Development of Stimuli-Responsive Organo-silica Nanoparticles for Enhanced Drug Delivery.

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Background: Glioblastoma multiforme (GBM) is an aggressive primary brain tumor with high invasiveness, therapy resistance, and restricted drug penetration due to the blood-brain barrier (BBB). Conventional treatments such as surgery, radiotherapy, and chemotherapy provide limited success, highlighting the need for advanced drug delivery systems. Mesoporous silica nanoparticles (MSNs) have been explored as drug carriers due to their high surface area, tunable porosity, and functionalizability, but their limited biodegradability presents challenges for clinical application. To address this, mesoporous organosilica nanoparticles (MONs) and periodic mesoporous organosilicas (PMOs) have been developed by integrating organic moieties into the silica framework to enhance biocompatibility. Among these, hollow mesoporous organosilica nanoparticles (HMONs) offer a promising platform, featuring a biodegradable disulfide (-S-S-) bonded framework and a hollow core that allows high drug loading and controlled, redox-responsive release.

Methods: The synthesis of HMONs was carried out in a two-step process, beginning with the preparation of MSNs via a sol-gel approach, followed by the deposition of an organic-inorganic hybrid layer. The core was subsequently removed using an ammonia-based etching process.

Results: The synthesized HMONs had a particle size of 70 nm, a pore size of 7 nm, a pore volume of 0.6 cm^3/g, and a surface area of 273 m^2/g. The zeta potential was measured at -30 mV with a polydispersity index (PDI) of 0.1. DOX loading efficiency was 84%, and drug release exhibited a concentration-dependent redox response, with 92% and 82% of the loaded drug released at 10 mM and 5 mM GSH, respectively. Preliminary biocompatibility studies showed no significant toxicity to U87 cell lines at concentrations up to 200 µg/Ml.

Conclusions: These findings support the potential of HMONs as a biodegradable and redox-responsive drug delivery system for GBM therapy.