NOx Synergy™

*Supports Healthy Nitric Oxide Levels**

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NOx Synergy™ is a comprehensive formula designed to support healthy nitric oxide (NO) levels, cardiovascular health, and athletic performance.* It is provided in a convenient grape flavored powder to allow serving size flexibility and better patient compliance.* NOx Synergy™ may help attenuate the effects of oxidative stress and promote healthy blood flow and energy production.*

Formula Highlights

- Features 1.5 g of L-arginine and 1.5 g of L-citrulline per serving
- Grape and apple extracts standardized to contain 95% polyphenols
- Delivers targeted amounts of creatine, taurine, magnesium, and the bioactive form of folate to support healthy nitric oxide levels*
- Contains the antioxidants L-glutathione and vitamin C to support endothelial health*
- Great-tasting grape flavor sweetened with PhytoSweet® stevia blend
- Easy-to-mix in water or any other beverage
- Convenient powdered delivery, allowing serving size flexibility
- Gluten-free, dairy-free, non-GMO, and soy-free

Benefits*

- Supports healthy nitric oxide levels
- Supports healthy blood flow
- Supports cardiovascular health
- Supports athletic performance
- Promotes energy production

Supplement Facts

Serving Size 9 grams (approx. one scoop)
Servings Per Container 30

Amount Per Serving		% Daily Value
Calories	5	
Total Carbohydrate	1 g	1%**
Vitamin C (as Ascorbic Acid)	300 mg	333%
Folate (as Quatrefolic® [6S]-5-methyltetrahydrofolate, glucosamine salt)	170 mcg DFE	43%
Pantothenic Acid (as d-Calcium Pantothenate)	100 mg	2000%
Magnesium (from Creatine MagnaPower®)	120 mg	29%
Magnesium Creatine Chelate (Creatine MagnaPower®)	1.5 g	*
L-Arginine	1.5 g	*
L-Citrulline	1.5 g	*
Taurine	1 g	*
Creatine (from Creatine MagnaPower®)	675 mg	*
Grape and Apple Extracts (*Vitis vinifera*)(fruit) (*Malus pumila*)(skin)[standardized to contain 95% polyphenols]	250 mg	*
L-Glutathione	100 mg	*

**Percent Daily Values are based on a 2,000 calorie diet.
*Daily Value not established.

Other Ingredients: Tartaric acid, natural flavor, partially hydrolyzed guar gum, PhytoSweet® blend (rebaudioside M, steviol glycosides [from *Stevia rebaudiana* leaf]).

Nitric oxide (NO) is a vasodilator that promotes increased blood supply to tissues, which increases the delivery of oxygen and nutrients, and facilitates the clearance of metabolic by-products.[1] NO regulates hormone secretion, nutrient metabolism, cardiac contractility, smooth muscle relaxation, and promotes a healthy microbial balance.[1-4] NO is a messenger molecule that attenuates the atherosclerotic process by decreasing monocyte adhesion and atheroma formation.[2] Healthy NO levels may support healthy blood pressure by supporting vasodilation, reducing sodium reabsorption, promoting sodium and water excretion, and modulating extracellular and plasma volume.[2] Clinical studies suggest that impaired NO production, bioavailability, or activity is associated with endothelial dysfunction in cardiovascular disease, hypertension, obesity, and atherosclerosis.[5]

L-arginine (Arg) is a precursor to NO and has been shown to increase NO bioavailability in vitro.[2] Arg can be obtained from dietary sources or endogenous metabolism.[2] Human studies suggest that Arg supplementation promotes healthy NO levels and may be clinically relevant to individuals with metabolic syndrome or erectile dysfunction.[3] A systematic review and meta-analysis of randomized, placebo-controlled clinical trials observed that normotensive or hypertensive individuals who were administered Arg supplementation of ≤9 g per day had significantly decreased systolic and diastolic blood pressure regardless of study duration, sex, health status, or body mass index, and was generally well tolerated.[2]

Arg supplementation may support athletic performance through its role in NO production.* In clinical trials, NO has been shown to increase blood flow and improve muscle contraction, oxygen supply to muscles, glucose uptake, muscle fatigue, mitochondrial respiration, and oxidative phosphorylation.[6,7] A systematic review and meta-analysis evaluated the effects of Arg supplementation versus a placebo on aerobic and anaerobic performance in athletes.[6] The athletes administered Arg supplementation of 0.15 g/kg of body weight ingested between 60 minutes and 90 minutes before exercise displayed improved aerobic and anaerobic physiological parameters and performance outcomes.[6]

L-citrulline (Cit) can serve as an endogenous precursor to Arg, thereby increasing NO production. In human studies, Cit supplementation has been shown to support cardiovascular health and athletic performance.[4,7,8] Some research suggests that Cit supplementation may be more effective than Arg supplementation in promoting healthy NO levels due to different metabolic pathways.[1,4] Unlike Arg, Cit is not metabolized in the liver or intestine.[1,4] A systematic review and meta-analysis studying the acute effects of Cit supplementation on high-intensity strength and power performance observed a significant benefit for those taking Cit supplementation compared to a placebo.[7]

