Abstract
Ordered pore structure, large surface area, and substantial pore volume are all definitive characteristics of mesoporous silica nanoparticles (MSNs) that have gained them considerable interest in the biomedical field as drug delivery agents. Modifying the surface of MSNs with derivatives of hydrophilic polyethylene glycol (PEG) has been shown to increase cell viability, reduce hemolysis, and prevent macrophage uptake relative to bare MSNs. Incorporating a second organosilane, hydrophobic chlorotrimethyl silane (TMS), in a process known as co-modification has further improved colloidal stability in biological environments like blood serum. Additionally, TMS contributes to a hydrophobic environment inside the MSN pores, allowing for high retention of hydrophobic cancer therapeutics like doxorubicin. However, this hydrophobic pore interior is partially compromised in co-modified particles which employ the traditional straight chained PEG due to PEG migration into the pores. Consequently, this migration lowers the available pore volume, limiting drug loading capacity.

Herein, sub-50 nm diameter co-modified MSNs incorporating TMS and a novel PEG-silane (bis(triethoxysilyl)propyl)-polyethylene oxide, i.e. arc-PEG) are predicted to have an increased drug loading capacity and delivery of doxorubicin relative to traditional co-modified particles. This is due to the bulky structure of arc-PEG (~3000 MW) and the presence of two silane bonding groups which will attach to create an arc structure on the surface. These features can prevent its migration into the pores or imbue the MSNs with other useful properties. This study includes synthetic optimization, full characterization, drug delivery studies, and an investigation of the long-term stability of these particles in biological media.