Journal of Pharmaceutical Sciences xxx (2018) 1-8

Contents lists available at ScienceDirect

Journal of Pharmaceutical Sciences

journal homepage: www.jpharmsci.org

Pharmaceutical Nanotechnology

Preparation and Evaluation of Multifunctional Autofluorescent Magnetic Nanoparticle–Based Drug Delivery Systems Against Mammary Cancer

Zhi Li [1, 2], Junya Zhang [1], Xiao Li [1], Xinhong Guo [1, 2, *], Zhenzhong Zhang [1, 2, *]

[1] School of Pharmaceutical Sciences, Zhengzhou University, 100 Kexue Avenue, Zhengzhou 450001, People's Republic of China
[2] Henan Key Laboratory of Targeted Therapy and Diagnosis of Tumor and Major Diseases, Henan Province, Zhengzhou 450001, People's Republic of China

ARTICLE INFO

Article history:
Received 18 May 2018
Accepted 12 June 2018

Keywords:
cancer
controlled delivery
controlled release
drug delivery system(s)
nanoparticle(s)
targeted drug delivery

ABSTRACT

The Fe_3O_4@C@$NaYF_4$:Yb,Er nanocarriers of multifunction were synthesized. The mitoxantrone was selected as model drug, and these nanoparticles have high drug loading (0.63 mg/mg). The temperature of Fe_3O_4@C@$NaYF_4$:Yb,Er in water reached 60°C with 808 nm irritation (2.5 W/cm^2). The cumulative release of these nano drug carriers significantly increased because of the increase in temperature, and the 4T1 cell growth inhibition rates were 59.15%, almost 2.25-fold higher than mitoxantrone group (p <0.05). Because the nanoparticles had autofluorescence under 808 nm irritation, the nanocarriers could be traced in both *in vitro* and *in vivo* studies. Based on magnetic field, the fluorescence signal of these nano drug carriers could be observed at tumor region during 2-9 h *in vivo* study. The nanocarriers with magnetic and 808 nm laser group, tumor growth inhibition rate achieved almost 83.14%. These nanoparticles are an outstanding potential carrier for antitumor drugs, which can improve curative effect for tumor while reducing toxicity.

Introduction

During the past decade, magnetic carriers have gained considerable attention in drug delivery system because of their unique properties, such as excellent biocompatibility, small size, low toxicity, thermal therapy, high tunable surface modifications, and targeted by an external magnetic field application.[1,2] However, some reported magnetic nanoparticles (NPs) were of low efficiency as drug carriers owing to limitations in drug loading, not spreading in the general circulation and being recognized and eliminated by the mononuclear phagocyte system.[3,4] Recently, modification or coating for magnetic NPs by materials has been broadly studied, such as biodegradable polylactide microspheres containing magnetic NPs,[5] tyrosine-decorated biocompatible Fe_3O_4 magnetic NP,[6] and polyacrylic acid–coated iron oxide magnetic NPs.[7] But polymer nano drug carrier system hinders tumor cell endocytosis, greatly reduces the efficacy of small molecule drug absorption into the cell; in addition, nanoscale drug delivery system, even being absorbed into cells through endocytosis, often released slowly or released incompletely in cells, results in low drug utilization and ineffective treatment. Moreover, all traditional drug delivery systems have a common problem and it is the separation of drug tracer and tumor therapy, and to trace the drug, the popular method is to encapsulate quantum dots or organic molecules in the carrier.

However, the use of traditional luminescent materials, organic molecules, and quantum dots are often subjected to inherent limitations, such as chemical instability, fluorescence quenching, high autofluorescence background, broad emission bandwidth, long-term toxicity, and so on.[8,9] Now, particularly, the potential of lanthanide-doped upconversion nanoparticles (UCNPs) has been placed on developing luminescent probes owe to their promise in biological research and biomedical applications. Compared with other fluorescent labeling technology, UCNPs provide a number of advantages, higher detection sensitivity, outstanding photostability, chemical inertness, long luminescence lifetimes, and large tissue penetration depths.[10,11] In recent years, there have been significant progresses in upconversion emission tuning.[12] Researcher can profit from these advances to fabricate luminescent nanoprobes for bioprobes for biodetections. Typical probes involve Yb/Er, Yb/Tm, Yb/Er,Yb/Tm, and Yb/Ho doped UCNPs.[13,14]

* *Correspondence to:* Xinhong Guo and Zhenzhong Zhang (Tel: +86 371 67781910).
E-mail address: wyx040123@126.com (Z. Zhang).

