Preparation of Biomagnetism Composite Material for Medical Applications

Abdulsalam Khashan Swadi
Directorate of Materials Research, Ministry of Science and Technology/Baghdad
Dr. Thair Latif Muzel
Directorate of Materials Research, Ministry of Science and Technology/Baghdad
Abdulkareem Ibraheem Aboud
Directorate of Materials Research, Ministry of Science and Technology/Baghdad
Email:akswadi@yahoo.com
Dr.Eman Abdulwahed Othman
Directorate of Materials Research, Ministry of Science and Technology/Baghdad

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ABSTRACT

The colloidal non-aqueous precipitation method was used to prepare a biocompatible magnetic ceramic–polymer composite [Hydroxyapatite/ Polyvinylachohol (HAP/PVA)] for medical applications. The starting materials used for preparing hydroxyapatite (HAP) were calcium nitrate and diammonium hydrogen phosphate, while the biodegradable polyvinylachohol (PVA) and nanosized iron oxide particles (γ-Fe_2O_3) were used to generate a biocompatible magnetic gel film. The results showed that the specimens of composite containing up to 30wt% hydroxyapatite didn't explore any of phase separation; further the incorporated of the ferrite enhanced the affectivity and the stability of the composite. The surface morphology and magnetic properties of the gel films were studied and the magnetization measurements were carried out at 5-300K^o. it showed that no remnant magnetization at 300 K^o, but at 5 K^o hysteretic loop was observed leading to confirm that the superparamagnetic nature of the nanosized maghemite particles didn't affect in presence of the polymer and its behavior considered as superparamagnetic material.

Key words: Hydroxyapatite, Hyperthermia, Biodegradable Polymer, Biocompatible

تحضير متراكبات حيوية - مغناطيسية للتطبيقات الطبية

الخلاصة

طريقة الترسيب من المحاليل الرغوية استخدمت لتحضير متراكب (سيرايك- بوليمر) ذو التوافقية الحياتية مع انسجة الجسم في التطبيقات الطبية لحقل ترميم العظام وكذلك للاستفادة من ذلك المتراكب بعد تفعيله مغناطيسيا لعلاج بعض الاورام السرطانية بطريقة العلاج بالمعاملة الحرارية العالية (hyperthermia) . المواد الاساسية في التحضير هي نترات الكالسيوم وثنائي امونيم-فوسفورلانتاج مادة الهيدروكسي ابتايت (HAP) والتي تصنف باعتبارها مادة شبيهة بمادة سيراميك العظام والاسنان ،

وبولي فنيل الكحول (PVA) المصنف كاحد المواد البوليمرية ، واوكسيد الحديدوز (γ-Fe_2O_3) وذلك لجعل المتراكب على هيئة هلامية (gel) وذو صفة مغناطيسية. النتائج بينت ان النماذج المحضرة بنسبة اعلى من 30% من السيراميك (الهيدروكسي ابتايت) لم تضهر اي طور انفصالي لمواد المتراكب المحضر. نتائج فحوصات حيود الاشعة السينية اظهرت المتراكب الناتج بهيئة بلورية متماسكة ومنتظمة وخالية من الشوائب. صور التراكيب المجهرية اظهرت دقة التجانس السطحي للمركب . الخواص المغناطيسية تمت دراستها بقياس حلقة الهسترة عند الدرجات الحرارية من 5-300 كلفن حيث تم ملاحظة منحنى الهسترة عند 5كلفن وهذا يعطي الدليل على الطبيعة المغناطيسية العالية للجسيمات النانوية للهلام المغناطيسي المتكون مع المتراكب حيث لايؤثر وجود البوليمر على الخواص المغناطيسية مما يعطي انطباعا بان المتراكب المحضر يتمتع بصفات مغناطيسية عالية.

الكلمات المفتاحية: الهيدروكسي ابتايت ، العلاج الحراري للسرطان ، البوليمرات القابلة للتحلل ، التوافقية الحياتية

INTRODUCTION

Metals, polymers, and ceramics were used as bone replacement materials. Metals were regarded to be biologically inert, while ceramics and polymers considered as inert or bioactive. Most metals used in surgery were providing assistant for bone without interacting with the surrounding tissues. The currently needing for biomaterials used in bone tissue engineering is not only to create strength but also to explore bioactivity that can interact within tissues without causing any disadvantage effects. So the attributes of bioceramics based on calcium/phosphor and the polymers were making them the most implanted materials in bone tissue engineering (1–6).

