

Hydrogen acts as a therapeutic antioxidant by selectively reducing cytotoxic oxygen radicals

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Abstract

Acute oxidative stress induced by ischemia-reperfusion or inflammation causes serious damage to tissues, and persistent oxidative stress is accepted as one of the causes of many common diseases including cancer. We show here that hydrogen (H_2) has potential as an antioxidant in preventive and therapeutic applications. We induced acute oxidative stress in cultured cells by three independent methods. H_2 selectively reduced the hydroxyl radical, the most cytotoxic of reactive oxygen species (ROS), and effectively protected cells; however, H_2 did not react with other ROS, which possess physiological roles. We used an acute rat model in which oxidative stress damage was induced in the brain by focal ischemia and reperfusion. The inhalation of H_2 gas markedly suppressed brain injury by buffering the effects of oxidative stress. Thus H_2 can be used as an effective antioxidant therapy; owing to its ability to rapidly diffuse across membranes, it can reach and react with cytotoxic ROS and thus protect against oxidative damage.

Figure 1: Molecular hydrogen dissolved in medium selectively reduces hydroxyl radicals in cultured cells.

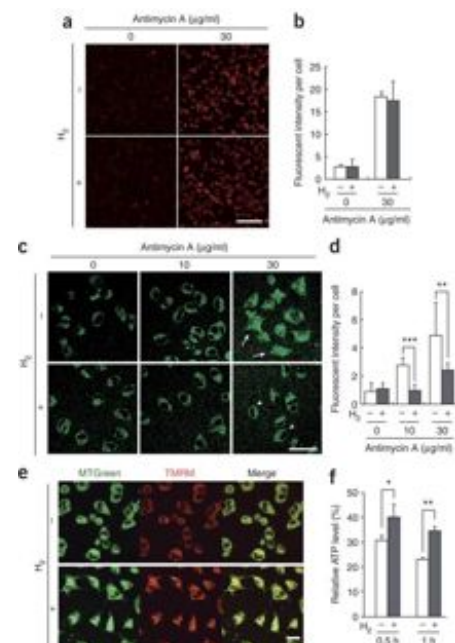


Figure 2: Molecular hydrogen protects cultured PC12 cells by scavenging hydroxyl radicals.

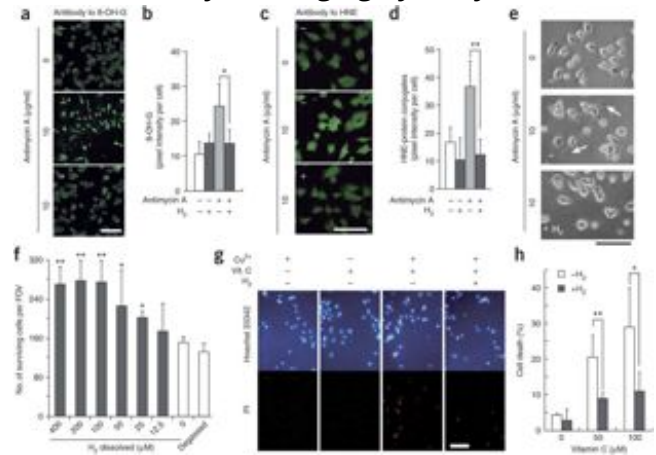


Figure 3: Spin-trapping identifies the free radical species that H₂ reduces.

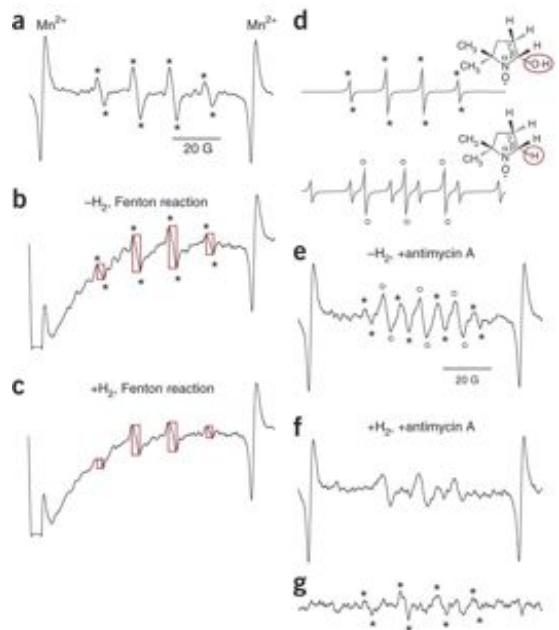


Figure 4: Molecular hydrogen dissolved in solution scavenges hydroxyl radicals at 23 °C and pH 7.4 in cell-free systems.

