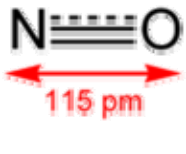
Nitric oxide

From Wikipedia, the free encyclopedia

Nitric oxide (common name) or **nitrogen monoxide** (systematic name) is a chemical compound with chemical formula NO. This gas is an important signaling molecule in the body of mammals, including humans, and is an extremely important intermediate in the chemical industry. It is also an air pollutant produced by combustion of substances in air, like in automobile engines and fossil fuel power plants.

NO is an important messenger molecule involved in many physiological and pathological processes within the mammalian body both beneficial and detrimental.[1] Appropriate levels of NO production are important in protecting an organ such as the liver from ischemic damage. However sustained levels of NO production result in direct tissue toxicity and contribute to the vascular collapse associated with septic shock, whereas chronic expression of NO is associated with various carcinomas and inflammatory conditions including juvenile diabetes, multiple sclerosis, arthritis and ulcerative colitis.[2]

Nitric oxide should not be confused with nitrous oxide (N_2O), an anesthetic and greenhouse gas, or with nitrogen dioxide (NO_2), a brown toxic gas and a major air pollutant. However, nitric oxide is rapidly oxidised in air to nitrogen dioxide, as Humphrey Davy found to his

Nitric oxide	
	
Preferred IUPAC name	
Nitric oxide	
Systematic name	
Nitroso	
Other names	
Nitrogen(II) oxide	
Identifiers	
CAS number	10102-43-9 ✓, 15917-77-8 (^{15}N) ✓
PubChem	145068 ✓, 12858183 (^{15}N) ✓
ChemSpider	127983 ✓, 21170263 (^{15}N) ✓
UNII	31C4KY9ESH ✗
EC number	233-271-0
UN number	1660
DrugBank	DB00435
KEGG	C00533
ChEBI	16480
RTECS number	QX0525000
ATC code	R07AX01 (http://www.whocc.no/atc_ddd_index/?code=R07AX01)
SMILES	[N]=O
InChI	InChI=1S/NO/c1-2
InChI key	MWUXSHHQAYIFBG-UHFFFAOYSA-N
Gmelin Reference	451
3DMet	B00122
Properties	
Molecular formula	NO
Molar mass	30.006 g/mol
Appearance	colourless gas paramagnetic
Density	1.269 g/cm^3 (liquid) 1.3402 g/l (gas)

discomfort when he inhaled the gas early in his career.

Despite being a simple molecule, NO is a fundamental player in the fields of neuroscience, physiology, and immunology, and was proclaimed "Molecule of the Year" in 1992.[3]

Contents

Melting point	−163.6 °C, 110 K, -262 °F
Boiling point	−150.8 °C, 122 K, -239 °F
Solubility in water	7.4 ml/100 ml (STP)
Solubility	soluble in alcohol, CS_2
Refractive index (n_D)	1.0002697
Structure	
Molecular shape	linear, $C_{\infty v}$
Thermochemistry	
Std enthalpy of formation $\Delta_f H^{\circ}_{298}$	+90.29 kJ/mol
Standard molar entropy S°_{298}	210.76 $JK^{-1}mol^{-1}$
Pharmacology	
Bioavailability	good
Routes of administration	Inhalation
Metabolism	via pulmonary capillary bed
Elimination half-life	2–6 seconds
Hazards	
MSDS	External MSDS (http://avogadro.chem.iastate.edu/MSDS/nitric_oxide.pdf)
EU Index	Not listed
R-phrases	R26, R34
S-phrases	(S1), S9, S26, S36, S45
NFPA 704	
Flash point	Non-flammable
Related compounds	
Related nitrogen oxides	Nitrous oxide Dinitrogen trioxide Nitrogen dioxide Dinitrogen tetroxide Dinitrogen pentoxide
(what is this?) (verify) (http://en.wikipedia.org/w/index.php?title=Nitric_oxide&diff=cur&oldid=269505247) Except where noted otherwise, data are given for materials in their standard state (at 25 °C, 100 kPa)	
Infobox references	

