

Abstract

Six Malaysian plants from the family of Lauraceae were investigated for their alkaloidal content. Three plants from the genus *Phoebe* i.e. *Phoebe grandis*, *Phoebe scortechinii* and *Phoebe lanceolata*, and the other three from the genus *Dehaasia* i.e. *Dehaasia longipedicellata*, *Dehaasia candolleana* and *Dehaasia incrassata* have been studied. A total of about 50 compounds were isolated in which sixteen are new alkaloids. The alkaloids isolated from bark and leaves of *Phoebe* and *Dehaasia* species are summarized below (Table and structures). Structural elucidation was performed with the aid of spectroscopic methods notably; UV, IR, MS, 1D and 2D NMR (COSY, HMQC, HMBC, NOESY).

Crude alkaloids of *Phoebe grandis*, *Phoebe scortechinii* and *Dehaasia longipedicellata* have the IC₅₀ values below 8 µg/ml (upper unit for the parasite lactate dehydrogenase test, pLDH). These alkaloid extracts demonstrate good properties as *anti-plasmodial* activities against sensitive and resistant strain of *P. falciferum* *in vitro*.

In addition, eleven selected alkaloids isolated from the genus of *Phoebe* and *Dehaasia* have been tested for CNS activity using radioligand receptor binding assays. Norhexahydromecambrine A **187** showed significant activity (64 % inhibition) to inhibit binding upon ³H-scopolamine, which labels muscarinic receptor. Phobegrandine B **29**, sinoacutine **81**, norboldine **98**, phoebescortechiniine A **175**, tetrahydropronuciferine **177**, grandine B **180**, grandine C **183**, pallidinine **188**, pallidine **189** and melonine **190** showed weak activity (< 50% inhibition).

Abstrak

Enam tumbuhan Malaysia dari keluarga Lauraceae telah dikaji kandungan alkaloidnya. Tiga tumbuhan adalah daripada genus *Phoebe* iaitu *Phoebe grandis*, *Phoebe scortechinii* dan *Phoebe lanceolata*, dan tiga tumbuhan lain daripada genus *Dehaasia*, iaitu *Dehaasia longipedicellata*, *Dehaasia candolleana* dan *Dehaasia incrassata*. Sebanyak 50 sebatian telah dipisahkan di mana 16 daripadanya adalah baru. Alkaloid yang telah dituliskan daripada kulit batang dan daun spesis-spesis *Phoebe* dan *Dehaasia* ditunjukkan di bawah (Jadual dan struktur). Penentuan struktur-struktur alkaloid dijalankan menggunakan kaedah spektroskopik UV, IR, MS, 1D dan 2D NMR (COSY, HMQC, HMBC dan NOESY).

Ekstrak alkaloid daun *Phoebe grandis*, *Phoebe scortechinii* dan *Dehaasia longipedicellata* didapati mempunyai nilai IC_{50} di bawah 8 $\mu\text{g/ml}$ (tahap tertinggi untuk ujian parasit lactate dehydrogenase). Ekstrak-ekstrak ini telah menunjukkan aktiviti-aktiviti yang baik sebagai *anti-plasmodial* dalam melemahkan sensitiviti *P. falciferum in vitro*.

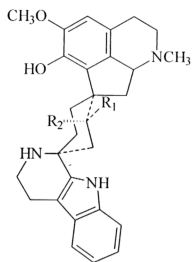
Seterusnya, sebelas alkaloid utama daripada spesis *Phoebe* dan *Dehaasia* telah diuji untuk activity CNS menggunakan assai '*radioligand receptor binding*'. Norhexahydromecambrina A **187** menunjukkan aktiviti yang bermakna (64% halangan) untuk menghalang pengikatan ^3H -scopolamine yang melabel penerima muscarinic. Phoebe grandina B **29**, sinoacutina **81**, norboldina **98**, phoebescortechiniina A **175**, tetrahydropronuciferina **177**, grandina B **180**, grandina C

183, pallidinina **188**, pallidina **189** dan milonina **190** cuma menunjukkan aktiviti yang lemah (< 50 % halangan).