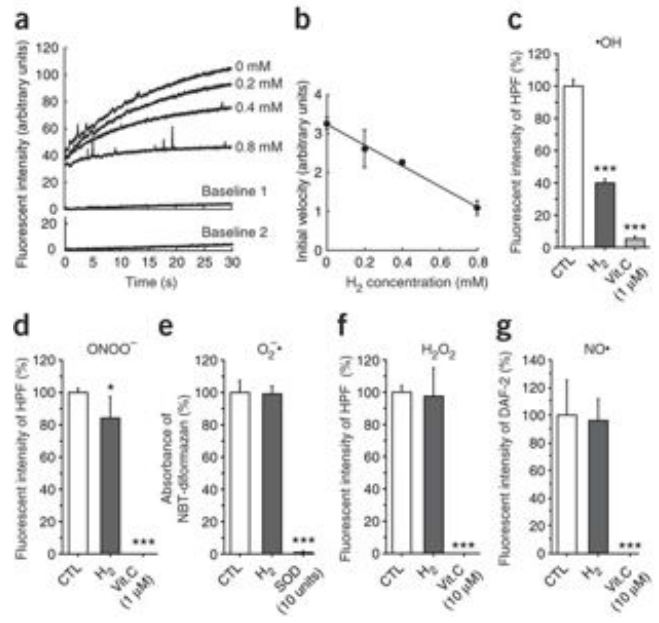


Figure 5: Inhalation of hydrogen gas protects against ischemia-reperfusion injury.

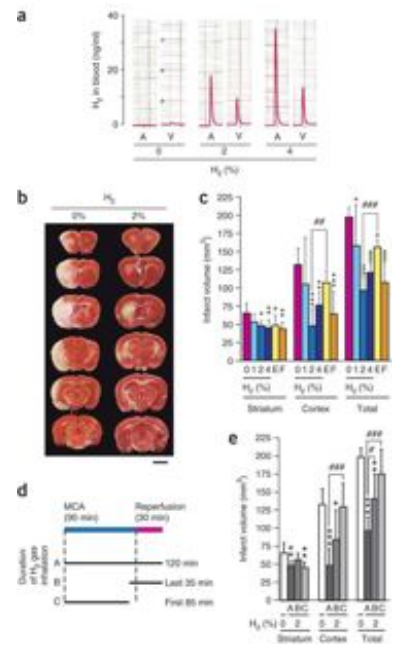
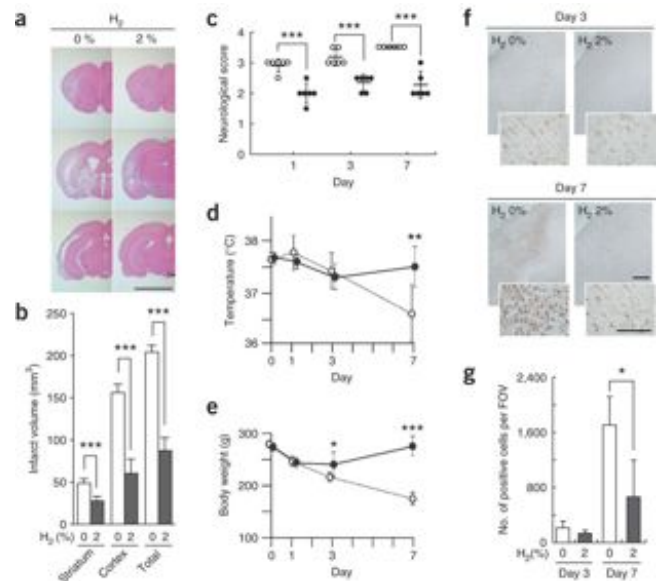


Figure 6: Inhalation of H₂ gas improved brain injury after 1 week.



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Contributions

S.O. conceived the experiments. S.O., I.O., K.K. and Y.K. designed the experiments. I.O., S.A. and S.O. performed data analysis. I.O., M.I., K.T., M.W., K.N, K.Y., S.A. and S.O. performed the experiments. S.O. and I.O. wrote the paper.

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Ethics declarations

Competing interests

The authors declare no competing financial interests.

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