On the other hand, human and animal studies suggest that the combined effect of Cit and Arg supplementation may be more beneficial than one amino acid alone.[1] For instance, in healthy men, a combination of 1 g per day of Arg and 1 g per day of Cit increased plasma Arg levels more effectively than either 2 g per day of Arg or 2 g per day of Cit alone.[1] A study showed that male soccer players who supplemented with 1.2 g per day of Arg and 1.2 g per day of Cit for one week had significantly improved power output and subjective perception of "leg muscle soreness" and "ease of pedaling" during a cycling test, and elevated plasma Cit, Arg, and NO levels.[1]

NOx Synergy™ includes glutathione as an adjunct to Cit. The combination of these compounds has been shown to increase plasma levels of NO in vivo and in vitro.[9] Glutathione may be particularly beneficial for attenuating oxidative reduction of NO and sustained release of NO in the body.[9] Glutathione and Cit combined may support muscle protein synthesis and muscle performance after resistance training.[9]

Folate (as Quatrefolic® [6S]-5-methyltetrahydrofolate glucosamine salt) is included to promote tetrahydrobiopterin (BH4) bioavailability within the vascular endothelium, as demonstrated in vitro and in vivo.[10] BH4 is a required cofactor for nitric oxide synthase (NOS) activity.[10] Inadequate levels of BH4 may result in the generation of superoxide radicals, rather than NO, from endothelial NOS (eNOS).[10] NOS-derived superoxide reacts with NO to produce highly reactive peroxynitrite radicals, which rapidly oxidize BH4 and trigger the uncoupling of NOS.[10] Depletion of BH4 and uncoupling of NOS are associated with many cardiovascular pathologies.[10] In individuals with compromised endothelial function, folic acid supplementation helped to restore endothelium-dependent vasodilation.[10] Sufficient folate is also required for the proper metabolism of homocysteine, which may play a role in circulating levels of NO and support healthy endothelial function.[11] In vitro, folic acid administration improved endothelial function by reducing homocysteine and increasing BH4 and NO production.[12]

Grape (*Vitis vinifera*) and apple (*Malus pumila*) extracts hold antioxidant properties and may promote vasodilation.* In human and rodent models, supplementation with various grape/grape seed extracts has been shown to promote healthy blood pressure at rest and during exercise.[13-15] Grape seed extract is proposed to activate eNOS and, in turn, increase NO production.[16] In a randomized controlled trial with prehypertensive middle-aged adults, the individuals receiving 400 mg per day of grape seed extract supplementation had significantly improved systolic and diastolic blood pressure and vascular elasticity compared to a placebo.[17] Rodent models have demonstrated that apple extract polyphenols hold endothelial-dependent vasorelaxation properties and result in a significant increase in NO production.[18]

Vitamin C plays a vital role in supporting vascular health.[19] Vitamin C is necessary for collagen synthesis, stimulating endothelial proliferation, inhibiting apoptosis, scavenging free radicals, and supporting normal blood flow through nitric oxide interactions.[19] As a potent antioxidant, vitamin C may help attenuate the oxidative stress and inflammation associated with vascular dysfunction.[19]

Taurine is an amino acid that regulates vascular relaxation through the modulation of NO.[5] Human studies suggest taurine may support cardiovascular health and athletic performance.[20] Rodent models highlight that taurine increases NO levels and bioavailability, while hypertensive animal models demonstrate that taurine promotes healthy blood pressure.[5,21] A randomized controlled trial (n = 120) administered taurine supplementation (1.6 g per day) or a placebo to hypertensive individuals for 12 weeks.[21] The individuals receiving taurine supplements displayed significantly decreased blood pressure and improved endothelium-dependent and endothelium-independent vasodilation.[21]

Creatine and magnesium provide a stable, synergistic pairing that may promote cardiovascular health, muscle performance, and energy production.* Magnesium supports healthy blood pressure by stimulating local vasodilator mediators, including NO, and modulating endothelium-dependent and endothelium-independent vasodilation.[22,23] Systematic reviews and meta-analyses have demonstrated an inverse association between magnesium intake and cardiovascular risk, including promoting healthy blood pressure.[23-25] It is proposed that creatine may benefit vascular health by attenuating oxidative stress and improving NO bioavailability.[26]

Dietary supplementation of creatine (3 g per day) to adults may significantly contribute to energy storage and metabolism in the skeletal muscle and promote athletic performance.[20] A 4-week clinical study reported that individuals performing exercise training and taking creatine supplements (20 g per day for 6 days, then 2 g per day for the remainder of the study) displayed improved maximal muscle strength and reduced exercise-associated muscle damage in adults.[20] The combination of magnesium and creatine may further support athletic performance.* Elite soccer players who were administered 0.7 g/kg per day of magnesium creatine chelate for 16 weeks displayed improved repeated sprint ability test results, and increased speed and power compared to a placebo.[27]

Recommended Use: Mix 9 grams (approximately one scoop) in 8 ounces of water per day or as directed by your health-care practitioner.

For a list of references cited in this document, please visit:

https://www.designsforhealth.com/api/library-assets/literature-reference---nox-synergy-tech-sheet-references

Dosing recommendations are given for typical use based on an average 150 pound healthy adult. Healthcare practitioners are encouraged to use clinical judgement with case-specific dosing based on intended goals, subject body weight, medical history, and concomitant medication and supplement usage.

***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.**

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