

**BIOLOGICALLY ACTIVE ALKALOIDS FROM
*ALSTONIA ANGUSTILOBA***

KU WAI FOONG

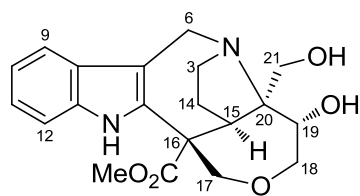
**DISSERTATION SUBMITTED IN FULFILLMENT
OF THE REQUIREMENTS FOR THE DEGREE OF
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**DEPARTMENT OF CHEMISTRY
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UNIVERSITY OF MALAYA
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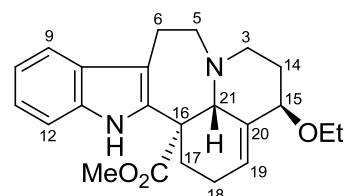
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Abstract

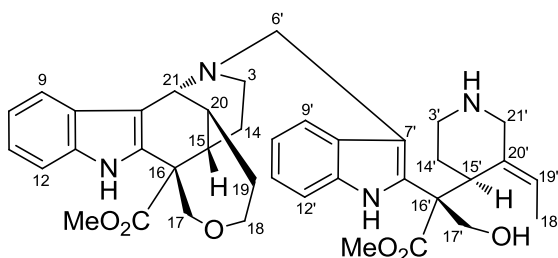
The alkaloidal content of Malaysian plant, *Alstonia angustiloba* Miq., was investigated and the results are summarized as below (Table). A total of 20 alkaloids were isolated and characterized, of which, three were new alkaloids, viz., angustilobine C (**1**), andransinine (**2**), and angustiphylline (**3**). Angustilobine C (**1**) and andransinine (**2**) are alkaloids of the angustilobine- and andranginine type, respectively, while angustiphylline (**3**) is a new bisindole alkaloid constituted from the union of uleine and *secovallesamine* moieties. Alkaloids **1** and **2** were obtained from the leaf extract while the bisindole **3** was isolated from the bark extract. In addition to the new alkaloids, seventeen known alkaloids were also obtained which were: 19,20-*E*-vallesamine (**4**), 17-*O*-acetylvallesamine (**5**), yunnannensine (**6**), angustilobine A (**7**), angustilobine B (**8**), *nor*-6,7-*seco*angustilobine B (**9**), *nor*-6,7-*seco*-19,20 α -epoxyangustilobine B (**10**), undulifoline (**11**), condylocarpine (**12**), 20*S*-tubotaiwine (**13**), *N*(4)-demethylechitamine (**14**), 17-*O*-acetyl-*N*(4)-demethylechitamine (**15**), alstolucine B (**16**), vincamine (**17**), 16*R*,19*E*-isositsirikine (**18**), venoterpine (**19**), and cantleyine (**20**). Angustilobine C (**1**) showed moderate cytotoxicity towards both drug-sensitive and vincristine-resistant KB cells (IC₅₀ 7.76 and 7.33 $\mu\text{g/mL}$, respectively), while andransinine (**2**) reversed multidrug resistance in vincristine-resistant KB cells (KB/VJ300 cells, IC₅₀ 1.61 $\mu\text{g/mL}$ in the presence of 0.1 $\mu\text{g/mL}$ of vincristine).



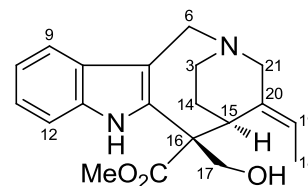
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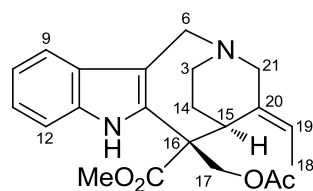
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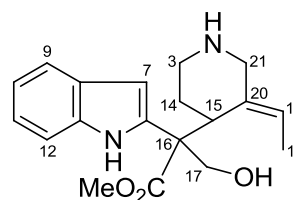
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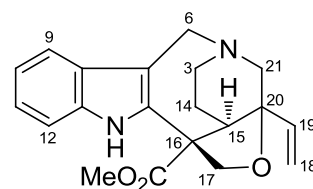
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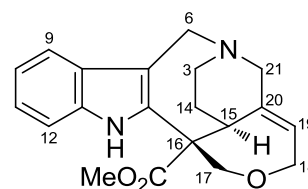
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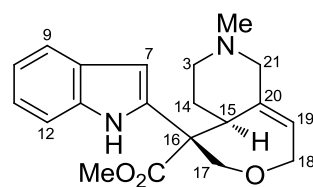
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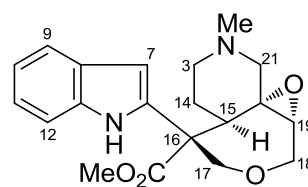
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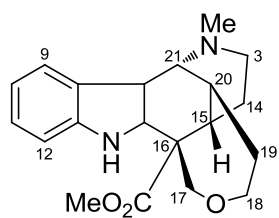
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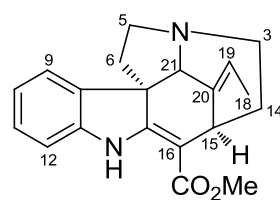
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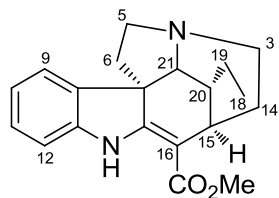
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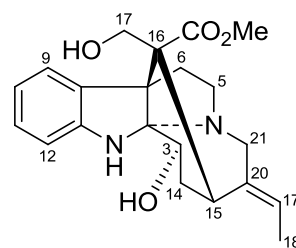
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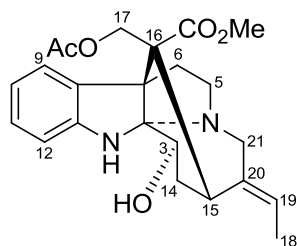
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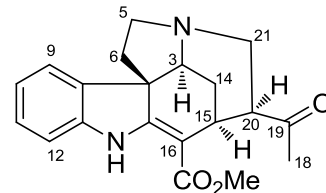
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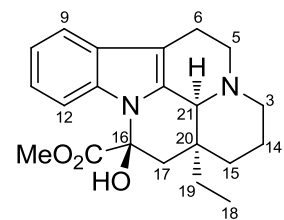
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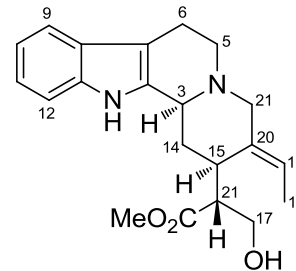
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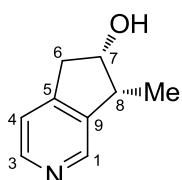
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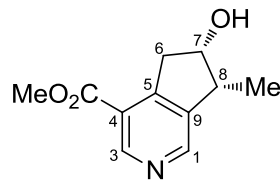
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18



