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Anti-tumor potential of *Hottentotta zagrosensis* scorpion low molecular weight venom fractions: VEGF-mediated angiogenesis inhibition in Glioblastoma cells

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Abstract

Glioblastoma (GBM) is an aggressive and treatment-resistant brain tumor with poor clinical outcomes. In the recent years, natural bioactive compounds have attracted growing interest as sources of novel anticancer agents. Among these, Peptides derived scorpion venom (PESV) has emerged as a particularly promising reservoir of low-molecular-weight peptides with potent therapeutic potential. PESV from Hottentotta zagrosensis scorpion have attracted interest for their antitumor properties, particularly their ability to inhibit angiogenesis. This study examined the effects of PESV on angiogenesisin C6 glioblastoma cells. For this purpose, the venom from scorpion of H. zagrosensis was collected. The lyophilized whole venom was fractionated usingultra-filtration prior to load on SDS-PAGEand stained with silver. This process showed two protein bands, with the majority of molecular masses of 10kDa and a smaller band of5kDa. The concentration of vascular endothelial growth factor (VEGF) in Glioblastoma cells significantly decreased following the treatment with Temozolomide (TMZ) compared to the control group. Similarly, exposure to 75 µg and 150 µg of peptides derived from H. zagrosensis venom (PESV) also resulted in a significant reduction in VEGF levels compared to the control. The reduction of VEGF levels in the PESV groups (75 and 150 µg/mL) is dose-dependent, and notably, the extent of VEGF reduction at the high PESV dose (150 µg/mL) is comparable to the effect of TMZ, indicating the strong anti-angiogenic potential of these peptides. In conclusion, this study provides robust preclinical evidence that peptide fractions extracted from the venom of *H. zagrosensis* scorpion exhibit significant suppression of angiogenesis indicating its promise as a potential therapeutic candidate for GBM.

Key words: *Hottentotta zagrosensis*, venom, ultra-filtration, SDS-PAGE, Khuzestan

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