It is a well-known that hydroxyapatite (HAP) was used clinically for filling bone defects. So HAP is biocompatible and non-toxic, having a structure similar to natural bone minerals and to form direct bond with bone tissues. For that, in recent years, various kinds of bioactive bone materials were developed to solve this problem (3-6).

Polyvinyl alcohol (PVA) was considered as synthetic biocompatible polymer for it has a large number of hydroxyl groups leaded it to react with several types of functional groups. It is in wide use in the system of sensors and in drug delivery. Bioceramics were able for osteoconductive but extremely brittle. Thus a composite containing bioceramics and biopolymer could offer the osteogenic property and the composite could offer good mechanical properties (7).

Magnetism was found to play in wide applications of health care, as example, the magnetite Fe_3O_4 is biocompatible and therefore considered as one of the most biomaterials benefit to use for various applications ranging from cell separation, drug delivery and hyperthermia. Hyperthermia is a type of cancer's treatment in which body tissue is exposed to high temperatures (up to 42-46°C) to damage and/or kill cancer cells (8-12).

The objective of this research is to explore new approaches to generate highly pure magnetic ceramic/polymer composite (HAP/PVA) using a colloidal non-aqueous precipitation method at room temperature, and to control of the HAP microstructure

which expected to be advantageous in adjusting the amount of HAP that can be incorporated into the composite.

EXPERIMENTAL

The starting materials used for prepare the composite were, calcium nitrate tetrahydrate ($Ca(NO_3)_2.4H_2O$, Fluka) and orthophosphoric acid (H_3PO_4, 85 %, Aldrich), tetrahydrofuran (THF, 99%, Aldrich) which used as the solvent and poly vinyl alcohol (PVA, Mw = 25,000 and 125,000- Merck) was used as the biodegradable polymer. The pH of the reaction was adjusted with NH_4OH (30%, Merck). Four samples of the composites (HAP/PVA) containing 10, 20, 30, and 40 wt % of HAP were prepared, respectively. According to the reaction formula:

$$10\ Ca(NO_3)_2.4H_2O + H_3PO_4 + 20NH_4OH = Ca_{10}(PO_4)_6(OH)_2 + 6H_2O + 20NH_4NO_3$$

At the beginning, H_3PO_4 added to tetrahydroflouran (THF) followed by the slow addition of NH_4OH with stirring for 30 min until a pH adjusted to 10. $Ca(NO_3)_2.4H_2O$ is then added in proper proportion to achieve a Ca/P ratio of 1.67 with continues stirred. The reaction is allowed to aging period for 24 h. The polymer PVA was dissolve in the (THF) at room temperature. After stirring for 3 h, NH_4OH is added to achieve a pH of 10 in order to disperse the HAP particles. The HAP formation was dispersed in the polymer matrix with stirred until the viscous solution has produce, and then poured into a small dish. After that, nanosized iron oxide (γ-Fe_2O_3, ~100 nm) was added to the above components to produce the magnetic gel compound. Glutaraldehyde was used as crosslinking agent (at slightly acidic pH, about 6) using 1M nitric acid.

The prepared composites were characterized for elemental composition by the technique of atomic absorption spectroscopy (AAS, 760 Shimadzu –Japan]. The phase's patterns were estimated using X-ray diffraction technique (XRD diffractometer, X 6000 Shimadzu- Japan) and surface morphology by scanning electron microscopy (SEM). The magnetic properties of the all samples of composite prepared were measured using vibrating sample magnetometer (VSM) by placed a small piece of magnetic composite in a gelatin capsule and inserted in the VSM device.

RESULTS AND DISCUSSIONS

The variations in pH of the solution were found to affect the chemical reaction due to solubility altered, further the powder's agglomeration tendency. The longer aging time allowed the reagents to be fully reacted forming the precipitates of the desired compound. After dissolving the PVA polymer and stirring for over 3 hours, the pH is adjusted near 10 by adding NH_4OH.

