Effect of Active Hexose Correlated Compound (AHCC) and Tabebuia Ipe (IPE) on the Production of Nitric Oxide in Hepatocytes

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[Objective] Active hexose correlated compound (AHCC), which is extracted from mushroom (*Basidiomycetes*), is “complex compound” containing a variety of polysaccharides and other components, in which α-1,4 glucan with acetylation is the major component. The application of AHCC has been rapidly increased for complementary and alternative medicine. Particularly in clinical studies, AHCC has been reported to improve the prognosis of postoperative hepatocellular carcinoma patients. However, the molecular mechanism of AHCC is not fully understood.

IPE (Tabebuia Ipe), which is extracted from plant resin in Brazil, is folk remedy medicine. Recently, IPE is interested in antibiotic and anticancer effects. However, it has not been reported about the effect of IPE to liver dysfunction.

On disease state of liver, nitric oxide (NO) generated by inducible nitric oxide synthase (iNOS) is considered one of causal factors for various hepatopathy. In this study, the possibility of AHCC-regulation and IPE for NO production by iNOS was pursued as one of liver protecting mechanisms.

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

[Results] IL-1β stimulated the IκB/NF-κB pathway, resulting in the activation of NF-κB (nuclear translocation and DNA binding), which was followed by the induction of iNOS and NO production. The addition of IL-1β and AHCC (1-10 mg/ml) and/or IPE (0.5-2 mg/ml) markedly inhibited NO production, with a maximal effect at AHCC 8 mg/ml (80% inhibition) and IPE 2 mg/ml (90% inhibition). AHCC and IPE also decreased the levels of iNOS protein and mRNA. Transfection experiments revealed that IPE decreased the transactivation activity of the iNOS promoter, but AHCC had no effect on the transactivation activity of promoter. In contrast, AHCC and IPE inhibited the activity of iNOS-Luc containing 3’UTR with AU-rich elements (six of ARE), which shows the stabilizing activity of iNOS mRNA. An electrophoretic mobility shift assay demonstrated that IPE inhibited the activation of NF-κB, but AHCC had no effect on the activation of NF-κB. Furthermore, IPE decreased the mRNA levels of the NF-κB subunit p65 and prevent nuclear translocation of p65.

[Conclusions] These findings suggest that AHCC inhibits the induction of iNOS at transcriptional step, which is followed by the decrease of NO production in hepatocytes, and that IPE inhibits iNOS induction at the step of NF-κB activation. Such studies may provide the foundation for novel pharmacological approaches to reduce hepatic inflammation and injury.