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D-aspartic Acid Supplementation Effects on Body Composition: A Systematic Review of Randomized Clinical Trials on Trained Males

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Abstract

Context: D-Aspartic acid (DAA) is an amino acid found in the brain and reproductive system. Some investigations have reported beneficial effects of DAA on brain function and reproductive system health by increasing testosterone through the hypothalamic-pituitary-gonadal axis. However, its effect on body composition is unknown. Given testosterone's role in muscle growth, this study aimed to evaluate the effect of DAA supplementation on the body composition of trained males.

Evidence Acquisition: PubMed, Scopus, Embase, and Web of Science (until 1 August 2021) were searched for this systematic review. Inclusion criteria assumed as clinical trials assessed the effect of DAA on body composition in trained males. After including articles by keywords, the articles were reviewed for meeting the eligibility criteria. Three independent researchers conducted the search and full-text review.

Results: Among 134 articles located during the primary search, five articles (47 interventions and 43 controls) were included in the study based on eligibility criteria. All included clinical trials had a low risk of bias. A review of the relevant literature concludes that different doses of DAA (three grams, six grams, 7.12, and 12 grams) in different intervention periods (two weeks, four weeks, and 12 weeks) have no effects on body composition in trained males.

Conclusions: DAA supplementation is a low-level booster of testosterone and has no significant effect on the testosterone level in professional male athletes, and cannot alter the body composition.

Keywords: Testosterone, D-Aspartic Acid, Body Composition, Athletes

1. Context

D-Aspartic acid is an essential amino acid present in the central nervous system and regulates the brain's hormone secretion and brain development (1). Animal studies demonstrated the effects of DAA on memory, learning, and cognition (2, 3). This amino acid also has a critical role in sexual function, observed in animal studies (4, 5). The effects of DAA on sexual function are attributable to nitric oxide production in the brain (6, 7). High levels of DAA have been observed in rat testicular veins, epididymis, parenchymal testicular cells, and spermatozoa (8). In addition, animal studies have suggested that DAA increases the release of gonadotropin-releasing hormone (GnRH), luteinizing hormone (LH), and growth hormone (GH) by affecting the hypothalamic-pituitary-gonadal axis (HPG axis), resulting in testosterone production by testes (9).

Testosterone boosting is helpful for muscle growth (10). Many athletes, especially bodybuilders, try to boost their testosterone levels to increase muscle mass and improve recovery from exercise. Nutritional supplementation is a valuable source for improving testosterone levels which are safe (11). D-Aspartic acid is also a popular dietary supplement consumed by athletes with the intention of increasing testosterone levels (12). Given its potential role in testosterone production, some assume that DAA supplementation improves body composition by improving testosterone formation and muscle growth. Therefore, plenty of professional athletes consume it to improve muscle mass and body composition; however, it is up to doubt whether the testosterone boosting resulting from DAA consumption can improve the body composition or not.

In this study, we conduct a systematic review to evaluate the effect of DAA in changing the body composition in the trained male.

2. Evidence Acquisition

2.1. Study Design and Eligibility Criteria

This systematic review was conducted to assess the impact of D-aspartic acid supplementation on body composition in an exercised population. A primary search was conducted to identify relevant articles, determine the risk of bias of the articles meeting inclusion, and avoid duplication of sources. The question of the study was designed based on the PICO. The PICO tool focuses on the population, intervention, comparison, and outcomes of an article (13). The main question in this research based on the PICO tool was considered as below:

Population: Healthy, physically active humans

Intervention: D-aspartic acid consumption

Comparison: placebo

Outcome: Body composition change

The inclusion criteria for this study were assumed as studies describing the association between D-aspartic acid and body composition in exercised human population until 2020. Inclusion criteria were assumed as (1) any clinical trial investigating the effect of D-aspartic acid on body composition (2) no limitation in patient age, race, gender, and date. Furthermore, exclusion criteria were assumed as follows: (1) study of D-aspartic acid on non-human population (2) unreliable and duplicated data (3) case reports, case series, and systematic review studies.

2.2. Search Strategy and Identification

Research databases included PubMed, Web of Science, Scopus, and Embase. The systematic search was based on "title and abstract," and the keywords (1) "D aspartic acid," "DAA," and “D aspartate” (2) "Body composition," "Muscle mass," and "Fat-free mass." In addition, 'AND' was used for combining the keywords. After the systematic search, all records were collected in a single Endnote library. Duplications were deleted based on "title, author, year" or "title, author, journal" similarity. The remaining references were exported to an Excel file for the screening.

