L-Arginine

designs for health®

*Natural support for cardiovascular health and immune function**

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Designs for Health's L-Arginine provides 750 mg of the amino acid arginine per capsule. Arginine is needed for protein structure and function but has biological roles that go far beyond this. It can be synthesized endogenously (primarily in the kidneys), and this typically generates an adequate supply of arginine, but arginine is classified as a conditionally essential amino acid for infants and children, and for adults under catabolic stress or with dysfunction of the small intestine or kidney.[1] Pregnancy, strenuous exercise, trauma and recovery from surgery may also increase the need for arginine.

Role in Nitric Oxide Synthesis & Cardiovascular Function
L-Arginine is best known for its protective role in cardiovascular health. It is a precursor to nitric oxide (NO), a compound produced via nitric oxide synthase (NOS). There are three isoforms of NOS: endothelial (eNOS), neuronal (nNOS), and inducible (iNOS).

Endothelial nitric oxide synthase plays a critical role in cardiovascular health and blood vessel function. eNOS is synthesized by the endothelial cells lining the inner surface of blood vessels and is involved in production of NO, which regulates vascular tone and facilitates blood flow by promoting vasodilation in all types of blood vessels, including arteries.[2] (eNOS has also been detected in cardiac muscle cells, platelets, and select neurons of the brain.)

NO is predominantly recognized for this vascular relaxing effect, which may help in blood pressure regulation.[3] Beyond this, it helps protect the endothelium by inhibiting vascular inflammation, proliferation of vascular smooth muscle cells, leukocyte adhesion, and platelet adhesion and aggregation.[2,3] The loss of NO-mediated vasodilation is associated with alterations in the structure and function of the vascular endothelium leading to coagulation abnormalities and is considered to be an early step in the development of atherosclerosis.[2] NO is critical for healthy vascular function; aside from influencing vasodilation, it is antiproliferative, anti-inflammatory and antithrombotic.[4] Decreased availability of arginine is believed to be behind the reduction in NO production that may contribute to vascular malfunction or damage.

Through effects on nitric oxide availability, L-arginine may support*:

- Healthy blood pressure
- Endothelial and blood vessel function
- Proper platelet aggregation and blood clotting
- A healthy inflammatory response
- Neuronal communication and synaptic plasticity
- Healthy immune function
- Erectile function deficiencies on metabolic testing

Supplement Facts

Serving Size 1 capsule

Amount Per Serving		% Daily Value
L-Arginine	750 mg	*

*Daily Value not established.

Other Ingredients: Cellulose (capsule), vegetable stearate.

The use of statin drugs for primary prevention of cardiovascular disease or events is a subject of much debate and controversy. To the extent that these drugs are effective in either primary or secondary prevention, it is increasingly believed that the mechanism is unrelated to the lowering of LDL cholesterol and may be based in statins' pleitropic effects, including effects on eNOS. Statins stimulate and upregulate eNOS, thereby increasing endothelial NO production, including under hypoxic conditions.[5,6] The increase in eNOS may favorably affect platelet aggregation and thrombosis, as well as contribute to increased cerebral blood flow.[7] This may underlie the purported beneficial effects of statins for secondary prevention of stroke,[6] also independent of cholesterol lowering. In mouse models of stroke, eNOS-knockout mice show increased infarct sizes, suggesting that protective effects are likely mediated at least in part by eNOS and therefore, arginine.

A neuronal form of nitric oxide synthase (nNOS) is expressed in central and peripheral neurons and some other cell types. Its functions include influencing synaptic plasticity in the central nervous system, central regulation of blood pressure, smooth muscle relaxation, and vasodilatation via peripheral nitrergic nerves.[3] In the peripheral nervous system, NO derived from nNOS acts as an "atypical neurotransmitter" that mediates vasodilation, penile erection, and relaxing components of gut peristalsis.[3] nNOS has been identified in the spinal cord, sympathetic ganglia, adrenal glands, peripheral nitrergic nerves, in the epithelial cells of various organs, kidney macula densa cells, pancreatic islet cells, and in vascular smooth muscle, with the largest pool in terms of tissue mass being found in skeletal muscle.[3] nNOS-containing nitrergic nerves are responsible for penile erection by promoting relaxation of smooth muscle in the corpus cavernosum. Residual nNOS activity is essential for the pro-erectile effect of drugs such as sildenafil and tadalafil, which work via inhibition of phosphodiesterase 5 (PDE5).[3] PDE5 is also significantly expressed in pulmonary arteries, so apart from their effect on erectile function, these two drugs have been approved for the treatment of pulmonary arterial hypertension.[8] It may be that adequate NOS activity and arginine/NO availability is necessary for this effect as well.

Inducible nitric oxide synthase is needed for the immune system. It is identified primarily in macrophages, and as its name indicates, is induced by bacterial lipopolysaccharide, cytokines, and other agents.[3] Macrophages produce large amounts of NO, believed to be largely responsible for their cytotoxicity.

The following nutrients need to be optimized for maximizing nitric oxide production and protection from oxidation (conversion to peroxynitrite radical): natural folate (from foods or 5-MTHF supplementation), vitamin A, vitamin E isomers (as gamma-tocopherol or mixed tocotrienols), vitamin C and various other antioxidants (such as grape flavonoids and glutathione).