Reactions

- When exposed to oxygen, NO is converted into nitrogen dioxide.

$$2\ NO + O_2 \rightarrow 2\ NO_2$$

This conversion has been speculated as occurring via the ONOONO intermediate. In water, NO reacts with oxygen and

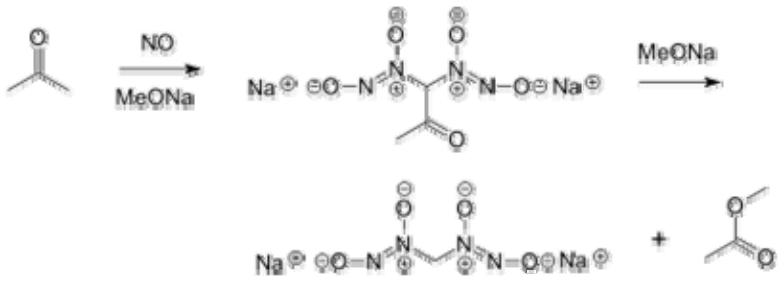
water to form HNO_2 or nitrous acid. The reaction is thought to proceed via the following stoichiometry:

$$4\ NO + O_2 + 2\ H_2O \rightarrow 4\ HNO_2$$

- NO will react with fluorine, chlorine, and bromine to form the XNO species, known as the nitrosyl halides, such as nitrosyl chloride. Nitrosyl iodide can form but is an extremely short-lived species and tends to reform I_2.

$$2\ NO + Cl_2 \rightarrow 2\ NOCl$$

- Nitroxyl (HNO) is the reduced form of nitric oxide.
- Nitric oxide reacts with acetone and an alkoxide to a *diazeniumdiolate* or *nitrosohydroxylamine* and methyl acetate:[4]



This is a very old reaction (1898) but of interest today in NO prodrug research. Nitric oxide can also react directly with sodium methoxide, forming sodium formate and nitrous oxide.[5]

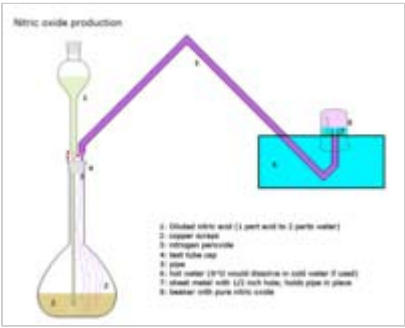
Preparation

Commercially, NO is produced by the oxidation of ammonia at 750 °C to 900 °C (normally at 850 °C) in the presence of platinum as catalyst:

$$4\ NH_3 + 5\ O_2 \rightarrow 4\ NO + 6\ H_2O$$

The uncatalyzed endothermic reaction of O_2 and N_2, which is performed at high temperature (>2000 °C) by lightning has not been developed into a practical commercial synthesis (see Birkeland–Eyde process):

$$N_2 + O_2 \rightarrow 2\ NO$$


Nitric oxide production

In the laboratory, nitric oxide is conveniently generated by reduction of nitric acid with copper:

$$8\ HNO_3 + 3\ Cu \rightarrow 3\ Cu(NO_3)_2 + 4\ H_2O + 2\ NO$$

or by the reduction of nitrous acid in the form of sodium nitrite or potassium nitrite:

$$2\ NaNO_2 + 2\ NaI + 2\ H_2SO_4 \rightarrow I_2 + 4\ NaHSO_4 + 2\ NO$$
$$2\ NaNO_2 + 2\ FeSO_4 + 3\ H_2SO_4 \rightarrow Fe_2(SO_4)_3 + 2\ NaHSO_4 + 2\ H_2O + 2\ NO$$

$$3\ KNO_2\ (l) + KNO_3\ (l) + Cr_2O_3(s) \rightarrow 2\ K_2CrO_4(s) + 4\ NO\ (g)$$

The iron(II) sulfate route is simple and has been used in undergraduate laboratory experiments.

So-called NONOate compounds are also used for NO generation.

