Coffee Diterpene Derivatives as Anti-angiogenesis Agent

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Among the several compounds present in coffee, the coffee specific diterpenes have been identified as important chemo-protective agents which possess anti-carcinogenic properties.(1) Diterpenes are pentacyclic alcohols present in considerable quantity (up to 20%) in coffee oil.(2) Although large proportions (98%) of diterpenes exist esterified with various fatty acids - mainly palmitic acid, free diterpenes occur as minor components (0.7 to 3.5%).(3) Although there is substantial research sug-gesting the anti-carcinogenic properties of coffee diterpenes, in particular free cafestol and kahweol, available data regarding their anti-an-giogenic properties is still scarce. Few studies have demonstrated the anti-angiogenic properties of free cafestol (4) and kahweol,(5) however there is no study regarding the angiogenesis properties of diterpene esters, namely cafestol palmitate (CP) and kahweol palmitate (KP). Given that angiogenesis plays an important role in many pathological conditions, including cancer growth and metastasis, the present study aimed to compare and characterize whether CP and KP could inhibit angiogenesis in an *in vitro* model. For this purpose, human microvas-cular endothelial cells (HMVECs) were incubated with 50 μM of CP and KP. Subsequently, cell viability, cell migration, proliferation and apoptosis were assessed. In addition, capillary-like structures formation on Matrigel was also analysed.

According to our findings, both compounds inhibited angiogenesis steps on HMVECs, although a more significant effect was observed for KP. Incubation of HMVECs at concentration of 50 μM of CP and KP, did not sustain toxic effects under MTS assay. However, incubation of cells with higher concentrations of CP and KP (75 and 100 μM) decreased cell viability significantly ($p \leq 0.05$). Compared to control, a significant anti-proliferative effects on HMVECs assessed by bromodeoxyuridine (BrdU) was observed for both compounds. Moreover, treatment withCP and KP led to impairment of migratory capacity. Nevertheless, in-rease in apoptosis as tested by double-chamber and terminal trans-ferase dUTP nick end labeling (TUNEL) assay was observed for CP andKP, the effect was not statistically significant ($p \geq 0.05$). In addition, treatment of HMVECs with CP and KP led to decrease in the assembly of capillary-like structures on matrigel assay.

Taken together, these data indicate that CP and KP can be considered a promising strategy against angiogenesis-dependent disorders. Our findings further indicate that KP exerts more potent anti-angiogenic effects than CP, which may explain the more beneficial health effects reported for kahweol.

Referências

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