ASSEMBLY AND RELEASE OF DICLOFENAC ACID-PILLARED HYDROTALCITES

X. PENG†‡, K. HUANG‡, S. ZHANG† and J. LIU†

† *Department of Chemistry and Environmental Engineering, Changsha University, Changsha 410003, China.*

‡ *School of Chemistry and Chemical Engineering, Central South University, Changsha 410083China .*

pxiahui@yahoo.com.cn

***Abstract*— A pharmaceutically active material diclofenac was intercalated into a layered double hydroxide by co-precipitation method, release studies suggest that the result diclofenac acid-pillared hydrotalcites (Dic-LDHs) have significant sustained release effect. The complex materials were characterrized using XRD, FTIR, DSC-TG, EA and ICP. The result show that the interlayer distance of the Dic-LDHs is expanded to 1.83nm and the thermal stability of material increases after the intercalation of diclofenac.**

***Keywords*— Diclofenac acid, Hydrotalcites, Release, Assembly.**

I. INTRODUCTION

Layered double hydroxides (LDHs), which are referred to as hydrotalcite-like compounds or as anionic clays, are an important class of ionic lamellar solids (Cavani *et al.*, 1991). They can be described by the general formula: $[M^{2+}_{1-x}M^{3+}_{x}(OH)_2]^{x+}(A^{n-})_{x/n}$. m H_2O, where M^{2+} and M^{3+} can be any divalent and trivalent metal ions (with ionic radius similar to Mg^{2+}), x is the metal ratio $M^{3+}/(M^{2+}+M^{3+})$ and A^{n-} is the interlamellar charge-compensating anions (Bouraada *et al.*, 2008). Their structure are made of brucite-like layers ($Mg(OH)_2$) with partial substitution of divalent cations by trivalent cations resulting in a net positive charge balanced by interlayer anions associated with variable amounts of water (Gennequin *et al.*, 2008). They have been widely investigated owing to their potential applications as ion exchangers, catalyst supports and so on (Carpani *et al.*, 2004; Terry, 2004). Recently, LDHs have been investigated for storage and delivery of some drugs, such as NSAIDs (nonsteroidal anti-inflammatory drugs) widely used in rheumatism treatment.

Diclofenac (Dic) is an important analgesic and anti-inflammatory drug, widely used in the treatment of post-operative pain, rheumatoid arthritis, and chronic pain associated with cancer (Sparidans *et al.*, 2008). Similar to other NSAIDs, Dic use is associated with rare, but serious and sometimes fatal, gastrointestinal (GI) side effects, including ulceration, and hemorrhage, so it is an ideal candidate for incorporation in a controlled release device to diminish its adverse effects after oral administration. Different approaches have been taken to decrease NSAID-induced GI toxicity (Mehta *et al.*, 2008). For example, incorporation of NSAIDs with phospholipid has been suggested to improve GI safety of these drugs (Khazaeinia and Jamali, 2003). Another way to reduce the side effect from the treatment with NSAIDs is the concomitant use of antacids. LDHs, a commercially available antacid, shows high efficiency in the treatment of NSAIDs induced gastro duodenal lesions. Furthermore, the concomitant use is considered as an approach to improve drug solubility and decrease gastric irritation (Khan *et al.*, 2001; Gordijo *et al.*, 2005).

The salts of acid drugs dissociate in aqueous solution, obtaining an anionic form of the drug that can significantly interact with LDHs by anion exchange. LDHs are often used as matrices for several pharmaceuticals. Salicylate and naproxen were intercalated into the interlayer space of hydrotalcites, characterizing the solids obtained by several physicochemical techniques and studying their thermal behaviour (del Arco *et al.*, 2004). Naproxen intercalated into LDHs was also studied by Wei *et al.* (2004), highlighting that the thermal stability of the intercalated naproxen is significantly enhanced compared with the pure form, which suggests that this drug-inorganic layered material may have prospective application as the basis of a novel drug delivery system. Adsorption of medical broad spectrum drugs as aspirin on LDHs appears sufficiently weak and the drug is easily removed by water, and do not modify the medical effects of the drug (Linares *et al.*, 2004). He *et al.* (2004) studied several organic UV absorbents intercalated into Zn_2Al LDHs: organic compounds in the interlayer space still maintain the original structure and UV absorption ability. The immobilization of the non-steroidal antiinflammatory drug ibuprofen and Cu-ibuprofen compounds on magnesium–aluminum LDHs by three routes (ion-exchange, co-precipitation, reconstruction) was studied by Gordijo *et al.* (2005), comparing the pharmacological potential of the materials considering the amounts of the immobilized drugs and their buffering properties. Bonina *et al.* (2008) studied Diclofenac-hydrotalcites used for in vitro release experiments to evaluate the percutaneous absorption of diclofenac. This sample was selected for the in vivo experiments. The result showed the diclofenac-hydrotalcite appeared to be useful for an efficient application on human skin as inhibitor of the UV-induced erythemas, also better than the usual gel samples.

In this paper, we report the intercalation of DIC (2-(2,6-dichloranilino) phenylacetic acid) into LDHs by co-precipitation method. The intercalation will be a way to prepare sustained and controlled release prepgration of diclofenac. Initial studies suggest that the medical of