CHAPTER 2

Literature Review

2.1 Plants of Combretaceae

The *Combretum* is a genus in the Combretaceae family. The genus comprises about 370 species of trees and shrubs, roughly 300 of which are native to tropical southern Africa, about 5 to Madagascar, some 25 to tropical Asia and approximately 40 to tropical America. This genus is absent from Australia. Nineteen species of *Combretum* are enumerated in Thailand [Hooker, 1879 ; Nanakorn, 1986].

2.2 Genus *Combretum*

In southern Africa, the Combretaceae family is divided in to six genera: *Combretum*, *Lumnitzera*, *Meiostemon*, *Quisqualis*, *Pteleopsis* and *Teminalia*. Of the six genera in southern Africa, *Combretum* and *Terminalia* are the most important and widely used for medicinal purposes. The taxonomy of *Combretum* is complex. Flowering plants are grouped into families and families are devided up into genera, which may also have subgenera. Each is split into species and some species may have two or more subspecies or varieties. The genus *Combretum* has two subgenera, these being subgenus *Combretum* and subgenus *Cacoucia*. Subgenus *Combretum* is divided into 11 sections and subgenus *Cacoucia* is divided into 5 sections. The subgenera and sections of the genus *Combretum* are presented in Table 2.1 [Kotze, 2000].

2.3 Taxonomy of *Combretum* species

2.3.1 Taxonomic hierarchy as applied to the taxon of *Combretum*

Kingdom : Plantae	- Plants
Subkingdom : Viridaeplantae	- -
Phylum : Tracheobionta	- Vascular plants
Subphylum : Euphyllophytina	- -
Inflaphylum : Radiatopses	- -
Class : Magnoliopsida	- Dicotyledons
Subclass :	- Rosidae
Superorder : Myrtanae	- -
Order : Myrtales	- -
Suborder : Lythrineae	- -
Family : Combretaceae	- -
Genus : *Combretum*	- *Combretum* spp.

2.3.2 Botanical aspects of genus *Combretum*

Shrubs or woody climbers, rarely small tree with long pendent or scandent branches; deciduous [Hooker, 1879 ; Nanakorn, 1986].

1) Indumentum : simple hairs or glandular hairs (stalked glands) or scales; most prominent on young parts, leaves, flowers and fruit.

2) Leaves : usually opposite, rarely ternate; hairy or glabrous, often conspicuously scaly; part of petiole sometimes persisting after the leaves are shed forming a thorn, pubescent or glabrous, without glands.

3) Inflorescence : spikes, racemes or panicles often subtended by bracts.

4) Flower : bisexual, 4-or 5-merous, sessile or shortly pedicillate, often scaly.

5) Calyx : cupuliform or infundibuliform, caducuous.

6) Petals : 4, or 5 usually early caducuous, or absent.

7) Stamens : twice the number of calyx-segments.

8) Ovary : with 2-4 ovules; style free.

9) Fruit : a drupe with 5 ridges, or a 4-, or 5-winged nut.

Table 2.1 The subgeneric classification of species of the genus *Combretum* occurring in southern Africa

***Combretum* Loefl.**	
Subgenus *Combretum*	**Subgenus *Cacoucia***
Section *Hypocrateropsis*	**Section *Lasiopetala***
Combretum celastroides	*Combretum obovatum*
Combretum imberbe	**Section *Conniventia***
Combretum padoides	*Combretum microphyllum*
Section *Combretastrum*	*Combretum paniculatum*
Combretum. umbricola	*Combretum platypetalum*
Section *angustimarginata*	**Section *Oxystachya***
Combretum caffrum	*Combretum oxystachyum*
Combretum erythrophyllum	**Section *Megalantherum***
Combretum kraussii	*Combretum wattii*
Combretum vendee	**Section *Poivrea***
Combretum woodii	*Combretum bracteosum*
Section *Macrostigmatea*	*Combretum mossambicense*
Combretum engleri	
Combretum kirkii	
Combretum sp.nov.	
Section *Metallicum*	
Combretum collinum	
Section *Glabripetala*	
Combretum fragrans	
Section *Spathulipetala*	
Combretum zeyheri	
Section *Ciliatipetala*	
Combretum albopunctatum	
Combretum apiculatum	
Combretum edwardsii	
Combretum moggii	

Table 2.1 (continued)

***Combretum* Loefl.**		
Combretum molle		
Combretum petrophilum		
Combretum psidioides		
Section *Fusca*		
Combretum coriifolium		
Section *Breviramea*		
Combretum hereroense		
Section *Elaeagnoida*		
Combretum elaeagnoides		

According to Thai forest bulletin [1986], the species of the genus *Combretum* found in Thailand are as Table 2.2 [Nanakorn, 1986].

Table 2.2 The species name of the genus *Combretum* found in Thailand

Scientific name	Thai name
Combretum acuminatum Roxb.	Khamin khruea (Prachin Buri).
Combretum apetalum Wall.	Dok soi (Central, Northern).
Combretum chinense Roxb.	Sakae thao (Peninsular).
Combretum decandrum Roxb.	Sakae khruea (Peninsular).
Combretum deciduum Coll. & Hemsl.	Haen khruea (Northern).
Combretum griffithii Heur. & M.A.	Khamin khruea, Haen khruea tua phuu (Northen); Chaang mang, Chaang mang noi (Chiang Mai).
Combretum latifolium Bl.	Kae dam (Nong Khai); Thua pae thao (Chiang Mai); Man daeng, Khruea uat chueak (Peninsular); Haen lueang (Kanchanaburi).
Combretum nanum Buch.-Ham. *ex* D. Don	Kae dam (Nong khai).
Combretum nigrescens King	Sakai (Peninsular).
Combretum pilosum Roxb.	Nguang chum (Nakhon Phanom); Teentang tuamae (Lampang); Khruea khao muak (Nong Khai).
Combretum porterianum (Clarke) Wall. *ex* Craib	Nuai sut (Peninsular).
Combretum procursum Craib	Kae (Nakorn Ratchasima); Sakae khruea, Sakae thao (Central).
Combretum punctatum Blume	Sakae wan, Sakae khruea (Northern).
Comretum quadrangulare Kurz	Kae (North-eastern); Khon khae, Chong khae (Phrae); Sang kae (Prachin Buri); Phaeng (Northern); Sakae, Sakae naa (Central).
Combretum sundaicum Miq.	Sangkae thao (Peninsular).
Combretum tetralophum Clarke	Krot, Thaowan krot (Central); Phum kot (Phitsanulok); Sakai nam (Narathiwat); Ee-laa-ku (Yawee-Narathiwat).

Table 2.2 (continued)

Scientific name	Thai name
Combretum trifoliatum Vent.	Khot sang, Yaan tut (Surat Thani); Chut (Peninsular); Ben (Khon Kaen); Puei (Nakhon Phanom); Yaa yotdam (Northern).
Combretum winitii Criab	Khruea ma thua nao (Northern).
Combretum yunnanense Exell	Chaang mang (Northern).

2.4 Chemical constituents of *Combretum* species

A number of compounds have been isolated from the genus *Combretum.* They can be classified as flavonoids, triterpenes, triterpene saponins, steroids, lignans and miscellaneous substances (Table 2.3).

The aerial parts, roots, flowers, seeds and leaves of the *Combretum* species were investigated for their chemical constituents ; flavonoids, triterpenes, triterpene saponins, steroids and lignans have been reported. The major compounds isolated from the species of *Combretum* are phenanthrenes, stilbenoids, polyphenol and triterpenoids [Banskota, 2003 ; Eloff, 2008].

Table 2.3 The chemical constituents and part used of *Combretum* species

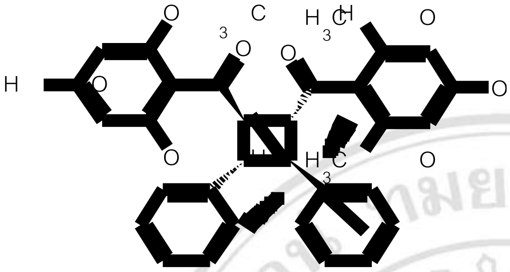
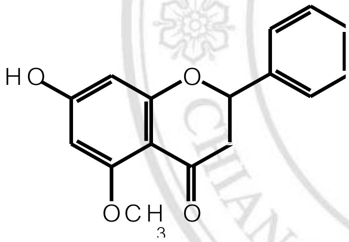
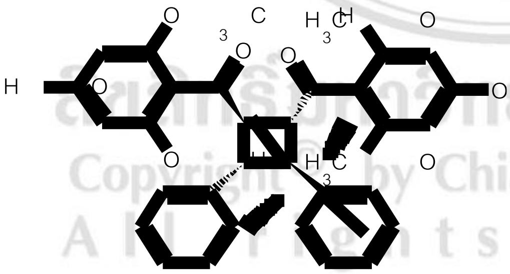
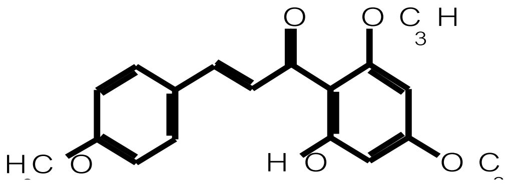
Chemical compound	Part used	Reference
Combretum albopunctatum Suess.		
Cyclobutane [1] 	aerial part	[Eloff, 2008]
Combretum apiculatum Sond.		
Alpenitin [2] 	leaves	[Eloff, 2008] [Serage, 2003]
Cyclobutane [1] 	aerial part	[Eloff, 2008]
Flavokawain [3] 	leaves	[Eloff, 2008] [Serage, 2003]

Table 2.3 (continued)

