NOx SYNERGY™

SUPPORT FOR OPTIMAL NITRIC OXIDE LEVELS

210 G POWDER | NPN80077402 | NOX210-CN

NOx Synergy™ is a comprehensive formula designed to optimize nitric oxide (NO) levels in the body. It is provided in a delicious berry flavoured powder for convenient dosing and ease of patient compliance.

NOX SYNERGY™ MAY HELP TO:

- increase the body's production of NO
- extend the half-life of NO in the body
- protect NO from producing peroxynitrites (harmful free radicals)
- enhance the production of ATP

ARGININE AND CITRULLINE

Arginine is a critical substrate for the synthesis of NO, a compound that relaxes endothelial cells throughout the cardiovascular system. NO also inhibits platelet aggregation and superoxide radical generation. Arginine supplementation has been shown to reverse the endothelial dysfunction associated with common cardiovascular risk factors and also ameliorates symptoms of certain cardiovascular disorders, including coronary and peripheral arterial disease, ischemia/reperfusion injury and heart failure.[1]

Supplemental arginine may be beneficial due to high arginase activity in the small intestine, where approximately 40% of arginine is degraded during digestion, and only 50% of dietary arginine enters the systemic circulation.[1]

Citrulline is included as an adjunct to arginine, as citrulline is converted to arginine in various cells. Unlike arginine, citrulline is not metabolized in the intestine or liver and does not induce tissue arginase. In fact, it inhibits arginase, and citrulline entering peripheral tissues—particularly the kidneys and vascular endothelium—may be readily converted to arginine, thus raising arginine levels and enhancing NO production.[2] Studies show that citrulline raises plasma arginine levels significantly higher than arginine itself and has a longer half-life in the body, so citrulline can be thought of as a potent "time-released arginine."[3] Research suggests that one of citrulline's primary physiological roles is serving as a precursor to arginine in the kidneys.[4,5]

In regard to the influence of citrulline on increasing NO synthesis and stimulating a positive downstream effect, a study involving men with mild erectile dysfunction demonstrated that 1.5g/day of citrulline improved erectile function in 50% of participants.[3]

NOx Synergy™ includes glutathione as an adjunct to citrulline. The combination of these compounds has been shown to increase plasma levels of NO in humans in vivo. It may be particularly beneficial for recovery from intense physical activity and may enhance muscle protein synthesis after resistance training.[6]

BENEFITS OF NOX SYNERGY™

Athletic performance: by increasing blood flow to muscles and enhancing ATP production, exercise can be performed at a higher intensity for a longer duration; muscle contraction may be more efficient, potentially leading to a greater anabolic effect. Additionally, antioxidants in NOx Synergy™ may help aid recovery from intense athletics.

FOLATE (AS 5-MTHF)

Folate, as 5-MTHF, is included as a precursor to tetrahydrobiopterin (BH4), a required cofactor for activity of the enzyme nitric oxide synthase (NOS).[7] Inadequate levels of BH4 result in the generation of superoxide radicals, rather than NO, from endothelial NOS (eNOS).[8] When low BH4 bioavailability occurs, oxygen activation is "uncoupled" from arginine oxidation, and NOS produces superoxide instead of NO. NOS-derived superoxide reacts with NO to produce highly

reactive peroxynitrite radicals, which rapidly oxidize BH4 and trigger uncoupling of NOS. Depletion of BH4 and uncoupling of NOS may result in hypertension, ischemia/reperfusion injury, overload-induced heart failure and atrial fibrillation.[9] Sufficient folate is also required for proper metabolism of homocysteine.[10]

GRAPE (*VITIS VINIFERA*) AND APPLE (*MALUS PUMILA*) EXTRACTS

A proprietary combination of apple and grape polyphenols are included for their potent antioxidant and vasodilating properties. These polyphenols have been shown to enhance vasodilation by increasing the activation of the eNOS enzyme. Animal models have shown grape-derived polyphenols to be effective in increasing NO synthesis and availability by enhancing eNOS activity.[11] Studies using red wine polyphenols demonstrate that these compounds—most potently, the tannins and anthocyanins—cause vasorelaxation in rat aortas.[12] Studies in humans confirm the health benefits of wine and grape polyphenols.[13,14] This formula also includes vitamin C for its role in supporting healthy blood vessels. This nutrient is a required cofactor for building collagen, which is a key structural component of blood vessels. Additionally, working synergistically with the antioxidant compounds in grape and apple extracts, vitamin C exerts vasoprotective benefits, including helping to maintain capillary integrity.

