HYPOCHLORHYDRIA: Cranberry juice might increase absorption of dietary vitamin B-12 in people with hypochlorhydria due to its acidity (2817).

Typical Dosages & Routes of Administration that are Commonly Used

ORAL: For urinary tract infections, a typical dose is 3 oz cranberry juice cocktail (33% pure cranberry juice) daily for preventing infections and 12-32 oz per day for treating infections (615). Six capsules of dried cranberry powder are equivalent to 3 oz cranberry juice cocktail (615). Some sources recommend 300-400 mg of concentrated cranberry juice capsules twice daily (7010). Fresh or frozen cranberries may also be used; 1.5 oz is equivalent to 3 oz cranberry juice cocktail (3). Approximately 1500 grams of fresh fruit produce 1 L of juice. Cranberry juice cocktail is approximately 33% pure cranberry juice, sweetened with fructose or artificial sweetener (11515).

Comments

Avoid confusing cranberry fruit with high-brush cranberry (Viburnum opulus), which is also known as cramp bark (6,11).

The American cranberry (Vaccinium macrocarpon) is native to the northeastern and north central US and eastern Canada, and the fruit is cultivated commercially for food use and as a beverage base (2818). Cranberries, along with blueberries and Concord grapes, are the only fruits native to North America (2821). The Pilgrims called the cranberry "crane berry" because the stem and flower resembled the neck, head, and beak of the crane, and the name was shortened to the word used today (2821).

The European cranberry (Vaccinium oxycoccos) is native to the same areas of North America as its American cousin, as well as central and northern Europe and temperate areas of Asia (2819). The fruit of European cranberry is commercially important in Russia (2820). Approximately 1500 grams of fresh cranberries produce 1 L of pure cranberry juice.

CREATINE

This Product is Also Known As

Creatine Monohydrate.

CAUTION: Do not confuse creatine with its metabolite, creatinine.

Scientific Names

N-amidinosarcosine; N-(aminoiminomethyl)-N methyl glycine.

People Use This For

Orally, creatine is used to increase exercise performance and muscle mass in athletes (2101,2103) and older adults (4570,4571,4572). Creatine has also been used to treat heart failure (4562,4563), neuromuscular disease (4564), and mitochondrial cytopathy (4565), gyrate atrophy of the choroid and retina (4577,4578), and to lower cholesterol (4573). It is also used to slow the progression of amyotrophic lateral sclerosis (ALS, Lou Gehrig's disease) (209,209) and for various muscular dystrophies (6182).

Intravenously, creatine has been used in cardiac surgery (4586,4587).

Safety

POSSIBLY SAFE ...when used orally and appropriately (2100,2101,2103,3996). A one year study of 5-8 grams of creatine per day for 12 months found no adverse effects on blood and urine markers of health in a group of 17 college football players compared to a control group. This unpublished study was presented at the American College of Sports Medicine 2000 meeting (6117).

There is insufficient reliable information available about the safety of the long-term use of creatine or the use of creatine in children. Concerns about prolonged suppression of endogenous creatine have been raised, but not studied (3997).

PREGNANCY AND LACTATION: Insufficient reliable information available; avoid using.

Effectiveness

POSSIBLY EFFECTIVE ...when used orally for enhancing muscle performance during repeated bouts of brief, high-intensity exercise. Numerous studies have shown creatine to be beneficial for certain types of high-intensity exercises (2100,2101,2102,4591,4592,4593,4594,4601,4602,4604,4605,6015); however, some studies have shown no effect for other exercises (4582,4595,4596,4597,4606,6183). A meta-analysis of 32 creatine studies showed no effect of creatine supplementation on various measures of anaerobic performance, including fatigue, power, speed, strength, and work values. This unpublished study was presented at the American College of Sports Medicine 2000 meeting (6117). Creatine appears to be more effective for repeated maximal energy bursts than for single event performance (4593,4598,4599,4606). Many variables seem to determine the effect of creatine on performance, including whether the subject is well-trained or sedentary, the type of sport being tested, diet, and the dose regimen of creatine. Benefits have been shown in such sports as weight lifting, cycling sprints, and short-term kayaking bouts. Sports that may not benefit from creatine supplementation include sprints in running and swimming. It is possible that the benefit in certain sports is offset by weight gain from creatine supplementation (4576,4601,4604,4605,6015). Acute creatine loading may be more effective than chronic use (4603). Most studies have used 20 grams daily for 5 days for

