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Separation of the defect-free Fe₃O₄-Au core/shell fraction from magnetite-gold composite nanoparticles by an acid wash treatment

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Abstract

Some undesired nanoparticles, such as malformed structures or incomplete core/shell Fe₃O₄-Au nanocomposites, might be formed when Fe₃O₄-Au core/shell nanocomposites are being synthesized. These impurities should be separated before any applications are performed. In this investigation, magnetic cores (Fe₃O₄) were synthesized using a conventional fabrication method involving coprecipitation of Fe²⁺ and Fe³⁺. Carboxyl-capped magnetite-gold composite nanoparticles, measuring ≤50 nm, were then synthesized using a plant extract (*Eucalyptus camaldulensis*). The prepared carboxyl-capped magnetite-gold composite nanoparticles were further subjected to acid treatment for 18 h and characterized with different instrumentation methods. The results of the investigation showed that acid treatment can be applied successfully to separate defect-free Fe₃O₄-Au core/shell nanoparticles from different types of Fe₃O₄-Au nanocomposites, without any considerable changes in their physiochemical properties.

Keywords: Magnetite nanocomposite, Fe₃O₄-Au core/shell, Acid washing, Biosynthesis, Separation

Background

Magnetic nanoparticles (MNPs) have been known as one of the nanostructures that provide the widest uses in biomedicine [1-5]. For example, MNPs that are composed of magnetite (Fe₃O₄) or maghemite (γ-Fe₂O₃) have unique thermal, chemical, and magnetic properties that make these particles particularly well suited for medical applications [5,6]. However, producing nanoparticles (NPs) with high stability and biocompatibility presents one of the greatest challenges. To address this, MNPs should be covered with an external quite inert shell, in order to protect the magnetic core against chemical changes. In addition, the surfaces of these particles should be functionalized with organic molecules, to allow them to bind chemically to other biomolecules such as DNA, proteins, amino acids, etc. [7-9]. Gold is a chemically quite inert element, and no single acid dissolves it. This metal is resistant to chemical reactions that take place in biological fluids and

is a very useful element for providing a coating layer to protect MNPs [10,11]. Also, gold metal does not decrease the magnetic properties of Fe₃O₄ MNPs and, consequently, will not limit the applications in which these particles are used [12,13].

