Ceftriaxone Intercalated Nanostructures Used to Improve Medical Treatment

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The development of antibiotic resistance in bacteria possesses a huge threat to public health by nullifying the effect of even the most efficient antibiotics. From years, LDHs type nanomaterials have been used as drug carriers for a wide variety of pharmaceutically active molecules due to their delivery properties, making these inorganic-organic nanohybrids very efficient antimicrobial agents. The major purpose of this work was to synthesize and characterize ceftriaxone intercalated layered nanostructures for further use to treat some infections, mostly of them child infections. The novel nanohybrid materials were prepared by ion exchange route and coprecipitation method. Structural and morphological characterization was performed by FTIR, EDX and SEM techniques. The results revealed a high incorporation of the drug in the interlayer space of promising nanostructures.

Keywords: nanostructures, ceftriaxone, SEM, antimicrobial agents, medical treatment.

Usually drug administration consist in drug spreading through blood circulation leading to increased concentrations in undesired parts of patient's body thus causing serious side effects. There are many cases where systemic drug administration practice does not guarantee satisfactory pharmacokinetic profile because of drug concentration decreased levels. Additionally, drug delivery systems are designed to overcome these problems and to ensure a suitable drug release profile. Maintaining drug concentrations at desired levels for longer time is accomplished by using carriers that slowly release drug content. Layered double hydroxides (LDHs) nanoparticles can be used as drug carriers due to their ability of modifying surface and size distribution in order to reduce the risk of toxic side effects by targeting specific cells or tissues. These biocompatible inorganic materials possess a higher stability and lower toxicity than other drug delivery systems [1-3].

Layered double hydroxides, also known as hydrotalcites (a natural occurring hydroxycarbonate of magnesium and aluminium) or anionic clays have the structure similar to that of brucite, $Mg(OH)_2$, where metal cations fill octahedral holes every two sheets. Partial substitution of Mg/Al gives the possibility to develop positive charged layers balanced by anions and water molecules located in the interlayer space. A great advantage of these nanomaterials is that the metal cations can be substituted by others such as Fe, Zn, Co, Mn, Ni (divalents) and Co, Cr, V, Ga (trivalents) and also the interlayer anions can be replaced by a wide variety of inorganic or organic anions [4-16].

Ceftriaxone, a third generation cephalosporin, is used to treat severe infections such as community-acquired pneumonia, gonorrhea and meningitis being a time-dependent killer. Intercalation of this antibiotic into LDHs structure (fig. 1) improves antimicrobial treatment by increasing intracellular delivery thus reducing toxic side effects [17-28].

This work refers to designing of ceftriaxone-LDHs nanohybrid as a controlled drug delivery system. Layered double hydroxide nanoparticles are used as antibiotic carriers with improved medical treatment.

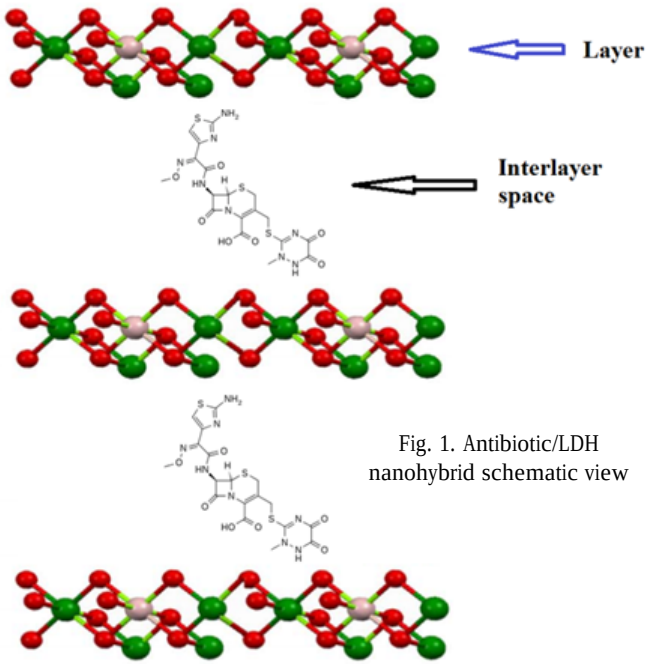

Fig. 1. Antibiotic/LDH nanohybrid schematic view

Experimental part

Materials and methods

Ceftriaxone drug-based nanocomposite was prepared by intercalation of antibiotic into the interlayer gallery of layered double hydroxide by co-precipitation. Ceftriaxone, $Mg(NO_3)_2 \cdot 6H_2O$ and $Al(NO_3)_3 \cdot 9H_2O$ compounds in a molar ratio of 0,2:2:1 were dissolved in double distilled water. The *p*H of mixed solution was adjusted at 9.0 by adding a $NaOH/Na_2CO_3$ aqueous solution. Then, the solution was vigorously stirred for 20h and the obtained precipitate of Ceftriaxone/LDH nanohybrid was washed with double distilled water, filtered and dried for further structural and morphological analysis.

