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Human Kinetics
SCHOLARLY REVIEW

Beta-Alanine for Improving Exercise Capacity, Muscle Strength, and Functional Performance of Older Adults: A Systematic Review

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Background/Objective: Beta-alanine supplementation increases muscle carnosine content and also improves exercise capacity and performance in young adults, with mixed findings emerging from the few studies investigating its effects on older participants. Therefore, this study aimed to systematically review the evidence regarding the effects of beta-alanine on exercise capacity, muscle strength, and functional performance of older adults. ***Methods:*** This systematic review was conducted following the specific methodological guidelines of the Preferred Report Items for Systematic Reviews and Meta-Analyses and the Physiotherapy Evidence Database scale. Furthermore, the Cochrane risk-of-bias assessment tool was used. The search was carried out in five relevant databases (MEDLINE, Embase, Web of Science, Scopus, and Cochrane Library) from inception up to March 2024. ***Results:*** Of the 1,749 registers identified, only five met the established criteria and were included in this systematic review. A total of 163 older adults (mean age ± *SD*: 69.1 ± 2.8 years; range: 66.2–72.7 years) were included across all five studies. The majority of studies included participants from both genders. The mean intervention duration ± *SD* was 11.7 ± 1.0 weeks. The mean daily dosage was 2.7 ± 0.4 g/day (range: 2.4–3.2 g/day). ***Conclusion:*** Overall, exercise capacity may be improved following supplementation protocols with dosages ranging from 2.4 to 3.2 g/day. Muscle strength and functional performance do not seem to be improved by beta-alanine since these tasks are not significantly impacted by acidosis buildup.

Keywords: carnosine, sarcopenia, senior

Key Points

- This study suggests that exercise capacity of older adults may be improved following supplementation protocols (2.4–3.2 g/day).
- Muscle strength and performance in functional tests do not seem to be improved by beta-alanine.

In addition to the muscle strength, power, and mass decreases (i.e., sarcopenia) observed during the chronological aging process, older individuals may also present impairments in fatigue resistance, which in turn may negatively impact physical parameters such as balance, gait speed, and increased risk of falls (Emerson et al., 2014; Kannus et al., 2005; Madureira et al., 2010). Furthermore, older individuals with reduced exercise tolerance and lower fatigue threshold may present impairments on functional independence (Shephard, 2009), which highlights the relevance of an active lifestyle adopted throughout the whole lifespan.

It has been previously reported that exercise-induced neuromuscular fatigue is influenced by aging (Zarzissi et al., 2020), which might be explained by cardiovascular, pulmonary, and neuromuscular alterations that play a role in exercise capacity and performance decreases within the aging process. For example, changes in the skeletal muscle as so in the corticospinal tract and afferent feedback activity have been previously described as playing important roles in the increased peripheral fatigue observed in older compared with younger adults (Zarzissi et al., 2020). Furthermore, the reduced exercise tolerance usually observed in this population may also be related to impairments in the oxygen extraction by the skeletal muscle cells during exercise (Fuller et al., 2021).

Carnosine is an intracellular dipeptide located in the cytoplasm of skeletal muscle cells (especially Type II fibers) where it is synthesized from the amino acids L-histidine and beta-alanine (BA). Since skeletal muscle cells have a high L-histidine content (Harris et al., 2012), carnosine synthesis is limited by BA availability (Blancquaert et al., 2017), which can be obtained by uracil degradation in the liver and also by nutritional sources of carnosine (especially meat; Harris et al., 2006). Due to its relevant hydrogen ion (H+) buffering capacity over the physiological pH range (Harris et al., 2006; Tallon et al., 2007), higher muscle carnosine content has been shown to attenuate fatigue during exhaustive dynamic exercise (Derave et al., 2007) and induce higher calcium sensitivity of the contractile apparatus (Dutka & Lamb, 2004). Notwithstanding, previous studies have described an inverse relationship between age and carnosine content (Stuerenburg & Kunze, 1999; Tallon et al., 2007), with older adults displaying a 53% lower carnosine content in Type II muscle fibers compared with their younger counterparts (Tallon et al., 2007). From this perspective, it seems reasonable to suggest that, in addition to the aforementioned factors, lower exercise tolerance and fatigue threshold presented by older adults might also be explained by the reduced muscle carnosine content. Therefore, strategies that

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could result in increased carnosine levels within the skeletal muscle and augmented potential of buffering intramuscular H+ accumulation would be able to elicit improved exercise capacity, better fatigue tolerance, and also functional performance in older adults (Emerson et al., 2014; Kannus et al., 2005).

An overwhelming body of evidence has pointed to BA supplementation as a feasible means to significantly increase skeletal muscle carnosine content. Harris et al. (2006), for example, observed that 28 days of BA supplementation significantly increased skeletal muscle carnosine levels (60%), whereas Hill et al. (2007) demonstrated a further 20% increase when BA supplementation was continued for an additional period of 5 weeks. Additionally, distinct supplementation protocols have elicited significant improvements in performance parameters of exercise tasks with durations above 60 s (Hobson et al., 2012). However, it is of great relevance to note that the majority of studies investigating the effects of BA on exercise performance and capacity were limited to performing the assessments in younger rather than older adults, with some conflicting evidence emerging from these investigations for the latter. Although somewhat difficult to reconcile, the inconsistencies in the current body of evidence may reside on the different sample characteristics of each study (e.g., age range, training status), as well as the supplementation protocols adopted (e.g., duration, daily and total dosage) and the tests adopted to detect eventual effects of BA supplementation in exercise capacity, muscle strength, and functional performance outcomes. Accordingly, a systematic review would be useful to synthesize the available evidence regarding this topic, offer a comprehensive view of the current state of knowledge, and identify gaps in the existing knowledge, pointing directions to further research as well. Therefore, the current study aimed to systematically review the available evidence regarding the effects of BA supplementation on exercise capacity, muscle strength, and functional performance-related parameters of older adults.

Methods

Protocol Registration

This systematic review was registered with PROSPERO (CRD42024518272; https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=518272) and follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (Moher et al., 2009).

