MASTER'S THESIS

Preparation and characterization of noble metal-magnetite hybrid nano/micro composites towards drug delivery and heterogeneous catalysis

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Abstract

This thesis describes the preparation and characterization of core-shell noble metal-magnetite hybrid hollow nanocomposites utilizing hierarchical architecture. The hollow magnetite ($h$$Fe_3O_4$) nanoparticles were prepared by hydrothermal method, forming the cavity via Oswald ripening. Further surface modifications involved both inorganic and organic coatings, conferring the intracellular drug delivery ability and the catalytic enhancement.

In the first part, a series of hierarchical core-shell nanostructures flower-like $h$$Fe_3O_4$@AlOOH was synthesized through solvothermal method and sol-gel process. The formation of cavity accessible $h$$Fe_3O_4$@γ-AlOOH was achieved using silica-templated solvothermal treatment where the Kirkendall effect was observed. The morphologies of the as-prepared nanocomposites were characterized by scanning electron microscope (SEM), transmission electron microscope (TEM), dynamic light scattering (DLS), thermogravimetric analysis (TGA) and Fourier-transform infrared spectroscopy (FTIR). Then, the nano-encapsulation of platinum drug using hollow magnetite and its derivatives, has been developed with improved loading efficiency via co-solvent system. A dimethylformamide/water co-solvent system was found to be the most efficient system to encapsulate water-insoluble cisplatin. The platinum content was further quantitatively and qualitatively analyzed by inductively coupled plasma mass spectrometry (ICP-MS) and FTIR spectroscopy. The enhancement of loading efficiency could be driven by emulsification due to the diffusion of hydrophobic cisplatin into the hollow cavity of iron oxide nanoparticles. By incorporating water, the loading efficiency of $h$$Fe_3O_4$ and $h$$Fe_3O_4$@γ-AlOOH increased from 1-2% to 27% and from 6% to 54%, respectively. The grafting of cisplatin on AlOOH nanoflakes might account for the high loading efficiency of

flower-like *h*Fe_3O_4@AlOOH.

As a complement to naked *h*Fe_3O_4, a cell-penetrating poly(disulfide)s (CPD)-decorated hollow iron oxide nanoparticle was synthesized by immobilizing both cysteine and MPTMS as an initiator, followed by *in situ* polymerization to form *h*Fe_3O_4-Cys-CPD-$CONH_2$ and *h*Fe_3O_4-MPS-CPD-$CONH_2$. The morphologies were characterized by TEM/energy-dispersive X-ray spectroscopy (TEM/EDX) and the compositions of the as-prepared iron oxide nanocomposites were characterized by TGA, FTIR and X-ray photoelectron spectroscopy (XPS) and ICP-MS. The CPD coating not only serve as a protective layer, but also prevent the encapsulated cisplatin from a premature release. The *h*Fe_3O_4-MPS-CPD-$CONH_2$ exhibit promising features for the intracellular delivery of cisplatin, demonstrating a glutathione (GSH)-responsive drug release. Comparing with other *h*Fe_3O_4 nanoparticles, an enhancement of cellular uptake of *h*Fe_3O_4-MPS-CPD-$CONH_2$ could be observed by optical microscope, showing rapid accumulation of the *h*Fe_3O_4-MPS-CPD-$CONH_2$ nanocomposites in the primary human renal proximal tubular epithelial cells (HRPTEpiCs) cell in 2 h. At 24 h, *h*Fe_3O_4 (F), *h*Fe_3O_4-MPS (FS) and *h*Fe_3O_4-MPS-CPD-$CONH_2$ (FSC) together with cisplatin treatment did not cause any significant cytotoxicity to the cells when the particle concentration is less than 10 μg/mL. Interestingly, FSCC showed a certain extent of toxicity with increasing Fe and Pt concentration along with the treated time. It may suggest that the *h*Fe_3O_4-MPS-CPD-$CONH_2$ nanoparticle, as a cisplatin carrier, could enhance the drug efficiency by increasing cellular uptake of the nanoparticles in HRPTEpiCs together with the boosted cytotoxicity. Based on these data, *cisplatin*- *h*Fe_3O_4-MPS-CPD-$CONH_2$ (FSCC) treatments with the concentration less than 20 μg/mL and duration no more than 24 h could maintain around 70% of the cell viability of the HRPTEpiCs. The

hypothesis, at which CPD serves as an efficient carrier for intracellular cisplatin delivery, could be confirmed by both microscopic images and the cell viability test.

In the second part, a series of Au/Fe_3O_4 hybrid nanocomposites was prepared to investigate their catalytic efficiencies using 4-nitrophenol reduction as a model system. The flower-like *h*Fe_3O_4@γ-AlOOH@SiO_2-NH_2@Au was prepared by using protonated ammonium on *h*Fe_3O_4@γ-AlOOH@SiO_2-NH_2 to entangle gold nanoparticles (AuNPs) via electrostatic attraction. In comparison to numerous of catalytic studies, the turnover frequency (TOF) of *h*Fe_3O_4@γ-AlOOH@SiO_2-NH_2@Au shows a superior conversion rate up to 7.57 min^{-1} (4-nitrophenol per Au per min) for the 4-nitrophenol using sodium borohydride as a reductant. A rapid conversion of 4-nitrohpenol was observed using flower like composites that converted the 4-nitrophenol within 2 min. Our result suggests that silica residue hinders the reduction rate of the 4-nitrophenol. A significant deviation from pseudo first order was observed for densely AuNPs-functionalized nanoflower system, *h*Fe_3O_4@γ-AlOOH@SiO_2-NH_2@Au2X, which is different from most of the 4-nitrophenol reductions reported in literature. The *h*Fe_3O_4@γ-AlOOH@SiO_2-NH_2@Au also demonstrates catalytic activity when heated up to 800 °C before reduction. The recyclability was examined using magnetically recycled *h*Fe_3O_4@γ-AlOOH@SiO_2-NH_2@Au, which showed insignificant decrease in the catalytic efficiency. To prove the concept, platinum nanoparticles (PtNPs) immobilized *h*Fe_3O_4@γ-AlOOH@SiO_2-NH_2@Pt and *h*Fe_3O_4@γ-AlOOH@SiO_2-NH_2@Pt/Au were also prepared via electrostatic attraction to verify the feasibility of endowing modular functionality via post modification.

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