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Review

The role of hydrogen sulfide in burns

Farhana Akter *

London Deanery, United Kingdom

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ABSTRACT

Hydrogen sulfide is a novel gasotransmitter that has been shown to play a major role in regulating vascular tone. However, the role of hydrogen sulfide in inflammation, sepsis and burns has only recently been studied. In animal studies, hydrogen sulfide has been shown to play a role in both promoting and inhibiting inflammation. Understanding the role of H_2S in sepsis and shock is particularly important due to the high mortality associated with both conditions. In animal sepsis models, hydrogen sulfide appears to increase survival. Severe burns are associated with an inflammatory response that causes increased permeability and edema. Currently, there are few studies that have examined the exact role of hydrogen sulfide in burns. However, the role of hydrogen sulfide in inflammation enables us to hypothesize its role in burns. This review highlights the role of hydrogen sulfide in the mechanisms of action underlying inflammation, wound healing and sepsis as well as examining the potential role of hydrogen sulfide in burns. The authors of this article hope that this review will stimulate research to discover the exact role of this fascinating molecule in burns.

Contents

* *Correspondence to*: 68 Primrose Close, Beds, LU3 1EY, United Kingdom. Tel.: +44 07910964309.
E-mail address: fakter555@gmail.com.

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Table 1 – Classification of gasotransmitters.

(1) Small molecules of gas.
(2) Freely permeable to the membrane.
(3) Endogenously generated.
(4) Have specific functions at physiological concentrations.
(5) Cellular effects may or may not be mediated by second messengers.

1. Introduction

Over the last few decades, the scientific community has seen an increase in the number of studies on the endothelium and local mediators of the endothelium, such as nitric oxide (NO). More recently, the toxic gas hydrogen sulfide (H_2S) has been recognized as a signaling molecule, and it has been proposed that H_2S is an important endogenous gaseous transmitter with signaling activities similar to NO and another gaseous transmitter, carbon monoxide [1]. To distinguish NO, CO, and H_2S from classical neurotransmitters and humoral factors, these endogenous gaseous transmitters have been defined as "gasotransmitters" based on several criteria (Table 1) [1]. The role of NO and H_2S in inflammation, sepsis and wound healing has been the subject of numerous studies in recent years. NO is of great interest because it is thought to play a complex role in burns and because it has therapeutic potential. The role of H_2S in the pathophysiology of burns is not well known. Studies investigating the role of H_2S in burns are limited and have predominantly been restricted to animal models. However, the known role of H_2S in inflammation and sepsis enables us to hypothesize the role of H_2S in burns and provides us with clues about the therapeutic potential of H_2S. This review highlights the potential uses of H_2S and its mechanism of action in burns, inflammation and sepsis.

2. Hydrogen sulfide background

2.1. H_2S chemistry and biology

H_2S is a colorless gasotransmitter with a characteristic rotten egg smell. Under physiological conditions (aqueous solutions at pH 7.4), one-third of H_2S is un-dissociated and two-thirds is hydrolyzed to sulfide and hydrosulfide ions in the following reaction: $H_2S \Leftrightarrow H^+ + HS^- \Leftrightarrow 2H^+ + S^{2-}$ [2]. In mammalian tissues and blood, the concentration of H_2S is 1–160 μM under physiological conditions [3]. Higher concentrations of H_2S are present in the brain (50–160 μM) and blood (10–100 μM) [4].

H_2S is produced in the central nervous system and in peripheral organs via two enzymatic pathways: cystathionine β-synthase (CBS) and cystathionine γ-lyase (CSE) [5]. In mammals, CBS is present in large amounts in the brain, particularly in purkinje cells and the hippocampus [6], whereas CSE activity is highest in peripheral tissues, especially the liver, kidney, blood vessels and vascular smooth muscle [7] (Fig. 1).

3. Hydrogen sulfide in inflammation and sepsis

3.1. Hydrogen sulfide as a promoter of inflammation

Bhatia et al. [8] demonstrated that H_2S has a key role in inducing edema, which is a cardinal sign of inflammation. They used carrageenan to induce edema in rat's paws, a well-known method for testing inflammatory reactions [9]. Injection of carrageenan led to edema formation as determined by an increase in the weight of the hind paws of rats. The rats

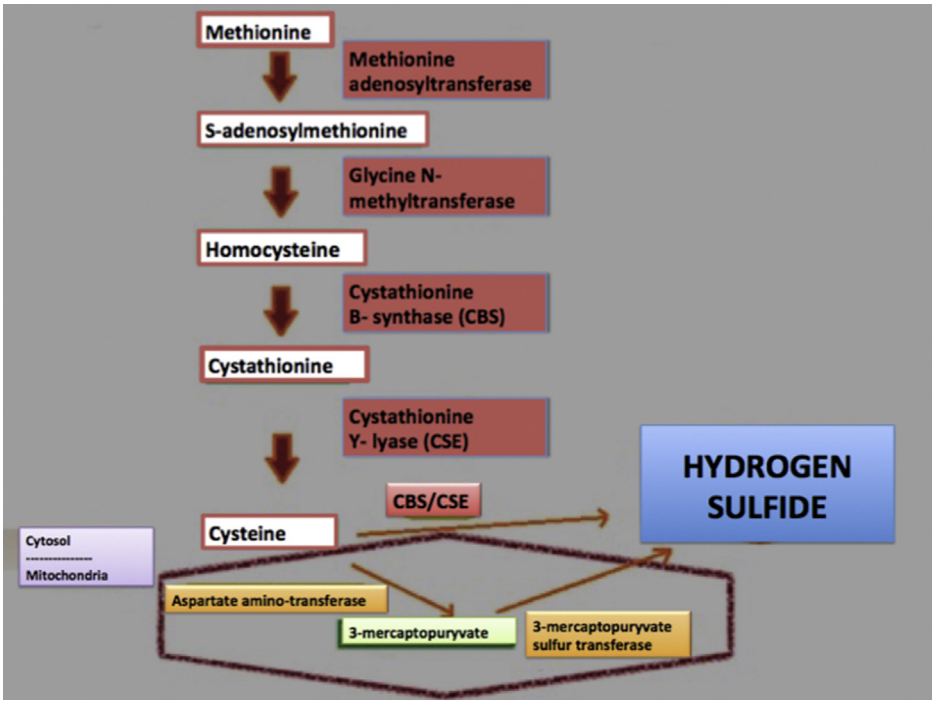

Fig. 1 – Hydrogen sulfide synthesis.