The XRD pattern of the composite prepared is showed in Figure (1), which revealed the presence of semi-crystalline PVA polymer and HAP in the polymer matrix. In order to confirm the crystalline nature of hydroxyapatite present in the composite, the PVA and ammonium nitrate were removed by washing in THF and distilled water, respectively. A strong peak at 31.78 represents the pattern of the final powder corresponded to crystalline hydroxyapatite (HAP). The results confirmed that the composite prepared of (apatite-magnetite) was dissolved at a rate dependent on the amount of iron in the lattice of apatite. So the dissolution at 37^{o}C was found to be about 5 ppm over a period of one hour. Also the temperature required for heating the ceramic for hyperthermia treatments

was increased the solubility and also from the internal stress of temperature gradient within the ceramic (11, 12)

Heat treatment at atmosphere was affected the iron transportability, which produced a hematite, while nitrogen be useful for the formation of iron containing apatite, so the selection of a reducing atmosphere could produce magnetite with a fine dispersed in a bioactive hydroxyapatite phase.

The HAP microstructure images were obtained as rough surfaces free of particular facets as showed in Figure (2), it revealed as spherical with no distinct orientation due to the presence of ammonium nitrate. The HAP mean particle size was found at the range of (10–100) nm and appeared to be in homogenous distribution in PVA polymer matrix.

Scanning electron microscopy (SEM) was used to evaluate the size and the shape of the magnetite particles (γ-Fe_2O_3, ~100 nm). The image showed in Figure (3) revealed the magnetic composite particles which at the size range of (70 – 100 nm) and in approximately as uniform distribution.

Table (1) showed the magnetization measurement of different samples of HAP/PVA composites with various weights ratio. It was appeared that almost no remnant magnetization was showed at 300 K^o, but at 5 K^o the hysteretic loop was observed Figure (4), leading to confirm that the superparamagnetic nature of the nanosized maghemite particles didn't change in presence of the polymer network and the composite itself behaved as a superparamagnetic material.

CONCLUSIONS

Composites containing HAP and PVA were successfully synthesized by a non-aqueous based chemical reaction. The process leads to the generation of a single phase of stiochiometric HAP since the pH level of the solution was maintained in excess of 10. Analysis of the composite indicates a homogeneous distribution of the HAP particles within the polymer matrix. The magnetic gel which produced out of crosslinked magnetic nanoparticles in the polymer network was found to be stable and possess the magnetic properties of the nanoparticles.

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Table(1) Saturation Magnetization, Coerecivity and Retentivity of Different HAP/PVA Composites with Different Weights Ratio.

Sample No.	Magnetization (emu/gm)	Corecivity (Gauss)	Retentivity (emu/gm)
10% wt HAP/PVA	12.8	1060	6.9
20% wt HAP/PVA	14.5	1100	7.5
(30% wt)HAP/PVA	15.4	1149	8.18
40% wt HAP/PVA	17. 3	1173	8.69

