial electron transport chain (instead of O_2) [16].

However, authors of clinical studies have completed the mechanistic approach explaining the ergogenic effect of beetroot juice:

- a reduced ATP cost of muscle force production, linked to an inhibition of the actomyosin ATPase and the Ca^{2+} ATPase :
  The ATP cost of contraction in skeletal myocytes is essentially the sum of ATP consumption via the interaction between actin and myosin (actomyosin-ATPase) and calcium (Ca^{2+}) pumping in the sarcoplasmic reticulum (Ca^{2+}-ATPase), with membrane depolarization (Na-K-ATPase) making a further small contribution to the total ATP turn- over. NO has been demonstrated to slow cross-bridge cycling kinetics, reduce ryanodine activity, and therefore Ca^{2+} release and inhibit Ca^{2+} -ATPase activity, and NO may therefore have a regulatory influence on the ATP cost of force production. [17]
- a better glucose mobilization: a NO-mediated increase in myocyte glucose uptake, particularly in the case of intermittent effort [47]
- reduced O_2 cost of exercise is not compensated by an elevation in anaerobic metabolism:
  Bailey in 2010 demonstrated that the calculated muscle ATP total was significantly reduced with NO_3^- supplementation as a consequence of a reduced ATP_{Ox} and ATP_{PCr} : BR attenuated the reduction in muscle phosphocreatine concentration (a marker of anaerobic energetic pathway) [17]

Results of clinical studies are a combination of all these synergistic pathways.

3.2 Clinical studies findings

Clinical studies findings has been the followings:

- an exercise O2 cost reduction ($V0_2$ ⇲), particularly high for submaximal (low to moderate) effort [50,17,37,65,52,53,54,55,56]
- a decrease of the O_2 debt (measured mainly by deoxyhemoglobin level) and anaerobic metabolism (Phosphocreatin level) , which allows a better recovery after sport [50,17,56,57]
- an increase of exercise performance (significant increase of time-to-exhaustion of 7-22%, of distance, etc...) for cycling, knee extension, running, intermittent team-sport, rowing, swimming [50,51,58,52,55,56,57,47,59,60,18,61,62]
- for athletic and/or intense effort : an increase of VO_2 may happen instead of a 0_2 cost reduction. It nevertheless leads to a performance increase. According to Breese *et al.* 2013,

type II muscle fiber recruited preferentially than type I during intense effort have a high O_2 demand which is difficult to match: BRJ improve the local matching of O_2 delivery [47,18]

These findings linked to beetroot supplementation appear to be dose-dependent: Wylie in 2013 and Hoon in 2014 have demonstrated that an acute dose of 240-260 mg of nitrate from BRJ is not sufficient. Additionally, it appears that no additional benefit is gained from doses larger than ~8–9 mmol (around 560 mg of nitrate). [52][64]
These effects were observed after either a single bolus (2-3 h prior to exercise) or a long-term (2-15 days) supplementation, but effects seems to be more efficient after long-term ingestion (approximately 6 days). Vanhatalo in 2010 has lead the unique clinical study comparing both supplementation types. Specific mechanistic explanation is a mitochondrial biogenesis: a sustained exposure of mammalian cells to NO over 6 days has been shown to induce mitochondrial biogenesis through cGMP-dependent pathways [37][63]

These findings suggest that daily doses in the 5–9 mmol of nitrate (equivalent to 310-560 mg) range tend to be most beneficial for those seeking improvement to exercise performance, preferably during 6 days.

To be noted: 4 clinical studies on 25 were not conclusive:
- 3 of them concern well-trained men
- another one was based on a low nitrate dose: 240 mg

3.3 Benefits illustration through some key clinical trials

ON ACTIVE PEOPLE, 6 days:

Bailey and colleagues, from Exeter University (UK), were pioneers in 2009 with the first clinical study on beetroot juice and sport performance:
- Bailey *& al*, 2009: randomized double-blind crossover clinical study on 8 men. Cycle ergometer at moderate and severe work rates. Daily dose of 341 mg nitrate from 500 ml beetroot juice during 6 days [50]
- Bailey *& al*, 2010: randomized double-blind crossover clinical study on 7 men. Knee-extension at low and high intensity. Daily dose of 316 mg nitrate from 500 ml beetroot juice during 6 days [17]