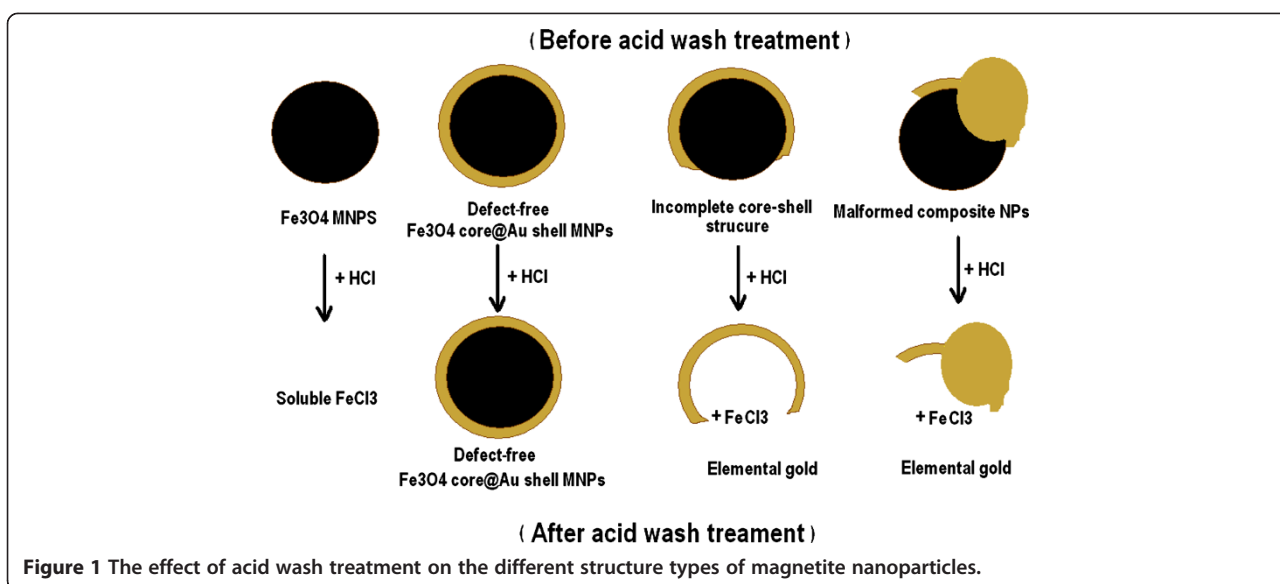
At present, a number of different chemical and biological methods have been reported for fabricating magnetite Fe₃O₄-Au composite NPs [4,6,9]. These nanocomposites contain both defect-free Fe₃O₄ core@Au shell MNPs and other types of Fe₃O₄-Au nanocomposites such as malformed structures or incomplete core/shell Fe₃O₄-Au nanocomposites (Figure 1). As mentioned above, the importance of the external inert shell in protecting the magnetic core is well established, and different reports have been published on the synthesis of Fe₃O₄ core@Au shell MNPs [4,13]. However, in these studies, no further treatments such as acid washing have been applied for separating the defect-free Fe₃O₄ core@Au MNPs from other types of Fe₃O₄-Au nanocomposites. An intact gold layer on the Fe₃O₄ nucleus can protect the core against acid wash treatment. In contrast, Fe₃O₄ minerals in malformed structures or other structures with incomplete inert shell will be dissolved with exposure to acid. In the current study, carboxyl-capped

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Fe₃O₄-Au composite MNPs were prepared by a combined chemical and biological reducing method [14]. Hydrochloric acid (HCl) was used to dissolve all types of Fe₃O₄-Au composite MNPs, except for Fe₃O₄@Au core/shell MNPs. In the next step, the remaining Fe₃O₄ MNPs with defect-free gold shell, which has been designated in this report as 'Fe₃O₄ core@Au shell MNPs,' were separated from the reaction mixture with a magnet and fully characterized using different instrumentation methods.

Results and discussion

This study reports a simple acid wash treatment for separating defect-free Fe₃O₄ core@Au shell MNPs from other types of Fe₃O₄-Au composite NPs (i.e., malformed structures and incomplete core/shell MNPs) (Figure 1). First, crude magnetite Fe₃O₄-Au nanocomposites were synthesized using the method described above, and their shapes and sizes were studied by transmission electron microscopy (TEM). Figure 2 shows two representative TEM images recorded from the drop-coated film of the Fe₃O₄-Au nanocomposites that were fabricated by a recently described semi-biosynthesis method [14]. Two dark and gray particles with sizes of ≤50 nm can be observed in the TEM images that have been illustrated in Figure 2a,b.

It should be noted that Fe₃O₄ magnetite NPs are seen as a gray color because elemental gold (Au) has a higher electron density than Fe₃O₄ and, consequently, more electrons are transmitted in bright field imaging [15]. The analysis of the gray particles by energy-dispersive spectroscopy (EDS) confirmed the presence of Fe and O element signals (Figure 2c). The peaks shown in Figure 2c are attributed to Fe and O elements, and this confirmed the existence of iron-oxide NPs (copper and carbon peaks existed due to

the grid used for TEM imaging). The EDS pattern of the dark particles indicated the presence of gold, iron, and oxygen, as illustrated in Figure 2d. The EDS experiment was repeated to analyze different other dark NPs, and the obtained EDS spectra confirmed that the other dark NPs were also made up of both elemental gold and Fe₃O₄ magnetite ingredients (Figure 3a,b). In addition, further analysis of some gray particles (Figure 3a) by EDS showed a gold element signal with lower density, confirming the presence of other types of Fe₃O₄-Au nanocomposites, especially malformed Fe₃O₄-Au composite NPs (Figure 3c).