Eligibility Criteria

Studies were required to meet the following inclusion criteria: (a) human chronic interventions published in English and in peer-reviewed journals; (b) comparing BA with a nonsupplemented placebo (PLA) control group; (c) studies that reported on outcomes based on exercise capacity, muscle strength, and also functional performance as sit-to-stand (STS), timed up and go, and gait tests. For the purpose of this review, exercise capacity tests were defined as those requiring exertion to the point of volitional fatigue (open tasks) (Saunders et al., 2017); (d) the participants were apparently healthy older adults without any chronic disease or musculoskeletal injury. Studies that eventually employed co-interventions (e.g., resistance and/or endurance exercise training) were also considered for this review. For data management, removal of duplicates, and finding the full texts of the articles, the referencing software Endnote (version X9, Clarivate Analytics) was adopted.

Search Strategy and Information Sources

The literature search was conducted for four relevant databases (MEDLINE, Embase, Web of Science, and Scopus) from inception up to March 2024. The MeSH terms were combined as follows: (((aged) OR (older[Title/Abstract])) OR (elderly[Title/Abstract])) AND ((beta alanine[Title/Abstract]) OR (β-alanine[Title/Abstract] OR (carnosine[Title/Abstract])) AND ((performance[Title/Abstract] OR (capacity[Title/Abstract] OR (function[Title/Abstract] OR (functionality[Title/Abstract] OR (muscle strength[Title/Abstract]))). The search strategies for all databases are included as Supplementary Material (available online). Two researchers conducted the review independently (de Camargo and Brigatto). The discrepancies between researchers were discussed and a third researcher not involved in the study was consulted when necessary.

Study Selection and Data Extraction

The titles and abstracts of all studies were independently evaluated by two investigators (de Camargo and Brigatto). Duplicated studies were excluded, and the remaining ones were screened, assessed for eligibility criteria, and then forwarded to data extraction. Data extraction was performed by two independent reviewers (de Camargo and Brigatto) for the following variables: authors, year of publication, sample size, age (mean ± *SD*), intervention duration, supplementation protocol, assessed outcomes, and main results findings for each individual study. When multiple time points for the outcomes were assessed, the last time point available was considered as the postintervention value for analysis. The procedures for data extraction were standardized using an Excel spreadsheet. The data extracted are presented in Table 1.

Risk-of-Bias Assessment

The risk of bias of each included study was independently assessed by two authors (de Camargo and Brigatto) using the Revised Cochrane risk-of-bias tool for Randomized Trials (RoB2; Sterne et al., 2019). The following domains were assessed: (a) bias arising in the randomization process, (b) bias due to deviations from intended interventions, (c) bias due to missing outcome data, (d) bias in the measurement of the outcome, and (e) bias in the selection of the reported result. Each domain was classified as having (a) LOW risk of bias, (b) SOME CONCERN of risk of bias, and (c) HIGH risk of bias.

Quality Assessment

Methodological quality was assessed with the Physiotherapy Evidence Database scale, which is based on the Delphi list (Verhagen et al., 1998). A total score out of 10 is derived for each study from the number of criteria that are satisfied. The quality of the included studies was assessed independently by two assessors, and disagreements were resolved by a third independent assessor not involved in the study. Only studies scoring at least 3 were considered in the initial analysis.

Results

Studies and Participants Characteristics

The initial search process returned 1,749 studies. After that, 251 duplicated studies were excluded. Then, titles and abstracts of the remaining studies were read, from which 1,472 were excluded.

Table 1 Summary of the Included Studies Assessing the Effects of Beta-Alanine on Exercise Capacity, Muscle Strength, and Functional Performance in Older Adults

Study	Sample size	Age (years)	Duration	Supplementation protocol	Outcome measures	Main findings
Stout et al. (2008)	BA = 12	72.7 ± 11.2	90 days	2.4 g/day (3 × 800 mg)	PWC_{FT}	Significant increases in PWC_{FT} only for BA group
	PLA = 14					
Del Favero et al. (2012)	BA = 12	64.5 ± 5.5	12 weeks	3.2 g/day (2 × 1.6 g)	TTE	Significant increases in TTE only for BA group
	PLA = 6				STS	No between-group differences in STS and TUG
					TUG	
McCormack et al. (2013)	BA = 15	70.6 ± 4.2	12 weeks	1.6 g/day (2 × 800 mg) 2.4 g/day (2 × 1,200 mg)	PWC_{FT}	Significant increases in PWC_{FT} only for BA groups
	PLA = 16				STS	Significantly larger increases in STS for BA (2.4 g/day)
Bailey et al. (2018)					HS	No increase from baseline in HS (both groups)
	BA + NEX = 5	70.6 ± 3.7	12 weeks	3.2 g/day (2 × 1.6 g)	STS	No further effects of BA in any of the outcomes
	BA + EX = 8	66.2 ± 6.1			6MW	
	PLA + NEX = 6	68.5 ± 5.0			1RM	
Ostfeld et al. (2023)	BA = 38	70.6 ± 8.7	10 weeks	2.4 g/day (2 × 1.2 g)	HS	No increase from baseline in HS (both groups)
	PLA = 41				STS	No between-group differences in STS

Note. BA = beta-alanine group; PLA = placebo group; EX = exercise group; NEX = nonexercise group; PWC_{FT} = physical working capacity at the fatigue threshold; TTE = time to exhaustion; STS = sit-to-stand test; TUG = timed up and go test; HS = handgrip strength; 6MW = 6-min walking test; 1RM = one-repetition maximum.

The remaining 19 articles were fully read and five studies were considered eligible according to our previously set criteria. The search procedures are detailed in Figure 1. A total of 163 older adults (mean age ± *SD*: 69.1 ± 2.8 years; range: 66.2–72.7 years) were included across all five studies. The majority of studies included participants from both genders. The mean intervention duration ± *SD* was 11.7 ± 1.0 weeks. The mean daily dosage was 2.7 ± 0.4 g/day (range: 2.4–3.2 g/day), and the total dosage of BA supplementation throughout the intervention period (Daily dosage × Total duration) ranged from 201.6 to 268.8 g. For the assessment methods adopted for muscle strength outcomes, one study adopted maximal dynamic (Bailey et al., 2018) and two isometric testing (Bailey et al., 2018; Ostfeld et al., 2023). Three studies assessed functional-related parameters through STS test (Del Favero et al., 2012; McCormack et al., 2013; Ostfeld et al., 2023), one used timed up and go test (Del Favero et al., 2012), and one adopted 6-min walk test (6MW; Bailey et al., 2018). None of the studies assessed the effects of supplementation in previously trained subjects. Dropout rates throughout the studies ranged from 0% to 26%.

