Inhibitory effects of quercetin derivatives on phosphodiesterase isozymes and high-affinity [3H]-rolipram binding in guinea pig tissues

柯文昌

Chan ALF;Huang HL;Chien HC;Chen CM;Lin CN;Ko WC

摘要

Abstract

Background. L-arginine transport mediated by type-2 cationic amino acid transporter (CAT-2) isozymes is one crucial mechanism that regulates nitric oxide (NO) production via inducible nitric oxide synthase (iNOS). We sought to investigate the effects of heme oxygenase-1 (HO-1) overexpression on CAT-2 isozymes, e.g., CAT-2, CAT-2A, and CAT-2B. Materials and Methods. Adult male Sprague Dawley rats were allocated to receive lipopolysaccharide (LPS), normal saline, hemin (a HO-1 inducer), tin protoporphyrin (SnPP, a HO-1 inhibitor), LPS plus hemin, or LPS plus hemin plus SnPP. After maintaining for 6 h, rats were sacrificed and the expression and activity of individual enzyme was evaluated. Results. LPS increased HO activity, HO-1 concentration, NO production, L-arginine transport, and concentrations of iNOS, CAT-2, and CAT-2B in rat lungs and kidney. LPS also increased HO activity, HO-1 concentration, NO production, L-arginine transport, and iNOS concentration but decreased CAT-2 and CAT-2B concentrations in rat liver. LPS increased CAT-2A concentration in rat liver but did not affect CAT- 2A concentration in rat lungs and kidney. Hemin further increased HO activity and induced HO-1 overexpression in the lungs, kidney, and liver from LPStreated rats. In addition, the effects of LPS on NO production, L-arginine transport, and concentrations of iNOS and CAT-2 isozymes were significantly attenuated by hemin. SnPP, on the other hand, reversed the effects of hemin. Conclusions. HO-1 overexpression significantly attenuates endotoxin-induced increases in NO production production and L-arginine transport. Induction of HO-1 overexpression also significantly attenuates the effects of endotoxin on the expression of iNOS and CAT-2 isozymes in septic rats.