

Nitric Oxide: FAQ

Nitric Oxide (NO) Biochemistry

What is NO and why is NO important?

- NO is an important signaling molecule because it controls virtually every aspect of human physiology.
- Regulates all cardiovascular function/homeostasis
- Regulates immune and inflammatory balance
- Regulates cellular energetics and aging
- Regulates neurotransmission (NANC—non adrenergic non cholinergic neurotransmitter)
- Regulates metabolism
- Regulates gastro intestinal function
- Helps activate GLUT 4 transport of glucose into cells
- Critical to sexual function-vasodilation/innervates erectile tissue
- Scavenges superoxide anion (especially important in neuronal damage and microglial activation)
- Supports telomerase activity that protects the genes
- Regulates, protects and even increases mitochondria (energy factories)
- Controls stem cells in the process of healthy cell regeneration
- NO is the 'miracle molecule' responsible for circulation, where it widens blood vessels and micro-circulation allowing oxygen and nutrient delivery to all cells. This supports healthier tissues that are more resistant to the ravages of aging.

What are vascular effects of NO?

- Direct vasodilation (flow dependent and receptor mediated)
- Indirect vasodilation by inhibiting vasoconstriction (inhibits angiotensin II and sympathetic vasoconstriction)
- Anti thrombotic effect by inhibiting platelet adhesion to vascular endothelium
- Anti inflammatory by inhibiting leukocyte adhesion to vascular endothelium
- Anti proliferative effect by inhibiting smooth muscle hyperplasia in artery walls

What disrupts NO production?

- Physical inactivity
- Inflammatory diets (SAD) and decreased nitrate rich veggies
- Lack of stomach acid
- Environmental factors such as pollution
- Medications such as PPIs, NSAIDs like Vioxx, antibiotics, antiseptic mouth washes
- Individual genomics such as decreased activity/expression of NOS or its cofactors
- With aging, our production of NO decreases (around age 40, our NO production decreases approximately 50%)

What are some other cofactors for NOS (Nitric Oxide Synthase), which can affect endogenous production on NO?

- O₂
- NADPH
- BH₄
- FAD
- FMN
- Heme

What are some conditions associated abnormal NO production and bioavailability?

- Hypertension
- Obesity
- Dyslipidemia
- Diabetes Type 1 and 2
- Heart Failure
- Atherosclerosis
- Cigarette smoking
- Aging

What are 2 endogenous pathways for NO production?

- L-Arginine pathway (utilizes NOS pathways)
- Nitrate – Nitrite – NO

Why supplement NO production?

- By age 40, there is significant loss of NO production and bioavailability in the population, which increases the development of endothelial dysfunction.
- Restoring NO availability starts with endothelial repair, which cannot be otherwise accomplished without NO.
- NO restoration significantly improves function in every area because the target is the body's core mechanism for homeostasis.

Why not supplement with L-Arginine for NO production?

- Increasing L-Arginine supplementation will not make more NO because the NOS enzyme systems get saturated with very low concentration of L-Arginine (so more L-Arginine is not necessarily better).
- L-Arginine supplementation is not effective in many due to NOS dysfunction and is actually harmful when endothelial dysfunction is present.
- Tolerance develops with chronic L-Arginine therapy in younger people even with functioning NOS activities.
- Intracellular L-Citrulline is used for synthesis of L-Arginine for NO production
- Extracellular L-Arginine is not used for synthesis of NO

Neo 40 increases Nitric Oxide

What does Neo 40 do?

- Only clinically proven nutraceutical that provides an exogenous source of authentic NO.
- Neo 40 technology generates physiological levels of NO gas.
- Neo 40 is not a cofactor or substrate based product.
- Provides the body the nutrients necessary for restoring NO.

How does Neo 40 work to generate NO?