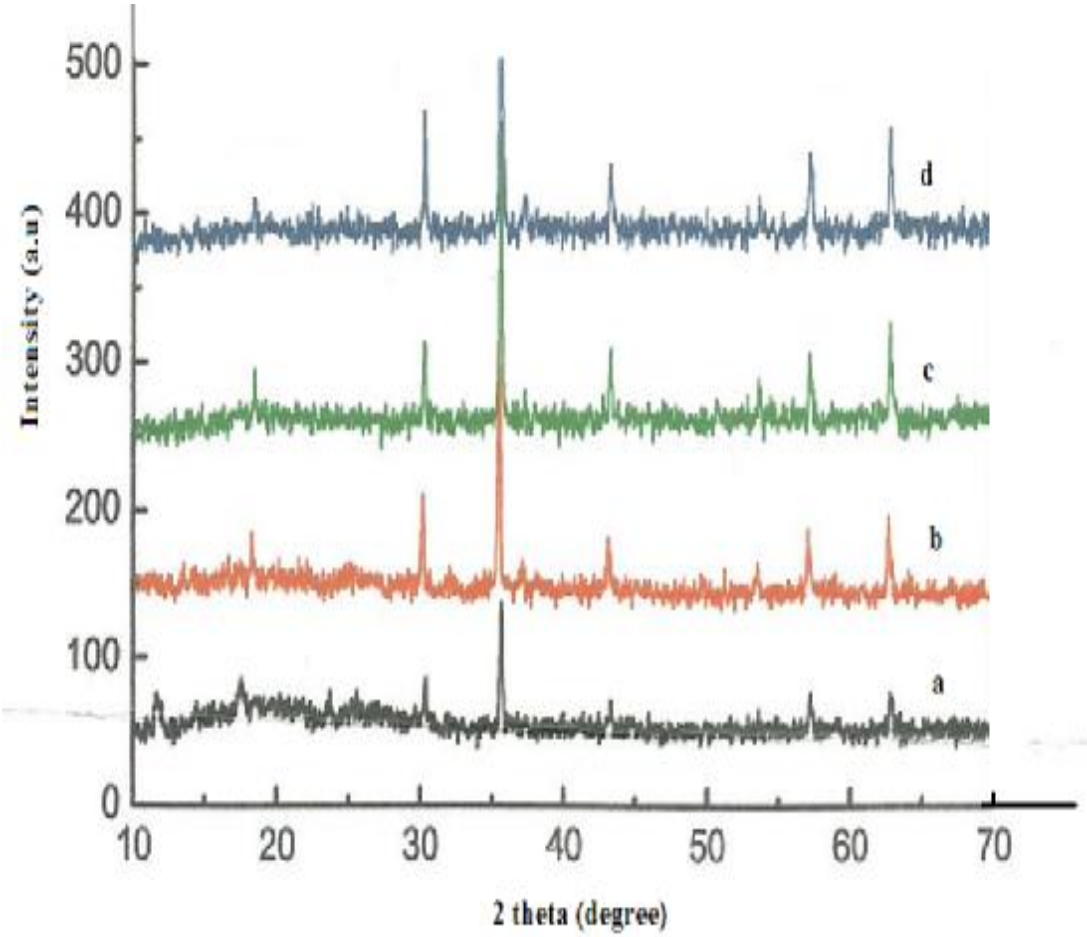

Figure (1) XRD Patterns of HAP/PVA Biomagnetism Composite at various weights ratio of HAP (a) 10% wt (b) 20% wt, 30% wt and (d) 40% wt.