Risk-of-Bias Assessment

Figure 2 presents the results of the risk-of-bias assessment for each study included in the review. Four investigations were classified as presenting "some concerns" (Bailey et al., 2018; Del Favero et al., 2012; McCormack et al., 2013; Stout et al., 2008), which derived from the "randomization process" and "selection of the reported result" items. In addition, one study presented "high" risk of bias (Ostfeld et al., 2023), which derived from possible differences (although not statistically significant) in baseline values between the groups (BA and PLA), suggesting eventual problems with the randomization process.

Quality Assessment

The methodological quality of the studies using the Physiotherapy Evidence Database scale was as follows: two studies (Del Favero et al., 2012; Stout et al., 2008) achieved "excellent" quality and the other three studies (Bailey et al., 2018; McCormack et al., 2013; Ostfeld et al., 2023) achieved "good" quality (Table 2).

Discussion

BA Supplementation and Exercise Capacity/Performance in Older Adults

In addition to the impairments in neuromuscular and cardiovascular systems, the literature has pointed out that reductions in exercise capacity and performance in older subjects might also be related to a lower capacity to resist fatigue, especially during high-intensity exercise tasks. Although several buffering agents act in order to control the muscle cell's pH during exercise, the decrease in muscle carnosine levels observed during the aging process may play a relevant role in decreasing buffering capacity of the muscle, diminishing the ability to withstand the buildup of H+ during anaerobic activities that rely on glycolytic energy pathway (Stout et al., 2008). For example, similar exercise capacity was observed between older and younger subjects performing four sets to the point of fatigue during high- (80% of one-repetition maximum

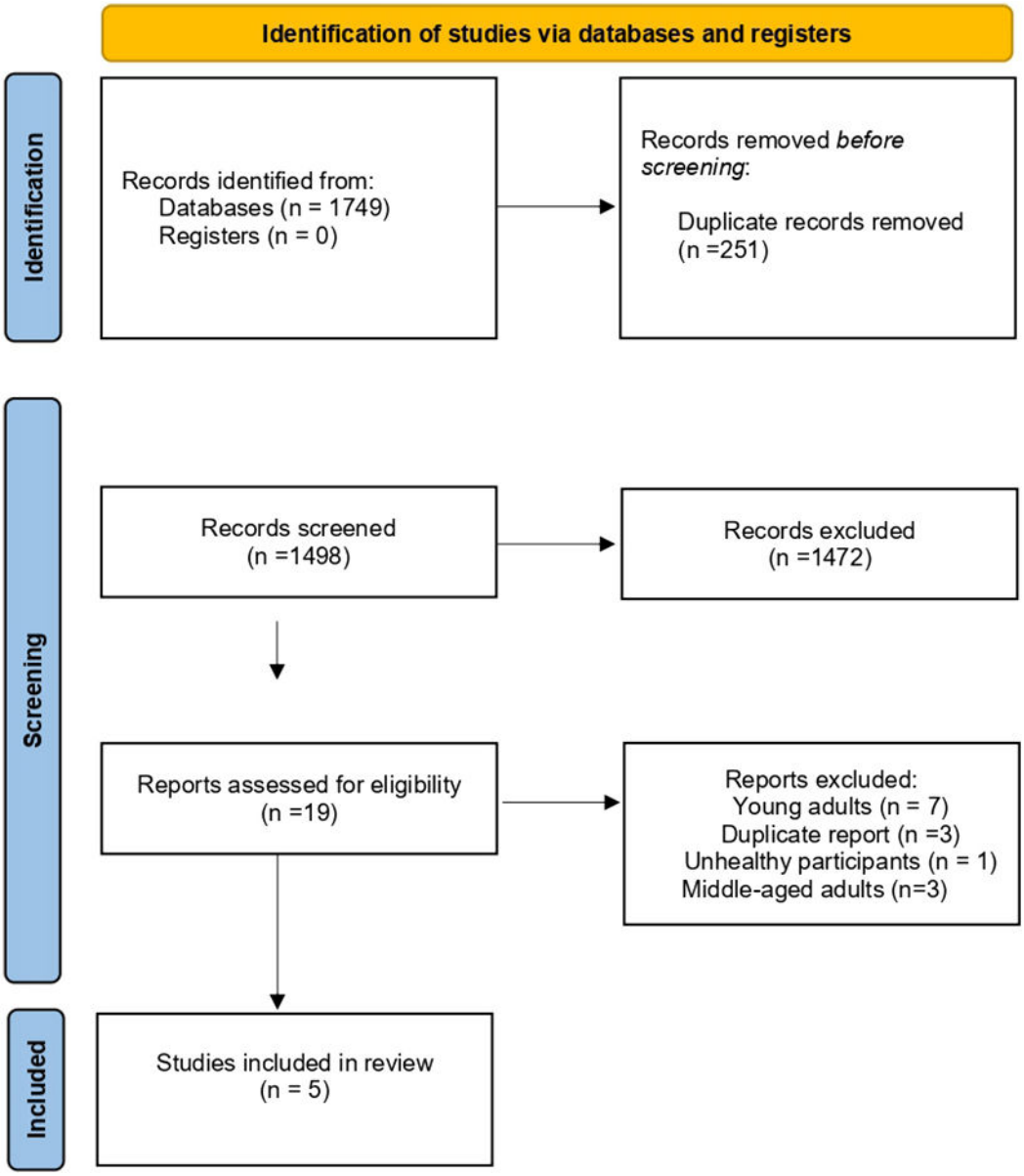

Figure 1 — Preferred Report Items for Systematic Reviews and Meta-Analyses flow diagram of search and screening stages.

