Desorption Studies of Nimesulide on Layered Double Hydroxides

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It is estimated that over 40 to 70% of all new chemical entities developed by pharmaceutical companies are poorly water-soluble.[1,2] There are number of factors which affect drug dissolution rate which include particle size, polymorphism and wettability, and various formulation strategies to improve solubility of poorly water-soluble drugs have been employed, such as encapsulation of drugs into liposomes, nanoparticles and porous polymer films.[2,3] Layered double hydroxides (LDHs), also known as anionic clays, are candidates in potential to carry and improve drug solubility because of their lamellar structure, rich ionic surface and inherent positive charge. Also, depending on chemical composition, LDHs can exhibit low toxicity, biocompatibility and high stability, besides LDHs may be functionalized with surfactants, proteins and antibodies, and can be synthesized by trivial and affordable methods.[4] The aim of this work was focused on the preparation of LDHs derived from Mg/Fe (2:1) and Mg/Al (2:1) to incorporate a non-steroidal anti-inflammatory nimesulide (NMS) to improve the drug solubility in water and different buffered phosphate solutions with pH 4.0 and 7.4 at 40 °C. The synthesized LDHs and solid dispersions prepared with LDHs and NMS (LDH Mg/Fe-NMS and Mg/Al-NMS) were characterized by X-ray diffraction, atomic absorption and scanned electron microscopy. The loading and desorption kinetics of NMS from solid dispersions were analyzed in solutions by UV-vis spectroscopy and reversed-phase high performance liquid chromatography. The results showed an average loading of NMS around 40% w/w in all dispersions, and for LDH Mg/Fe-NMS a faster release of drug (close to 1h) was observed when it was compared with LDH Mg/Al-NMS (around 2h) and free NMS (superior to 24h to reach equilibrium), independently of solution pH. The dissolution rate also was monitored, and the results suggested an increase of solubility of NMS in both LDH-NMS at least two- to five-fold higher than compared to free NMS in the same conditions. These preliminary results are promising to use LDHs as carries to improve water solubility of weakly ionizable drugs. Details of the synthesis, characterization and desorption kinetics of the compounds will be presented.

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