The Effect of Addition of $\text{Fe}_3\text{O}_4$ and Sintering Temperature on Properties of the Magnetite/Hydroxyapatite Particles Produced through the Coprecipitation Technique

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Abstract. Nowadays, the composite of magnetite/hydroxyapatite has become one of the main topics in biomedical field especially as drug delivery system. In this paper, the effect of sintering temperature and $\text{Fe}_3\text{O}_4$ addition on the properties of coprecipitation produced by magnetite/hydroxyapatite composite is investigated. The magnetite was first dispersed into 100 mL aqua dest and mixed with 33.7 mmol Ca(NO$_3$)$_2.4\text{H}_2\text{O}$ while stirring for 15 minutes. Subsequently, the mixture was reacted with 20 mmol (NH$_4$)$_2\text{HPO}_4$ for 120 minutes at 90ºC. The mixture pH of 11 during process was controlled by adding NH$_4$OH 25%. The mixture was left to stand for 1 day, washed and then the precipitate was separated from the mixture. The precipitate was dried at 90ºC for 1 day and it ended with sintering for 2 hours. The composite powder was characterized by field emission scanning electron microscopy (FESEM), X-ray diffraction (XRD), and vibrating sample magnetometer (VSM). The result showed that increase in the amount of of $\text{Fe}_3\text{O}_4$ in the composite, it produced the larger crystalline $\text{Fe}_3\text{O}_4$ size of 15.59 nm, a decrease in crystallinity to 14.22%, and a higher saturation magnetization was 17.2 emu/g. The higher sintering temperature causes an increase in the size of a hydroxyapatite crystal to 22.94 nm, an increase in crystallinity to 22.55%, and a lower saturation magnetization was 4.0 emu/g.

1. Introduction
Drug delivery system is a technology that exemplifies drug delivery for targeted delivery and controlled the release of drugs. Even though, drugs are increasingly improving, yet there is still side effect even the most sophisticated molecular biology strategies due to the interaction of the body part that are not the target of the drugs. This is one of the reasons that limits the further development of drugs for various diseases such as cancer, neurodegenerative diseases, and infectious diseases [1].

Iron oxide has become one of the main topics in biomedical engineering because it has good potential as drug delivery agent. Iron oxide can provide using magnetic resonance imaging (MRI) which can be directed or held on some point with the help of magnetic field [2]. Unfortunately, when it is used directly as drug delivery agent, it will be biofouling in blood plasma and leading to formation of aggregates, which triggers the reticular endothelial system to segregate it. Therefore, there is a need to modify the iron oxide to minimalize the biofouling and aggregation [3].
Calcium phosphate has been accepted as bioactive and biodegradable material, because hydroxyapatite does not have high toxicity and very good at ion exchange. Besides, hydroxyapatite consist of inorganic component that can be found in the bone hard tissue and shows excellent biocompatibility with bone tissues [4]. Several studies have been reported, Gu et al [5], has successfully synthesized composite magnetite/hydroxyapatite with the combination of gas-liquid chemical preparation and hydrothermal method. The result indicates that the composite had a large specific surface area, high pore volume, and good magnetic separability. It is suitable for targeted drug delivery systems. Liu et al [6], has develop magnetite/hydroxyapatite nanoparticles through homogeneous precipitation method. The magnetite/hydroxyapatite nanoparticles calcined at 400°C possess good magnetism and photocatalytic activity in comparison with other calcined temperature. Sato and Nakahira [4], examine about the effect of Fe addition to hydroxyapatite. The powder obtained that granular crystals with a diameter 10 nm and most of Fe additions is presented as iron oxide phase at the surface of hydroxyapatite particles. This paper reported the effect of sintering temperature and the amount Fe$_3$O$_4$ on the properties of the Fe$_3$O$_4$/hydroxyapatite composites synthesized by the coprecipitation method.

2. Materials and Method
2.1 Materials
Materials used in this research were FeCl$_2$.4H$_2$O (Merck, Germany), FeCl$_3$.6H$_2$O (Merck, Germany), Ca(NO$_3$)$_2$.4H$_2$O (Merck, Germany), (NH$_4$)$_2$HPO$_4$ (Merck, Germany), NH$_4$OH solution (Merck, Germany).