creatine loading; however, various other regimens have been studied. One study used 9 grams daily for 5 days and was beneficial in weight lifters, while another study used 20 grams daily for 3 days and did not show a benefit in single sprints in cyclists (4576,4599,6015). Due to the variety of study methodologies and conflicting findings, it has yet to be determined exactly who can benefit from creatine supplementation and what dosing schedule might be most effective. So far, the data have been inconclusive. All studies have been limited by small sample size; all have involved less than 40 subjects and most less than 25. ...when used orally to increase strength and endurance in patients with congestive heart failure (4562,4563). In two open-label short-term studies, supplemental creatine improved exercise tolerance, but had no effect on ejection fraction (4562,4563). ...when used orally to treat gyrate atrophy of the choroid and retina (4577,4578). Two small studies have shown that creatine supplementation slows visual deterioration (4573,4578). ...when used orally short-term to improve muscle strength and daily-life activity in adults and children with various muscular dystrophies (6182). In a small double-blind, placebo controlled, crossover trial, creatine monohydrate daily for eight weeks mildly improved muscle strength and daily-life activity in a group of children and adults with facioscapulohumeral dystrophy, Becker dystrophy, Duchenne dystrophy, or sarcoglycan-deficient limb girdle muscular dystrophy (6182).

LIKELY INEFFECTIVE ...when used for increasing endurance or for improving performance in highly trained athletes (2103,2105,2106,4570). ...when used to improve isometric strength and body composition in adults over age 60 (4570,4571,4572). In three well-designed studies, creatine dosed at 20 grams per day for 5 days followed by lower maintenance doses had no beneficial effect on exercise except reducing muscle fatigue (4570,4571,4572). In one study it had no effect on quadriceps fatigue after repeated sets of explosive work (6183).

There is insufficient reliable information available about the effectiveness of creatine for its other uses.

Possible Mechanism of Action & Active Ingredients

Creatine is found primarily in skeletal muscle (95%), but also in heart, brain, testes, retina, and other tissues (3997,3998). The body synthesizes 1 to 2 grams of creatine a day primarily in the liver, kidneys, and pancreas (3997). Dietary sources, such as fish and meats, supply an additional 1 to 2 grams (3977). One pound of fresh uncooked steak contains about 2 grams of creatine (4575). Creatine is irreversibly converted to creatinine and excreted by the kidneys (3997). Creatine in skeletal muscles exists in dynamic equilibrium with phosphocreatine (3997). Body stores of phosphocreatine in skeletal muscle serve as a precursor to the energy molecule, adenosine triphosphate (ATP). Higher levels of creatine can enhance the ability to renew ATP for short energy bursts (10 to 20 seconds) and improve resynthesis of phosphocreatine during recovery from intense exercise, although faster resynthesis has been questioned (2103,3997,4576,4580). Supplementation variably increases total creatine (4574,4583). People such as vegetarians, who have lower initial total creatine, are more likely to respond to supplemental creatine, while people with higher initial levels may not respond (4574). Creatine levels return to baseline within 28 days of discontinuing supplementation (2101,4582). Skeletal muscle has a saturation point at which additional supplemental creatine will not increase intracellular creatine levels (3999). Excess supplementation increases urinary creatine and creatinine (4576). In patients with gyrate atrophy, an inherited metabolic disease in which phosphocreatine is depleted, supplemental creatine increased myofibrillar protein synthesis resulting in muscle accretion (4576,4587). Although some laboratory evidence identifies creatine as a muscle builder, most clinical evidence supports increased water retention as the primary cause of creatine-induced weight gain (4575,4576,4579,4588). Five days of creatine loading (20 grams per day) in healthy adults resulted in increases in body weight and fat-free mass, but did not affect blood pressure, renal function, or plasma CK activity (4569). Body mass changes were greater in men than women (4569). One small study suggests that creatine may reduce lactate production, as evidenced by lower increases in blood lactate levels in well trained males who received the supplement (4604). However, another small study did not show a reduction in blood lactate accumulation with creatine (4592). Creatine might have a beneficial effect on lipid levels in some people (4573). Creatine has been used in preliminary clinical studies to increase high-intensity strength in people with neuromuscular disease (4564) and increase the strength of high-intensity anaerobic and aerobic type activities in people with mitochondrial cytopathies (4565). Early laboratory evidence suggests that creatine might be useful in diseases such as amyotrophic lateral sclerosis, Huntington's disease, and Parkinson's disease (4566,4567,4568).

Adverse Reactions Including Known Allergies

Creatine use can cause gastrointestinal pain, nausea, and diarrhea (2103,4576). Although not reported in clinical studies, 25% of male collegiate athletes taking creatine reported muscle cramping (4584). A one year study of 5-8 grams of creatine per day for 12 months in a group of 17 college football players found no adverse effects on blood and urine markers of health. When researchers compared blood and urine samples they found no differences in serum creatinine, urea nitrogen, uric acid, muscle and liver enzymes, blood lipids, electrolytes, and percentage of whole blood red and white cells in the creatine group compared a control group. Also, there was no increase in the incidence of injury or cramping in the creatine group. This unpublished study was presented at the American College of Sports Medicine 2000 meeting (6117). A theoretical increase in the risk of dehydration subsequent to intracellular fluid shifts has led most creatine manufacturers to caution about adequate hydration with creatine supplementation (217,4576). Creatine typically causes a weight gain of 0.5 to 1.6 kg (see Mechanism of Action) that increases with prolonged supplementation (3997). Creatine can also cause renal dysfunction (184,2118), although renal toxicity among people with healthy kidneys appears to be rare (2120,3996). There is one report of acute interstitial nephritis and focal tubular injury after four weeks of creatine at 5 grams four times daily (184). Supplemental creatine, loaded at 15 grams per day for one week, then 2 grams per day, caused a significant decline in creatinine

