

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

¹Maha A. Al-Kinani, ¹Adawiya J. Haider, *²Sharafaldin Al-Musawi

¹Applied Science Department/ Laser branch, University of Technology, Baghdad, Iraq

*²College of Biotechnology, Al-Qasim green University, Babylon, Iraq



Article information

Article history:

Received: April, 11, 2021

Accepted: April, 26, 2021

Available online: April, 26, 2021

Keywords:

Drug delivery,
Nanoparticles,
Chitosan,
Fe@Au NPs,
Nanoformulation

Correspondence:

Sharafaldin Al-Musawi
dr.sharaf@biotech.uoqasim.edu.iq

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.

DOI: [10.53293/jasn.2021.11023](https://doi.org/10.53293/jasn.2021.11023), Department of Applied Science, University of Technology

This is an open access article under the CC BY 4.0 license.

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 ($\lambda = 1064, 532$) nm, R.R = 3 Hz, $\tau = 5$ 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 NPs by 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°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 (500 μ l) 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:

$$R = V \sum n-i C_i + V_0 C_n / m \text{ drug} \quad \text{Eq. (1)}$$

where the drug release final is R, the concentrations of curcumin are C_i and C_n , 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 μ l) 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 μ M) 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 μ l. 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 \pm 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

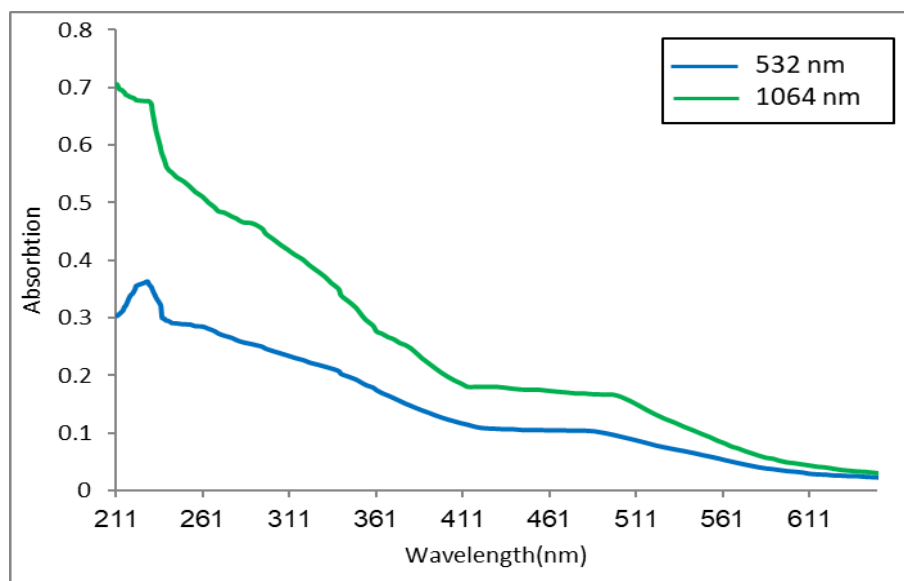


Figure 1. Fe@Au NPs colloidal in DDW absorption spectra at different laser wavelength.

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 curves 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].

