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Fabrication of succinic acid- γ -Fe₂O₃ nano core-shells

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ABSTRACT

Core–shell nano-structures were synthesized by adsorbing succinic acid on γ -Fe₂O₃ nanoparticles (hereafter referred to as core–shell nanoparticles or core–shells). Streptomycin was chosen as a model drug to attach on γ -Fe₂O₃ core–shells. Vibration spectroscopic data confirmed the specific adsorption of organic ligands (i.e., succinic acid or streptomycin) onto γ -Fe₂O₃ via bi-dentate, bi-nuclear complex. Possible molecular configurations between organic ligands and γ -Fe₂O₃ were examined by density functional theory (DFT) using Fe₆(OH)₁₈(H₂O)₆ ring cluster. The measured vibration frequencies and bond distances (i.e., Fe–O–Fe, Fe–O_w, and Fe–OH units) of the optimized γ -Fe₂O₃ cluster matched well with the calculations.

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1. Introduction

The γ -Fe₂O₃ nanoparticles are extensively examined due to their magnetic properties and wide applications as ferrofluids, recording tapes [1], data storage devices, biomedical work and catalysis [1,2]. The design and fabrication of magnetic nanoparticles with a controllable size and uniform dispersion is important research in materials science. The inherent structure of γ -Fe₂O₃ core-shell nanoparticles makes them very useful in biomedical applications, namely enzymes and protein separation, RNA and DNA purification, magnetic resonance imaging (MRI) and drug delivery. The utilization of iron-based nanoparticles in other scientific areas is also gaining momentum largely due to their environmental benignness [3-8]. The surface of a given nanoparticles is generally tailored with synthetic or natural polymers to improve their stability, reactivity, biocompatibility and floatability. Previously, modifications of surface sites were carried out with various functional agents such as polyethylene, polyethylene glycol, and silica [9,10]. The grafting sites on nanostructures immobilize foreign molecules, and the surface-derived functional groups act reversibly for bio-entities. Carboxylic groups on polymeric surfaces immobilize oligonucleotides and protein via covalent bonding [5]. These surface carboxyl groups can readily be derivatized; hence, they can improve the dispersion of iron oxide nanoparticles by shifting the iso-electric point [11,12].

Streptomycin, one of the oldest antibiotics in the world, is used to control the incidence of tuberculosis (TB). (Chemical structure, Fig. 1-S: support documents). Streptomycin, 1-(4-(4-(3,5-dihydroxy-6-(hydroxymethyl)-4-(methylamino)tetrahydro-2H-pyran-2-yloxy)-5-formyl-5-hydroxy-3-methyl tetra hydrofuran-2-yloxy)-2,5,6-trihydroxycyclohexane-1,3-

diyl)diguanidine is an aminoglycosidic antibiotic with three components: streptidine, streptose and N-methyl-L-glucosamine. It is also used in the treatment of infections caused by Gramnegative bacteria. Under alkaline conditions, streptomycin is an effective bactericide against rapidly dividing extracellular *Mycobacterium tuberculosis.* However, the major drawbacks associated with application of this drug are the requirements of parenteral dosing and its toxicity. The use of this drug has also declined due to poor gastrointestinal absorption that precluded effective oral administration. However, streptomycin is one of the most cost-effective ATDs and it is recommended in certain categories of TB patients, e.g., patients showing re-lapse or treatment failure, compulsory withdrawal of ionized and rifampicin, TB meningitis, HIV-infected TB patients receiving protease inhibitors, and certain cases of multi-drug resistant TB [13].

