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Efficient fabrication of smart pH-responsive gold nanohybrids for targeted anticancer drug delivery systems

Cancer has become the main leading cause and reason of death worldwide. Chemotherapy is the most common cancer treatment by using anticancer drugs. However, its treatment is limited by its high toxicity to healthy tissues, causing undesirable side effects. Accordingly, research has combined drugs with nanocarriers, especially gold nanohybrids (AuNHs), to achieve better therapeutic effects. Moreover, AuNHs have been extensively studied for their potential applications in anticancer drug delivery systems. This work reported an efficient method to fabricate smart pH-responsive AuNHs stabilized by folate-targeted pullulan derivative (FTPD) for delivery of camptothecin (CPT) to improve the selectivity, efficacy, and safety of these systems. Monodispersed FTPD@AuNHs were successfully synthesized by the green reduction with the addition of FTPD as a reducing/capping/stabilizing/functionalizing agent. After that, the combination of FTPD@AuNHs-CPT was prepared by subsequent loading of CPT into FTPD@AuNHs via intermolecular interactions. These systems were characterized by TEM, EDS, DLS, Zeta-potential, UV-VIS, XRD, and FTIR analyses, offering sphere-shaped particles with an average size of 11.0 nm. The UV-VIS spectrum of FTPD@AuNHs-CPT showed a redshift from 519 to 528 nm, confirming the formation of a protective layer on the AuNHs surface upon binding to CPT to form the larger NHs. pH-responsive FTPD@AuNHs-CPT demonstrated a faster release rate under acidic conditions. At the end of 72 h, the cumulative amount of CPT released from FTPD@AuNHs-CPT at pH 5.0 was 66.2%, whereas the release rate at pH 7.4 was 29.8%. The FTPD@AuNHs-CPT exhibited 2.8-fold higher cytotoxicity against human lung cancer cells (Chago-k1) than CPT. These systems also displayed high intracellular uptake by folate receptor-mediated endocytosis and induced cell death through the apoptosis pathway by arresting the cell cycle at the G0-G1 phase (9.3-11.4%). Consequently, it is suggested that FTPD@AuNHs-CPT should be considered as a new way for targeted anticancer drug delivery systems.

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