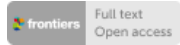


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## Hydrogen (H<sub>2</sub>) Inhibits Isoproterenol-Induced Cardiac Hypertrophy via Antioxidative Pathways

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Affiliations

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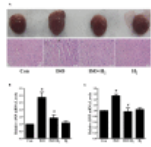
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### Abstract

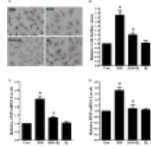
**Background and Purpose:** Hydrogen (H<sub>2</sub>) has been shown to have a strong antioxidant effect on preventing oxidative stress-related diseases. The goal of the present study is to determine the pharmacodynamics of H<sub>2</sub> in a model of isoproterenol (ISO)-induced cardiac hypertrophy. **Methods:** Mice (C57BL/6J; 8–10 weeks of age) were randomly assigned to four groups: Control group ( $n = 10$ ), ISO group ( $n = 12$ ), ISO plus H<sub>2</sub> group ( $n = 12$ ), and H<sub>2</sub> group ( $n = 12$ ). Mice received H<sub>2</sub> (1 ml/100g/day, intraperitoneal injection) for 7 days before ISO (0.5 mg/100g/day, subcutaneous injection) infusion, and then received ISO with or without H<sub>2</sub> for another 7 days. Then, cardiac function was evaluated by echocardiography. Cardiac hypertrophy was reflected by heart weight/body weight, gross morphology of hearts, and heart sections stained with hematoxylin and eosin, and relative atrial natriuretic peptide (ANP) and B-type natriuretic peptide (BNP) mRNA levels. Cardiac reactive oxygen species (ROS), 3-nitrotyrosine and p67 (phox) levels were analyzed by dihydroethidium staining, immunohistochemistry and Western blotting, respectively. For *in vitro* study, H9c2 cardiomyocytes were pretreated with H<sub>2</sub>-rich medium for 30 min, and then treated with ISO (10 μM) for the indicated time. The medium and ISO were re-changed every 24 h. Cardiomyocyte surface areas, relative ANP and BNP mRNA levels, the expression of 3-nitrotyrosine, and the dissipation of mitochondrial membrane potential (MMP) were examined. Moreover, the expression of extracellular signal-regulated kinase1/2 (ERK1/2), p-ERK1/2, p38, p-p38, c-Jun NH2-terminal kinase (JNK), and p-JNK were measured by Western blotting both *in vivo* and *in vitro*. **Results:** Intraperitoneal injection of H<sub>2</sub> prevented cardiac hypertrophy and improved cardiac function in ISO-infused mice. H<sub>2</sub>-rich medium blocked ISO-mediated cardiomyocytes hypertrophy *in vitro*. H<sub>2</sub> blocked the excessive expression of NADPH oxidase and the accumulation of ROS, attenuated the decrease of MMP, and inhibited ROS-sensitive ERK1/2, p38, and JNK signaling pathways. **Conclusion:** H<sub>2</sub> inhibits ISO-induced cardiac/cardiomyocytes hypertrophy both *in vivo* and *in vitro*, and improves the impaired left ventricular function. H<sub>2</sub> exerts its protective effects partially through blocking ROS-sensitive ERK1/2, p38, and JNK signaling pathways.

**Keywords:** MAPK; NADPH oxidase; cardiac hypertrophy; hydrogen; mitochondrial damage; reactive oxygen species; β-adrenoceptor.

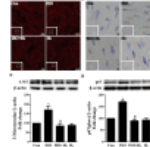
### Figures



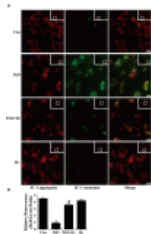
**FIGURE 1** Effects of hydrogen (H<sub>2</sub>...



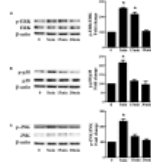
**FIGURE 2** Effects of H<sub>2</sub> - rich...



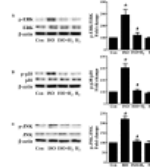
**FIGURE 3** Effects of H<sub>2</sub> on...



**FIGURE 4** Effects of H<sub>2</sub> - rich...



**FIGURE 5** The time-dependent effects of ISO...



**FIGURE 6** Effects of H<sub>2</sub> - rich...

All figures (7)

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