Coordination chemistry

Main article: Metal nitrosyl

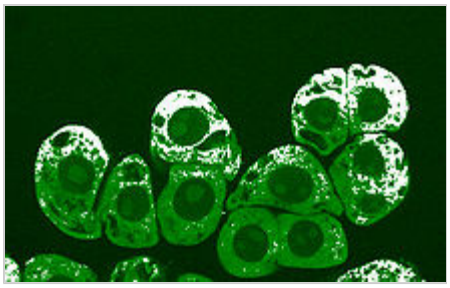
NO forms complexes with all transition metals to give complexes called metal nitrosyls. The most common bonding mode of NO is the terminal linear type (M-NO). The angle of the M-N-O group can vary from 160° to 180° but are still termed as "linear". In this case, the NO group is considered a 3-electron donor under the covalent (neutral) method of electron counting, or a 2-electron donor under the ionic method.[6] In the case of a bent M-N-O conformation, the NO group can be considered a one-electron donor using neutral counting, or a 2-electron donor using ionic counting.[7] One can view such complexes as derived from NO^+, which is isoelectronic with CO.

Nitric oxide can serve as a one-electron pseudohalide. In such complexes, the M-N-O group is characterized by an angle between 120° and 140°.

The NO group can also bridge between metal centers through the nitrogen atom in a variety of geometries.

Measurement of nitric oxide concentration

The concentration of nitric oxide can be determined using a simple chemiluminescent reaction involving ozone:[8] A sample containing nitric oxide is mixed with a large quantity of ozone. The nitric oxide reacts with the ozone to produce oxygen and nitrogen dioxide. This reaction also produces light (chemiluminescence), which can be measured with a photodetector. The amount of light produced is proportional to the amount of nitric oxide in the sample.



Nitric oxide (white) in conifer cells, visualized using DAF-2 DA (diaminofluorescein diacetate)

$$NO + O_3 \rightarrow NO_2 + O_2 + \text{light}$$

Other methods of testing include electroanalysis (amperometric approach), where NO reacts with an electrode to induce a current or voltage change. The detection of NO radicals in biological tissues is particularly difficult due to the short lifetime and concentration of these radicals in tissues. One of the few practical methods is spin trapping of nitric oxide with iron-dithiocarbamate complexes and subsequent detection of the mono-nitrosyl-iron complex with electron paramagnetic resonance (EPR).[9][10]

A group of fluorescent dye indicators that are also available in acetylated form for intracellular measurements exist. The most common compound is 4,5-diaminofluorescein (DAF-2).[3]

Production environmental effects

From a thermodynamic perspective, NO is unstable with respect to O_2 and N_2, although this conversion is very slow at ambient temperatures in the absence of a catalyst. Because the heat of formation of NO is endothermic, its synthesis from molecular nitrogen and oxygen requires elevated temperatures above 1000 °C. A major natural source is lightning. The use of internal combustion engines has drastically increased the presence of nitric oxide in the environment. One purpose of catalytic converters in cars is to minimize NO emission by catalytic reversion to O_2 and N_2.

Nitric oxide in the air may convert to nitric acid, which has been implicated in acid rain. Furthermore, both NO and NO_2 participate in ozone layer depletion. Nitric oxide is a small highly diffusible gas and a ubiquitous bioactive molecule.

Technical applications

Although NO has relatively few direct uses, it is produced on a massive scale as an intermediate in the Ostwald process for the synthesis of nitric acid from ammonia. In 2005, the US alone produced 6 million metric tons of nitric acid.[11] It finds use in the semiconductor industry for various processes. In one of its applications it is used along with nitrous oxide to form oxynitride gates in CMOS devices.

Miscellaneous applications

Nitric oxide can be used for detecting surface radicals on polymers. Quenching of surface radicals with nitric oxide results in incorporation of nitrogen, which can be quantified by means of X-ray photoelectron spectroscopy.