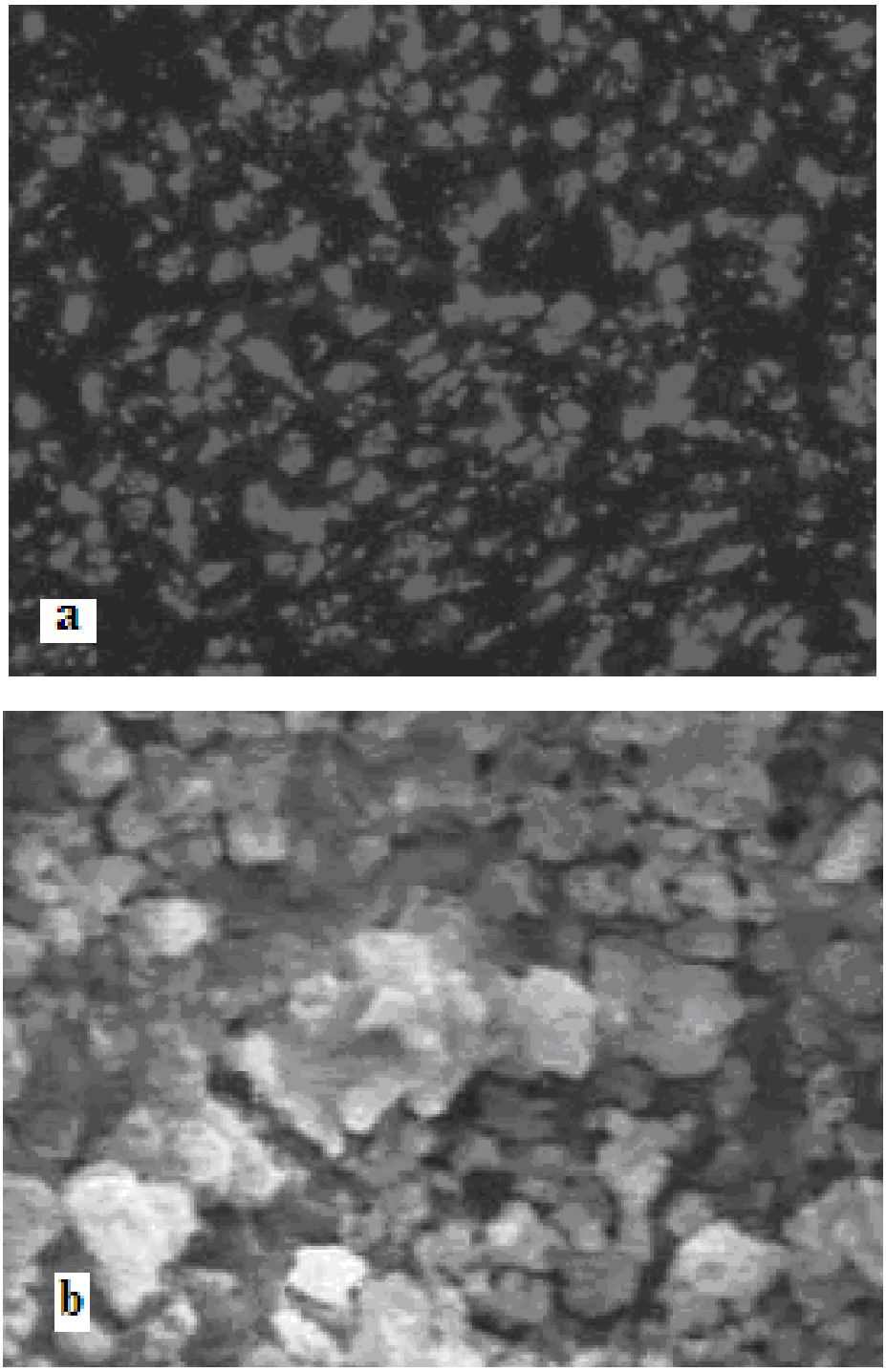

Figure (2) Micrograph Images of HAP/PVA Composites Containing HAP (a) 20 wt. % and (b) 40 wt. %.

