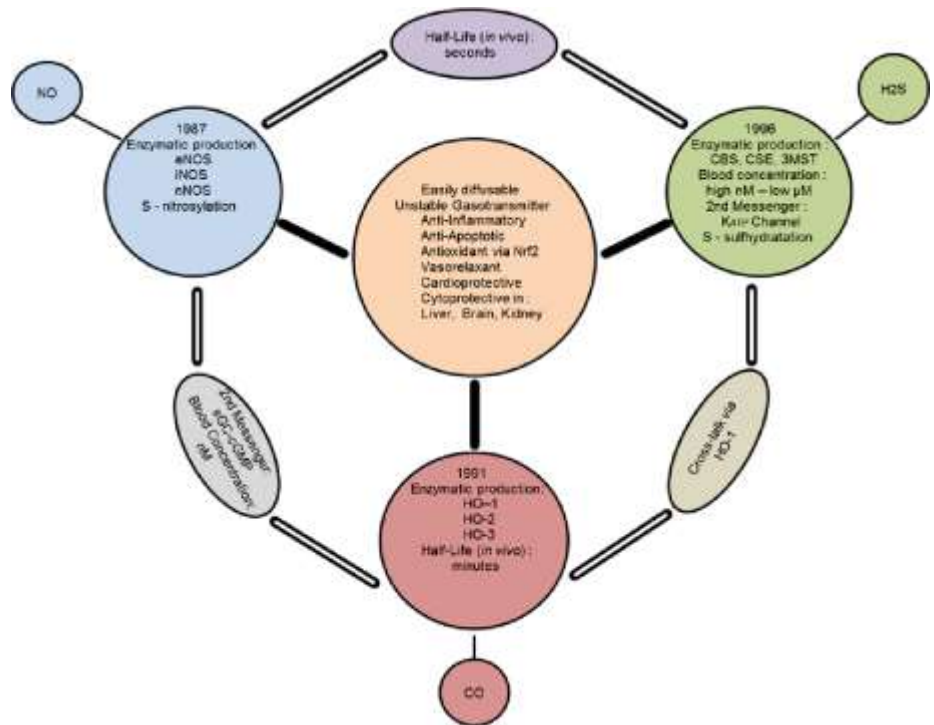


# H<sub>2</sub> as a gaseous signal modulator

**Gaseous signaling molecules** are gaseous molecules that are either synthesized internally (endogenously) in the organism, tissue or cell or are received by the organism, tissue or cell from outside (say, from the atmosphere or hydrosphere, as in the case of oxygen) and that are used to transmit chemical signals which induce certain physiological or biochemical changes in the organism, tissue or cell.



Oxidative stress impacts multiple signaling pathways, including the extracellular signal-regulated protein kinase (ERK)1/2, NF- $\kappa$ B, JNK, and nuclear factor-erythroid 2p45-related factor 2 (Nrf2) pathways. Along with selectively scavenging  $\cdot$ OH, H<sub>2</sub> may alleviate oxidative stress-induced injury by targeting these pathways. Studies has confirmed that H<sub>2</sub> could exert anti-inflammatory effects by regulating Toll-like receptor 4 (TLR4) signaling, and anti-apoptotic effects through Ras-ERK1/2-MEK1/2 and Akt pathway inactivation. H<sub>2</sub> may also protect against allergic reactions by directly modulating Fc $\epsilon$ RI-related signaling, rather than through radical-scavenging activity.

Since H<sub>2</sub> may influence multiple signaling pathways to exert broad effects, crosstalk between these pathways likely influences H<sub>2</sub> therapeutic outcomes. The effects of H<sub>2</sub> as a gaseous signal modulator in a therapeutic setting may involve a network of signaling molecules.

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