Phloretin, a polyphenol most commonly found in apples, has been shown to inhibit the expression of inflammatory cytokine-induced adhesion molecules in aortic endothelial cells. It has also been demonstrated to reduce platelet aggregation, suggesting that phloretin could be protective against the onset and progression of cardiovascular disease.[15] Other apple polyphenols inhibit expression of pro-inflammatory genes in human cells in vitro in a dose-dependent manner.[16]

TAURINE

This sulfonic acid derivative of cysteine has been shown to affect cardiovascular function through multiple mechanisms. It is anti-arrhythmic, hypotensive, and may decrease platelet aggregation. It also has a normalizing effect on cardiac muscle function with regard to calcium status, as it may strengthen contraction at low calcium levels, and beneficially relax the force of contraction at high calcium levels.[17] Human and animal studies have shown taurine to reduce intimal thickening, arteriosclerosis, oxidative stress, and inflammation associated with diabetes, hypertension, and smoking-induced vascular events. Taurine supplementation in hypertensive patients has been shown to alleviate hypertension symptoms, as well as reverse arterial stiffness in type 1 diabetics.[18]

CHELATED CREATINE/MAGNESIUM COMPLEX

The combination of creatine and magnesium is a synergistic pairing of two compounds with powerful effects on cardiovascular health and muscle performance. The production of ATP involves the transfer of a phosphate group from creatine to ADP, and this transfer is dependent on the availability of magnesium ions. The chelated creatine/magnesium complex in this formula provides a stable, highly effective form of creatine with the presence of magnesium, wherein magnesium repletion facilitates the anabolic activity of creatine.

Magnesium is well-regarded for its hypotensive and relaxing effects, and a magnesium deficiency is associated with several conditions related to blood vessel function and blood flow.[9,19] Creatine has long been recognized for its beneficial effects on muscle performance.[20] Supplemental creatine stimulates strength and muscle mass, but its efficacy is limited by the lactamation reaction, which transforms some creatine into anabolically inert creatinine. Pairing creatine with magnesium inhibits this conversion, thus increasing the amount of creatine available for supporting muscle cells.

Supplementing with this creatine/magnesium chelate helps increase muscle strength as well as the speed of muscle mass growth, since larger amounts of ATP may facilitate greater force stimuli and muscle contraction. Creatine has also been demonstrated to increase muscle anaerobic capacity and aerobic recovery by stimulating mitochondrial activity.[21] According to research, the effects of a combined magnesium/creatine chelate are significantly more potent than the administration of creatine and magnesium from separate sources.[22,23]

Medicinal Ingredients (per one scoop/2 tsp./7g):

L-Arginine	1.5 g
L-Citrulline	1.5 g
Taurine (2-Aminoethanesulfonic acid)	1 g
Creatine ((alpha-Methylguanido) acetic acid, Magnesium creatine chelate)	675 mg
Vitamin C (Ascorbic acid)	300 mg
Fruit Blend (*Vitis vinifera* - Fruit, *Malus domestica* - Fruit) (95% Polyphenols)	250 mg
Magnesium (Magnesium creatine chelate)	120 mg
L-Glutathione	100 mg
Vitamin B5 (Pantothenic acid, Calcium D-pantothenate)	100 mg
Folate (L-5-Methyltetrahydrofolic acid, glucosamine salt)	100 mcg

Non-Medicinal Ingredients: Natural flavour, citric acid, stevia leaf. **Recommended Dose:** Adults: Mix one scoop/approx. 2 tsp. in 8-10 oz of water immediately before consumption. Take once per day or as directed by a health care practitioner. 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.

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REFERENCES

For a list of references cited in this document, please visit: http://mkt.s.designsforhealth.com/techsheets/NoxSynergyReferences.pdf