Discovery of endothelial barrier protection by natural product

ABSTRACT

Vascular endothelial cells emerge as a key regulator of vascular homeostasis. Disruption of vascular endothelial barrier leads to vascular hyperpermeability which in turn contributes to a broad spectrum of the most dreadful of human diseases, including heart diseases, diabetes, atherosclerosis, and cancer. The search for permeability-modulating agent still far lacking, thus, it is a need to search for a new agent to reduce endothelial hyperpermeability. Bixa orellana L. has been traditionally used to treat a number of ailments, including internal inflammation. Preliminary data showed that its leaves are able to suppress inflammation induced by carrageenan. Hence, this study aimed to investigate the anti-hyperpermebility effect of B. orellana leaf extract (AEBO) and elucidate its mechanism of action induced by histamine. The anti-hyperpermeability activity of the extract was evaluated using histamineinduced rat paw oedema, increased peritoneal vascular permeability, nitric oxide (NO) and vascular endothelial growth factor (VEGF) measurement in animal model, while, phospholipase C (PLC) – NO – cyclic guanosine monophosphate (cGMP) signaling pathway was determined via in vitro. AEBO produced a significant inhibition of histamine-induced paw edema starting at 60 min time point, with maximal percentage of inhibition (60.25%) achieved with a dose of 150 mg/kg. Up to 90% of increased peritoneal vascular hyperpermeability successfully suppressed by AEBO. NO and VEGF from inflammed paw tissues was also found to be downregulated in the AEBO group. Histamine-induced increased endothelial permeability was significantly attenuated by pretreatment with AEBO in a time- and concentration-dependent manner. Moreover, AEBO also suppressed PLC, calcium, NO and cGMP signaling cascade when endothelial cells were challenged with histamine. Protein kinase C activity was also significantly abolished by AEBO under histamine condition. In conclusion, the present data suggest that AEBO could suppress histamine-induced increased vascular permeability and the activity may be closely related with the inhibition of the PLCNO-cGMP signaling and PKC activity.

Keyword: Bixa Orellana; Histamine; Vascular permeability