Original Article: New Advances on Modulating Nanomagnetic Cores as the MRI-Monitored Drug Release in Cancer

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ABSTRACT

Multifunctional magnetic nanostructures were considered by different functional organic groups to use as a drug delivery arrangement in cancer therapy. The modulating nonmagnetic core-shell, yolk-shell structures, and the MRI-monitored drug release cells were applied in cancer therapy. Furthermore, magneto-fluorescent nanocarriers with fluorescent and superparamagnetic features were used in bioimaging and MRI, respectively.

Introduction

Superparamagnetic iron oxide nanoparticles are applied for different biomedical applications, covering imaging and physiological activities in cells and tissues. Herein, carbon-coated core-shell superparamagnetic iron oxide nanoparticles (FC-SPIONs) are used as a compound to support network outgrowth [1-3]. They are used in theranostic fields like MRI, bioimaging, hyperthermia therapy, and targeted drug delivery [4-7]. The theranostic applications need to have a tinny size of

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particles and long-standing strength in biological media. According to FDA approval, Fe_3O_4 MNPs have received much attention in terms of biocompatibility and biodegradability [7, 8]. Thus, Fe_3O_4 MNPs are applied to undergo a complicated biological process. So, there is a need to design prolonging blood circulation time to interact with Fe_3O_4 MNPs [8]. Different organic functional groups were immobilized onto the MNPs surfaces like aminosilane, amino acid, citric acid, polyphosphate, and protein to give them stability and biocompatibility [8-11].

The use of magnetic drug carriers such as Gd [12, 13] and Mn-based chelates are valuable [14, 15] for positive or T1-weighted imaging, and superparamagnetic iron oxide nanoparticles (SPIONs) as the drug carrier and checking the progress of the disease as well [16, 17]. Another point is to have acceptable contrast agents (CAs) in MRI method as a non-invasive technique to show the detail of soft tissue at high resolution [18].

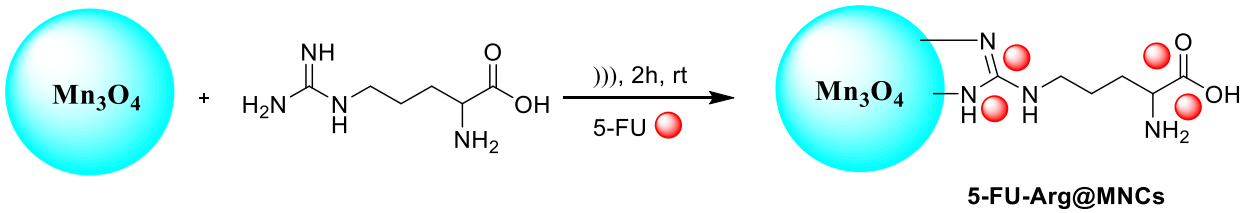
While there are various reports of MRI-monitored drug release research, some of which accomplished on both MRI technique and targeted drug release, which are included in this review.

The current demand for cancer theranostics is an aim to target, guide, and control the release of therapeutics.[19, 20]. Therefore, external drug delivery procedure is by light, magnetic field, heat, electric field, and ultrasound created directing organized management [21]. In our previous work, yolk-shell nanostructures for drug delivery were reviewed as a new class of hollow structure [22]; however, in this paper, the importance of the magnetic cores was considered in MRI and cancer therapy.