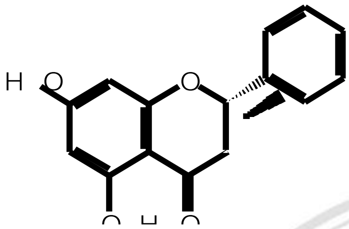
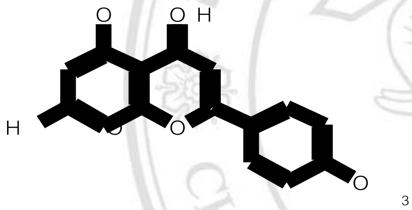
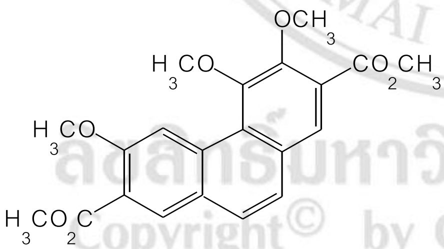
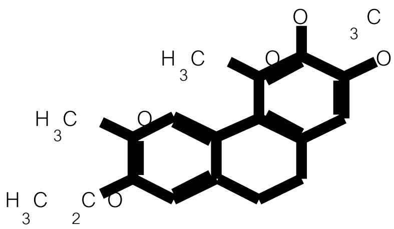
Plant and chemical compound	Plant part	Reference
Pinocembrin[4] 	leaves	[Eloff, 2008] [Serage, 2003]
Combretum caffrum (Eckl. & Zeyh.) Kuntze		
Acacetin [5] 	twigs, leaves and fruits	[Pettit, 1987]
7-Acetoxy-2,3,4,6-tetramethoxy-phenanthrene [6] 	stem	[Pettit, 1986]
7-Acetoxy-2,3,4,6-trimethoxy-9,10-dihydrophenanthrene [7] 	stem	[Pettit, 1986]

Table 2.3 (continued)

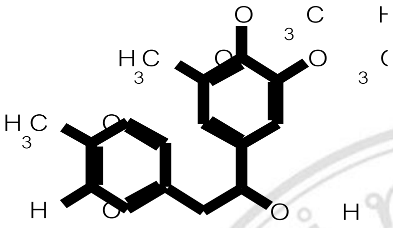
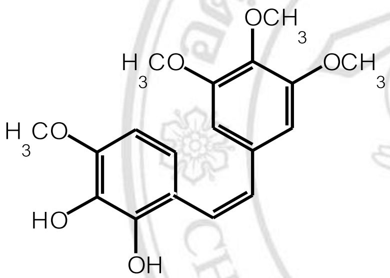
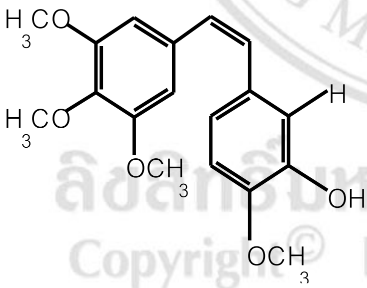
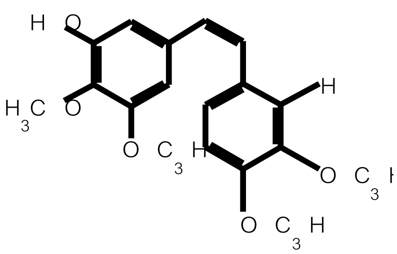
Plant and chemical compound	Plant part	Reference
Combretastatin [8] 	stem twigs, leaves and fruits	[Pettit, 1986] [Pettit, 1987]
Combretastatin A-1 [9] 	stem	[Pettit, 1986 ; 1987]
Combretastatin A-4 [10] 	stem	[Pettit, 1995]
Combretastatin A-5 [11] 	stem	[Pettit, 1995]

Table 2.3 (continued)

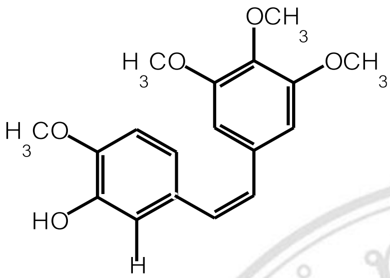
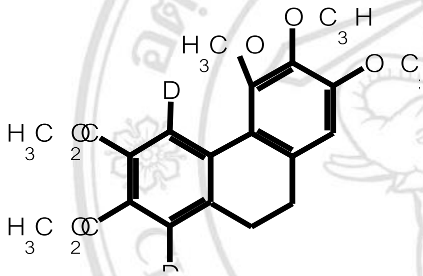
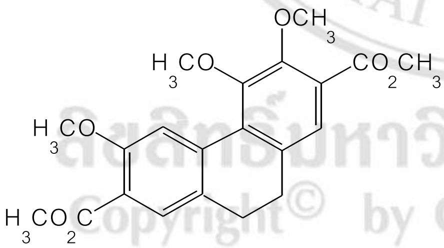
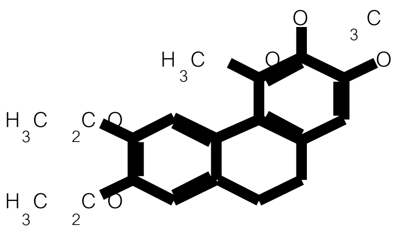
Plant and chemical compound	Plant part	Reference
Combretastatin A-6 [12] 	stem	[Pettit, 1995]
6,7-Diacetoxy-2,3,4-trimethoxy-5,8-dideuterio-9,10-dihydrophenanthrene [13] 	stem	[Pettit, 1986]
2,7-Diacetoxy-3,4,6-trimethoxy-9,10-dihydrophenanthrene [14] 	stem	[Pettit, 1986]
6,7-Diacetoxy-2,3,4-trimethoxy-9,10-dihydrophenanthrene [15] 	stem	[Pettit, 1986]

Table 2.3 (continued)

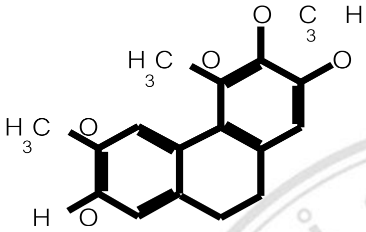
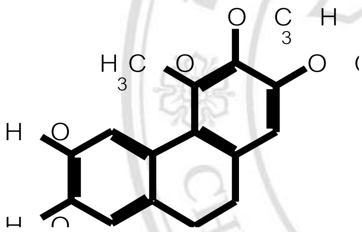
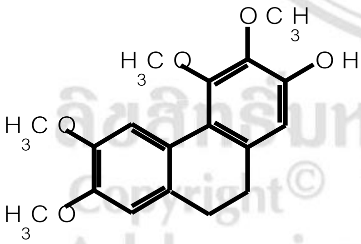
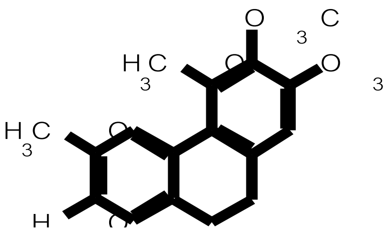
Plant and chemical compound	Plant part	Reference
2,7-Dihydroxy-3,4,6-trimethoxy-9,10-dihydrophenanthrene [16] 	stem	[Pettit, 1986]
6,7-Dihydroxy-2,3,4-trimethoxy-9,10-dihydrophenanthrene [17] 	stem	[Pettit, 1986]
2-Hydroxy-3,4,6,7-tetramethoxy-9,10-dihydrophenanthrene [18] 	stem	[Pettit, 1986]
7-Hydroxy-2,3,4,6-tetramethoxy-9,10-dihydrophenanthrene [19] 	stem	[Pettit, 1986]

Table 2.3 (continued)

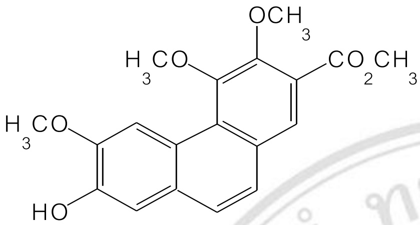
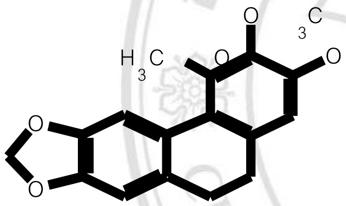
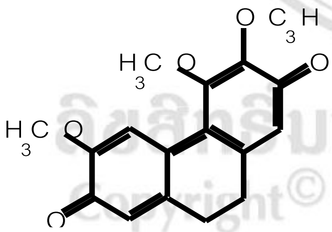
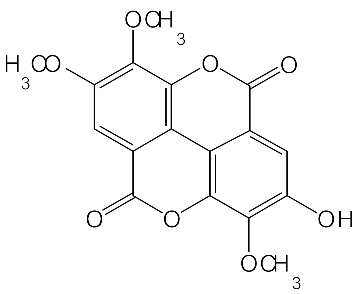
Plant and chemical compound	Plant part	Reference
7-Hydroxy-2,3,4,6-tetramethoxy-phenanthrene [20] 	stem	[Pettit, 1986]
6,7-Methylenedioxy-2,3,4-trimethoxy-9,10-dihydrophenanthrene [21] 	stem	[Pettit, 1986]
3,4,6-Trimethoxy-2,3,4-trimethoxy-9,10-dihydrophenanthrene-2,7-quinone [22] 	stem	[Pettit, 1986]
3,3',4'-Tri-*O*-methylellagic acid [23] 	twigs, leaves and fruits	[Pettit, 1987]

Table 2.3 (continued)

