Mol Cell Biochem. 2015 May;403(1-2):231-41. doi: 10.1007/s11010-015-2353-y. Epub 2015 Feb 24.

Simultaneous oral and inhalational intake of molecular hydrogen additively suppresses signaling pathways in rodents

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PMID: 25707580 DOI: 10.1007/s11010-015-2353-y

Abstract

Molecular hydrogen (H2) is an agent with potential applications in oxidative stress-related and/or inflammatory disorders. H2 is usually administered by inhaling H2-containing air (HCA) or by oral intake of H2-rich water (HRW). Despite mounting evidence, the molecular mechanism underlying the therapeutic effects and the optimal method of H2 administration remain unclear. Here, we investigated whether H2 affects signaling pathways and gene expression in a dosage- or dose regimen-dependent manner. We first examined the H2 concentrations in blood and organs after its administration and found that oral intake of HRW rapidly but transiently increased H2 concentrations in the liver and atrial blood, while H2 concentrations in arterial blood and the kidney were one-tenth of those in the liver and atrial blood. In contrast, inhalation of HCA increased H2 equally in both atrial and arterial blood. We next examined whether H2 alters gene expression in normal mouse livers using DNA microarray analysis after administration of HCA and HRW. Ingenuity Pathway Analysis revealed that H2 suppressed the expression of nuclear factor-kappa B (NF-κB)-regulated genes. Western blot analysis showed that H2 attenuated ERK, p38 MAPK, and NF-κB signaling in mouse livers. Finally, we evaluated whether the changes in gene expression were influenced by the route of H2 administration and found that the combination of both HRW and HCA had the most potent effects on signaling pathways and gene expression in systemic organs, suggesting that H2 may act not only through a dose-dependent mechanism but also through a complex molecular network.

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