2.2 Methodology
The magnetite was synthesized using Liu et al [6] method as reference by mixing 18.5 mmol FeCl$_2$.4H$_2$O and 37 mmol FeCl$_3$.6H$_2$O and into this mixture 25% NH$_4$OH solution was slowly dropped until the pH was maintained at 10. The reaction mixture then was heated at 90°C for 90 min and then it was cooled down until room temperature. The precipitate from the reaction then separated by magnetic separation, washed with aquadest, and then dried at 120°C in the oven.

The composite was synthesized using Liu et al [6] method that described as follows, the magnetite obtained from the previous synthetic was then dispersed in 100 ml aquadest. Therefore, into this solution 33.7 mmol Ca(NO$_3$)$_2$.4H$_2$O (10%, 15%, and 20% mol Ca(NO$_3$)$_2$.4H$_2$O) was added then mixed for 15 min and continued by adding 20 mmol (NH$_4$)$_2$HPO$_4$. Into this mixture 25% NH$_4$OH solution was slowly dropped until the pH was maintained at 11. The reaction took place for 120 min at 90°C and then it was cooled down until room temperature. The precipitate was then separated by magnetic separation, washed with aquadest, and then dried at 120°C in the oven. After that, the composite was sintered at 200, 400, 600, 800 °C.

2.3 Characterization Technique
The crystalline phases of composites magnetite/hydroxyapatite were analyzed using powder X-ray diffraction (XRD). The morphology of the composites magnetite/hydroxyapatite was observed using field emission scanning electron microscopy (FESEM). Vibration sample magnetometer (VSM) was used to determine the saturation magnetization value of the sample.

3. Result and Discussion :
3.1 Visual Analysis
The colour of synthesized magnetite powder with coprecipitation method is black. The magnetite deposit that produced is magnetic properties, because when it is brought close to an external magnet, the resulting precipitate interacts with an external magnet. Figure 1(a) is the condition of the magnetite solution before being exposed to an external magnet. After the 20 seconds, the magnetite will be completely attracted by the magnet within a span of 20 seconds as shown in Figure 1(b). The magnetic properties of a precipitate appear when it is exposed to an external magnet and then disappear when
the magnetic field is removed. This shows that the magnetite samples produce superparamagnetic properties, namely materials that contain a magnetic moment and can be strongly attracted by a magnet.

![Figure 1](image1.png)

**Figure 1.** The obtained magnetite was dispersed in water (a), and the magnetite particles was perfectly attracted by external magnet (b).

Teja and Koh [7] asserted that magnetite had black pigment, so it is known as black iron oxide. The dispersed magnetite as shown in Figure 1(a) will be attracted gradually by the external magnetic field and will be completely attracted in 20 seconds as shown in Figure 1(b). Magnetic properties of magnetite is superparamagnetic which is the material can be strongly attracted by magnet.

### 3.2 X-Ray Diffraction (XRD) Analysis

The X-ray diffraction pattern was used to analyse the samples composition and crystal characterization. Figure 2 shows XRD patterns of magnetic/hydroxyapatite sintered is at 400°C and the composition of Fe₂O₃ are 10%, 15%, and 20% mol Ca(NO)₃.4H₂O. It can be seen that there is an influence from the composition of Fe on composite properties that produced. The highest intensity of hydroxyapatite is densest at 10% Fe composition with a peak height of 990.91 cts of hydroxyapatite and a peak height of magnetite is 180.11 cts, it is followed by a composition of 15% and 20% Fe at 814.14 cts and 697.24 cts for hydroxyapatite, while for magnetite it is obtained 365.16 cts and 434.82 cts. A high intensity peak indicates that the sample has high crystallinity and a wide peak indicates that the sample is nanometers in size. Therefore, it can be concluded that the composition of 10% Fe has better crystallinity of hydroxyapatite than 15% Fe composition and 20% Fe composition. The decrease in the peak intensity of hydroxyapatite at the composition of 15% Fe and 20% Fe composition occurred because the percentage of the resulting magnetite content is more than the 10% Fe composition. The percentage of magnetite content is increased with the increase in the percentage of Fe composition. Liu et al. [6] said that the more magnetite content causes a decrease in the peak intensity of hydroxyapatite and an increase in the intensity of magnetite.
**Figure 2.** X-ray diffraction of magnetite/hydroxyapatite composite for Fe₃O₄ amount of (a) ICDD Ha; (a) 10%; (b) 15%; (c) 20% after sintered at 400°C

Figure 3 shows that XRD patterns of magnetic/hydroxyapatite with 15% Fe₃O₄ sintered at 200, 400, 600, and 800°C. It can be seen that the peak intensity of hydroxyapatite will increase by increasing sintering temperature.

