

International Conference and Exhibition on

Marine Drugs and Natural Products

July 25-27, 2016 Melbourne, Australia

Kukoamine B ameliorates rodent polymicrobial sepsis via simultaneous blockade of primary PAMPs and induced inflammatory disorders

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Kukoamine B (KB) is an alkaloid compound isolated from the traditional Chinese herb Cortex Lycii. KB has been identified as a novel dual antagonist for LPS and CpG DNA; two major pathogens associated molecular patterns (PAMPs) for triggering sepsis. However, its inhibitory effects against LPS and CpG DNA *in vivo* and the potential therapeutic implications in treating sepsis need to be well elucidated. In this study, the impact of KB on survivals of different rodent sepsis models was analyzed. Organ distribution and clearance of LPS and CpG DNA in the presence of KB were detected. The antagonistic effects of KB against LPS and CpG DNA, including inflammatory associated cytokines production, coagulation parameters, major organ functions were evaluated in rats CLP model. We found that KB could bind bacterial LPS from different bacterial origins and inhibit the induced release of pro inflammatory cytokines. KB attenuates the activity of LPS and CpG DNA *in vivo*, accelerates their circulatory clearance and increases liver uptake. KB effectively improves the survival of different murine sepsis models. KB also ameliorates the production of pro and anti-inflammatory cytokines and serum biomarkers of sepsis in CLP rats, KB efficacy in reversing their acidosis state, suppressing DIC and organ dysfunctions and limiting acute lung injuries secondary to sepsis. Overall, KB is effective in simultaneously blockade of LPS and CpG DNA *in vivo* and improves the outcomes in rodent sepsis models. KB may become a promising candidate drug for the treatment of sepsis.

Biography

Xin Liu has received his PhD in Southwest Hospital, Third Military Medical University, China in 2010. He currently serves as an Associate Professor in the same institute. His research interest lies mainly on investigating therapeutic intervention of sepsis by means of natural products. He has co-operated with his fellow researchers to screen more than 140 traditional Chinese herbs and identify a couple of novel anti-sepsis compounds.

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