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Review

Therapeutic role of nitric oxide as emerging molecule

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ABSTRACT

NO has many physiological roles; in inflammation, pain, rheumatoid arthritis, immune system, gastroprotection, as antioxidant and reported to be a free radical scavenger.Intensive research on the biological functions of NO and other reactive nitrogen oxide species demands exogenous sources of NO donors as research tools and pharmaceuticals. Since the mid-1980s, the development of new NO donors has offered several advantages over theprevious NO donors, such as spontaneous release of NO, donation of NO under controlled rates, and even the targeting of NO to certain tissues. Nitric oxide releasing derivatives of conventional NSAIDs have been synthesized not only to avoid gastrotoxicity, but also for making them fit for topical delivery, targeting them to brain and increase their analgesic and anti-inflammatory activity. “Hybrid nitrates” have vital role in different like NSAIDs, Anti-platelet, Antileukemic, Glaucoma, Antihypertensive, Antimalarial etc.

Contents

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1. Introduction

1.1. Nitric oxide (NO)

Nitric oxide is a ubiquitous signaling molecule having an ability to freely diffuse across the cell membranes and unlike other classical neurotransmitters, NO cannot be regulated by storage, release and reuptake process. Instead of that, the biosynthesis of NO dynamically modulated to provide the appropriate levels. Nitric oxide (NO) has long been identified that the signal molecule acetylcholine dilates blood vessels in both humans and animals. Nitric oxide has been known as an important neurotransmitter substance which is involved in the pathophysiology of many neurological disorders, such as epilepsy, schizophrenia, drug addiction, anxiety, major depression, etc [1]. The biological importance of nitric oxide in cardiovascular and nervous systems is now more than 20 years old, but its clinical implications are under investigation. The release of nitric oxide (NO) from nitroglycerine and its action on vascular smooth muscle was discovered by Ferid Murad in 1977. The role of endothelium in acetylcholine-induced vasorelaxation was identified by Robert Furchgott and John Zawadski in 1980 and nitric oxide was recognized as endothelial-derived relaxing factor (EDRF) by Louis Ignarro and Salvador Moncada in 1987 [2]. The half life of nitric oxide is considered to be very small (3–6 s). Nitric oxide is involved in different physiological processes of the body by modulating different biochemical reactions, the best example taken is in the brain, nitric oxide has been involved in neurotransmission, neuromorphongenesis, synaptic plasticity, regulation of gene expression, modulating sexual and aggressive behaviors, learning, perception of pain, aggression and depression [3]. In the year of 1992, nitric oxide was designated by other wonderful name called as "**Molecule of the Year**" name given by science, a prevalence of the literature has brought insights into its numerous roles in many brain related disorders including stress and major depression [4].

Ignarro and co-workers found that this wonderful molecule nitric oxide (NO) was identical to endothelium-derived relaxing factor (EDRF) [5]. Nitric oxide was not established earlier in mammals due to its instability, NO is an unstable gas, which is rapidly converted to free radicals like NO_3^- and NO_2^- in the presence of H_2O and O_2. Nitric oxide is a critical signaling molecule, involved in modulating the plethora of physiological responses including:

a Maintenance of blood pressure in the cardiovascular system [6–8]
b Stimulating host defenses in the immune system [9]
c Regulating neural transmission in the brain [10]
d Platelet aggregation [6–8]
e Learning and memory [11,12]
f Male sexual function [11,12]
g Cytotoxicity and cytoprotection [11,12]
h Development of arteriosclerosis among others 11,12]
i Inflammation [13]
j Gastroprotection [14]

On one hand, NO exerts beneficial results on the body by playing an important role such as antibacterial, antiparasital, antiviral agent. The lethal reaction occurs if the high amount of nitric oxide reacts with concurrently produced superoxide anions, which further generate highly toxic compounds, such as peroxynitrite and hydroxyl radicals. NO is colorless gas, soluble in water (1.9 μmol/L at 25° C) [15] (Fig. 1).

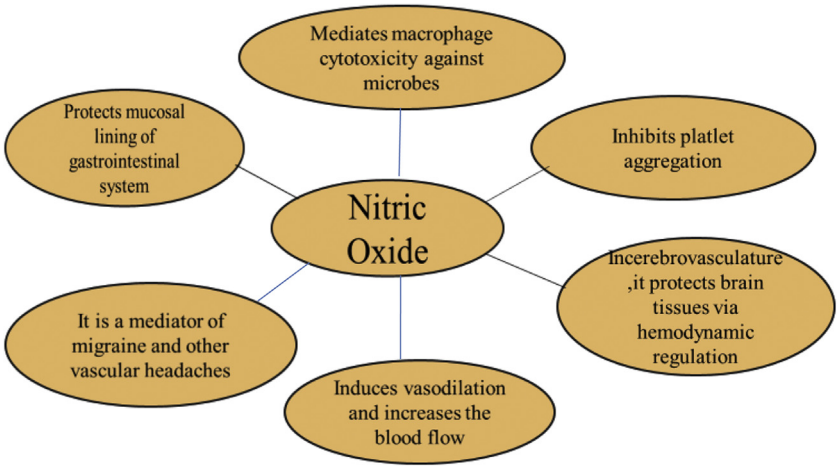

Fig. 1. Role of NO in biological systems.