УДК 612.127.4

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Abstract: Nitric oxide is a signaling molecule formed from nitrogen (N) and oxygen (O), which is literally called NO. Nitric oxide plays a major role in vascular relaxation (regulation of blood pressure, erectile dysfunction), immune response, inflammation, antithrombotic activity and memory formation.

KEY WORDS: nitric oxide, pathogenesis, oxidative potential, nebivolol, NO-synthase isoforms, oxidative potential.

BIOLOGY OF NITRIC OXIDE

History

In 1998, Louis Ignarro and two American scientists pharmacist – Ferid Murad and Robert Furchgott – was awarded the Nobel prize in physiology or medicine for establishing the functional role of nitric oxide in the cardiovascular system. These scientists were able for the first time to prove the importance of nitric oxide (NO) for the provision of blood organs and its role in the body as a carrier of information,which are also hormones regulating metabolism and organ functions.

What is the reason for this growing scientific interest in nitrogen oxide? It turned out that nitric oxide controls both intracellular and intercellular processes in living cells. Many diseases-hypertension, myocardial ischemia, thrombosis, cancer - caused by violation of physiological processes that regulate nitric oxide. It is for this reason that nitric oxide is of great interest to biologists and physicians of various specialties.

Structure

Nitric oxide is a small signaling molecule synthesized from the amino acid L-arginine by a family of nitric oxide synthase comprising eNOS (endothelial, NOS-III), iNOS (inducible, NOS-II) and nNOS (neuronal, NOS-I). This family of enzymes acts as dimers in conjunction with a variety of cofactors, including tetrahydrobiopterin, flavin adenine dinucleotide (FAD), flavin mononucleotide (FMN), iron and zinc. While the regulation and modulation of each isoform varies considerably, all isoforms accelerate the l-arginine reaction with NADPH and oxygen to produce NO, citrulline and NADPH.

How nitric oxide transmits the signal

The explanation of the action of nitric oxide as a signal molecule of the gas led to the fact that the gas molecule is produced by one cell, immediately transferred to other cells and then acts as a signal molecule in the cells. For example, NO, produced by eNOS in endothelial cells, is transferred to smooth muscle cells, where it gives rise to a cascade of reactions due to the activation of soluble guanylate cyclase, which accelerates the production of cyclic GMF[1].

The rise in cGMP levels causes the activation of G protein kinase (PKG), which in turn phosphorylates the phosphatase of myosin light chains (MLC) (thus

activating them). In turn, activated MLC phosphatase MLC dephosphorylated, which leads to relaxation of smooth muscle cells and thus relaxation of blood vessels. Nitric oxide transmits the signal by stimulating its receptor, soluble guanylyl cyclase and increasing the cellular level of the signal molecule called cyclic guanidine monophosphate (cGMP).

Additional participants in the regulation of vascular tone include a family phosphodiesterase (PDE 1 to 11), which accelerate the hydrolysis of cGMP at the 3' end product[2], effectively inhibiting due to NO relaxation of the blood vessels. Due to the physiological importance of PDE in controlling cGMP levels, they become a popular target when it comes to vessel relaxation and blood flow. Examples include drugs such as Cialis and Levitra, all of which inhibit PDE5, which is particularly expressed in smooth muscle cells.

Oxidation potential

NO can theoretically break up into a molecule known as peroxynitrite (OONO -), which is the result of a NO reaction with superoxide anions (O_2 -). [3]OONO-also acts as a reactive signaling molecule, although the end result is the formation of some structures that are negative to the body; OONO - can nitrosylate (transmit nitrogen group) against amino acids to form compounds such as 3-nitrotyrosine or S-nitrosocysteine, the formation of protein CARBONYLS or nitrosylation phospholipids containing polyunsaturated fatty acids (PUFA).

[4] In this sense, nitric oxide can be used as a substrate by superoxide to form reactive compounds that have a negative impact on health, despite the fact that NO is relatively favorable to the body. Nitric oxide can be transformed (by means of a connection to superoxide radicals) into a form of peroxynitrite, which can then form a set of molecules that bind to an unhealthy state and are presumably related to pathologies.

Pharmacology

Additional nitric oxide

NO, which is synthesized in the body and subsequently released into the bloodstream, has a half-life period of 5 seconds or less, while in the laboratory can create some complexes to increase the half-life to 445 s or so for research purposes. These short half-life periods indicate a rapid decomposition of the nitric oxide molecule into constituents (nitrogen and oxygen), with proper storage of NO can increase storage life, as confirmed, only up to 5 days, [5] with the use of Mylar cylinders, which slow down the destruction.

Physiology

Cardiovascular system

Nitric oxide is related to the relaxation of nasty vascular muscles, which is a mechanism underlying the cardioprotective action of nitric oxide (by reducing blood pressure).

Neuronal action

Nitric oxide modulates ion channels, innate excitability, causes synaptic plasticity and can penetrate cell membranes. Neuronal nitric oxide synthase (nNOS) is capable of forming a dimer with a protein known as PSD95, [6] this complex is a positive regulator of depression, since the inhibition of NNOs-PSD95 interaction has

an antidepressant effect. This complex is activated after activation of NMDA-receptor.[7]

Conclusion

Thus, the variety of effects of nitric oxide is due to the formation of physiologically active metabolites NO and its interaction with various molecular targets, and is dose-dependent. Analysis of the literature showed that many aspects of NO have not been fully studied and are often contradictory. Nevertheless, clarifying the mechanism of action of nitric oxide deserves close attention and further research, as it contributes to solving many fundamental problems of biology and is of great practical importance for medicine.

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