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| **Title:** | A new mechanism of thermal sensitivity for rapid drug release and low systemic toxicity in hyperthermia and thermal ablation temperature ranges |
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| **Abstract:** | Purpose: The aim of this paper was to introduce a new mechanism of thermal sensitivity in nanocarriers that results in a relatively low drug release at physiological temperature and rapid release of the encapsulated drug at hyperthermia and thermal ablation temperature range (4060 degrees C). Materials and methods: The nanocarriers were synthesised by coating mesoporous silica nanoparticles with a thin layer of polyacrylamide. The low gelation temperature of the protective shell provides preferred routes for drug diffusion when the nanocarriers are heated within the hyperthermia temperature range. In order to determine the gelation point of polyacrylamide shell, differential scanning calorimetry was used. Various chemical, morphological, thermal, as well as drug loading capacities of these nanocarriers were characterised and their drug release behaviour was examined using magnetic resonance - guided focused ultrasound (MRgFUS). Results: Drug |

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| | release measurements at different temperatures using doxorubicin showed 11.5 +/- 2.4% leakage in aqueous solution at 37 degrees C after 30 min, while this value was significantly increased to 67.6 +/- 2.5% at 60 degrees C. A 39.2 +/- 2.2% release of doxorubicin was also obtained due to the sonication of drug-loaded nanoparticles for 5 x 20 s using MRgFUS. Conclusion: The nanocarriers developed do not exhibit a sharp transition temperature. However, a relatively high loading efficiency as well as rapid drug release at thermal ablation temperature range makes these nanostructures promising candidates for application as adjuvants to various thermal modalities such as radiofrequency and high intensity focused ultrasound. |
| **Keyword:** | core-shell structure; gelation point; mrgfus; polyacrylamide; thermosensitive liposomes; silica nanoparticles; triggered release; biomedical applications; n-isopropylacrylamide; mild hyperthermia; in-vitro; delivery; doxorubicin; transition |
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