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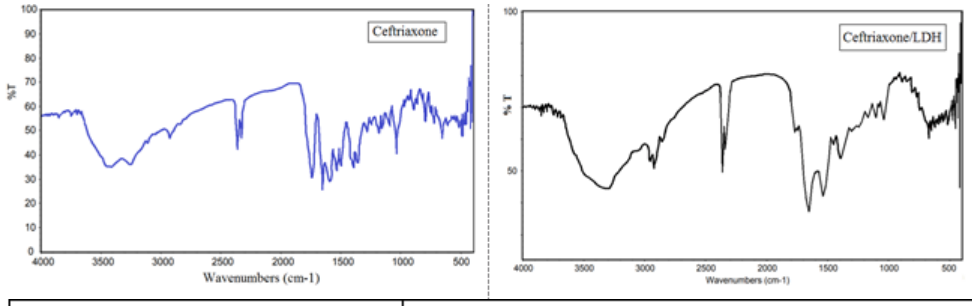

Fig. 2. IR spectra for Ceftriaxone and Ceftriaxone/LDH

Sample	Elements					
	Al	Mg	C	O	N	S
LDH	36.17	8.64	4.74	50.49	0	0
Ceftriaxone/LDH	33.36	6.5	10.58	46.7	3.64	1.35

Table 1
ELEMENTS OF LDH AND CEFTRIAXONE/LDH SAMPLES

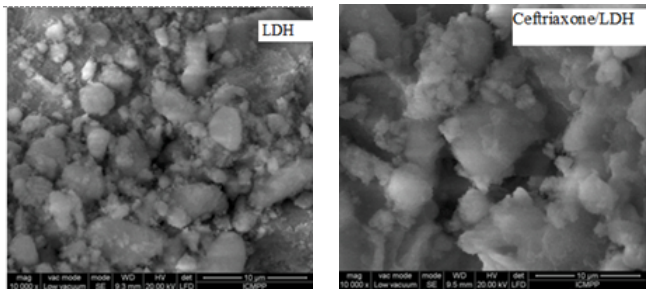

Fig. 3. SEM images of LDH and Ceftriaxone/LDH nanoparticles

Results and discussions

FTIR characterization is an important analysis for identification of intercalated ceftriaxone molecules into LDH structure (fig. 2). IR spectra for ceftriaxone present characteristic peaks at nearly 3430 cm^{-1} asigned to N-H stretching vibration of H-bonded amide group, at 1740 cm^{-1} attributed to C=O stretching vibration and 1590 cm^{-1} to C=N stretching vibration.

For ceftriaxone/LDH nanocomposite the peaks noticed at 3380 cm^{-1} corresponds to the -OH groups stretching vibration, at around 2450 cm^{-1} to C-H stretching vibration. Band around 1640 cm^{-1} and 1290 cm^{-1} are attributed to C=O groups and for C-C and C-N stretching vibration.

Elemental analysis was determined by Energy Dispersive X-Ray (EDX) technique.

SEM micrographs of LDH and Ceftriaxone/LDH samples are shown in figure 3. Antibiotic loaded hydrotalcite suggest the presence of aggregates specific for layered double hydroxides nanoparticles.

The sheet-like morphology is characterized by a particle size about 150 nm and thickness that suggest the small number of layers. They are larger than LDH sample but in the same area and aggregation degree.

Conclusions

The inclusion of active ingredients has been carried out using layered double hydroxides as inorganic matrices so as to offer advantages such as high drug loading and sustained release.

Intercalation of ceftriaxone into layered structure of anionic clays was realized in order to improve the antibiotic efficiency and to accomplish the controlled release of the drug respectively. Structural and morphological features of the obtained nanostructures confirmed that ceftriaxone molecules were intercalated into interlayer gallery of LDHs thus proving stabilization of drug molecules in anionic clay lattice. The obtained ceftriaxone - LDH nanohybrids have a huge potential for uses in some formulations containing antibiotics in order to improve medical treatment.

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