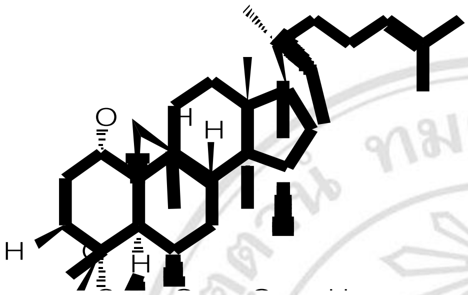
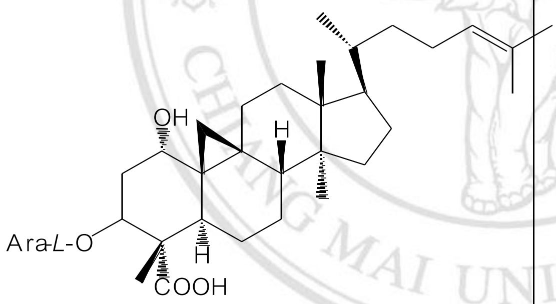
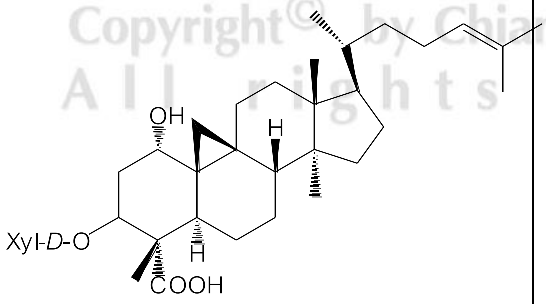
Plant and chemical compound	Plant part	Reference
Combretum edwardsii		
Mollic acid [24]	leaves	[Rogers, 1988a]
		
Mollic acid 3-*O*- *α*-*L*-arabinoside [25]	leaves	[Rogers, 1988a]
		
Mollic acid 3-*O*- *β*-*D*-xyloside [26]	leaves	[Rogers, 1988a]
		

Table 2.3 (continued)

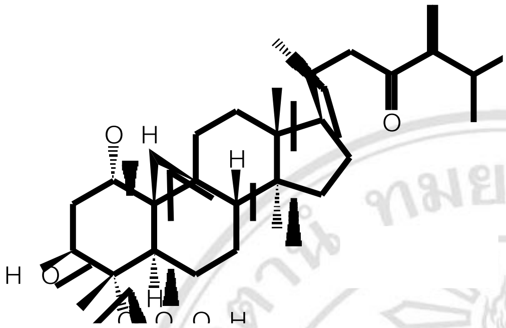
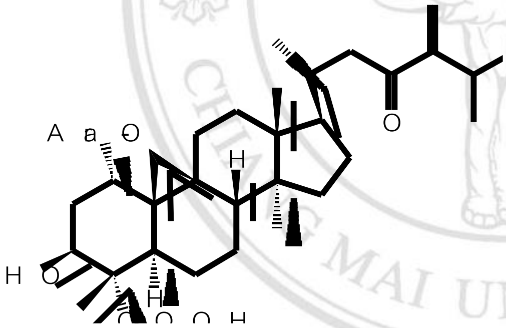
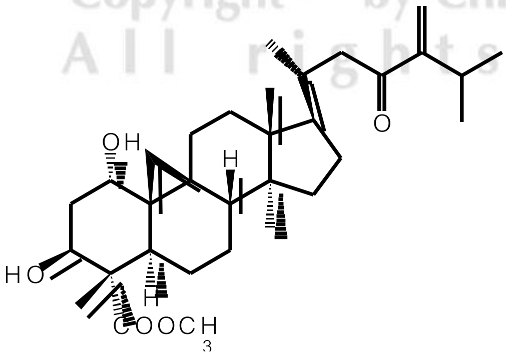
Plant and chemical compound	Plant part	Reference
Combretum elaeagnoides Klotzsch		
Jessic acid [27]	leaves	[Osborne, 1984]
		
Jessic acid *α*-*L*-arabinoside [28]	leaves	[Osborne, 1984]
		
Methyl jessate [29]	leaves	[Osborne, 1984]
		

Table 2.3 (continued)

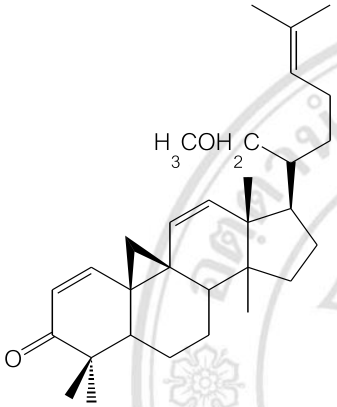
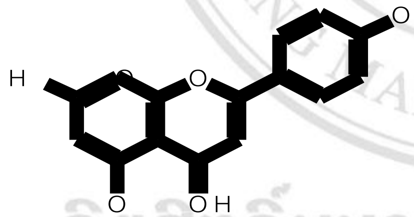
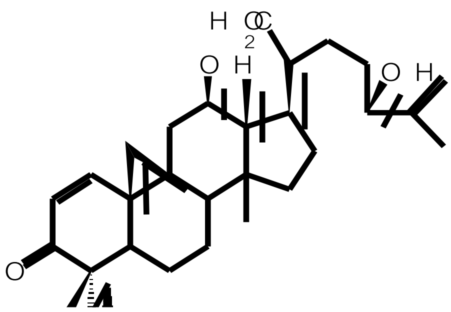
Plant and chemical compound	Plant part	Reference
Combretum erythrophyllum (Burch.) Sond.		
21-Acetoxy-3-oxo-cycloart-1,11,24-triene [30] 	leaves	[Rogers, 1998]
Apigenin [31] 	leaves	[Martini, 2004]
12β,24(*S*)-Dihydroxy-3-oxo-cycloart-1,25(26)-dien-21-oic acid [32] 	leaves	[Rogers, 1998]

Table 2.3 (continued)

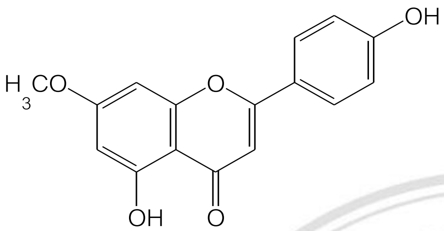
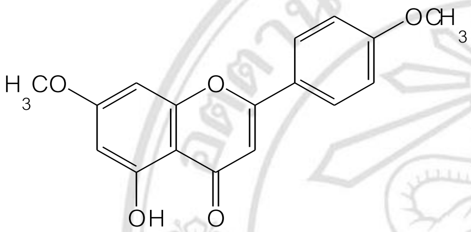
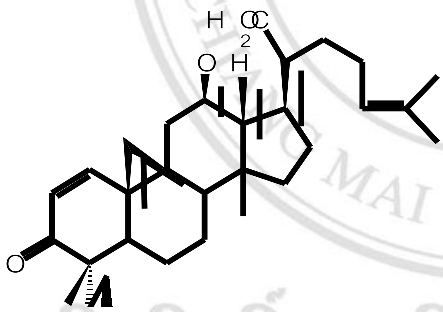
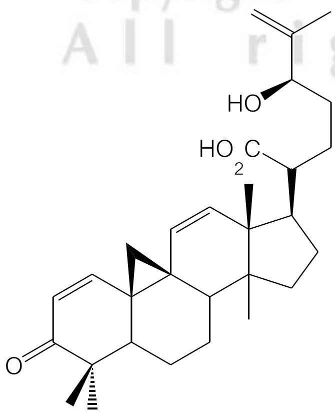
Plant and chemical compound	Plant part	Reference
Genkwanin [33] 	leaves	[Martini, 2004]
5-Hydroxy-7,4'-dimethoxyflavone [34] 	leaves	[Martini, 2004]
12β-Hydroxy-3-oxo-cycloart-1,24-dien-21-oic acid [35] 	leaves	[Rogers, 1998]
24(*R/S*)-Hydroxy-3-oxo-cycloart-1,11,25(26)-trien-21-oic acid [36] 	leaves	[Rogers, 1998]

Table 2.3 (continued)

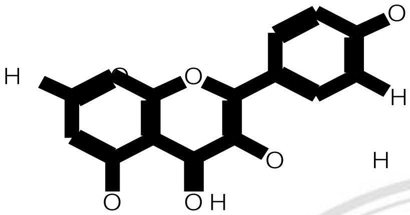
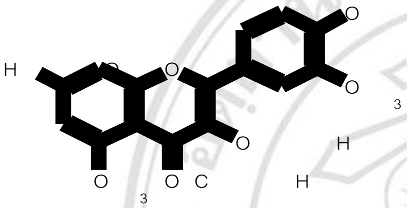
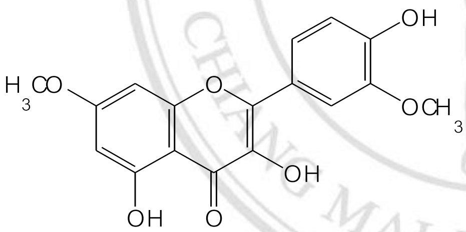
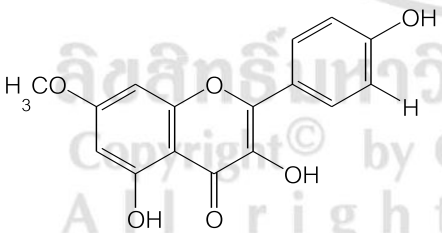
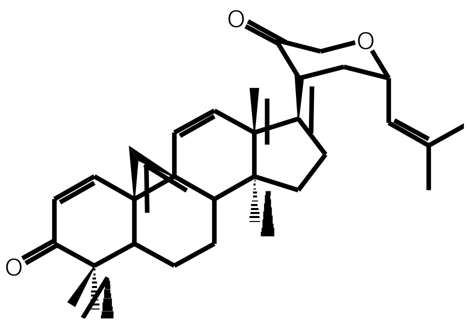
Plant and chemical compound	Plant part	Reference
Kaempferol [37] 	leaves	[Martini, 2004]
Quercetin-5,3'-dimethylether [38] 	leaves	[Martini, 2004]
Rhamnazin [39] 	leaves	[Martini, 2004]
Rhamnocitrin [40] 	leaves	[Martini, 2004]
3-Oxo-cycloart-11-en-21-oic acid [41] 	leaves	[Rogers, 1998]