Challenges in developing new drugs not only include identifying novel active compounds but also improving their delivery at the biological level. Most of the active compounds on the market are poorly soluble in water, and it is expected that they will be less soluble in the future [14]. Therefore formulation of poorly water soluble active compounds is an important challenge to be faced. Due to

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Table 1

Surface characterization data of $\gamma\text{-}\text{Fe}_2\text{O}_3$ and $\gamma\text{-}\text{Fe}_2\text{O}_3\text{-}\text{water interface}.$

Parameter	Value	Source
pH _{zpc}	8.13	Ref. [12]
pH _{IEP}	8.03	This study
Site density (sites/nm ²)	5.66	This study
Specific surface area (m ² /g)	150	This study
Particle size (nm)	10-20	This study

their inherent environmental benignness, iron derived compounds can be considered as potential substrates for controlled delivery of drugs. Therefore we determined the physico–chemical interactions of streptomycin and γ -Fe₂O₃ nanoparticles by spectroscopic, experimental and theoretical methods. Streptomycin was selected as the model drug. Particular attention was paid to select mild acidity conditions of experimental solutions as required for biological systems. The reactivity of γ -Fe₂O₃ surface sites was quantified by a cluster molecular model based on density functional theory (DFT)[15]. Therefore the chemical data presented here will provide an essential first step to assess the suitability of γ -Fe₂O₃/ γ -Fe₂O₃ nano-core shells as a drug carrier under controllable fashion.

The succinic acid- γ -Fe₂O₃ core-shells were synthesized by a co-precipitation method and streptomycin was attached to the surface in methanolic medium. The term "core-shell" was used against "surface coating" due to the following reasons. Core-shells are nanostructures that have a core made of a material coated with another material. When a core material is coated with a polymeric or inorganic layer because the polymeric or inorganic layer would endow hybrid structure with additional function/property on top of the function/property of the core hence synergistically emerged functions can be envisioned [16–18]. Henceforth, the succinic acid coated γ -Fe₂O₃ particles are designated as core-shells or core-shell nanoparticles. All ab initio calculations were performed using a cluster model by DFT to affirm the molecular configurations that resulted from experimental data.

2. Materials and methods

2.1. Materials

The iron derived particles were characterized by X-ray diffraction (XRD) and the γ -Fe₂O₃ phase. The surface structure, particle size and morphology of γ -Fe₂O₃ were examined by transmission electron microscopy (TEM). Unless otherwise stated, all chemicals used were either from Aldrich (USA) or FLUKA (Switzerland). The water used was de-ionized-distilled water produced by All-Glass Distillation Unit.

2.2. Synthesis of γ -Fe₂O₃ nanoparticles

The γ -Fe₂O₃ was synthesized by the co-precipitation of Fe (II) and Fe (III) containing solutions in 1 M NaOH as detailed in Ref. [12]. An aqueous iron solution with a molar ratio of Fe (II)/Fe (III)=0.5 was prepared in 1 M HCl. This solution was titrated with 100 ml 1 M NaOH under vigorous shaking. The reaction was carried out under inert atmosphere in a glove box filled with 99.5% Ar. After the titration was completed the reaction mixture was stirred for 30 min prior to centrifugation at 2500 rpm. The supernatant solution was removed and precipitate was rinsed with distilled water several times to remove the remaining ions. The solid residue was freeze dried and re-dispersed in 500 ml distilled water under sonication. Table 1 showed the basic surface properties of the γ -Fe₂O₃ phase. The black colloid thus obtained was stored for further use.

2.3. Synthesis of succinic acid coated- γ -Fe₂O₃ core-shell nanoparticles

Succinic acid coated γ -Fe₂O₃ nanoparticles were synthesized using the same co-precipitation method. However, in this case, the aqueous solution of iron species was spiked with 0.025 mole succinic acid prior to titration with 1 M NaOH. The colloid suspension thus obtained was centrifuged at 2500 rpm and the precipitate was washed with de-ionized, distilled water several times before drying at 60 °C.

2.4. Synthesis of streptomycin–succinic acid coated γ -Fe₂O₃ nanoparticles

Succinic acid- γ -Fe₂O₃ core–shell nanoparticles (~0.1 g) were mixed in 50 ml methanol solution. A portion of 0.25 g streptomycin was added to the solution and stirred for 12 h. This experiment was conducted under acid different conditions, i.e., pH = 3.0, 7.0 and 11.0. The filtered precipitate was washed with methanol followed by water several times. Finally, the solid residue was dried at 60 °C [19].

