

NitroFX, NitroXtreme and Nitric Oxide

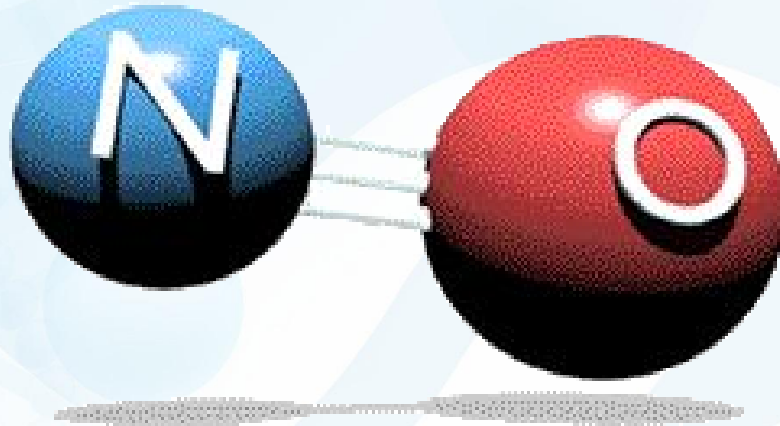
The Science Behind the Kyani Nitric Oxide
Precursors

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Nitric Oxide

“The Molecule of Life”



Nitro FX

The importance of Nitric Oxide

Underscored when three pharmacologists were awarded the Nobel Prize in Physiology or Medicine in 1998 for their research in Nitric Oxide.



Nitric Oxide Precursors

- The first recognized nitric oxide precursor was the amino acid arginine, which is converted to NO by a family of enzymes called Nitric Oxide Synthases (NOSs)
- NitroFx and NitroXtreme represent a second generation of Nitric Oxide precursors. They activate in seconds and are 100% arginine-free.

Nitrates, Nitrites and Nitric Oxide

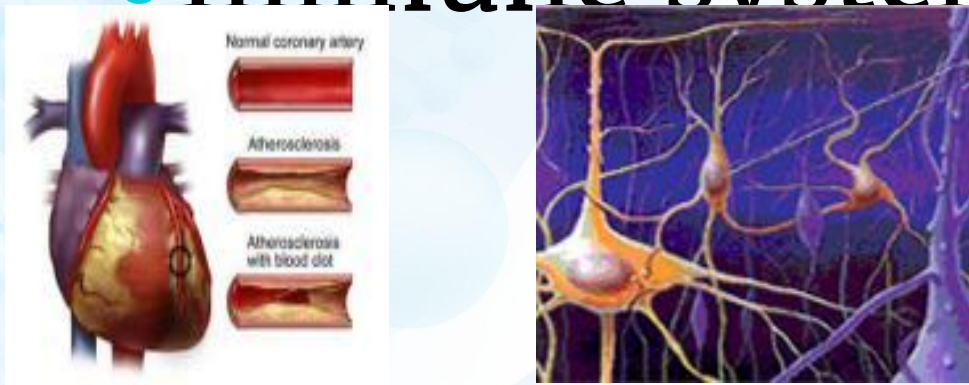
- Nitrate = NO_3
- Nitrite = NO_2
- Nitric oxide = NO

Nitrates and Nitrites Are Recycled in the body

- In the stomach, the nitrites are converted to NO, and the some of the nitrates are absorbed.
- Nitrates in the bloodstream are concentrated in the saliva, where they are converted to nitrites, then swallowed and converted to NO in the stomach.
- NO in the body is converted back to nitrites and nitrates, and the cycle continues

Nitric Oxide: Effects on

- Cardiovascular system
- Nervous system
- Immune system

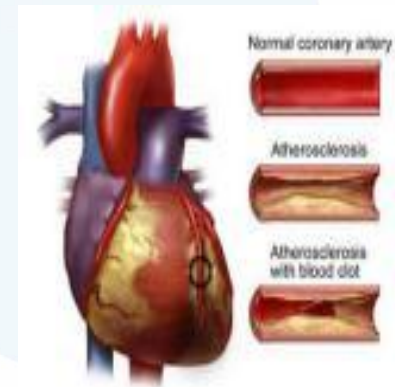


Nitric Oxide: Cardiovascular Effects

- NO signals the smooth muscle cells and induces increased compliance, enhancing blood flow throughout the vascular tree.
- Also regulates function in platelets (blood cells responsible for blood clots) to inhibit excess aggregation or blood clotting.

