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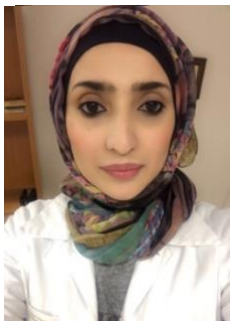
Lomustine and *n*-propyl gallate co-encapsulated liposomes for targeting glioblastoma multiforme via intranasal route: *ex vivo* permeability and *in vitro* cell line study



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The study aimed to develop the *n*-propylgallate (PG) and lomustine (LOM)-loaded liposomes suitable for nose to brain delivery for targeting the glioblastoma multiforme. Lomustine is a chemotherapeutic compound that may increase the anti-proliferative effect when applied with PG. Nose to brain delivery of LOM may reduce its toxicity issues in systemic circulation via other invasive routes. The characterization including encapsulation efficiency, loading capacity, *in vitro* drug release and *ex*-vivo permeation studies, were performed. The MTT assay was also directed to assess the anti-proliferative effects of LOM-loaded formulations. Additionally, the IC_{50} values representing the anti-proliferative effects of PG and LOM encapsulated liposomes were analyzed. We also studied the cellular uptake by loading liposomes with propidium iodide (PI) and fluorescein isothiocyanate (FITC) fluorescent dye. The particle size of the fabricated liposomal formulations was less than 175 nm with homogenous distribution and negative surface charge (ranging from -36.7±5.0 mV to -28±6.0 mV). The liposomes co-encapsulated with PG and LOM showed anti-proliferative effects on U87 (glioblastoma) and A2780 (ovarian cancer) and NIH/3T3 (murine embryonic fibroblast) cell lines within the investigated concentrations. Our study evaluation suggested the application of this novel combination comprises of PG and LOM nano-formulations as a favorable approach for glioblastoma targeting via intranasal route. Fluorescent microscopic study of PI and FITC-loaded liposomes revealed cellular uptake process was strongly time dependent.

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