In the next step, a simple dissolution method using hydrochloric acid (1 N) was performed to separate acid-stable magnetite particles, coated with an intact gold layer, from those containing bare Fe₃O₄ MNPs, malformed structures or incomplete core/shell nanocomposites (Figure 1). It should be noted that defect-free Fe₃O₄ core@Au shell MNPs are stable against acid and can easily be separated after the acid wash process by applying an external magnetic field. In contrast, during acid wash treatment, malformed structures or incomplete Fe₃O₄@Au core/shell MNPs are decomposed to gold metal and soluble ferric iron (Figure 1). In addition, bare Fe₃O₄ MNPs are also completely dissolved in HCl solution (1 N) (Figure 1). Figure 4a shows a test tube containing Fe₃O₄-Au nanocomposites that has been mixed with HCl and incubated for 18 h. Also, Figure 4b,c demonstrates two tubes containing acid-stable NPs before and after separation by a magnet.

The upper illustration in Figure 5 shows different TEM images of the acid-stable NPs after washing with distilled water. As shown in this illustration, dark NPs with sizes of less than 50 nm can be observed in TEM images, indicating different magnetite NPs with higher electron density.

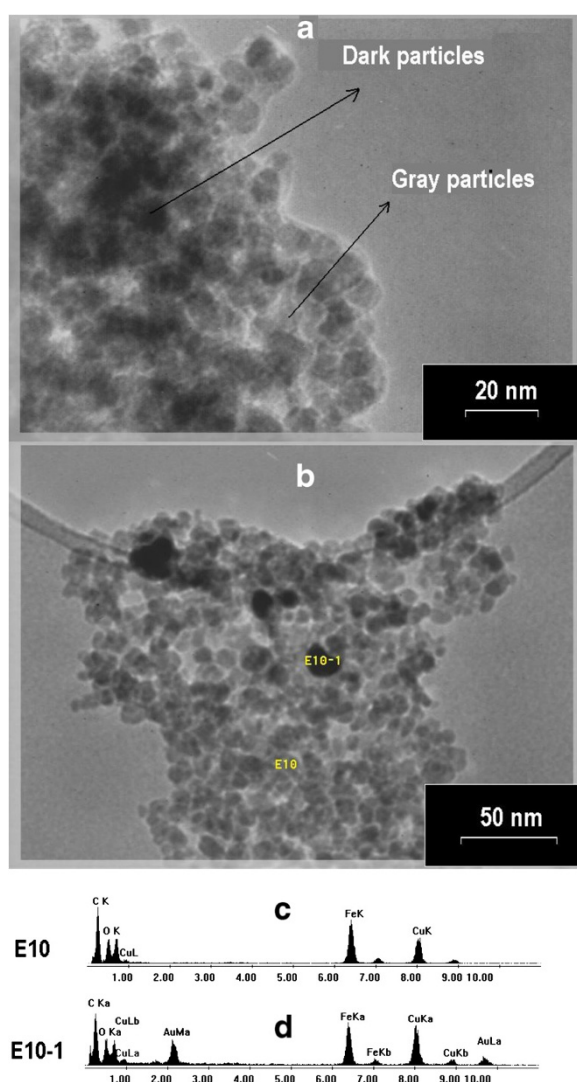


Figure 2 Transmission electron microscopic images. Of both magnetic-gold composite nanoparticles (dark particles) and bare Fe_3O_4 magnetite nanoparticles (gray particles), recorded by different magnification (a and b). Lower illustrations show energy-dispersive spectroscopy patterns of these gray (c) or black (d) nanoparticles.