Nitric Oxide: Cardiovascular Applications

- Hardening of the Arteries
- Plaque Build-Up
- High Blood Pressure
- Obstruction of the Arteries

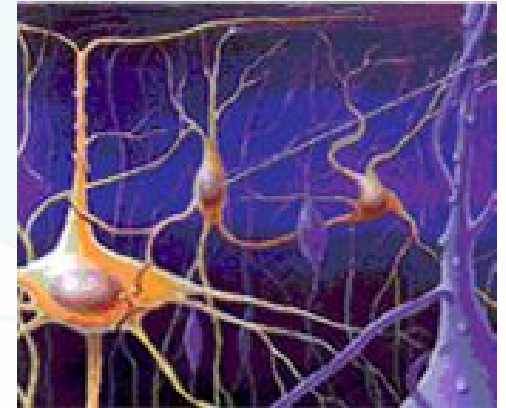


Nitric Oxide: Neurologic effects

- Brain-derived NO affects several types of nerve cells
- Important in neurotransmitter pathways, both in the central and peripheral nervous systems.
- Regulates production and release of many hormones

Nitric Oxide: Neurologic applications

- Mental Health
- Anti-aging properties – release of human growth hormone (HGH)
- Regeneration of damaged axons of neurons
- Diabetic neuropathy

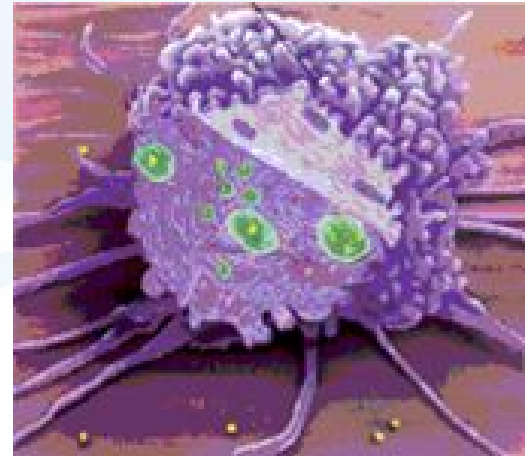


Nitric Oxide: Immunologic effects

- Macrophage-derived NO
- Important in the immune system
- Helps macrophages kill bacteria

Nitric Oxide: Immunologic applications

- Bacterial and viral infection
- General immunity
- Inflammation



NitroXtreme: More Power

- Significant increase in potency
- Faster acting because of more rapid absorption
- Longer sustained action because of higher concentration
- Includes co-factors to increase N.O. generation and dramatically broaden the health benefit.
- Additional ingredients: Magnesium, Niacin, Zinc, CoQ-10, Chromium and Quick-Sorb®.

CoQ10

- A natural, fat-soluble nutrient present in virtually every cell in the body
- Vital to the production of Adenosine Triphosphate (ATP) which is 90% of the energy in the body
- Promotes cardiovascular health and improved blood flow
- Aides in strengthening the immune system and promoting good periodontal health

Magnesium

- Converts carbohydrates, protein and fats to energy
- Supports muscle relaxation and contraction as well as nerve transmission
- Promotes healthy systolic and diastolic blood pressure
- Promotes healthy glucose metabolism

Zinc (Zn)

- A component of numerous enzymes including the enzyme that converts L-arginine into Nitric Oxide
- Plays a role in protein synthesis, blood sugar balance, wound healing and brain function
- Promotes healthy skin, and a strong immune system
- Promotes healthy fetal and reproductive health
- Promotes healthy prostate function

Chromium

- Assists uptake of blood sugar into the cells
- Promotes regulation of blood sugar levels
- Reduces the risk of insulin resistance
- Supports lean body mass