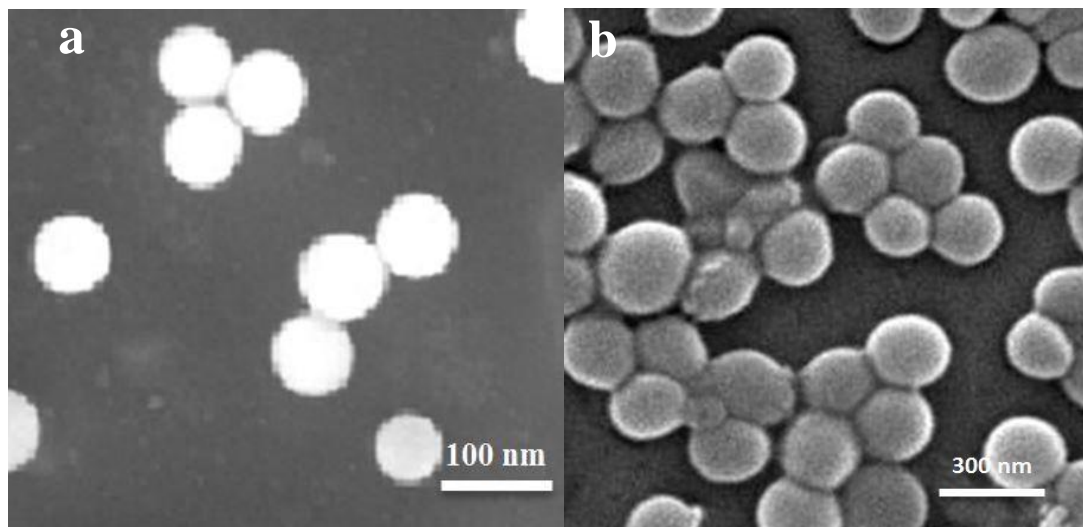


Figure 2. SEM image at laser wavelength 532 nm of (a) Fe@Au NPs, (b) FA-CU-CS-Fe@Au NPs.

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].

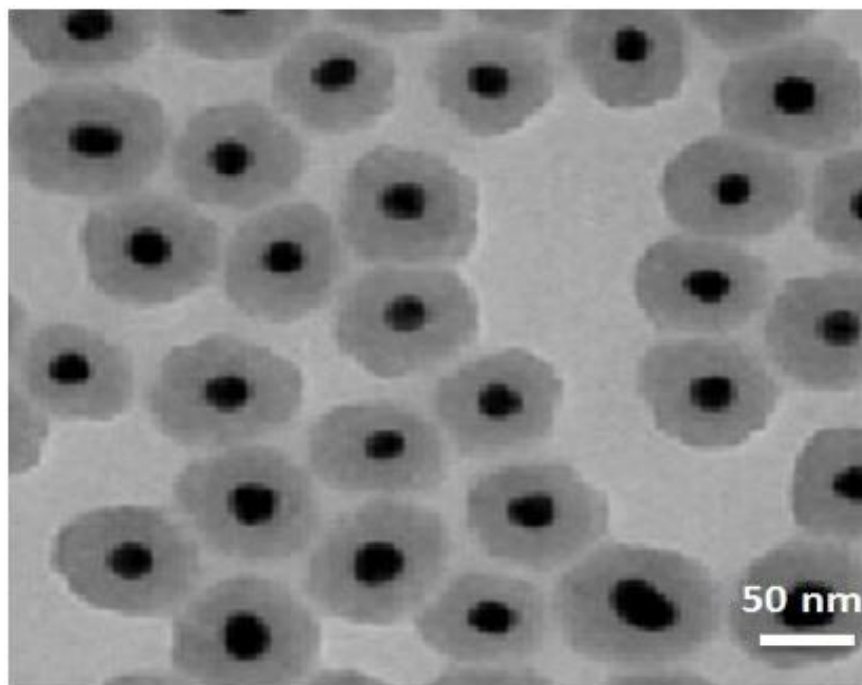


Figure 3. TEM micrographs of Fe@Au NPs at laser wavelength 532nm.

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].

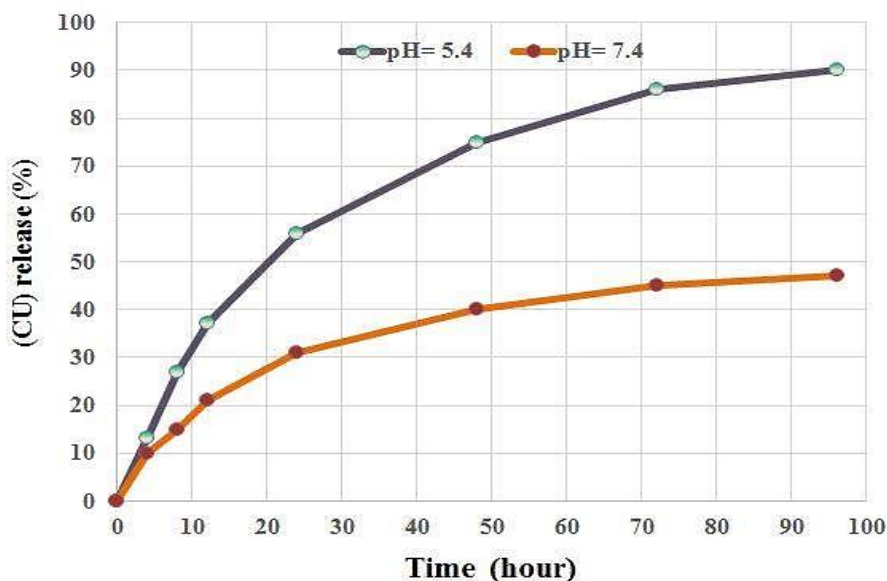


Figure 4. release profile of CU at pH of (7.4 and 5.4)

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) μ M 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.