The chemical composition of these NPs was studied using the X-ray diffraction (XRD) method and is depicted in the lower illustration in Figure 5. The Fe_3O_4 composite MNPs were observed after the acid leaching process and verified the connection between MNPs and elemental gold (also lower illustration in Figure 5). Some negligible impurities may be remained after acid leaching, so advanced characterization methods such as high resolution TEM or elemental mapping is necessary to differentiate between the core/shell structure and other impurities. The magnetite properties of prepared Fe_3O_4 -Au composite MNPs before and after acid wash treatment with HCl (1 N) were also investigated, using the vibrating sample magnetometer (VSM) method. The magnetic hysteresis curves of bare (a)

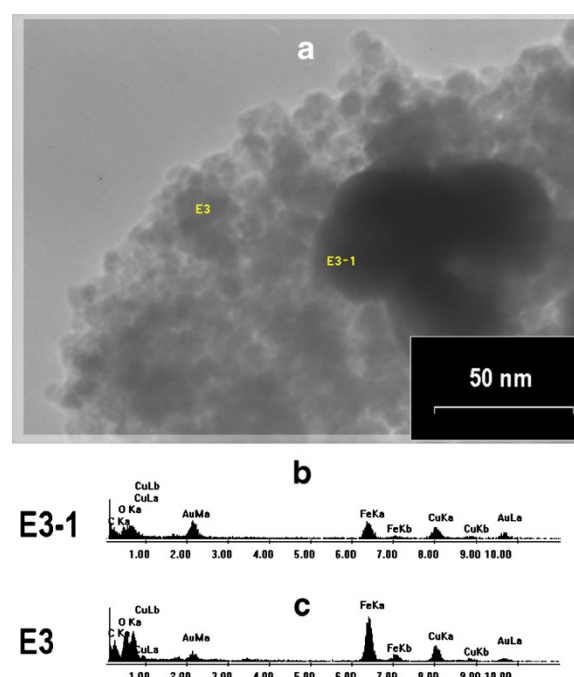


Figure 3 Another transmission electron micrograph of magnetic-gold composite nanoparticles, prepared by the semi-biosynthetic method (a). Lower illustration shows energy-dispersive spectroscopy patterns of a core/shell Fe_3O_4 -Au composite nanoparticle (b) and other types of Fe_3O_4 -Au nanocomposites, especially malformed Fe_3O_4 -Au composite nanoparticles (c).

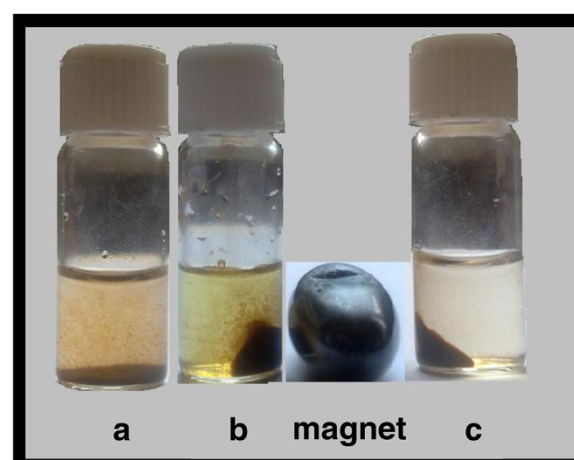


Figure 4 The images of different test tubes that contain Fe_3O_4 -Au composite MNPs. In exposure with 1 N hydrochloric acid (a) and after separation with external magnetite field (b). Tube (c) shows the defect-free core/shell fraction of Fe_3O_4 -Au nanocomposites separated by a magnet and washed three times with distilled water.

Fe_3O_4 MNPs, (b) Fe_3O_4 -Au composites MNPs, and (c) Fe_3O_4 core@Au shell MNPs are demonstrated in Figure 6 and show magnetite saturation conditions for all magnetite nanomaterials. No considerable change was observed in superparamagnetism properties of this magnetite material (Fe_3O_4) either before or after the acid washing process with HCl (1 N) for 18 h (Figure 6b,c). Furthermore, we have tested HCl solutions with higher normality of 2, 3, 4, and 5 N for the dissolution of non-core/shell composite NPs, but in all experiments, non-magnetic properties were observed from the remaining nanomaterials (data not shown).