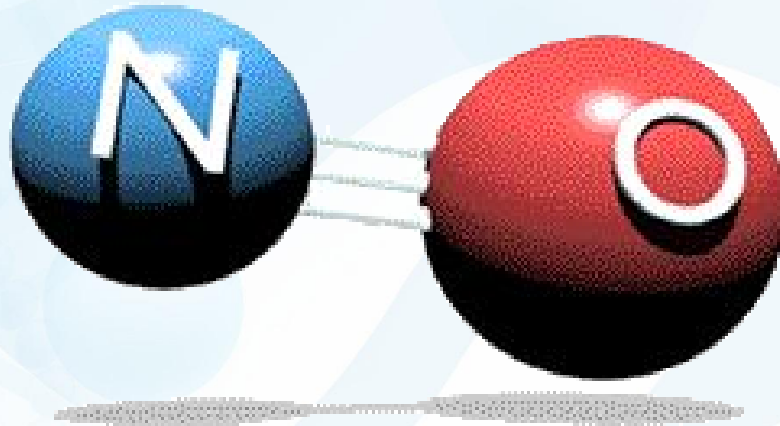
NitroFX or NitroXtreme?

- Both provide an excellent source of organic nitrates and nitrites, manufactured under GMP conditions.
- Concentrations of nitrates and nitrites are tightly controlled and highly reproducible
- NitroXtreme has higher concentrations of nitrates and nitrites and a bolder taste
- Additional ingredients in NitroXtreme allow for a longer acting effect on nitric oxide production, as well as quicker absorption into the body



Nitric Oxide

- A short-lived gaseous molecule
- Plays a key role in numerous biological processes essential for human health.



NitroFX and NitroXtreme

- Contain concentrates of the Noni plant, which has high levels of nitrates and nitrites.
- Nitrates and nitrates serve as precursors of NO.

Next Up

- The biochemistry used to convert nitrates and nitrites into NO
- The science behind the functions served by NO throughout the body.

Nitrogen – A Key Element for Human Health!

- Nitrogen gas (N_2) is the most abundant element in the atmosphere
- Represents the largest pool of nitrogen on our planet
- The nitrogen cycle serves to convert N_2 to a form that can be used in biological processes
- In the first step, atmospheric nitrogen is converted into ammonia (NH_4^+), a process called nitrogen fixation.

Biochemical Pathways

- Ammonia is modified to different nitrogen oxides, including nitrite (NO_2^-) and nitrate (NO_3^-).
- The process of denitrification completes the cycle
- Nitrate is reduced first to nitrite, nitric oxide, nitrous oxide and finally back to nitrogen gas (N_2), which can then diffuse back into the atmosphere.

Nitric Oxide

- As a gas, NO has an extremely short half life (fraction of a second)
- Even during that short time it can activate a number of enzymes and these activated enzymes cause NO-mediated effects that can last for several hours.
- Any NO that is not used immediately in a biologic process is rapidly converted back to nitrite and nitrate.
- The metabolic steps in the nitrogen cycle depend heavily on bacteria (different metabolic pathways)

Nitric Oxide

- The metabolic steps in the nitrogen cycle depend heavily on bacteria, which have metabolic pathways not found in plants or animals to catalyze the different steps of the cycle.

Pathways to Nitric Oxide

- Arginine is converted to NO by enzymes called Nitric Oxide Synthases
- Nitrate ingestion greatly enhances production of nitric oxide.
- High concentrations of nitric oxide are produced from nitrates by the acidity in the stomach.

Moving through the GI tract...

- Any nitrate that escapes conversion to NO in the stomach enters the circulation or passes into the small intestine and is absorbed into the circulation
- Nitrate is delivered to the salivary glands
- Saliva containing nitrate is actively secreted into the mouth.
- Bacteria in the mouth then convert (“reduce”) nitrate to nitrite .
- The process of nitrate reduction also occurs in the heart and multiple other organ systems throughout the body.

Biological Processes Dependent on Nitric Oxide

- Regulation of blood flow
- Cellular signaling
- Response to low oxygen levels
- Inhibition of platelet stickiness
- Lung function
- Immunity
- Metabolic (energy) regulation
- Nerve transmission
- Pain reduction

Low NO levels found in...

- Atherosclerosis
- Angina
- Stroke
- Metabolic syndrome of obesity, hypertension and hyperlipidemia.

What Sources Provide Nitrate and Nitrite?

- Vegetables – especially green leafy vegetables
- Noni plant – outstanding source

NitroFX and NitroXtreme are derivatives of Noni Concentrate.

How Much Nitrate and Nitrite is There?

- Concentrations of nitrates are at least two orders of magnitude higher than those of nitrites.
- The half-life for nitrate is 5-6 hours
- The half life for nitrite is only 20 minutes.

