UNIVERSITI TEKNOLOGI MARA

SYNTHESIS OF CALCIUM-ALUMINIUM-CIPROFLOXACIN LAYERED DOUBLE HYDROXIDE – PHYSICOCHEMICAL PROPERTIES AND EVALUATION ON ANTIBACTERIAL ACTIVITY AND CYTOTOXICITY

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PhD

September 2021

AUTHOR'S DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Teknologi MARA. It is original and is the results of my own work, unless otherwise indicated or acknowledged as referenced work. This thesis has not been submitted to any other academic institution or non-academic institution for any degree or qualification.

I, hereby, acknowledge that I have been supplied with the Academic Rules and Regulations for Post Graduate, Universiti Teknologi MARA, regulating the conduct of my study and research.

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Faculty	:	Applied Sciences
Thesis Title	:	Synthesis of Calcium-Aluminium-Ciprofloxacin Layered Double Hydroxide – Physicochemical Properties and Evaluation on Antibacterial Activity and Cytotoxicity
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ABSTRACT

Layered double hydroxides (LDHs) have been proposed as drug delivery systems of fluoroquinolones including ciprofloxacin (CPX) to overcome their low bioavailability and prevent the emergence of resistant bacteria. CPX is used in the treatment of various bacterial infections. However, there are cases of side effects associated with CPX such as gastrointestinal irritation, tendon problem and skin cancer. Since these issues have become a major concern in the pharmaceutical industry, more studies on the alteration of drug behaviour were carried out to avoid these harmful side effects. In this study, calcium-aluminium-layered double hydroxide (CAL) carrier with a molar ratio of 3:1 (Ca:Al) was initially synthesized by hydrothermal technique. Subsequently, a fluoroquinolone antibacterial drug, CPX was incorporated into the interlayer of the CAL host by anion exchange method to produce calcium-aluminium-ciprofloxacin-layered double hydroxide (CAC). The successful intercalation was confirmed by powder X-ray diffraction (PXRD) pattern analysis, Fourier transform infrared spectroscopy (FTIR), carbon, hydrogen, and nitrogen analysis (CHN), thermogravimetric and differential thermogravimetic analysis (TGA/DTG), and inductively coupled plasma-atomic emission spectrometry (ICP-AES). The material was also characterized by using field emission scanning electron microscope (FESEM), transmission electron microscopy (TEM), and accelerated surface area and porosity (ASAP) analysis. Well crystallized nanohybrid was obtained at the concentration of 0.2 M CPX. The basal spacing of CAC (0.2 M CPX) synthesized in this study is 17.3 Å, which resulted from the expansion of CAL due to the inclusion of CPX in the interlayer space of the CAL carrier with a loading percentage of 75.9% (w/w). The FTIR spectra of CAC show resemblance to the peaks of CAL and CPX, indicating the inclusion of the drug into the CAL interlayers. The release percentages of the drug into phosphate-buffered saline (PBS) at pH 1.2, pH 4.8, pH 6.8 and 7.4 are 65%, 67%, 58% and 60%, respectively, and are best described by the pseudo-second order kinetic model. Cytotoxicity studies of CPX, CAL and CAC on human lung fibroblast (MRC5) cells and normal mouse embryonic (3T3) cells showed no significant toxicity until 100 μg/mL. The antimicrobial activity of CPX, CAL, and CAC were investigated against *Escherichia coli*, *Klebsiella pneumoniae*, and *Staphylococcus aureus* by disc diffusion method. All tested treatments were found effective against all tested strains and there is no significant difference between the CPX and CAC as it was similar in their antibacterial activities. The MICs of the synthesized nanocomposite, CAC against *Escherichia coli, Klebsiella pneumoniae* and *Staphylococcus aureus* were found to be 50, 40, and 60 μg/mL, respectively and the MBCs of the nanocomposite against all the pathogenic bacteria is similar at 5 mg/mL. Therefore, this study proved that CAL nanocarrier can successfully serve as a controlled release and drug delivery system for the antibacterial drug, CPX.

ACKNOWLEDGEMENT

Every good and perfect gift is from above, praise be to God! In the name of the Lord, with His beautiful love and mercy, I am totally blessed to complete my PhD within the stipulated time. My doctoral thesis is dedicated to all members of my personal network who connect, inspire, collaborate, and share with me personally and professionally. I am thankful for their encouragement and great contribution to this research.

First and foremost, I would like to express my deepest appreciation and gratitude to my dedicated supervisor, Assoc. Prof. Dr. Siti Halimah Binti Sarijo and my co-supervisors, Assoc. Prof. Dr. Sharifah Aminah Binti Syed Mohamad, Dr. Zaemah Binti Jubri and Dr. Hamizah Binti Mohd Zaki for their excellent supervision, guidance, and motivational support throughout years of my study. I am honoured to have great mentors, who have guided me through what started as daunting maze, which eventually turned into a pathway of intellectual discovery.

Special thanks to my fellow friends for their companion since the first day I started my postgraduate journey. I am incredibly grateful for those of you who stood by to support me along the way. My sincere thanks to all the helpful UiTM officers and kind lab staffs for always giving hands whenever in need during the early days of my project. Not to forget, big thanks to Dr. Norazalina Saad and Mrs. Sumaiyah Megat for their valuable contribution during my academic writing and paper publishing. May the peace of God be with all of you.

Precious thanks and appreciation to my beloved family, especially to my parents, Jadam Jinggan and Deisy Betau Layang, my younger brothers Francis Ngelai and Dominic Daniel, my sister-in-law Izuarina Casandra Dorcas and my late grandmother Cecelia Jenoh Geraman who just passed away on 5th July 2021, for their understanding, endless love, tremendously support and prayers. Thank you for never letting me fight this battle alone and joining me in this scholarly adventure. This piece of victory is dedicated to all of you.

A heartfelt thank goes out to the Faculty of Applied Sciences and Universiti Teknologi MARA (UiTM) for providing adequate research facilities and giving me opportunity to complete my PhD in this institution. This thesis has been made possible in part due to financial support from Research Entity Initiative (REI) (File No: 600-IRMI/REI 5/3 (008/2019) by UiTM.

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