UNIVERSITI TEKNOLOGI MARA

INTERCALATION OF FLUFENAMIC ACID INTO MAGNESIUM-ALUMINUM-LAYERED DOUBLE HYDROXIDE AND ZINC-ALUMINUM-LAYERED DOUBLE HYDROXIDE FOR THE FORMATION OF CONTROLLED RELEASE DRUGS

MONICA LIMAU ANAK JADAM

Thesis submitted in fulfillment
of the requirements for the degree of
Master of Science (Chemistry)

Faculty of Applied Sciences

MAY 2018

ABSTRACT

Flufenamic acid, a non-steroidal anti-inflammatory drug (NSAID) was successfully intercalated into Magnesium-Aluminum-layered double hydroxide (Mg/Al-LDH) and Zn-Al-layered double hydroxide (Zn/Al-LDH) by self-assembly method at concentration of 0.6 M flufenamic acid and molar ratio of Mg/Zn:Al = 2. The nanocomposites were synthesized until reached their optimum pH to enhance the intercalation process. The optimum pH for Magnesium-Aluminum-flufenamic acid (Mg/Al-FA) is at pH10 and Zn-Al-flufenamic acid (Zn/Al-FA) is at pH7.5. Upon the successful intercalation of the drug, release profiles and the factors govern its release from their matrices into various aqueous media were determined. The relatively phase-pure with well-ordered layered nanohybrid materials were successfully synthesized by self-assembly method at optimum condition. Expansion of basal spacing was observed from 9.8 Å in the Mg/Al-LDH to 23.5 Å in the Mg/Al-FA-LDH and 8.9 Å in the Zn/Al-LDH to 21.0 Å in the Zn/Al-FA-LDH nanocomposite obtained from the analysis by using PXRD. The results were supported by the data obtained from the whole analysis using FTIR, TGA/DTG, UV-Vis, CHNS, ASAP and ICP-AES. Controlled release study of the drug into the aqueous solutions of sodium carbonate solution, sodium chloride solution and saline solution were performed. The release of drug into the aqueous media is in the order of; sodium carbonate > sodium chloride > saline solution with the percentage release of 50%, 30% and 20% for Mg/Al-FA-LDH and 53%, 42% and 20% for Zn/Al-FA-LDH, respectively. The release profiles are best described by pseudo-second order kinetic model as shown by the regression values of about 1.0. The FA anion was successfully intercalated into Mg/Al-LDH and Zn/Al-LDH with the percentage loading of guest anions which are 63.37% and 63.40%, respectively. This study shows that the Mg/Al-LDH and Zn/Al-LDH can be used as a matrix for controlled release formulation of FA drug. The release of FA from the matrix was found to be controlled by the anion in the release aqueous solution as well as the type of the release media.

ACKNOWLEDGEMENT

Glory is to God and praised be to the Lord. In the name of the Lord, with His beautiful mercy and amazing guidance, I am totally blessed to be able to complete my master's degree within 2 years. I would like to express my gratitude and deepest appreciation to my dedicated supervisor, Assoc. Prof. Dr. Siti Halimah Binti Sarijo and my co-supervisor, Assoc. Prof. Dr Faizah Binti Md Salleh and Dr. Hamizah Binti Mohd Zaki for their excellent supervision, guidance and motivational support throughout years of my study.

Special thanks to my fellow friends, especially to my only special best friend, Idayu Razali, my lovely soul sisters Kak Aida, Kak Aqilah, Kak Mudah and Kak Ana for their unforgettable moral support and companion since the first day I started my postgraduate journey. Not to forget Kak Nik Hana, Kak Sarah, and Kak Fiza, thank you for always making me feel belong and making my postgraduate journey happen. I am so blessed and truly, truly thankful for being surrounded by such an amazing personality. My sincere thanks and gratitude to all the very helpful UiTM officers for always giving hands whenever in need. Thank you to the kind hearted lab staffs; especially to En. Ahmad Kambali, En. Azrin and Puan Haslina who have helped me during the early days of my project.

Precious thanks and appreciation to my beloved family, especially to my parents, Jadam Jinggan and my younger brothers Francis Ngelai and Dominic Daniel, my beloved grandmother Cecelia Jenoh Geraman, for their unlimited love, support and understanding throughout the years of my study. I would like to dedicate this piece of victory to all of you. Thank you very much for never letting me fight this battle alone and always being a safe place for me to run to when the issues of this life become too much to bear. May the peace of God be with all of you.

I would like to give credit to Ministry of Higher Education (MOHE) of Malaysia for sponsoring my education under MyBrain15 (MyMaster) Program. This thesis has been made possible in part due to financial support from Fundamental Research Grant Scheme (FRGS) from Minister of Education (MOE) and also private grant from Malaysia Toray Science Foundation (MTSF).

TABLE OF CONTENTS

CHAPTER ONE
INTRODUCTION

1.1 RESEARCH BACKGROUND

1.1.1 Nanocomposites

Nanocomposites can be defined as materials or substances with one or more components consisting of phase with at least one dimension having less than 100 nanometers. Nanocomposite derived from addition of nanoparticles has better properties including great mechanical strength, good electrical or thermal conductivity and toughness in structure. Some nanocomposites show advanced property such as flame retardancy, thermal stability and chemical resistance (Xu and Lu, 2006). Nanoparticles have been widely used for many applications such as in automotive, food industry, films and cosmetic product (Sekhon, 2014).

1.1.2 Layered Double Hydroxides

The assembly of molecular species of biological origin and inorganic substrates through interactions on the nanometric scale constitutes the basis for the preparation of nanohybrid materials (Hussein *et al.*, 2004). Layered double hydroxides (LDHs) have been recently used to prepare organic or inorganic hybrids, by intercalating anionic drug molecules in the interlayer space, thus becoming protected against changes originated by damping, light or heat. In the case of drug delivery, the inorganic solid acts as matrix to prepare systems with controlled drug release formulation (Arco *et al.*, 2010).

Layered Double Hydroxides (LDHs) are materials that have brucite type layer made up of mixed metal hydroxides of divalent and trivalent metals. The exchangeable intercalated negatively charged species in between the two surface layers compensate the positive charge of the brucite layer. LDHs also known as hydrotalcite-like minerals or anionic clays, which can be found in nature as minerals and easily being synthesized in the laboratory (Xu and Lu, 2006).