

Anti-malarial and anti-inflammatory effects of *Gleichenia truncata* mediated through inhibition of GSK3 β

Abstract

Gleichenia truncata is a highland fern from the Gleicheniaceae family known for its traditional use among indigenous communities in Asia to treat fever. The scientific basis of its effect has yet to be documented. A yeast-based kinase assay conducted in our laboratory revealed that crude methanolic extract (CME) of *G. truncata* exhibited glycogen synthase kinase-3 (GSK3)-inhibitory activity. GSK3 β is now recognized to have a pivotal role in the regulation of inflammatory response during bacterial infections. We have also previously shown that lithium chloride (LiCl), a GSK3 inhibitor suppressed development of *Plasmodium berghei* in a murine model of malarial infection. The present study is aimed at evaluating *G. truncata* for its anti-malarial and anti-inflammatory effects using in vivo malarial and melioidosis infection models respectively. In a four-day suppressive test, intraperitoneal injections of up to 250 mg/kg body weight (bw) *G. truncata* CME into *P.berghei*-infected mice suppressed parasitaemia development by >60%. Intraperitoneal administration of 150 mg/kg bw *G. truncata* CME into *Burkholderia pseudomallei*-infected mice improved survivability by 44%. *G. truncata* CME lowered levels of pro-inflammatory cytokines (TNF- α , IFN- γ) in serum and organs of *B. pseudomallei*-infected mice. In both infections, increased phosphorylations (Ser9) of GSK3 β were detected in organ samples of animals administered with *G. truncata* CME compared to controls. Taken together, results from this study strongly suggest that the anti-malarial and anti-inflammatory effects elicited by *G. truncata* in part were mediated through inhibition of GSK3 β . The findings provide scientific basis for the ethnomedicinal use of this fern to treat inflammation-associated symptoms.