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Study the Effect of Laser Wavelength on Polymeric Metallic Nanocarrier Synthesis for Curcumin Delivery in Prostate Cancer Therapy: In Vitro Study

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Abstract

Drug delivery using nanocarriers is recommended to decrease the drug amount. To improve the different therapeutic characteristics of curcumin (CU) such as solubility, bioavailability, maintenance endorsement, and make it a promising, successful antitumor drug used for prostate cancer treatment. It was introduced to folate decorated chitosan (CS) coated Fe@Au NPs (FA-CU-CS-Fe@Au NPs). Fe@Au nanoparticle contains magnetic Fe NP's core with a fine layer of Au NP's synthesized using the method Pulsed, Laser, Ablation in Liquid (PLAL). These Fe@Au NP's characterized by UV-Visible Spectrophotometer, High-Resolution, Transmission Electron Microscopy, (HRTEM), and Field Emission Scanning, Electron, Microscopy (FESEM). The smallest nanosize and the best result was obtained at different laser wavelength (532, 1064) nm. The mean size gained of Fe@Au NPs were (67.65, 77.88) nm. Obtained results exhibited that the laser wavelength plays a key role in the size, and dispersity of Fe@Au NPs. CU loaded FA-CS-Fe@Au NPs MTT assay on human prostate cancer cell line (PC3) proved that CU cytotoxicity can improve when they are loaded on (FA-CS-Fe@Au NPs) when comparing it with free CU.

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1. INTRODUCTION

Cancer is characterized by the proliferation of uncontrolled cells, in which cells that grow to become an abnormal cell mass is called a tumor. Chemotherapy, surgery, and radiation therapy were developed for the treatment of different cancer types, but normal cells were also will be affected, damaged, and died [1,2]. prostate cancer incidence and the death rate of the cancer present vary differently. It is predestined that 1 in 6 men will be detected with prostate cancer at some point during their lives but only 1 in 36 is expected to die because of it. The risk of prostate cancer is higher in men over the age of 55–65. Various studies were made to raise the performance of cancer therapy by decrease hurtful effects in normal cells. A favorable strategy over recent years appeared to manufacture core-shell iron-gold biocompatible nanomaterials, for usages, they are widely in the biotechnological and biomedical areas, comprise bio-targeting for cancer therapy, drug carriers, bio-detection, and bio-separation [3-6]. Nano-materials can be a beneficial tool to decrease the radiation therapy side effects in natural cells nearly a tumor cell [7]. The high atomic numbers of nanoparticles can be intensive as sanitizing agents in the carcinoma cells and the absorption property of their increased [8-10]. Because nanoparticles have small size exhibit new physical properties that differ greatly from those of the (bulk) solid-state [11]. The gold addition in Fe@Au can

promote the stability and dispersibility of core particles (Fe) and their characteristic enhance [12,13]. The fabrication of (Au) shell (Fe) core nanoparticles has attracted attention because of potential applications like targeted delivery, medical imaging, bio-separation, electrochemical sensors, and cancer treatment [14]. Gold protects the iron core from oxidation [15]. A favored coating material is Au using the functionality particular surface, from therapy with agents bio-medical or chemical [16,17]. A clean and flexible technique for the manufacture of core-shell colloids nanoparticle is Pulsed Laser Ablation in Liquids (PLAL) [18]. One of the most complex phenomena is the process of pulsed laser ablation of a target product in liquids, it is top-down nanomaterials generation processes, noticed when interacts the radiation of laser with a material solid. Radiation of laser is focused on a metal target within the particular solution fabrication nanoparticles dispersion [19-21]. The structures and properties of the production are easily dominated by modifying conditions of experimental like solutions, external environment, target materials, and laser parameters, the process can be performed at normal temperature and pressure [22-25]. The purpose of this study is to prepare and synthesized nanoencapsulation as drug delivery by PLAL method with a new formulation of FA-CU-CS-Fe@Au NPs to treat prostate cancer (PC3) and normal cell line (RWPE-1).

2. Materials and Methods

2.1 Production of Fe@Au NPs

To laser ablation of (Gold, Iron) a beam of Nd:YAG laser ((λ = 1064, 532) nm, R.R = 3 Hz, τ = 5 ns, 100 pulses) first: focused vertically to the Fe plate surface diameter (1 cm), at the target surface the spot size of the beam (1mm^2). Inside a glass container containing DDW water Fe plate placed, the plate of Fe target was (99.99% pure) [15]. The DDW height above the target (10 cm). In the PLAL of the Fe target, the watercolor turns to gray color, indicating the formation of Fe NPs. And from the subsequent ablation of (99.99% pure) Au target in preparing already, Fe NPs colloidal Fe@Au NPs were prepared.

