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Review

# Ergogenic dietary aids for the elderly

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ABSTRACT

Ergogenic dietary aids might be useful adjunctive therapy to enhance the effects of exercise in the elderly, who lose physical function with age. Many such aids have been tested in athletes and untrained younger persons in laboratory and athletic performance settings, with positive results, although not all studies have demonstrated benefit. Some substances have been tested in the elderly, including creatine, caffeine, β-hydroxy-β-methylbutyrate, ubiquinone, and carnitine. The published medical evidence for the use of these substances is considered in this review article. All studies have involved a few subjects for a short period. Studies of creatine alone or together with exercise in old persons have yielded mixed results. These studies have confirmed that creatine in older individuals, as in younger individuals, can increase the short-term capacity to perform quick, repeated episodes of intense activity. An investigation of caffeine has suggested that in older as in younger individuals, caffeine increases endurance but may not improve other parameters of exercise capacity. Evidence has implied β-hydroxy-β-methylbutyrate can increase the ability to perform certain short-term activities requiring strength, but not others. Carnitine has been reported to decrease fatigue and increase endurance in older persons. An investigation of ubiquinone has shown no benefit. Further testing has involved the combinations of agents, such as creatine and caffeine, and combinations of β-hydroxy-β-methylbutyrate, showing some small improvements in physical function. Future research with these and potentially other combinations over a longer duration will be needed to establish the safety and efficacy of ergogenic dietary aids.
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## Introduction

The number of physically limited elderly is expected to double, from slightly more than 20 million to more than 40 million, in the next 25 y [1]. Exercise has been found to decrease falls, increase mobility, and improve the ability of elderly persons to perform activities of daily living, but not all elderly persons have shown a uniform benefit [2–5].

One possible means to enhance the effect of exercise might be to provide adjunctive ergogenic agents to participants. The safety, availability, and cost are important considerations in the choice of such agents. This review evaluates what is known about the potential ergogenic agents that might benefit the elderly.

## Methodology

A search for published evidence was conducted using the PubMed database and the search terms *ergogenic*, *elderly*, *exercise*, and *physical performance*. When specific substances were identified from the original search, additional articles were obtained by using the names of the substances as search terms. After articles deemed irrelevant to the topic of the review and substances for which no published evidence of benefit existed were excluded, additional articles were collected from the references of the original set of articles.

## Results

Using this search strategy, 327 articles were reviewed, and 19 were found to be trials of ergogenic substances that included elderly subjects. All were controlled with placebo. There were 14 trials of creatine, two of carnitine, and one each of β-hydroxy- β-methylbutyrate (HMB), ubiquinone, and caffeine. Six lasted longer than 2 mo, and only one was as long as 6 mo.

### *Creatine*

Creatine, a substance endogenously produced from amino acids in the liver, is one of the most commonly used ergogenic

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dietary aids [6]. It can be ingested as a supplement, which is usually made from fish or meat [6]. In the muscle, it can be found in a free or phosphorylated form [6].

Creatine is believed to have multiple actions [6]. In the muscle, most creatine combines with a phosphate group to create phosphoryl creatine [6]. Phosphoryl creatine in turn phosphorylates adenosine diphosphate (ADP), promoting the diffusion of phosphate between myosin and the mitochondria, which facilitates the linking between myosin heads and preserves muscle tension [6]. Lower phosphocreatine levels increase the concentrations of phosphofructokinase, which induces glycolysis and increases adenosine triphosphate (ATP) levels [6]. Phosphocreatine may also promote protein synthesis and muscle hypertrophy. In addition, it serves to buffer the pH, absorbing hydrogen ions from creatine kinase, and when ADP becomes ATP [6]. Creatine, by augmenting the calcium influx into the sarcoplasmic reticulum, can shorten the time for repeated maximal isometric contractions [6]. Creatine and phosphocreatine may have different actions on mitochondrial respiration, creatine by augmenting the sensitivity of mitochondrial respiration of skeletal muscle to ADP, and phosphocreatine by lowering it [6].