Table 2.3 (continued)

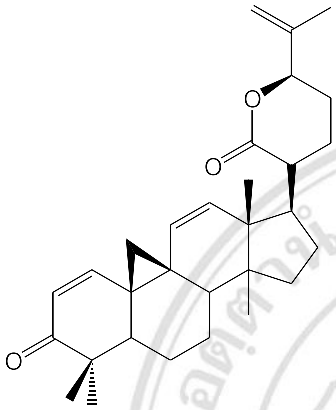
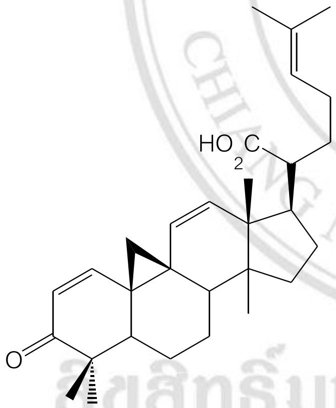
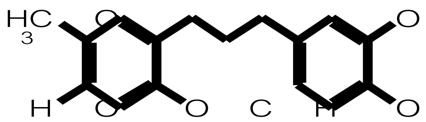
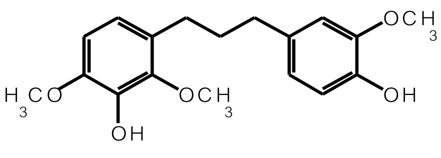
Plant and chemical compound	Plant part	Reference
3-Oxo-cycloart-1,11,25(26)-trien-24(*R*),21-olide [42] 	leaves	[Rogers, 1998]
3-Oxo-cycloart-1,11,24-trien-21-oic acid [43] 	leaves	[Rogers, 1998]
Combretum griffitii Heur. & M.A.		
Griffithanes A [44] 	stem	[Moosophon, 2011]
Griffithanes B [45] 	stem	[Moosophon, 2011]

Table 2.3 (continued)

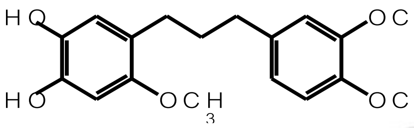
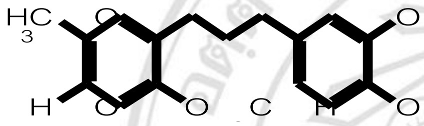
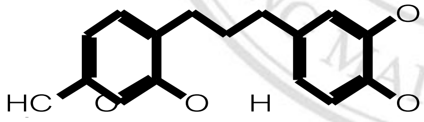
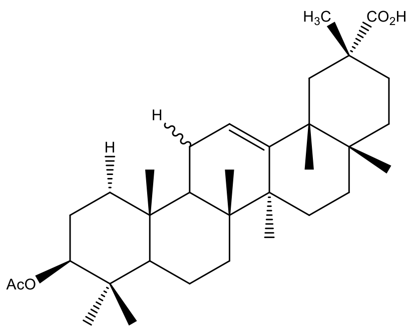
Plant and chemical compound	Plant part	Reference
Griffithanes C [46] 	stem	[Moosophon, 2011]
Griffithanes D [47] 	stem	[Moosophon, 2011]
1-(2-Hydroxy-4-methoxyphenyl)-3-(4-Hydroxy-3-methoxyphenyl) propane [48] 	stem	[Moosophon, 2011]
Combretum imberbe Wawra		
3*β*-acetoxy-olean-12-en-29-oic acid methyl ester [49] 	leaves	[Rogers, 1988b]

Table 2.3 (continued)

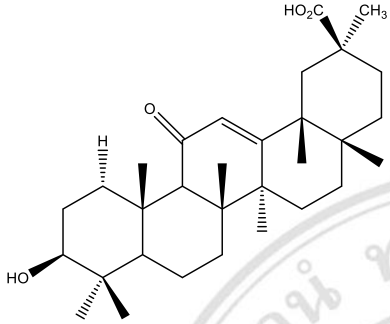
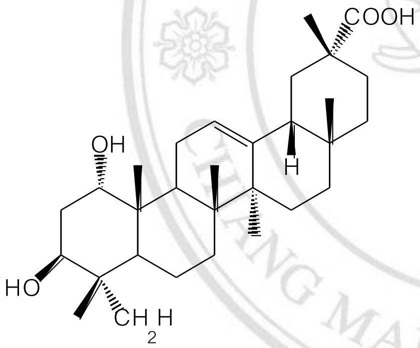
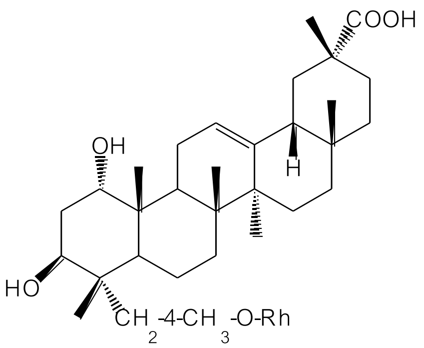
Plant and chemical compound	Plant part	Reference
Glycyrrhetic acid [50] 	leaves	[Rogers, 1988b]
1*α*,3*β*-Hydroxyimberbic acid (1*α*,3*β*-Dihydroxy-olean-12-en-29-oic acid) [51] 	leaves	[Katerere, 2003] [Eloff, 2008]
1*α*,3*β*-Hydroxyimberbic acid-23-*O*-*α*-*L*-4-acetylrhamnopyranoside (1*α*,3*β*,23-Trihydroxy-olean-12-en-29-oate-23-*O*-*α*-*L*-4-acetylrhamnopyranoside) [52] 	leaves	[Katerere, 2003] [Eloff, 2008]

Table 2.3 (continued)

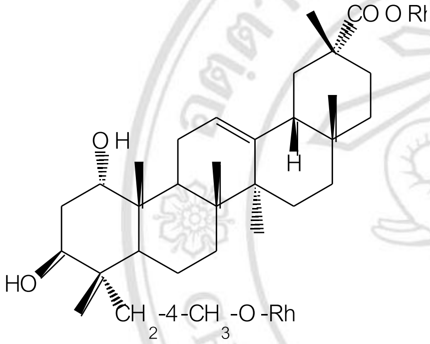
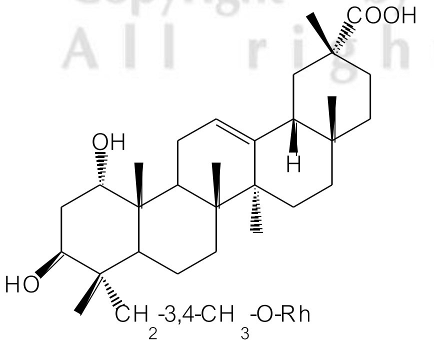
Plant and chemical compound	Plant part	Reference
1*α*,3*β*-Hydroxyimberbic acid-23- *O*-*α* – [*L*-4-acetyl-rhamnopyranosyl]-29-*O*-*α*-rhamnopyranoside (1*α*,3*β*,23-Trihydroxy-olean-12-en-29-oate-23-*O*-*α*-*L*-4-acetyl-29-dirhamnopyranoside) [53] 	leaves	[Katerere, 2003] [Eloff, 2008]
1*α*,3*β*-Hydroxyimberbic acid-23-*O*-*α*-*L*-3,4-diacetylrhamnopyranoside (1*α*,3*β*-Trihydroxy-olean-12-en-29-oate-23-*O*-*α*-*L*-3,4-acetylrhamnopyranoside) [54] 	leaves	[Katerere, 2003] [Eloff, 2008]

Table 2.3 (continued)

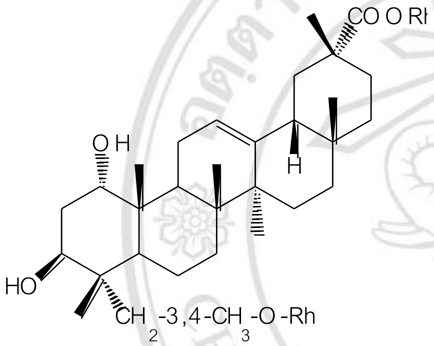
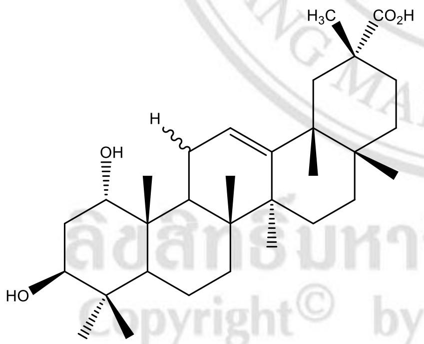
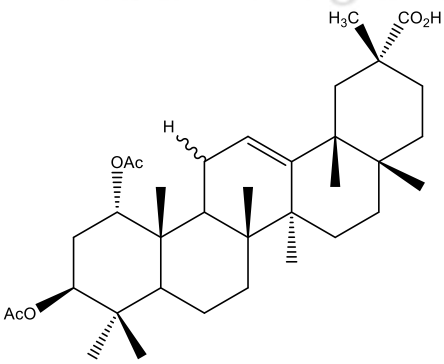
Plant and chemical compound	Plant part	Reference
1*α*,3*β*-Hydroxyimberbic acid-23-*α* –[*L*-3,4-diacetyl-rhamnopyranosyl]-29-*O*-*α*-rhamnopyranoside (1*α*,3*β*,23-Trihydroxy-olean-12-en-29-oate-23-*O*-*α*-*L*-3,4-acetyl-29-dirhamnopyranoside) [55]	leaves	[Katerere, 2003] [Eloff, 2008]
		