The existence of a carboxyl group on the surface of the prepared magnetite-gold nanocomposites fabricated by a semi-biosynthetic with ethanol extract of *Eucalyptus camaldulensis* has previously been demonstrated by the Fourier transform infrared spectroscopy (FTIR) method [10] and confirmed in this investigation (Figure 7a). IR peaks, centered at 3,430 and 1,720 cm^{-1} , confirmed the presence of a carboxyl group on the surface of the semi-biosynthesized Fe_3O_4 -Au nanocomposites (Figure 7a). Furthermore, this carboxyl group can also be detected on the surface of Fe_3O_4 -Au core/shell composites MNPs after

acid wash treatment (Figure 7b) showing that carbonyl groups have not been chemically changed or degraded during acid treatment of Fe_3O_4 -Au composite MNPs.

However, it should be noted that the magnetite properties of Fe_3O_4 -Au composite MNPs was not optimized during this study, and further optimization process should be performed on the magnetization of the Fe_3O_4 -Au composite MNPs which makes them better candidate for biomedical applications. Also, no assay was carried out to determine the biocompatibility of the above Fe_3O_4 -Au core/shell composites MNPs and merit further investigation.

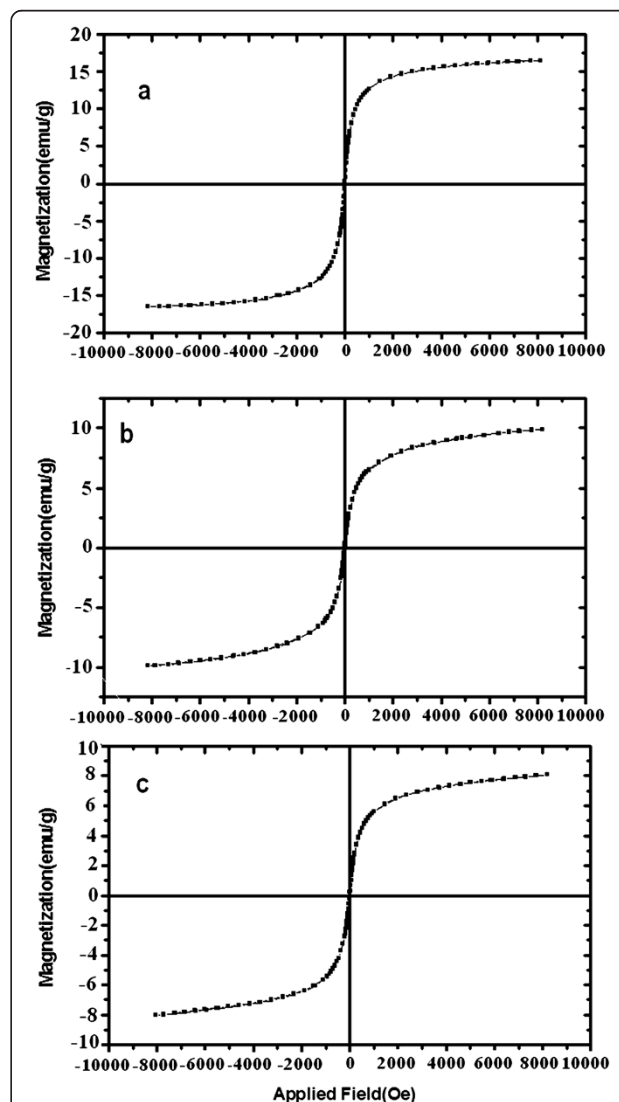
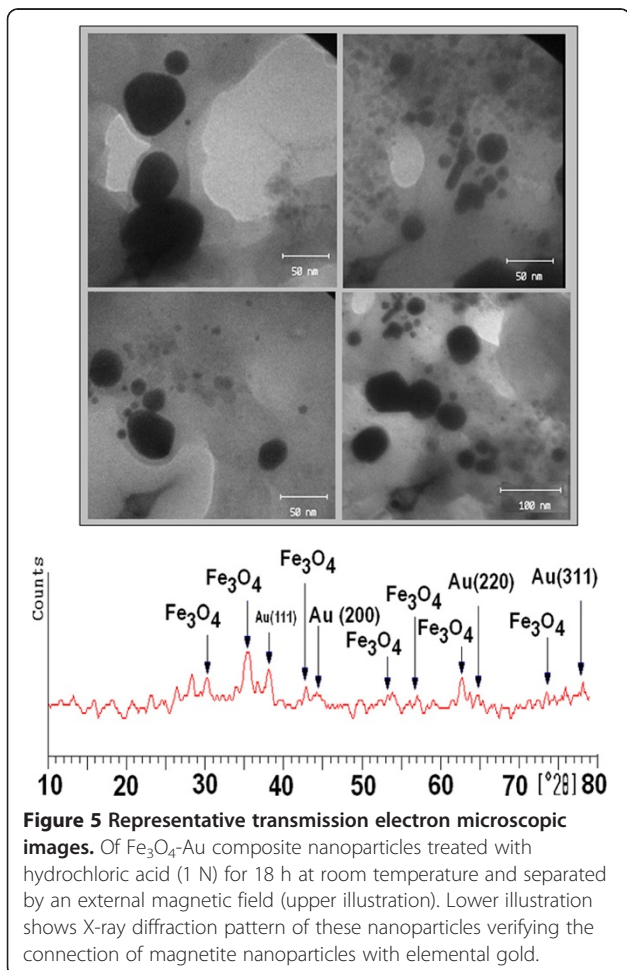


