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Nitric Oxide: A Small molecule with diversifying impacts

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Abstract

Ever since Nitric oxide (NO) was discovered it has been the most studied molecule as it had so much diversity in its biological function based on organ and site specificity. It has been evolved as an important physiological mediator involved in cellular signaling in the cardiovascular, gastrointestinal, genitourinary, respiratory and nervous system. It's failure to be in normal range have been indicated as a cause of various diseases. The drug designing and its therapeutic efficacy is based on the production and inhibition of NO. The main areas of its involvement are in neurotransmission, non-specific immunity and inflammatory response and its regulation in blood pressure.

It has both beneficial and deleterious effects, of which beneficial effects includes the inhibition of leukocyte adhesion, protection against tumor necrosis factor, and also its role an as antioxidant such as offering protection against hydrogen peroxide, and many more. Its deleterious effects include the cytotoxic effects, inhibition of enzyme functions, induction of DNA damage, lipid peroxidation, etc. On the basis of enormous work that has been done on NO's , presumes it as a double edge sword mediator, which has beneficial physiological effects as well as detrimental pathological effect making its development into a drug quite challenging. So there is a tremendous potential in the field of NO research, so that NO can be further regulated by pharmaceuticals and can be further exploited for treatment using NO or the regulators of NO.

Key words: Nitric Oxide, Antioxidant, Second Messenger, DNA damage and Cytotoxicity

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Nitric oxide (NO), a colorless and odorless gas was discovered in 1980 as a chemical entity known as endothelial derived relaxing factor (EDRF) [1]. Since then the molecule has become one of the most highly studied and important biological molecules. It has been evolved as an important physiological mediator involved in cellular signaling in the cardiovascular, gastrointestinal, genitourinary, respiratory and nervous system [2]. The imbalance of NO in tissues has been indicated for the development of several disease state. Hence the production of NO and its inhibition can lead to the development of many therapeutic molecule [3]. Nitric oxide is biosynthesized from amino acid L-arginine, that is present in high concentrations in blood, in extracellular fluid, and as well even at higher concentrations within the cells. The synthesis of NO is the outcome of a series of oxido-reductive events involving a large number of co-factors, which binds to the specific binding sites on the NO synthase that work as a catalyzer [4]. The NO synthase has three different isoforms as they are tailored for the location and stimuli where the NO is required. The main areas of its involvement are in neurotransmission, non-specific immunity and inflammatory response and its regulation in blood pressure [5].

The most beneficial effects of NO involves the inhibition of leukocyte adhesion, protection against tumor necrosis factor, and also its role an as antioxidant such as offering protection against hydrogen peroxide, alkyl hydroperoxide and superoxide induced free radical damage. Nitric oxide plays

an important role in vascular biological, immuno surveillance system, renal function, bronchodilation, cellular adhesion [6]. In addition to these NO has been shown to be involved in the oxidation war chest of the immune system by virtue of involvement of anti-tumor and anti-pathogen host response [7].

Besides its therapeutic implications, the synthesis of NO is seen as a source of oxygen free radicals either alone or via the formation of peroxy nitrite, which has been generated as the resultant end product of the reactions between NO and superoxide. These generated oxygen free radicals have been suggested to be responsible for some the cytotoxic effects of these molecules. There are several deleterious effect of NO such as, inhibition of enzyme functions, induction of DNA damage [8, 9], induction of lipid peroxidations, the depletion of antioxidants stores and also it increases the susceptibility to radiations, alkylating agents and toxic metals. The susceptibility of cell by cytotoxic agents are enhanced when NO per se is present. Still there is confusion regarding the NO's involvement in the physiologic derailment because of its multifaceted and paradoxical action in various cytotoxic mechanisms. [10].

On the basis of enormous work that has been done on NO's suggests that they can regulate cellular and the whole body activity in a surprisingly versatile way. This uniquely acts as a double edge sword mediator, which has beneficial physiological effects as well as detrimental pathological effect making its development into a drug quite challenging. So there is a tremendous potential in the field of NO research, so that NO can be further regulated by pharmaceuticals and can be further exploited for treatment using NO or the regulators of NO.

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