Antioxidant-activity-and-dose-enhancement-factor-of-CeO-nanoparticles-synthesized-by-precipitation-method2018IOP-Conference-Series-Materials-Science-a

by Agus Subagio

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Antioxidant activity and dose enhancement factor of CeO_2 nanoparticles synthesized by precipitation method

I Nurhasanah[1], W Safitri[1], Z Arifin[1], A Subagio[1], and T Windarti[2]

[1] Department of Physics, Faculty of Science and Mathematics, Diponegoro University
[2] Department of Chemistry, Faculty of Science and Mathematics, Diponegoro University, Prof. H. Soedarto St., S.H., Semarang 50275, Indonesia

nurhasanah@fisika.undip.ac.id

Abstract. CeO_2 nanoparticles (CeO_2 NPs) have been considered as promising antioxidant and radioprotectant due to its mixed valence state that can prevent cell damage induced by ionizing radiation. The aim of this study is to investigate the antioxidant activity and dose enhancement factor (DEF) of CeO_2. The NPs were synthesized by using a precipitation method. The structure of CeO_2 NPs was characterized with an X-ray diffractometer (XRD). The antioxidant activity of CeO_2 NPs was analyzed by the reduction of 1,1-diphenyl-2-picrylhydrazil (DPPH) stable free radical using UV-vis spectroscopy. The dose enhancement factor (DEF) of CeO_2 NPs was examined using X-ray radiation with an energy of 6 MV. The radioprotective ability of CeO_2 NPs was evaluated by mixing CeO_2 NP suspension with *E. coli* and exposing it to X-ray radiation with a dose of 2 Gy. The XRD pattern analysis reveals that CeO_2 NPs possess a cubic fluorite structure. CeO_2 NPs show activity with IC50 value of 4.4 mg/ml. CeO_2 NPs also show the ability to absorb X-ray radiation with DEF value < 1 and reduce the *E. coli* damage induced by X-ray radiation. The amount of irradiated *E. coli* in the presence of 0.2 mg/ml CeO_2 NPs was found to be 23 times larger than that irradiated *E. coli* in the absence of CeO_2 NPs.

1. Introduction

The application of nanoparticles in radiotherapy has been a subject of considerable interest. Radiotherapy is the reliable way for cancer treatment by exposing cancer cells to ionizing radiation. During radiotherapy of cancer, the ionizing radiation resulted in an increased rate of not only cancer cell death but also normal cell death. The main challenge in the cancer therapy is to increase the radiation ability to kill cancer cells by increasing the dose effectiveness and minimizing damage to the surrounding normal cells. The dose effectiveness to kill cancer cells could be increased by using radiosensitizer, while radioprotector is used to protect normal cell [1-3]. Many free-radical scavengers or antioxidants have been investigated and used to overcome the effects of radiation on normal cell. Amifostine is the only compound as radioprotector recommended by US FDA (Food and Drug Administration) [4, 5]. However, this compound has limitations due to short life and poor penetration to the location where the free radicals produced.

The current nanotechnology makes it possible to develop a variety of nanoparticles tobe used for biomedical application with superior properties. Nanoantioxidants, including inorganic nanoparticles have shown promise as high-performance therapeutic nanomedicine in attenuating oxdative stresses. However, the small size and large surface area of nanoparticles resulted in particles aggregation and led

to difficulty in the handling of nanoparticles in liquid [6]. A few metal oxides nanoparticles were reported as antioxidants, including TiO_2 [7], ZnO [9-11], and CeO_2 [12-17]. Among metal oxide nanoparticles, applications of CeO_2 nanoparticles (CeO_2 NPs) in biomedical have experienced growing attention due to lower toxicity than the other oxide nanoparticles that commonly investigated such as TiO_2 and ZnO. Furthermore, CeO_2 nanoparticles are known as catalysts that have pharmacological potential and promising therapeutic agent. The redox reaction that occurs between Ce^{3+} and Ce^{4+} with superoxide and oxidizing hydrogen peroxide are similar to the behavior of antioxidant enzymes [18, 19]. The antioxidant properties of CeO_2 NPs are determined by the presence Ce^{3+} which depend on shape, size, valence states and synthesis method [13-15].

