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| **Table 1. Characteristics of 11 included trials** | | | | | | | | | | | | | | | |
| Included trials | Registration | Design | Disease | No. of Participants(T/C) | Age (years) | No. of Male/Female | Disease duration | EF（%） | Administration route | Experimental group | Control group | Intervention duration | Follow-up duration | Outcome index | Adverse events |
| 1. **Four trials in HFrEF** | | | | | | | | | | | | | | | |
| AR Coggan 201525 | NCT01682356 | double-blind, placebo-controlled, randomized crossover | HFrEF | 9 | 57±10 | 5/4 | 10±7 | 28±11 | oral | 140 mL of a concentrated BRJ  supplement (Beet It Sport®, James White Drinks, Ipswich, UK) containing 11.2 mmol of NO3- | the same volume of NO3- depleted BRJ | 2 hours | None | 1. HR during rest and exercise 2. SBP during rest and exercise 3. DBP during rest and exercise | 1 |
| AR Coggan 201821 | none | randomized, double-blind, placebo-controlled, crossover | HFrEF | 8 | 52±5 | 6/2 | 6±3 | 34±2 | oral | 140 mL of a concentrated BRJ  supplement (Beet It Sport®, James White Drinks, Ipswich, UK) containing 11.2 mmol of NO3- | the same volume of NO3- depleted BRJ | 2 hours | None | 1.VO2peak 2.Ve/VCO2 slope 3. RER 4. HR during exercise 5. SBP during exercise 6. DBP during exercise | None |
| DM Hirai 201720 | NCT02401126 | double-blind, randomized crossover | HFrEF | 10 | 63±5 | 10/0 |  | 32±2 | oral | nitrate-rich beetroot juice(70 ml, Beet It Sport; James White Drinks,Ipswich, UK).Each 70-ml bottle of nitrate-rich juice has an average nitrate content of 6.45 mmol (0.4 g) | nitrate-depleted beetroot juice | 9 days | None | 1.VO2 during rest | No event |
| MN Woessner 202026 | ACTRN12615000906550 | randomised, double-blind, crossover design | HFrEF | 16 | 62.6±3.6 | 15/1 |  | 30.4±1.8 | oral | nitrate-rich beetroot juice (210 ml, 16 mmol nitrate)(James White Drinks, Ipswich, UK). | nitrate-depleted placebo (210 ml, <0.1 mmol nitrate) (James White Drinks, Ipswich, UK). | 5 days | None | 1.VO2 peak  2.exercise time  3.SBP during rest  4.DBP during rest | No event |
| 1. **Seven trials in HFpEF** | | | | | | | | | | | | | | | |
| BA Borlaug 201527 | NCT01932606 | double-blind, randomized, placebo-controlled, parallel-group | HFpEF | 14/14 | T69±6  C70±8 | T5/9  C6/8 |  | T65±6  C62±6 | infusion | sodium nitrite (50 μg/kg/min) (Hope Pharmaceuticals, Scottsdale, Arizona) | placebo (normal saline solution) | 15 min | None | 1.VO2 during rest and exercise 2.RA during rest and exercise 3.PA during rest and exercise 4.PCWP during rest and exercise 5.CO during rest and exercise 6.HR during rest and exercise 7.SBP during rest and exercise 8.DBP during rest and exercise | No event |
| BA Borlaug 201628 | NCT02262078 | double-blind, randomized, placebo controlled, parallel-group | HFpEF | 13/13 | T67±9  C72±10 | T7/6  C5/8 |  | T62±4  C62±6 | inhale | nebulized sodium nitrite (90 mg, Mast Therapeutics) administered via the Solo-Idehaler device (Aerogen Galway, Ireland/DTF Saint-Etienne, France) | placebo (inhaled normal saline) | 10min | None | 1.VO2 during rest and exercise 2.RA during rest and exercise 3.PA during rest and exercise 4.PCWP during rest and exercise 5.HR during rest and exercise 6.SBP during rest and exercise | No event |