2.5. Analytical methods

The pH of the suspensions was determined by a pH sensing electrode (model H 112, Kyoto, Japan) and reference electrode (R 116, Kyoto, Japan) with a potentiometric auto-titrator (AT 400 Kyoto, Japan). The pH_{IEP} of γ -Fe₂O₃ suspensions were measured by electrokinetic mobility (Zeta Meter 4.0, USA). Infrared analyses were carried out using a FTIR spectrometer at 4 cm⁻¹ spectral resolution (Nicolet 6700, USA). The γ -Fe₂O₃, different core–shells, succinic acid and streptomycin were mixed separately with spectroscopic grade KBr at 1:6 (w/w) ratio, crushed in agate mortar and pestle to achieve homogeneous mixtures. All spectra were collected at the transmission mode.

2.6. Molecular cluster modeling

The cluster modeling method based on density functional theory (DFT) was used to calculate surface complexes, vibration frequencies and bond lengths. Because of its computational advantages, DFT has evolved as the most important quantum mechanical approach in solid-state geometry optimization [20,21], and it can handle large systems that are intractable by Hartee–Fock methods [22,23]. DFT is based on the fact that the ground-state properties of a molecular system are uniquely defined by the electron density ($\rho(\mathbf{r})$) [15]. In DFT, the energy functional ($E[\rho]$) is written as a sum of four terms [24]:

$$E[\rho(\mathbf{r})] = -\sum_{\mathbf{A}=1}^{M} \int \frac{\mathbf{Z}_{\mathbf{A}}}{|1 - \mathbf{R}_{\mathbf{A}}|} \rho(\mathbf{r}) d\mathbf{r} + \sum_{i=1}^{N} \varphi_{i}(\mathbf{r}) \left(\frac{-\nabla^{2}}{2}\right) \varphi_{i}(\mathbf{r}) d\mathbf{r}$$
$$+ \frac{1}{2} \int \int \frac{\rho \mathbf{r}_{1} \rho \mathbf{r}_{2}}{|\mathbf{r}_{1} - \mathbf{r}_{2}|} d\mathbf{r}_{1} d\mathbf{r}_{2} + E_{XC} |\rho(\mathbf{r})|$$

where, $\mathbf{Z}_{\mathbf{A}}$ is the charge on nucleus \mathbf{A} , \mathbf{r} is a position vector, $\mathbf{R}_{\mathbf{A}}$ is the position vector of nucleus \mathbf{A} , M is the number of nuclei, N is the number of electrons, φ_i is the spatial orbital occupied by the *i*th electron, and $E_{XC}|\rho(\mathbf{r})|$ is the exchange correlation energy functional. The first term on the right-hand side of the equation corresponds to the potential energy due to nucleus–electron interactions, the second term is the kinetic energy for N non-interacting electrons, and the third term represents the energy for electron–electron repulsions. Inter-nuclear repulsions are constant and are accounted for separately. The equation serves to define $E_{XC}|\rho(\mathbf{r})|$ as the energy needed to be added to the other terms to reproduce the exact energy of

the molecular system. Thus, $E_{XC}|\rho(\mathbf{r})|$ contains contributions associated with electron exchange and correlation, and also contains a contribution arising from the difference between the true kinetic energy and the kinetic energy of *N* non-interacting electrons. The functional approximation used for $E_{XC}|\rho(\mathbf{r})|$ is the distinguishing feature of different DFT methods. Molecular modeling calculations were performed with Gaussian 03 code and all models were built with Gauss View [25]. Optimized molecular structures were determined by searching in the potential energy surface for minima with respect to each atomic coordinate using the DFT calculations. An octahedral cluster consisting of two Fe (III) ions was used as to simulate γ -Fe₂O₃ surface (Fig. 2-S). The two octahedra were connected by surface -OH bridges as they were in the bulk crystal structure. The cluster was optimized by DFT method using B3LYP functional with 6-31G (d, f) basic set. Minimum energy structures were verified by IR data for any imaginary frequencies (i.e., unstable vibrational modes). Calculated frequencies vs. experimental frequencies were plotted to examine the best-fit scale-factor "m" which was calculated as

 $v(\text{scaled}) = m \cdot v(\text{DFT/basis sets})$

where, *m* is the scale factor obtained from the slope of the plot and ν was the calculated frequencies for selected theory/basis set. These molecular calculations were repeated to succinic acid, streptomycin, succinic acid- γ -Fe₂O₃ core–shell particle and drug loaded core–shell particle [26]. In order to gain better accuracy, the scale factor should be close to one. In the present calculations, the scaling factor varied from one which implies differences with respect to harmonic and anharmonic frequency modes. However, there is no prior requirement that each vibrational mode should be scaled by the same factor. Therefore, the scaling factor was adjusted to receive a good agreement with experimental data.

