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Investigation of the role of OXR1-P21-Nrf2 signaling pathway on oxidative stress in monocrotaline-induced pulmonary hypertension model in rat: the protective role of Crocin

Maryam Radan, Mahin Dianat and Vahid Bayati
Ahvaz Jundishapur University of Medical Sciences, Iran

Abstract

Pulmonary arterial hypertension (PAH) is a severe and multifactorial syndrome that restricts flow through pulmonary arterial circulation The pathogenesis of pulmonary arterial hypertension involves reactive oxygen species and inflammation. The eukaryotic oxidation resistance gene1 (OXR1) is involved in protection against oxidative stress. The cyclin-dependent kinase inhibitor 1A (P21) and nuclear factor (erythroid-derived 2)-like 2 (Nrf2) play important roles in controlling ROS levels by regulating antioxidant enzymes. It is documented that degraded or diminished Nrf2 activity contributes to oxidative stress which, in turn, leads to many pathological conditions. P21 can stabilize and activate Nrf2 and consequently, activated Nrf2 upregulates several antioxidant enzymes. mechanism underlying the possible prevention of oxidative damage by OXR1 pathway is not clear in pulmonary system disorders. The present experiment focused on the role of OXR1-P21-Nrf2 signaling pathway in pulmonary hypertension model with emphasis on the oxidative stress. The rats were divided into groups, receiving: Saline; MCT; Crocin (7.5, 15 and 30 mg/kg); MCT+Crocin. Twenty-one days after substance administration, we evaluated the pulmonary hemodynamic (PAP), arterial blood gas analysis, bronchoalveolar lavage fluid, total protein in BALF, cytokines production, pulmonary edema and cardiac hypertrophy, lung histopathology, antioxidant enzymes activity and gene expression of OXR1, P21 and Nrf2 using the RT-PCR. The Nrf2 localization also evaluated immunohistochemically. The obtained results showed that the pulmonary hypertension caused to changes in oxidative stress profile which is associated with decreases of OXR1-P21-Nrf2 gene expression. Co-treatment with crocin preserved pulmonary hemodynamic parameters by improving antioxidant statues. the signaling pathway identification in pulmonary hypertension and the protective effect of Crocin as an antioxidant agent can be used in future basic and clinical supplemental studies.

Ahvaz Jundishapur University of Medical Sciences

Biography: Maryam Radan has completed her PhD at the age of 30 from Jundishapur University of Medical Sciences, Ahvaz, Iran. She is the faculty member (Assistant Professor) of Physiology Department-Jundishapur University of Medical Sciences,Ahvaz, Iran. She is an integrative cardiopulmonary physiologist focusing on understanding the integrated mechanisms underlying the pulmonary, hypertension and heart failure utilizing animal models. Her expertise includes pulmonary circulation, isolated perfused heart and echocardiography to understand in vivo function at cell-to-organ levels. she combine these approaches with cell culture and immunohistochemistry.

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