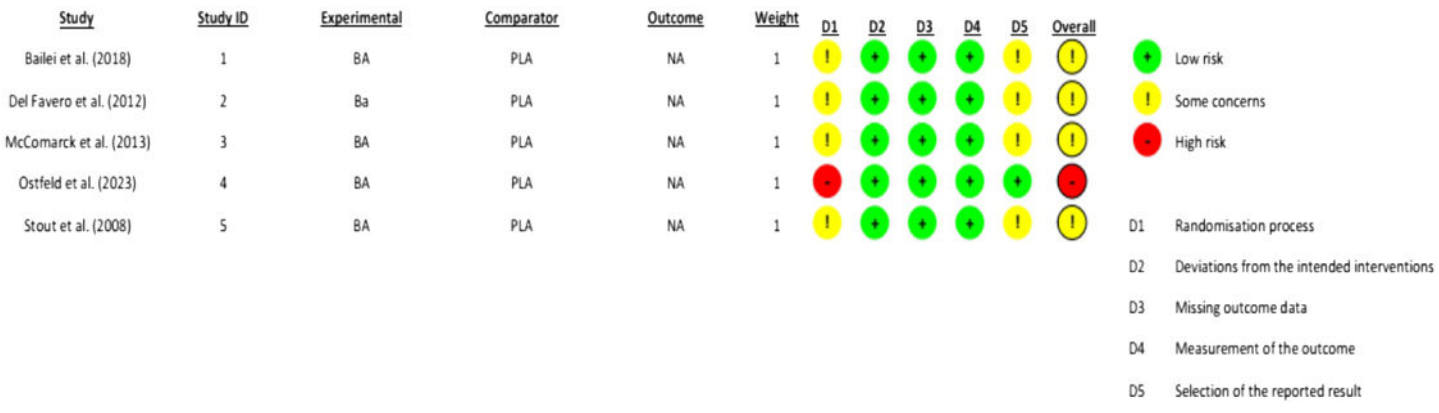

Figure 2 — Risk-of-bias assessment for the studies included in the systematic review. BA = beta-alanine group; NA = not applicable; PLA = placebo group.

Table 2 PEDro Ratings of the Included Studies

	Criteria											
Studies	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**Total**
Bailey et al. (2018)	1	1	1	1	1	1	1	0	0	0	1	7
Del Favero et al. (2012)	1	1	1	1	1	1	1	1	1	1	1	10
McCormack et al. (2013)	1	1	1	1	1	1	1	0	0	1	1	8
Ostfeld et al. (2023)	1	1	1	0	1	1	1	0	0	1	1	7
Stout et al. (2008)	1	1	1	1	1	1	1	1	1	1	1	10

Note. 0 = not fulfilled criteria; 1 = fulfilled criteria; Items in the PEDro scale: 1 = eligibility criteria were specified; 2 = subjects were randomly allocated to groups; 3 = allocation was concealed; 4 = the groups were similar at baseline regarding the most important prognostic indicators; 5 = there was blinding of all subjects; 6 = there was blinding of all therapists who administered the therapy; 7 = there was blinding of all assessors who measured at least one key outcome; 8 = measures of one key outcome were obtained from 85% of subjects initially allocated to groups; 9 = all subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome were analyzed by "intention to treat"; 10 = the results of between-group statistical comparisons are reported for at least one key outcome; 11 = the study provides both point measures and measures of variability for at least one key outcome. PEDro = Physiotherapy Evidence Database.

[1RM]) but not low-intensity (30% 1RM) resistance exercise protocols (Sardeli et al., 2020), which reinforces that older adults may present impaired fatigue tolerance during activities with the most acidosis buildup.

Distinct factors may explain why older individuals display a reduced carnosine concentration compared with the younger. First, since carnosine synthesis is mainly dependent on BA availability, which occurs naturally in fresh meat sources, changes toward a diet with lower meat consumption over the years may negatively impact muscle carnosine content (Everaert et al., 2011). Indeed, individuals with daily ingestion of 1.7 g of protein/kg of body mass present higher carnosine content compared with those consuming 1.0 g/kg (Varanoske et al., 2017). The second cause of a decrease in muscle carnosine with aging usually mentioned is the atrophy of Type II muscle fibers. Since carnosine content is high in Type II compared with Type I muscle fibers (Baguet et al., 2011), a decreasing area of the first (even if the carnosine content per kilogram of muscle remains unaltered) may elicit a reduction in the content of carnosine at the whole muscle level (Tallon et al., 2007).

Although it seems plausible to suggest that, based on the premise that exercise capacity may be a relevant determinant of healthy independent living (Akerman et al., 2015), increasing muscle carnosine content through BA supplementation would offer some benefit for the older adult, a scarce number of longitudinal studies to the present date investigated the effects of BA in exercise capacity-related parameters of this population. The first study was performed by Stout et al. (2008), who aimed to assess whether BA supplementation (2.4 g/day) could improve the physical working capacity at the fatigue threshold (PWC_{FT}; determined by the electromyography activity of the vastus lateralis muscle during incremental cycling test and defined as the highest power output that does not result in a significant increase in the electrical activity of the thigh muscle over time) of active (nontrained) older men and women (72.7 mean age) compared with a PLA group. After the intervention period (90 days), significant increases from baseline in PWC_{FT} were observed for the BA group (28.6%) but not for the PLA group ($p > .05$). Furthermore, when analyzing individual data, 67% and 21.5% of the participants in BA and PLA groups (respectively) presented significant improvements in PWC_{FT} after the intervention weeks. Interestingly, these percentage increases presented by the older adults assessed by Stout et al. (2008) were markedly higher compared with younger women (13.9%) even with increasing doses (3.2–6.4 g/day) over a 12-week intervention period (Stout et al., 2007). Therefore, one can suggest that the distinct improvements in PWC_{FT} noted between these two investigations can mainly be explained by the differences in the age of the participants, suggesting that older adults may display higher improvements in exercise capacity that their younger counterparts when submitted to BA supplementation protocols. Future studies should be addressed in order to confirm this hypothesis.

The PWC_{FT}, which has been pointed out as a more suitable and sensitive test to detect improved exercise capacity in older individuals compared with others that require maximal effort (i.e., VO_2max; Devries et al., 1987), was also adopted for assessing the effects of BA supplementation on exercise capacity of older subjects in another study (McCormack et al., 2013). Interestingly, while no increases were observed for the PLA group (−5.9%), PWC_{FT} was significantly improved for the BA group receiving 1.6 g/day (17.8%), with no further increases being observed with an increased daily dosage of 2.4 g (13.6%). It is important to note that, despite using equal daily dosages (2.4 g), the percentage increases in PWC_{FT} differed between Stout et al. (2008) and McCormack et al. (2013). Some methodological aspects of each study should be considered in order to understand these differences in the magnitude of improvements. For Stout et al. (2008), only active older subjects were recruited, and 20% of the sample was considered as inactive in McCormarck et al. (2013). Therefore, although further specifications about the habitual exercise practices were not provided, differences regarding the fitness level of the participants must help justify these discrepancies in the magnitude of improvements observed between both investigations since muscle carnosine loading by BA supplementation seems to be dependent on the training status of the muscle (Bex et al., 2014). The difference in the magnitude of the results of the PWC_{FT} between Stout et al. (2008) and McCormarck et al. (2013) may also be related to the total dosage of BA consumed during the supplementation period. The total dose of BA ingested by the participants in Stout et al. (2008) was approximately 216 g, which represents ~ 20% more BA than that consumed by the participants in McCormarck et al. (2013) (~181 g). Although further investigations in older subjects are warranted, the total dosage provided within supplementation protocols seems to modulate the improvements in exercise capacity. This is supported by an investigation from Hill et al. (2007) that showed an improved total work done in cycling tests when male participants were exposed to a 10-week versus 4-week supplementation protocol (daily dosage ranging from 4 to 6.4 g). Together, these data seem to point out that BA supplementation is an effective

ergogenic aid for improving PWC_{FT} in older adults. These findings may represent clinical significance for this population since PWC_{FT} is significantly associated with sarcopenia-related body composition (appendicular lean mass; $r = .572$) and functional outcomes (STS [$r = .440$] and handgrip strength [HS; $r = .485$]), with a ~5% decrease in the odds of sarcopenia classification for each 1-W increase in PWC_{FT} (Emerson et al., 2014).