Table: The alkaloids isolated from the genus *Phoebe* and *Dehaasia*

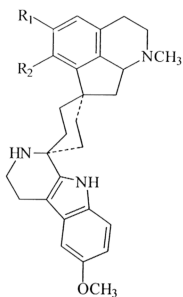
Species	Plant Part	Remarks	Type of skeleton		
<i>Phoebe grandis</i> KL 4224	Leaves	Phoebegrandine E 176	Indoloquinolizidine		
		Tetrahydroglaziovine 178	Proaporphine		
		Phoebegrandine C 173	Proaporphine-tryptamine		
		Phoebegrandine A 28	Proaporphine-tryptamine		
		Phoebegrandine B 29	Proaporphine-tryptamine		
		Phoebegrandine D 174	Proaporphine-tryptamine		
	Bark	Boldine 97	Aporphine		
		Grandine A 179	Proaporphine		
		Grandine B 180	Proaporphine		
		Norboldine 98	Aporphine		
Laufornine 160		Proaporphine			
<i>Phoebe grandis</i> KL 4994	Leaves	Tetrahydropronuciferine 177	Proaporphine		
		Tetrahydroglaziovine 178	Proaporphine		
		Phoebescortechiniine A 175	Proaporphine-tryptamine		
		Phoebegrandine A 28	Proaporphine-tryptamine		
	Bark	Grandine C 183	Proaporphine		
		Grandine D 184	Proaporphine		
		Norhexahydromecambrine A 187	Proaporphine		
		Laufornine 116	Proaporphine		
		<i>Phoebe scortechinii</i> KL 4886	Leaves	Tetrahydropronuciferine 177	Proaporphine
				Phoebescortechiniine A 175	Proaporphine-tryptamine
Phoebegrandine A 28	Proaporphine-tryptamine				
	Phoebegrandine B 29		Proaporphine-tryptamine		
Bark	Hexahydromecambrine A 186		Proaporphine		
	Grandine B 180		Proaporphine		
	Grandine C 183	Proaporphine			
	Norboldine 98	Aporphine			
	Norhexahydromecambrine A 187	Proaporphine			

Species	Plant Part	Remarks	Type of skeleton
<i>Phoebe lanceolata</i> KL 4763	Leaves	Liriodenine 135 Roemerine 47 Norboldine 98 Laurotetanine 99	Oxoaporphine Aporphine Aporphine Aporphine
	Bark	Liriodenine 135 Roemerine 47 Sebiferine 71 Norboldine 98 Asimilobine 57 Boldine 97	Oxoaporphine Aporphine Morphinandienone Aporphine Aporphine Aporphine
<i>Dehaasia longipedicellata</i> KL 4719	Leaves	(+)-Milonine 190	Morphinandienone
		(+)-Pallidinine 188	Morphinandienone
		(-)-Pallidine 189	Morphinandienone
		(-)-Sinoacutine 81	Morphinandienone
		(-)-8,14-Dihydrosalutaridine 191	Morphinandienone
<i>Dehaasia candolleana</i> KL 4683	Leaves	Perakensol 193	Phenantrene
		(-)-Sebiferine 71	Morphinandienone
		(+)-Sebiferine 192	Morphinandienone
		Pallidine 189	Morphinandienone
<i>Dehaasia incrassata</i> KL 4640	Bark	(-)-3', 4'- Dihydrostephasubine 198	Bisbenzylisoquinoline
		(-)-Norstephasubine 201	Bisbenzylisoquinoline
		(-)-Gyrolidine 194	Bisbenzylisoquinoline
		Stephasubine 202	Bisbenzylisoquinoline



