

# Nitric Oxide Fuel™



## CLINICAL APPLICATIONS

- Support Circulatory Health
- Support Cardiovascular Health
- Optimize Muscle Synthesis, Muscle Function, and Adaptation to Exercise
- Support Anti-Inflammatory Pathways

*Nitric Oxide Fuel™ is a patented, (U.S. PATENT: 6,905,707), extended-release formulation that combines the highest quality source of pure arginine alpha-ketoglutarate with ACTINOS™, a proprietary whey peptide fraction that upregulates nitric oxide synthase. This powerful ingredient has been proven to increase nitric oxide levels by 950% over baseline arginine-derived nitric oxide.‡*

**All 360 Medicine® Formulas Meet or Exceed cGMP quality Standards**

## DISCUSSION

Nitric Oxide Fuel™ elevates the plasma level of L-arginine, a “semi-essential” amino acid considered the most potent nutraceutical ever discovered. It is perhaps the only nutraceutical whose remarkable properties are validated by a Nobel Prize in Medicine (1998). More than 60,000 clinical studies have brought L-arginine to the forefront of modern medicine as a nutrient that offers a wide range of health benefits.

As the substrate of nitric oxide-generating enzymes (NO synthetases), L-arginine is considered a direct nitric oxide (NO) precursor. Nitric oxide is an endogenously produced cellular signaling molecule involved in a variety of endothelium-mediated effects in the vasculature.<sup>[1]</sup> The plasma concentration of L-arginine might be a rate-limiting factor for NO production. Oral supplementation with L-arginine has been demonstrated in humans to increase smooth muscle relaxation, inhibit platelet aggregation, and inhibit expression of adhesion molecules and endolelin-1.<sup>[2]</sup> L-arginine drives the biosynthesis of NO in tissues including the vascular endothelium and skeletal muscle.<sup>[3]</sup> Acting via the cGMP intracellular signaling system, NO increases blood flow without increasing blood pressure.<sup>[4]</sup> In short, NO causes vasodilation by inhibiting smooth muscle contraction. Increased blood flow results in increased nutrient uptake and glucose utilization into muscle, especially during exercise.<sup>[4]</sup>

In addition to the cardiovascular/circulatory benefits, L-arginine is involved in ammonia detoxification, hormone secretion and immune health. It supports the synthesis of protein.<sup>[5]</sup> The generation of nitric oxide may act as a molecular switch that activates PGC-1 $\alpha$ , the master regulator of mitochondrial biogenesis and energy metabolism.<sup>[6]</sup> Many athletes have safely and effectively used it to increase ‘muscle pump’ during and for several hours after a workout, increase overall workout capacity (muscular endurance), and increase post-exercise recovery.<sup>[7]</sup>

ACTINOS® is a mixture of both high and low molecular weight fractions of proteins and peptides derived from whey through patent-pending technology. Strong evidence suggests that these fractions are NOS activators that boost NO production by factors unrelated to arginine, Ca<sup>++</sup>, or bradykinin. ACTINOS possibly increases the transcription of NOS gene and its role in reducing the negative feedback mechanism on NO production. The synergistic activity of the size-based fractions of ACTINOS has been shown to increase NO production in human endothelial cells in vitro from 9.5 to 12.7 times compared to a control.<sup>[8]</sup>



Nitric Oxide Fuel is manufactured in the U.S. using the highest purity commercially-available (>98.0%) L-arginine alpha-ketoglutarate. This patented formulation is specially designed to deliver L-arginine alpha-ketoglutarate in a controlled manner over a period of about 4-6 hours. A considerable fraction of an oral L-arginine dose is metabolized pre-systemically or excreted from the gut; then eliminated by glomerular filtration and almost completely reabsorbed by the renal tubules.<sup>[9]</sup>

‡ Results confirmed in in-vitro studies.

ACTINOS® is a registered trademark of Glanbia plc.

### Supplement Facts

Serving Size: 3 Caplets  
Servings Per Container: 20

	Amount Per Serving	%Daily Value
Arginine <i>alpha</i> -ketoglutarate‡	1980 mg	**
ACTINOS <sup>®</sup> ™ Whey Peptide Fraction‡	150 mg	**

\*\* Daily Value not established.

‡ Controlled delivery formulation

**Other Ingredients:** Dicalcium phosphate, cellulose ethers and composites, pectin (citrus fruit extract), seaweed extract, corn extract, magnesium stearate, talc USP.

### DOSING:

Take three caplets twice per day as follows: three caplets 30 minutes before breakfast and three caplets again 30 minutes before lunch with 8 ounces of water each time.

### REFERENCES

1. Moncada S, Higgs EA. Nitric oxide and the vascular endothelium. *Handb Exp Pharmacol.* 2006;(176 Pt 1):213-5 [PMID: 16999221]
2. Tousoulis D, et al. Mechanisms of disease: L-arginine in coronary atherosclerosis—a clinical perspective. *Nat Clin Pract Cardiovasc Med.* 2007 May;4(5):274-83. [PMID: 17457351]
3. Boger, RH, Bode-Boger, SM: The clinical pharmacology of L-arginine. *Annu Rev Pharmacol Toxicol* 41:79-99, 2001 [PMID: 11264451]
4. Preli, RB, Klein, KP, Herrington, DM: Vascular effects of dietary L-arginine supplementation. *Atherosclerosis* 162:1-15, 2002 [PMID: 11947892]
5. Nisoli E, et al. Effects of nitric oxide on proliferation and differentiation of rat brown adipocytes in primary cultures. *Br J Pharmacol.* 1998 Oct;125(4):888-94 [PMID: 9831929]
6. Nisoli E, Carruba MO. Nitric oxide and mitochondrial biogenesis. *J Cell Sci* 2006; 119:2855-2862 [PMID: 16825426]
7. Rassaf T, et al. Nitric oxide synthase-derived plasma nitrite predicts exercise capacity. *Br J Sports Med.* 2007 Oct;41(10):669-73; [PMID: 17496072]
8. Inhouse report. Glanbia Nutritionals Inc., 2006 CFMN-CSR-0506-1
9. Tangphao O, et al. Pharmacokinetics of intravenous and oral L-arginine in normal volunteers. *Br J Clin Pharmacol.* 1999 Mar;47(3):261-6 [PMID: 10215749]

### CONTRAINDICATIONS:

Diabetics, women who are pregnant or nursing and individuals being treated for high blood pressure or taking prescription drugs should consult their physician before using this formula. Use cautiously if history of cold sores. Not recommended for individuals allergic to corn products, gluten or citrus fruit. Not intended for use by individuals under the age of 18 years.

### STORAGE

Store at 59-86° F (15-30° C). Protect from light and moisture.

\*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.