It is important to note that the aforementioned investigations did not expose the participants to a structured exercise training program concomitantly to the supplementation protocols. To the present date, the effects of implementing a combined supplementation plus exercise training protocol (resistance-type) on neuromuscular outcomes of older adults were assessed by only one study (Bailey et al., 2018). After the 12-week experimental period, both fatigue rate and index (upper and lower limbs) were not enhanced by BA in a muscular endurance test (20 repetitions at 50% 1RM). These results are not surprising since the ergogenic effects of BA supplementation have been shown to be more pronounced in exercise capacity rather than in performance tasks (effect sizes = 0.49 vs. 0.10, respectively; Saunders et al., 2017). In addition, exercise duration has been pointed out as the main influencing factor on the efficacy of BA supplementation, with a time frame of 0.5–10 min likely to result in the greatest gains and very short-duration exercise clearly resulting in no significant benefits (Saunders et al., 2017).

The aforementioned increases in exercise capacity-related parameters reflect an enhanced buffering potential by muscle cells. Notwithstanding, none of them assessed muscle carnosine content pre and post the supplementation period, limiting inferences about the real effects of this variable on the performance testing. The first study that measured BA-induced increases in muscle carnosine of older individuals was performed by Del Favero et al. (2012), in which 18 participants (men and women) were submitted to a 12-week supplementation period (3.2 g/day) and tested for a time to exhaustion incremental test. A significant increase in muscle carnosine content was noted in the BA group (85.4%) when compared with the PLA group (7.2%). In addition, time to exhaustion was significantly improved in BA (26.9%) compared with the PLA group (6.8%). Furthermore, a positive and significant correlation ($r = .62$) was observed between the increases in muscle carnosine content and time to exhaustion. These data show that aging does not seem to impair BA uptake by the muscle cell nor muscle carnosine synthesis.

Although few studies are available to the present date, the current evidence suggests that the adoption of BA supplementation (even without an exercise training program implemented) may elicit positive effects on tasks that require exertion to the point of volitional fatigue in an older population. Therefore, older individuals engaged in exhausting physical/leisure activities may benefit from ingesting 2.4–3.2 g/day of BA during a period of 10–12 weeks.

BA Supplementation for Muscle Strength and Functional Performance of Older Adults

It is widely known that older adults experience significant reductions in muscle strength and power over the years, which can negatively impact the performance of daily living tasks (Foldvari et al., 2000; Hyatt et al., 1990). In this sense, exercise training and nutrition interventions have been adopted in order to counteract these deleterious effects of aging on muscle function. Moreover, one may assume that ergogenic aids that could enhance muscle strength/power outcomes would also result in improved functional performance. Although BA seems to positively influence exercise capacity and improve fatigue tolerance (as aforementioned), it is not clear whether and to which extent these adaptations would somehow influence the capacity of older adults to perform daily living activities and also improve the quality of life in this population.

To the present date, the effects of implementing BA supplementation on parameters of muscle strength and functionality of older individuals have been shortly explored by the literature. Some of the studies assessing the effects of BA on muscle strength parameters of older adults adopted the HS test, which has been shown to significantly associate with muscle both strength- and functional-related parameters (Bohannon, 2015; Pratama & Setiati, 2018) and also pointed out as a potential biomarker of malnutrition among older populations (Bohannon, 2019). McCormack et al. (2013) reported that both 1.6 and 3.2 g daily doses failed to increase HS of older participants after 12 weeks, with similar results being reported in a study that included both middle-aged and older female cyclists who did not display improvements in HS after 28 days of a 3.2 g/day protocol (BA: −2.4%; PLA: −2.3%; Glenn et al., 2016). Although one may assume that HS may not necessarily reflect overall strength status (Felicio et al., 2014), a study that implemented an isotonic (1RM) test also failed to observe significant increases in muscle strength outcomes emerging from BA supplementation (Bailey et al., 2018). During a 12-week intervention period, healthy older men and women (mean age 68 years) were exposed to a supplementation protocol implemented alongside a resistance training program. Although the training regimen adopted was able to elicit significant increases in muscle strength for both chest press and leg press exercises, BA supplementation did not enhance these adaptations. Furthermore, peak and average power output during muscular endurance testing (50% of 1RM) did not differ between groups. These results are in accordance with recent findings in younger adults submitted to an 8-week BA supplementation protocol (Benvenutti Bueno de Camargo et al., 2023). Therefore, based on the scarce investigations available, it can be suggested that the performance in tasks such as HS and 1RM tests may not be influenced by BA supplementation due to its short duration and consequent low acidosis buildup.

Few studies to the present date investigated possible effects of BA supplementation on functional performance parameters of older adults. McCormack et al. (2013), for example, observed that the experimental group ingesting 2.4 g/day of BA presented significantly larger improvements (28.6%) in the STS performance compared to the 1.6 g/day group (3.5%) and the placebo group (12.0%). Conversely, STS performance was not affected by supplementation in other studies (Bailey et al., 2018; Del Favero et al., 2012). Some methodological aspects of each study must be considered to explain these divergent results in STS performance. First, 68% of the participants in McCormack et al. (2013) already performed some type of physical exercise and 11% were considered as being physically active. Otherwise, only inactive older subjects were recruited in Del Favero et al. (2012). Therefore, differences in the physical activity habits of the participants between these two studies may explain these distinct results. Moreover, the baseline values of STS in the participants receiving BA were different between the studies (13.3 ± 3.6 repetitions and 16.0 ± 2.0 repetitions for McCormarck et al. [2013] and Del Favero et al. [2012], respectively). In a recent investigation, implementing a 12-week resistance training program improved the performance of STS, TUG, and gait speed tests in older men and women (Bailey