The influence of aging on creatine metabolism has not been well studied. Older persons have less muscle creatine than younger persons [7]. The creatine-to-phosphocreatine ratio is slightly higher in older age, although the ratio of ATP to ADP is not altered with age [7,8]. In a comparison study of subjects of different ages, the supplementation of younger subjects (range 20–32 y) induced a greater increase in serum creatine and phosphocreatine than in older subjects (mean age 63–83 y) [9]. The supplementation of creatine may serve to stem the senescent decrease of type 2 muscle fibers, possibly as a result of increasing muscle hypertrophy, augmenting the expression of myogenic transcription factors, increasing satellite cell mitotic activity, and increasing ATP concentrations [7]. The supplementation of creatine might also increase the activity of the phosphocreatine energy system, which may enable greater work during exercise for longer periods [7].

Creatine has had variable effects on rodent aging models. Mice belonging to an inbred mouse strain, C57Bl/6J, ate a 1% creatine-supplemented diet or a standard diet [10]. The creatine-supplemented mice had a 9% longer life span than the control mice and performed better on cognitive testing. Senescence-accelerated mice ingested a 2% creatine supplement from 2.5 to 5 mo of age [11]. However, creatine did not prevent the age-related loss of muscle fibers.

In the laboratory, athletes who consumed creatine increased their isometric force and endurance. Ten younger men who consumed creatine 10 g/d for 15 d had significantly greater maximum voluntary knee extensor isometric force and endurance [12]. Sixteen young men 18 to 23 y old who took 5 g/d for 4 d had decreased muscle contraction and relaxation times during isometric elbow flexion [13].

Athletes who have ingested creatine have obtained performance benefits. Approximately four-fifths of all studies have demonstrated improvements at doses of 5 to 20 g/d for up to 2.5 mo [14–19]. Several investigations have tested the effects of creatine in the elderly, with mixed results. In one study, 30 men (mean age 70.4 y) took 0.3 mg $\cdot$ $kg^{-1}$ $\cdot$ $d^{-1}$ or a placebo for 5 d [20]. Subjects who ingested creatine had increased lean tissue mass and endurance while exercising using a leg press and performing knee extensions. Three months after the creatine supplementation stopped, the improvements persisted [21]. Fifteen men took creatine 20 g/d for 1 wk followed by 10 g/d for 2 wk or a placebo in a double-blinded, placebo, crossover trial [22]. In another investigation, 18 men 59 to 72 y old took creatine 0.3 kg/d or a placebo for 7 d, with improvements in strength power and fat-free mass [23]. Seventeen elderly subjects 60 to 78 y old took creatine 5 g/d or a placebo for 5 d [24]. Those subjects who consumed creatine had a small increase in mass but no improvement in their ability to perform isokinetic exercise. In a longer intervention, 28 participants, all at least 65 y old, ingested creatine 5 g/d or a placebo for 2.5 mo [25]. Those individuals taking creatine had significant improvements (approximately 25–40%) in measurements of dynamic and isometric strength [26]. Twenty men 60 to 82 y old took creatine 4 g/d for 20 d. There was a small increase in body mass but not in knee extensor exercise performance. When 32 persons 67 to 80 y old took creatine 20 g for 5 d and 3 g for the remainder of 2 wk or a placebo, no differences in measured exercise parameters were observed [27]. Twelve older men took creatine 5 g/d or a placebo, but no changes were noted in the degree of muscle fatigue or isometric voluntary force [28].

Creatine has also been used as an adjunctive therapy to exercise. Forty-six men 55 to 75 y old started an exercise program lasting 75 min/d 10 times a month [29]. Participants took creatine 5 g/d or a placebo, and the program lasted 6 mo to 1 y. Although the creatine group had more total creatine in the muscle biopsy, their exercise performance was no better than the placebo group. Older trained cyclists were compared with sedentary older and younger men in their ability to pedal a cycle ergometer after creatine or placebo ingestion [30]. The participants took creatine 5 g/d for 3 d; although the two groups of sedentary subjects significantly improved their exercise ability, the trained cyclists did not. The investigators speculated that trained subjects might have increased levels of catecholamines, which increased their creatine levels even in the absence of supplementation, thus decreasing the effect of further creatine intake.