2.3. Screening and Selection

Three researchers reviewed the abstract of articles for meeting the eligibility criteria. In the context of doubt about the article's inclusion, its inclusion in the study was based on the supervisor's decision. After the initial abstract review, databases were searched for full-text articles, and if the full-text of the articles was not available, ResearchGate was searched for full-text availability, and the author was contacted. After the screening process, the full text of articles was reviewed by the researchers for final inclusion. In addition, for the bias reduction, a manual search was conducted based on the references of included articles and searching cited articles in PubMed and Google Scholar.

3. Results

We identified a total of 134 articles after searching the databases. After deleting duplicates (n = 76), the researcher screened 58 articles for meeting the eligibility criteria. Among 58 articles, 54 articles were excluded from further consideration. Four articles were full-text reviewed; moreover, one article was included through a manual search of Google Scholar. Finally, five articles were included in this study. The flowchart of the study is presented in Figure 1.

3.1. Bias Assessment

We collected data from included full texts and imported them to an Excel sheet which was categorized into article information, outcomes, and quality assessment. The revised Cochrane risk-of-bias tool for randomized trials (ROB 2) was used as the quality assessment tool for included studies (14). The result of the bias assessment is presented in Table 1.

3.2. Study Characteristics

In the study of Willoughby et al. in 2013, the resistance-trained men with at least 1-year experience in training underwent a randomized, double-blind clinical trial to investigate the effect of DAA on body composition, sex hormones, and muscle strength. The intervention was conducted as a 4-week supplementation with 12 grams daily of DAA in the intervention group (10 resistance-trained males) and placebo supplementation in the control group. All participants engaged in resistance exercise four times per week (16 times overall). It was shown that muscle strength and body composition increased in both placebo and control groups, but there were no significant differences between the two groups. In addition, the serum levels of the gonadal hormone were unchanged in both groups after the intervention (15).

In another study by Willoughby et al. in 2014, twenty resistance-trained males underwent a randomized clinical trial with 7.12 grams of N-methyl-DAA (NMDA) in 28 days of resistance training four times per week. No significant differences were observed for total body water between the supplementation group and the placebo group. In addition, NMDA supplementation had no effects on LH, FSH, and testosterone (16).

In the 2017 LaMacchia et al. investigation, 15 young male athletes were included in a randomized, double-blind clinical trial to evaluate the effects of two weeks of DAA supplementation on muscle strength and body composition. It was concluded that DAA could increase muscle strength but had no effects on body composition and serum testosterone (17).

