Bixa orellana leaf extract suppress histamine-induced endothelial hyperpermeability via the PLC-NO-cGMP signaling cascade

ABSTRACT

Background: Histamine is established as a potent inflammatory mediator and it is known to increased endothelial permeability by promoting gap formation between endothelial cells. Previous studies have shown that aqueous extract of Bixa orellana leaves (AEBO) exhibits antihistamine activity in vivo, yet the mechanism of its action on endothelial barrier function remains unclear. Therefore, the current study aimed to determine the protective effect of AEBO against histamine-induced hyperpermeability in vitro. **Methods:** The endothelial protective effect of AEBO was assess using an in vitro vascular permeability assay kit. Human umbilical vein endothelial cells (HUVEC) were used in the current study. HUVEC were pre-treated with AEBO for 12 h before histamine induction. Vascular permeability was evaluated by the amount of FITC-dextran leakage into the lower chamber. In order to elucidate the mechanism of action of AEBO, phospholipase C (PLC) activity, intracellular calcium level, nitric oxide (NO) concentration, cyclic guanosine monophosphate (cGMP) production and protein kinase C (PKC) activity were determined following histamine challenge. **Results:** Histamine-induced increased HUVEC permeability was significantly attenuated by pretreatment with AEBO in a time- and concentration-dependent manner. Upregulation of PLC activity caused by histamine in HUVEC was suppressed by pretreatment with AEBO. Pretreatment with AEBO also blocked the production of intracellular calcium induced by histamine in HUVEC. In addition, AEBO suppressed the NO-cGMP signaling cascade when HUVEC were challenged with histamine. Moreover, PKC activity was significantly abolished by pretreatment with AEBO in HUVEC under histamine condition. **Conclusion:** In conclusion, the present data suggest that AEBO could suppress histamine-induced increased endothelial permeability and the activity may be closely related with the inhibition of the PLC-NO-cGMP signaling pathway and PKC activity.

Keyword: Bixa orellana; Histamine; Endothelial permeability