2.2 FA-CU-CS-Fe@Au NPs preparation

11 mg of chitosan (CS) powder was dissolved in 50ml DDW and 50ml G-Acetic acid. CS solution adds to the solution of Fe@Au NPs, then curcumin (CU) drug-specific amount (10 mg) was mixed with the solution of Fe@Au-CS. (5ml) Folic acid (FA) add to CU-CS-Fe@Au NPs. By stirring continuously for (8 h) at (1000) rpm/min in a water bath, formed a water-in-oil microemulsion [15]. To obtained nanoencapsulation FA-CU-CS-Fe@Au NPsby using a microsyringe filter, the solution was filtration.

2.3 FA-CU-CS-Fe@Au NPs characterization

The nanoformulation was analyzed using spectrophotometer UV-Visible (UV-Visible, Aquarius 7000, Italia), TEM (Carl Zeiss AG - Zeiss EM900, Germany), and SEM (FE-SEM, Hitachi S-4160, Japan).

2.4 Drug release profile

Buffers different used like phosphate (0.01 M), and (pH=7.4), and citrate (0.01 M), and (pH=5.4) in 37^{o}C to drug release value measurement from Fe@Au-CS-CU-FA NPs. 1ml solution nanoformulation added to the dialyze bag and placed in (100ml) phosphate and citrate buffers separately. Tween 80 was utilized as an emulsion to prevent precipitation of drugs released. To perform the release process use a shaking water bath. At (0, 4, 8, 12, 24, 48, 72, and 96) h the sampling was done. The (500µl) was aliquoted freeze-dried in every process of sampling and resolved in 2ml methanol [16]. By fluorescence spectroscopy, CU release measurement was done. By using the following equation CU freeing was measured:

$$\mathbf{R= V \Sigma n\text{-}i\ Ci + V_0\ Cn / m\ drug} \qquad \textbf{Eq. (1)}$$

where the drug release final is R, the concentrations of curcumin are Ci and Cn, the volume of sample is V, the initial volume of drug is V_0, the mass of curcumin drug in the nanoparticle is m, the times of sampling and

precipitated was rinsed and suspended again with DDW are i and n.

2.5 MTT Assay

To MTT 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide solution preparation, MTT powder (5) mg was solved in (1 ml) PBS. For the study of MTT, the plates with 96 wells were used and cultured with 10^4 cells. Then DMEM medium of (200 µl) was added to every well. After that cells are left to grow and multiply in 24 hours. In this stage, the doses different of (10-60 µM) of the void drug (CU), (FA-CU-CS-Fe@Au NPs) nanoencapsulation, and the bare NPs (FA-CS-Fe@Au NPs) that solved in (2%) V/V in DMSO compared to the medium that was added in the cells formed from the wells [1]. Every experiment was performed in three wells, and was at least repeated three times. At (24 and 48) h after treatment, the MTT analysis was performed. After 4 h incubation with MTT, solutions were completely evacuated and then replaced in each well with DMSO 100 µl. In the shaker, the plates were placed, for 15 minutes then evaluated by an ELISA reader (BioTek Power Wave XS).

2.6. Statistical Analysis

By the use of SPSS (Version 24), software and statistical analyses were performed by Excel 2016 (Microsoft office, USA) software graphical representations were showed. p values less than 0.05 were considered statistically significant. As mean ± SD of three independent experiments the data are presented here.

3. Results and Discussion

3.1. UV–Visible absorption spectrum

The Fe@Au NPs core-shell UV–visible absorption spectra, synthesized by shoot Au decorated Fe NPs colloidal