See the DFH white paper on "Safety of arginine/citrulline supplementation in healthy subjects versus those with cardiovascular or diabetic pathologies or with previous myocardial infarct" for details on nutritional assessments and nutritional interventions that may be implemented along with arginine supplementation.

Designs for Health's NOx Synergy™ is a formula that may be used as an alternative to standalone arginine capsules. It provides arginine combined with citrulline, folate (as 5-MTHF), powerful antioxidants (vitamin C, grape flavonoids, glutathione), nutrients that support healthy blood pressure (taurine, pantothenic acid), and creatine.

Common sources of arginine in the North American diet include meat, poultry, fish, dairy products and eggs. Nuts, peanuts and almonds in particular, are rich sources of arginine, and a high arginine content is believed to contribute to the noted beneficial role of nut consumption on cardiovascular health.[9,10] Analyzing NHANES data using 24-hour food recall, researchers determined that individuals with higher arginine intake had lower C-reactive protein (CRP) compared to those with lower intakes. Adjusting for age, sex, race, exercise, total caloric intake, BMI, smoking status, diabetes, hypertension and fiber intake, it was found that subjects with the highest arginine intake were 30% less likely to have high CRP (> 3.0) compared to those with lower intake. Compared to those in the highest quartile of arginine intake, those in the lowest quartile had nearly double the likelihood of having elevated CRP.[11]

Blood Pressure
Meta-analyses looking at arginine supplementation show that compared to placebo, supplementation with arginine results in lower systolic and diastolic blood pressures.[12] Arginine supplementation (along with B6, B12 and folate) in adults with mild-to-moderate hypertension resulted in improvement in blood pressure, with tendency toward larger nighttime decreases (nocturnal dipping), indicating improved cardiovascular function.[13] A review of meta-analyses evaluating the effect of L-arginine on blood pressure found that arginine supplementation results in small but significant reductions in systolic and diastolic blood pressure in hypertensive adults, including pregnant women with gestational hypertension or preeclampsia; however, some analyses have found that in pregnant women, reductions were significant only in diastolic pressure and not in systolic.[14-17] Generally speaking, effective doses of arginine are high and yield only modest results, but combined with other interventions that may improve blood pressure and endothelial function (e.g., magnesium, low-carbohydrate diet[18-20]), arginine may be a helpful adjunct.

Erectile Function
Owing largely to its influence on NO, arginine has been shown to improve erectile function in men with erectile dysfunction (ED). A systematic review and meta-analysis of studies evaluating arginine supplementation in men with mild-to-moderate ED found that arginine resulted in significant improvements in erectile function, overall satisfaction, intercourse satisfaction and orgasmic function.[21] Randomized controlled trials show that the combination of arginine with ED medications (sildenafil or tadalafil) is more effective for improving ED than either alone.[22,23] (Designs for Health cautions against using arginine with ED medications, however. See note below.)

Protective Role in Metabolic Syndrome, Type 2 Diabetes and Obesity
Elevated blood pressure is included in the diagnostic criteria for metabolic syndrome and CVD is the number one cause of death in those with type 2 diabetes (T2D). With this in mind, there may be a beneficial role for arginine supplementation in these patients.[24] In patients with impaired glucose tolerance (IGT) and metabolic syndrome (MetSyn), compared to placebo, 18 months of arginine supplementation reduced risk for progression to T2D over the next 9 years.[25] Arginine supplementation has been shown to reduce adiposity in animals and humans, in part by decreasing growth of white adipose tissue and stimulating mitochondrial biogenesis and development of brown adipose tissue, as well as increasing lipolysis and metabolism of glucose and fatty acids while inhibiting fatty acid synthesis.[26-29]

In a study of obese, insulin-resistant patients with T2D who followed a hypocaloric diet plus an exercise program, two cohorts—arginine supplementation and placebo—both showed significant decreases in body weight, waist circumference, daily glucose profiles, fructosamine and insulin, but arginine supplementation resulted in greater reductions in fat mass and waist circumference while preserving more fat-free mass and inducing greater improvements in fructosamine and mean daily glucose profile, with improvements also seen in assessments of endothelial function and oxidative stress compared to placebo.[30] A double-blind RCT in subjects with IGT and MetSyn showed that 18 months of arginine supplementation plus lifestyle changes resulted in no change in incidence of progression to diabetes, but significantly increased return to normal glucose tolerance compared to placebo plus lifestyle change. At a 30-month follow-up point, subjects who had been in the arginine arm showed greater probability of remaining free of diabetes.[31]

Recommended Use:

- As a dietary supplement, take one capsule per day, or as directed by your health care practitioner.
- Arginine may be used along with LibidoStim-M™ or LibidoStim-F™ but is not recommended with erectile dysfunction medications.
- Zinc plays a structural (but not catalytic) role in all forms of NOS so it may be prudent to assess zinc status in those who may benefit from L-Arginine.[3] Consider adding Zinc Supreme™ if indicated.

For a list of references cited in this document, please visit:
http://catalog.designsforhealth.com/assets/itemresources/L_Arginine_References.pdf

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.