RESEARCH ARTICLE

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# Synthesis by Sol-Gel Route, Chemical, and Biological Characterization of Hybrid Material Composed by Fe(II)C and poly($\epsilon$-caprolactone)

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**Sol–gel route represents a valuable technique to obtain functional materials, in which organic and inorganic components are closely connected. Imbalance of the iron level in the body causes several diseases. In particular, the low level of iron, during pregnancy, is responsible of the iron deficiency anemia, and even of neurodegenerative diseases. The aim of this work is the synthesis of iron (II) therapeutic systems by sol–gel method. Different weight percentages of poly($\epsilon$-caprolactone) (PCL 7wt%) and ferrous citrate (Fe(II)C 6wt%) for drug delivery applications are embedded in a $SiO_2$ matrix. Fourier transform infrared (FTIR) spectroscopy is used to study the interactions among different components in the hybrid materials. $SiO_2$/Fe(II)C/PCL materials have been proposed as valuable antibacterial agents against *Escherichia coli and Enterococcus faecalis.***

## 1. Introduction

The sol–gel method, which involves the hydrolysis reactions of the precursors leading to the formation of a colloidal suspension and its evolution in a gel by condensation process, is a useful technique employed to obtain hybrid organic-inorganic materials.[1,2] Hybrid materials are commonly used in the biomedical fields as tools employed, for example, as carriers for the drug delivery or as implant components that combine the properties of both the inorganic and organic phases.[3] The importance of iron as constitutive element involved in several biological functions, such as erythropoiesis, mitochondrial activities, DNA synthesis, and repair, and many enzymatic reactions required for cell survival has been reported by many authors.[4–6] Disfunction of iron regulation and iron deficiency may contribute to several diseases [7,8] and the interest about new hybrid materials containing Fe(II) is in constant growth. Given the biocompatibility and low cytotoxicity of biopolymers such as PCL they are widely studied for biomedical application.[9,10] Here, we evaluate the possibility to synthesize a hybrid material made up of silica, Fe(II) citrate, and PCL by means of sol–gel synthesis.

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## 2. Experimental Section

### 2.1. Ferrous Citrate Preparation

A total of 25 g of citric acid monohydrate (>99.5%, Fluka, Munich, Germany) were completely dissolved in 500 mL of ultrapure water to which 6.0 g of iron powder (>99%, Sigma-Aldrich, St. Louis, MO, USA) were added. The solution was boiled and stirred under magnetic stirring until all the iron powder disappeared and consequently the ferrous citrate complex (Fe(II)C) appeared. Then, the mixture was cooled at room temperature and the gray/pearly precipitated complex was filtered off under vacuum with a paper filter and washed with water. Finally, the obtained solid was freeze dried.

### 2.2. Sol-Gel Synthesis

The sol–gel method was used to synthesize the hybrid material. The precursor of silica matrix, tetraethyl orthosilicate (TEOS; $Si(OC_2H_5)_4$; Sigma-Aldrich, Darmstadt, Germany), was added to a solution of 99.8% ethanol (EtOH, Sigma-Aldrich, Darmstadt), and distilled water with Fe(II)C 6wt%. The gel material was obtained by hydrolysis and condensation reactions. In order to prepare $SiO_2$/Fe(II)C/PCL hybrid, PCL 7wt%, dissolved in chloroform, was added to silica sol. The remaining solvent in the wet gel was removed by incubating in an oven at 40 ∘C for 24 h.[11] **Figure 1** shows the flow chart of the hybrid synthetic procedure.