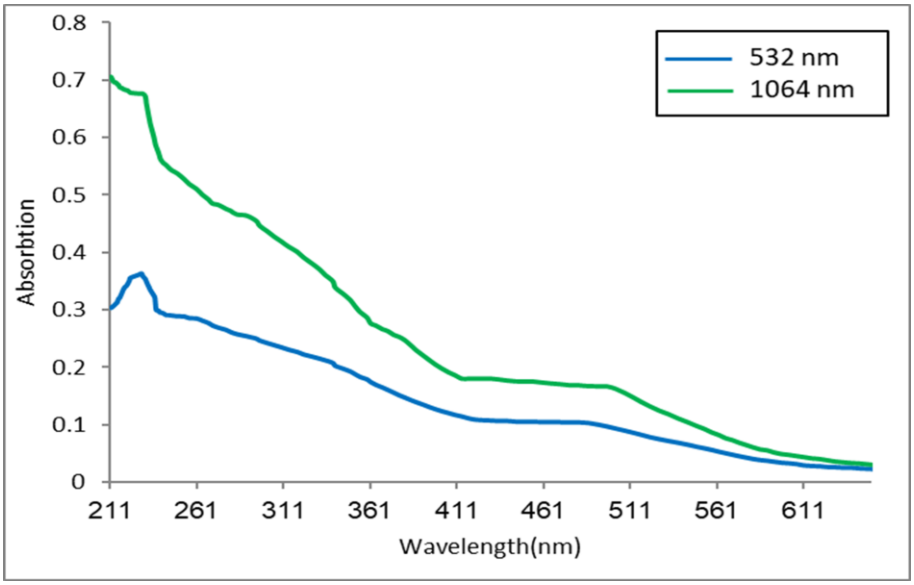

Figure 1. Fe@Au NPs colloidal in DDW absorption spectra at different laser wavelength.

solution with laser pulses and different laser wavelength (532, 1064) nm (Table. 1). Figure (1) shows absorption bands, of Fe NPs core peak at 227 and 231nm at wavelength (532, 1064) nm respectively [25]. Au nanoshell surface plasmon resonance appeared at 502 and 508 nm at wavelength (532, 1064) nm respectively [22]. By increasing particle size carves were showed a redshift toward wavelengths longer [26].

3.2. Core-shell Fe@Au NPs morphological characteristics

Figure (2) shows a uniform distribution excellently of NPs spherical in the nanoparticles synthesized [27]. Fe@Au core-shell NPs SEM images at laser wavelength 532 nm are shown in figure (2-a). The images showed the synthesized nanoparticles' average sizes of 67.65 nm. Figure (2-b) showed the FA-CU-CS-Fe@Au NPs synthesized with an average size of 212.8 nm. To investigate the ability of the gold shell to keep the Fe core from oxidation [28].

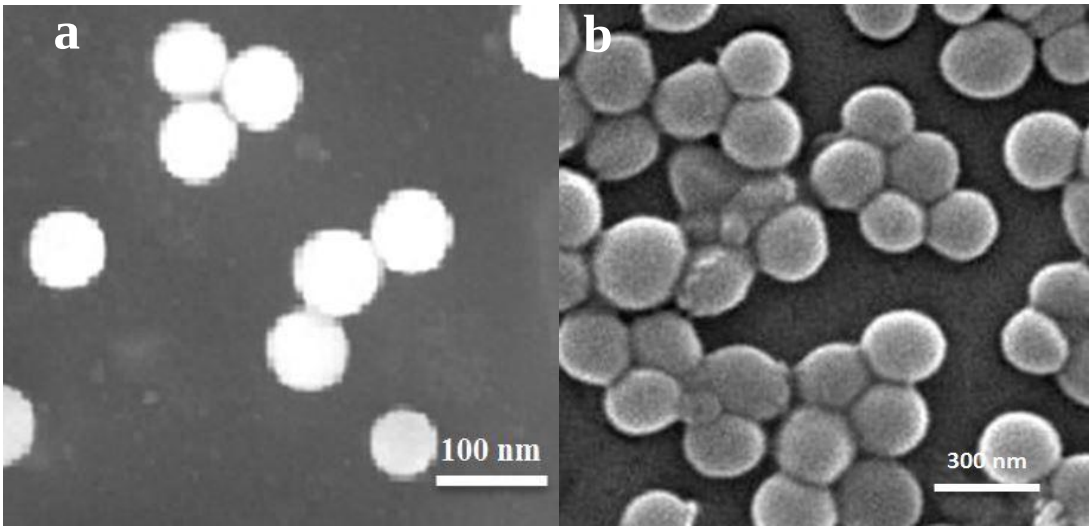

Figure 2. SEM image at laser wavelength 532 nm of (a) Fe@Au NPs, (b) FA-CU-CS-Fe@Au NPs.

Figure (3) illustration micrographs TEM of nanoparticles synthesized with laser wavelength 532 nm. Figure (3) shows Fe@Au NPs core-shell which has a spherical form with around 63.65 nm nearly uniform in size. The Au NPs shell has around 31.18 nm a nearly uniform size. In figure (3) the Fe NPs core was much darker than the gold shell nanoparticles [29, 30].