Imberbic acid [56]	leaves	[Rogers, 1988b]
		
Imberbic acid diacetate [57]	leaves	[Rogers, 1988b]
		

Table 2.3 (continued)

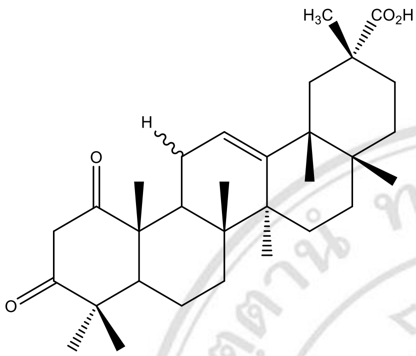
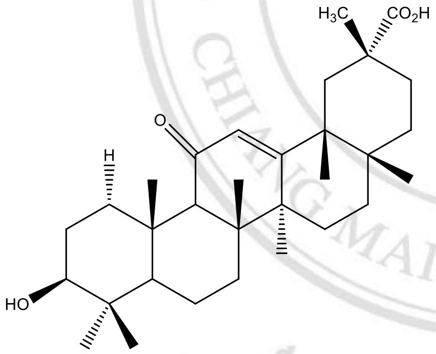
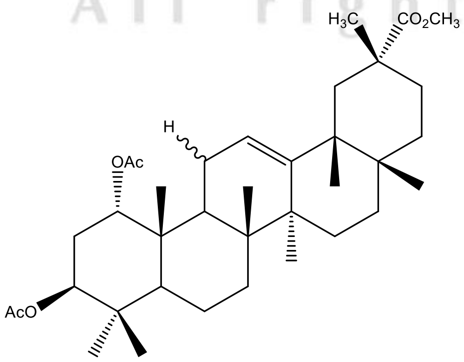
Plant and chemical compound	Plant part	Reference
Imberbic acid diketone [58] 	leaves	[Rogers, 1988b]
Liquiritic acid [59] 	leaves	[Rogers, 1988b]
Methyl imberbate diacetate [60] 	leaves	[Rogers, 1988b]

Table 2.3 (continued)

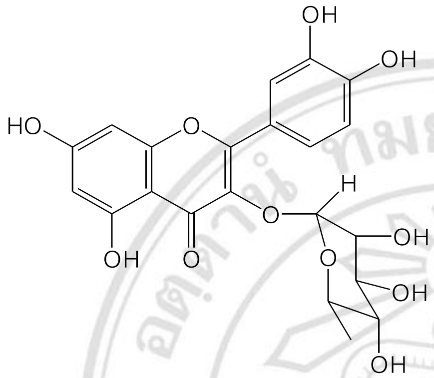
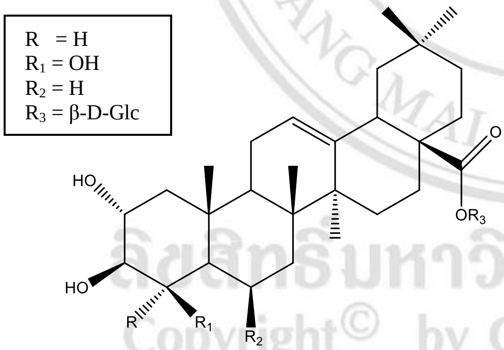
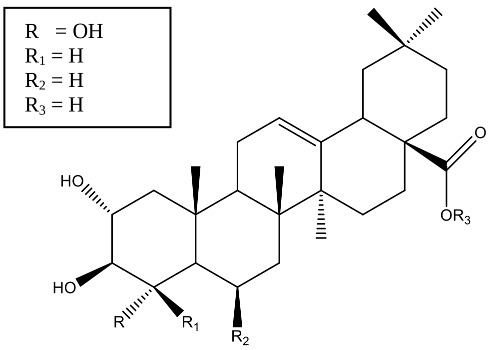
Plant and chemical compound	Plant part	Reference
Combretum lanceolatum Pohl *ex* Eichler Quercetin [61] 	flowers	[Dechandt, 2013]
Combretum laxum Jacq. *β-D*-Glucopyranosyl-2*α*,3*β*,24-trihydroxyolean-12-en-28-oate [62] 	stem	[Bisoli, 2008]
Arjunolic acid [63] 	stem	[Bisoli, 2008]

Table 2.3 (continued)

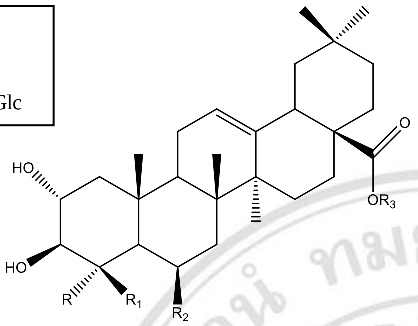
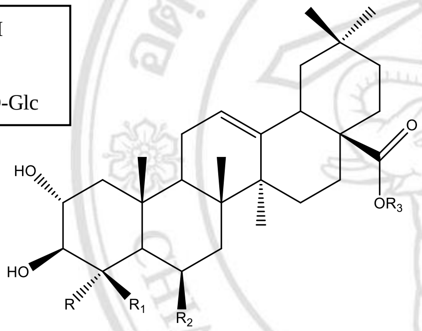
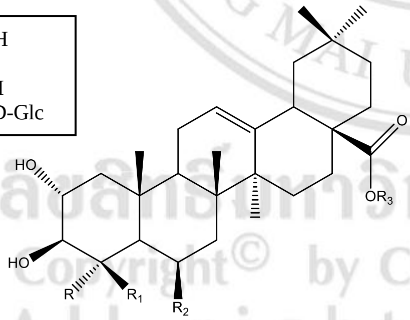
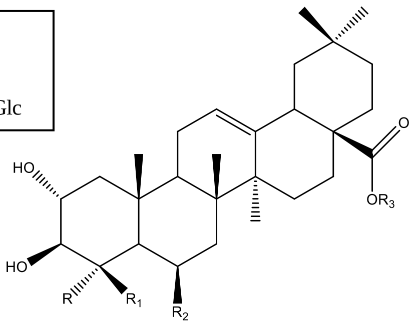
Plant and chemical compound	Plant part	Reference
Arjunglucoside II [64] R = OH R_1 = H R_2 = H R_3 = β-D-Glc 	stem	[Bisoli, 2008]
Bellericoside [65] R = OH R_1 = OH R_2 = H R_3 = β-D-Glc 	stem	[Bisoli, 2008]
Chebuloside II [66] R = OH R_1 = H R_2 = OH R_3 = β-D-Glc 	stem	[Bisoli, 2008]
β-D-Glucopyranosyl-2*α*,3*β*,6*β*-trihydroxyolean-12-en-28-oate [67] R = H R_1 = H R_2 = OH R_3 = β-D-Glc 	stem	[Bisoli, 2008]

Table 2.3 (continued)

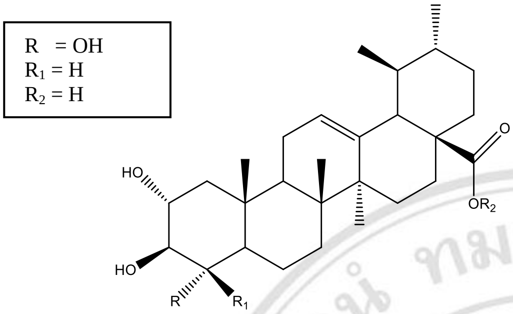
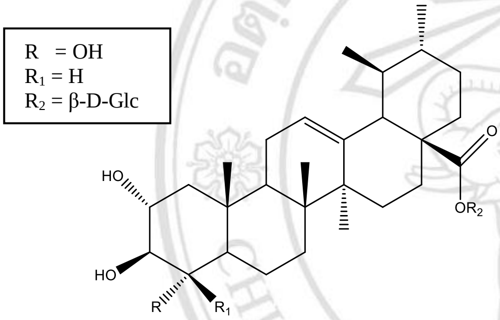
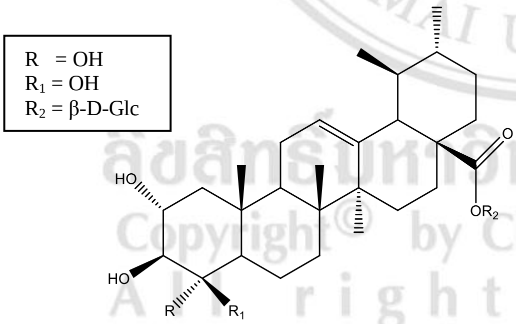
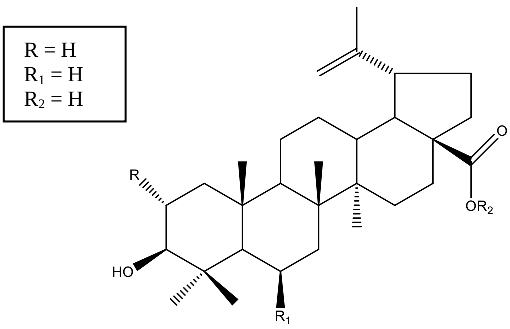
Plant and chemical compound	Plant part	Reference
Asiatic acid [68] 	stem	[Bisoli, 2008]
Quadranoside IV [69] 	stem	[Bisoli, 2008]
β-D-Glucopyranosyl-2*α*,3*β*,23,24-tetrahydroxyurs-12-en-28-oate [70] 	stem	[Bisoli, 2008]
Betulinic acid [71] 	stem	[Bisoli, 2008]

Table 2.3 (continued)

