Extract of Salvia miltiorrhiza (Danshen) induces Nrf2-mediated heme oxygenase-1 expression as a cytoprotective action in RAW 264.7 macrophages.


Source

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Abstract

ETHNOPHARMACOLOGICAL RELEVANCE:

Danshen (Salvia miltiorrhiza) is widely used in traditional herbal medicines for relief of a variety of symptoms related to complications arising from vascular diseases such as hypertension, diabetes, and atherosclerosis. Induction of heme oxygenase-1 (HO-1) expression protects against oxidative stress-induced cell damage, which plays an important role in cytoprotection in a variety of pathological models.

MATERIALS AND METHODS:

In the present study, we investigated the effect of Danshen on the up-regulation of HO-1, an inducible and cytoprotective enzyme in RAW 264.7 macrophages. Molecular mechanisms underlying the effects, especially protective effects, was elucidated by analyzing the activation of transcription factors and their upstream signalling, and by evaluating the inhibitory effect of HO-1 on ROS production.

RESULTS:

Danshen induced HO-1 mRNA expression and protein production, and nuclear translocation of NF-E2-related factor 2 in RAW 264.7 macrophages. Pharmacological inhibitors of PI3K/Akt and MEK1 attenuated HO-1 induction in Danshen-stimulated RAW 264.7 macrophages. Furthermore, Danshen pretreatment reduced intracellular production of reactive oxygen species after stimulation with hydrogen peroxide; this effect was reversed by the HO-1 inhibitor ZnPP.

CONCLUSION:

Danshen induced HO-1 expression through PI3K/Akt-MEK1-Nrf2 pathway and reduced intracellular production of reactive oxygen species via induction of HO-1 expression. The results support a role of HO-1 in the cytoprotective effect of Danshen.

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