3. Results and discussion

3.1. XRD and TEM analyses

The crystal structure of the synthesized nanoparticles was examined by XRD using Cu K α radiation. As shown in Fig. 1(a) the XRD pattern matched well with the standard γ -Fe₂O₃ crystalline phase [27]. Six peaks, characteristic to the γ -Fe₂O₃ phase occurred at 2θ = 31.7°, 36.7°, 41.1°, 53.4°, 57.0° and 62.6° and they were identified as (220), (311), (400), (422), (511) and (440), respectively [28,29]. The variation of this XRD pattern with different treatments showed monotonous behavior (data not included). According to the TEM data shown in Fig. 1(b), the γ -Fe₂O₃ nanoparticles were uniformly distributed with a highly crystalline spherical shape with an average dimension in the range 5-20 nm. These values were in good agreement with the calculated dimensionalities of the γ -Fe₂O₃ particles (~14.3 nm) based on XRD data (such calculations were not possible with treated γ -Fe₂O₃). The Fe₂O (w/w) ratio estimated by the energy dispersive spectroscopy (EDS) was 2:3 which confirmed the presence of the γ -Fe₂O₃ phase. In the bulk structure, the γ -Fe₂O₃ nanoparticles were spinel type. However as shown in Fig. 1(b), when the γ -Fe₂O₃ particles were dried, they tend to agglomerate.

3.2. IR spectroscopic data

The interactions of γ -Fe₂O₃ and organic ligands, i.e., succinic acid and streptomycin were probed by transmission IR spectroscopy. As shown in Fig. 2(a)–(e), the IR spectroscopic patterns of individual organic ligands were first determined, and subsequently they were compared against the corresponding organic- γ -Fe₂O₃ complexes to elucidate possible bonding mechanism/s. Based on



Fig. 1. (a) XRD pattern of γ -Fe₂O₃ particles under different treatments. Six peaks, characteristic to γ -Fe₂O₃ phase occurred at 2θ = 31.7°, 36.7°, 41.1°, 53.4°, 57.0° and 62.6° were identified by the Miller Indices (220), (311), (400), (422), (511) and (440), respectively. (b) TEM image of the γ -Fe₂O₃ particles.

spectral data, once the plausible molecular configurations were resolved, a cluster modeling method was used to validate them. Fig. 2(d) showed the IR spectrum of succinic acid between 400 and 4000 cm⁻¹. The important spectral bands that showed variations upon different treatments of γ -Fe₂O₃ surface sites were summarized in Table 1-S (support documentation). The stretching vibrations at 2981 cm⁻¹ and around 3440 cm⁻¹ due to $v(CH_2)$ and v(COOH), respectively were distinct. The bands at 1727 and 1693 cm⁻¹ respectively, were ascribed to symmetric and asymmetric stretching of v(C=0) whereas those at 1420 cm⁻¹ and 1202 and $1309 \,\mathrm{cm}^{-1}$ respectively, were due to $\upsilon(C=0)$ and $\upsilon(COOH)$ stretching vibrations [30,31]. Fig. 2b shows a comparison of the IR spectra of succinic acid coated γ -Fe₂O₃ particles (i.e., core-shells) with respect to pure succinic acid. A broad band shown around 3436 cm^{-1} was due to H-bonded \equiv Fe–OH sites. As both –COOH and \equiv Fe–OH groups were present and they both tend to make H bonding, the bands at 3440 and 3436 cm⁻¹ could be assigned to those OH modes of the two groups. The band due to surface -OH bending vibrations was shown at 1642 cm⁻¹. The broad band in the vicinity of 615 cm⁻¹ indicated de-protonated surface sites, i.e., \equiv Fe-OH $\rightarrow \equiv$ Fe-O⁻. When succinic acid interacted with the surface, the bands due to asymmetric and symmetric stretching of $v(CH_2)$ were shifted from 2981 to 2851 and 3440 to 2923 cm⁻¹, respectively. The band at 1202 cm^{-1} due to υ (–C–OH) stretching of -COOH had shifted to 1238 cm⁻¹. A new band appeared at 1297 cm⁻¹ which showed surface-succinic acid bonding as



