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# COMMENT Hydrogen inhalation therapy for inflammation and eye diseases: a review of the literature

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An exhaustive survey of existing literature was conducted to investigate the relationship between hydrogen inhalation therapy, inflammation, and ocular disordhers. The burgeoning body of evidence indicates that hydrogen inhalation therapy might be a promising approach to alleviate not only inflammation but also related eye diseases.

Liang et al. investigated the effect of hydrogen gas inhalation on age-related macular degeneration in mice [1]. Hydrogen gas, an antioxidant, was found to reduce leakage in choroidal neovascularization, a key feature of the disease. The treatment also suppressed inflammation and the expression of vascular endothelial growth factor, potentially inhibiting disease progression [1].

Li et al. presented that  $H_2$  is a non-toxic gas that can alleviate oxidative damage and inflammation, offering protective effects on cells [2]. It can be administered in various forms and has shown promise in treating multiple eye diseases, including cataracts and diabetic retinopathy. Despite its potential, further studies are needed to optimize its use.

Otsuka et al. used a rat model to investigate the effects of hydrogen gas inhalation on retinal ischemia reperfusion injury [3]. Their results showed that hydrogen gas reduced inflammation, structural changes, and glial cell increase caused by the injury, suggesting its potential therapeutic benefits [3].

Artamonov et al. addressed that molecular hydrogen, a minor atmospheric component, has diverse biological effects such as an anti-inflammatory and antioxidant effect [4]. Over 2000 articles have been published on hydrogen medicine, indicating its potential in regenerative medicine. Their review aims to systematize the nature, characteristics, and mechanisms of hydrogen's influence on various cells, including stem cells [4].

 $H_2$ , with antioxidant properties, has been studied by Johnsen et al. for various therapeutic uses [5]. Over 2000 publications and numerous clinical trials reflect its potential as a new drug substance. Positive results have been found in major disease areas. Despite challenges in administration due to explosive hazards and low solubility, innovative solutions are being explored. The question remains: will  $H_2$  be a future drug substance, and if so, what form and indications will it have? [5].

Cheng et al. stated that  $H_2$ , the smallest diatomic molecule, has shown preventive and therapeutic effects on various diseases [6]. Its mechanism, especially as a selective radical scavenger, is still unclear. The protective role of  $H_2$  may be due to its ability to regulate mitochondrial homeostasis by activating the Keap1-Nrf2 antioxidant system. Their review focused on  $H_2$ 's mechanism as a mitochondriatargeting nutrient in different disease models, aiming to provide theoretical support for its medical applications [6].

Cejka et al. addressed that oxidative stress, often linked with ocular diseases, is caused by an imbalance between reactive oxygen species (ROS) production and antioxidant defences [7].  $H_2$ , a potent antioxidant, can cross blood-brain and blood-ocular barriers, effectively neutralizing ROS. Its anti-inflammatory, antiapoptotic, cytoprotective, and mitohormetic properties, coupled with its non-toxicity, make it ideal for therapeutic use. Studies show that  $H_2$  treatment can suppress oxidative stress, potentially preventing or improving ocular diseases and slowing the progression of severe degenerative diseases [7].

Zhang et al. investigated that glaucoma, an optic neuropathy, is linked to intraocular pressure and aging [8]. A theory suggested mitochondrial dysfunction plays a role in its mechanism, leading to oxidative stress from excessive reactive oxygen species. Other features included mitochondrial DNA damage, defective quality control, and ATP reduction. Their review explored these mechanisms and potential treatments like medications, gene therapy, and red-light therapy [8].

Perveen et al. concluded that molecular hydrogen or  $H_{2r}$  an odorless and colorless gas, has potential therapeutic effects on a range of diseases, including COVID-19 pneumonia [9]. It can be administered through inhalation, drinking water, or saline injection.  $H_2$  acts as an antioxidant, regulates the immune system, and reduces inflammation and cell death. Despite its promising future in therapeutics, the fundamental process of  $H_2$  is not fully understood. Their review focused on its antioxidative, antiapoptotic, and anti-inflammatory effects [9].

This study has shown that hydrogen gas, an antioxidant, can reduce leakage in choroidal neovascularization, a key feature of age-related macular degeneration. Hydrogen gas can also alleviate oxidative damage and inflammation, offering protective effects on cells. It has shown promise in treating multiple eye diseases, including cataracts and diabetic retinopathy. Despite its potential, further studies are needed to optimize its use. Hydrogen gas has also been found to reduce inflammation, structural changes, and glial cell increase caused by retinal ischemia reperfusion injury. Despite challenges in administration due to explosive hazards and low solubility, innovative solutions are being explored. The protective role of hydrogen may be due to its ability to regulate mitochondrial homeostasis by activating the Keap1-Nrf2 antioxidant system. Studies show that hydrogen

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## **COMPETING INTERESTS**

The author declares no competing interests.

### ADDITIONAL INFORMATION

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