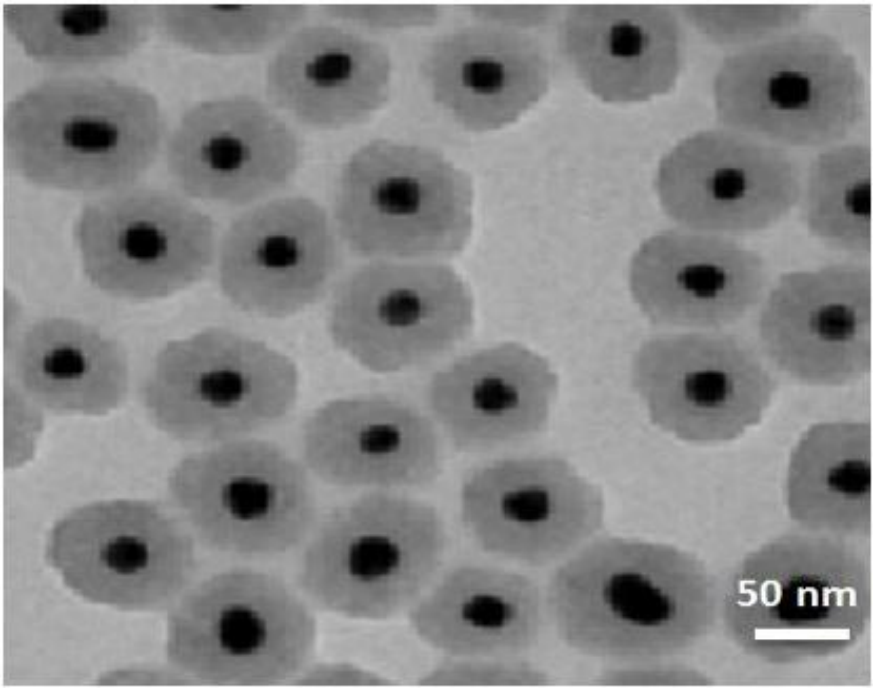

Figure 3. TEM micrographs of Fe@Au NPs at laser wavelength 532nm.

3.2. Release profile

Figure (4) presented for 96 h releases CU from (FA-CU-CS-Fe@Au NPs) and the result shows that the release time is faster at pH (5.4), when compared with pH (7.4). In comparison with free CU release profiles, there are similar release profiles at pH (7.4 and 5.4), under the planned state it noticed a faster CU liberation profile at pH (5.4) compare with pH (7.4) [14].

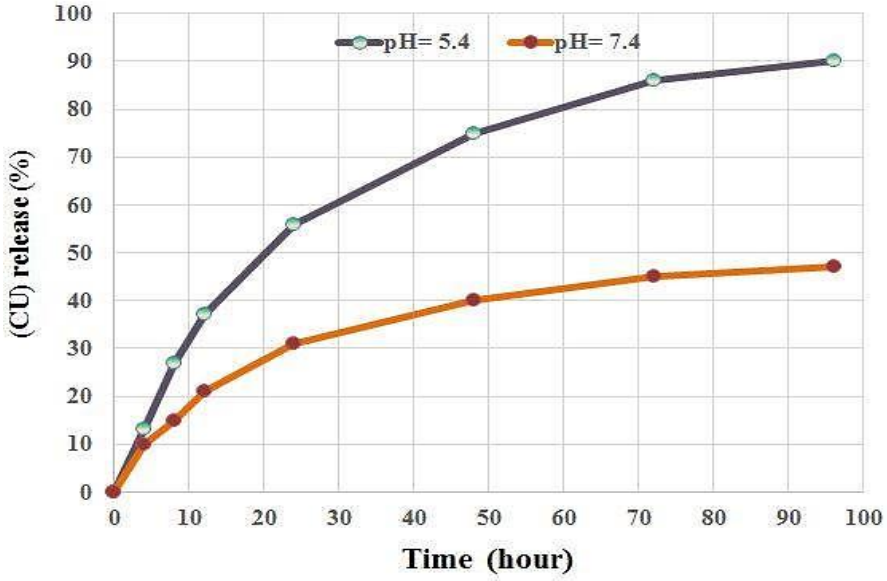

Figure 4. release profile of CU at pH of (7.4 and 5.4)