Fig. 2. The IR spectra of: (a) streptomycin, (b) succinic acid- γ -Fe₂O₃, and (c) streptomycin attached succinic acid- γ -Fe₂O₃ core-shells. Succinic acid core-shells were prepared by co-precipitation by spiking with 0.025 M succinic acid prior to 1 M NaOH addition. Streptomycin attachment onto succinic acid- γ -Fe₂O₃ core-shells were done in methanol medium. Refer to the text for details.

≡Fe−O−C at ≡Fe sites [32]. The bonding of succinic acid by the conversion of −C==O → −C−O → −Fe−O−C via −OH radicals of −COOH groups was evidenced by the band disappearance at 1639 cm⁻¹ and the appearance of new bands at 1398 and 1556 cm⁻¹ due to symmetry reduction [30–35]. Therefore, the adsorption of succinic acid on γ-Fe₂O₃ led to the formation of a binuclear, bidentate complex (Fig. 4(a)).

As shown in Fig. 3, the solution pH showed a marked influence on the IR spectra of core shells particularly in the 1300–1750 cm⁻¹ spectral region. This spectral region has also been used to probe molecular configurations given [36]: $\Delta[\nu(COO^{-})] > 200 \,\mathrm{cm}^{-1}$ (monodentate below complex), $\Delta[\nu(COO^{-})] < 110 \, \text{cm}^{-1}$ (bidentate complex) and $140 \text{ cm}^{-1} < \Delta[\nu(\text{COO}^{-})] < 200 \text{ cm}^{-1}$ (bridging complex). Here $\Delta[\nu(COO^{-})]$ was the spectral difference of the symmetric and asymmetric stretching of COO⁻ groups. Along these arguments, the IR bands of the same spectral window were used to ascertain molecular configurations of organic ligand/core-shells as a function of pH. The IR spectra of both sample A (sample synthesized at pH 3) and sample B (sample synthesized at pH 7) showed a remarkable similarity. Yet, the IR spectrum of the sample C (sample synthesized at pH 11) was significantly different. As theoretical calculations suggested the molecular configurations of both samples



Fig. 3. FTIR spectra of succinic acid- γ -Fe₂O₃ core-shells as a function of pH. The selected pH values ranged from 3 to 11 to cover the conditions that match the biologically important environments. The pH adjustments were made with calibrated 0.120 M HCl or 0.211 M NaOH.

A and B can be ascribed to a bidentate, binuclear complex (Fig. 4(a)). However, such a conclusion cannot be made for the sample C due to the following reasons. The IR band at 1693 cm⁻¹ (succinic acid) was shifted to 1716 cm⁻¹ and the new bands appeared at 1589 and 1400 cm⁻¹ which were due to anti-symmetric and symmetric stretching vibrations of carbonyl and $-COO^-$ groups, respectively. When compared to samples A and B, in the sample C, a new band appeared around 1436 cm⁻¹ and the band at 1398 cm⁻¹ remained unchanged. In all cases $\Delta[\nu(COO^-)] > 200 \text{ cm}^{-1}$ which implied the formation of monodendate succinic acid- γ -Fe₂O₃ complex (Fig. 4(b)).