https://doi.org/10.1016/j.xphs.2018.06.009
0022-3549/

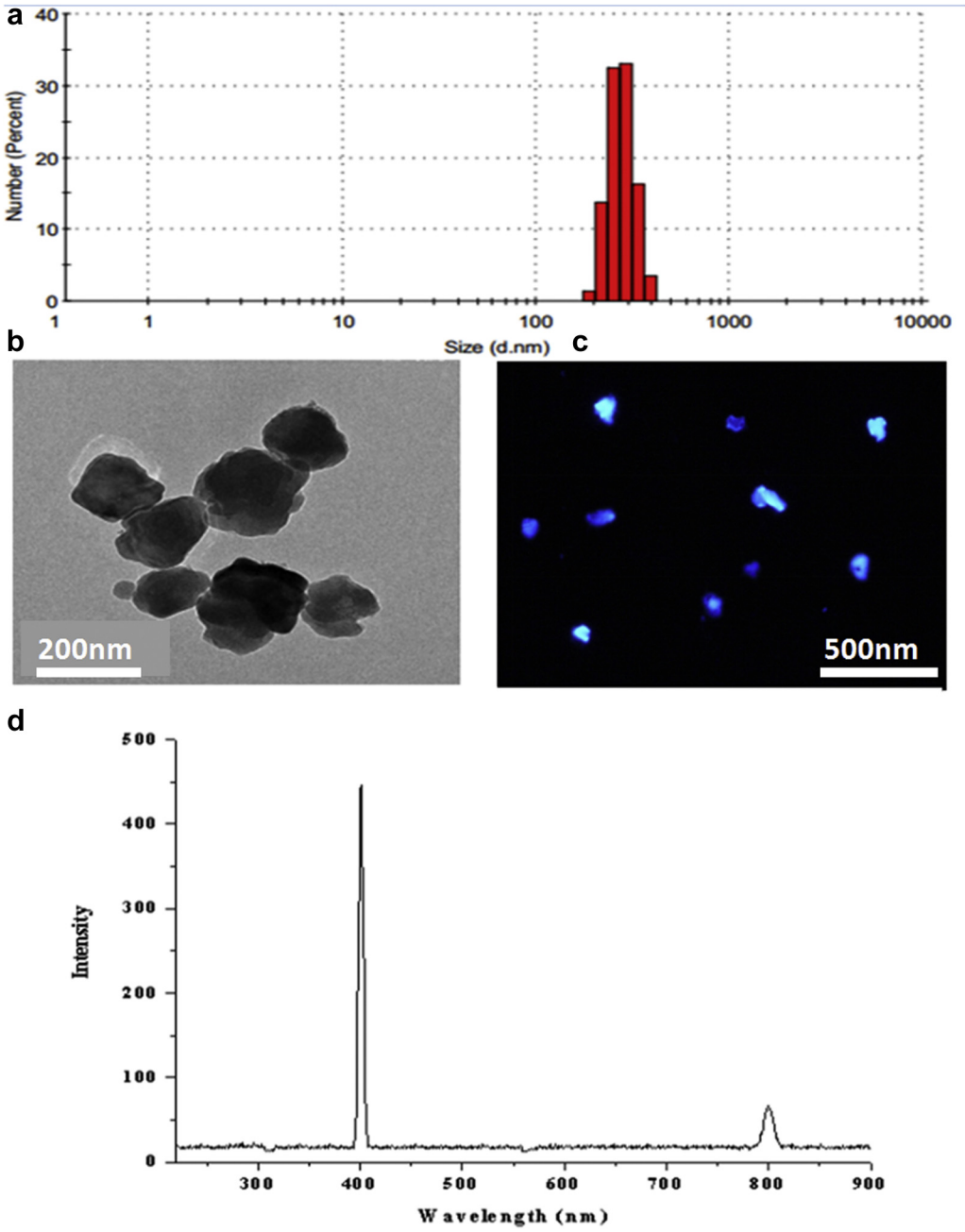

Figure 1. The size distribution (a) and TEM images (b) of Fe_3O_4@C@$NaYF_4$:Yb,Er. (c) The fluorescence photographs (under purple light field) of Fe_3O_4@C@$NaYF_4$:Yb,Er. (d) The fluorescence image of Fe_3O_4@C@$NaYF_4$:Yb,Er. TEM, transmission electron microscopy.

Whereas, UCNPs alone were seldom used as drug carrier due to solid construction and less active function.[15,16]

In this article, we designed and structured the composite nanocarrier with magnetic NPs and upconversion materials to implement the integration of positive target therapy and fluorescence tracking. In our previous studies, the surface of Fe_3O_4@C is filled with plentiful hydroxy and carboxyl, which can combine with drug through hydrogen bond, intermolecular interaction, and so on.[17,18] The compositing nanocarrier passive target with positive target was due to enhanced permeability and retention effect and external magnetic field.[19,20] The Fe_3O_4@C combined with upconversion materials were prepared with co-precipitation method; after that, some properties of this nanocarrier were discussed.

Methods

Material, Cells, and Animals

Mitoxantrone (MTO) hydrochloride was obtained from Yi kang si da Industries (Beijing, China); $YCl_3 \cdot 6H_2O$ (99.99%), $YbCl_3 \cdot 6H_2O$ (99.99%), and $ErCl_3 \cdot 6H_2O$ (99.99%) were obtained from Energy Chemical (Shandong China). N-propyl alcohol and ethylene diamine tetraacetic acid were obtained from Chemical Reagent Co. Ltd. (Dingsheng China). 3-(4,5-dimethylthiazol-2-yl)-2, 5-diphenyl tetrazolium bromide (MTT) was obtained from Sigma-Aldrich (St. Louis, MO); RPMI-1640 and fetal bovine serum were obtained from Biological Industries.