In other investigations, creatine was combined with protein for its effect on exercise. In one study, 35 men 59 to 77 y old took creatine 0.1 g/kg with or without protein 0.3 g/kg for 2.5 mo or a placebo [31]. Subjects who took creatine with additional protein had an improved bench press strength by more than 25% than those who took creatine alone. Forty-two men 48 to 72 y old took creatine 5 g/d and whey protein 35 g for 3.5 mo or protein or creatine alone or a placebo [32]. All groups gained body mass and improved their strength, but there was no difference between groups.

Creatine has demonstrated the most benefit in a short-term administration in which individuals performed repetitive motion exercises [6]. In older individuals and over longer periods of administration, the benefits have not been clear-cut [7]. Trials of combinations of creatine with other substances, such as protein, have also yielded mixed results. Differences in the doses and lengths of administration and the exercise techniques used to study the benefits of creatine may account for some discrepancies in the results. Its exact mechanism of action and whether long-term benefits endure after the cessation of ingestion remain to be determined [33].

### *Caffeine*

Caffeine has long been studied as an ergogenic agent. Although its mechanism of action has not completely been elucidated, caffeine, which is structurally similar to adenosine, acts on adenosine receptor sites in multiple cell types, including myocytes, cardiac myocytes, and adipocytes [34]. One of its actions is to induce epinephrine release.

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Caffeine has multiple effects on physical performance, including increasing attention, improving endurance, and augmenting the conversion of stored lipids into free fatty acids [34]. Much of the research on the benefit of caffeine has been conducted in younger individuals, including trained athletes. Caffeine improves short- and long-term endurance in bicyclists, soccer players, swimmers, skiers, and rowers. However, in general, the impact of caffeine on anaerobic exercise in athletes has yielded mixed results [34].

In one study, caffeine was tested for its effect on the physical performance of elderly subjects. Thirty individuals (15 men and 15 women) 75 y old who consumed a mean of 486 mg (equivalent to 4.9 cups of coffee a day, but included two subjects who did not drink caffeine) were included in the study [35]. Subjects were not allowed to drink caffeine for 2 d before the start of the trial. At the onset of the experiment, participants were given a capsule of caffeine 6 mg/kg or a placebo, and they performed several exercises 1 h later. The individuals who ingested the caffeine had significantly greater endurance, less perceived effort, and greater isometric submaximal strength, but they performed no better than those who consumed a placebo on the other tests.

Caffeine, like creatine, has shown optimal effect in short-term trials in trained individuals [36], but has been tested only in a single study in the elderly in which it did confer benefit. It may be especially important in its effect on the perception of fatigue and pain. Its role during anaerobic metabolic conditions is worthy of future consideration.

### β-Hydroxy- β-methylbutyrate

The HMB is derived from the amino acid leucine and converted to HMB in the cytosol of cells [37]. It has been used by athletes as an over-the-counter nutritional supplement to augment muscle size and strength. The mechanism of the action of HMB is not well understood but may be the result of its ability to preserve and maintain cellular protein, increasing coenzyme Q10 (CoQ10) levels, and improving oxidative capacity [37]. In many investigations, individuals who consumed HMB improved their exercise performance. Cyclists and other trained and untrained athletes who consumed HMB 250 mg/d to 6 g/d were able to improve their exercise capacity [38–43]. A meta-analysis was performed on the effects of HMB in athletes and sedentary individuals and concluded that HMB induced minor total lower body strength improvements in untrained men but not in trained men [44].

