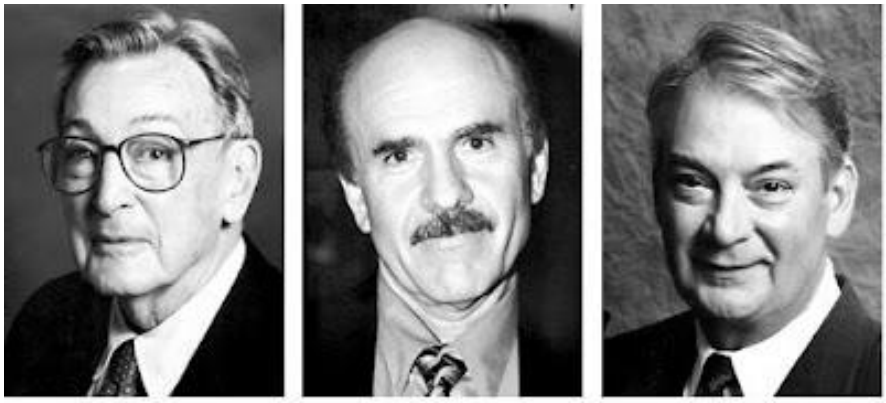
Nitric Oxide (NO): Molecule of the Year 1992



Dr. Robert F. Furchgott.
Professor of Pharmacology,
The State University of New York.

Dr. Louis Ignarro(1941-)
Professor of Pharmacology
UCLA School of Medicine,
Los Angeles

Dr. Ferid Murad (Father of Nitric Oxide)
Chairman of
Integrative Biology Department,
The University of
Texas Medical School, Houston

Nitric oxide is a molecular compound with a chemical formula of NO. Despite being a simple molecule, NO is an important biological regulator acting as cellular signaling molecule involved in many physiological and pathological processes. It is therefore a fundamental component in the field of physiology, neuroscience, cardiology and immunology. NO was proclaimed "molecule of the year" in 1992 by the journal- Science. Realization dawned upon researchers in the 80's that more than a century old pharmaceutical agents in use, such as nitroglycerine, amyl nitrite were precursors to nitric oxide.

Ferid Murad (1936-) was born to an Albanian immigrant father and an American mother. He received his MD and PhD from University of Cleveland- Ohio, and taught pharmacology at the University of Virginia and Stanford University. Murad, Chairman of Integrative Biology Department, while working on nitroglycerine at the University of Texas Medical School, Houston, showed that

nitroglycerine and several related drugs released nitric oxide which relaxed smooth muscle cells causing powerful vasodilatation, in 1977. Furchgott and Ignarro built on this work around 1980. Robert F Furchgott (1916-), Professor of Pharmacology at the State University of New York, arrived on his own to the identification of nitric oxide, while trying to study contradictory effects of drugs on blood vessels. He concluded that endothelial cells produced an unknown signalling molecule that relaxed vascular smooth muscles. He called this signal molecule EDRF (endothelium-derived relaxing factor). Louis J Ignarro (1941-) Professor of Pharmacology at UCLA School of Medicine in Los Angeles concluded independently through a series of analysis (1986) that EDRF was identical to nitric oxide. This prompted increase in research activity worldwide.

Nitric oxide is a powerful vasodilator, perhaps the only gaseous signalling molecule, a biological messenger playing a role in a variety of biological processes. NO is biosynthesized endogenously from L-arginine, oxygen by various nitric oxide synthases (NOS) enzymes. Endothelium synthesized NO, signalling the surrounding smooth muscles to relax resulting in vasodilatation and increased blood flow. NO is highly reactive and diffuses freely across membranes. However, it has a short life span of few seconds. These attributes make NO ideal for a transient paracrine (between adjacent cells) and autocrine (within a single cell) signalling molecule. Nitric oxide is also generated by phagocytes (monocyte, macrophages and neutrophils) as part of immune response. It is also a signalling molecule against oxidative stress.

Monoxide may act as nitric oxide agonist. Likewise Sildenafil citrate (Viagra) stimulates erection primarily by enhancing nitric oxide pathway in the penis. Nitrate rich vegetables, in particular leafy greens such as spinach and beetroot have shown to increase cardio protective levels of NO with a corresponding reduction of BP in hypertensive patients.

The vasodilator antihypertensive Nitric oxide/oxygen blends are used in critical care to promote capillary and pulmonary dilatation to treat pulmonary hypertension in neonatal patients in post meconium aspiration etc. Nitric oxide use is not approved in non neonatal population. Although it improves hypoxemia in acute lung injury and ARDS, its effects are short-lived.

Ferid Murad, Luis Ignarro and Dr.Robert F Furchgott shared Nobel Prize in Physiology and Medicine in 1998, for their discoveries concerning nitric oxide as a signalling molecule in the body.