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Enhancing anticancer drug release through stimuli-responsive transferrin-gated silica nanocarriers: tuning a pH-sensitive framework versus pH-sensitive surface linker

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Introduction: Stimuli-responsive nanosystems has emerged as a promising approach to improve the anticancer drug delivery, due to the increase in the specificity of spatio-temporal release. Understanding the design of nanosystems and its impact on drug release is crucial for enhancing intracellular performance. Following cellular uptake, intracellular trafficking and the duration of these processes can significantly influence the efficacy of nanomedicine [1,2]. Therefore, in this work we aimed to develop, characterize, and evaluate the release kinetics of doxorubicin (DOX) from pH-responsive transferrin gated mesoporous silica nanoparticles, using two strategies: a pH-sensitive surface linker (MSN) and a pH-sensitive framework (dMSN).

Methods: The pH-based stimuli-sensitive feature of the nanosystems was achieved through two approaches: (i) using an imine bond in the pH-sensitive surface linker strategy (post-synthesis conjugation), and ii) incorporating an organosilane containing imine bonds (synthesis by co-condensation) [3]. The morphology of the nanoparticles synthesized by a modified Stöber method was observed by transmission electron microscopy. Characterizations were performed using dynamic light scattering, zeta potential, FT-IR spectroscopy, N2 adsorption/desorption isotherms, thermogravimetry, UV-vis spectroscopy, and NMR. The release profiles were monitored at pH 7.4 and pH 5.0. Kinetic analysis was performed using conventional mathematical models such as zero-order, first-order, and power law. To evaluate the drug-matrix interaction, an empirical three-parameter compartmental model was used.

Results: Experimental results demonstrated the successful loading of DOX in mesoporous silica nanoparticles, with an average size of ca. 100 nm. Two types of nanoparticles were obtained: (1) those superficially functionalized with transferrin through an imine bond, and (2) those synthesized by co-condensation with an organosilane and subsequently surface-functionalized with transferrin. The release profiles exhibited a higher release at pH 5.0 compared to pH 7.4. Non-degradable nanomaterials followed zero-order kinetics for drug release, while DOX release from degradable matrix nanomaterials was better described by first-order kinetics. Additionally, non-Fickian anomalous transport mechanisms were observed in all release scenarios.

Conclusions: Tuning the framework of mesoporous silica nanoparticles to achieve controlled

release, including burst release, could be a better strategy to optimize anticancer drug delivery silica platforms.

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References

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