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Development of biocompatible fluorescent gelatin nanoparticles for cell imaging applications

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ABSTRACT

In recent years, fluorescent carbon dots (CDs) have attracted a great deal of attention in imaging and related biomedical applications due to their excellent photoluminescence properties, low cost, high quantum yield and low cytotoxicity in comparison with semiconductor quantum dots based on metallic elements. In this paper, a new design for development of CDs/gelatin nanoparticles (CDs/GNPs) is described. The obtained fluorescent nanocarriers were characterized using FT-IR, SEM, XRD, DLS, PL analysis. Afterwards, the performance of developed NPs was investigated through different in-vitro tests such as MTT assay, fluorescence microscopy analyses. Methotrexate (MTX) was successfully loaded into the fluorescent NPs at physiological pH (7.4) by ionic interactions between anionic carboxylate groups of MTX and cationic amino groups on the surface of NPs. The MTT assay revealed that the MTX-loaded nanocarriers have higher cytotoxicity in MCF-7 breast cancer cells than nanocarriers without MTX. Upon the obtained results, our fluorescent nanocarriers hold great potential as drug carriers for the targeted MTX delivery to the cancer cells and biological fluorescent labelling.

Keywords: Carbon Dots, Gelatin Nanoparticles, Cell imaging, Methotrexate

1. INTRODUCTION

Recent years, fluorescent nanomaterials have gained greater attention owing to their unique optical properties and a wide range of potential in medical applications [1-3]. Up to now, different types of fluorescent nanomaterials such as semiconductor quantum dots, polymer dots, carbon nanodots and liposome fluorescent nanomaterials have been synthesized and studied in various applications [4-6]. By comparing semiconductor quantum dots (QDs) based on metallic elements, such as PbSe, CdSe, CdS, and Ag_2S with fluorescent carbon-based nanodots (CDs), CDs are the excellent fluorescent nanomaterials due to their good biocompatibility, easy to modify, and low toxicity biocompatibility [7]. So, CDs were used as promising materials for various applications such as gene transmission, bioimaging, biosensing, disease detection and drug delivery [8-10]. Moreover, to develop these fluorescent nanoparticles (NPs) with effective drug delivery systems, the use of natural biopolymeric nanocarriers can be proposed to load of these fluorescent materials [11, 12]. Among the natural biopolymers, gelatin is one of the desirable materials used in foodstuff, pharmaceutical, cosmetic and medical applications due to its excellent biodegradability and biocompatibility. Furthermore, gelatin is a non-toxic and natural polyampholyte biopolymer gained either by partial acid (type-A) or alkaline (type-B) hydrolysis of collagen [13-15]. In general, gelatin-based NPs (GNPs) are considered as a useful biomaterial nanocarrier for drugs and bioactive molecules because of its excellent surface chemical modification potential and cross-linking possibility. The complex of fluorescent nanodots/GNPs showed potential applications in drug delivery and bioimaging, simultaneously. In this regard, several works have been studied and reported for fluorescent GNPs [16-18]. However, the toxicity of QDs may hold back their *in-vivo* applications due to the direct release of cytotoxic metals of QDs into the biological system which could damage normal cells because of severe toxicity [19-21]. Thus, to overcome this problem, CDs can be used as a fluorescent dye with excellent biocompatibility and easy combination with natural biopolymer nanocarrier. As we know, no previous investigations have been reported about the synthesis of CDs embedded GNPs. Methotrexate (MTX) is one of the most widely used therapeutic agents to treat various cancers such as breast cancer, choriocarcinoma, lung cancer and bladder carcinoma [22-24]. Moreover, MTX has structural similarity with folic acid (FA) which would be able to enter cells through a similar transport system of FA as a targeting ligand on the surface of cancer cells [25-27]. Thus, in this paper, we report the preparation of fluorescent GNPs with the loading of MTX on the surface of NPs as a targeting and therapeutic agent. In the first step, CDs with an excellent fluorescence quantum yield of 75% were prepared by the one-step hydrothermal method process [28]. Then, CDs/GNPs were synthesized via two-step dissolution method. Then, MTX as