Extended Abstract

Developing a new generation of nanoscale theragnostic with simple compositions and multidimensional features to achieve improved diagnoses and treatment outcomes while avoiding side effects is highly desirable, but it remains a great challenge. Fluorescent hybrid nanomaterials with a paramagnetic Gd_2O_3 core were applied as contrast agents for both in vivo fluorescence and magnetic resonance imaging. These hybrid particles were obtained by encapsulating Gd_2O_3 cores within a polymer shell carrying organic fluorophores covalently tethered to the inorganic network.

In this thesis work, we report a facile one-pot method for the synthesis of ultra-small (1–3 nm) gadolinium oxide (Gd_2O_3) nanoparticles using bovine albumin protein and chitosan as a capping agent and ascorbic acid as a mild reducing agent. We exclusively acquired multifluorescent Gd_2O_3 NCs without adding any dopants or impurities in aqueous suspension. The average particle size for BSA-capped and Chitosan-capped Gd_2O_3 was estimated to be in the range of nanometre (nm), respectively. The size range of prepared clusters lies within the optimal range for maximal contrast enhancement. The surface functionality, composition, and oxidation state of prepared particles is examined through FTIR and XPS spectra, whereas the crystallinity of Gd_2O_3 is interrogated via XRD planes. BSA-capped Gd_2O_3 nanoclusters exhibit strong tuneable emission spanning from 400-620nm (visible region) with broad full width at half maximum of (FWHM) ~140 nm, resulting in white light emission (WLE). The relative quantum yield was found to be 1.85% and 4.6% for blue and green emissions, respectively. Cytotoxicity measurement in HEK 293 (Human embryonic kidney cell) and cancerous MDA-MB-231 (Breast cancer cell line) studies revealed nearly 100% cell viability, encouraging its application in cell imaging. These nanoclusters possessed distinctive properties such as wide-range pH stability, ionic tolerability, prolonged photostability, and anomalous colloidal stability

(more than 24 months). The above findings report white light-emitting gadolinium oxide (Gd_2O_3) nanoclusters as an optical probe for *in-vitro* fluorescence imaging.

Although the MRI-based contrast agent is famous for their high spatial resolution, they suffer from low intensity. The idea of multimodal imaging emerges to complement the weakness of one imaging modality with the strength of the others. In this context, chitosan-derived Gd_2O_3 NCs can be used as a contrast agent in MRI and fluorophores in fluorescence imaging. Prepared chitosan-derived NCs not only exhibit a wide emission range with high absolute quantum yield (4.4 % and 7.1 % in blue and green emission respectively) but also exhibit higher longitudinal proton relaxivities (7.9) than positive contrast agents like Gd-DOTA, which are commonly used for clinical magnetic resonance imaging. Furthermore, to assess imaging capability, malignant glioma brain cell lines, viz., U-87 MG cells, were utilized, and the data revealed significant cytoplasmic accumulation in the red, green, and blue regions. The Z-stack study revealed the presence of Gd_2O_3 NCs in the depth of cells. In contrast, IVIS imaging is performed to visualize real-time tracking of particles within the physiological condition. Furthermore, an *in-vitro* cytotoxicity study in U-87 MG cells and an *in-vivo* study on Charles foster rats revealed the nontoxic behavior of the prepared particles and confirmed their candidature for biological cell imaging/labeling purposes.

Furthermore, understanding thermodynamic parameters, nucleation rate, and interfacial energy is critical for forecasting the stability, size, and phase of the produced cluster, which can be modified to acquire desirable features. For that purpose, determining temperature-dependent nucleation rate is a crucial parameter to accessing the kinetic and thermodynamic barrier linked with developing subatomic-sized nuclei, which tend to restrain the nucleation process. In this study, we exclusively compute the nucleation rate, thermodynamic parameters, and interfacial energy of ultra-small gadolinium oxide nanoclusters at high temperatures. Here, the apparent value of activation energy (E_a) and pre-exponential kinetic factor (A_a) was precisely computed by utilizing the most accurate Vyazovkin advanced and KAS iso-conversional method, which was further exploited to estimate the thermodynamic parameters, nucleation rate, and interfacial energy of ∼1 nm-sized gadolinium nanoclusters, in the temperature ranging from 555 to 780 K by appraising thermogravimetric data. The obtained *Z(α)* master plot suggested the existence of random nucleation within the BSA matrix of Gd_2O_3 nanoclusters at high temperatures over a specified conversion value. Additionally, four mathematical models were proposed using the above finding to interpret the nucleation rate and interfacial energy concerning high temperature and specified conversion points for the first time. This study revealed that these particles are suited for dual-modality imaging and freely circulate in the blood vessels without undesirable accumulation in vital organs. Additionally, the kinetic study suggested excellent thermal stability of prepared clusters, and the solid-state decomposition mechanism was determined to be R_3 according to the Piu model.

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