Nitric Oxide in the Stomach

- Nitric oxide in the stomach is a first line of defense
- Nitric oxide in high concentrations is known to kill bacteria
- Gastric nitric oxide helps control of blood flow to the cells of the stomach and the production of mucus – promotes intestinal health

Nitric Oxide in the Intensive Care Unit

- ICU patients on ventilators do not produce much saliva, and they do not swallow much of what they produce.
- Treated with potent antibiotics to prevent infection
- H2 blockers or proton-pump inhibitors increase the pH in the stomach (decreased acidity)
- Extremely low levels of nitric oxide in the stomach
- High risk of developing stomach ulcers and bacterial infections in the stomach

Hemoglobin and Nitric Oxide

- Interaction between hemoglobin and NO only recently recognized
- The oxygen binding status of hemoglobin affects its ability to convert nitrite to NO
- Conversion of nitrite to NO is most active during periods of rapid deoxygenation.
- What are the consequences of this?
 - provides a mechanism whereby the body is able to produce more NO in times of low oxygen
 - results in increased dilation of the blood vessels, more blood flow and hence more oxygen.
 - may be one of the mechanisms used by the body to increase vasodilation in times of hypoxia

NO and Anemia

- Patients who are anemic are known to be at risk from the events associated with low NO availability including hypertension.
- NO can be generated by leafy green vegetables and by NitroFX and NitroXtreme

Other Globin Molecules also bind NO

- Myoglobin is also known to play a role in nitrite bioactivation.
- Myoglobin converts nitrite to NO in the heart muscle in much the same way that hemoglobin does in the intravascular space.
- Nitrite has a cardio-protective effect mediated through myoglobin .
- A similar molecule in the nervous system, called neuroglobin, also has the ability to convert nitrite to NO through the process of reduction.

NO and the Cardiovascular System

- The first reports of dilating the coronary arteries by pharmacologic doses of inorganic nitrite were published almost 100 years ago.
- There is a vasodilatory effect of much lower levels of circulating nitrite
- Organic nitrites, derived from plants, are much more potent than inorganic nitrite.
- The preferential conversion of nitrite to NO under conditions of hypoxia has important clinical applications in the care of patients with myocardial ischemia

Scientific Evidence: Nitrates, Nitrites and Heart Health

- Increased consumption of fruits and vegetables provides a cardio-protective effect (Mediterranean Diet, DASH Diet)
- Administration of inorganic nitrate reduces blood pressure

Heart and Kidney Study

- Animal model of high blood pressure and renal disease
- Nitric oxide deficiency induced by chronic blockage of NOS (nitric oxide synthase)
- Nitrite supplementation provided in the diet
- Improved the blood pressure
- Protected against kidney injury

Other Studies of Nitrite Supplementation

- Mouse and rat models of heart disease – improved cardiac function
- decreased ulcer formation and improved mucus secretion in the stomach in a rat model of gastric ulcers
- Human studies:
 - decreased platelet aggregation
 - decreased blood pressure
 - improved endothelial function
 - decreased oxygen consumption with moderate or maximal exercise
 - improved work efficiency

More Science

- In mouse models of serious bacterial infection causing dangerously low blood pressure, nitrite improved survival and reduced mitochondrial damage, tissue damage from ischemia, hypothermia and oxidative stress
- Inhaled nitric oxide has been used to treat babies with high blood pressure in the pulmonary circulation
- Inhaled nitrite has improved hypertension in the pulmonary circulation in animal studies

Transplantation Studies

- Rat model of cardiac transplantation,
- Oral supplementation of nitrite
- Graft survival improved from 50 days in animals on a control diet to over 120 days in animals receiving nitrite supplementation in their drinking water.
- Animals receiving a low-nitrite diet had reduced survival of the allograft, to an average of 31 days

Fighting Infection

- NO acts against multiple types of bacteria
- In an animal model of cystic fibrosis, nitrite was successfully used to clear *Pseudomonas aeruginosa*, a common bacterial infection in this disease
- In animal models, the combination of vitamin C with nitrite is comparable to antibiotics in fighting urinary tract infections

So...Like Mama Always Said...

For optimal health –

- **EAT YOUR VEGETABLES!!!**
- **And take NitroFX or NitroXtreme three times a day**

