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Bioactive Molecule (Pravastatin) incorporated in Layered Double Hydroxide Nanomaterials

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Abstract – The sodium salt of the cholesterol lowering agent pravastatin (Pr) was incorporated in Mg-Al LDH (Layered Double Hydroxide) by co-precipitation method. X-ray diffraction (XRD) patterns show that both samples present the peaks (012), (110) and (113) related to the formation of lamellar materials. The increase in basal spacing (d_{003} ~ 3.0-3.1 nm) suggest that the anionic species are arranged in a trilayer in interlayer region. Elemental analysis data found (and calculated) of $Mg_2Al.2Pr$ and $Mg_2Al.3Pr$ were 34.71(41.07) and 34.43 (41.07) for carbon and 6.37(7.29) and 6.40(7.29) for hydrogen, respectively, that confirm the presence of the organic species.

Layered Double Hydroxides, also known as hydrotalcite like-compounds, have received increasing attention as host materials for organic species that have biological activity due to side effects commonly produced by the drugs.[1] The emerging inorganic materials beyond biocompatible present antacid character.[1] The substance intercalation between the layers can also improve the molecule stability against degradation processes such as hydrolysis and photo-reactions and keep the sustained release of the guest species.[2] In this study, synthetic routes and experimental parameters were evaluated for the confinement of anionic form of pravastatin (shown in Fig. 1) which is used to reduce blood cholesterol levels and preventing cardiovascular disease.[3] Samples were synthesized by co-precipitation method, using molar ratio Mg^{+2}/Al^{+3} = 2 and varying the molar ratio Pr^{-}/Al^{+3} in 2 and 3. The XRD patterns (Fig. 2) of the obtained materials show the formation of lamellar materials by the presence of (012), (110) and (113) reflections. The enhanced in interlayer distance d_{003} from 0.771 nm ($Mg_2Al.Cl$) to 3.197 nm in $Mg_2Al.2Pr$ and 3.064 nm in $Mg_2Al.3Pr$ indicate the arrangement of trilayer of biological molecule in the interlayers spacing. Thermal analysis data reveal that guest thermal stability is equal or slightly higher than the non-intercalated species. Sodium pravastatin presents two main events of weight loss (175 – 290 °C and 300 – 517 °C) that corresponds to combustion of the organic species. The both materials exhibited two weight loss events above 177 °C. In the temperature range of 177 - 610 °C (ca. 63%) for $Mg_2Al.2Pr$ and 180-615°C (ca. 64%) for $Mg_2Al.3Pr$ being a continuous weight loss process. The slow weight loss event (177 ~ 460 °C) may involve simultaneously partial dehydroxylation of the brucite-like layers and decomposition of pravastatin anions, whereas the weight loss at 450 to 615 °C occurs the complete combustion of guest anion and dehydroxylation of the host layers. FTIR spectra of these materials shows the main absorption bands of the ion derived of pravastatin such as νC-H of the ring (2968 cm^{-1} and 2875 cm^{-1}) and $\nu_{as}COO^-$ (1560 cm^{-1}). The present results imply that the intercalation in LDH of guest molecule is the same for both materials even using different excess of the anion derived of pravastatin.

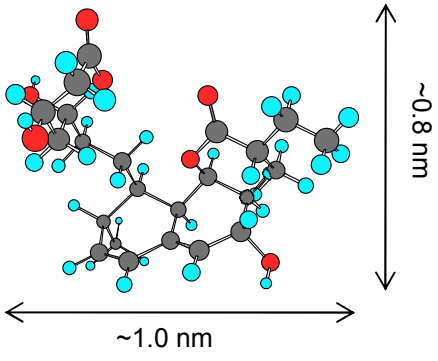

Figure 1: Structure of anionic form of pravastatin. Color codes: gray C; red O and blue H.

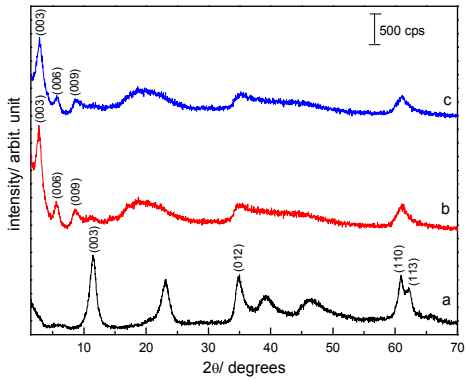

Figure 2: XRD of (a) $Mg_2Al.Cl$, (b) $Mg_2Al.2Pr$ and (c) $Mg_2Al.3Pr$.

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