- Nitrate-Nitrite-NO pathway via the entero-salivary pathway
- Not NOS dependent.
- Not O₂ dependent, in fact, there is robust activity in hypoxia and acidity
- Neo 40 has a 2 Phase NO restoration system
- Phase 1 – generates therapeutic NO in first 10 minutes
- Phase 2 – NO permeates the system while supporting nutrients help to restore the body's own NO production
- No tolerance development

Laboratory and Clinical Verification of Neo 40

What laboratory proof verifies Neo 40 benefits?

- Endothelial function testing
- Carotid ultrasound showing increased vasodilation and plaque regression
- Thermography to show improved peripheral circulation
- Decrease in peripheral blood pressure measurement
- Improvement in central blood pressure measurements (pulse wave analysis)
- Measurement of improved inflammatory balance

Are there any published studies on Neo 40?

- Neo 40 has been clinically proven in 5 published trials with 4 issued patents (more pending)
- 15 years of sound basic science
- Neo 40 was funded by and created at the University of Texas Therapeutic Institute with over a decade of research with intentions of being a typical hard core drug, however as the natural plant based chemistry became the basis for its efficacy and safety, it could not be issued as a drug.
- Neo 40 has drug like strength and efficacy without drug drawbacks.

Are those published studies easily available to read?

On www.neogenismedical.com these studies, as well as other 3rd party NO research, located under Research and Education are available after you have logged in.

Neogenis Diagnostic Salivary Indicator Strips

What do the Neogenis diagnostic salivary indicator strips measure?

- Measures saliva nitrite level
- Salivary nitrite level is able to function as a surrogate biomarker for NO
- Only non invasive salivary NO indicator in the marketplace giving instant NO evaluation

What if someone has been using Neo 40 regularly but the indicator strip does not show increased levels?

It does not mean the lozenge is not working. It means your ability to recycle nitrate is compromised and this breakdown in NO production puts you at risk for cardiovascular dysfunction, precisely the people who need NO support the most.

Dosing, Results and Cautions of Neo 40

What is the suggested dosing protocol?

- 1 lozenge twice daily, 12 hours apart for the 1st 30 days
- After 30 days or when clinical symptoms improve, continue with once daily
- For blood pressure support, dose as needed
- Testing with Neogenis Test Strips, frequently, demonstrates NO evaluation

How long does the improvement in detectable NO activity last per dose of Neo 40?

10-12 hours with Neo 40

How long will it take to see results?

- Neo 40 delivers immediate NO
- Arteries dilate and blood flow begins to increase through out body
- Blood vessels become flexible and compliant
- Hours - endogenous production of NO improved approximately 15%
- Weeks – better auto regulation of blood flow
- Improved mitochondrial function shown by improved exercise capacity performance
- Baseline blood pressure in pre-hypertension decreased by 12mm Hg systolic and 6mm Hg diastolic
- Triglycerides decrease by 27%
- Decrease CV risk factors
- Decrease oxidative stress
- Months – existing plaque within arteries more stable and has begun to regress

Are there any known side effects of Neo 40?

- No known side effects
- Safe for long-term use
- No tolerance built
- If mouth becomes sensitive to the lozenge, hydrate prior to use. Continually move lozenge around in the mouth and follow with water after dissolving.
- With severe dry mouth, patients can chew and swallow however reaction is a little slower.
- Rarely, patients may experience minor gassiness or varied minor sensations as vessels dilate (that have been previously constricted for prolonged periods of time).

Is it possible to have too much NO?

- Yes, too much NO is associated with headaches, dizziness and low blood pressure. However 2 lozenges a day is a completely safe dose, regardless of health level, age or diet.
- Neo 40 is roughly equivalent to eating a spinach salad when you were younger and your body was able to make its own NO.

Are there any cautions with prescription medications?

Consult with a physician before use if a patient is taking

- 1)organic nitrate medications such as nitroglycerin or isosorbide dinitrate
- 2)erectile dysfunction drugs since the combination may cause an unsafe drop in blood pressure
- 3)'blood thinner' medications
- 4)blood pressure medications

Discontinue use and contact physician if dizziness or fainting occurs

Can Neo 40 Professional be taken with an erectile dysfunction medication?

