Design and Synthesis of Multifunctional Nanoparticles for Biocatalysis and Targeted Delivery of Anticancer Drug

Banalata Sahoo (Roll No. 09CY9728)

THESIS ABSTRACT

Nano-biotechnology is an emerging research area where nanomaterials find applications in biomedical fields especially in biocatalysis, cancer diagnosis and therapy. Judicious integration of nanotechnology and biology in a single entity offers many exciting possibilities for healthcare in the future. In this thesis work, several versatile, novel, and inexpensive chemical routes were established to prepare different types of aqueous dispersible functionalized nanoparticles viz. Fe_3O_4 magnetic nanoparticles, $MnFe_2O_4$ superparamagnetic nanoparticles, gold-Fe_3O_4 nanocomposites, hollow silica nanoparticles, mesoporous silica-$MnFe_2O_4$ nanocomposites. Characterization of these nanoparticles and evaluation of their performance as (a) support for immobilization of enzymes used as biocatalysts (b) carrier for targeted delivery of anticancer drugs, have been successfully carried out. In addition, the applicability of some of the magnetic nanoparticles as MRI contrast agent is evaluated.

The enzyme-substrate combinations that are used as biocatalysts are (i) phosphonate functionalized Fe_3O_4 nanoparticles for urease, (ii) amine functionalized Fe_3O_4 nanoparticles for lipase, and (iii) Fe_3O_4-gold nanocomposites for papain. The activities and reusabilities of the immobilized enzymes are then evaluated. The immobilized enzymes were found to retain their activity and follow kinetics similar to corresponding free enzymes. This immobilization strategy resulted in good reusability without significant loss of catalytic activity. This process of enzyme immobilization is simple, robust and applicable to other enzymes, making it potentially suitable for industrial applications. The high retention of catalytic activity of the enzymes upon immobilization onto these nanoparticles, with concomitant resusability opens up new opportunities in biotechnological applications.

An ideal targeted drug delivery system usually consists of the following – a carrier capable of encapsulating and releasing drugs at targeted organs (or sites), a targeting moiety, a signaling functionality. In this work we prepared i) hollow silica nanoparticles, ii) nanoparticle composites of superparamagnetic $MnFe_2O_4$ and mesoporous silica, iii) pH and temperature responsive polymer-tethered Fe_3O_4 magnetic nanoparticles as carrier for targeted delivery of anticancer drugs. All these particles are then functionalized with cancer cell targeting folate moiety and a fluorescent molecule (RITC) for cell imaging. These multifunctional nanoparticles are then loaded with an anticancer drug Doxorubicin, DOX, and their anticancer activity was evaluated *in vitro* by various biological techniques. *In vitro* biological studies revealed that the DOX-loaded folate-targeted nanoparticles achieved excellent efficacy for simultaneous targeting and destroying cancer cells. They specifically accumulate and release the payloads on HeLa cells through receptor-mediated endocytosis. Moreover, folate functionalized silica-$MnFe_2O_4$ nanocomposites showed promise as a MRI agent that is capable of specifically imaging the cancer cells. From all the biological studies, it is envisioned that these DOX-loaded multifunctional nanoparticles synthesized by us are excellent candidates that may serve as vehicles in cancer-specific targeting, imaging and therapeutic application in a single entity.

Keywords: ***Magnetic nanoparticles, iron oxide, $MnFe_2O_4$, hollow nanoparticles, mesoporous silica, enzymes, cancer, folic acid, Doxorubicin (DOX), MRI contrast agent***