Various Magnetic Cores

Mn_3O_4 Magnetic nanostructures

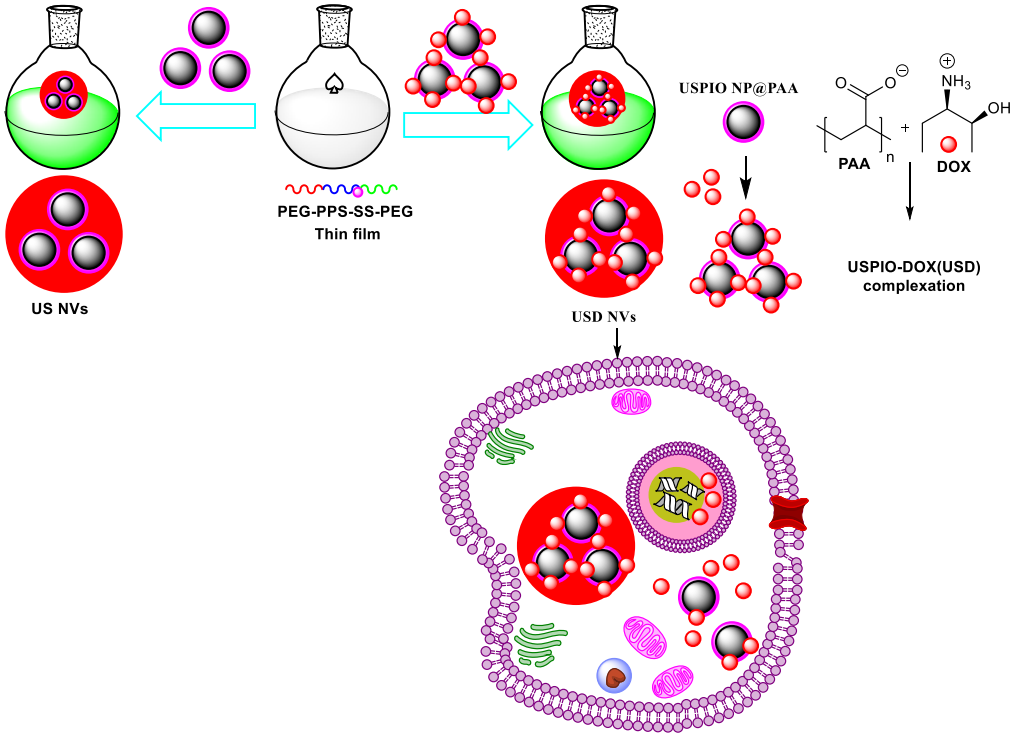
Mn_3O_4 nanocuboids (MNCs), which were provided through precipitation processes, were treated with arginine (Arg) as a stabilizer under ultrasonicated conditions to obtain Arg@MNCs [23, 24]. In the next step, 5-Fluorouracil (5-FU), which is one of the applicable drugs in chemotherapy, was loaded on the Arg@MNCs to provide 5-FU-Arg@MNCs as a diagnostic carrier for cancer therapy (Scheme 1) [25].



Scheme 1. Formation of 5-FU-Arg@MNCs Nanocarriers

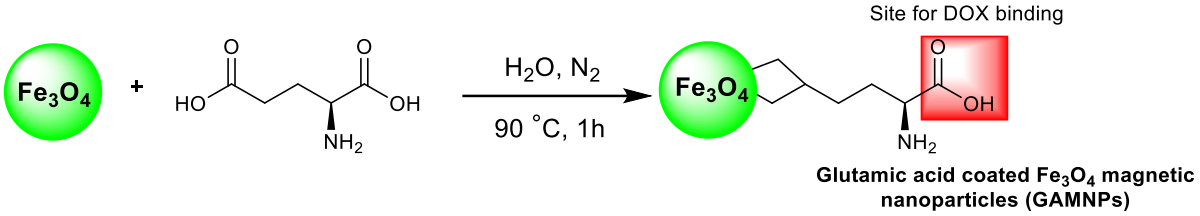
Fe_3O_4 magnetic nanostructures

Yolk-shell nanostructure with glutathione-responsive drug release and T1 MRI activation in cancer diagnostics was designed by Du and co-workers. At first, iron oxides were provided as ultrasmall paramagnetic nanostructure features (USPIO NPs), which were mixed with poly (acrylic acid) (PAA) to provide USPIO NPs@PAA [26]. On the other hand, for the synthesis of PEG-PPS-SS-PEG amphiphilic polymers, Poly (ethylene glycol) methyl ether was applied as primary compounds to provide PEG-Tosyl and PEG thioacetate; which was converted to the PEG-PPS-disulfide pyridine by PEG thioacetate in MeOH. Then, propylene sulfide and disulfide dipyridine were added to provide PEG-PPS-disulfide pyridine, which was mixed with HS-PEG-NH_2 to prepare PEG-PPS-SS-PEG as a thin film. USPIO NPs@PAA was mixed with doxorubicin hydrochloride (DOX) solutions to yield USD, which was loaded on thin-film to provide USD NVs (Scheme 2) [27].