Fig. 2(a) showed the IR spectrum of pure streptomycin for comparison purposes with those of streptomycin core-shells. As shown in Fig. 2(b), two shoulder bands appeared around 3211 cm⁻¹ (broadened due to OH) and 1590 cm⁻¹ which were assigned due to -N-H stretching and bending modes, respectively. An IR band at 1669 cm⁻¹ corresponds to -COH bond stretching and those at 618 and 1116 cm⁻¹ were due to -S-O vibrations whereas the band at 1040 cm⁻¹ was assigned due to cyclic -C-O-C stretching. The -C=N vibrations appeared together with N-H bending around 1580 cm⁻¹. The band at 1463 cm⁻¹ corresponded to C–O stretching of carbonyl group and the band at 1396 cm⁻¹ was due to C-OH vibrations [37,38]. Fig. 2(c) showed the IR spectrum of streptomycin attached to succinic acid-y-Fe₂O₃ core-shells (hereafter denoted as streptomycin-core shell). The IR bands at 618, 1040 and 1116 cm⁻¹ due to S-O vibrations had disappeared in streptomycin-core shells possibly due to SO₄²⁻ stripping. In principle, the streptomycin and core-shell sites interacted in several ways leading to a chemical bond; streptomycin can be tagged with free or succinic acid coated Fe (III) sites via -- NH or -- CHO [37]. As shown in Fig. 2(c), the bands due to N–H vibrations remained unchanged [38]. The band at 1669 cm⁻¹ due to carbonyl stretching disappeared, and a new band appeared around 1436 cm⁻¹ indicating strong interactions of organic ligands with the γ -Fe₂O₃ sites [30,31]. As shown in Fig. 2(c), the $\Delta[\nu(COO^{-})]$ value of the two bands at 1597 and 1436 cm^{-1} differed by $\sim 161 \text{ cm}^{-1}$ showing the formation of a bridging streptomycin-core-shell complex (Fig. 5(c)). However, the exact position of the band at 1436 cm^{-1} showed some ambiguity due to the overlap of $\nu(COO^{-})$ stretching and $\delta(CH_2)$ scissoring modes. The shoulder bands at 1441 cm⁻¹ and 1425 cm⁻¹ favored a bridging complex, viz. $\Delta [\nu(COO^{-})] = 140 \text{ cm}^{-1}$ [30,31,39-42]. Our spectral data did not provide any conclusive evidence for intimate interactions between (surface coated) succinic acid and streptomycin [37]. The free Fe (III) sites on succinic coated-y-Fe₂O₃ core-shells behaved as active centers for strepto-



Fig. 4. Postulated succinic acid and γ-Fe₂O₃ complexes (a) bi-dentate complex and (b) bridging complex. These complexes were optimized using B3LYP functional and 6-31G (*d*, *f*) basis set. Atomic distances were in Å.

mycin binding. When streptomycin was loaded into core-shells, the protons of –CHO radicals reacted with surface OH sites forming H₂O. The resulted –C=O groups interacted with free =FeOH sites forming a bridging complex.

3.3. Molecular cluster modeling

The properties of γ -Fe₂O₃ nanoparticles were modeled using Fe₆(OH)₁₈(H₂O)₆ ring clusters of six edge sharing octahedra joining via –OH groups. The resulting model showed a "hole" in the structure (Fig. 1-S: Support documentation). The calculated bond lengths of Fe–Fe and bulk –OH were 2.93 Å and 1.75–1.98 Å respectively. These values were in agreement with the crystallographic data [43–45]. In most cases, the calculated vibration frequencies of the different bonding modes of Fe₆(OH)₁₈(H₂O)₆ cluster were also in agreement with the experimental data. As shown in Fig. 6, a perfect match between calculated vs. experimental data was noted in the bending mode vibrations of surface –OH (spectral range 900–1024 cm⁻¹). The apparent discrepancy shown in stretching vibrations of –OH could be accounted for the H-bonded interactions [47,48]. Based on these observations, it was concluded that the structural properties of the γ -Fe₂O₃ nanoparticles can best be described by the Fe₆(OH)₁₈(H₂O)₆ cluster.

In analogy to α -Fe₂O₃ [46], a given surface of γ -Fe₂O₃ could be terminated either by Fe (III) or oxygen ions yielding polar sites. As shown in Fig. 2-S, the half-vacant O-terminated sites were unstable when compared to Fe (III)-terminated analogs. It was believed that both these sites catalyze surface hydroxylation by adsorbed H₂O via migration of protons to O-sites to form –OH. The steric hindrance of the surface –OH prevented further H₂O attachments to Fe (III) sites. Therefore, the water molecules and surface –OH groups were expected to form a network of H-bonded interactions.