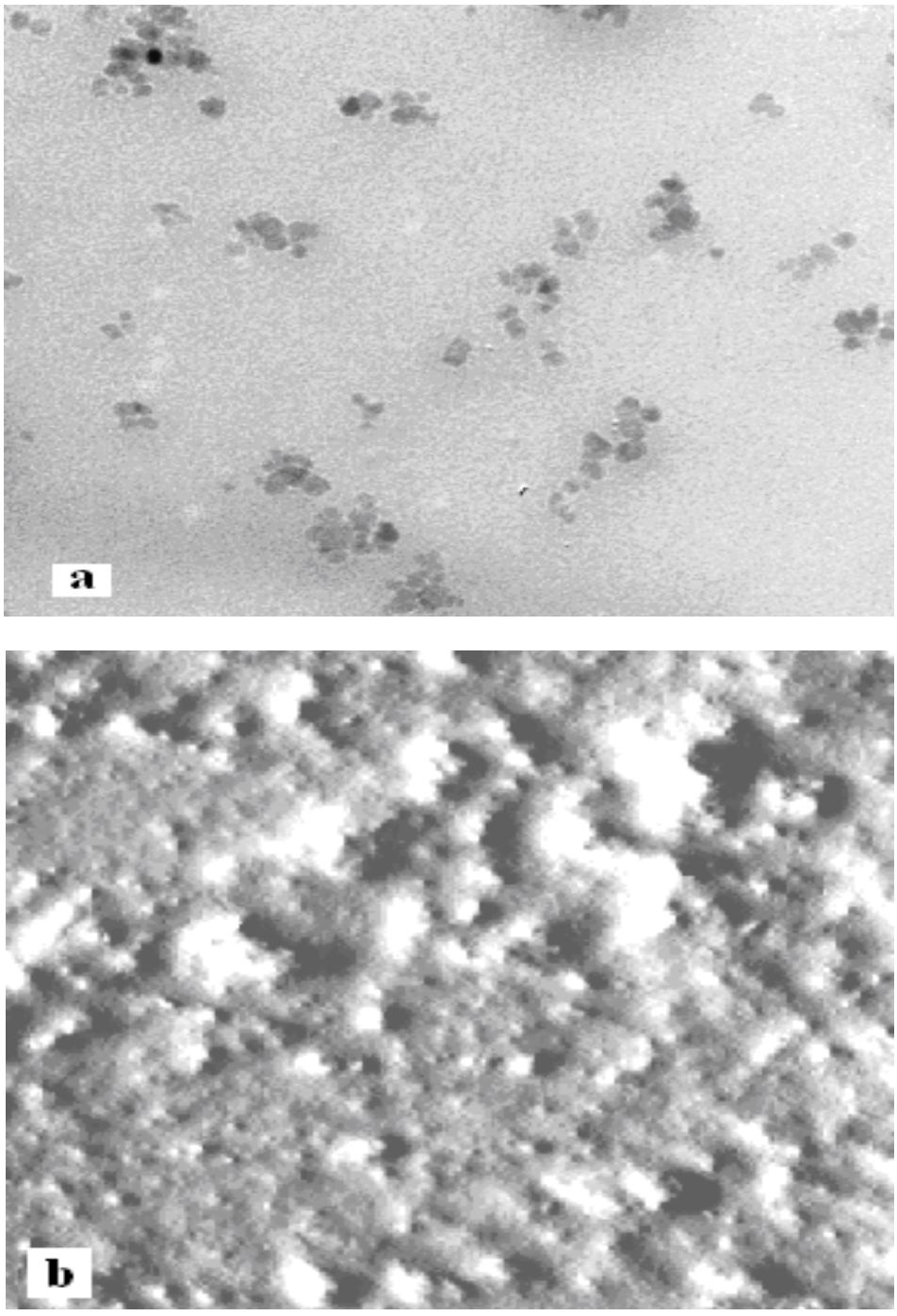

Figure (3) Micrograph for (a) Maghemite (γ-Fe_2O_3) Particles and (b) PVA Magnetic Gel.

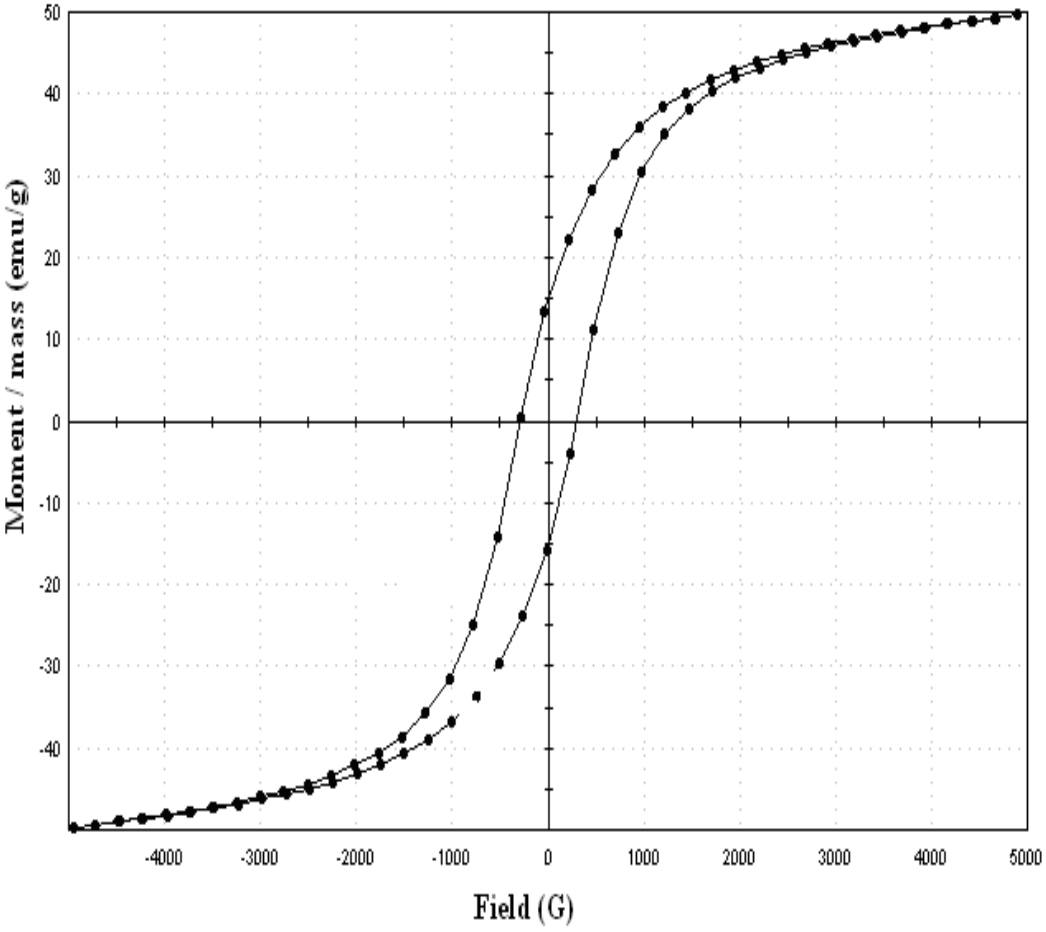

Figure (4) Hysteretic Plot for Magnetic 40 wt % HAP/PVA Composite.