173: $R_1 = H$, $R_2 = OH$

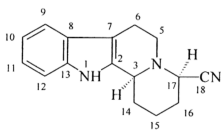
174: $R_1 = OH$, $R_2 = H$



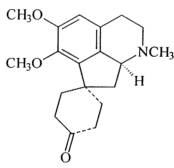
175: $R_1 = OCH_3$, $R_2 = OCH_3$

28: $R_1 = OCH_3$, $R_2 = OH$

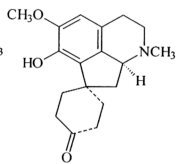
29: $R_1 = OH$, $R_2 = OCH_3$



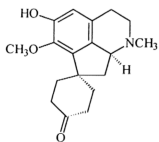
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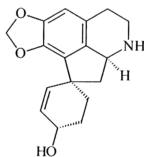
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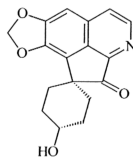
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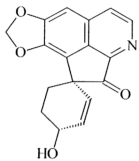
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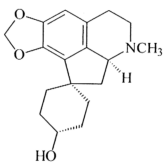
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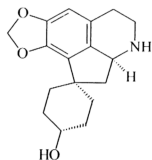
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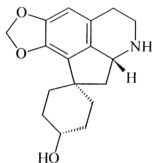
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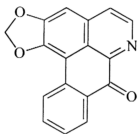
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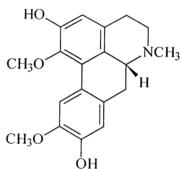
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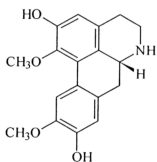
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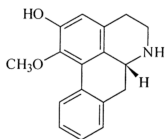
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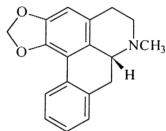
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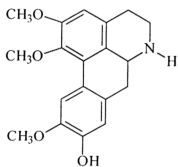
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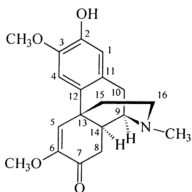
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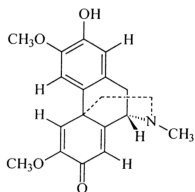
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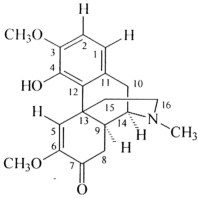
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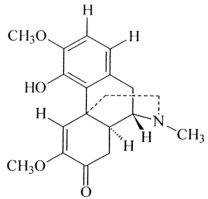
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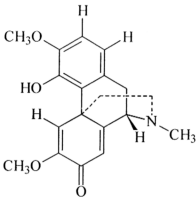
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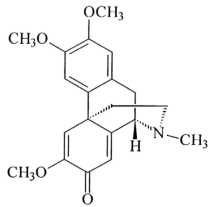
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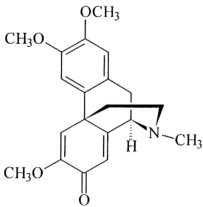
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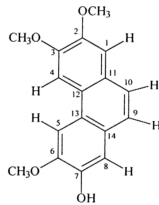
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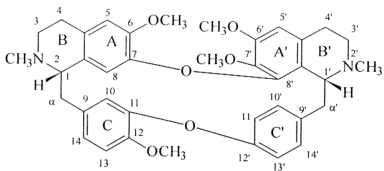
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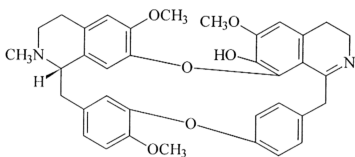
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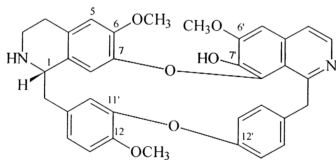
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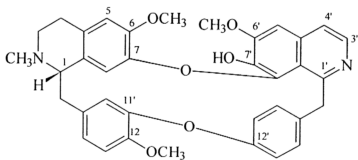
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