et al., 2018). However, BA supplementation (3.2 g/day) did not enhance these training-induced adaptations. Although not completely clear, these results may be explained by the absence of further improvements induced by the supplementation in muscle strength and power outcomes reported by the study since there is a strong association between these variables and improvements in functional tasks' performance (Foldvari et al., 2000; Hyatt et al., 1990). The absence of effects of BA on functional performance had also been reported in a previous investigation with no exercise training program concomitantly being performed (Del Favero et al., 2012). These results are not surprising since short-duration tests, which are not markedly influenced by acidosis buildup within the muscle, were adopted in these studies to assess the effects of BA on functional parameters. Therefore, since the performance in exercises lasting from 0.5 to 10 min has shown the greatest effects induced by BA (Saunders et al., 2017), potential significant BA-induced adaptations in functional performance assessed through longer duration tests should not be disregarded. Therefore, since the performance in exercises with duration ranging from 0.5 to 10 min has shown the larger effects induced by BA, eventual significant BA-induced adaptations in functional performance assessed through tests presenting longer duration must not be discarded. Additionally, the lack of changes in these parameters may also be explained by the fact that the participants recruited by the aforementioned studies were healthy and functional at baseline. A future goal, therefore, should be to study the effects of BA supplementation in individuals who display a higher degree of sarcopenia and frailty. Therefore, based on the scarce available evidence, muscle strength and functional performance outcomes of older subjects do not seem to be improved by BA supplementation protocols.

Limitations of the Studies and Future Directions

Although it seems limited, due to the scarce number of investigations to the present date, to point out the real effects of BA on exercise capacity, muscle strength, and functional performance of older individuals, important limitations of the aforementioned studies must be pointed out. First, exclusively older participants with satisfactory general health conditions were included in the present review study. From this perspective, eventual improvements on muscle strength and function induced by a BA supplementation protocol must not be completely discarded in older populations displaying a considerable sarcopenia/frailty status. It is also relevant to highlight that muscle carnosine content of older participants provided with BA supplementation was assessed in only one study (Del Favero et al., 2012), which limits associations between the improvements in exercise capacity reported by some studies and eventually increased muscle carnosine content. Although the improvements in the aforementioned exercise capacity-related outcomes may be indeed acknowledged due to increases in muscle carnosine content, one can suggest that eventual reward effect of the supplementation must not be discarded (Bellinger & Minahan, 2016; Liu et al., 2012), first, due to the sensation of paresthesia reported by some of the participants who received BA in one study (McCormack et al., 2013) and also by the lacking of control regarding side effects of supplementation in other investigation (Stout et al., 2008). Then, based on this information, one may assume that the blinding process was not effective in these studies, which may have influenced some of the participants when performing the tests. Moreover, a strict control of the adherence throughout the supplementation protocol imposed was weakly adopted by the studies (being reported in only three investigations [Del Favero et al., 2012; McCormack et al., 2013; Ostfeld et al., 2023]), which could eventually compromise the magnitude of the estimated effects observed in some of these investigations. Another important aspect of the studies analyzed was the lacking details regarding the sample size calculation. First, none of the studies reported the primary outcome assessed and adopted to calculate the sample size required. Furthermore, the magnitude of the effect expected to be observed between groups was not described in any of the studies included. In this sense, it should not be completely discarded that these studies were unpowered to detect significant between-group differences (Type II error). Finally, since no study assessed the effects of BA in exclusively older participants with physical training background, it remains to be further investigated whether and to which extent the previous training experience could modulate some of the ergogenic effects of BA supplementation.

Conclusions

Although a relatively scarce number of studies to the present date aimed to investigate the effects of supplementing BA in older adults, the present study suggests that exercise capacity may be improved following supplementation protocols with dosages ranging from 2.4 to 3.2 g/day, even with no structured exercise program being concomitantly performed. In addition, although further studies are required, muscle strength and performance in functional tests do not seem to be improved by BA since these tasks are not significantly impacted by acidosis buildup. The aforementioned limitations of the studies included in this systematic review should be carefully considered by health professionals when making evidence-based decisions as to implement (or not) BA supplementation for the older population.

References

Akerman, J.P., Heckman, G.A., & McKelvie, R.S. (2015). Exercise capacity and aging. *American Journal of Lifestyle Medicine, 9*(4), 252–265. https://doi.org/10.1177/1559827614542224

Baguet, A., Everaert, I., Hespel, P., Petrovic, M., Achten, E., & Derave, W. (2011). A new method for non-invasive estimation of human muscle fiber type composition. *PLoS One, 6*(7), Article e21956. https://doi.org/10.1371/journal.pone.0021956

Bailey, C.H., Signorile, J.F., Perry, A.C., Jacobs, K.A., & Myers, N.D. (2018). Beta-alanine does not enhance the effects of resistance training in older adults. *Journal of Dietary Supplements, 15*(6), 860–870. https://doi.org/10.1080/19390211.2017.1406422

Bellinger, P.M., & Minahan, C.L. (2016). Performance effects of acute β-alanine induced paresthesia in competitive cyclists. *European Journal of Sport Science, 16*(1), 88–95. https://doi.org/10.1080/17461391.2015.1005696

Benvenutti Bueno de Camargo, J., Brigatto, F., Zaroni, R., Germano, M., Souza, D., Bacurau, R., Marchetti, P., Braz, T., Aoki, M., & Lopes, C. (2023). Does beta-alanine supplementation enhance adaptations to resistance training? A randomized, placebo-controlled, double-blind study. *Biology of Sport, 40*(1), 217–224. https://doi.org/10.5114/biolsport.2023.112967

Bex, T., Chung, W., Baguet, A., Stegen, S., Stautemas, J., Achten, E., & Derave, W. (2014). Muscle carnosine loading by beta-alanine supplementation is more pronounced in trained vs. untrained muscles. *Journal of Applied Physiology, 116*(2), 204–209. https://doi.org/10.1152/japplphysiol.01033.2013

Blancquaert, L., Everaert, I., Missinne, M., Baguet, A., Stegen, S., Volkaert, A., Petrovic, M., Vervaet, C., Achten, E., De Maeyer, M., De Henauw, S., & Derave, W. (2017). Effects of histidine and β-alanine supplementation on human muscle carnosine storage. *Medicine and Science in Sports and Exercise, 49*(3), 602–609. https://doi.org/10.1249/MSS.0000000000001213