The adsorption of succinic acid and streptomycin onto γ -Fe₂O₃ was also modeled using the same Fe₆(OH)₁₈(H₂O)₆ cluster. We postulated that the –CHO \rightarrow –COOH conversion was surface mediated. This fact provided a basis to examine the mechanism/s of succinic



Fig. 5. Postulated configuration of streptomycin–succinic acid-γ-Fe₂O₃ surface complex (a) γ-Fe₂O₃ cluster, (b) succinic acid, and (c) streptomycin.



Fig. 6. A comparison of experiment derived and calculated vibrational frequencies of succinic acid- γ -Fe₂O₃ nanoparticles. Similar plots were obtained for other surface complexes (data not shown). Pure Hartree–Fock (HF) calculations overemphasized bonding, therefore all frequencies were experienced large systematic errors. In contrast pure DFT functional required no scaling, or the errors were random. However the hybrid DFT functional required scaling consistent with their inclusion of some HF character. Presently we used 1.0053 as the scaling factor at B3LYP/6-31G (*d*, *f*) level which was comparable with the data shown in Ref. [52].

acid or streptomycin adsorption onto the solid via —COOH. Three coordination modes do exist: a mono-dentate mode where one carboxylate oxygen was coordinated to a surface Fe (III) site, a bidentate mode involving a de-protonated molecule where the two carboxylate oxygen atoms were bonded to the same Fe (III) site and a bridging mode where the two oxygen atoms of carboxylate were coordinated to two surface Fe (III) sites.

Fig. 6 showed the optimized structure of streptomycin attached to succinic acid- γ -Fe₂O₃ core–shells. It clearly indicated that the bonding between succinic acid and γ -Fe₂O₃ complex was bi-dentate, bi-nuclear. Therefore, the inner-sphere complexes essentially dominated in the adsorption [49]. As shown in Fig. 6, in all cases the DFT calculations of vibration frequencies of the succinic acid and streptomycin–succinic acid–Fe₆(OH)₁₈(H₂O)₆ clusters were in good agreement with the experimental data. The oxophilic character of Fe (III) ion and basic oxygen atoms of the bi-dentate carbonyl group enhanced the interaction of the iron oxide cluster with streptomycin and succinic acid forming a 6-member ring. As proposed, the succinic acid–Fe₆(OH)₁₈(H₂O)₆ and streptomycin–succinic acid–Fe₆(OH)₁₈(H₂O)₆ clusters were formed by removing water from respective surface complexes [50].

average O-Fe (III)-O angle of the optimized The Fe₆(OH)₁₈(H₂O)₆ cluster was 105.5°. The calculated Fe (III)–O bond distance (1.582 Å) was in good agreement with the experimental value (1.5893 Å). The calculated -Fe (III)-O stretching frequency was 1079.6 cm^{-1} which was in general agreement with the experimental value (1011.3 cm^{-1}). The calculated H₂O–Fe (III) and Fe (III)–O bond distances were 2.15 Å and 1.633 Å respectively. The C-O-Fe (III) (oxygen in carbonyl group) bond lengths were 2.13 Å and 2.13 Å, respectively for succinic acid and streptomycin. The HO-Fe (III) bond distance (1.81 Å) was about 0.34 Å shorter than that of the H₂O–Fe (III) and about 0.20 Å larger than that of -O-Fe (III). Moreover, during the ligand exchange, a binuclear geometry was formed for each carbonyl oxygen atom that coordinated with the surface. Even though, the cluster model suggested that the streptomycin and succinic acids favored binuclear coordination, it was hypothesized that a binuclear bi-dentate geometry, if formed, would be even more stable [51].

4. Conclusions

A new method was proposed to functionalize γ -Fe₂O₃ nanoparticles coating with succinic acid (or core-shells). Specific interactions of core-shells and streptomycin were interpreted due to bi-dentate, bi-nuclear bridging complexes. The calculated bond distances and IR frequencies showed a good agreement with the relevant experimental data.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.colsurfa.2012.03.061.

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