

ZnFe₂O₄ nanoparticles for potential application in radiosensitization

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Abstract. Radiosensitizer is a material that can increase the effects of radiation in radiotherapy application. Various materials with high effective atomic number have been developed as a radiosensitizer, such as metal, iron oxide and quantum dot. In this study, ZnFe₂O₄ nanoparticles are included in iron oxide class were synthesized by precipitation method from the solution of zinc nitrate and ferrite nitrate and followed by calcination at 700°C for 3 hours. The XRD pattern shows that most of the observed peaks can be indexed to the cubic phase of ZnFe₂O₄ with a lattice parameter of 8.424 Å. SEM image reveals that nanoparticles are the sphere-like shape with size in the range 84–107 nm. The ability of ZnFe₂O₄ nanoparticles as radiosensitizer was examined by loading those nanoparticles into *Escherichia coli* cell culture which irradiated with photon energy of 6 MV at a dose of 2 Gy. ZnFe₂O₄ nanoparticles showed ability to increase the absorbed dose by 0.5 to 1.0 cGy/g. In addition, the presence of 1 g/L ZnFe₂O₄ nanoparticles resulted in an increase radiation effect by 6.3% higher than if exposed to radiation only. These results indicated that ZnFe₂O₄ nanoparticles can be used as the radiosensitizer for increasing radiation effect in radiotherapy.

1. Introduction

Radiotherapy has been long used in cancer treatment by application of X-ray and high-energy particles radiation. The problem in radiotherapy is the optimization of the cancer cell killing and preserving healthy tissues. One strategy to enhance the cell killing is the use radiosensitizers. Recently, research focused on the development of nanomaterials for radiosensitizer under irradiation with X-ray and high-energy particle. Several nanomaterials have been developed as radiosensitizer ie heavy metal with a high atomic number, iron oxide, and quantum dot [1]. Materials with high atomic numbers can increase the number of secondary electrons formation which can increase the radiation absorbed dose. Gold and gadolinium nanoparticles are heavy metal which commonly used as radiosensitizer [2, 3]. Another radiosensitizer proposed for radiotherapy is an iron oxide which has the ability to increase free radicals formation. Free radicals such as superoxide played the main role in the death of cancer cells indirectly [4, 5].

ZnFe₂O₄ nanoparticles with low toxicity have been intensively studied for medical applications such as hyperthermia treatment [6], magnetic resonance imaging (MRI) [7] and drug delivery [8]. ZnFe₂O₄ nanoparticles were explored as radiosensitizer because it's effective atomic number higher than the effective atomic number of the body's tissues and included in the class of iron oxide [9]. In this study, ZnFe₂O₄ nanoparticles were synthesized by precipitation method. These method has been used for production ZnFe₂O₄ [10-13]. ZnFe₂O₄ nanoparticles were evaluated as a radiosensitizer by measuring



the ability to increase the absorbed dose and loading into *E. coli* culture as the living system to determine the enhancing radiation effect.

2. Experimental

2.1. Preparation of ZnFe_2O_4 nanoparticle

ZnFe_2O_4 nanoparticles were synthesized by precipitation method from the mixed solution of iron nitrate $[\text{Fe}_3(\text{NO})_3 \cdot 9\text{H}_2\text{O}]$ and zinc nitrate $[\text{Zn}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}]$. A stoichiometric amount of iron nitrate and zinc nitrate with molar ratio of 1:2 were dissolved in distilled water. Ammonium hydroxide was used as precipitant and mixed with nitrate solution under magnetic stirring at 80°C and pH until 10. The precipitate was obtained then aged for 2 hours. The solid was filtered and washed with distilled water, dried at 100°C for 2 hours in an oven. The reddish brown solid was calcined at 700°C for 3 hours and grinded in a mortar to obtain fine powder ZnFe_2O_4 nanoparticles.

2.2. Characterization of ZnFe_2O_4 nanoparticles

The structure and phase of ZnFe_2O_4 nanoparticles were characterized by X-ray diffraction (XRD). XRD pattern was obtained using PW 1710 diffractometer. The crystallite size was determined using Scherer formula. Scanning electron microscope (SEM) JEOL JSM-6360 was used to obtain the morphological image of ZnFe_2O_4 nanoparticles.

Absorbed dose measurement was carried out using linac with energy radiation of 6 MV, 2 Gy of dose, SSD of 100 cm, the field $(10 \times 10) \text{ cm}^2$, the position of the detector located at a depth of 1 cm below phantom surface. Furthermore, the absorbed dose was measured without and with ZnFe_2O_4 nanoparticles for the different mass of 1 g, 2 g, 3 g, 4 g and 5 g. ZnFe_2O_4 nanoparticles were placed on the phantom surface and above the sensitive area detector. The ability of ZnFe_2O_4 nanoparticles as radiosensitizer was investigated by loading those nanoparticles into *E. coli* culture and irradiated using the energy of 6 MV with 2 Gy of dose. A number of bacteria survival was calculated using total plate count method.