Principal findings: significant difference versus placebo in percentage:

		VO_2 (O_2 cost)	Phosphocreatin (anaerobic metabolism)	Deoxyhemoglobin (O_2 debt)	Exercise tolerance (time to exhaustion)
Moderate work rates	Cycling	-19%	-36%	-13%	+14%
	Knee-extension	-25%	NA	NA	*Not significant*
High work rates	Cycling	NA	- 59%	*Not significant*	+17%
	Knee-extension	-21%	NA	NA	+25%

NA: not analyzed

ON SUBELITES PEOPLE, 1 day:

Lansley in 2011 [51], still belonging to the Exeter University, evaluated beetroot nitrates benefit on subelites cyclists. This was the first study to investigate the effects of dietary nitrate supplementation on athletic performance.

Study design: randomized double-blind crossover clinical study on 9 competitive male. Cycling: 4 km and 16,1 km time-trials. One acute dose of 384 mg nitrate in 500 ml of beetroot (BR) juice

Plasma [nitrite] was significantly increased 2.5 h after BRJ supplementation (+138%), and systolic blood pressure was reduced (125 mm Hg versus placebo 131 mm Hg), consistent with an increased NO bioavailability.

BR ingestion resulted in greater cycling Power Output (PO increase: +4,6% for 4,1 km and + 6% for 16 km) with no change in VO_2. As a consequence, Beetroot juice improved 4 km performance by 2,8% (6,27 min versus 6,45 min) and 16,1 km performance by 2,7% (26,9 min versus 27,7 min).

3.4 Systematic review

The following table presents the systematic literature review of nitrate supplementation and sport performance, between 2007 and 2014.

[64] [65] [66] [67] [68] [69] [70] [71] [72] [73]

Legend : Trained participants / Inconclusive study

	Study design	Participants	Exercise test	NO_3^- dose (mmol/ day)	NO_3^- dose (mg/day)	Nitrate source	BRJ nitrate concentration (ppm)	Acute dose	Long-term dose	Time of ingestion	Change in plasmatic NO_2^-	Nitrate group results on exercise performance
Larsen 2007	randomized, double-blind crossover	9 well-trained men	cycle ergometer: maximal incremental test	7	434	Na NO3			2 x 3 days		+ 82%	↘ VO2 *(-5,3%)* only for submaximal efforts + increased gross efficiency (work rate/Energy Expenditure) = +6,6%
Larsen 2010	randomized, double-blind crossover	7 male and 2 female	(combined arm and legs) cycle ergometer	7	434	Na NO3			2 days		+ 133%	↘ VO2 (-5,5%) and ↘ VO2max (-2,7%) ↗ time to exhaustion (+6,9%)
Bayley 2009	double-blind, placebo-controlled crossover	8 men	cycle ergometer: at moderate (<VT) and severe (>VT) work rates	5,5	341	500 ml BRJ	682		4-6 days			moderate work rates: ↘HHb (muscle deoxy-hemoglobin /index of O_2 extraction) and VO_2 (-19%) severe work rate : ↘ $V0_2$ kinetics & ↗ time to exhaustion (+14 %)
Bayley 2010	randomized, double-blind crossover	7 active males	knee extension	5,1	316	500 ml BRJ	632		6 days			low intensity : ↘VO_2 (-25%) low and high intensity: PCr degradation reduction (-36%) and (-59%), and reduced muscle ATP turnover rate (-35%)
Vanhatalo 2010	balanced, randomized croosover	8 healthy moderately fit men and women	cycle ergometer : 2×5-min at 90% VT and a maximal test	5,2	322	500 ml BRJ	645	x	5 days and 15 days	2,5 h pre-exercise	+ 36 %	O_2 cost reduced for acute and long-term supplementation (around 4%). $\dot{V}O_2$max **increased** after 15 days of supplementation
Vanhatalo 2011	randomized, double-blind crossover	9 moderately trained men and women	knee extension in normoxia and hypoxia	9,3	577	750 ml BRJ	769	x		24 h prior to hypoxia trials	+ 50%	in hypoxia : ↗time to exhaustion, ↘ PCr beakdown, ↘ (faster) PCr recovery time
Lansley 2011	randomized, double-blind crossover. Placebo NO3-depleted beetroot	9 physically active men	Walking and running at moderate (<VT) and severe (>VT) exercise intensities	6,2	384	500 ml BRJ	769		6 days		+ 104%	↘ VO_2 at walking (-12%), at moderate-intensity (-7%) and at high intensity running (-7%); ↗VO_2 primary amplitude at moderate intensity; ↗ time to exhaustion (+15%); nevetheless, no change in mitochondrial oxydative capacity (expected) and PCr and pH