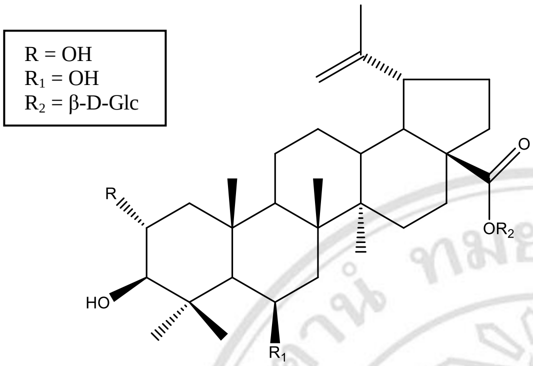
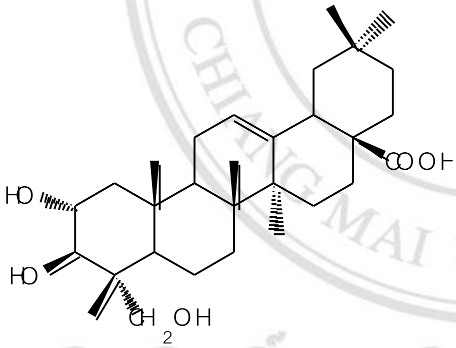
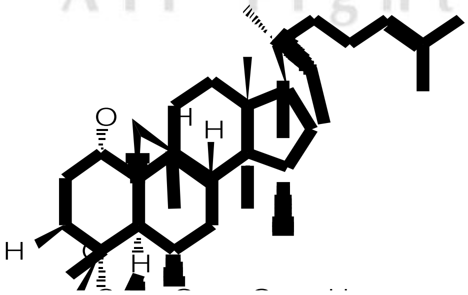
Plant and chemical compound	Plant part	Reference
Quadranoside I [72] 	stem	[Bisoli, 2008]
Combretum leprosum Mart.		
Arjunolic acid [63] 	roots	[Facundo, 1993]
Mollic acid [24] 	leaves	[Facundo, 1993]

Table 2.3 (continued)

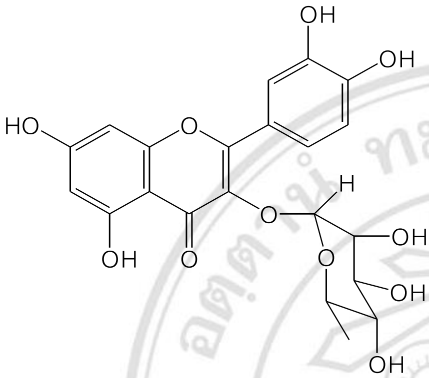
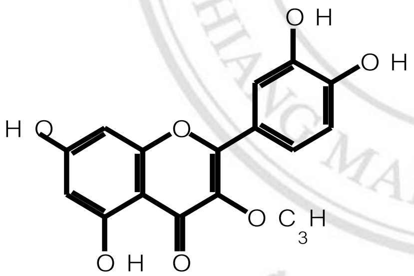
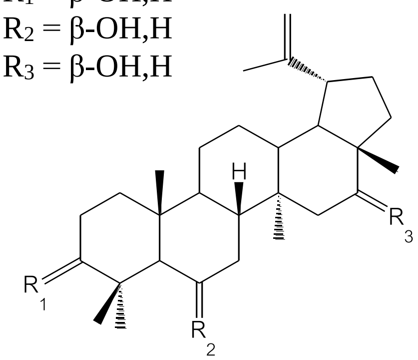
Plant and chemical compound	Plant part	Reference
Quercetrin (3-*O*-*α*-*L*-Rhamnopyranosylquecertin) [61] 	leaves	[Facundo, 1993]
Scoparol (3-*O*-Methylquercetin) [73] 	leaves	[Facundo, 1993]
3*β*,6*β*,16*β*-Trihydroxylup-20(29)-ene [74] R_1 = β-OH,H R_2 = β-OH,H R_3 = β-OH,H 	leaves flowers	[Facundo, 1993] [Pietrovski, 2006]

Table 2.3 (continued)

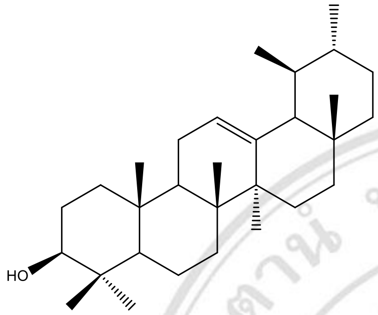
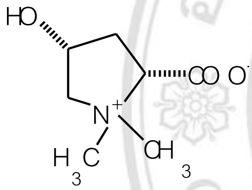
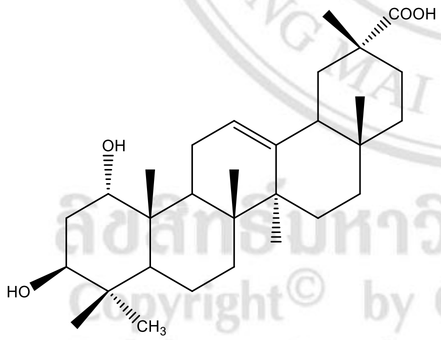
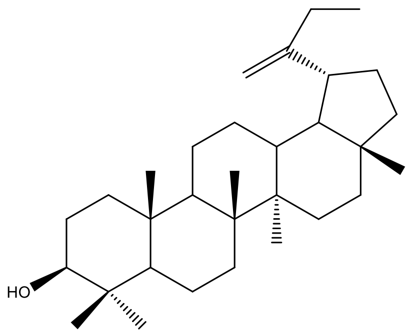
Plant and chemical compound	Plant part	Reference
Combretum micranthum G. Don		
α-Amyrin [75] 	leaves	[Dawe, 2013]
4-Hydroxyproline betaine [76] 	leaves	[Eloff, 2008]
Imberic acid (1α,3β-dihydroxy-12-oleanen-29-oic) [77] 	leaves	[Dawe, 2013]
Lupeol [78] 	leaves	[Dawe, 2013]

Table 2.3 (continued)

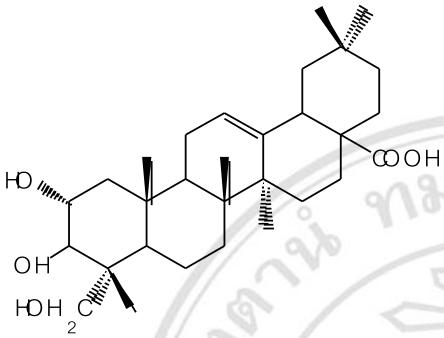
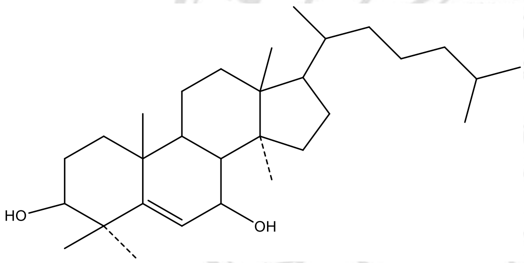
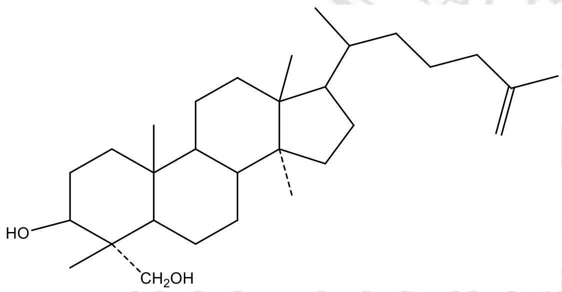
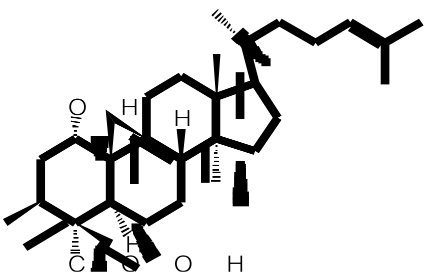
Plant and chemical compound	Plant part	Reference
Combretum molle R. Br. *ex* G. Don		
Arjunolic acid [63] 	leaves	[Eloff, 2008]
Combretene-A [79] 	arial part	[Ahmed, 2004]
Combretene-B [80] 	arial part	[Ahmed, 2004]
1α-Hydroxycycloartane glycoside [81] 	leaves	[Pegal, 1985]

Table 2.3 (continued)

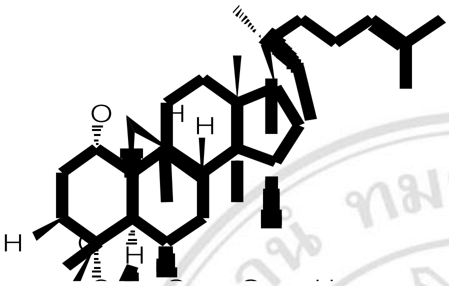
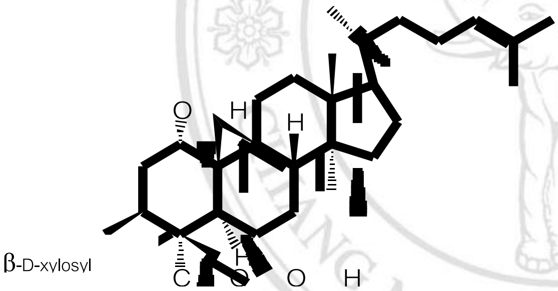
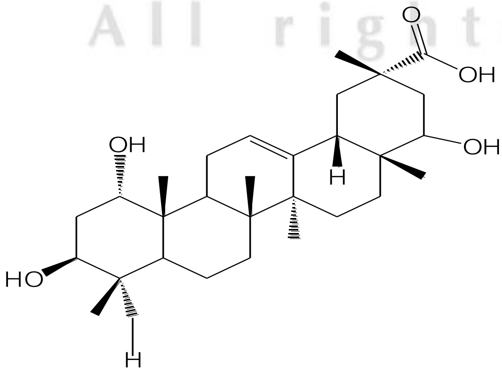
Plant and chemical compound	Plant part	Reference
Mollic acid [24] 	leaves aerial part	[Pegal, 1985] [Eloff, 2008] [Ahmed, 2004]
Mollic acid 3-*β*-*D*-xyloxide [82] 	leaves	[Pegal, 1985]
Combretum padoides Engl. & Diels 1,22-Dihydroxy-12-oleanen-30-oic acid [83] 	leaves	[Angeh, 2007]

