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Title: Photo-active carbon nitride and gold nanostuctures as autononomous and magnetically augmented entities for therapeutic & imaging applications

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Abstract:

Cancer and infectious diseases are presently two major causes of global mortality. Even with colossal development in the field of medical sciences, conventional treatment methods need to be altered or combined with advanced techniques for better management of these diseases. Nano-engineering is emerging as a solitary platform to integrate organic and inorganic moieties in a single entity to synergize more than one treatment modality for better therapeutic outcome. The present thesis converges on the development of multifunctional nanomaterials that can accomplish unimodal or multimodal therapy in conjunction with imaging. The first part deals with the synthesis, characterization and application of graphitic carbon nitride quantum dots (g-CNQDs) as photodynamic agent for both anti-bacterial and anti-cancer applications. Firstly, we tested the ability of g-CNQDs to inhibit the growth of gram-positive and gram-negative pathogenic bacteria under white light irradiation. Later, we have shown that under visible blue light excitation, g-CNQDs generate intracellular reactive oxygen species (ROS) causing significant cancer cell death. Subsequently, the thesis delves into synthesis of mesoporous magnetic nanoparticles (MMNP) decorated with carbon nitride and curcumin (MMCN-Cur) for combined magnetic hyperthermia, chemotherapy and photodynamic therapy. Here, curcumin and g-C3N4 act as a photosensitizer to catalyze ROS production under the influence of blue light. On application of Alternating Magnetic Field exposure, the local heat generated by MMCN not only triggers the release of curcumin but also induce cellular damage leading to apoptotic cell death. Apart from imparting significant T2 weighted contrast to glioma cells, a combination of mild magnetic hyperthermia, photodynamic effect and high oxidative stress-induced significant cellular damage leading to cancer cell apoptosis. The final chapter elaborates the development of degradable iron oxide nanoassemblies (IONs) and their surface functionalization with ultra-small gold nanoparticles for photothermal radiosensitization applications. Gold nanoparticles, lesser than 5 nm size are capable of getting cleared from the body, however do not possess desirable near infra-red absorption for in vivo photothermal applications. Hence, there is an undeniable necessity for tuning their photo-transduction properties without compromising the size required for renal & hepato-biliary clearance. Primarily, water-stable IONs with controlled primary crystallite size and overall spherical shape were prepared using PEI or gelatin as stabilization agents. After functionalizing them with either plasmonically intercoupled ultrasmall gold nanoparticles or organic photo-transducer coupled gold nanoclusters, they were evaluated for photothermal radiotherapy application. All the nanoparticles developed in this thesis have an intrinsic potential for one or more therapeutic (hyperthermia, photodynamic therapy, radiation therapy, photothermal therapy) and diagnostic (MR, PAI, Optical imaging) applications. Further systemic toxicity, biodistribution and therapeutic studies in pre-clinical models would reveal their suitability for clinical translation.

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