Background

L-arginine is an amino acid that is necessary for the body to make protein and is found in red meat, poultry, fish, and dairy foods. It was studied in the early- and mid-1990s for its potential effects on wound healing, post-operative recovery, AIDS-related wasting, and angina pectoris, among other conditions. In the last decade, L-arginine has been marketed as an ergogenic (i.e., performance-enhancing) supplement, most notably in the “nitric oxide” class of supplements.

The ostensible ergogenic potential is through three mechanisms. First, the substrate L-arginine along with O₂ is converted to citrulline and NO (nitric oxide). Nitric oxide causes vasodilation (widening of blood vessels), which can increase blood flow to tissues such as myocardial and skeletal muscle. The primary theory behind its use as an ergogenic aid is this vasodilation, which is thought to increase blood and nutrient flow to skeletal muscle.¹ ² Second, L-arginine is a substrate in the pathway for the production of creatine, which is produced in the liver.¹ ² (Creatine is covered in a separate monograph.) Third, under certain conditions, L-arginine is known to increase the release of endogenous growth hormone.¹ ³ ⁸

Dose Range and Upper Limit

Food and Nutrition Board DRI:

RDA/AI: Not relevant for this substance.

Upper Limit: Not relevant for this substance. Normal dietary intake approximates 5.4 g/100 g of mixed dietary proteins.⁹

The Observed Safe Level (OSL) for L-arginine is considered to be 20 grams per day in healthy adults.¹⁰

Doses Used In Randomized Clinical Trials: Most human studies on L-arginine have used doses of five to nine grams per day, or alternatively, 0.1 g/kg/day.⁶ ¹¹⁻¹⁷

Toxicology Data: No NOAEL (no observed adverse effect level) or LOAEL (lowest observed adverse effect level) could be determined⁹ for L-arginine.¹⁰

Evaluation of Potential Benefits

The primary putative ergogenic benefits of L-arginine are related to the performance of military tasks that call for increases in peak power, improvement in VO₂max (a measure of aerobic fitness), and muscle endurance. Studies on L-arginine have been small and show mixed results for the ergogenic benefit of supplementation at the doses discussed above (see Dose Range and Upper Limit) ³ ¹¹⁻¹³,¹⁶⁻¹⁸⁻²⁰ Although there are some studies showing benefits of L-arginine supplementation vis-à-vis peak power and VO₂max ¹¹⁻¹³,¹⁶⁻¹⁸ some other studies show none.¹⁴,¹⁷,¹⁸

Some studies have looked at the purported ergogenic mechanisms, including the release of endogenous growth hormone. Although L-arginine supplementation likely increases growth hormone secretion while a person is at rest, supplementation in conjunction with exercise does not appear to increase endogenous growth hormone more than exercise alone.⁴⁻⁸,¹⁹

There is little evidence to support the claim that L-arginine taken in conjunction with creatine increases the creatine found in skeletal muscle.¹⁵

Potential Detrimental Effects on…

Military Performance: Although L-arginine is a naturally occurring amino acid, it is known to cause abdominal bloating and diarrhea when taken as a supplement. ²¹ In small studies, it has been shown to increase airway reactivity in asthmatic patients.²² As a potential vasodilator, it has the potential to affect mechanisms leading to vascular headaches.²³
Military Survivability: L-arginine has been linked to several anecdotal reports of adverse events requiring medical attention. Such events have included palpitations, headache, and elevated blood pressure. Many of these adverse events were associated with multiple-ingredient products (i.e., “nitric oxide” products) in which L-arginine was one component, and it is uncertain as to which product or combination of products led to the adverse events.

Other Health Risks
L-arginine is often included in multiple-ingredient “nitric oxide” products, making it difficult to attribute adverse events and health risks to any one ingredient or combination of ingredients. Any combination product should be used with caution.

Interactions with Medications or Other Bioactive Substances
All interactions with L-arginine are theoretical and are related to L-arginine’s vasodilatory effects. L-arginine supplementation should be used with caution in patients taking:

- Antihypertensive medications and nitrates. Vasodilation caused by L-arginine could have an additive effect with antihypertensives and could cause hypotension.
- Phosphodiesterase type 5 (PDE-5) inhibitors (e.g., sildenafil, vardenafil, tadalafil). Vasodilatory effects of PDE-5 inhibitors could in theory have additive effects with those of L-arginine.
- Triptan medications. Vasodilator mechanisms of triptans could compete with the vasodilatory effects of L-arginine. Similar effects can occur when L-arginine is used in combination with supplements such as coenzyme Q-10 and fish oil.

For details of these and other potential interactions, visit the Natural Medicines Comprehensive Database.

Withdrawal Effects
None noted.

Concern and Benefit Estimate (see Dietary Supplement Risk Matrix)

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<thead>
<tr>
<th>Benefit potential:</th>
<th>Low to Moderate</th>
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<tbody>
<tr>
<td>Risk (safety concern):</td>
<td>Moderate</td>
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Classification score: 8

L-arginine supplements exceeding normal dietary intakes—used either singly or in combination dietary supplement products—have little proof of benefit with significant safety concerns.

References