In one investigation, 32 elderly participants with a mean age of 70 y took HMB 3 g/d for 2 mo or a placebo [38]. All exercised twice a week using 10 to 12 repetitions of upper and lower extremity resistance exercises. Those who took HMB had a significantly smaller fat-free mass and a significantly improved strength in latissimus dorsi pulldown and leg curl exercises but not in the other arm and leg exercises.

A review of these studies, noting mixed results, considered possible explanations for the lack of uniformity in benefit [37]. Among these were a lack of validity of the tests, variations in HMB dosage, short duration of trials, a lack of specificity between the exercise training and the testing conditions, and overtraining during exercise. The review concluded that adverse drug reactions were not observed at doses of 3 to 6 g/d.

### Ubiquinone (CoQ10)

Ubiquinone is an electron transport quinone found in the mitochondria of all animal cells. Its use has been tested in athletes and sedentary individuals, with mixed results. In a double-blinded, placebo, cross-over trial, 15 sedentary young men took CoQ10 100 mg/d or a placebo for 2 mo, performed exercises with lift loads of 75 g/kg of body weight five times for 30 s each, had a month washout period followed by 2 mo with the other treatment, and then repeated the exercise [45]. The CoQ10 supplementation improved the mean power at the end of the fifth lift.

However, other studies have shown no benefit. Twenty trained and 19 untrained young adults took CoQ10 200 mg or a placebo for 2 wk [46]. Subjects had to perform cycle ergometry and a leg-extension test on the first and last days of the trial. No significant changes in exercise performance were observed. In a trial involving the elderly, two small groups of individuals, one consisting of 8 participants 60 to 74 y old and the other consisting of 11 younger participants 22 to 38 y old, participated [47]. Each group took part in a double-blinded, placebo-controlled, cross-over trial in which they took CoQ10 120 mg/d or a placebo for 6 wk, after which they performed cycle ergometry. There was no difference in the exercise outcomes between groups. Young cyclists who consumed CoQ10 1 mg $\cdot$ $kg^{-1}$ $\cdot$ $d^{-1}$ for 1 mo showed no improvement in aerobic and anaerobic respiration or decreased fatigue thresholds [48].

### Carnitine

Another potential ergogenic compound is carnitine. Carnitine is an amino acid that aids the entrance of acetyl coenzyme-A into the mitochondria when fatty acids are oxidized to produce energy [49,50]. Athletes who took carnitine 2 g twice a day for 1 wk showed a significantly improved swimming ability in five 100-yard swims [51]. Ninety-six subjects (age range 71–88 y) took carnitine 2 g twice a day or a placebo for 6 mo. Individuals ingesting carnitine showed a significant improvement in subjective fatigue scale scores [49,52]. Thirty older persons (mean age 69 y) with emphysema who took carnitine 2 g/d for 1.5 mo added to an exercise regimen show improvements in 6-min walk time [53]. Thus, carnitine has some potential as an ergogenic agent, but evaluations of its use thus far have been quite limited.

### Other substances

There are several substances that may be ergogenic in the elderly but have not yet been tested in older persons. Resveratrol is a plant polyphenol found in numerous fruits and plants including grapes [54]. Mice that ingested a high-fat diet with resveratrol avoided decreases in exercise performance that were observed in mice that consumed a high-fat diet alone [55]. Senescence-accelerated mice that consumed a diet with 0.2% resveratrol maintained greater exercise performance than those that ingested a placebo [56]. However, human trials of resveratrol in exercise have not yet been performed. Another substance derived from fruits, the juice of the *Morinda citrifolia* (noni), was subjected to a preliminary evaluation of its ergogenic potential. Old mice were given doses of juice (10, 20, or 40 mL/kg of body weight) for 3 wk [57]. All groups of mice given the noni juice had statistically significantly better exercise times than the control mice. A polyphenol from the plant *Ecklonia cava* was tested in young athletes, in which 20 men 18 to 23 y old drank the polyphenol 0.4 g/L in a 180-mL drink daily or a placebo for 1 wk 30 min before walking for 30 min on a treadmill [58]. Subjects who drank the polyphenol showed significantly greater endurance in walking time than individuals who consumed the placebo.