Bohannon, R.W. (2015). Muscle strength: Clinical and prognostic value of hand-grip dynamometry. *Current Opinion in Clinical Nutrition and Metabolic Care, 18*(5), 465–470. https://doi.org/10.1097/MCO.0000000000000202

Bohannon, R.W. (2019). Grip strength: An indispensable biomarker for older adults. *Clinical Interventions in Aging, 14*, 1681–1691. https://doi.org/10.2147/CIA.S194543

Del Favero, S., Roschel, H., Solis, M.Y., Hayashi, A.P., Artioli, G.G., Otaduy, M.C., Benatti, F.B., Harris, R.C., Wise, J.A., Leite, C.C., Pereira, R.M., De Sá-Pinto, A.L., Lancha-Junior, A.H., & Gualano, B. (2012). Beta-alanine (Carnosyn™) supplementation in elderly subjects (60-80 years): Effects on muscle carnosine content and physical capacity. *Amino Acids, 43*(1), 49–56. https://doi.org/10.1007/s00726-011-1190-x

Derave, W., Özdemir, M.S., Harris, R.C., Pottier, A., Reyngoudt, H., Koppo, K., Wise, J.A., & Achten, E. (2007). β-Alanine supplementation augments muscle carnosine content and attenuates fatigue during repeated isokinetic contraction bouts in trained sprinters. *Journal of Applied Physiology, 103*(5), 1736–1743. https://doi.org/10.1152/japplphysiol.00397.2007

Devries, H.A., Tichy, M.W., Housh, T.J., Smyth, K.D., Tichy, A.M., & Housh, D.J. (1987). A method for estimating physical working capacity at the fatigue threshold (PWCFT). *Ergonomics, 30*(8), 1195–1204. https://doi.org/10.1080/00140138708966008

Dutka, T.L., & Lamb, G.D. (2004). Effect of carnosine on excitation-contraction coupling in mechanically-skinned rat skeletal muscle. *Journal of Muscle Research and Cell Motility, 25*(3), 203–213. https://doi.org/10.1023/B:JURE.0000038265.37022.c5

Emerson, N.S., Fukuda, D.H., Stout, J.R., Robinson, E.H., McCormack, W.P., Scanlon, T.C., Warren, A.M., Wells, A.J., Gonzalez, A.M., Mangine, G.T., Fragala, M.S., & Hoffman, J.R. (2014). Physical Working Capacity at Fatigue Threshold (PWCFT) is associated with sarcopenia-related body composition and measures of functionality in older adults. *Archives of Gerontology and Geriatrics, 59*(2), 300–304. https://doi.org/10.1016/j.archger.2014.04.012

Everaert, I., Mooyaart, A., Baguet, A., Zutinic, A., Baelde, H., Achten, E., Taes, Y., De Heer, E., & Derave, W. (2011). Vegetarianism, female gender and increasing age, but not CNDP1 genotype, are associated with reduced muscle carnosine levels in humans. *Amino Acids, 40*(4), 1221–1229. https://doi.org/10.1007/s00726-010-0749-2

Felicio, D.C., Pereira, D.S., Assumpção, A.M., de Jesus-Moraleida, F.R., de Queiroz, B.Z., da Silva, J.P., de Brito Rosa, N.M., Dias, J.M.D., & Pereira, L.S.M. (2014). Poor correlation between handgrip strength and isokinetic performance of knee flexor and extensor muscles in community-dwelling elderly women. *Geriatrics and Gerontology International, 14*(1), 185–189. https://doi.org/10.1111/ggi.12077

Foldvari, M., Clark, M., Laviolette, L.C., Bernstein, M.A., Kaliton, D., Castaneda, C., Pu, C. T., Hausdorff, J.M., Fielding, R.A., & Fiatarone Singh, M.A. (2000). Association of muscle power with functional status in community-dwelling elderly women. *Journals of Gerontology - Series A Biological Sciences and Medical Sciences, 55*(4), M192–M199. https://doi.org/10.1093/gerona/55.4.M192

Fuller, A., Okwose, N., Scragg, J., Eggett, C., Luke, P., Bandali, A., Velicki, R., Greaves, L., MacGowan, G.A., & Jakovljevic, D.G. (2021). The effect of age on mechanisms of exercise tolerance: Reduced arteriovenous oxygen difference causes lower oxygen consumption in older people. *Experimental Gerontology, 149*, Article 111340. https://doi.org/10.1016/j.exger.2021.111340

Glenn, J.M., Gray, M., Stewart, R.W., Moyen, N.E., Kavouras, S.A., DiBrezzo, R., Turner, R., Baum, J.I., & Stone, M.S. (2016). Effects of 28-day beta-alanine supplementation on isokinetic exercise performance and body composition in female masters athletes. *Journal of Strength and Conditioning Research, 30*(1), 200–207. https://doi.org/10.1519/JSC.0000000000001077

Harris, R.C., Tallon, M.J., Dunnett, M., Boobis, L., Coakley, J., Kim, H.J., Fallowfield, J.L., Hill, C.A., Sale, C., & Wise, J.A. (2006). The absorption of orally supplied β-alanine and its effect on muscle carnosine synthesis in human vastus lateralis. *Amino Acids, 30*, 279–289. https://doi.org/10.1007/s00726-006-0299-9

Harris, R.C., Wise, J.A., Price, K.A., Kim, H.J., Kim, C.K., & Sale, C. (2012). Determinants of muscle carnosine content. *Amino Acids, 43*(1), 5–12. https://doi.org/10.1007/s00726-012-1233-y

Hill, C.A., Harris, R.C., Kim, H.J., Harris, B.D., Sale, C., Boobis, L.H., Kim, C.K., & Wise, J.A. (2007). Influence of β-alanine supplementation on skeletal muscle carnosine concentrations and high intensity cycling capacity. *Amino Acids, 32*(2), 225–233. https://doi.org/10.1007/s00726-006-0364-4

Hobson, R.M., Saunders, B., Ball, G., Harris, R.C., & Sale, C. (2012). Effects of β-alanine supplementation on exercise performance: A meta-analysis. *Amino Acids, 43*(1), 25–37. https://doi.org/10.1007/s00726-011-1200-z

Hyatt, R.H., Whitelaw, M.N., Bhat, A., Scott, S., & Maxwell, J.D. (1990). Association of muscle strength with functional status of elderly people. *Age and Ageing, 19*(5), 330–336. https://doi.org/10.1093/ageing/19.5.330