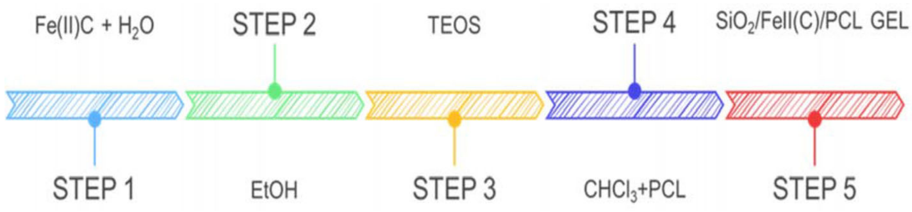


**Figure 1.** Flowchart of the sol–gel synthesis

### 2.3. Fourier Transform Infrared (FTIR) Analysis of the Hybrid Material

Prestige 21 Shimadzu (Kyoto, Japan) FTIR instrument equipped with a DTGS detector was used to evaluate the different interactions among the inorganic and organic components of the hybrids. The samples were analyzed in KBr pelletized disks containing about 2 mg of each sample and about 198 mg of KBr. The disks with a diameter of 13 mm and a thickness of 2 mm were obtained by pressing the sample powder and KBr into a cylindrical holder using a Specac manual hydraulic press. Analysis was performed with Fourier transform infrared (FTIR) transmittance over a wavenumber range of 4000–400 $cm^{-1}$ with resolution of 2 $cm^{-1}$ (60 scans). The FTIR spectra were processed by Prestige software (IR solution).

### 2.4. Antibacterial Activity

Antibacterial properties of the synthesized hybrid materials were evaluated against the Gram (-) *Escherichia coli* (ATCC 25922) and Gram (+) *Enterococcus faecalis* (ATCC 9212) bacteria. To this purpose, each bacterial culture was diluted in distilled saline water (0.9% NaCl) to produce a bacterial cell suspension of $10^5$ CFU $mL^{-1}$. *E. coli* was plated on TBX Medium (Tryptone Bile X-Gluc) (Liofilchem, Roseto degli Abruzzi (Te), Italy), while *E. faecalis* was inoculated in Slanetz–Bartley Agar Base (Liofilchem, Italy) in the presence of 100 mg of the hybrid powders. Afterward, the bacteria were incubated with and without the material for 24 h at 44°C and 48 h at 36°C, respectively. The diameter of inhibition halos (IDs) in relation to Petri dish diameter (PD) (6 cm) were calculated. Tre samples were analyzed and four measurements for each sample were carried out to determine the mean and the standard deviation. Results are expressed as Bacterial Viability (in percentage).

$$Bacterial\ Viability = \frac{PD - ID}{PD} * 100 \tag{1}$$

Bacteria viability without samples is expressed as 100%. The mean standard deviation is expressed as relative standard deviation (RSD).

## 3. Result

FTIR spectra, reported in **Figure 2**, were useful to demonstrate the formation of the hybrid material. Indeed, FTIR spectrum of the $SiO_2$/Fe(II)C/PCL (Figure 2d) shows both the main peaks of silica (Si-O-Si stretching at 1080 $cm^{-1}$ with a shoulder at 1200 $cm^{-1}$, Si-O bending at 460 $cm^{-1}$) and the presence of the