This paper describes the antioxidant activity and dose enhancement factor of CeO_2 NPs synthesized by precipitation method. The antioxidant activity of nanoparticles CeO_2 was examined using DPPH method. The dose enhancement factor of CeO_2 NPs was determined using the absorbed dose of X-ray radiation measurement. The capability of CeO_2 NPs as radioprotector was evaluated by loading those CeO_2 NPs into *E. coli* culture under X-ray irradiation.

2. Experiment

The CeO_2 NPs were synthesized by precipitation method from cerium nitrate solution as described in previous report [20]. The solution of 0.08 M cerium nitrate (Sigma-Aldrich) was prepared in demineralized water/isopropanol mixed solvent with a volume ratio of 1:6. NH_4OH was then added drop by drop under stirring into the solution until a pH value of 10 was reached. Precipitates were repeatedly washed by isopropanol. The precipitates were then dried at 60 °C for 2 hours and calcined at 500 °C for 2 hours.

The crystallinity and phase of CeO_2 NPs was characterized by X-ray powder diffractometry (XRD) with Cu K_α radiation (λ = 1.54060 A). UV-Vis transmittance of the CeO_2 NPs was examined using UV-Vis spectrophotometer. Antioxidant activity of CeO_2 NPs was evaluated using DPPH (1,1-diphenyl-2-picrylhydrazyl) radical scavenging method. The suspension of CeO_2 NPs with different concentration (1.5, 3.0, 4.5, 6.0, 7.5, and 9.0 mg/mL) were sonicated using sonicator bath at room temperature for 10 minutes to avoid agglomeration. The absorbance of samples (the mixture of CeO_2 NPs and DPPH solution) and control (DPPH solution without CeO_2 NPs) were measured by UV-Vis spectrophotometer. The ability of CeO_2 NPs to scavenge DPPH radical was calculated using equation (1). Furthermore, the required concentration to inhibit 50% of DPPH (IC_{50}) was determined by linear regression.

$$\% \text{ inhibition} = \frac{A_c - A_s}{A_c} \times 100\% \quad (1)$$

To investigate dose enhancement factor (DEF), the absorbed dose of CeO_2 NPs with various mass of 0,5 g, 1 g, 2 g, and 2,5 g was measured using detector. Measurements were made for photon energy of 6 MV and dose rate of 200 cGy/min, SSD of 100 cm, the field size of (2x2) cm^2, and detector position at 1 cm below phantom surface. The absorbed dose was measured in the absence and in the presence of CeO_2 NPs. The dose enhancement factor (DEF) was defined as ratio of radiation dose in the presence of CeO_2 NPs to radiation dose in the absence of CeO_2 NPs.

The protection effect of CeO_2 NPs was investigated by mixing CeO_2 NPs suspension with *E. coli* culture at various concentrations in the range 0.02 to 0.1 mg/mL. The *E. coli* cultures were irradiated by using a photon energy clinical linear accelerator (LINAC) of 6 MV X-ray with a dose rate of 200 cGy/min, a depth of 10 cm and source-to-surface distance (SSD) of 90 cm. The number of live *E. coli* was determined by using total plate count method.

3. Results and discussion

The X-ray diffraction (XRD) pattern of CeO_2 NPs synthesized using precipitation method is shown in Figure 1. The XRD pattern reveals that the prepared nanoparticles are polycrystalline of cubic fluorite

CeO_2 structure. Four preferred diffraction peaks at the 2θ values of about 28.46°, 32.97°, 47.44° and 56.18° are observed corresponding to (111), (200), (220), and (311) planes, respectively. Those diffraction peaks are in good agreement with the Joint Committee on Powder Diffraction Standard (JCPDS) No. 34-0394. No other peaks related to impurities or other phases are detected in the XRD pattern which confirmed the prepared CeO_2 NPs are single phase crystalline of CeO_2. This result was confirmed by Rietveld refinement as shown in Figure 1(b). The Rietveld refinement shows good agreement between experimental and simulated XRD pattern with the refinement factors being R_{wp} 9.6 % and R_p = 7.55% with the goodness-of-fit (χ^2) = 1.146. The refined cell parameter of CeO_2 NPs is 5.419 Å which is slightly larger than that of bulk CeO_2 (5.411 Å) indicating the prepared CeO_2 NPs consist of nanocrystallite. The crystallite size was calculated using Scherer formula to be about 9 nm.