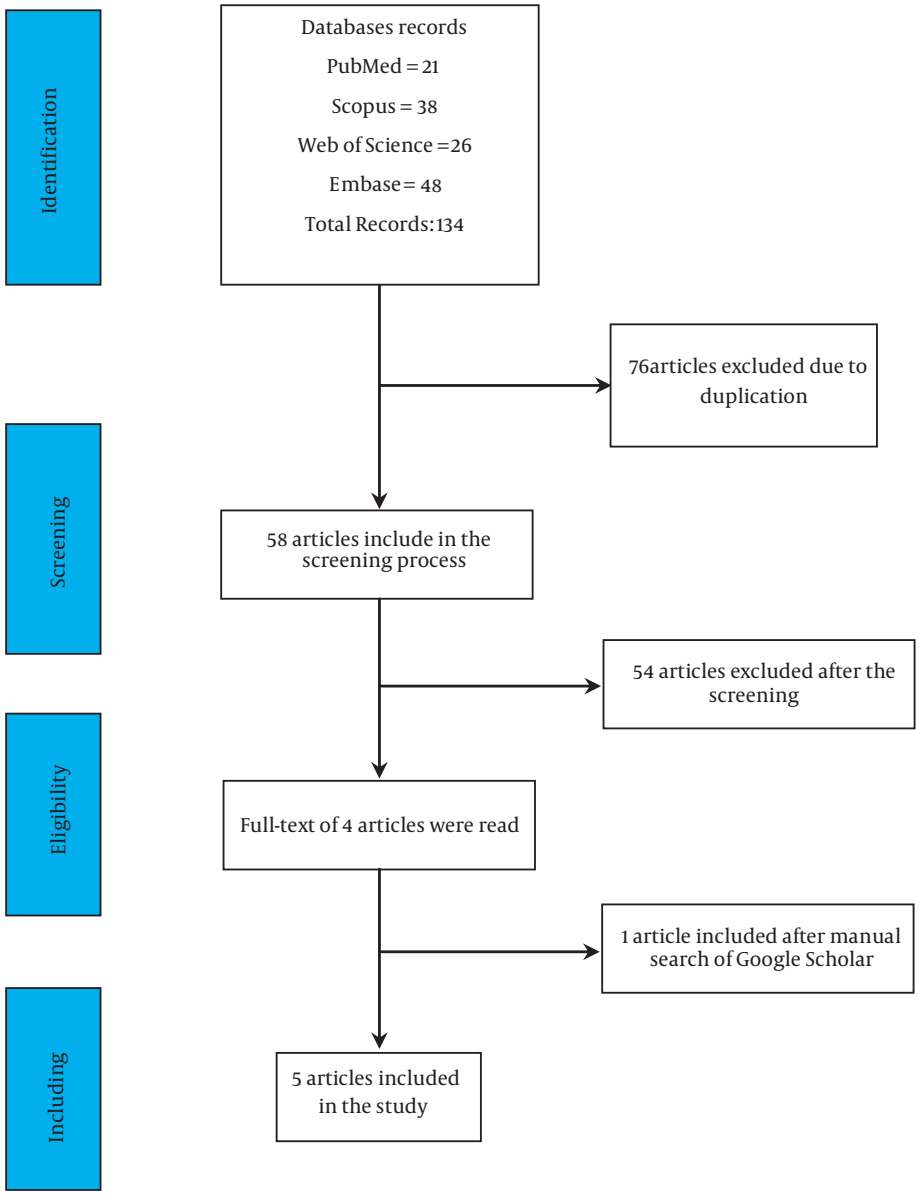

Figure 1. Flowchart of the study

Table 1. Bias Assessment Based on ROB 2

Study	Sequence Random?	Allocation Concealed?	Imbalance Suggest Problem?	Risk of Bias
Willoughby et al. (15)	Yes	Yes	Yes	Low
Willoughby et al. (16)	Yes	Yes	Yes	Low
LaMacchia et al. (17)	Yes	Yes	Yes	Low
Melville et al. (18)	Yes	Yes	Yes	Low
Crewther et al. (19)	Yes	Yes	Yes	Low

In another study in 2017, DAA supplementation was administered to ten resistance-trained men to assess its effectiveness on testosterone levels and muscle hypertrophy. It was shown that 12 weeks of DAA supplementation (6 grams per day) in resistance-trained men completing four days per week of resistance training had no significant effects on serum testosterone. In addition, DAA was no different than placebo in relation to muscle hypertrophy and body mass (18).

Similarly, Crewther et al. reported that two weeks of DAA supplementation (3 grams daily) had no effects on testosterone levels or body composition in professional male climbers (19).

The summary of included studies is presented in Table 2.

3.3. DAA Effects on Body Composition

It was concluded that different doses of DAA (three grams, six grams, 7.12, and 12 grams) in different intervention periods (two weeks, four weeks, and 12 weeks) have no effects on body composition (free fat mass, muscle mass, total body mass, total body water) in male athletes. In fact, consuming this supplementation is effective for testosterone boosting, but this is not enough for improving body composition.

4. Discussion

In the current study, we conducted a systematic review to evaluate the effects of DAA on the body composition of male athletes. It was concluded that DAA supplementation has no effect on the body composition of male athletes. In addition, it has conflicting results on testosterone levels of athletes and limited results on muscle strength of athletes that should be re-evaluated in future studies. To the best of our knowledge, this is the first systematic review for assessing DAA on the body composition of male athletes.

Testosterone is an endogenous androgenic steroid, the critical hormone for steroid synthesis in both males and females. This hormone also has other androgenic effects, including masculinizing and anabolic (muscle building) actions (20, 21). Improvements in skeletal muscle mass by enhancing testosterone levels may intensify muscle strength and physical function (22). It is also associated with total body cell mass improvement, visceral and trunk fat shrinkage, and improved insulin responsiveness (23). It has been observed that testosterone supplementation can alter body composition during strenuous exercise and low-energy diets (24). Therefore, many athletes use exogenous testosterone as a supplementary tool to enhance physical endurance, muscle mass, and muscle strength (25, 26).

Exogenous testosterone therapy is associated with severe complications, including cardiovascular events, prostate cancer, and breast cancer (27). Thus, it would be better to administer supplements that boost testosterone levels to prevent adverse effects of exogenous testosterone. Some studies revealed that supplements including vitamin D (28), Ashwagandha (29), Tribulus Terrestris (30), Fenugreek (31), Ginger (32), Zinc (33), L-arginine (34), magnesium (35), and DAA (36) are testosterone boosters. Nowadays, many athletes use testosterone boosters, assuming that they may gain muscle mass quickly, and the consumption of these products has an increasing trend (37). In fact, due to the prohibition of anabolic steroids by the world anti-doping agency (WADA), these products are used as a replacement for anabolic steroids in athletes (38).

