Journal of Molecular Structure 1086 (2015) 246–254

Contents lists available at ScienceDirect

Journal of Molecular Structure

journal homepage: www.elsevier.com/locate/molstruc

Synthesis and spectroscopic investigations of iron oxide nano-particles for biomedical applications in the treatment of cancer cells

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HIGHLIGHTS

- Ferric oxide nano-particles have an anticancer medicinal application.
- This article aimed to synthesize of Fe_2O_3 nanoparticles using a friendly procedure.
- Ferric(III) complexes of the hippuric, itaconic, and tyrosine amino acid used as a precursors.
- The Fe_2O_3 prepared has a single phase with particle size 20–60 nm.
- Iron oxide nano-particles affected on the treatment of breast carcinoma cancer cells.

ARTICLE INFO

Article history:
Received 9 November 2014
Received in revised form 22 December 2014
Accepted 30 December 2014
Available online 20 January 2015

Keywords:
Fe_2O_3
Hippuric acid
Itaconic acid
Tyrosine
Nano-scale
Anticancer activity

ABSTRACT

Recently, upon the great importance of synthesized nano-particles especially ferric oxides on medicinal applications, these nano-particles have been prepared here using friendly and low cost biological precursors moieties via a thermal decomposition method. The Fe_2O_3 nano-particles preparation method is based on thermal degradation of ferric complexes of hippuric acid, itaconic acid, or tyrosine amino acid at 600 °C. The used precursors were characterized by several characterization techniques such as micro-analysis, conductance, infrared spectra, electronic spectra, and thermogravimetric (TG/DTG). The calcinations stages were identified from the thermogravimetric analyses of ferric complexes. The narrow size distribution in nano-scale range for the Fe_2O_3 crystals have been studied using X-ray powder diffraction (XRD), scanning electron microscope (SEM), X-ray energy dispersive spectrometer (EDX) and transmission electron microscopy (TEM) analyzer. XRD data indicate that a single phase Fe_2O_3 nano-particles are obtained with particle size ranging from 20 to 60 nm. The cytotoxic activity of the Fe_2O_3 nanoparticles was tested against the breast carcinoma cells (MCF-7 cell line). The results of inhibitory concentration fifty (IC_{50}) were existed within the 3.10–3.81 μg limit.

Introduction

In the literature survey, many studies discuss about several procedures developed to prepare iron oxide nano-particles "NPs". Parameters such as cost and efficiency of the procedure, nano-particles size, stability, and biocompatibility of iron oxide NPs have to be taken into account [1–5]. Among common procedures used we can cite co-precipitation, thermal degradation, hydrothermal, microemulsion, sonochemical, electrochemical [1,2], laser pyrolysis [3], iron reducing bacteria [4,5] and synthetic route leading to a high quality nano-scaled iron oxide particles. On the other hand, the co-precipitation is one of the most conventional methods for the preparation of iron oxides (Fe_3O_4 or Fe_2O_3) by mixing 1:2 M ratio of Fe(III) and Fe(II) ions in alkaline medium at low temperature [6]. The type of anions attached to iron metal (e.g., nitrates, acetates, chlorides, sulfates, etc), temperature, stirring rate, the pH value, and the ionic strength of the media have to be controlled to improve shape, morphology, structure, and magnetic properties of iron oxide nano-particles [6,7]. Kang et al., [8] have discussed the co-precipitation (Fe(II)/Fe(III)) synthesis of Fe_3O_4 with

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http://dx.doi.org/10.1016/j.molstruc.2014.12.085
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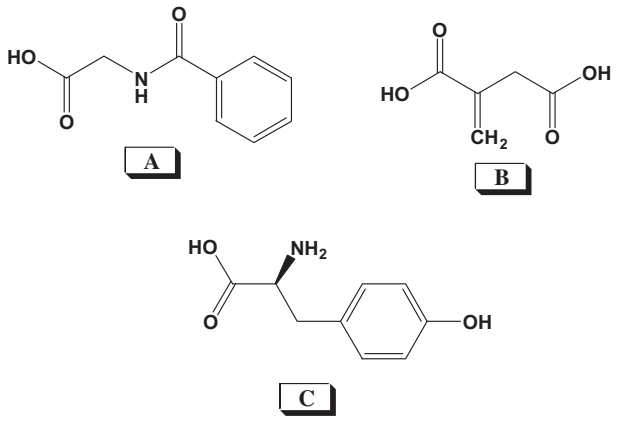

Fig. 1. Structures of (A) hippuric acid, (B) itaconic acid, and (C) tyrosine compounds.

mono-dispersed, and nano-particle scale diameter within ~8.5 nm in an aqueous alkaline medium at pH = 11–12. Recent works on this field have been performed to produce successful mono-dispersed NPs adding surfactants like dextran or polyvinyl alcohol to the reaction mixtures [9,10]. Surfactants in the co-precipitation method are used as a protecting agent of the form of particle size. The major drawback of surfactants use on iron oxides NPs synthesis is the high pH value of the reaction mixture which has to be adjusted in both synthesis and purification steps [11].