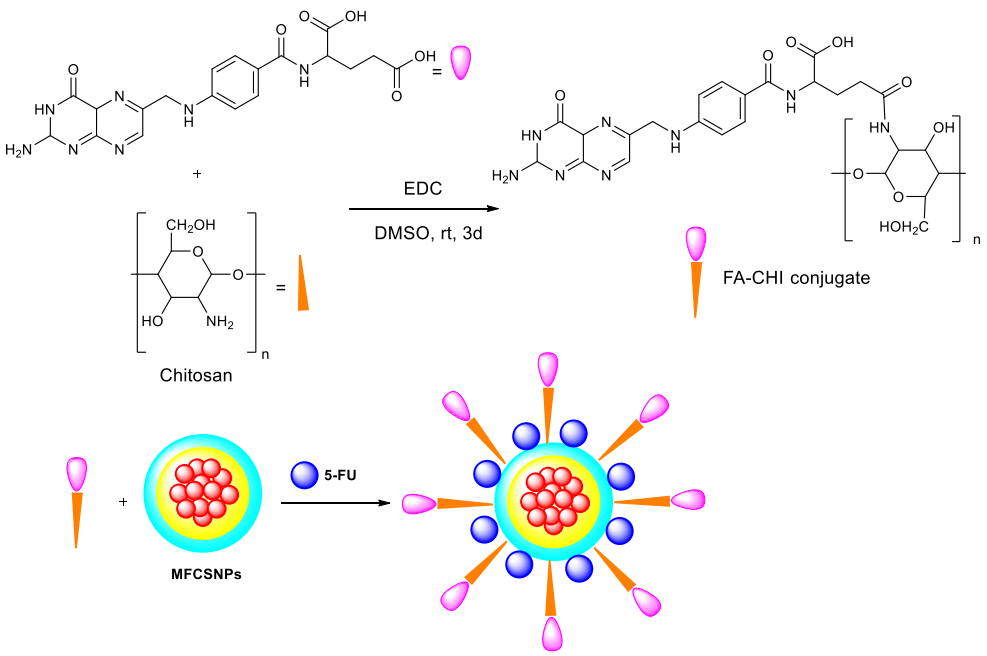
Scheme 2. Formation of USD NVs Nanocarriers

Glutamic acid-coated Fe_3O_4 nanoparticles (GAMNPs) were provided through the immobilization of glutamic acid on the Fe_3O_4 to give Fe_3O_4 GAMNPs, which were modified by doxorubicin hydrochloride (DOX) and methotrexate (MTX) to yield DOX-MTX-GAMNPs as chemotherapeutic drugs (Scheme 3) [28, 29].



Scheme 3. The synthesis of DOX-MTX-GAMNPs Nanocarriers

Randhawa and co-workers designed a Multifunctional-fluorescent magnetic nanostructure (MFCSNPs-FA-CHI-5FU) to be applied in imaging and drug delivery. MFCSNPs were synthesized by the reaction of ferrocene, acetone, and H_2O_2 solution to give the black precipitate. On the other hand, the treatment of Folic Acid (FA) and Chitosan (CHI) yields FA-CHI using *N*-(3-(dimethylamino)propyl)-*N*-ethylcarbodiimide hydrochloride (EDC). Multifunctional Magneto-Fluorescent Nanocarriers were provided by the reaction of MFCSNPs, 5-FU, and FA-CHI conjugates in water, which could be applied in targeted drug delivery and MRI techniques [30].



Scheme 4. The synthesis of MFCSNPs-FA-CHI-5FU Nanocarriers

Conclusion

In summary, different core-shell or yolk-shell nonmagnetic particles were used to be functionalized by organic groups for loading targeted drugs in cancers. Various responsive release of drugs was designed based on nanocarriers in MRI, in which the hemocompatibility and the biocompatibility of the magnetic nanoparticles are highly essential.

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