



Miktoarm Star Micelles Containing Curcumin Reduce Cell Viability of Sensitized Glioblastoma

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Abstract:

Glioblastoma multiforme (GBM) is the most common and lethal primary intracranial tumor in humans. Monotherapeutic interventions have not been successful. The objective of the current studies was to establish the effective combination therapy consisting of pifitrin as a sensitizer, and curcumin as therapeutic incorporated into miktoarm micelles. A2B type miktoarm stars were prepared using a combination of click chemistry with ring opening polymerization on a core with orthogonal functionalities. These self-assemble into spherical micelles with hydrophobic core and hydrophilic corona structure. Micellar delivery systems for curcumin based on these miktoarm star polymers were prepared, characterized and tested on cultures sensitized with pifitrin. The results show that: (1) pifitrin and temozolamide in combination with curcumin cause significant cell death compared with the individual therapeutics (incorporated or not in micelles), and (2) repeated exposure to the same treatments is necessary to fully prevent a re-growth of glioblastoma cells both in 2D and 3D cultures. Although the incorporation of curcumin into A2B star polymer micelles did not increase the extent of cell death compared with curcumin alone, the advantage of micelles is that they significantly increase the aqueous solubility of curcumin and sustain its release; this will likely reduce the frequency of its administration required to be effective in vivo. A2B miktoarm polymers could be a new viable delivery system for curcumin and other anticancer drugs with similar limitations.

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