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Hybrid lipid/clay carrier system containing *Bixa orellana L.*: a tool for drug delivery

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1. Introduction

Nanocomposite systems attract considerable interest in the pharmaceutic and cosmetic fields due to the wide range of advantageous properties compared to free polymers, such as the high potential to provide predictable, accurate, and reproducible patterns of controlled release and specific delivery of bioactive molecules [1]. Studies have shown the hybridization of different clays with polymers or surfactants by strong secondary interactions of the mineral compounds with their guests. Nanostructured lipid carriers (NLC) associated with clays have gained attention in pharmaceutical areas due to their ability to transport hydrophobic drugs. Additionally, lipid-based nanoparticles are considering "nano-safety, stable, biocompatible, and have low dermal toxicity [2]. In this context, Bixa orellana L. or "annatto," has been proposed as a potential active ingredient in pharmaceuticals by its biological activity as healing, antioxidant, antibacterial, and anti-leishmaniasis properties [3]. The purpose of the present study was to produce and characterize NLCs with AO in association with Laponite (L) nanoparticles ($Na^{+}_{0.7}[(Si_8Mg_{5.5}Li_{0.3})\ O_{20}(OH)_4]^{-}_{0.7}$) [4][5].

2. Materials and methods

2.1. Preparation of nanoparticles

The production of NLC (n) was performed by the fusion-emulsification´s method, where the structural lipids cetyl palmitate (CP) or myristyl myristate (MM, 10 % (w/w)), AO (2 and 4 %, w/w), and the colloidal stabilizer Poloxamer 188 (PL, 11.7 % (w/w)) were used. Hybrid compounds contained Lipid-based nanoparticles plus L (3 %, w/w) were prepared by a simple mix of clay into the lipid colloidal system for 24 hours and stored after the process at 25 ºC.

2.2. Physicochemical characterization

Particle size, polydispersity index (PDI), and zeta potential (ZP) were measured by photon correlation spectroscopy (PCS). The morphology of uranyl-stained samples was analyzed by ultra-high-resolution transmission electron microscope with HAADF FEI TITAN G2 (UHRTEM) coupled with X-ray spectroscopy (EDX) detector.

3. Results and Discussion

Fig. 1 shows Structural properties of lipid-based nanoparticle and hybrid systems with and without AO (0-4 %, wt). DLS measurements were presented in terms of (a) size (nm), polydispersity index (PDI), and (b) zeta potential and pH values. The sizes and polydispersity of nanoparticles and hybrid systems were around 180nm, and PDI > 0.3. Zeta potential (mV) of samples ranged from -16.23 ± 0.60 to -42.73 ± 0.29. The pH values differed according to the change in liquid lipid (AO) concentration, ranging between 5.30 and 6.91 to the samples without L and around 8.52-8.61 to

the samples with L. Formulations without clay are more sensitive to the presence of AO. In addition, Fig. 1b shows that the presence of AO was the most important factor that generated changes in zeta potential values. The hybrid systems demonstrated stability over ten weeks in terms of size, zeta potential, and polydispersion.

Morphology of the nanohybrids also was assessed by TEM was found to be very similar to DLS results: spherical structures, with well-delimited shape and size of around 200 - 250 nm. Fig. 2 shows the microphotographs, the XEDS spectra, and elemental X-Ray maps of the systems containing MM.

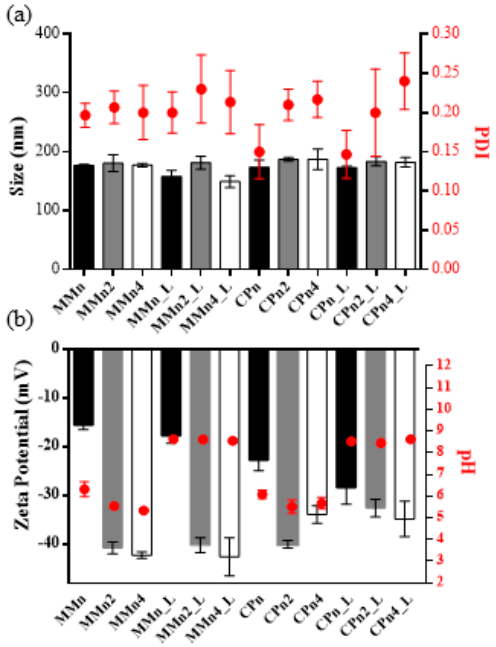

Fig. 1. Structural properties of lipid-based nanoparticle and hybrid system.

The selected areas in Fig. 2a show peaks of lipids (organic components, C and O) in a green graph (inside NLC), and clay (inorganic components, O, Mg, and Si) and C in a blue graph. A weak Cu peak corresponding to the support (grids) used to prepare the samples was observed also. The Fig. 2a, at region pointed by arrows, showed L outside of nanoparticle and no changes in shape or size. The same was observed at Fig. 2b and 2c for MMn2_L and MMn4_L formulations respectively. In addition, X-ray map presented in Fig. 2c highlights Si and Mg revealing the elemental composition of L and its distribution in the hybrid systems. No changes were observed in nano-hybrid prepared with CP.

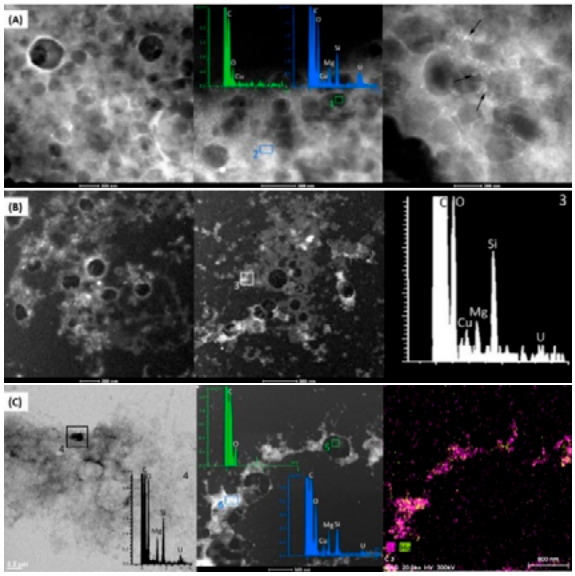

Fig.2. UHRTEM microphotographs, XEDS analysis and elemental X-Ray maps of MMn_L (a), MMn2_L (b) and MMn4_L (c). scale bars =200 nm.

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