BIOLOGICALLY ACTIVE ALKALOIDS FROM *KOPSIA*

YAP WAI SUM

FACULTY OF SCIENCE

UNIVERSITY OF MALAYA

KUALA LUMPUR

2011

BIOLOGICALLY ACTIVE ALKALOIDS FROM *KOPSIA*

YAP WAI SUM

DISSERTATION SUBMITTED IN FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF SCIENCE

DEPARTMENT OF CHEMISTRY
FACULTY OF SCIENCE
UNIVERSITY OF MALAYA
KUALA LUMPUR

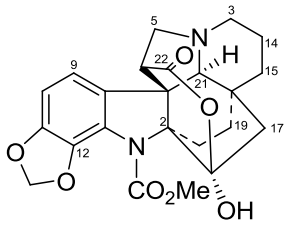
2011

ABSTRACT

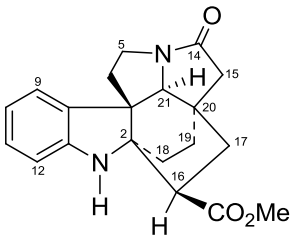
Two Malaysian plants *viz*., *Kopsia pauciflora* and *Kopsia grandifolia* were investigated for their alkaloidal constituents. A total of 40 alkaloids were isolated and characterized from *K. pauciflora*, of which 12 are new alkaloids. The new alkaloids isolated include seven aspidofractinine alkaloids (**1**, **2**, **3**, **4**, **5**, **6**, **7**), and five eburnane alkaloids (**8**, **9**, **10**, **11**, **12**). *K. grandifolia* yielded a total of eight alkaloids. Of these, three are new. The new alkaloids are grandilodine A (**41**), grandilodine B (**42**), and grandilodine C (**43**). Grandilodine A (**41**), grandilodine C (**43**), and lapidilectine B (**47**) were found to reverse multidrug resistance in vincristine-resistant KB cells.

ABSTRAK

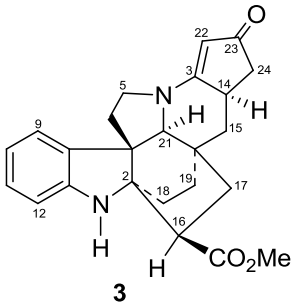
Dua jenis tumbuhan dari Malaysia iaitu *Kopsia pauciflora* dan *Kopsia grandifolia* telah dikaji dari segi kandungan alkaloidnya. Sebanyak 40 alkaloid telah diasingkan dan dicirikan dari *K. pauciflora*, di mana 12 alkaloid adalah baru. Alkaloid-alkaloid baru tersebut terdiri daripada tujuh alkaloid *aspidofractinine* (**1**, **2**, **3**, **4**, **5**, **6**, **7**), dan lima alkaloid *eburnane* (**8**, **9**, **10**, **11**, **12**). *K. grandifolia* telah menghasilkan sebanyak lapan alkaloid. Di kalangan alkaloid-alkaloid itu, tiga alkaloid adalah baru. Alkaloid-alkaloid baru tersebut ialah grandilodine A (**41**), grandilodine B (**42**), dan grandilodine C (**43**). Grandilodine A (**41**), grandilodine C (**43**), dan lapidilectine B (**47**) telah menunjukkan aktiviti dalam *reversal of multidrug resistance in vincristine-resistant KB cells*.



