Effect of Active Hexose Correlated Compound on the Production of Nitric Oxide in Hepatocytes

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Abstract

Background: Active hexose correlated compound (AHCC) is a” complex compound” containing polysaccharides. AHCC has been reported to improve the prognosis of postoperative hepatocellular carcinoma patients. However, the molecular mechanism of this improvement is not fully understood. In the diseased liver, nitric oxide (NO) generated by inducible nitric oxide synthase (iNOS) is considered to be a causal factor for various hepatopathies. In this study, the possibility of AHCC regulation of NO production by iNOS was pursued as a potential liver-protecting mechanism.

Methods: Primary cultured rat hepatocytes were treated with interleukin-1β (IL-1β) in the presence or absence of AHCC. NO production, iNOS induction, and iNOS signal were analyzed.

Results: IL-1β stimulated iNOS induction through the activation of nuclear factorκB (NFκB), leading to NO production. The addition of AHCC inhibited NO production, showing >80% inhibition at 8 mg/mL. AHCC also decreased the levels of iNOS protein and mRNA. However, AHCC influenced neither the degradation of inhibitory protein κB (IκB) nor the activation of NFκB stimulated by IL-1β. Transfection experiments with an iNOS promoter-luciferase construct (iNOS-Luc) revealed that AHCC had no effect on the transactivation activity of the iNOS promoter. By contrast, AHCC inhibited the activity of iNOS-Luc containing a 3'untranslated region (UTR) with adenosine and uridine (AU)–rich elements, which shows the stabilizing activity of iNOS mRNA. Conclusions: Results indicated that AHCC inhibits the induction of iNOS at the level of transcription, causing a decrease in NO production in hepatocytes. AHCC seems to decrease the levels of iNOS mRNA by reducing mRNA stabilization rather than inhibiting its synthesis.

It is possible that the inhibitory effect of active hexose correlated compound (AHCC) on the production of nitric oxide through the inhibition of inducible nitric oxide synthase induction is associated with AHCC-induced protection against liver failure.
Active Hexose Correlated Compound Inhibits the Expression of Proinflammatory Biomarker iNOS in Hepatocytes

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Abstract

Background/Aims: Excess production of nitric oxide (NO) by inducible nitric oxide synthase (iNOS) has been implicated as proinflammatory biomarker in liver injury. The application of active hexose correlated compound (AHCC) as a functional food in complementary and alternative medicine has increased. The possibility that AHCC might inhibit iNOS induction was investigated as a potential liver-protective effect.

Methods: Hepatocytes were isolated from rats by collagenase perfusion and cultured. Primary cultured hepatocytes were treated with interleukin-1β in the presence or absence of AHCC-sugar fraction (AHCC-SF).

Results and Conclusion: AHCC-SF inhibited the production of NO and reduced expressions of iNOS mRNA and its protein. AHCC-SF had no effects on either IκB degradation or nuclear factor-κB (NF-κB) activation. In contrast, AHCC-SF inhibited the upregulation of type I interleukin-1 receptor (IL-1RI) through the inhibition of Akt phosphorylation. Transfection experiments with iNOS promoter-luciferase constructs revealed that AHCC-SF reduced the levels of iNOS mRNA at both promoter transactivation and mRNA stabilization steps. AHCC-SF inhibited the expression of iNOS gene antisense transcript, which is involved in iNOS mRNA stabilization. These findings demonstrate that AHCC-SF suppresses iNOS gene expression through a IκB/NF-κB-independent but Akt/IL-1RI-dependent pathway, resulting in the reduction of NO production. AHCC-SF may have therapeutic potential for various liver injuries.

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