Figure 6 Magnetite properties of fabricated nanoparticles. Measured by vibrating sample magnetometer; bare Fe_3O_4 nanoparticles (a), Fe_3O_4 -Au nanocomposites before (b) and after (c) acid wash treatment.

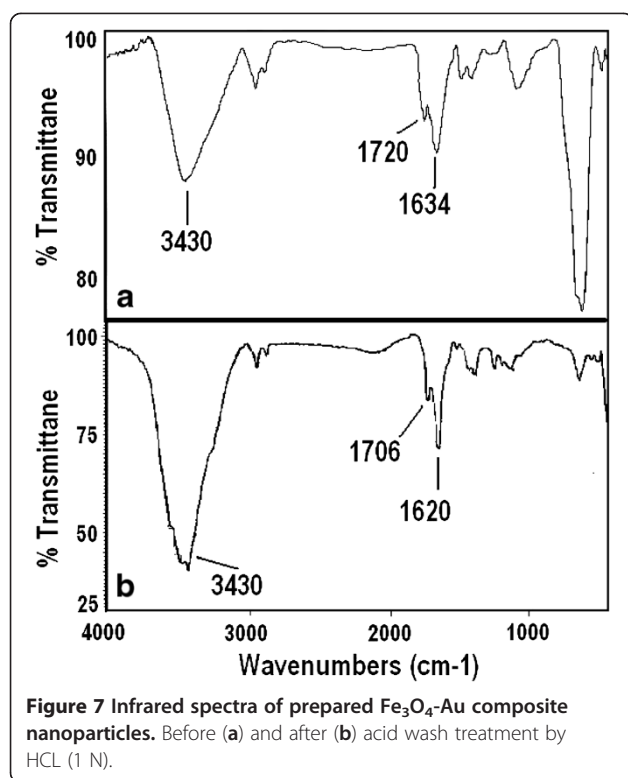


Figure 7 Infrared spectra of prepared Fe_3O_4 -Au composite nanoparticles. Before (a) and after (b) acid wash treatment by HCL (1 N).

