Ellagitannin derivatives induced inhibitory effects on the migration of metastatic melanoma cells

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Introduction: Cancer is recognized as one of the main leading causes of death and an important barrier to life expectancy worldwide. Melanoma is a life-threatening form of skin cancer with increasing incidence and mortality rates. Spread of melanoma cells to nearby lymph nodes, which is due to their highly metastatic nature, makes their eradication very challenging. Ellagitannins are hydrolysable tannins that are abundant in walnut, almond, black strawberry, raspberry and pomegranate. Urolithins are gut microbiota-derived metabolites of ellagitannins with valuable pharmaceutical activities. The aim of present study was to investigate effects of urolithin A (UA), urolithin B (UB) and methyl-UA (mUA) on the migration of melanoma cells *in vitro*.

Methods: Synthesis of UA, UB and mUA was carried out using 2-bromo-5 benzoic acid, 2-bromo-5-methoxy benzoic acid and resorcinol. To conduct migration assay, B16F10 cells, a mouse melanoma cell line, were seeded in 24-well plates and after 24 h, a straight scratch was made by a sterile pipette tip. Afterwards, cells were washed and treated with 40 μM UA, UB and mUA and incubated at 37˚C in the presence of 5% CO_2 for 24 and 48 h. Of note, untreated cells and cells treated with 0.4% DMSO were used as control groups. At the end of each time point, migration of cells to the scratched region was monitored and taken photographs were analyzed by imageJ software.

Results: Findings of current research indicated that UA and UB significantly ($p \leq 0.01$) decreased the migration of B16F10 cells. To note, calculated migration (%) for untreated and DMSO controls was as 84.1 and 95.5, respectively. Nevertheless, migration (%) was calculated as 35.7, 43 and 73.3 for UA, UB and mUA, respectively.

Conclusion: Ellagitannin derivatives tested in the present study exerted considerable inhibitory effects on the migration of melanoma cells. However, to introduce UA and UB as anti-metastatic agents, more investigations are required to assess their effects on human melanoma cells, as well as animal models.

Keywords: Melanoma, Migration, Ellagitannin, Urolithins.