	Study design	Participants	Exercise test	NO_3^- dose (mmol/ day)	NO_3^- dose (mg/day)	Nitrate source	BRJ nitrate concentration (ppm)	Acute dose	Long-term dose	Time of ingestion	change in plasmatic NO_2^-	Nitrate group results on exercise performance
Lansley 2011	randomized, double-blind crossover. Placebo NO3-depleted beetroot	9 competitive male cyclists	cycling: 4km and 16.1km time-trials	6,2	384	500 ml BRJ	769	x		2,5 h pre-exercise	39%	→VO2; ↗Power output (4.5%-6%); ↗ work/VO2 (7-11%); ↗ performance (~3.0%)
Bescos 2011		13 male trained cyclists and trialthletes	cycling : 4×6-min at 35%-65% of PPO and a maximal test		533	Na NO3		x	3 hours pre-exercise		+16% (only !)	no significant effect on submaximal O_2 cost, on time to exhaustion, on maximal power, and on blood lactate; VO_2max, however, was significantly reduced by 3.7%.
Bescos 2012	randomized, double-blind crossover	13 male trained cyclists and trialthletes	40-min cycling distance trial		700	Na NO3			2 x 3 days		+79%	no significant effect
Murphy 2012		11 moderately fit men and women	5 km run trial	8	500	baked BR		x		75 min pre-exercise		higher mean velocity (+ 3,2%), and even higher during last 1,8 km (+5%)
Engan 2012	randomized, double-blind crossover	12 trained apneic men and women	serie of incremental apneic exercise	5	310	70 ml BRJ	4429	x		2,5 h		↗ apneic duration (+11%) higher 0_2 saturation in sub-maximal performance
Bond 2012		14 well-trained male rowers	simulated 6 x 500 m rowing with 90 s rest	5,5	341	BRJ	?		6 days			↗ performance by reporting shortened rowing repetition time, particularly 4–6 (-1.7%)
Bond 2013		12 active women	Cycling at 40%, 60%, and 80% of VO2max	12	750	BRJ	?	x		2h pre-exercise	+ 300%	- ↘ VO_2 (22%, 14% and 13% at respectively 40-60-80 % VO_2max) - increased cerebral arterial blood flow velocity and reduced the cerebrovascular resistance (CVR), the rate-pressure product (RPP, an index of myocardial oxygen demand)

	Study design	Participants	Exercise test	NO_3^- dose (mmol/ day)	NO_3^- dose (mg/day)	Nitrate source	BRJ nitrate concentration (ppm)	Acute dose	Long-term dose	Time of ingestion	change in plasmatic NO_2^-	Nitrate group results on exercise performance
Cermak 2012	NO3-depleted BR as PL	12 trained cyclists + triatletes	10 km trial : 2 × 30-min at 45% and 65% of PPO	8	496	2x 70 ml BRJ	3543		6 days	2-5 h pre-exercise		- cycling: steady-state exercise at 45-65% VO_2max: O_2 cost ↘ of 2,5% and 5,4% - 10-km trial: ↘ time (-1,2%) and ↗average power output (2%)
Cermak 2012		20 trained cyclists	1hour time-trial (75% PPO)	8,7	539	2x 70 ml BRJ	3853			2 h pre-exercise	+124%	no significant result
Wylie 2013	randomized, double-blind crossover NO3-depleted BR as PL	10 active males	moderate-intensity and severe-intensity cycle	4,2 (70 ml) 8,4 (140 ml) 16,8 (280 ml)	260 (70 ml) 520 (140 ml) 1040 (280 ml)	up to 4x 70 ml BRJ	3714	x		2,5 h pre-exercise		-lower dose (4,2): no improvement of physiological response to exercise - higher dose 8,2 and 16,8 : ↘ $V0_2$ respectively by 1,7 % and 3% ↗ time to task failure : respectively +14% and +12%.
Wylie 2013	randomized, double-blind crossover NO3-depleted BR as PL	14 recreational team-sport players	intense intermittent Yo-Yo recovery level 1 test	29 mmol (3628 mg NO3/L)	1 798	490 ml BRJ in multiple dose	3669			30 h pre-exercise	+ 400%	• Overall, ↗$[NO_2^-]$ around 400% • However, during the exhaustive test, $[NO_2^-]$ declined by 20% in PL and by 54% in BR relative to the pre-exercise baseline, suggesting that NO_2^- may have served as a substrate for NO production during high-intensity exercise. * exercise performance is 4,2% greater (distance) * mean blood glucose was lower
Christensen 2013		10 elite cyclists	endurance + intense intermittent trials	8	496	500 ml BRJ	992		6 days		+ 300% of nitrate + nitrite	no significant effect