Increased blood flow in the corpus cavernosum of the penis and clitoral engorgement is facilitated by the production of NO. Current ED medications such as Viagra and Cialis work through a NO pathway, so without NO, these medications do not work. This is reason that these phosphodiesterase inhibitor medications only work in approximately 50% of the population. Neo 40 has been shown to significantly improve NO levels.

Will Neo 40 Professional interfere with sleep?

NO helps promote sleep because of its vasodilation (relaxation) effects. As a NANC (non adrenergic non cholinergic) neurotransmitter, it has a calming effect. However, there are some B vitamins (methylcobalamin and 5-MTHF) which some find energizing. If you experience sleeplessness, take it earlier in the evening yet keep dosing 12 hours apart.

Ingredients of Neo 40 Professional

What is Neo 40 Professional?

Clinical strength version of Neo 40 for increased potency/efficacy of NO production and restoration with biologically active form of folate (5-MTHF), methylcobalamin and hawthorn berry for additional endothelium benefits.

Why is the 5-MTHF in Neo 40 Professional?

5-Methyltetrahydrofolate supports the methylation cycle and stimulates formation of BH4, one of the rate limiting co-factors of the NOS enzyme systems for manufacturing NO.

Why is the hawthorn berry in Neo 40 Professional?

Hawthorn is used to support the circulatory system, treat angina, high blood pressure, congestive heart failure and cardiac arrhythmia and has been found to strengthen the heart. Hawthorn is widely regarded in Europe as a safe and effective treatment for the early stages of heart disease and has been used for a number of ailments including angina, myocarditis and arteriosclerosis. It has also been indicated for strengthening blood vessels, vascular insufficiency and blood clots, restoring the heart muscle wall, lowering cholesterol and to aid digestion.

Why is methylcobalamin in Neo 40 Professional?

Methylcobalamin is the activated form of vitamin B12, which is essential for the methylation cycle pathways. Methylcobalamin donates a methyl group to homocysteine converting it back to methionine. High blood levels of homocysteine may increase endothelial cell injury. Hyperhomocysteinemia has been correlated with occurrence of blood clots, heart attacks and strokes.

Why is vitamin C in Neo 40 Professional?

Vitamin C is an essential nutrient for man. It is a well-known antioxidant. Vitamin C is a cofactor in at least 8 known enzymatic reactions, one of which is collagen formation. This is important in wound healing and supporting the integrity of capillary health.

Why the L-Citrulline in Neo 40 Professional?

The cell uses intracellular L-Citrulline to synthesize L-Arginine in the manufacture NO.

Remember, the cell does not use extracellular L-Arginine to make NO.

Why the Sodium Nitrite in Neo 40 Professional?

Basic science as well as clinical studies demonstrates that nitrate and/or nitrite can restore NO homeostasis as an endothelium independent source of NO.

NOS independent source of NO (remember as we age, as well as previously mentioned health issues, NOS functionality is impaired)

Are there any cautions with other nutraceutical products?

No known adverse side effects, however there are multiple benefits by increasing and opening up the microcirculation. This action may facilitate not only the absorption of other nutraceuticals in the intestinal tract, but also improved circulation aids in the delivery of these nutrients through out the body. It is possible that lower doses of targeted nutraceuticals will be needed to affect outcomes.

By supporting the production and availability of NO, as well as actually restoring NO function, this affects every single physiological function in the body. Many blood chemistry values can be corrected by the use of just one supplement, which affects every cell, tissue, organ and system in the body.

Who may benefit from Neo 40?

- Patients over the age of 40 or anyone who is aging
- Patients with circulation issues
- Patients with low energy
- Patients with sexual dysfunction
- Patients on antacids (PPIs)
- Patients interested in disease prevention