World Academy of Science, Engineering and Technology
International Journal of Pharmacological and Pharmaceutical Sciences
Vol:8, No:12, 2014

# Antiulcer Potential of Heme Oxygenase-1 Inducers

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**Abstract :** Heme oxygenase-1 (HO-1), also known as heat shock protein 32 (HSP32), has been shown to be implicated in cytoprotection in various organs. Its activation plays a significant role in acute and chronic inflammation, protecting cells from oxidative injury and apoptosis. This inducible isoform of HO catalyzes the first and rate-limiting step in heme degradation to produce equimolar quantities of biologically active products: carbon monoxide (CO), free iron and biliverdin. CO has been reported to possess anti-apoptotic properties. Moreover, it inhibits the production of proinflammatory cytokines and stimulates the synthesis of the anti-inflammatory interleukin-10 (IL-10), as well as promotes vasodilatation at sites of inflammation. The second product of catalytic HO-1 activity, free cytotoxic iron, is promptly sequestered into the iron storage protein ferritin, which lowers the pro-oxidant state of the cell. The third product, biliverdin, is subsequently converted by biliverdin reductase into the bile pigment bilirubin, the most potent endogenous antioxidant among the constituents of human serum, which modulates immune effector functions and suppresses inflammatory response. Furthermore, being one of the so-called stress proteins, HO-1 adaptively responds to different stressors, such as reactive oxygen species (ROS), inflammatory cytokines and heavy metals and thus protects cells against such conditions as ischemia, hemorrhagic shock, heat shock or hypoxia. It is suggested that pharmacologic modulation of HO-1 may represent an effective strategy for prevention of stress and drug-induced gastrointestinal toxicity. HO-1 is constitutively expressed in normal gastric, intestinal and colonic mucosa and up-regulated during inflammation. It has been proven that HO-1 up-regulated by hemin, heme and cobalt-protoporphyrin ameliorates experimental colitis. In addition, the up-regulation of HO-1 partially explains the mechanism of action of 5-aminosalicylic acid (5-ASA), which is used clinically as an anti-colitis agent. In 2009 Ueda et al. has reported for the first time that mucosal protection by Polaprezinc, a chelate compound of zinc and L-carnosine used as an anti-ulcer drug in Japan, is also attributed to induction of HO-1 in the stomach. Since then, inducers of HO-1 are desired subject of research, as they may constitute therapeutically effective anti-ulcer drugs.

**Keywords :** heme oxygenase-1, gastric lesions, gastroprotection, Polaprezinc
**Conference Title :** ICPP 2014 : International Conference on Pharmacy and Pharmacology
**Conference Location :** Bangkok, Thailand
**Conference Dates :** December 18-19, 2014