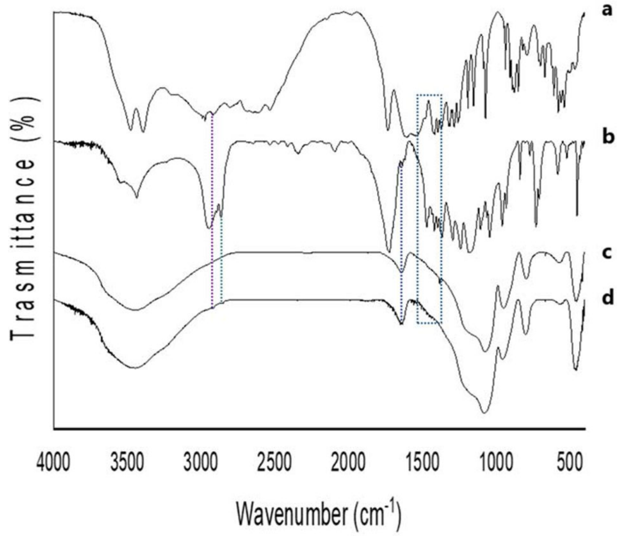


**Figure 2.** FTIR spectra of (**a**) $SiO_2$, (**b**) PCL, (**c**) Fe(II)C, and (**d**) the hybrid $SiO_2$/Fe(II)C/PCL.

asymmetric and symmetric stretching of the -$CH_2$ groups, belonging to the PCL and Fe(II)C, that correspond to the bands at 2945 and 2865 $cm^{-1}$. Moreover, from the shoulder, there is an additional band, in which the peaks due to the -$CH_2$ bending modes and COO- vibrations of the PCL and Fe(II)C are visible. Finally, the increase of the -OH stretching and bending modes at 3450 and 1650 $cm^{-1}$ could be a further demonstration of the interaction between SiO2, PCL, and Fe(II)C by H-bonds.[12–16]

To evaluate the effect of the hybrid on the microbial growth, *E. coli* and *E. faecalis* were used as bacterial strains. The hybrid material was grinded in a mortar to obtain a powder. Both bacteria were inoculated in absence and in the presence of 100 mg of sample. The results (**Figure 3**A) showed no antibacterial activity against both the gram(+) and the gram(-), indeed there are no differences between the bacterial viabilities (Figure 3B) of the bacteria essayed with and without the hybrid.

## 4. Conclusion

In the present study, Fe(II)C and PCL were added to the silica matrix by sol–gel method. FTIR spectrum of the obtained material shows the bands of citrate and the typical peaks of both the polymer and silica. Therefore, the different shape and position of some bands confirm the formation of the hybrid matter, suggesting the presence of H-bonds between the inorganic and the organic components. The synthesized hybrid material showed no

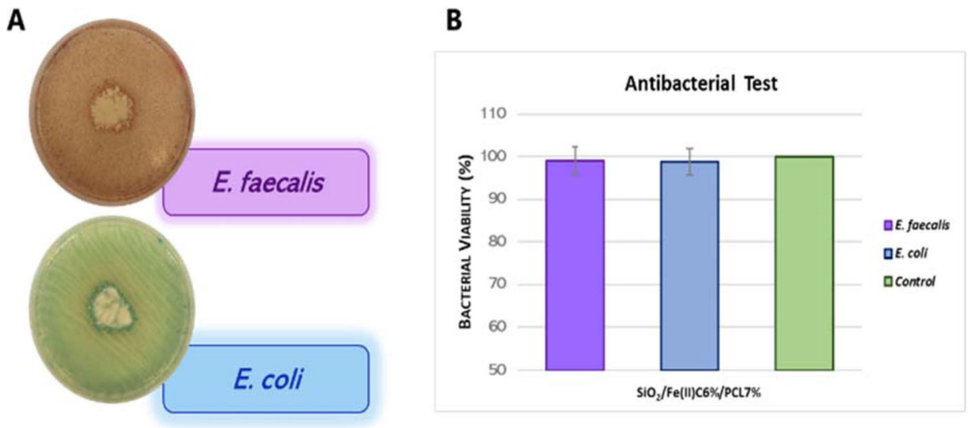


**Figure 3.** **A**) Plate images of antibacterial test of $SiO_2$/Fe(II)C6%/PCL7% in the presence of *E. faecalis* and *E. coli* strains. **B)** Bacterial viability results of $SiO_2$/Fe(II)C6%/PCL7%. Control is considered as 100% viability in the absence of samples.

antibacterial activity against both the *E. coli* and *E. faecalis,* indeed neither inhibition halos nor reduction of the bacterial viabilities were visible after the test.

## Conflict of Interest

The authors declare no conflict of interest.

## Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author.

## Keywords

antibacterial activity, ferrous citrate, FT-IR spectroscopy, PCL, sol-gel technique

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