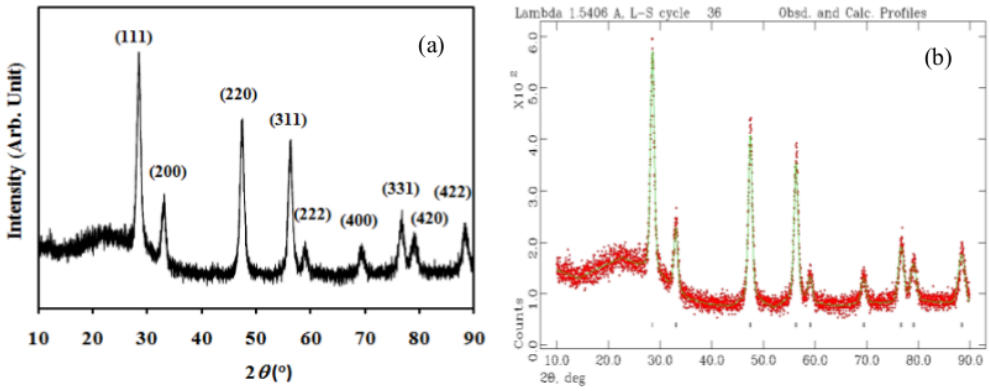

Figure 1. XRD pattern (a) and Rietveld refinement (b) of CeO_2 NPs synthesized by precipitation method.

The UV-Vis absorbance spectrum of the CeO_2 NPs is shown in Figure 2. The peak of absorbance was observed at wavelength of 207 nm and 303 nm corresponding to characteristic absorption peak of Ce^{3+} and Ce^{+4} of CeO_2 NPs. The sprectrum reveals that CeO_2 NPs consist of Ce^{3+} and Ce^{4+} ions. The present of Ce^{3+} ion has an important role on the antioxidant activity of CeO_2 NPs [14].

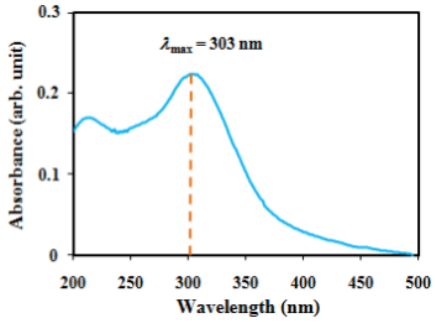

Figure 2. Absorbance spectrum of CeO_2 NPs.

In this study we use DPPH as a stable free radical to determine the radical scavenging activity of CeO_2 NPs. The absorbance of DPPH decreased due to the scavenging of DPPH by donation of electron

or hydrogen from antioxidant substance to form the stable DPPH molecule. The radical scavenging activity values were expressed as percentage of inhibition as ratio of percentage of sample absorbance decrease and the absorbance of DPPH solution in the absence of antioxidant substance at absorption peak of DPPH (λ = 520 nm). Figure 3 shows radical scavenging activity of CeO_2 NPs. The inhibition of DPPH increased up to 67% at concentration of CeO_2 NPs of 9 mg/mL. In another study, CeO_2 NPs prepared by co-precipitation method and coated by polysaccharide showed DPPH scavenging activity with % inhibition of 85% [13] whereas, CeO_2 NPs prepared by hydrothermal and solvothermal methods showed DPPH scavenging activity up to 55% and 30% respectively [15]. The DPPH scavenging activity of our CeO_2 NPs is smaller than levan-coated CeO_2 NPs, but higher that that CeO_2 NPs prepared by hydrothermal and solvothermal methods. The CeO_2 NPs posses antioxidant activity with IC_{50} value of 4,38 mg/ml. The CeO_2 NPs exhibited the higher antioxidant activity than ZnO nanoparticles (IC50 ~ 8 – 10 mg/mL) that reported in the literature [9-11]. The antioxidant properties of CeO_2 NPs would be explained as due to transfer of electron from CeO_2 NPs to odd electron located at nitrogen atom in DPPH.