Biological functions

Main article: Biological functions of nitric oxide

NO is one of the few gaseous signaling molecules known and is additionally exceptional due to the fact that it is a radical gas. It is a key vertebrate biological messenger, playing a role in a variety of biological processes. Nitric oxide, known as the 'endothelium-derived relaxing factor', or 'EDRF', is biosynthesized endogenously from L-arginine, oxygen and NADPH by various nitric oxide synthase (NOS) enzymes. Reduction of inorganic nitrate may also serve to make nitric oxide. The endothelium (inner lining) of blood vessels uses nitric oxide to signal the surrounding smooth muscle to relax, thus resulting in vasodilation and increasing blood flow. Nitric oxide is highly reactive (having a lifetime of a few seconds), yet diffuses freely across membranes. These attributes make nitric oxide ideal for a transient paracrine (between adjacent cells) and autocrine (within a single cell) signaling molecule.[12] The production of nitric oxide is elevated in populations living at high altitudes, which helps these people avoid hypoxia by aiding in pulmonary vasculature vasodilation. Effects include vasodilatation, neurotransmission (see gasotransmitters), modulation of the hair cycle, production of reactive nitrogen intermediates and penile erections (through its ability to vasodilate). Nitroglycerin and amyl nitrite serve as vasodilators because they are converted to nitric oxide in the body. Sildenafil citrate, popularly known by the trade name *Viagra*, stimulates erections primarily by enhancing signaling through the nitric oxide pathway in the penis.

Nitric oxide (NO) contributes to vessel homeostasis by inhibiting vascular smooth muscle contraction and growth, platelet aggregation, and leukocyte adhesion to the endothelium. Humans with atherosclerosis, diabetes, or hypertension often show impaired NO pathways.[13] A high salt intake was demonstrated to attenuate NO production, although bioavailability remains unregulated.[14]

Nitric oxide is also generated by phagocytes (monocytes, macrophages, and neutrophils) as part of the human immune response. Phagocytes are armed with inducible nitric oxide synthase (iNOS), which is activated by interferon-gamma (IFN-γ) as a single signal or by tumor necrosis factor (TNF) along with a second signal.[15] On the other hand, transforming growth factor-beta (TGF-β) provides a strong inhibitory signal to iNOS, whereas interleukin-4 (IL-4) and IL-10 provide weak inhibitory signals. In this way the immune system may regulate the armamentarium of phagocytes that play a role in inflammation and immune responses. Nitric oxide secreted as an immune response is as free radicals and is toxic to bacteria; the mechanism for this includes DNA damage[16][17][18] and degradation of iron sulfur centers into iron ions and iron-nitrosyl compounds.[19] In response, however, many bacterial pathogens have evolved mechanisms for nitric oxide resistance.[20] Because nitric oxide might serve as an *inflammometer* in conditions like asthma, there has been increasing interest in the use of exhaled nitric oxide as a breath test in diseases with airway inflammation.

Nitric oxide can contribute to reperfusion injury when an excessive amount produced during reperfusion (following a period of ischemia) reacts with superoxide to produce the damaging oxidant peroxynitrite. In contrast, inhaled nitric oxide has been shown to help survival and recovery from paraquat poisoning, which produces lung tissue–damaging superoxide and hinders NOS metabolism.

In plants, nitric oxide can be produced by any of four routes: (i) L-arginine-dependent nitric oxide synthase,[21][22][23] (although the existence of animal NOS homologs in plants is debated),[24] (ii) by plasma membrane-bound nitrate reductase, (iii) by mitochondrial electron transport chain, or (iv) by non -enzymatic reactions. It is a signaling molecule, acts mainly against oxidative stress and also plays a role in plant pathogen interactions. Treating cut flowers and other plants with nitric oxide has been shown to lengthen the time before wilting.[25]

An important biological reaction of nitric oxide is S-nitrosylation, the conversion of thiol groups, including cysteine residues in proteins, to form S-nitrosothiols (RSNOs). S-Nitrosylation is a mechanism for dynamic, post-translational regulation of most or all major classes of protein.