3. Results and discussion

3.1. Structure and morphology analysis

The XRD pattern of nanoparticles is shown in figure 1. A pattern shows that nanoparticles contain three phases ie most strong peaks can be indexed as high-quality crystalline of ZnFe_2O_4 which is agreement with JCPDS 22-1012. Several peaks can be ascribed from low crystalline of ZnO and Fe_2O_3 phases indicating the obtained nanoparticles is still contained small another phase. However, the obtained value of lattice parameter is 8.424 \AA comparable to the value of 8.427 \AA [14] and 8.429 \AA [15] and close to the value reported in JCPDS 8.441 \AA . Therefore, the major phase of nanoparticles in this study can be referred as spinel cubic structure of ZnFe_2O_4 . Crystallite sizes in the range 11.85 nm to 22.63 nm were obtained by using full width at half maximum (FWHM) of the dominant peaks (220), (311), (511), (440), and (400) to Scherer formula.

The morphology of the ZnFe_2O_4 nanoparticles was observed using SEM image as presented in figure 2. It was found that the prepared nanoparticles consist of spherical clusters with sizes in the range 84.44 nm-106.67 nm.

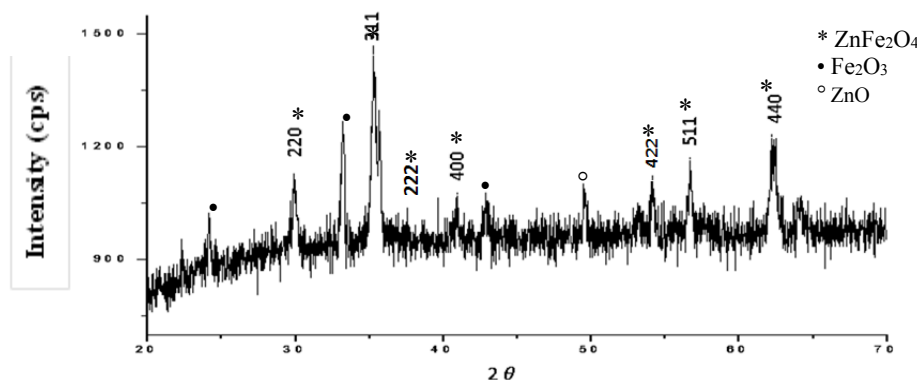


Figure 1. The XRD graphs of ZnFe_2O_4 nanoparticles.

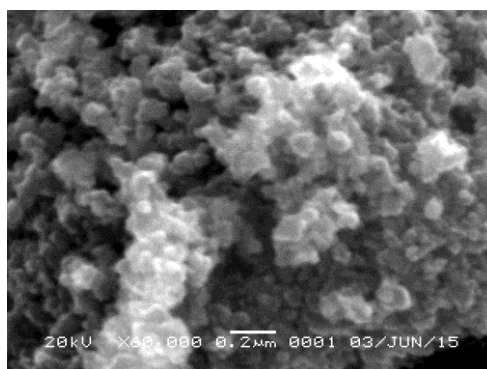


Figure 2. SEM image of ZnFe_2O_4 nanoparticles.

3.2. Radiosensitizer ability study

The increase in absorbed dose by radiosensitizer can enhance radiation effect to the living system. Potential ZnFe_2O_4 nanoparticles as a radiosensitizer can be evaluated from the ability those nanoparticles to increase absorbed dose. The increase in absorbed dose was determined by subtracting the measured absorbed dose without ZnFe_2O_4 nanoparticles to the measured absorbed dose ZnFe_2O_4 nanoparticles for various mass. Figure 3 shows the increase in absorbed dose for the various mass of ZnFe_2O_4 nanoparticles.

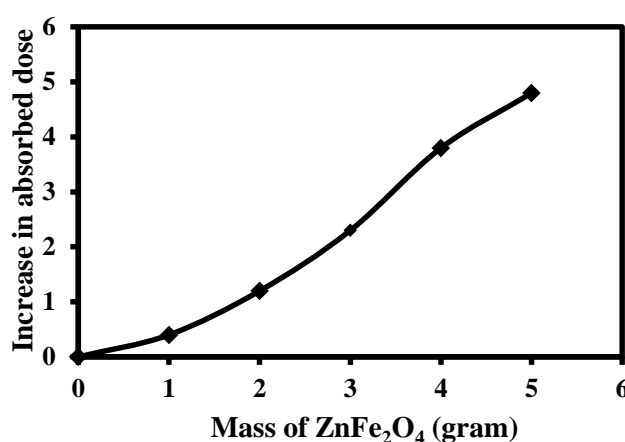


Figure 3. The increase in absorbed dose for various mass of ZnFe_2O_4 nanoparticles.

