

BIOLOGICALLY ACTIVE ALKALOIDS
FROM *KOPSIA*

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**BIOLOGICALLY ACTIVE ALKALOIDS
FROM *KOPSIA***

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**DISSERTATION SUBMITTED IN FULFILMENT OF
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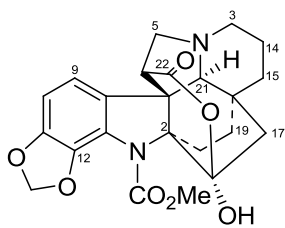
2011

ABSTRACT

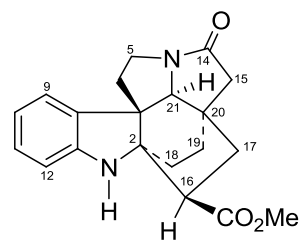
Two Malaysian plants viz., *Kopsia pauciflora* and *Kopsia grandifolia* were investigated for their alkaloidal constituents. A total of 40 alkaloids were isolated and characterized from *K. pauciflora*, of which 12 are new alkaloids. The new alkaloids isolated include seven aspidofractinine alkaloids (**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

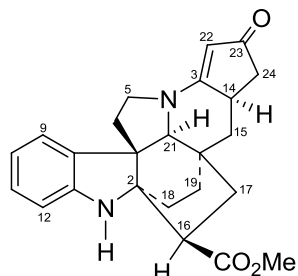
Dua jenis tumbuhan dari Malaysia iaitu *Kopsia pauciflora* dan *Kopsia grandifolia* telah dikaji dari segi kandungan alkaloidnya. Sebanyak 40 alkaloid telah diasingkan dan dicirikan dari *K. pauciflora*, di mana 12 alkaloid adalah baru. Alkaloid-alkaloid baru tersebut terdiri daripada tujuh alkaloid *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*.



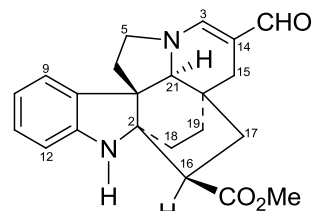
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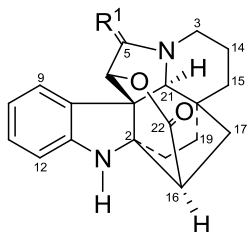
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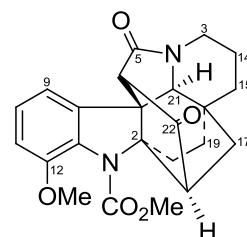


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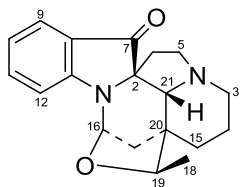


5 R¹ = H, H

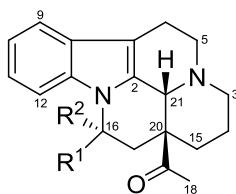
6 R¹ = O



7

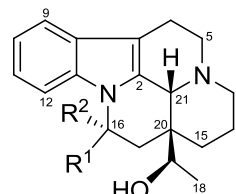


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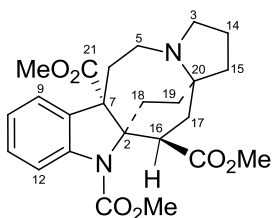
9 R¹, R² = O

10 R¹ = H, R² = OH

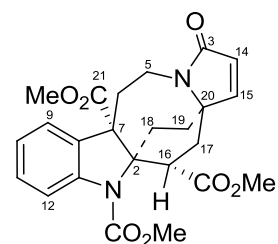


11 R¹ = H, R² = nil, Δ^{16,17}

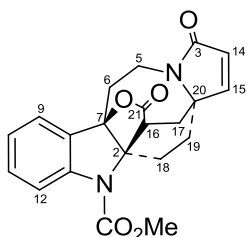
12 R¹ = H, R² = OEt



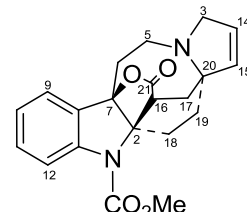
41



42



43



47

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

Plant	Plant part	Alkaloid
<i>K. pauciflora</i>	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)
		<i>N</i> (1)-Carbomethoxy-5,22-dioxokopsane (15)
		Kopsanone (16)
		Kopsifine (17)
		Decarbomethoxykopsifine (18)
		Paucidactine B (19)
		Kopsamine (20)
		Kopsamine <i>N</i> -oxide (21)
		Kopsinine (22)
		<i>N</i> (1)-Methoxycarbonyl-12-methoxy- $\Delta^{16,17}$ -kopsinine (23)
		<i>N</i> (1)-Methoxycarbonyl-12-hydroxy- $\Delta^{16,17}$ -kopsinine (24)
		Kopsinine <i>N</i> -oxide (25)
		<i>N</i> (1)-Methoxycarbonyl-11,12-dimethoxykopsinaline (26)

