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Switching off Hsp70 abrogates crocin mediated cardioprotective effect in experimental model of acute myocardial infarction
S. Bharti; N. Rani; D.S. Arya
All India Institute of Medical Sciences, New Delhi, India

Purpose: We established previously that Crocus sativus and its carotenoid crocin protects the myocardium via augmenting the endogenous antioxidant defense system. Since, heat shock protein70 (Hsp70) actively participates in shielding the cell from oxidative stress, programmed or necrotic cell deaths; we hypothesized that Hsp70 might be the actual mediator behind the cardioprotective effects of crocin.

Methods: To document this interplay between crocin and Hsp70, we administered crocin (20mg/kg/day, p.o.) and Hsp70 inhibitor, KNK437 (25mg/kg/day, i.p.) for 14 days followed by left anterior descending coronary artery ligation for 45 minutes and reperfusion for 60 minutes on the 15th day.

Results: Intriguingly, crocin pretreatment significantly ameliorated (P < 0.05) hemodynamic status, myocardial architecture and decreased infarct size in ischemia-reperfusion challenged myocardium. This improvement in functional and morphological changes were corroborated with suppression of inflammatory (IKK-beta/NF-kappaB and TNF-alpha), apoptotic (TUNEL positivity and Bax expression) and cardiac injury markers (CK-MB, LDH and BNP), along with upregulation of Hsp70 protein expression. In addition, crocin bolstered the antioxidant defense system as manifested by augmented activities of GSH, GSHPx and overexpression of MnSOD protein expression levels. Surprisingly, co-treatment with KNK437 abrogated the crocin-induced cardioprotection with significant amplification in infarct size, inflammation, apoptosis and oxidative stress markers. Conclusion: For the first time, present study unravels that crocin attenuates ischemia-reperfusion injury through augmenting Hsp70 expression and could be developed as a nutriment for alleviating acute myocardial infarction.