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Pharmacokinetics and pharmacodynamics of thymoquinone as a novel agent in sepsis management

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Sepsis or septic shock is a multiple organ failure syndrome and is one of the main causes of death in intensive care units. The induction of inflammation during sepsis is a complex biological cascade, which requires exhaustive therapeutic intervention. A series of experiments were designed to evaluate the effect of thymoquinone (TQ) treatment on a septic model and to elucidate the possible mechanism in the process. TQ significantly improved renal and hepatic functions alone and in combination with a nitric oxide inhibitor (L-NAME). TNF- α , IL-1 α , IL-2 and IL-10 levels were significantly decreased with TQ and L-NAME treatments as compared with untreated animals. Vascular activity of isolated aorta of septic mice pretreated with TQ and/or L-NAME demonstrated an endothelial dependent contractile tone in contrast to relaxation in normal controls. Pharmacokinetic studies showed that THQ represents a compound with rapid elimination and relatively slower absorption after oral administration. Plasma concentration-time curves demonstrated a rapid poly exponential decline following intravenous dosing. These findings suggest that TQ has a strong potential for combating the sequel of the multiple organ failure syndrome of sepsis where modulations in inflammatory cytokines, nitric oxide production and vascular reactivity appear to be important mechanisms through which TQ exhibits its effect.

Biography

Khalid M Alkharfy, PharmD, PhD is Professor at the College of Pharmacy, King Saud University, Riyadh, Saudi Arabia. He is the Director of Pharmacokinetic/ Pharmacodynamic Research Laboratory, and a member of the Biomarkers Research Program at the university. Professor Alkharfy received a Bachelor of Pharmaceutical Sciences from King Saud University, a Doctorate of Pharmacy from University of Tennessee School of Pharmacy, and a Doctorate of Philosophy in Clinical Pharmaceutical Sciences from the University of Pittsburgh. Other current focus is drug discovery and development. The research in his laboratory utilizes contemporary methods of drug analysis coupled with molecular techniques in the pursuit of generating new information about the pathogenesis and treatment of diseases using both animal models and clinical patient samples.

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