Table 2.3 (continued)

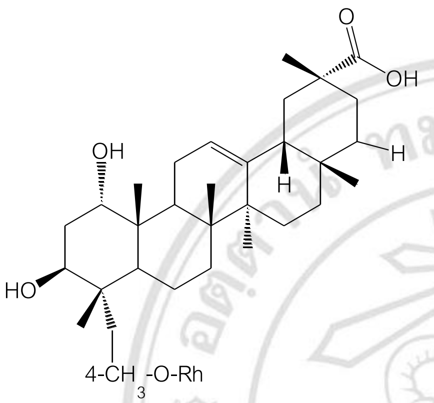
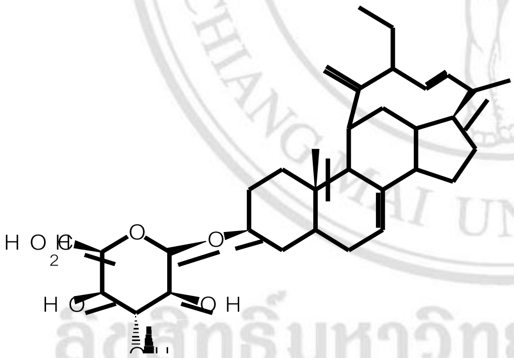
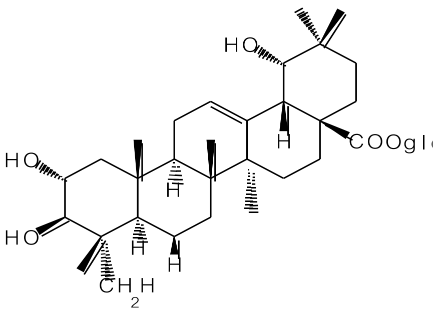
Plant and chemical compound	Plant part	Reference
1α,23β-Dihydroxy-12-oleanen-29-oic-acid-23β-*O*-α-4-acetylrhamnopyranoside [84] 	leaves	[Angeh, 2007]
24-Ethylcholesta-7,22,25-trien-*O*-β-*D*-glucopyranoside [85] 	leaves	[Angeh, 2007]
Combretum quadrangulare Kurz		
Arjunetin [86] 	seeds	[Adnyana, 2000a]

Table 2.3 (continued)

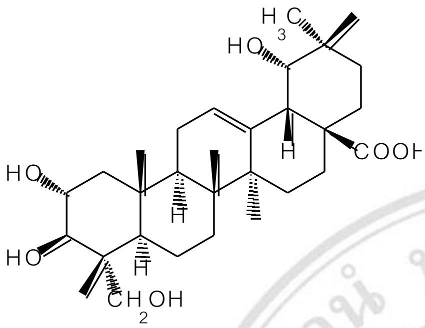
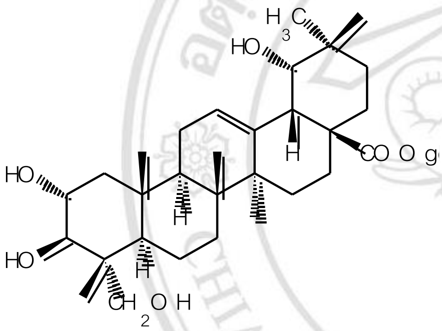
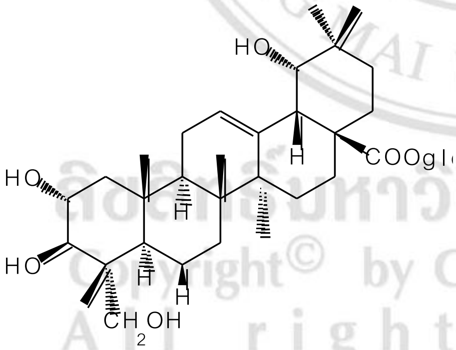
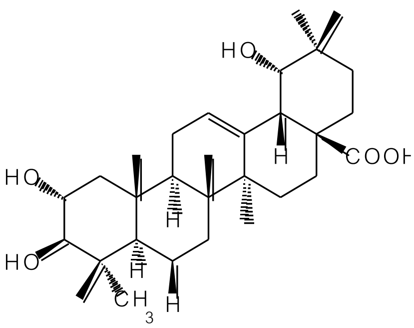
Plant and chemical compound	Plant part	Reference
Arjungenin [87] 	seeds	[Adnyana, 2000b]
Arjunglucoside I [88] 	seeds	[Adnyana, 2000b ; 2001b]
Arjunglucoside II [64] 	seeds	[Adnyana, 2000a ; 2001b]
Arjunic acid [89] 	seeds	[Adnyana, 2001b]

Table 2.3 (continued)

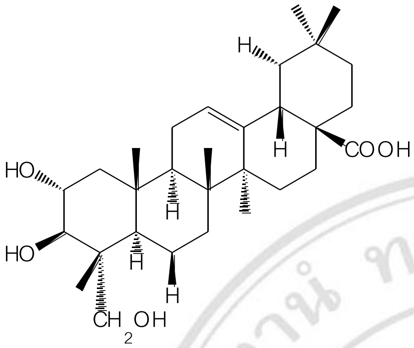
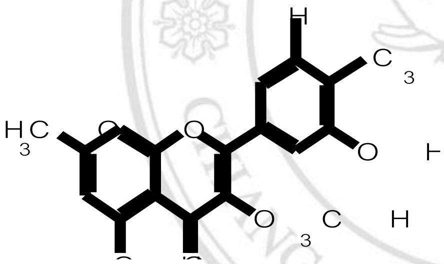
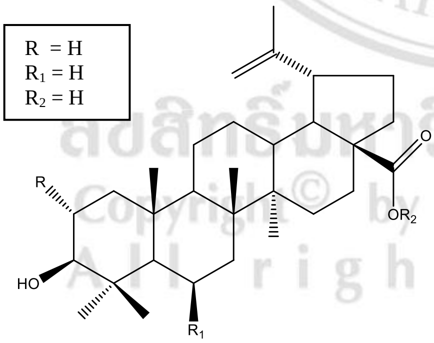
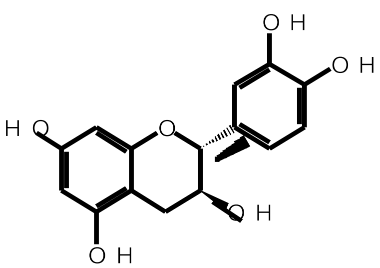
Plant and chemical compound	Plant part	Reference
Arjunolic acid [63] 	seeds	[Adnyana, 2001b]
Ayanin (3’,5-dihydroxy-3,4’,7-trimethoxy) [90] 	seeds flowers	[Banskota, 2003] [Castleden, 1985)]
Betulinic acid [71] 	leaves	[Banskota, 2000a]
(+)-Catechin [91] 	seeds	[Adnyana, 2000a ; 2001b]

Table 2.3 (continued)

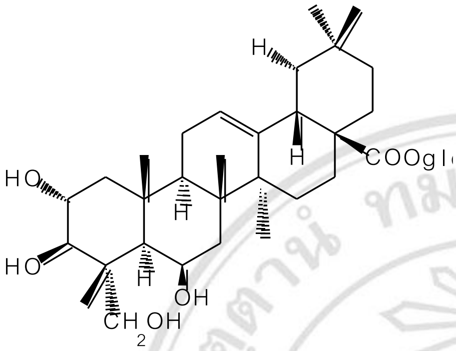
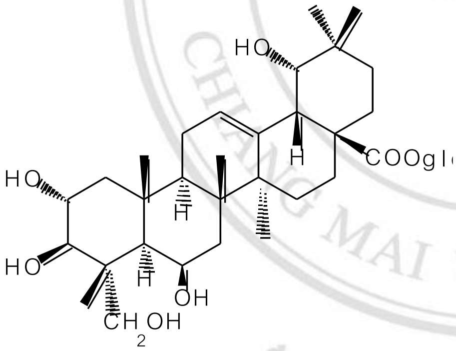
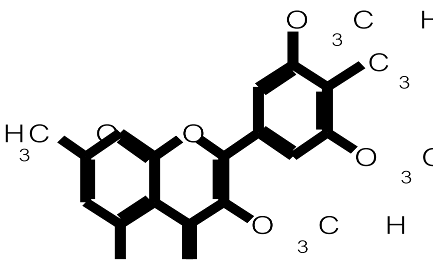
Plant and chemical compound	Plant part	Reference
Chebuloside II [66] 	seeds	[Adnyana, 2000a]
Combreglucoside [92] 	seeds	[Adnyana, 2000a]
Combretol (5-hydroxy-3,3',4',5',7-pentamethoxy) [93] 	flowers	[Castledol, 1985]

Table 2.3 (continued)