3.4. Cytotoxicity Assay

By the MTT assay on prostate cancer (PC3) and (RWPE-1) as a normal cell line of curcumin (CU) cytotoxicity effect was evaluated. In a 48 h time, the test was performed as shown in figure (5). At concentrations various of FA-CU-CS-Fe@Au NPs (10-60) μM for 24 and 48 h the cells were treated, but in the case of bare nanoparticle and void, curcumin treating. Then, the cells treating results were evaluated in 48 h time only. Nanoformulation FA-CU-CS-Fe@Au NPs significantly ($P<0.01$) inhibited the PC3 cancer cells growth time, and dose-dependent compared with free CU and bare nanoparticle but didn't show any change remarkable in cell growth and reproduction after treating cancer PC3 and normal RWPE-1 cell lines with treatments. Both bare nanoparticles and free CU therapy didn't indicate any cytotoxic influence remarkable in all used concentrations.

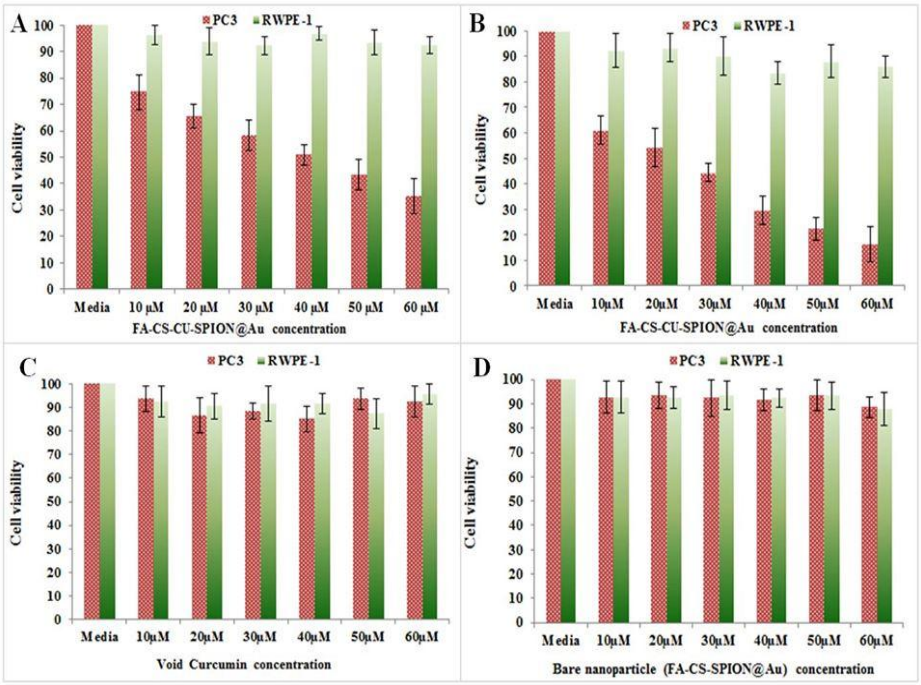

Figure 5. Cytotoxic effect of (10-60 µM) concentrations of FA-CU-CS-Fe@Au NPs after 24 h (A), 48 h (B), and void CU (C) & FA-CS-Fe@Au NPs (D) at 48 h on PC3 and RWPE-1 cell lines.

The FA-CU-CS-Fe@Au NPs IC50 value for PC3 cell lines was 54 µM within 24 h which was reduced relative to 28 µM in 48 h. These data conformed with the similar therapy effects study results of nanoformulation CU in chitosan-coated SPION [15, 29].

Table 1. Process of synthesis Fe@Au NPs

Sample	wavelength nm	particles sized (nm)
1	532	67.65
2	1064	77.88

Conclusion

This study confirmed that the grouping of MNPs with CU as a system to cancer chemopreventive treatment to increase anticancer effects and cytotoxic of CU on the PC3 cell line. In this research, Fe@Au NPs were synthesis by the PLAL method with different laser wavelengths (532, 1064) nm. Creating FA-CU-CS-Fe@Au NPs nanoparticles by encapsulated CU into Fe@Au after changing with CS and FA. Statistical analysis, for the results, represents important increases in quantities of necrosis, apoptosis, and cell death in FA-CU-CS-Fe@Au NPs compared with void CU or bare FA-CS-Fe@Au NPs on PC3 cells. The FA-CU-CS-Fe@Au NPs nano-carriers prepared showed a sustained-releasing behavior, good stability, and small size.

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