Table, continued

Plant	Plant part	Alkaloid
		Kopsilongine (27)
		Pleiocarpine (28)
		12-Methoxypleiocarpine (29)
		Pleiocarpine <i>N</i> -oxide (30)
		(+)-Eburnamenine (31)
		(+)-Eburnamonine (32)
		(-)-Eburnamine (33)
		(+)-Isoeburnamine (34)
		(+)-19-oxoeburnamine (35)
		(-)-19(<i>R</i>)-Hydroxyisoeburnamine (36)
		(+)-19(<i>R</i>)-Hydroxyeburnamine (37)
		(-)-Norpleiomutine (38)
		(-)-Demethylnorpleiomutine (39)
		(+)-Kopsoffinol (40)
<i>K. grandifolia</i>	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)

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TABLE OF CONTENTS

	Page
ABSTRACT	ii
ACKNOWLEDGEMENTS	vii
LIST OF FIGURES	x
LIST OF TABLES	xiv
LIST OF SCHEMES	xvii
CHAPTER ONE: INTRODUCTION	
1.1 General	1
1.2 The Alkaloids	2
1.3 Indole Alkaloids of the Apocynaceae	4
1.3.1 General	4
1.3.2 Classification of the Indole Alkaloids	5
1.4 The Genus <i>Kopsia</i>	7
1.4.1 General	7
1.4.2 Alkaloids of the Genus <i>Kopsia</i>	8
1.4.3 Occurrence and Distribution of Alkaloids in the Genus <i>Kopsia</i>	9
1.5 Objective of the Present Research	34
CHAPTER TWO: RESULTS AND DISCUSSION	
2.1 Alkaloids from <i>Kopsia pauciflora</i>	35
2.1.1 Compound 1	40
2.1.2 Compound 2	44
2.1.3 Compound 3	48

2.1.4 Compound 4	52
2.1.5 Compound 5	55
2.1.6 Compound 6	58
2.1.7 Compound 7	61
2.1.8 Compound 8	64
2.1.9 Compound 9	68
2.1.10 Compound 10	67
2.1.11 Compound 11	74
2.1.12 Compound 12	77
2.2 Alkaloids from <i>Kopsia grandifolia</i>	131
2.2.1 Grandilodine A (41)	133
2.2.2 Grandilodine B (42)	137
2.2.3 Grandilodine C (43)	141
2.3 Biological Activity	145
2.3.1 General	152
2.3.2 Cytotoxicity and Reversal of Multidrug Resistance (MDR)	152
 CHAPTER THREE: EXPERIMENTAL	
3.1 Source and Authentication of Plant Materials	154
3.2 General	155
3.3 Chromatographic Methods	155
3.3.1 Column Chromatography	155
3.3.2 Thin Layer Chromatography (TLC)	156
3.3.3 Centrifugal Preparative TLC	158
3.4 Spray Reagent (Dragendorff's Reagent)	158
3.5 Extraction of Alkaloids	159

3.6	Isolation of Alkaloids	159
3.6.1	General Procedure	159
3.6.2	Isolation of Alkaloids from <i>Kopsia pauciflora</i>	160
3.6.3	Isolation of Alkaloids from <i>Kopsia grandifolia</i>	160
3.7	Compound Data	163
3.8	Catalytic Hydrogenation of Lapidilectine A (43)	178
3.9	Cytotoxicity Assays	179
	References	180

LIST OF FIGURES

	Page	
2.1	Selected HMBCs of 1	41
2.2	X-ray crystal structure of 1 . Thermal ellipsoids are shown at the 50% probability level.	41
2.3	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of compound 1	43
2.4	Selected HMBCs of 2	45
2.5	X-ray crystal structure of 2 . Thermal ellipsoids are shown at the 50% probability level.	45
2.6	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of compound 2	47
2.7	Selected HMBCs and NOEs of 3	49
2.8	X-ray crystal structure of 3 . Thermal ellipsoids are shown at the 50% probability level.	50
2.9	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of compound 3	51
2.10	Selected HMBCs of 4	53
2.11	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of compound 4	54
2.12	Selected HMBCs of 5	55

