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Nitrite and Nitrite Reductases: From Molecular Mechanisms to Significance in Human Health and Disease

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ABSTRACT

Nitrite, previously considered physiologically irrelevant and a simple end product of endogenous nitric oxide (NO) metabolism, is now envisaged as a reservoir of NO to be activated in response to oxygen (O₂) depletion. In the first part of this review, we summarize and compare the mechanisms of nitrite-dependent production of NO in selected bacteria and in eukaryotes. Bacterial nitrite reductases, which are copper or heme-containing enzymes, play an important role in the adaptation of pathogens to O₂ limitation and enable microorganisms to survive in the human body. In mammals, reduction of nitrite to NO under hypoxic conditions is carried out in tissues and blood by an array of metalloproteins, including heme-containing proteins and molybdenum enzymes. In humans, tissues play a more important role in nitrite reduction, not only because most tissues produce more NO than blood, but also because deoxyhemoglobin efficiently scavenges NO in blood. In the second part of the review, we outline the significance of nitrite in human health and disease and describe the recent advances and pitfalls of nitrite-based therapy, with special attention to its application in cardiovascular disorders, inflammation, and anti-bacterial defence. It can be concluded that nitrite (as well as nitrate-rich diet for long-term applications) may hold promise as therapeutic agent in vascular dysfunction and ischemic injury, as well as an effective compound able to promote angiogenesis. *Antioxid. Redox Signal.* 17, 684–716.