Mechanism of action

There are several mechanisms by which NO has been demonstrated to affect the biology of living cells. These include oxidation of iron-containing proteins such as ribonucleotide reductase and aconitase, activation of the soluble guanylate cyclase, ADP ribosylation of proteins, protein sulfhydryl group nitrosylation, and iron regulatory factor activation.[26] NO has been demonstrated to activate NF-κB in peripheral blood mononuclear cells, an important transcription factor in iNOS gene expression in response to inflammation.[27] It was found that NO acts through the stimulation of the soluble guanylate cyclase, which is a heterodimeric enzyme with subsequent formation of cyclic GMP. Cyclic GMP activates protein kinase G, which causes phosphorylation of myosin light chain phosphatase, and therefore inactivation of myosin light-chain kinase, and leads ultimately to the dephosphorylation of the myosin light chain, causing smooth muscle relaxation.[28]

Use in pediatric intensive care

Nitric oxide/oxygen blends are used in critical care to promote capillary and pulmonary dilation to treat primary pulmonary hypertension in neonatal patients[29][30] post-meconium aspiration and related to birth defects. These are often a last-resort gas mixture before the use of extracorporeal membrane oxygenation (ECMO). Nitric oxide therapy has the potential to significantly increase the quality of life and, in some cases, save the lives of infants at risk for pulmonary vascular disease.[31]

Pharmacology

Nitric oxide is considered an antianginal drug: it causes vasodilation, which can help with ischemic pain known as angina by decreasing the cardiac workload. By dilating the veins there is less blood returned to the heart per cycle.[32] This decreases the amount of volume that the heart has to pump. Nitroglycerin pills, taken sublingually (under the tongue), are used to prevent or treat acute chest pain. The nitroglycerin reacts with a sulfhydryl group (–SH) to produce nitric oxide, which eases the pain by causing vasodilation. Recent evidence suggests that nitrates may be beneficial for treatment of angina due to reduced myocardial oxygen consumption both by decreasing preload and afterload and by some direct vasodilation of coronary vessels[32]

References

1. ^ Hou, YC; Janczuk, A; Wang, PG (1999). "Current trends in the development of nitric oxide donors.". *Current pharmaceutical design* **5** (6): 417–41. PMID 10390607 (http://www.ncbi.nlm.nih.gov/pubmed/10390607) .
2. ^ Taylor, BS; Kim, YM; Wang, Q; Shapiro, RA; Billiar, TR; Geller, DA (1997). "Nitric oxide down-regulates hepatocyte-inducible nitric oxide synthase gene expression.". *Archives of surgery (Chicago, Ill. : 1960)* **132** (11): 1177–83. PMID 9366709 (http://www.ncbi.nlm.nih.gov/pubmed/9366709) .
3. ^ *a b* Elizabeth Culotta and Daniel E. Koshland Jr (1992). "NO news is good news. (nitric oxide; includes information about other significant advances & discoveries of 1992) (Molecule of the Year)". *Science* **258** (5090): 1862–1864. doi:10.1126/science.1361684 (http://dx.doi.org/10.1126%2Fscience.1361684) . PMID 1361684 (http://www.ncbi.nlm.nih.gov/pubmed/1361684) .
4. ^ Traube, Wilhelm (1898). "Ueber Synthesen stickstoffhaltiger Verbindungen mit Hülfe des Stickoxyds". *Justus Liebig's Annalen der Chemie* **300**: 81. doi:10.1002/jlac.18983000108 (http://dx.doi.org/10.1002%2Fjlac.18983000108) .
5. ^ Derosa, Frank; Keefer, Larry K.; Hrabie, Joseph A. (2008). "Nitric Oxide Reacts with Methoxide". *The Journal of Organic Chemistry* **73** (3): 1139. doi:10.1021/jo7020423 (http://dx.doi.org/10.1021%2Fjo7020423) . PMID 18184006 (http://www.ncbi.nlm.nih.gov/pubmed/18184006) .
6. ^ Robert H. Crabtree: "The Organometallic Chemistry of the Transition Metals" (http://books.google.com/books?id=0bXMwefSs-kC&pg=PA32) , John Wiley and Sons, 2005, ISBN 0471662569, p. 32.
7. ^ Robert H. Crabtree: "The Organometallic Chemistry of the Transition Metals" (http://books.google.com/books?id=0bXMwefSs-kC&pg=PA96) , John Wiley and Sons, 2005, ISBN 0471662569, pp. 96–98.
8. ^ Fontijn, Arthur.; Sabadell, Alberto J.; Ronco, Richard J. (1970). "Homogeneous chemiluminescent measurement of nitric oxide with ozone. Implications for continuous selective monitoring of gaseous air pollutants". *Analytical Chemistry* **42**: 575. doi:10.1021/ac60288a034 (http://dx.doi.org/10.1021%2Fac60288a034) .
9. ^ Vanin, A; Huisman, A; Vanfaassen, E (2002). *Iron dithiocarbamate as spin trap for nitric oxide detection: Pitfalls and successes*. **359**. pp. 27. doi:10.1016/S0076-6879(02)59169-2 (http://dx.doi.org/10.1016%2FS0076-6879%2802%2959169-2) .