The increase of absorbed dose increases with increasing mass of nanoparticles ZnFe_2O_4 . It was found that ZnFe_2O_4 nanoparticles exhibited the ability to increase of absorbed dose by 0.5 to 1 cGy/g. 1 Gy absorbed dose can produce 2×10^5 ionization, causing damage to 1000 single-strand DNA breaks and 40 double-strand breaks [16, 17]. This means that the increase in absorbed dose of 1 cGy is equivalent to an increase in ionization of 2×10^3 , 24 single-strand breaks and 1 double-strand breaks. From this view point can be suggested that ZnFe_2O_4 nanoparticles have potential as radiosensitizer.

The influence of ZnFe_2O_4 nanoparticles on the cell killing was investigated by loading those nanoparticles into *E. coli* cultures with various concentrations. The cultures were irradiated with the photon energy of 6 MV at a dose of 2 Gy. It was observed that *E. coli* survival decreases with the addition of ZnFe_2O_4 nanoparticles as can be seen in figure 4. The decrease in the percentage of bacteria survival indicates the addition of ZnFe_2O_4 nanoparticles enhances the radiation effect. Therefore, the radiation effect enhancement determined by subtracting the percentage of bacteria survival with the addition of ZnFe_2O_4 nanoparticles to the percentage of bacteria survival without ZnFe_2O_4 nanoparticles. Figure 5 reveals the radiation effect enhancement for various ZnFe_2O_4 nanoparticles concentrations. The radiation effect enhancement increases with increasing ZnFe_2O_4 nanoparticles concentrations. The addition of 1 g/L ZnFe_2O_4 nanoparticles enhances radiation effect of about 6.3% greater than if the culture exposed to radiation only without an addition of ZnFe_2O_4 nanoparticles. The radiation effect enhancement is occurred due to an increase in the number of free radicals formation because of ZnFe_2O_4 nanoparticles addition. These results suggest that ZnFe_2O_4 nanoparticles can be used as a radiosensitizer.

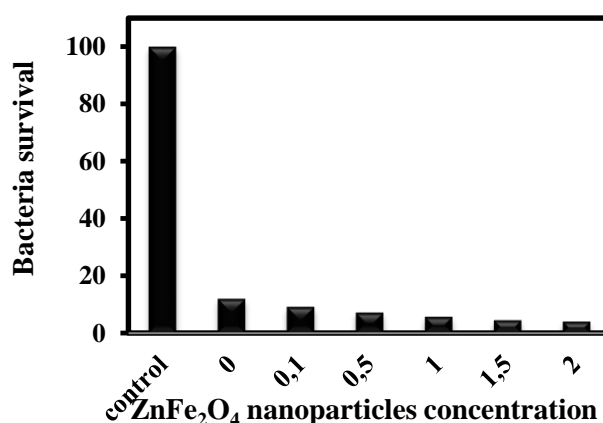


Figure 4. The percentage of bacteria survival for various ZnFe_2O_4 nanoparticles concentrations.

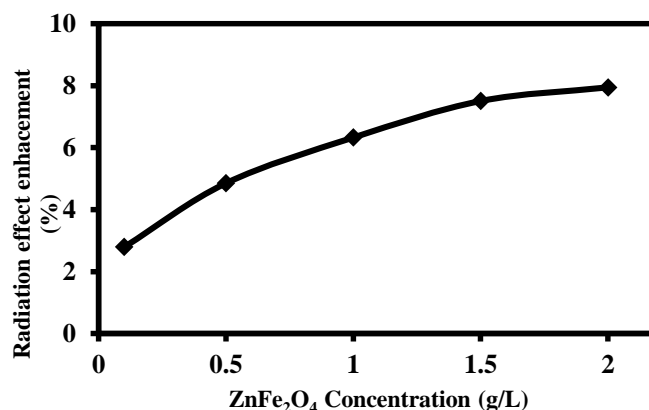


Figure 5. The radiation effect enhancement for various ZnFe_2O_4 nanoparticles concentrations.

4. Conclusions

ZnFe₂O₄ nanoparticle was synthesized by precipitation method. It has been found that nanoparticle is spinel structure with crystallite size in the range of 11.85 to 22.63 nm and spherical in shape. ZnFe₂O₄ nanoparticle was used as radiosensitizer which exhibited improve absorbed dose ability of 0.5–1 cGy/g. The use of ZnFe₂O₄ nanoparticle with concentration 1 g/L resulted in an increase in the effect of radiation by 6.3%. Therefore, the nanoparticles ZnFe₂O₄ exhibited potential as a radiosensitizer for radiotherapy application.

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