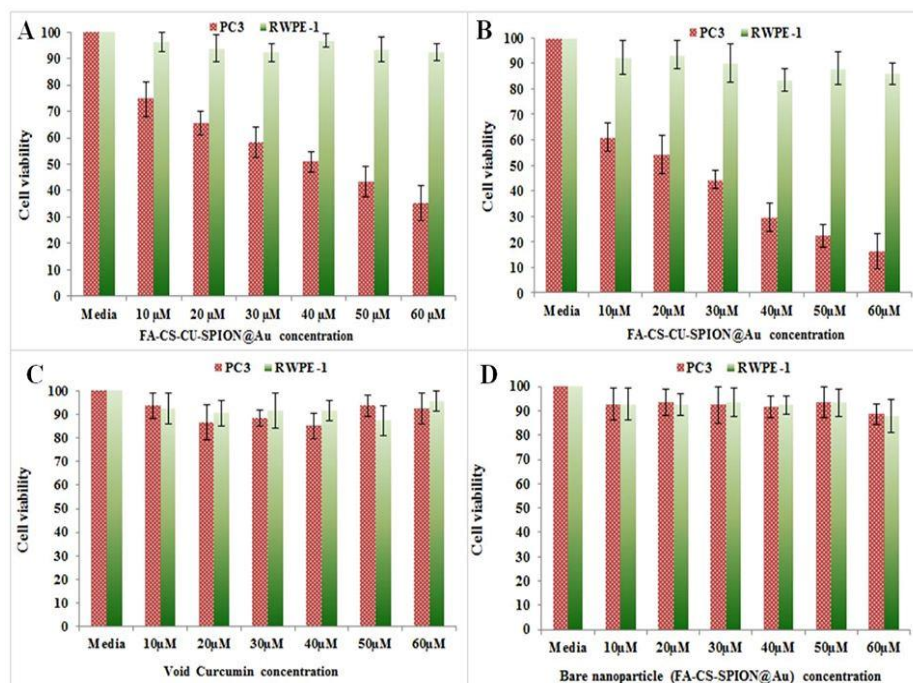


Figure 5. Cytotoxic effect of (10-60 μ M) concentrations of FA-CU-CS-Fe@ Au NPs after 24 h (A), 48 h (B), and void CU (C) & FA-CS-Fe@Au NPs (D) at 48 h on PC3 and RWPE-1 cell lines.

The FA-CU-CS-Fe@Au NPs IC₅₀ value for PC3 cell lines was 54 μ M within 24 h which was reduced relative to 28 μ M 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.

Acknowledgments

The authors acknowledge gratefully the technical support provided by the Genetic Engineering Department, Al-Qasim Green University (Babylon/Iraq), and the Laser Branch, Applied Science Department, University of Technology (Baghdad/Iraq).

