

Thesis Title Chemical Constituents and Biological Activities
from *Clausena harmandiana*, *Clausena lansium*,
and *Clausena wallichii*

Author Wisanu Maneerat

Degree Doctor of Philosophy (Applied Chemistry)

Advisor Asst. Prof. Dr. Surat Laphookhieo

ABSTRACT

Phytochemical investigation and biological activity studies from *Clausena* plants including *Clausena harmandiana*, *Clausena lansium*, and *Clausena wallichii* led to the isolation and identification of twenty-one new compounds (**WM22**, **WM23**, **WM25-WM27**, **WM29**, **WM32-WM35**, **WM37**, **WM42**, **WM56-WM54**, **WM57**, **WM62**, and **WM66**) along with fifty-three known compounds (**WM1-WM21**, **WM24**, **WM28**, **WM30**, **WM32**, **WM36**, **WM38**, **WM39-WM41**, **WM43-WM47**, and **WM67-WM74**). All structures were characterized by spectroscopic methods, including NMR, UV, IR, and MS spectral data for structural characterization. Some of isolated compounds were exhibited cytotoxicity and antibacterial activities.

Three new carbazole alkaloids, harmandianamines A (**WM50**), B (**WM49**), and C (**WM37**), together with fifteen known compounds (**WM3**, **WM5**, **WM14**, **WM15**, **WM36**, **WM38**, **WM39**, **WM43-WM48**, **WM70**, and **WM71**) were isolated from the twigs of *Clausena harmandiana*. The antibacterial activity against *Escherichia coli* TISTR 780, *Salmonella typhimurium* TISTR 292, *Staphylococcus aureus* TISTR 1466, and methicillin-resistant *Staphylococcus aureus* (MRSA) SK1

of some isolated compounds were also evaluated. Compound **WM47** exhibited significant antibacterial activity against MRSA SK1 with an MIC value of 0.25 µg/mL which was higher than that of the standard drug, vancomycin (MIC value = 1 µg/mL) whereas compounds **WM44** and **WM46** showed strong activity with MIC values of 4 and 8 µg/mL, respectively. Only compound **WM44** showed strong antibacterial activity against *Staphylococcus aureus* TISTR 1466 with an MIC value of 4 µg/mL.

A new phenylpropanoid derivative, harmandianone (**WM66**), along with five known compounds (**WM67–WM70** and **WM74**) were isolated from the acetone extract of *Clausena harmandiana* fruits. Compounds **WM66**, **WM68–WM70**, and **WM74** demonstrated weak antibacterial activities against *Escherichia coli* TISTR 780, *Salmonella typhimurium* TISTR 292, *Staphylococcus aureus* TISTR 1466 and methicillin-resistant *Staphylococcus aureus* (MRSA) SK1, with MIC values between 64 and 128 µg/mL.