2.13	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of compound 5	57
2.14	Selected HMBCs of 6	58
2.15	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of compound 6	60
2.16	Selected HMBCs of 7	61
2.17	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of compound 7	63
2.18	Selected HMBCs of 8	65
2.19	X-ray crystal structure of 8 . Thermal ellipsoids are shown at the 50% probability level.	65
2.20	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of compound 8	67
2.21	Selected HMBCs of 9	69
2.22	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of compound 9	70
2.23	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of compound 10	73
2.24	Selected HMBCs of 11	74
2.25	X-ray crystal structure of 11 . Thermal ellipsoids are shown at the 50% probability level.	75
2.26	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of compound 11	76
2.27	Selected HMBCs of 12	78
2.28	X-ray crystal structure of 12 . Thermal ellipsoids are shown at the 50% probability level.	78
2.29	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of compound 12	79
2.30	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of tetrahydroalstonine (13)	85
2.31	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of leuconoxine (14)	87
2.32	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of <i>N</i> (1)-carbomethoxy-5,22-dioxokopsane (15)	90
2.33	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of kopsanone (16)	91
2.34	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of kopsifine (17)	92

2.35	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of decarbomethoxykopsifine (18)	94
2.36	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of paucidactine B (19)	95
2.37	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of kopsamine (20)	97
2.38	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of kopsamine <i>N</i> -oxide (21)	98
2.39	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of kopsinine (22)	101
2.40	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of <i>N</i> (1)-methoxycarbonyl- 12-methoxy- $\Delta^{16,17}$ -kopsinine (23)	102
2.41	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of <i>N</i> (1)-methoxycarbonyl- 12-hydroxy- $\Delta^{16,17}$ -kopsinine (24)	103
2.42	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of kopsinine <i>N</i> -oxide (25)	106
2.43	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of <i>N</i> (1)-methoxycarbonyl- 11,12-dimethoxykopsinaline (26)	107
2.44	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of kopsilongine (27)	108
2.45	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of pleiocarpine (28)	111
2.46	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of 12-methoxypleiocarpine (29)	112
2.47	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of pleiocarpine <i>N</i> -oxide (30)	113
2.48	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of (+)-eburnamenine (31)	115
2.49	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of (+)-eburnamonine (32)	116
2.50	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of (-)-eburnamine (33)	118
2.51	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of (+)-isoeburnamine (34)	119
2.52	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of (+)-19-oxoeburnamine (35)	122
2.53	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of (-)-19(<i>R</i>)-	123

	hydroxyisoeburnamine (36)	
2.54	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of (+)-19(<i>R</i>)-hydroxyeburnamine (37)	124
2.55	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of (–)-norpleiomutine (38)	126
2.56	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of (–)-demethylnorpleiomutine (39)	128
2.57	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of (+)-kopsoffinol (40)	130
2.58	X-ray crystal structure of 41 . Thermal ellipsoids are shown at the 50% probability level.	134
2.59	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of grandilodine A (41)	136
2.60	Selected NOEs of 42	138
2.61	X-ray crystal structure of 42 . Thermal ellipsoids are shown at the 50% probability level.	138
2.62	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of grandilodine B (42)	140
2.63	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of grandilodine C (43)	143
2.64	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of lapidilectine A (44)	147
2.65	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of isolapidilectine A (45)	148
2.66	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of lapidilectam (46)	149
2.67	¹ H NMR spectrum (CDCl ₃ , 400 MHz) of lapidilectine B (47)	151
3.1	Isolation of alkaloids from the stem-bark extract of <i>Kopsia Pauciflora</i>	161
3.2	Isolation of alkaloids from the stem-bark extract of <i>Kopsia Grandifolia</i>	162
3.3	Isolation of alkaloids from the leaf extract of <i>Kopsia grandifolia</i>	162

LIST OF TABLES

	Page
1.1 Occurrence of alkaloids in <i>Kopsia</i>	9
2.1 Alkaloid composition of <i>K. pauciflora</i>	38
2.2 ¹ H and ¹³ C NMR spectroscopic data of compound 1	42
2.3 ¹ H and ¹³ C NMR spectroscopic data of compound 2	46
2.4 ¹ H and ¹³ C NMR spectroscopic data of compound 3	50
2.5 ¹ H and ¹³ C NMR spectroscopic data of compound 4	53
2.6 ¹ H and ¹³ C NMR spectroscopic data of compound 5	56
2.7 ¹ H and ¹³ C NMR spectroscopic data of compound 6	59
2.8 ¹ H and ¹³ C NMR spectroscopic data of compound 7	62
2.9 ¹ H and ¹³ C NMR spectroscopic data of compound 8	66
2.10 ¹ H and ¹³ C NMR spectroscopic data of compound 9	69
2.11 ¹ H and ¹³ C NMR spectroscopic data of compound 10	72
2.12 ¹ H and ¹³ C NMR spectroscopic data of compound 11	75
2.13 ¹ H and ¹³ C NMR spectroscopic data of compound 12	78
2.14 Known alkaloids from the stem-bark of <i>K. pauciflora</i>	80
2.15 ¹ H and ¹³ C NMR spectroscopic data of tetrahydroalstonine (13)	84
2.16 ¹ H and ¹³ C NMR spectroscopic data of leuconoxine (14)	86
2.17 ¹ H NMR spectroscopic data of <i>N</i> (1)-carbomethoxy-5,22-dioxokopsane (15), kopsanone (16), and kopsifine (17)	88
2.18 ¹³ C NMR spectroscopic data of <i>N</i> (1)-carbomethoxy-5,22-dioxokopsane (15), kopsanone (16), and kopsifine (17)	89
2.19 ¹ H and ¹³ C NMR spectroscopic data of decarbomethoxykopsifine (18) and paucidactine B (19)	93
2.20 ¹ H and ¹³ C NMR spectroscopic data of kopsamine (20) and	96