Organic moieties are useful to preclude the agglomeration of the iron oxide NPs through the synthesis process. Some of bioorganic precursor's moieties are of interest to enhance the medical compatibility of iron oxide nano-particles [11]. Moreover, organic moieties functionalized iron oxide nano-particles are useful for increasing the magnetic properties of iron NPs and for improving biocompatibility and biodegradability of functionalized organic materials. Actually, organic moieties containing some reactive groups for instance aldehyde, hydroxyl, carboxyl and amino are linked to the active bio-substance such as antibody, protein, DNA, enzyme, for medical applications [9–11]. Thermal decomposition route of some organic compounds like, $Fe(cup)_3$ (cup = N-nitrosophenyl hydroxylamine), $Fe(acac)_3$ (acac = acetylacetonate), or $Fe(CO)_5$ followed by an oxidation step can lead to a high-quality mono-dispersed iron oxide nano-particles [11]. For example, the thermal decomposition method for the preparation of mono-dispersed Fe_3O_4 nano-particles at high temperature using $Fe(acac)_3$ in phenyl ether with the presence of alcohol, oleic acid, and oleylamine has been presented by Sun and Zeng [12]. Alternatively, the direct thermal decomposition of $Fe(Cup)_3$ as only precursor lead to mono-dispersed Fe_2O_3 NPs [13]. Though, the thermal decomposition of $Fe(CO)_5$ followed by an oxidation step offer mono-dispersed Fe_2O_3 NPs [14]. Hyeon et al., [15] have studied the preparation of well crystallized mono-dispersed iron NPs by the thermal decomposition of ferric(III) pentacarbonyl in the presence of oleic acid at 100 °C with particle size ranged from 4 to16 nm. The search of the best way to prepare iron oxide NPs and their composites is mainly related to the great input of these particles in biomedical applications [16–22] being easily attached to bioactive molecules. The iron oxide NPs have been used as light scattering labels and luminescent optical markers [16–18] because of their potential applications as contrasting materials for magnetic resonance imaging [19–22], in vitro cell separation [23,24], targeted drug delivery [25] and hyperthermia [26,27]. It can be noted that particle size and surface morphology play an important role in the microbial applications [28–31]. The side effect of residual iron oxide nanoparticles with their toxicity and high-level accumulation on target tissue or organ can be overcame by functionalized bioactive molecules [32].

Furthermore, the chemistry of metal carboxylates continues to be an area of intense research in view of its diverse applications, ranging from the relevance of metal carboxylate complexes as model systems for the metal-active sites in bioinorganic chemistry [33,34] to their use as novel materials in material science. Metal oxides can be readily prepared from metal carboxylate which exhibits fascinating structural features by thermal decomposition methods [35]. The structure diversity of metal carboxylate complexes can be attributed to the versatile ligational behavior of the carboxylate group which can function like a bidentate ligand binding with single metal atom or alternatively as a bridging bidentate ligand coordinating two metal atoms or as a monodentate ligand [36–38].

Because of the numerous studies in the field of biomedical applications such as tissue engineering, the present work is focused on synthesis of magnetite ferric oxide nanoparticles demonstrating high effective ability against cancer cells. Iron oxide (Fe_2O_3) nanoparticles have been successfully synthesized by precipitation and thermal decomposition methods using precursor's complexes resulting from the coordination of ferric chloride $FeCl_3{\cdot}6H_2O$ and hippuric acid, itaconic acid, or tyrosine amino acid at 600 °C annealing temperature. The obtained nanoparticles have been characterized by X-ray powder diffraction (XRD), scanning electron microscope (SEM), X-ray energy dispersive spectrometer (EDX) and transmission electron microscopy (TEM). The cytotoxic activity of the ferric nanoparticles were tested against the human breast carcinoma cell lines (MCF-7).

Experimental

All chemicals $FeCl_3{\cdot}6H_2O$, hippuric acid, itaconic acid and tyrosine (Fig. 1) used throughout this study were Analar or extra pure grade and received from Aldrich chemical company.

Synthesis of precursor's ferric complexes

Ferric hippuric complex

The solid complex $[Fe(hip)_3]{\cdot}1½H_2O$ was prepared previously [39] by adding a water solution of ferric chloride hydrated (3 mmol) dropwisely to a stirred mixture of hippuric acid (6 mmol) in 55 mL of water–ethanol (10:1) and sodium hydroxide (6 mmol). The reaction mixture was heated to about 60 °C with constant stirring for two hours. The brown solution was left stand for two days, the precipitate formed was filtered off, washed with hot distilled water, and dried over silica gel in a desecrator.

Table 1
Elemental analysis results of precursor's ferric complexes found/calculated data.

Compounds	C%		H%		N%		Fe%	
	Calc.	Found	Calc.	Found	Calc.	Found	Calc.	Found
$[Fe(hip)_3]1.5H_2O$	52.51	51.45	4.37	4.57	6.80	6.35	9.07	8.89
$Fe_2(Ita)_3{\cdot}6H_2O$	29.80	29.69	3.97	3.92	–	–	18.49	18.41
$[Fe(tyr)_3]$	54.38	54.31	5.03	4.99	7.05	6.81	9.37	9.28