The XRD analysis also indicated that when the sintering temperature below 400°C the peaks at 2θ = 30.03°; 35.36°; 43.68°; 47.49°; and 62.92° were in agreement with those of pure magnetite nanoparticles (JPCDS no 19-0629) and the peaks at 2θ = 25.89°; 31.65°; 32.97°; 34.01°; and 49.54° were in agreement with those of pure hydroxyapatite nanoparticles (JPCDS no 9–0432). When the sintering temperature was higher than 400°C (600°C and 800°C), magnetite peaks disappeared and new peaks were detected. The new peaks were maghemite, so it can be said that magnetite transforms to hematite at sintering temperature above 400°C. These results were in agreement with that reported by Liu et al [6].

**Table 1.** Crystallinity degree of magnetite/hydroxyapatite composite

| Fe₃O₄ Composition | Sintering Temperature | Degree of Crystallinity |
|------------------|-----------------------|-------------------------|
| 10%              | 200                   | 17.16                   |
|                  | 400                   | 18.76                   |
|                  | 600                   | 19.92                   |

3.2.1 **Effect on Degree of Crystallinity**

Karavelidis et al [8] investigated the effect of crystallinity in polyester nanocarriers on drug release behaviour, it is said that degree of crystallinity is one of the important parameter. From Table 1, it can be seen that the peak of the composite magnetite/hydroxyapatite is getting lower along with increase in the composition of Fe₃O₄ in it. It means that the increase of the composition of Fe₃O₄ used in the composite affect the crystallinity of the magnetite/hydroxyapatite composite. When the XRD analysis was used to calculate the degree of crystallinity of the sample, it can be seen that at the composition of Fe₃O₄ was 10% and the sintering temperature is 200°C the sample degree of crystallinity (DOC) is 17.16% but when the composition of Fe₃O₄ was 15% and 20% the sample DOC became 13.16% and 8.72%, respectively. Khan et al [9] reported that in the absence of N₂ when synthesizing magnetite, poorly crystalline magnetite were produced. Thus, it affects the degree of crystallinity of the composite when the Fe₃O₄ composition is increased. Sato and Nakahira [4] reported when the composition of Fe₃O₄ is increased, the crystallinity of the magnetite/hydroxyapatite will be decreased.
In Table 1 it is also shown that when the sintering temperature is increased so then the peaks of the samples are getting sharper and higher. It means that if the sintering temperature increase, it will affect the crystallinity of the magnetite/hydroxyapatite composite. When the XRD analysis was used in observation to calculate the degree of crystallinity of the sample, it can be seen that when the composition of Fe₃O₄ is 15% and the sintering temperature was 200°C the DOC of sample is 13.16% and when the sintering temperature are 400, 600, and 800°C the DOC are 14.22% ; 16.65% and 22.55%. Al-Khazraj et al [10] have reported that when the sintering temperature gets higher, so does the crystallinity of the sample.

3.2.2 Effect on Crystalline Diameter
Scherrer’s equation was used to calculate the crystalline diameter of composite magnetite/hydroxyapatite. The calculation data is shown in Table 2.

Table 2. Crystalline diameter of magnetite/hydroxyapatite composite

| Fe₃O₄ Composition (%) | Sintering Temperature (°C) | Hydroxyapatite (nm) | Magnetite (nm) |
|----------------------|---------------------------|---------------------|----------------|
| 10                   | 200                       | 21.82778            | 14.11461       |
|                      | 400                       | 23.80839            | 14.77753       |
|                      | 600                       | 25.32857            | 16.42845       |
|                      | 800                       | 26.86284            | 18.90964       |
| 15                   | 200                       | 20.08042            | 15.28675       |
|                      | 400                       | 21.4436             | 15.58943       |
|                      | 600                       | 22.35172            | 16.92251       |
|                      | 800                       | 22.93615            | 17.65757       |
| 20                   | 200                       | 19.40209            | 17.33063       |
|                      | 400                       | 19.97549            | 17.54491       |
|                      | 600                       | 20.21124            | 18.1213        |
|                      | 800                       | 21.15066            | 19.22734       |