10. ^ Nagano, T; Yoshimura, T (2002). "Bioimaging of nitric oxide.". *Chemical reviews* **102** (4): 1235–70. doi:10.1021/cr010152s (http://dx.doi.org/10.1021%2Fcr010152s) . PMID 11942795 (http://www.ncbi.nlm.nih.gov/pubmed/11942795) .
11. ^ "Production: Growth is the Norm" Chemical and Engineering News, July 10, 2006, p. 59.
12. ^ Stryer, Lubert (1995). *Biochemistry, 4th Edition*. W.H. Freeman and Company. pp. 732. ISBN 0-7167-2009-4.
13. ^ Dessy, C.; Ferron, O. (2004). "Pathophysiological Roles of Nitric Oxide: In the Heart and the Coronary Vasculature". *Current Medical Chemistry – Anti-Inflammatory & Anti-Allergy Agents in Medicinal Chemistry* **3** (3): 207–216. doi:10.2174/1568014043355348 (http://dx.doi.org/10.2174%2F1568014043355348) .
14. ^ Osanai, T; Fujiwara, N; Saitoh, M; Sasaki, S; Tomita, H; Nakamura, M; Osawa, H; Yamabe, H *et al.* (2002). "Relationship between salt intake, nitric oxide and asymmetric dimethylarginine and its relevance to patients with end-stage renal disease." (http://content.karger.com/ProdukteDB/produkte.asp?Aktion=ShowPDF&ProduktNr=223997&Ausgabe=228460&ArtikelNr=63555) . *Blood purification* **20** (5): 466–8. doi:10.1159/000063555 (http://dx.doi.org/10.1159%2F000063555) . PMID 12207094 (http://www.ncbi.nlm.nih.gov/pubmed/12207094) . http://content.karger.com/ProdukteDB/produkte.asp?Aktion=ShowPDF&ProduktNr=223997&Ausgabe=228460&ArtikelNr=63555.
15. ^ Gorczyniski and Stanely, Clinical Immunology. Landes Bioscience; Austin, TX. ISBN 1570596255
16. ^ Wink, DA; et.al. (1991). "DNA deaminating ability and genotoxicity of nitric oxide and its progenitors". *Science* **254** (5034): 1001–3. doi:10.1126/science.1948068 (http://dx.doi.org/10.1126%2Fscience.1948068) . PMID 1948068 (http://www.ncbi.nlm.nih.gov/pubmed/1948068) . About killing of salmonella bacteria.
17. ^ Nguyen, T; Brunson D, Crespi CL, Penman BW, Wishnok JS, Tannenbaum SR (1992). "DNA damage and mutation in human cells exposed to nitric oxide in vitro" (http://www.pubmedcentral.nih.gov/articlerender.fcgi?tool=pmcentrez&artid=48797) . *Proc Natl Acad Sci USA* **89** (7): 3030–4. doi:10.1073/pnas.89.7.3030 (http://dx.doi.org/10.1073%2Fpnas.89.7.3030) . PMID 1557408 (http://www.ncbi.nlm.nih.gov/pubmed/1557408) . Free text.
18. ^ Li, CQ; Pang B, Kiziltepe T, Trudel LJ, Engelward BP, Dedon PC, Wogan GN (2006). "Threshold Effects of Nitric Oxide-Induced Toxicity and Cellular Responses in Wild-Type and p53-Null Human Lymphoblastoid Cells" (http://www.pubmedcentral.nih.gov/articlerender.fcgi?tool=pmcentrez&artid=2570754) . *Chem Res Toxicol* **19** (3): 399–406. doi:10.1021/tx050283e (http://dx.doi.org/10.1021%2Ftx050283e) . PMID 16544944 (http://www.ncbi.nlm.nih.gov/pubmed/16544944) . free text.
19. ^ Hibbs, JB; Taintor RR, Vavrin Z, Rachlin EM (1988). "Nitric oxide: a cytotoxic activated macrophage effector molecule". *Biochem Biophys Res Commun* **157** (1): 87–94. doi:10.1016/S0006-291X(88)80015-9 (http://dx.doi.org/10.1016%2FS0006-291X%2888%2980015-9) . PMID 3196352 (http://www.ncbi.nlm.nih.gov/pubmed/3196352) .
20. ^ C. A. Janeway, et al. (2005). *Immunobiology: the immune system in health and disease* (6th ed.). New York: Garland Science. ISBN 0-8153-4101-6.
21. ^ Corpas, F. J. *et al.* (2004). "Cellular and subcellular localization of endogenous nitric oxide in young and senescent pea plants" (http://www.pubmedcentral.nih.gov/articlerender.fcgi?tool=pmcentrez&artid=523336) . *Plant Physiology* **136** (1): 2722–33. doi:10.1104/pp.104.042812 (http://dx.doi.org/10.1104%2Fpp.104.042812) . PMID 15347796 (http://www.ncbi.nlm.nih.gov/pubmed/15347796) .
22. ^ Corpas, F. J. *et al.* (2006). "Constitutive arginine-dependent nitric oxide synthase activity in different organs of pea seedlings during plant development". *Planta* **224** (2): 246–54. doi:10.1007/s00425-005-0205-9 (http://dx.doi.org/10.1007%2Fs00425-005-0205-9) . PMID 16397797 (http://www.ncbi.nlm.nih.gov/pubmed/16397797) .
23. ^ Valderrama, R. *et al.* (2007). "Nitrosative stress in plants". *FEBS Lett* **581** (3): 453–61. doi:10.1016/j.febslet.2007.01.006 (http://dx.doi.org/10.1016%2Fj.febslet.2007.01.006) . PMID 17240373 (http://www.ncbi.nlm.nih.gov/pubmed/17240373) .
24. ^ Corpas et al.; Barroso, Juan B.; Del Rio, Luis A. (2004). "Enzymatic sources of nitric oxide in plant cells – beyond one protein–one function". *New Phytologist* **162**: 246–7. doi:10.1111/j.1469-8137.2004.01058.x (http://dx.doi.org/10.1111%2Fj.1469-8137.2004.01058.x) .
25. ^ Judy Siegel-Itzkovich. Viagra makes flowers stand up straight (http://www.studentbmj.com/issues/99/09/news/313.php) . *Student BMJ*, September 1999.
26. ^ Shami, PJ; Moore, JO; Gockerman, JP; Hathorn, JW; Misukonis, MA; Weinberg, JB (1995). "Nitric oxide modulation of the growth and differentiation of freshly isolated acute non-lymphocytic leukemia cells.".