Studies suggested that DAA can boost low testosterone levels by increasing the follicular stimulating hormone (FSH) and luteinizing hormone (LH), which affect Leydig cells in testosterone production (9). This supplement can also increase the circulating testosterone in the body and causes positive sexual effects, including increasing libido and improving sexual function. In the study of Topo et al. in 2009, 23 male volunteers consumed 3.12 grams of DAA daily for 12 days, which resulted in the increase of LH (by 33%) and testosterone (by 42%) in both humans and rats (39). In the study of Bloomer et al. in 2009, 10 overweight or obese men consumed the mixture of DAA/sodium nitrate/vitamin D3 for 28 days. This supplement was associated with a 10 - 15% increase in total and free testosterone and improved the libido in middle-aged obese men (40). However, some conflicting results are present in this regard. In the study of Melville et al. in 2015, two weeks of DAA consumption (three grams daily) had no effects on testosterone levels. In addition, six grams of DAA daily decreased the testosterone level (41). In addition, no effects on testosterone were seen in a long-term period (12 weeks) consumption of DAA (18). Similar results were seen in the study of Willoughby et al. (15, 16), LaMacchia et al. (17), and Crewther et al. (19).

It seems that DAA only can boost low testosterone levels in untrained men or men with sexual disorders. This supplement is not effective in the high-level boosting of testosterone, which is necessary for muscle growth. DAA is more prominent in untrained men, which is effective in their sexual function, but this supplement is not effective in athletes because professional athletes have higher levels of testosterone due to heavy exercise (20).

This study has some positive points. To the best of our knowledge, this is the first study that assessed this issue as a systematic review that can alter DAA supplementation attitude in athletes and coaches. Unfortunately, due to heterogenicity in data, we could not conduct a meta-analysis

Table 2. The Characteristics of the Included Studies

Study	Intervention Group	Intervention Time	No. Intervention (Control)	DAA Dosage	Body Composition Index	Conclusion
Willoughby et al. (15)	Resistance trained men	4 weeks of supplementation	10 interventions, 10 controls	12 grams daily	Total body mass (kg); Fat mass and fat free mass (kg); Total body water (kg)	Total body mass increased in both groups without significance. Fat mass, free mass, and total body water were unchanged
Willoughby et al. (16)	Resistance trained men	4 weeks of supplementation	10 interventions, 10 controls	7.12 grams of NMDA	Total body mass (kg); Fat mass and fat free mass (kg); Total body water (kg)	Total body mass and fat-free mass increased in both groups without significance. Total body water and fat mass were unchanged
LaMacchia et al. (17)	College male athletes	2 weeks of supplementation	9 interventions, 6 controls	3 grams daily	Total body weight (kg); Fat free mass (kg); Body fat percent (%)	Body composition was unchanged in both groups
Melville et al. (18)	Resistance trained men	12 weeks of supplementation	10 interventions, 9 controls	6 grams daily	Body mass (kg); Hypertrophy in quadriceps and calf muscle	Hypertrophy and body mass were increased in both groups with no significant difference
Crewther et al. (19)	Male climbers	2 weeks of supplementation	8 interventions, 8 controls	3 grams daily	Body mass (kg)	Body mass did not change in either placebo or intervention groups

which is one of the limitations of this study. In addition, due to improving the testosterone level and androgenic effects, the consumption of this supplementation is associated with some ethical issues among female athletes, and the data for this supplementation among females is significantly scarce.

4.1. Conclusions

DAA supplementation does not positively affect body composition, muscle hypertrophy, and fat-free mass in trained male athletes. In contrast, there is limited data to suggest that DAA supplementation may increase testosterone levels in males with pre-existing suppressed testosterone levels. In conclusion, DAA supplementation is not effective for increasing testosterone or altering body composition in healthy, physically active males. Trained males should be aware of the exact effects of DAA, which may be associated with reducing its consumption among professional athletes.

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Footnotes

Authors' Contribution: The main idea of this article is attributed to Mohammadyasin Lak. Dr. Kian Goudarzi and Dr. Mohammad Amin Shahrbaf, and Mohammadyasin Lak conducted the systematic search. The manuscript is written by Dr. Mohammad Amin Shahrbaf.

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