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## Discussion

Few studies have defined the potential of ergogenic aids in the elderly. Most of these investigations have used creatine, singly or in combination with other agents. These studies have confirmed that creatine in older individuals, as in younger individuals, can enhance the short-term capacity to perform quick, repeated episodes of intense activity [6]. A single trial of caffeine has suggested that in older as in younger individuals, caffeine increases endurance but may not improve other parameters of exercise capacity [35]. One trial of HMB implied an enhanced ability to perform certain short-term activities requiring strength, but not others [38]. Two studies of carnitine have implied an ability to decrease fatigue and increase endurance in older persons [49,53], but one measured a subjective parameter only [49], and neither assessed its potential effect on strength. The single trial of CoQ10 that included elderly subjects reported a negative result [47].

Given the limited proven efficacy of the individual substances tested thus far, preliminary efforts have begun to test combinations of these substances for their ergogenic potential. One such combination is creatine and caffeine. Twelve athletes consumed 0.3 mg · $kg^{-1}$ · $d^{-1}$ for 5 d, followed a placebo, then creatine 0.3 mg · $kg^{-1}$ · $d^{-1}$ for 5 d, and then caffeine 6 mg/kg [59]. The individuals who took the combination of creatine and caffeine had greater power during sprinting than those who consumed a placebo [59].

In another trial, 10 young individuals ingested a mixture of a commercial supplement containing caffeine, creatine, and amino acids or a placebo [60]. Those who took the supplement had a 10% greater anaerobic running capacity and a longer time to exhaustion [60].

However, creatine and caffeine may have antagonistic effects [61]. In one investigation in humans, leg muscle relaxation time, which had been shortened by creatine, was prolonged by caffeine [61].

Other investigations have combined creatine with other agents. In one study, 38 participants who were at least 65 y old took creatine 5 g/d and conjugated linoleic acids 6 g/d, used by athletes to improve strength in nutraceuticals, or a placebo while performing resistance training for 24 wk [62]. Individuals who took the combination showed a significantly improved ability to perform most of the exercises including the leg press, knee extension, arm flexion, and chest press. No adverse reactions were observed. In other studies, creatine has been added to HMB. Forty younger subjects ingested creatine 20 g for 7 d and then twice the dose for 2 wk with HMB 3 g/d [63]. Subjects who took the combination showed a significant improvement in muscle strength. However, in another study in athletes, 18 who took this combination for 1.5 mo noted no improvement in strength [64].

The HMB has been tested in addition to substances other than creatine. A ketoacid form of HMB, α-ketoisocaproate, which is often found in HMB-containing supplements, was tested for its additive effect on HMB during exercise. In a small trial, eight young untrained men took HMB 3 g with α-ketoisocaproate 0.3 g for 2 wk before performing three sets of 10 repetitions of biceps curls at 70% maximum muscle strength [65]. Those who took the combination had significantly greater biceps strength. Another 14 subjects who took a similar regimen and engaged in downhill running did not experience a benefit [66]. An additional compound of HMB and the amino acids arginine and lysine was investigated in a pilot study of 23 elderly women (mean age 76.7) who took HMB 2 g, arginine 5 g, and lysine 1.5g or a placebo for 3 mo [67]. Participants who took the compound had significantly more knee flexor force and handgrip strength.

A small trial combined carnitine with caffeine. Five athletes pedaled a cycle ergometer longer after consuming caffeine 5 mg/kg and carnitine 15 g than after ingesting either substance alone [68].

Thus far, trials of ergogenic substances have been small and of short duration. Therefore, the safety of these substances, which is an important consideration in the elderly who, because of a loss of metabolic reserve with age and a greater likelihood of already consuming other multiple substances, has not yet been established. Future research should determine if longer-term trials of the combinations of these agents prove safe and effective in the elderly.

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