Malaysian Tualang Honey a Potent Inhibitor of Angiogenesis

Ahmad Firdaus Abdul Khalid¹, Muhammad Nazrul Hakim Abdullah², Yoke Keong Yong¹

¹Department of Human Anatomy, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Malaysia, ²Department of Biomedical Science, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Malaysia

Background
Metastasis involves invasion and migration of new tissue is an important determinant of angiogenesis poses an attractive target for cancer therapy. The differentiation process in cancer progression involves blood vessel formation which includes migration, cell adhesion and tubule formation. Among the known anti-angiogenic, compounds that can be attained from natural sources are flavonoids and phenolic acids. Malaysian Tualang Honey (MTH) has been widely acknowledged to have high medicinal properties with high bioactive constituents as above.

Methods
The anti-proliferative effect of MTH was measured using the MTT assay. The anti-invasion and tube formation assay were investigated using a Transwell migration chamber and by in vitro tube formation in Matrigel respectively. The actin cytoskeleton and intercellular junction were examined by immunofluorescent staining.

Results
In this study, we reveal that MTH has anti-angiogenic property and explore the potential mechanisms for this effect. Twenty-four hours treatment with MTH inhibited the proliferation of human umbilical vein endothelial cells (HUVECs) with IC50 values of 6.6 ± 0.03% mg/mL with no toxicity. Our results showed that MTH exposure could significantly inhibit the proliferation of HUVECs in a dose-dependent manner at a low dose. Relative to the VEGF-induced control, the number of invading cells was significantly reduced (85.13% ± 1.49) in the MTH-treated groups. MTH also dramatically blocked (118154 micrometer ± 24.42) HUVEC tube formation when compared to VEGF-induced control. Furthermore, reduced formation of stress fibers in the actin cytoskeleton and tightening of intercellular junction in HUVEC were also noticed suggesting that MTH stabilizes endothelial junction and inhibits vascular leakage.

Conclusion
This study demonstrated that MTH exposure exhibits a potential anti-angiogenic effect through suppression of endothelial cell growth, invasion, migration and tube formation. This potential anti-angiogenic effect of MTH may play an important role in the anti-tumor activity.

Keywords:
Malaysian Tualang Honey, anti-angiogenic, anti-invasion, anti-tubular, stress fiber, human umbilical vein endothelial cells