clearance in a man receiving cyclosporine for steroid-resistant focal segmental glomerulosclerosis (2118). A small study of athletes taking an average of 10 grams of creatine daily for 1 to 5 years maintained renal function comparable to control athletes not taking supplements (3996). The effects of chronic creatine administration have not been adequately studied. There is one report of ischemic stroke in an athlete who consumed creatine monohydrate 6 grams, caffeine 400-600 mg, ephedra 40-60 mg, and a variety of other supplements daily for six weeks (1275). The FDA has received a total of 32 complaints of adverse effects linked to creatine, including seizures, cardiomyopathy, arrhythmias, rhabdomyolysis, and cardiac arrest, although causality has not been proven (4585). Theoretically, the lax manufacturing standards for nutritional supplements could put people using high doses of creatine at risk for significant exposure to toxic contaminants.

Possible Interactions with Herbs & Other Dietary Supplements

EPHEDRA: There is one report of ischemic stroke in an athlete who consumed creatine monohydrate 6 grams, caffeine 400-600 mg, ephedra 40-60 mg, and a variety of other supplements daily for six weeks (1275).

CAFFEINE: There is one report of ischemic stroke in an athlete who consumed creatine monohydrate 6 grams, caffeine 400-600 mg, ephedra 40-60 mg, and a variety of other supplements daily for six weeks (1275). Caffeine can interfere with the ergogenic effects of creatine supplementation (2117).

Possible Interactions with Drugs

NEPHROTOXIC DRUGS: Theoretically, creatine should be avoided by people taking drugs with nephrotoxic potential, such as Cyclosporin, Angiotensin-Converting-Enzyme Inhibitors, and Nonsteroidal Anti-inflammatory drugs on a prolonged basis.

Possible Interactions with Foods

CAFFEINE can interfere with the ergogenic effects of creatine supplementation (2117).

Possible Interactions with Lab Tests

SERUM CREATININE: Creatine is metabolized to creatinine. High serum creatinine levels can result despite normal renal function (2100,2103).

Possible Interactions with Diseases or Conditions

KIDNEY DYSFUNCTION: Creatine should be avoided by people with pre-existing renal disease or by people with diseases such as diabetes that increase the risk for renal dysfunction. (4576).

Typical Dosages & Routes of Administration that are Commonly Used

ORAL: For improving physical performance, several dosing regimens have been tried. Creatine is typically acutely loaded with 20 grams per day (or 0.3 grams per kg) for 5 days followed by a maintenance dose of 2 or more grams (0.03 grams per kg) daily (4576). Although 5 day loading is typical, 2 days of loading has also been used (4576). A loading dose of 9 grams per day for 6 days has also been used (6015). Some sources suggest that, instead of acutely loading, similar results can be obtained with 3 grams per day for 28 days (2104). During creatine supplementation, the water intake should be 64 ounces per day (2103,2104). For heart failure, 20 grams per day for 5-10 days was used in clinical trials (4562,4563). For gyrate atrophy, 1.5 grams per day has been used (4577,4578). For muscular dystrophies, 10 grams per day has been used by adults and 5 grams per day has been used by children (6182).

Comments

Creatine is allowed by the International Olympic Committee, National Collegiate Athletic Association (NCAA), and professional sports (3998,4575,4576). However, the NCAA no longer allows colleges and universities to supply creatine to their students with school funds. Students are permitted to buy creatine on their own and the NCAA has no plans to ban creatine unless sufficient medical evidence indicates that it is harmful (6140). With current testing methods, detection of supplemental creatine use would not be possible (4575). Creatine use is widespread among professional and amateur athletes and has been acknowledged by well-known athletes such as Mark McGuire, Sammy Sosa, and John Elway (3998). Following the finding that carbohydrate solution further increased muscle creatine levels more than creatine alone, creatine sports drinks have become popular (4576,4589). Annual consumption of creatine in the US is estimated to exceed 4 million kg (3998).

CROTON SEEDS

This Product is Also Known As

Tiglium, Tiglium Seeds.

Scientific Names

Croton tiglium.

Family: Euphorbiaceae.

People Use This For

Orally, croton seed oil is used as a purgative (3800).