	kopsamine <i>N</i> -oxide (21)	
2.21	¹ H NMR spectroscopic data of kopsinine (22), <i>N</i> (1)-methoxycarbonyl-12-methoxy- $\Delta^{16,17}$ -kopsinine (23), and <i>N</i> (1)-methoxycarbonyl-12-hydroxy- $\Delta^{16,17}$ -kopsinine (24)	99
2.22	¹³ C NMR spectroscopic data of kopsinine (22), <i>N</i> (1)-methoxycarbonyl-12-methoxy- $\Delta^{16,17}$ -kopsinine (23), and <i>N</i> (1)-methoxycarbonyl-12-hydroxy- $\Delta^{16,17}$ -kopsinine (24)	100
2.23	¹ H NMR spectroscopic data of kopsinine <i>N</i> -oxide (25), <i>N</i> (1)-methoxycarbonyl-11,12-dimethoxykopsinaline (26), and kopsilongine (27)	104
2.24	¹³ C NMR spectroscopic data of kopsinine <i>N</i> -oxide (25), <i>N</i> (1)-methoxycarbonyl-11,12-dimethoxykopsinaline (26), and kopsilongine (27)	105
2.25	¹ H NMR spectroscopic data of pleiocarpine (28), 12-methoxypleiocarpine (29), and pleiocarpine <i>N</i> -oxide (29)	109
2.26	¹³ C NMR spectroscopic data of pleiocarpine (28), 12-methoxypleiocarpine (29), and pleiocarpine <i>N</i> -oxide (30)	110
2.27	¹ H and ¹³ C NMR spectroscopic data of (+)-eburnamenine (31) and (+)-eburnamonine (32)	114
2.28	¹ H and ¹³ C NMR spectroscopic data of (-)-eburnamine (33) and (+)-isoeburnamine (34)	117
2.29	¹ H NMR spectroscopic data of (+)-19-oxoeburnamine (35), (-)-19(<i>R</i>)-hydroxyisoeburnamine (36), and (+)-19(<i>R</i>)-hydroxyeburnamine (37)	120
2.30	¹³ C NMR spectroscopic data of (+)-19-oxoeburnamine (35), (-)-	121

	19(<i>R</i>)-hydroxyisoeburnamine (36), and (+)-19(<i>R</i>)-hydroxyeburnamine (37)	
2.31	¹ H and ¹³ C NMR spectroscopic data of (–)-norpleiomutine (38)	125
2.32	¹ H and ¹³ C NMR spectroscopic data of (–)-demethylnorpleiomutine (39)	127
2.33	¹ H and ¹³ C NMR spectroscopic data of (+)-kopsoffinol (40)	129
2.34	Alkaloid composition of <i>K. grandifolia</i>	132
2.35	¹ H and ¹³ C NMR spectroscopic data of grandilodine A (41)	135
2.36	¹ H and ¹³ C NMR spectroscopic data of grandilodine B (42)	139
2.37	¹ H and ¹³ C NMR spectroscopic data of grandilodine C (43)	142
2.38	Known alkaloids from the stem-bark and leaf of <i>K. grandifolia</i>	144
2.39	¹ H NMR spectroscopic data of lapidilectine A (44), isolapidilectine A (45), and lapidilectam (46)	145
2.40	¹³ C NMR spectroscopic data of lapidilectine A (44), isolapidilectine A (45), and lapidilectam (46)	146
2.41	¹ H and ¹³ C NMR spectroscopic data of lapidilectine B (47)	150
2.42	Cytotoxic effects of alkaloids isolated from <i>K. pauciflora</i> and <i>K. grandifolia</i>	153
3.1	Source and authentication of plant materials	154
3.2	The hR _f values of alkaloids isolated from <i>Kopsia pauciflora</i> and <i>Kopsia grandifolia</i>	156

LIST OF SCHEMES

	Page
1.1 Strictosidine from tryptophan and loganin	5
2.1 A possible biogenetic pathway to 1	42
2.2 A possible biogenetic pathway to 2	46
2.3 A possible biogenetic pathway to 4	53
2.4 A possible biogenetic pathway to 8	66