Anti-malarial and anti-inflammatory effects of Gleichenia truncata mediated through inhibition of GSK3β

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. GSK3β 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 GSK3β 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 GSK3β. The findings provide scientific basis for the ethnomedicinal use of this fern to treat inflammation-associated symptoms.