References

- [1] Al-Musawi S, Kadhim MJ, Hindi NKK. "Folated-nanocarrier for paclitaxel drug delivery in leukemia cancer therapy". *J Pharm Sci & Res.* 10(4): 749-754, 2018.
- [2] A.Urruticoechea, et al., "Recent advances in cancer therapy: an overview" *Current Pharmaceutical Design Journal*, vol.16 (1) p.p.3-10, 2010.
- [3] M. Chen, S. Yamamuro, D. Farrell, S. Majetich, "Gold-coated iron nanoparticles for biomedical applications" *Applied Physics Journal*, vol.93 p.p.7551-7553, 2003.
- [4] Ma'mani L, Nikzad S, Kheiri-Manjili H, Al-Musawi S, Saeedi M, Askarlou S, Foroumadi A, Shafiee A. "Curcumin-loaded guanidine functionalized PEGylated I3ad mesoporous silica nanoparticles KIT-6: Practical strategy for the breast cancer therapy" *Eur J Med Chem.* 18;83:646-54, 2014. doi: 10.1016/j.ejmech.2014.06.069.
- [5] Y. Zheng, D. Hunting, P. Ayotte, L. Sanche, "Radiosensitization of DNA by gold nanoparticles irradiated with high-energy electrons" *Radiation Research Journal*, vol.169 p.p.19-27, 2008.
- [6] W. Chen, J. Zhang, "Using nanoparticles to enable simultaneous radiation and photodynamic therapies for cancer treatment" *Nanoscience and Nanotechnology - American Journal*, vol.6 p.p.1159-1166, 2006.
- [7] D. Herold, I. Das, C. Stobbe, R. Iyer, J. Chapman, "Gold microspheres: A selective technique for producing biologically effective dose enhancement" *International Journal of Radiation Biology*, vol.76 p.p. 1357-1364, 2000.
- [8] M. Ravichandran, S. Velumani, T. Jose, A. Vera, & L. Leija, "Biofunctionalized MnFe₂O₄@Au core-shell nanoparticles for pH-responsive drug delivery and hyperthermal agent for cancer therapy" *Artificial Cells, Nanomedicine, and Biotechnology An International Journal*, p.p.2169-1401, 2018.
- [9] I. Y. Goon, L. M. H. Lai, M. Lim, P. Munroe, J. J. Gooding, & R. Amal, "Fabrication and dispersion of gold-shell-protected magnetite nanoparticles: systematic control using polyethyleneimine" *Chemistry of Materials Journal*, vol. 21(4) p.p.673-681, 2009.
- [10] W. Wang, J. Luo, Q. Fan, M. Suzuki, I. S. Suzuki, M. H. Engelhard, Y. Lin, N. Kim, J. Q. Wang, and C. Zhong "Monodispersed core-shell Fe₃O₄@Au nanoparticles" *Physical Chemistry B Journal*, vol.109 p.p. 21593-21601, 2005.
- [11] A. Alivisatos, "Semiconductor Clusters, Nanocrystals, and Quantum Dots" *Science Journal*, vol. 271(5251) p.p.933-937, 1996.
- [12] R. Averitt, D. Sarkar, & N. Halas, "Plasmon Resonance Shifts of Au Coated Au₂S Nanoshells: Insight into Multicomponent Nanoparticle Growth" *Physical Review Letters Journal*, vol.78(22) p.p.4217-4220, 1997.
- [13] R. Baer, D. Neuhauser, & S. Weiss, "Enhanced Absorption Induced by a Metallic Nanoshell" *Nano Letters Journal*, vol.4(1) p.p. 85-88, 2004.
- [14] Al-Kinani, M.A., Haider, A.J. & Al-Musawi, S. "High Uniformity Distribution of Fe@Au Preparation by a Micro-Emulsion Method" *IOP Conf. Ser.: Mater. Sci. Eng.* 987 012013, 2020. doi:10.1088/1757-899X/987/1/012013.
- [15] Al-Kinani, M.A., Haider, A.J. & Al-Musawi, S. "Design and Synthesis of Nanoencapsulation with a New Formulation of Fe@Au-CS-CU-FA NPs by Pulsed Laser Ablation in Liquid (PLAL) Method in Breast Cancer Therapy: In Vitro and In Vivo". *Plasmonics.* 2021.; doi: 10.1007/s11468-021-01371-3.
- [16] Al-Kinani, M.A., Haider, A.J. & Al-Musawi, S. "Design, Construction and Characterization of Intelligence Polymer Coated Core-Shell Nanocarrier for Curcumin Drug Encapsulation and Delivery in Lung Cancer Therapy Purposes". *J Inorg Organomet Polym* 31, 70-79, 2021. doi: 10.1007/s10904-020-01672-w.
- [17] Al-Awady MJ, Balakit AA, Al-Musawi S, Alsultani MJ, Ahmed Kamil, Alabbasi M. "Investigation of Anti-MRSA and Anticancer Activity of Eco-Friendly Synthesized Silver Nanoparticles from Palm Dates Extract" *Nano Biomed. Eng.* , 11(2):157-169, 2019. doi: 10.5101/nbe.v11i2.p157-169.