Leukemia research **19** (8): 527–33. doi:10.1016/0145-2126(95)00013-E (http://dx.doi.org/10.1016%2F0145-2126%2895%2900013-E) . PMID 7658698 (http://www.ncbi.nlm.nih.gov/pubmed/7658698) .
27. ^ Kaibori M., Sakitani K., Oda M., Kamiyama Y., Masu Y. and Okumura T. (1999). "Immunosuppressant FK506 inhibits inducible nitric oxide synthase gene expression at a step of NF-κB activation in rat hepatocytes" (http://www.jhep-elsevier.com/article/S0168-8278(99)80270-0/abstract) . *J. Hepatol.* **30** (6): 1138–1145. doi:10.1016/S0168-8278(99)80270-0 (http://dx.doi.org/10.1016%2FS0168-8278%2899%2980270-0) . PMID 10406194 (http://www.ncbi.nlm.nih.gov/pubmed/10406194) . http://www.jhep-elsevier.com/article/S0168-8278(99)80270-0/abstract.
28. ^ Surks, HK (2007). "cGMP-dependent protein kinase I and smooth muscle relaxation: a tale of two isoforms.". *Circulation research* **101** (11): 1078–80. doi:10.1161/CIRCRESAHA.107.165779 (http://dx.doi.org/10.1161%2FCIRCRESAHA.107.165779) . PMID 18040024 (http://www.ncbi.nlm.nih.gov/pubmed/18040024) .
29. ^ Finer NN, Barrington KJ (2006). "Nitric oxide for respiratory failure in infants born at or near term". *Cochrane Database Syst Rev* (4): CD000399. doi:10.1002/14651858.CD000399.pub2 (http://dx.doi.org/10.1002%2F14651858.CD000399.pub2) . PMID 17054129 (http://www.ncbi.nlm.nih.gov/pubmed/17054129) .
30. ^ Chotigeat U, Khorana M, Kanjanapattanakul W (2007). "Inhaled nitric oxide in newborns with severe hypoxic respiratory failure". *J Med Assoc Thai* **90** (2): 266–71. PMID 17375630 (http://www.ncbi.nlm.nih.gov/pubmed/17375630) .
31. ^ Hayward, CS; Kelly, RP; MacDonald, PS (1999). "Inhaled nitric oxide in cardiology practice.". *Cardiovascular research* **43** (3): 628–38. doi:10.1016/S0008-6363(99)00114-5 (http://dx.doi.org/10.1016%2FS0008-6363%2899%2900114-5) . PMID 10690334 (http://www.ncbi.nlm.nih.gov/pubmed/10690334) .
32. ^ [a] [b] Abrams, J (1996). "Beneficial actions of nitrates in cardiovascular disease". *The American Journal of Cardiology* **77**: C31. doi:10.1016/S0002-9149(96)00186-5 (http://dx.doi.org/10.1016%2FS0002-9149%2896%2900186-5) .