19



20

Table. Alkaloidal Composition of *Alstonia angustiloba* Miq.

Plant Part	Alkaloid	
Leaves (21.0 kg)	Angustilobine C (1) [New]	
	Andransinine (2) [New]	
	19,20- <i>E</i> -Vallesamine (4)	
	17- <i>O</i> -Acetylvallesamine (5)	
	Angustilobine A (7)	
	Angustilobine B (8)	
	<i>Nor</i> -6,7- <i>seco</i> angustilobine B (9)	
	<i>Nor</i> -6,7- <i>seco</i> -19,20 α -epoxyangustilobine B (10)	
	Condylocarpine (12)	
	20 <i>S</i> -Tubotaiwine (13)	
	Alstolucine B (16)	
	Vincamine (17)	
	16 <i>R</i> ,19 <i>E</i> -Isositsirikine (18)	
	Stem-bark (20.0 kg)	Angustiphylline (3) [New]
		19,20- <i>E</i> -Vallesamine (4)
		Yunnanensine (6)
		Angustilobine A (7)
Angustilobine B (8)		
<i>Nor</i> -6,7- <i>seco</i> angustilobine B (9)		
Undulifoline (11)		
20 <i>S</i> -Tubotaiwine (13)		
<i>N</i> (4)-Demethylechitamine (14)		
17- <i>O</i> -Acetyl- <i>N</i> (4)-demethylechitamine (15)		
Venoterpine (19)		
Cantleyine (20)		

Abstrak (Bahasa Malaysia Version)

Kandungan alkaloid daripada *Alstonia angustiloba* Miq., tumbuhan daripada Semenanjung Malaysia telah dikaji dan keputusan tersebut dirumuskan dalam jadual. Sebanyak 20 alkaloid telah diasingkan dan dicirikan dimana tiga alkaloid merupakan alkaloid baru, iaitu angustilobine C (**1**), andransinine (**2**), dan angustiphylline (**3**). Angustilobine C (**1**) dan andransinine (**2**) adalah alkaloid jenis angustilobine dan andranginine, manakala angustiphylline (**3**) merupakan bisindole alkaloid yang terdiri daripada gabungan alkaloid-alkaloid berjenis uleine dan *secovallesamine*. Alkaloid **1** dan alkaloid **2** ditemui dalam ekstrak daun manakala alkaloid **3** ditemui dalam ekstrak kulit dahan. Di samping itu, sebanyak 17 alkaloid yang telah dikenalpasti juga ditemui dalam ekstrak tumbuhan ini. Antara alkaloid yang telah dikenalpasti adalah 19,20-*E*-vallesamine (**4**), 17-*O*-acetylvallesamine (**5**), yunnannensine (**6**), angustilobine A (**7**), angustilobine B (**8**), *nor*-6,7-*seco*angustilobine B (**9**), *nor*-6,7-*seco*-19,20 α -epoxyangustilobine B (**10**), undulifoline (**11**), condylocarpine (**12**), 20*S*-tubotaiwine (**13**), *N*(4)-demethylechitamine (**14**), 17-*O*-acetyl-*N*(4)-demethylechitamine (**15**), alstolucine B (**16**), vincamine (**17**), 16*R*,19*E*-isositsirikine (**18**), venoterpine (**19**), dan cantleyine (**20**). Alkaloid-alkaloid yang diperolehi daripada kajian ini telah disaring ketoksikannya terhadap sel KB. Angustilobine C (**1**) menunjukkan kesan sitotoksik yang sederhana terhadap sel-sel KB jenis ‘vincristine-sensitive’ dan ‘vincristine-resistant’ (IC₅₀ 7.76 dan 7.33 μ g/mL, masing-masing). Andransinine (**2**) menunjukkan aktiviti dalam ‘reversing multidrug resistance’ (sel-sel KB/VJ300, IC₅₀ 1.61 μ g/mL dengan kehadiran 0.1 μ g/mL vincristine).

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