
Abstract
Berberine hydrochloride (BBR), a plant alkaloid, has been used to treat intestinal inflammation or infection for years. Cyclooxygenase-2 (COX-2) is pro-inflammatory mediator and involved in the induction of gut inflammation. The expression of COX-2 in small bowel mucosa was determined and the mechanism by which BBR modulated COX-2 expression was explored in a rat model of endotoxemia induced by lipopolysaccharide (LPS). The results showed that without LPS stimulation COX-2 was constitutively expressed at low levels in control rats. LPS challenge rapidly induced COX-2 gene transcription resulting in high levels of inducible COX-2 expression in endotoxemic rats. BBR pre- and post-treatment had no marked effect on constitutive COX-2 expression but inhibited inducible COX-2 overexpression. LPS challenge increased the expression and phosphorylation of peroxisome proliferator-activated receptor gamma (PPARγ), p38 and activating transcription factor 2 and 3 (ATF2, ATF3), but the effects of LPS were inhibited by BBR treatment. GW9662 did not influence constitutive COX-2 expression but enhanced inducible COX-2 overproduction. Besides, GW9662 abolished the inhibitory effect of BBR on inducible COX-2, p38, ATF2, 3 expression and phosphorylation. Collectively, these results indicated that BBR gavage could attenuate the overexpression of inducible COX-2, not constitutive COX-2, in ileal mucosa during acute endotoxemia in part via activation of PPARγ pathway, which negatively interfered with p38/ATFs cascade.