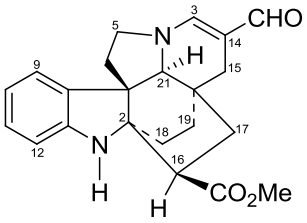
1



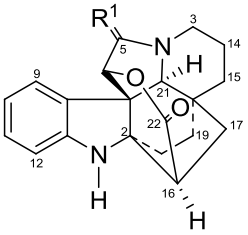
2



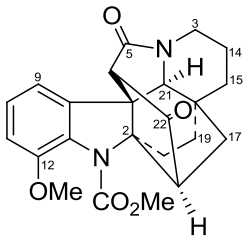
3



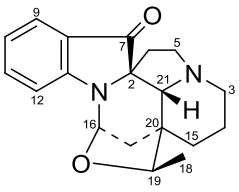
4



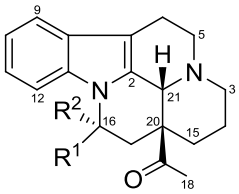
5 R^1 = H,H
6 R^1 = O



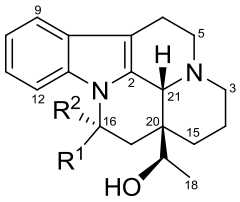
7



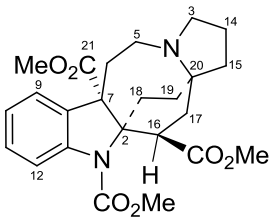
8



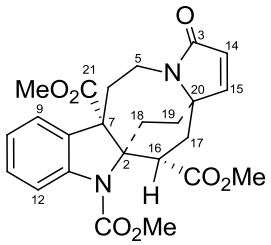
9 R^1, R^2 = O
10 R^1 = H, R^2 = OH



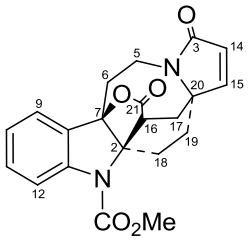
11 R^1 = H, R^2 = nil, $\Delta^{16,17}$
12 R^1 = H, R^2 = OEt



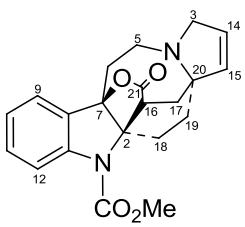
41



42



43



47

Table : Alkaloid composition of *K. pauciflora* and *K. grandifolia*

Plant	Plant part	Alkaloid
K. pauciflora	Stem-bark	Compound **1** [New]
		Compound **2** [New]
		Compound **3** [New]
		Compound **4** [New]
		Compound **5** [New]
		Compound **6** [New]
		Compound **7** [New]
		Compound **8** [New]
		Compound **9** [New]
		Compound **10** [New]
		Compound **11** [New]
		Compound **12** [New]
		Tetrahydroalstonine (**13**)
		Leuconoxine (**14**)
		N(1)-Carbomethoxy-5,22-dioxokopsane (**15**)
		Kopsanone (**16**)
		Kopsifine (**17**)
		Decarbomethoxykopsifine (**18**)
		Paucidactine B (**19**)
		Kopsamine (**20**)
		Kopsamine *N*-oxide (**21**)
		Kopsinine (**22**)
		N(1)-Methoxycarbonyl-12-methoxy-$\Delta^{16,17}$-kopsinine (**23**)
		N(1)-Methoxycarbonyl-12-hydroxy-$\Delta^{16,17}$-kopsinine (**24**)
		Kopsinine *N*-oxide (**25**)
		N(1)-Methoxycarbonyl-11,12-dimethoxykopsinaline (**26**)

Table, continued

Plant	Plant part	Alkaloid
		Kopsilongine (**27**)
		Pleiocarpine (**28**)
		12-Methoxypleiocarpine (**29**)
		Pleiocarpine *N*-oxide (**30**)
		(+)-Eburnamenine (**31**)
		(+)-Eburnamonine (**32**)
		(–)-Eburnamine (**33**)
		(+)-Isoeburnamine (**34**)
		(+)-19-oxoeburnamine (**35**)
		(–)-19(*R*)-Hydroxyisoeburnamine (**36**)
		(+)-19(*R*)-Hydroxyeburnamine (**37**)
		(–)-Norpleiomutine (**38**)
		(–)-Demethylnorpleiomutine (**39**)
		(+)-Kopsoffinol (**40**)
K. grandifolia	Stem-bark	Grandilodine A (**41**) [New]
		Grandilodine B (**42**) [New]
		Lapidilectine A (**44**)
		Isolapidilectine A (**45**)
		Lapidilectam (**46**)
		Kopsinine (**22**)
	Leaves	Grandilodine C (**43**) [New]
		Lapidilectine B (**47**)

ACKNOWLEDGEMENTS

I would like to express my deepest gratitude to Professor Dr. Kam Toh Seok for his supervision and guidance throughout the course of this study. I would also like to thank my co-supervisor Dr. Choo Yeun Mun for her help and advice.

My sincere appreciation to Dr. Lim Kuan Hon, Miss Gan Chew Yan, Miss Lim Siew Huah, Mr. Low Yun Yee, Miss Tan Shin Jowl, Miss Hong Fung Jiao, Mr. Ku Wai Foong, and Miss Nge Choy Eng for their invaluable help. Special thanks are due to my parents, Mr. and Mrs. Yap Wee Lim for their support and encouragement throughout the course of this study.

Financial support from the University of Malaya is gratefully acknowledged.

TABLE OF CONTENTS

LIST OF FIGURES

Page

LIST OF TABLES

LIST OF SCHEMES