| BA Borlaug 201829 | NCT02742129 | multicenter, randomized, double-blind, placebo-controlled, crossover | HFpEF | 105 | 68 | 46/59 |  | 61 | inhale | 80-mg ampules of inorganic sodium nitrite (AIR001 Inhalation Solution, Mast Therapeutics Inc, a subsidiary of Savara Pharmaceuticals Inc) | placebo | 4 weeks | None | 1.VO2 peak 2.NT-pro-BNP 3.KCCQ score 4.E/e' ratio 5.SBP during rest 6.DBP during rest 7.exercise time | 11 |
| HA Shaltout 201730 | none | randomized, double-blind, placebo-controlled | HFpEF | 10/9 | T68.0±6.2  C70.6±7.6 | T2/8  C1/8 |  |  | oral | The BRJ(70 ml; Beet It Sport Shot; James White Drinks, Ipswich, UK),contained 0.38 g (6.1 mmol) NO3− | placebo, the NO3− was removed,contained 0.0003 g (4.8 mmole) NO3− | 4 weeks | 1-4 days | 1.exercise time 2.VO2 peak 3.HR during exercise 4.SBP during exercise 5.DBP during exercise 6.RER during exercise 7.E/A ratio 8.E/e' ratio | No event |
| J Eggebeen 201631 | none | double-blinded,randomized crossover design | HFpEF | 20 | 69.0±6.8 | 3/17 |  |  | oral | The BRJ(70 ml; Beet It Sport Shot; James White Drinks, Ipswich, UK),contained 0.38 g (6.1 mmol) NO3− | placebo, the NO3− was removed,contained 0.0003 g (4.8 mmole) NO3− | 7-9 days | None | 1.exercise time 2.VO2 peak 3.HR during exercise 4.SBP during exercise 5.DBP during exercise 6.RER | No event |
| P Zamani 201532 | NCT01919177 | randomized, double-blind, crossover | HFpEF | 17 | 65.5±8.9 | 15/2 |  | 63.5±8.6 | oral | nitrate-rich beetroot juice (NO3−, BEET IT Sport, James White Drinks Ltd., Ipswich, UK) containing 12.9 mmoles of NO3− in 140 mL | identical nitrate-depleted placebo (PB, James White Drinks, LTD., Ipswich, UK) | 6 hours | None | 1.exercise time 2.VO2 peak 3.RER 4.Ve/VCO2 slope 5.HR during rest and exercise 6.CO during rest and exercise | No event |
| P Zamani 201733 | [NCT02256345](https://clinicaltrials.gov/ct2/show/NCT02256345" \o "https://clinicaltrials.gov/ct2/show/NCT02256345) | randomized, double-blind, crossover | HFpEF | 9 | 62.4±5.5 | 3/6 |  | 65.84±7.74 | oral | KNO3 given in two dosing regimens: 6 mmol twice daily for one week followed by dose-escalation to 6 mmol thrice daily for one week | KNO3 given in two dosing regimens: 6 mmol twice daily for one week followed by dose-escalation to 6 mmol thrice daily for one week | 1 week | None | 1.VO2 peak  2.exercise time  3.RER  4.Ve/VCO2 slope  5.SBP during exercise  6.DBP during exercise  7.HR during exercise  8.NT-pro-BNP  9.CO during rest and exercise  10.E/A ratio  11.E/e' ratio  12.KCCQ score | 4 |
| Abbreviation: T: treatment group; C: control group; EF: Ejection fraction;  Note: Outcomes: VO2 peak: peak oxygen uptake; VO2: oxygen uptake; RER: respiratory exchange ratio; Ve: ventilation; VCO2: carbon dioxide production; SBP: systolic blood pressure; DBP: diastolic blood pressure; PA: pulmonary artery pressure; HR: heart rate; CO: cardiac output; PCWP: pulmonary capillary wedge pressure; NT-pro-BNP: N-terminal fragment of the prohormone brain natriuretic peptide; KCCQ: Kansas City Cardiomyopathy Questionnaire; E: early mitral velocity; A: atrial mitral velocity; e’: mitral annulus velocity; RA:right atrial pressure. | | | | | | | | | | | | | | | |