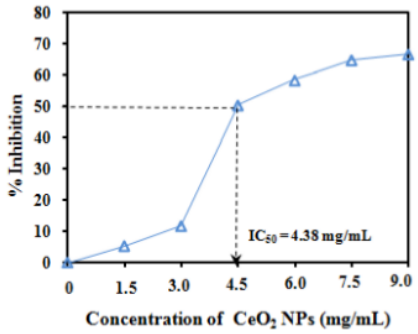

Figure 3. Radical scavenging activity of CeO_2 NPs.

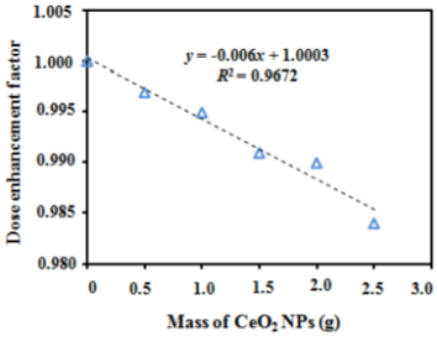

Figure 4. Dose enhancement factor for various mass of CeO_2 NPs.

Figure 4 depicts the dose enhancement factor (DEF) for various mass of CeO_2 NPs. The DEF values of CeO_2 NPs were 0.984 to 0.997 (DEF < 1). The DEF value decreased linearly as increase in mass of CeO_2 NPs. Its show the addition of CeO_2 NPs can decrease absorbed dose of about 1.2 cGy/g. The CeO_2 NPs are potent as radioprotector for preventing normal cell damage induced by X-ray radiation.

The protective effect of CeO_2 NPs was evaluated to protect *E. coli* from damages induced by X-ray radiation. Figure 5 demonstrates the protective effect of CeO_2 NPs. It can be seen that protective effect depends on concentration of CeO_2 NPs. X-ray radiation with dose of 2 Gy killed 98.92% *E. coli*. The increase in the amount of *E. coli* was found in *E. coli* treated with the presence of CeO_2 NPs. At the condition with addition of 0.02 mg/mL CeO_2 NPs, the amount of *E. coli* increased by 23 times larger than that irradiated *E. coli* without addition of CeO_2 NPs. These results suggested that CeO_2 NPs reduced the amount of *E. coli* death and protected *E. coli* damage induced by X-ray radiation. The amount of *E. coli* death increased with the increase in concentration of CeO_2 NPs. The CeO_2 NPs can reduce *E. coli* damage with concentration up to 0.06 mg/mL. However, the addition of CeO_2 NPs with concentration larger than 0.06 mg/ml did not act as radioprotector but as radiosensitizer. The protective effect mechanism of CeO_2 NPs is physical protection due to its ability to absorb radiation as described by DEF value < 1 and chemical protection through neutralization of reactive oxygen species (ROS) produced by radiolysis of water during irradiation [16]. The main protection mechanism that plays a role in our CeO_2 NPs is chemical protection. It is generally attributed to oxygen vacancy corresponding to surface Ce^{3+} fraction and/or Ce^{3+}/Ce^{4+} redox switch.

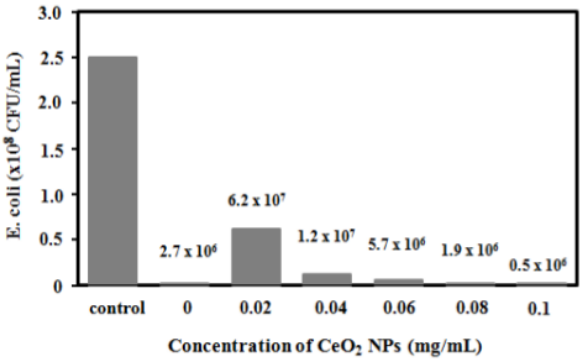

Figure 5. The number of X-ray irradiated *E. coli* with the presence of CeO_2 NPs at various concentration.

4. Conclusion

We have investigated the antioxidant activity and dose enhancement factor of CeO_2 NPs synthesized by precipitation method. The CeO_2 NPs possess good antioxidant activity and can reduce absorbed dose of X-ray radiation. The CeO_2 NPs with concentration of no more than 0.06 mg/ml show a protective effect on *E. coli* damage induced by X-ray radiation. These results indicated that CeO_2 NPs synthesized by precipitation method are a potent radioprotector. However, its effectiveness should be further investigated.

Acknowledgment

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