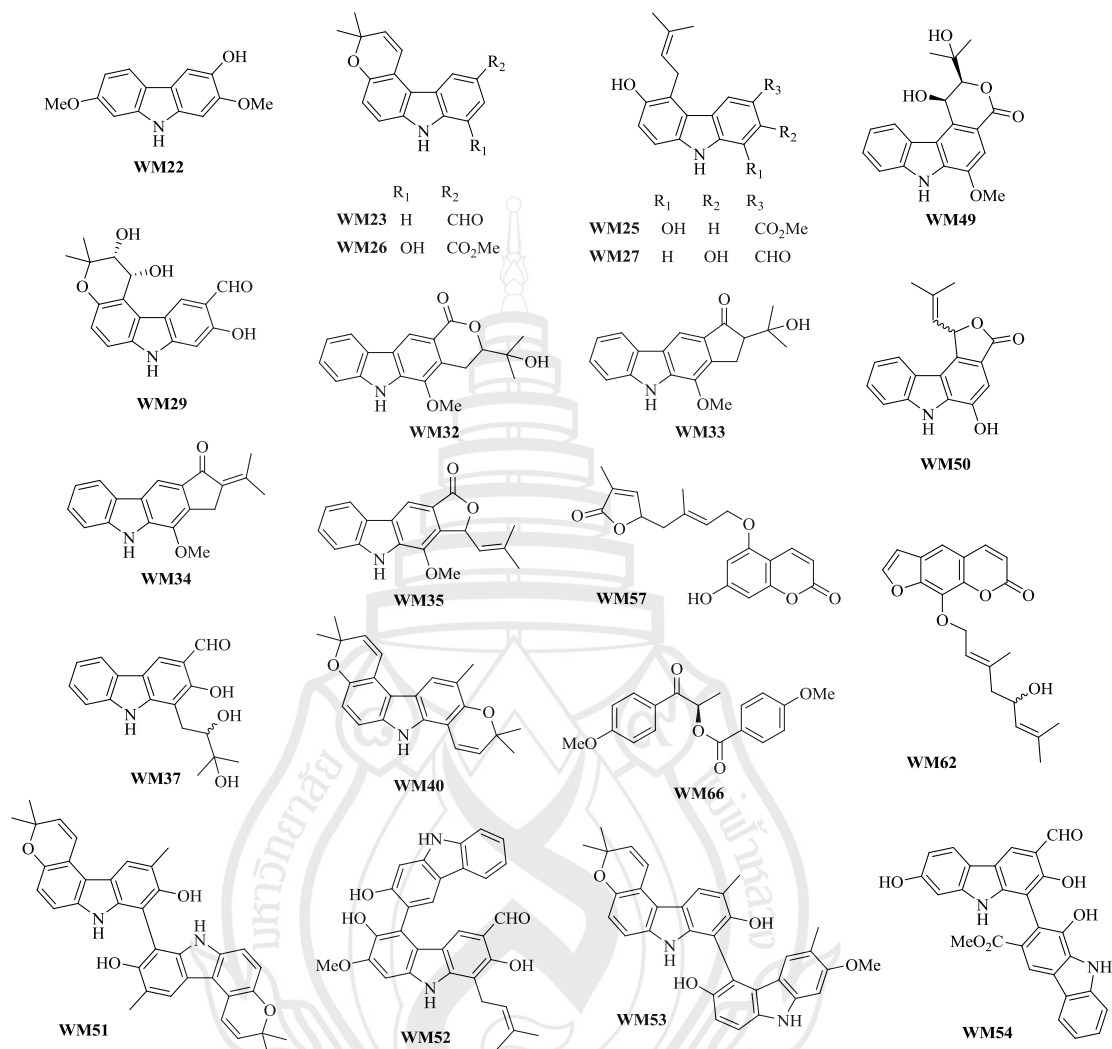
Three new carbazole alkaloids, mafaicheenamines A, (**WM32**), D (**WM34**), and E (**WM35**), together with eleven known compounds (**WM3**, **WM4**, **WM10**, **WM11**, **WM16**, **WM17**, **WM30**, **WM55**, **WM59**, **WM63**, and **WM64**) were isolated from the roots of *Clausena lansium*. Some of the isolates were evaluated for their cytotoxicity against three human cancer cell lines including oral cavity cancer (KB), breast cancer (MCF-7), and small-cell lung cancer (NCI-H187).

Four new compounds including two carbazole alkaloids, mafaicheenamines A (**WM32**) and C (**WM33**) and two new coumarins, clausenalansimins A (**WM57**) and B (**WM62**), along with fourteen known compounds (**WM4**, **WM16**, **WM17**, **WM30**, **WM31**, **WM58** – **WM61**, **WM63**, **WM64**, **WM56**, **WM65**, and **WM73**) were isolated from the twigs of *C. lansium*. Some of the isolated compounds were evaluated for their cytotoxicity against three human cancer cell lines including oral

cavity cancer (KB), breast cancer (MCF7), and small-cell lung cancer (NCI-H187) and antibacterial activity.

Six new carbazole alkaloids, clausenawallines A (**WM51**), B (**WM52**), C (**WM42**), D (**WM22**), E (**WM53**), and F (**WM54**), along with sixteen known compounds (**WM2**, **WM5**, **WM6**, **WM8**, **WM9**, **WM12**, **WM13**, **WM17-WM19**, **WM21**, **WM28**, **WM36**, **WM39**, **WM40**, and **WM41**) were isolated from the roots of *Clausena wallichii*. Compounds **WM40**, **WM52**, and **WM53** exhibited significant antibacterial activity against *Staphylococcus aureus* TISTR 1466 and methicillin-resistant *Staphylococcus aureus* (MRSA) SK1 with MIC values in the range of 4-16 µg/mL, whereas compound **WM54** showed the highest cytotoxicity against oral cavity cancer (KB) and small-cell lung cancer (NCI-H187) with IC₅₀ values of 10.2 and 4.5 µM, respectively.

Five carbazole alkaloids, clausenawallines G (**WM25**), H (**WM27**), I (**WM23**), J (**WM26**), and K (**WM29**), along with twelve known alkaloids (**WM1**, **WM2**, **WM6**, **WM14-WM16**, **WM19**, **WM20**, **WM24**, **WM28**, **WM79**, and **WM80**) were isolated from the twigs of *Clausena wallichii*. Their structures were established using spectroscopic methods. The antibacterial activity of compounds **WM23**, **WM25-WM27**, and **WM29** were also evaluated.



Keywords: Rutaceae/*Clausena*/*Clausena harmandiana*/*Clausena lansium*/*Clausena wallichii*/Cytotoxicity/Antibacterial activity