




Review

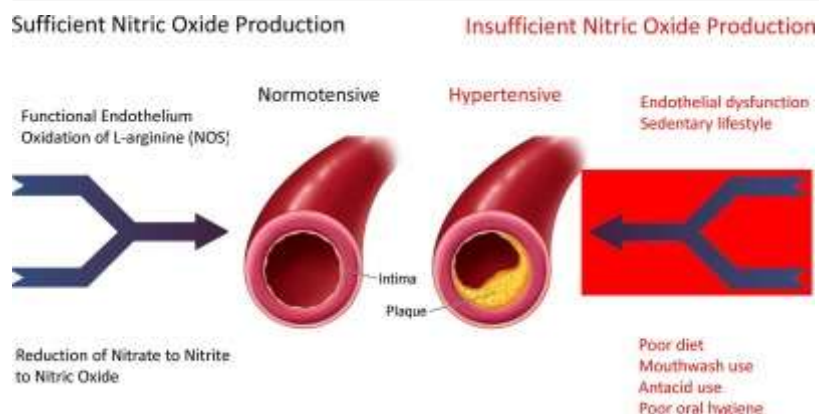
# Nitric oxide deficiency is a primary driver of hypertension

Nathan S. Bryan [Show more](#)  Share  Cite<https://doi.org/10.1016/j.bcp.2022.115325> [Get rights and content](#) 

## Abstract

Hypertension remains a global health crisis. High blood pressure is the number one modifiable risk factor in the onset and progression of cardiovascular disease. Despite many different classes of drug therapies approved for hypertension, the use of polypharmacy and recommendations on lifestyle modification, many patients still suffer from uncontrolled or unmanaged hypertension. Nitric oxide is a naturally produced vasodilator that controls and regulates vascular tone and therefore controls and regulates blood pressure. Research over the past 40 years reveals that loss of nitric oxide production, termed endothelial dysfunction, is the earliest event in the development of hypertension. Strategies aimed at preventing the loss of nitric oxide production and/or therapeutic strategies designed to restore nitric oxide production will likely have a positive effect on patients' health and lead to better management of blood pressure. This review article will focus on the loss of nitric oxide production as the primary contributor to hypertension and also discuss safe and clinically proven strategies to restore nitric oxide production and recapitulate nitric oxide based signaling in humans.

## Graphical abstract



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### Hypertension

Hypertension or commonly known as high blood pressure is the leading cause and risk factor for cardiovascular disease (CVD), including heart attack and stroke [1], the number one cause of death worldwide. Based on the latest guidelines, hypertension is defined by consistently having blood pressure greater than 130mmHg systolic and greater than 80mmHg diastolic [2]. Recent reports reveal that approximately 116 million Americans or nearly-one in two people suffer from hypertension [3]. ...

### Nitric oxide – Vasodilator and anti-Inflammatory

Nitric oxide or NO is a relatively new discovery in science and medicine. It was first realized only about 40years ago and has since opened up a new area in cardiovascular research. Over the past 4 decades, there are now more than 180,000 scientific articles published on NO. In 1998, the Nobel Prize in Physiology or Medicine was awarded to three U.S. Scientists responsible for its discovery. The science is clear on what NO is and how it affects every major chronic disease, including ...

### The oral microbiome regulates systemic blood pressure

The human microbiome constitutes many different bacterial species. In fact, there are ten times more bacteria that live in and on the human body than our own human cells. They are there to provide essential functions that are essential for survival of the human host, a true symbiotic relationship. Although much of the research has been conducted on the gut microbiome, the oral microbiome is gaining attention. A human nitrogen cycle has been identified that requires specific oral bacteria. This ...

## Sodium nitrite as a drug therapy

Now that we have a better understanding of what contributes to hypertension, we can begin to rationalize safe and effective therapies. As we began to solve this problem, we had certain requirements for any therapeutic innovation.

1. If the patient could not produce nitric oxide, either due to endothelial dysfunction or from inadequate dietary nitrate consumption or use of antiseptics, then the technology must provide an exogenous source of NO.  
...
2. The therapy should recapitulate NO based signaling ...

...

## The future of nitric oxide-based drug therapies

It is evident that loss of endogenous nitric oxide production and homeostasis is at least partly responsible for hypertension and is associated with most cardiovascular risk factors [107], [108], [109], [110], [111], [112]. Diet and lifestyle are critically important to controlling and combatting hypertension. Current drug therapy is not sufficient to manage hypertension. Moderate physical exercise promotes endothelial NO production [113]. The Dietary Approaches to Stop Hypertension (DASH) diet ...

## CRedit authorship contribution statement

**Nathan S. Bryan:** conceptualization, data curation, formal analysis, funding acquisition, investigation, methodology, product administration, resources, software - origin, excel, supervision, validation, visualization, writing, review and editing. ...

## Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: [N.S. Bryan is the inventor on dozens of

issued U.S. and International patents. He receives royalties on his patents from the University of Texas Health sciences Center at Houston. Dr. Bryan is company Founder of HumanN, Nitric Oxide Innovations, Pneuma Nitric Oxide, Bryan Nitric Oxide, Bryan Nitric Oxide Research Institute]. ...

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## Real-time and specific monitoring of nitric oxide and evaluating of the oxidative stress in living cells and zebrafish under the pollutant exposure using a carbon dot-based composite fluorescent probe

2024, Journal of Hazardous Materials

### *Citation Excerpt :*

...As shown in Table S2, the sensitivity of the proposed method for NO detection was superior to that of most previously reported methods. In addition, NO is widely distributed in various tissues of organisms; both low concentrations (from picomolar to nanomolar range) and high concentrations (in the micromolar range) are involved in various physiological functions such as cardiovascular regulation, neuromodulation, and immune surveillance [45]. SNP is commonly used as a donor of nitric oxide free radicals, as it constantly releases NO in aqueous solution under visible light irradiation....

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## Selection of goat $\beta$ -casein derived ACE-inhibitory peptide SQPK and insights into its effect and regulatory mechanism on the function of endothelial cells

2023, International Journal of Biological Macromolecules

*Citation Excerpt :*

...Then, three doses of SQPK (6.25, 12.5, 25  $\mu\text{g/mL}$ ) were selected for subsequent tests. Nitric oxide (NO) is a potent vasodilator that regulates blood pressure and can attenuate the epithelial-mesenchymal transition [33]. NO is produced by three isoforms of nitric oxide synthase (NOS), including neuronal NOS (nNOS), inducible NOS (iNOS), and endothelial nitric oxide synthase (eNOS)....

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## Oxidative stress disrupts vascular microenvironmental homeostasis affecting the development of atherosclerosis

2024, Cell Biology International

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