Gold Nanorods Stabilized by Drug-Conjugated Polymer for Synergistic Cancer Therapy

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Abstract

Taking advantages of gold nanorod (AuNRs) being capable of providing synergistic efficiency for cancer treatment via the combination of photothermal therapy and chemotherapy and their tunable properties as a function of stabilizer, this work aims to develop anticancer drug delivery system based on AuNRs stabilized with poly[(methacrylic acid)-*ran*-(methacryloyloxyethyl phosphorylcholine)] (PMAMPC). PMAMPC was synthesized by reversible addition-fragmentation chain transfer (RAFT) polymerization. Some carboxyl groups in PMAMPC were modified with cysteamine to introduce more thiol groups to increase active binding sites for each PMAMPC chains onto AuNRs surface. Remaining carboxyl groups were covalently bonded with hydrazine using EDC/NHS activation. Then, doxorubicin (DOX), an anticancer drug was conjugated to PMAMPC by acid-labile hydrazone linkage which should be rapidly destroyed under acidic environment in lysosomes. PMAMPC-DOX was coated on AuNRs surface via Au-S bonds. The resulting PMAMPC-DOX-AuNRs showed good colloidal stability and uniform size. Photothermal studies verified that the particles can convert the absorbed light into heat (> 70°C) when irradiated with NIR laser at 808 nm. *In vitro* drug release studies demonstrated that DOX release can be significantly accelerated at pH 5.0. Effective intracellular DOX release from the PMAMPC-DOX-AuNRs was verified by confocal laser microscopy. *In vivo* synergistic effect via hyperthermia and chemotherapy apparently outperform either treatment alone. These results suggested that PMAMPC-DOX-AuNRs could potentially be applied in pH-triggered drug delivery for cancer therapy.

Keywords: Anti-cancer drug, AuNRs, photothermal therapy, polymer stabilizer