Kannus, P., Parkkari, J., Niemi, S., & Palvanen, M. (2005). Fall-induced deaths among elderly people. *American Journal of Public Health, 95*(3), 422–424. https://doi.org/10.2105/AJPH.2004.047779

Liu, Q., Sikand, P., Ma, C., Tang, Z., Han, L., Li, Z., Sun, S., LaMotte, R.H., & Dong, X. (2012). Mechanisms of itch evoked by β-alanine. *Journal of Neuroscience, 32*(42), 14532–14537. https://doi.org/10.1523/JNEUROSCI.3509-12.2012

Madureira, M.M., Bonfá, E., Takayama, L., & Pereira, R.M.R. (2010). A 12-month randomized controlled trial of balance training in elderly women with osteoporosis: Improvement of quality of life. *Maturitas, 66*(2), 206–211. https://doi.org/10.1016/j.maturitas.2010.03.009

McCormack, W.P., Stout, J.R., Emerson, N.S., Scanlon, T.C., Warren, A.M., Wells, A.J., Gonzalez, A.M., Mangine, G.T., Robinson, E.H., Fragala, M.S., & Hoffman, J.R. (2013). Oral nutritional supplement fortified with beta-alanine improves physical working capacity in older adults: A randomized, placebo-controlled study. *Experimental Gerontology, 48*(9), 933–939. https://doi.org/10.1016/j.exger.2013.06.003

Moher, D., Liberati, A., Tetzlaff, J., & Altman, D.G. (2009). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *PLoS Medicine, 6*(7), Article e1000097. https://doi.org/10.1371/journal.pmed.1000097

Ostfeld, I., Ben-Zeev, T., Zamir, A., Levi, C., Gepner, Y., Springer, S., & Hoffman, J.R. (2023). Role of β-Alanine supplementation on cognitive function, mood, and physical function in older adults; double-blind randomized controlled study. *Nutrients, 15*(4), Article 923. https://doi.org/10.3390/nu15040923

Pratama, I.K., & Setiati, S. (2018). Correlation between hand grip strength and functional mobility in elderly patients. *Journal of Physics: Conference Series, 1073*(4), Article 042034. https://doi.org/10.1088/1742-6596/1073/4/042034

Sardeli, A.V., Santos, L.do.C., Ferreira, M.L.V., Gásparia, A.F., Santos, W.M.dos, Cavaglieri, C.R., & Chacon-Mikahil, M.P.T. (2020).

Elderly perform lower number of repetitions maximum than young at low instead high load resistance exercise. *Manual Therapy, Posturology & Rehabilitation Journal, 15,* 1–5. https://doi.org/10.17784/mtprehabjournal.2017.15.447

Saunders, B., Elliott-Sale, K., Artioli, G.G., Swinton, P.A., Dolan, E., Roschel, H., Sale, C., & Gualano, B. (2017). β-Alanine supplementation to improve exercise capacity and performance: A systematic review and meta-Analysis. *British Journal of Sports Medicine, 51*(8), 658–669. https://doi.org/10.1136/bjsports-2016-096396

Shephard, R.J. (2009). Maximal oxygen intake and independence in old age. *British Journal of Sports Medicine, 43*(5), 342–346. https://doi.org/10.1136/bjsm.2007.044800

Sterne, J.A.C., Savović, J., Page, M.J., Elbers, R.G., Blencowe, N.S., Boutron, I., Cates, C.J., Cheng, H.-Y., Corbett, M.S., Eldridge, S.M., Emberson, J.R., Hernán, M.A., Hopewell, S., Hróbjartsson, A., Junqueira, D.R., Jüni, P., Kirkham, J.J., Lasserson, T., Li, T., … Higgins, J.P.T. (2019). RoB 2: A revised tool for assessing risk of bias in randomised trials. *BMJ, 366*, Article l4898. https://doi.org/10.1136/bmj.l4898

Stout, J.R., Cramer, J.T., Zoeller, R.F., Torok, D., Costa, P., Hoffman, J.R., Harris, R.C., & O'Kroy, J. (2007). Effects of β-alanine supplementation on the onset of neuromuscular fatigue and ventilatory threshold in women. *Amino Acids, 32*(3), 381–386. https://doi.org/10.1007/s00726-006-0474-z

Stout, J.R., Sue, B.S., Smith, A.E., Hartman, M.J., Cramer, J.T., Beck, T.W., & Harris, R.C. (2008). The effect of beta-alanine supplementation on neuromuscular fatigue in elderly (55–92 years): A double-blind randomized study. *Journal of the International Society of Sports Nutrition, 5*, Article 21. https://doi.org/10.1186/1550-2783-5-21

Stuerenburg, H.J., & Kunze, K. (1999). Concentrations of free carnosine (a putative membrane-protective antioxidant) in human muscle biopsies and rat muscles. *Archives of Gerontology and Geriatrics, 29*(2), 107–113. https://doi.org/10.1016/S0167-4943(99)00020-5

Tallon, M.J., Harris, R.C., Maffulli, N., & Tarnopolsky, M.A. (2007). Carnosine, taurine and enzyme activities of human skeletal muscle fibres from elderly subjects with osteoarthritis and young moderately active subjects. *Biogerontology, 8*(2), 129–137. https://doi.org/10.1007/s10522-006-9038-6

Varanoske, A.N., Hoffman, J.R., Church, D.D., Wang, R., Baker, K.M., Dodd, S.J., Coker, N.A., Oliveira, L.P., Dawson, V.L., Fukuda, D.H., & Stout, J.R. (2017). Influence of skeletal muscle carnosine content on fatigue during repeated resistance exercise in recreationally active women. *Nutrients, 9*(9), Article 988. https://doi.org/10.3390/nu9090988

Verhagen, A.P., de Vet, H.C.W., de Bie, R.A., Kessels, A.G.H., Boers, M., Bouter, L.M., & Knipschild, P.G. (1998). The delphi list. *Journal of Clinical Epidemiology, 51*(12), 1235–1241. https://doi.org/10.1016/S0895-4356(98)00131-0

Zarzissi, S., Bouzid, M.A., Zghal, F., Rebai, H., & Hureau, T J. (2020). Aging reduces the maximal level of peripheral fatigue tolerable and impairs exercise capacity. *American Journal of Physiology–Regulatory Integrative and Comparative Physiology, 319*(6), R617–R625. https://doi.org/10.1152/AJPREGU.00151.2020