	Study design	Participants	Exercise test	NO_3^- dose (mmol/ day)	NO_3^- dose (mg/day)	Nitrate source	BRJ nitrate concentration (ppm)	Acute dose	Long-term dose	Time of ingestion	change in plasmatic NO_2^-	Nitrate group results on exercise performance
Breese 2013	(PL : NO3 depleted BRJ)	9 healthy men and women	cycling with intermittent exercise simulated competition =Cycling at moderate (<VT) and severe (>VT) exercise intensities	8	496	2 x 70 ml BRJ	3543		6 days		+ 435 %	BRJ group during M--> S exercise (but not for U--> M): speeder pulmonary VO_2 and muscle [HHb] kinetics and increased tolerance to severe intensity exercise (↗ time-to-task failure +22%) Nitrate may induce enhanced matching of 0_2 distribution to contracting skeletal muscle (specifically, type II muscle fibers). summary: Dietary supplementation with NO_3-rich BR juice speeds VO_2 kinetics and enhances exercise tolerance during severe-intensity exercise in recreationally active adults, when initiated from an elevated metabolic rate.
Fulford 2013	randomized, double-blind crossover	8 males	knee-extension	?	?	500 ml BRJ	?		15 days			PCr cost per unit force output was significantly reduced at this end of the exercise.
Muggeridge 2013	randomised, crossover	8 trained male kayakers	60%Wmax all-out sprints 1-km time-trial	5	310	70 ml BRJ	4429	x		3 h pre-exercise	+32%	Despite a reduction in VO_2, BR ingestion have no effect on performance. A smaller elevation in plasma nitrite following a single dose of nitrate and the individual variability in this response may partly account for these findings.
Muggeridge 2014	(PL : NO3 depleted BRJ)	9 trained male cyclists	Altitude: 15 min at 60% Wmax 16.1 km time-trial	5	310	70 ml BRJ	4429	x		3 h pre-exercise	+ 134%	steady state exercise = ↘ O_2 cost of and ↗ time trial performance (+2,9%).

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Thompson 2014		16 moderately fit men	cycle ergometer at 50% and 70% VO2max; All-out trial at 90% VO2max	5	310	BRJ	?	x		2 h pre-exercise	+ 79 %	50 % VO_2peak: trend to reduction VO_2. VO_2peak : ↗ time to exhaustion 16%
Hoon 2014		10 highly trained rowers	simulated 2000 m rowing	4,2 and 8,4	260 et 520	BRJ	?	x		2 h pre-exercise		↗performance at 8,4 mmol but not at 4,2 mmol. metabolism efficiency.
Hoon 2014		26 cyclists	cycle ergometer	4	254	70 ml BRJ	3629	x		150 min or 75 min pre-exercise		inconclusive and even detrimental to high-intensity cycling exercise those performing at a competitive level.
Pinna 2014		14 master swimmers	incremental test	5,5	341	500 ml BRJ	682		6 days		not reported	BRJ improved AEC (aerobic energetic cost =-10%) and workload (+6,3%) at AT (anaerobic threshold)

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