- [18] Al-Musawi S, Hadi AJ, Hadi SJ, Hindi NKK. "Preparation and Characterization of Folated Chitosan-Magnetic Nanocarrier for 5-Fluorouracil Drug Delivery and Studying its Effect in Bladder Cancer Therapy". *J Global Pharma Tech.* 11(7):628-637, 2019.
- [19] Svetlichnyi, V.A., Lapin, I.N. Structure and properties of nanoparticles fabricated by laser ablation of Zn metal targets in water and ethanol. *Russ Phys J* 56, 581–587 ,2013. <https://doi.org/10.1007/s11182-013-0071-z>.
- [20] Sylvestre, JP., Kabashin, A., Sacher, E. et al. Femtosecond laser ablation of gold in water: influence of the laser-produced plasma on the nanoparticle size distribution. *Appl. Phys. A* 80, 753–758, 2005. <https://doi.org/10.1007/s00339-004-3081-4>.
- [21] Mofazzal Jahromi, M., Al-Musawi, S., Pirestani, M., Fasihi Ramandi, M., Ahmadi, K., Rajayi, H., Mohammad Hassan, Z., Kamali, M., Mirnejad, R. "Curcumin-loaded Chitosan Tripolyphosphate Nanoparticles as a safe, natural and effective antibiotic inhibits the infection of Staphylococcus aureus and Pseudomonas aeruginosa in vivo". *Iran J Biotech.*12(3),: e1012, 2014. doi:10.15171/ijb.1012.
- [22] Albukhaty, S.; Al-Musawi, S.; Abdul Mahdi, S.; Sulaiman, G.M.; Alwahibi, M.S.; Dewir, Y.H.; Soliman, D.A.; Rizwana, H. "Investigation of Dextran-Coated Superparamagnetic Nanoparticles for Targeted Vinblastine Controlled Release, Delivery, Apoptosis Induction, and Gene Expression in Pancreatic Cancer Cells". *Molecules*, 25, 4721, 2020. doi: 10.3390/molecules25204721.
- [23] Al-Musawi, S.; Albukhaty, S.; Al-Karagoly, H.; Sulaiman, G.M.; Alwahibi, M.S.; Dewir, Y.H.; Soliman, D.A.; Rizwana, H. "Antibacterial Activity of Honey/Chitosan Nanofibers Loaded with Capsaicin and Gold Nanoparticles for Wound Dressing". *Molecules*, 25, 4770, 2020. doi: 10.3390/molecules25204770.
- [24] Al-Musawi, S; Albukhaty, S.; Al-Karagoly, H.; Sulaiman, G.M.; M S Jabir M.S; Naderi-Manesh H. "dextran-coated superparamagnetic nanoparticles modified with folate for targeted drug delivery of camptothecin" *Adv. Nat. Sci: Nanosci. Nanotechnol*, 11 (4), 2020.045009. doi: 10.1088/2043-6254/abc75b.
- [25] Albukhaty S, Al-Bayati L, Al-Karagoly H & Al-Musawi S. "Preparation and characterization of titanium dioxide nanoparticles and in vitro investigation of their cytotoxicity and antibacterial activity against Staphylococcus aureus and Escherichia coli". *Animal Biotechnology*,28:1-7, 2020. doi: 10.1080/10495398.2020.1842751.
- [26] Javed, B., & Mashwani, Z. U. "Synergistic Effects of Physicochemical Parameters on Bio-Fabrication of Mint Silver Nanoparticles: Structural Evaluation and Action Against HCT116 Colon Cancer Cells". *International journal of nanomedicine*, 15, 3621–3637, 2020. <https://doi.org/10.2147/IJN.S254402>.
- [27] Al-Musawi, S.; Albukhaty, S.; Al-Karagoly, H.; Almalki, F. "Design, and Synthesis of Multi-Functional Superparamagnetic Core-Gold Shell Coated with Chitosan and Folate Nanoparticles for Targeted Antitumor Therapy". *Nanomaterials*. 11, 1, 2020. doi: 10.3390/nano11010032.
- [28] Al-Musawi, S.; Ibraheem, S.; Mahdi, S.A.; Albukhaty, S.; Haider, A.J.; Kadhim, A.A.; Kadhim, K.A.; Kadhim, H.A.; Al-Karagoly, H. "Smart Nanoformulation Based on Polymeric Magnetic Nanoparticles and Vincristine Drug: A Novel Therapy for Apoptotic Gene Expression in Tumor" *Life*. 11, 71, 2021 doi: 10.3390/life11010071.
- [29] Al-Kaabi, W.J.; Albukhaty, S.; Al-Fartosy, A.J.M.; Al-Karagoly, H.K.; Al-Musawi, S.M.; Sulaiman, G.M.; Dewir, Y.H.; Alwahibi, M.S.; Soliman, D.A. "Development of Inula graveolens (L.) Plant Extract Electrospun/Polycaprolactone Nanofibers: A Novel Material for Biomedical Application". *Appl. Sci.*, 11, 828, 2021. doi: 10.3390/app11020828.
- [30] Proceedings of the World Molecular Imaging Congress 2014, Seoul, Korea, September 17-20, 2014. *Mol Imaging Biol* 17, 1–1352, 2015. <https://doi.org/10.1007/s11307-014-0809-1>