It can be seen that when the magnetite composition increase, hydroxyapatite crystalline diameter is smaller and the magnetite crystalline diameter is getting bigger. When the sintering temperature is 400°C and the magnetite composition are 10%, 15%, and 20% the hydroxyapatite diameter are 23.81; 21.44; and 19.98 nm. On the other side the magnetite diameter is 14.78; 15.59; and 17.55 nm. The effect of increasing Fe₃O₄ composition causes the crystal size of magnetite also
increase. This result is on agreement with Sato and Nakahira [4] that said when the Fe composition increases, the magnetite crystalline diameter will also increase. From Table 2 it can be seen that when the sintering temperature is increased, the hydroxyapatite and magnetite crystalline also increase. Hydroxyapatite crystalline diameter when the magnetite composition is 15% and the sintering temperature is 200, 400, 600, and 800°C is 20.08; 21.44; 22.35; and 22.93 nm. The magnetite crystalline diameter is 15.28; 15.58; 16.92; and 17.66 nm. The increase in crystalline diameter is due to particle agglomeration [6].

3.3 Field Emission Scanning Election Microscopy (FESEM) Analysis

From the FESEM analysis that is shown in Figure 4, there are two morphologies that can be found. The one is gray colour and the other is black. By the mechanism of the synthetizing composite magnetite/hydroxyapatite that reported by Ansar et al[3], hydroxyapatite will surround the magnetite. So can be concluded that the one with the gray colour and the shapes look like needle, it is mentioned as hydroxyapatite and the black colour is magnetite. This conclusion is on agreement with Liu et al [6] From Figure 4, it can be seen that when the temperature rises from 200°C to 400°C magnetite is increasingly enclosed by hydroxyapatite. So, it can be known that when the temperature rises, it will cause agglomeration in hydroxyapatite particles. This agglomeration is evidenced by the increase of hydroxyapatite particle diameter size from 20.08 nm into 21.44 nm.

**Figure 4.** FESEM analysis on composite magnetite/hydroxyapatite with 15% Fe₃O₄ at sintering temperature of (a) 200°C and (b) 400°C

3.4 Vibrating Sample Magnetometer (VSM) Analysis

Vibrating sample magnetometer (VSM) analysis used to measure the strength of magnets in the samples. Samples magnetization was measured by VSM at 25°C. Figure 5 shows hysteresis curve for magnetite/hydroxyapatite composite and saturation magnetization value of composite.
Figure 5. Hysteresis Curve for Magnetite/Hydroxyapatite composite

In Figure 5 shown the magnetic saturation value \( M_s \) of the composite samples shown different values at different levels of Fe. Saturation magnetization is the maximum magnetization or a condition where an increase in the intensity of the magnetic field \( H \) will not be increased the magnetic field density \( M \). The saturation magnetization value indicates the magnetization power of a material.

Table 3. Saturation magnetization \( M_s \) value of magnetite/hydroxyapatite composite

| Sintering Temperature (°C) | Fe\(_3\)O\(_4\) Composition (%) | Saturation Magnetization (emu/g) |
|---------------------------|-------------------------------|---------------------------------|
| 400                       | 10                            | 12.8                            |
| 400                       | 15                            | 17.2                            |
| 800                       | 15                            | 4.0                             |

The Table 3 shows that saturation magnetization \( M_s \) value of some composite magnetite/hydroxyapatite studied by a vibrating sample magnetometer, when the magnetite ratio in composite was 10% the \( M_s \) of the composite was 12.8 emu/g and when the magnetite ratio was increased into 15% as well as the \( M_s \) of the composite to 17.2 emu/g. So, it can be said that when the magnetite composition in the composite is increased the saturation magnetization also increases. However, when the sintering temperature is increased from 400°C into 800°C the saturation magnetization value is decreased from 17.2 emu/g into 4.0 emu/g. This change occurs due to the transformation of magnetite to maghemite when the sintering temperature is higher than 400°C. Several studies have reported the standard of saturation magnetization value that can be used in drug delivery application is 10 – 30 emu/g [11]. It is assumed that the composite with magnetite composition is 15% and the sintering temperature of 400°C has \( M_s \) that applicable in drug delivery.

4. Conclusion

Synthesis of magnetite / hydroxyapatite composites used the co-precipitation method. The result of XRD pointed out that the obtained composite was of Fe\(_3\)O\(_4\) and HAP. In this research, it can be implied that sintering temperature and magnetite composition in composite magnetite/hydroxyapatite affect the crystallinity and saturation magnetization. The study about the effect of sintering temperature and magnetite composition is essential for the effective implementation in the drug delivery system.
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