Conclusions

Different chemical or biological methods have been reported for synthesizing Fe_3O_4 MNPs and Fe_3O_4 core@Au shell MNPs [16-20]. However, when Fe_3O_4 -Au core/shell nanocomposites are synthesized, some undesired NPs, such as malformed structures or incomplete core/shell Fe_3O_4 -Au nanocomposites, may be formed. These types of MNPs are categorized as impurities and need to be removed from the final product. In the current study, an acid wash treatment has been developed to remove all undesired nanomaterials (Figure 1). The physiochemical properties of isolated Fe_3O_4 -Au composite MNPs before and after acid wash treatment were investigated by different characterization methods, such as TEM, EDS, XRD, VSM, and FTIR. The results show that the acid wash process did not change the surface chemistry and magnetite properties of Fe_3O_4 core@Au shell MNPs and can be used to reduce impurities and obtain the defect-free core/shell fraction of Fe_3O_4 -Au composite MNPs.

Methods

Semi-biosynthesis of magnetite Fe_3O_4 -Au nanocomposites

Carboxyl-capped magnetite Fe_3O_4 -Au nanocomposites were prepared at room temperature, using the previously

described methods [14,21]. For this purpose, $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ (0.487 g) and $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$ (0.25 g) were precisely weighted and dissolved in 200 ml of deionized water.

The mixture was then treated through a drop-by-drop addition of 10 ml NaOH solution (0.15 M), with mixing (200 rpm), under an argon atmosphere. The final pH of the reaction mixture was adjusted to pH12, with an excess volume of NaOH (0.15 M). The reaction mixture was then further incubated for 30 min at 80°C . The resulting black precipitate was separated by centrifugation ($8,000 \times g$). The separated MNPs were washed four times with deionized water. The prepared Fe_3O_4 MNPs were separated from the solution with a magnet. The reduction of Au^{3+} onto the surface of Fe_3O_4 MNPs was carried out using an ethanol extract prepared from *E. camaldulensis* leaves [14].

The *E. camaldulensis* leaves were air-dried at room temperature and then pulverized (50 g). The ethanol extract was prepared by macerating the powder (250 g) for 72 h with three changes of the solvent (1,000 ml) at room temperature. The combined solvent extracts were evaporated to yield a brownish or greenish viscous residue. A stock solution (10 mg/ml) of the plant extract was prepared in ethanol for further experiments and reserved in the refrigerator, at 4°C . Chloroauric acid was purchased from Merck, Darmstadt, Germany. MNPs (20 mg) were dispersed in 30 ml of aqueous HAuCl_4 (chloroauric acid) solution (1 mM) and mixed with 1 ml of an ethanol extract of *E. camaldulensis* (10 mg/ml). The resulting mixture was allowed to stand for 45 min at room temperature, and then the prepared magnetite Fe_3O_4 -Au nanocomposites were separated from the colloid by a magnet. Finally, the NPs were washed three times with distilled water and subjected to the next experiments.

Acid wash treatment

HCl solution (1 N) was used to remove bare Fe_3O_4 MNPs or other malformed structures from magnetite Fe_3O_4 -Au nanocomposites (Figure 1). Prepared composite NPs (100 mg) were mixed with HCl solution (600 ml, 1 N) and incubated for 18 h at room temperature. Then, the remaining composite NPs were separated from the solution by an external magnetic field. These separated NPs were washed three times with deionized water and subjected to further characterization.

Characterizations

All samples were characterized by transmission electron microscopy (model EM 208 Philips, Amsterdam, The Netherlands), EDS, XDS (Philips X'Pert Pro), and VSM. The surface chemistry of the composite MNPs before and after acid treatment was also studied by the FTIR (Nicolet Magna 550, Madison, WI, USA).

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

ARS is the leader of the group and the main writer of this study's manuscript. HM and AA both participated in synthesis and characterization of nanoparticles. Also, AA and HS commented on EDS and XRD experiments. All authors read and approved the final manuscript.

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