Further reading

- Butler A. and Nicholson R.; "Life, death and NO." (http://books.google.com/books?id=0d1Z0m76YeYC&printsec=frontcover) Cambridge 2003. ISBN 978-0-85404-686-7.
- van Faassen, E. E.; Vanin, A. F. (eds); "Radicals for life: The various forms of Nitric Oxide." (http://books.google.com/books?id=UJ4glFNEcn0C&printsec=frontcover) Elsevier, Amsterdam 2007. ISBN 978-0-444-52236-8.

External links

- International Chemical Safety Card 1311 (http://www.ilo.org/public/english/protection/safework/cis/products/icsc/dtasht/_icsc13/icsc1311.h
- National Pollutant Inventory – Oxides of nitrogen Fact Sheet (http://www.npi.gov.au/database/substance-info/profiles/67.html)
- 1998 Nobel Prize in Physiology/Medicine for discovery of NO's role in cardiovascular regulation (http://www.nobel.se/medicine/laureates/1998/index.html)
- Nitric Oxide and its Role in Diabetes, Wound Healing and Peripheral Neuropathy (http://www.diabetesincontrol.com/annodyne/burkeseries.php)
- Microscale Gas Chemistry: Experiments with Nitrogen Oxides (http://mattson.creighton.edu/NOx/index.html)
- Your Brain Boots Up Like a Computer (http://www.livescience.com/humanbiology/060817_brain_boot.html) – new insights about the biological role of nitric oxide.
- Assessing The Potential of Nitric Oxide in the Diabetic Foot (http://www.podiatrytoday.com/article/5164)

- New Discoveries About Nitric Oxide Can Provide Drugs For Schizophrenia (http://www.sciencedaily.com/releases/2007/11/071121213845.htm)
- Nitric Oxide at the Chemical Database (http://ull.chemistry.uakron.edu/erd/Chemicals/8000/6828.html)

Retrieved from "http://en.wikipedia.org/wiki/Nitric_oxide"
Categories: Oxides | Inorganic nitrogen compounds | Neurotransmitters | Nitrogen metabolism | Free radicals