

## Malaysian Tualang honey inhibits hydrogen peroxide-induced endothelial hyperpermeability

### ABSTRACT

Malaysian Tualang honey (TH) is a known therapeutic honey extracted from the honeycombs of the Tualang tree (*Koompassia excelsa*) and has been reported for its antioxidant, anti-inflammatory, antiproliferative, and wound healing properties. However, the possible vascular protective effect of TH against oxidative stress remains unclear. In this study, the effects of TH on hydrogen peroxide- ( $\text{H}_2\text{O}_2$ -) elicited vascular hyperpermeability in human umbilical vein endothelial cells (HUVECs) and Balb/c mice were evaluated. Our data showed that TH concentrations ranging from 0.01% to 1.00% showed no cytotoxic effect to HUVECs. Induction with 0.5 mM  $\text{H}_2\text{O}_2$  was found to increase HUVEC permeability, but the effect was significantly reversed attenuated by TH ( $p < 0.05$ ), of which the permeability with the highest inhibition peaked at 0.1%. In Balb/c mice, TH (0.5 g/kg-1.5 g/kg) significantly ( $p < 0.05$ ) reduced  $\text{H}_2\text{O}_2$  (0.3%)-induced albumin-bound Evans blue leak, in a dose-dependent manner. Immunofluorescence staining confirmed that TH reduced actin stress fiber formation while increasing cortical actin formation and colocalization of caveolin-1 and  $\beta$ -catenin in HUVECs. Signaling studies showed that HUVECs pretreated with TH significantly ( $p < 0.05$ ) decreased intracellular calcium release, while sustaining the level of cAMP when challenged with  $\text{H}_2\text{O}_2$ . These results suggested that TH could inhibit  $\text{H}_2\text{O}_2$ -induced vascular hyperpermeability in vitro and in vivo by suppression of adherence junction protein redistribution via calcium and cAMP, which could have a therapeutic potential for diseases related to the increase of both oxidant and vascular permeability.