Chlorhexidine-clay nanostructured materials of potential interest in biomedical applications

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INTRODUCTION AND OBJECTIVES

Since prehistoric times, clays have been used for human health applications (Carretero et al., 2013). Drug stability is often enhanced by encapsulation in clay minerals, based on intercalation processes in smectites such as montmorillonite, or adsorbed in microporous clays such as sepiolite, palygorskite or halloysite. The resulting clay-drug hybrids are increasingly used to control drug release over time and even to protect them from degradation (Viseras et al., 2007). Many researchers have contributed to the preparation of new clay-drug compounds by assembling clays and drugs with very different therapeutic activities. For example, in our research group we have assembled smectites (montmorillonite), microfibrous (sepiolite) and nanotubular (halloysite) clay minerals and related solids (e.g. DLH), with antidiabetic (e.g., metformin) (Rebitski et al., 2020), anticancer (e.g., 5-aminosalicylic acid (Ribeiro et al., 2014), analgesic (ibuprofen) and antimicrobial (salicylic acid) drugs (Lizuzzo et al., 2020). The present work describes the preparation and characterization of nanostructured hybrids based on the assembly of chlorhexidine (CHX) to montmorillonite and sepiolite. CHX is an antiseptic agent with bactericidal and fungicidal action, being on the World Health Organization's list of Essential Medicines required in a health care system (Wikipedia, retrieved 15/11/2024 from https://es.wikipedia.org/wiki/Clorhexidina). CXH is widely used in dental hygiene and general dentistry, being also used for topical cleaning and disinfection of wounds and burns, erosions and abrasions, gynecological cleaning, etc. The antimicrobial effect of chlorhexidine gluconate is due to the destruction of the microbial cell membrane. From the chemical point of view the CHX formulae is shown in Fig. 1, receiving the IUPAC name of (1E)-2-[6-[(amino-[(E)-[amino-[amino-(4-chloroanilino)methylidene]amino) methylidene]amino]hexyl]-1-[amino-(4-chloroanilino) methylidene] guanidine. Highly polar amino groups are well suited for intercalation, either as neutral species or capable of being protonated to be intercalated by ion-exchange mechanisms.

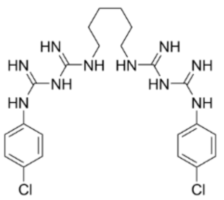

Fig. 1. Chemical structure of chlorhexidine

ADSORPTION OF CHLORHEXIDINE ON MONTMORILLONITE AND SEPIOLITE

Clay-chlorhexidine hybrid materials have been prepared using chlorhexidine (CHX) digluconate in 20% solution in water, supplied by Sigma Aldrich and high purity samples of two clay minerals: i) Na-montmorillonite (MONT) sample (marketed by Southern Clay Products, Inc., as Cloisite®Na), and ii) natural sepiolite (SEP) marketed by TOLSA S.A. as Pangel S9 ('rheological grade'). The CHX adsorption processes of MONT and SEP has been studied at 25°C using 100 mg of sepiolite and 25 mL of CHX aqueous solutions at different initial concentrations with the aim to obtain the corresponding adsorption isotherms. The clay-CHX dispersions are stirred in an orbital shaker for 48 hours, and then the solutions are centrifuged, separating the solid from the supernatant, the recovered solid being left to dry in an oven at 65ºC at the ambient atmosphere for a minimum of 12 h. The equilibrium concentrations of CHX present in the supernatants is determined by application of the Beer–Lambert law by acquiring the absorbance values from the UV-Vis spectra (CHX digluconate has an absorbance maximum at about 254 nm). Maximum values of CHX adsorption have been determined in the range of 40-65 mmoles/100 g of clay mineral.

CHARACTERIZATION OF CHLORHEXIDINE-CLAY HYBRID NANOMATERIALS

Various physicochemical techniques such as powder X-ray diffraction (XRD), IR spectroscopy (ATR and FTIR), elemental chemical analysis, UV-Vis spectroscopy (for liquids and solids) have been applied to characterize the CHX-clay compunds. XRD (Fig. 2) of the materials obtained by treatment of Na-montmorillonite with CHX indicate that chlorhexidine has the ability to intercalate the layers of the smectite. An increase in the basal spacing of about 0.5 nm is observed, which can be attributed to a planar arrangement of the CHX molecule on the interlamellar space of the phyllosilicate.

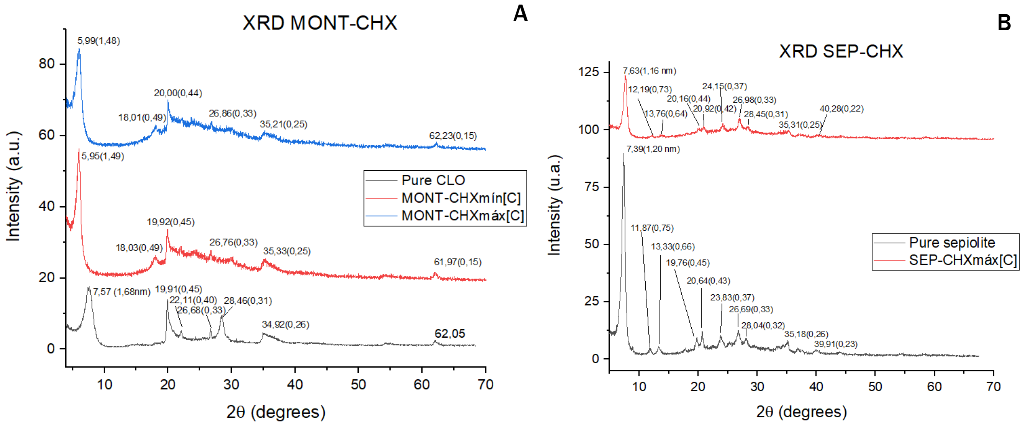

Fig. 2 Powder X-ray diffractograms of A) SEP-CHX and B) MONT-CHX (in parentheses: distances in nm)

The IR spectra of the resulting CHX-clay solids show typical adsorption bands of amino groups and C-H stretching and deformation vibrations (see e.g. bands at 2935, 2860, 1420 and 1370 cm^{-1}) and UV-Vis spectra (255, 292 and 355 nm) are characteristic of CHX having the ability to form molecular aggregates.

CONCLUSIONS

Chlorhexidine, as a digluconate solution, interacts with montmorillonite and sepiolite generating nanostructured materials in which the drug associates with the clay, intercalating on the montmorillonite and adsorbing on the external surface of the sepiolite. These materials are potentially of application for the controlled delivery of CHX. The bactericidal properties and release kinetics of the antiseptic assembled to the clay minerals remain to be studied.

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