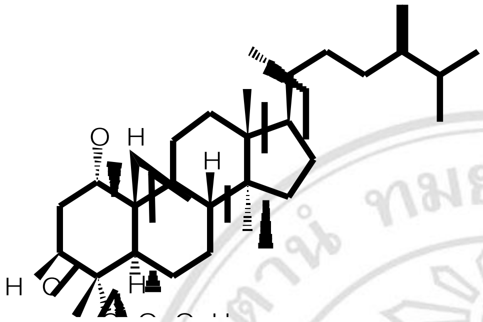
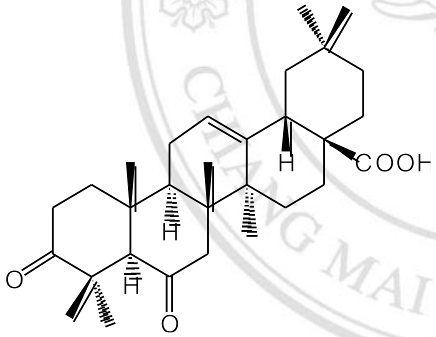
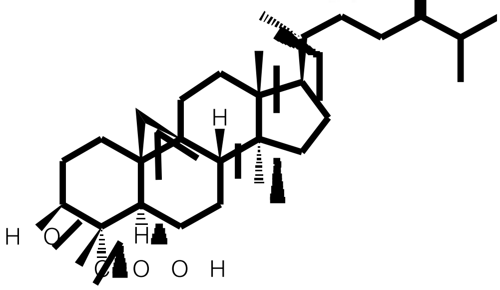
Plant and chemical compound	Plant part	Reference
23-Deoxojessic acid [94] 	leaves	[Banskota, 2000b]
3,6-Diketo-olean-12-en-28-oic acid [95] 	seeds	[Banskota, 2003]
4*β*,14*α*-Dimethyl-5*α*-ergosta-9*β*,19-cyclo-24(24')-en-3*β*-hydroxy-4*α*-carboxylic acid [96] 	leaves	[Banskota, 2003]

Table 2.3 (continued)

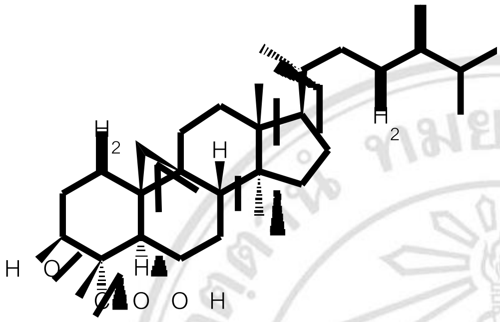
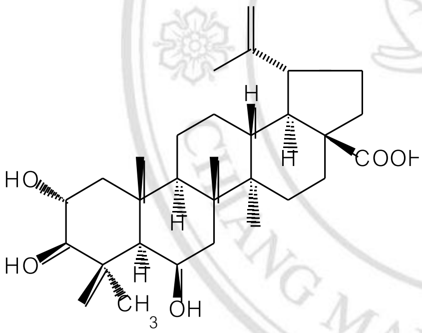
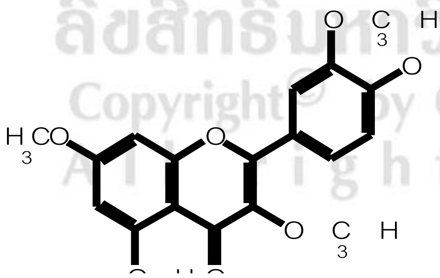
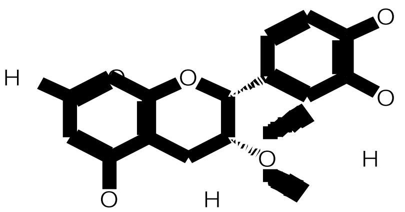
Plant and chemical compound	Plant part	Reference
4*β*,14*α*-Dimethyl-5*α*-ergosta-9*β*,19-cyclo-24(31)-en-3*β*-hydroxy-4*α*-carboxylic acid [97] 	leaves	[Adnyana, 2001b]
2*α*,6*β*-Dihydroxybetulinic acid [98] 	seeds	[Adnyana, 2000b]
5,4'-Dihydroxy-3,7,3'-trimethoxyflavone [99] 	leaves	[Banskota, 2000a]
(-)-Epicatechin [100] 	seeds	[Adnyana, 2000b ; 2001b]

Table 2.3 (continued)

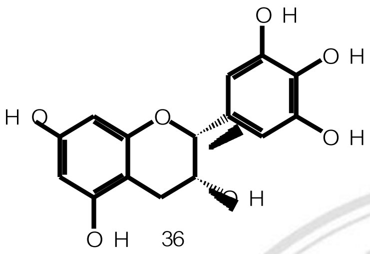
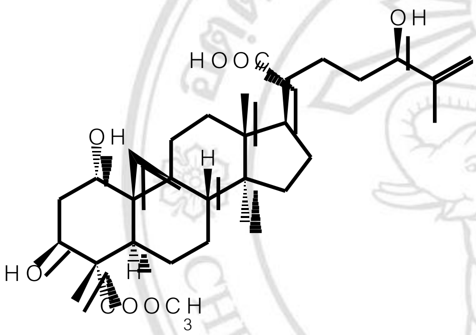
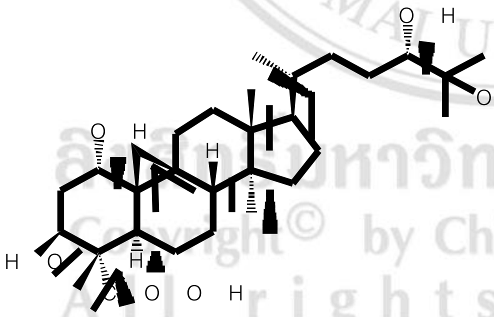
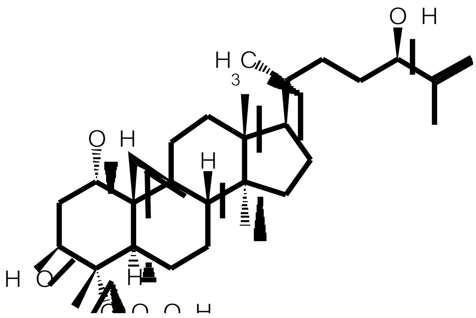
Plant and chemical compound	Plant part	Reference
(-)-Epigallocatechin [101] 	seeds	[Adnyana, 2000a ; 2001b]
24-Epiquadrangularic acid G [102] 	leaves	[Banskota, 2000c]
24-Epiquadrangularic acid L [103] 	leaves	[Banskota, 2003]
24-Epiquadrangularic acid M [104] 	leaves	[Banskota, 2003]

Table 2.3 (continued)

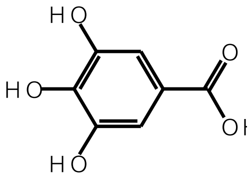
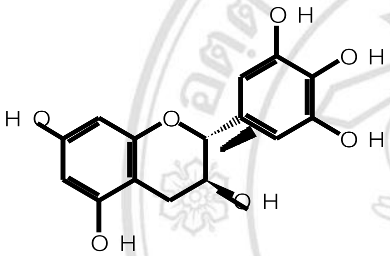
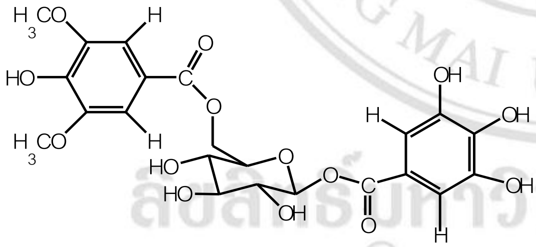
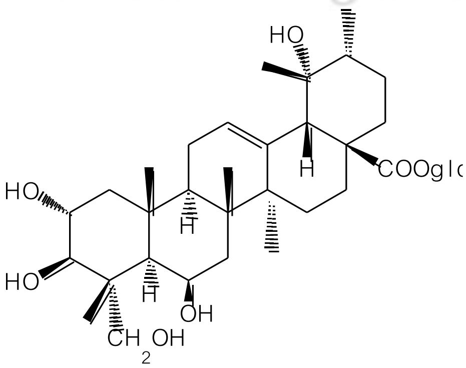
Plant and chemical compound	Plant part	Reference
Gallic acid [105] 	seeds	[Adnyana, 2000b]
(+)-Gallocatechin [106] 	seeds	[Adnyana, 2000b ; 2001b]
1-*O*-Galloyl-6-*O*-(4-hydroxy-3,5-dimethoxy) benzoyl-*β*-*D*-glucose [107] 	seeds	[Adnyana, 2001a]
28-*O*-*β*-*D*-Glucopyranosyl-6*β*,23-dihydroxytormentic acid [108] 	seeds	[Adnyana, 2000a]

Table 2.3 (continued)

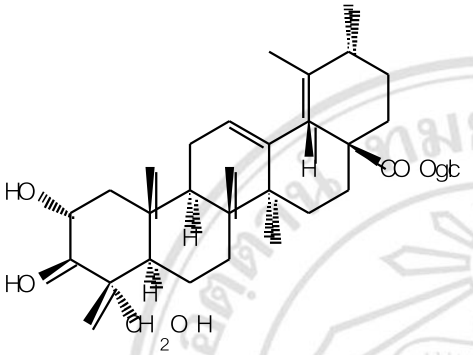
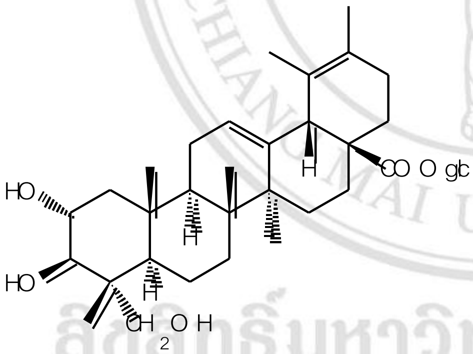
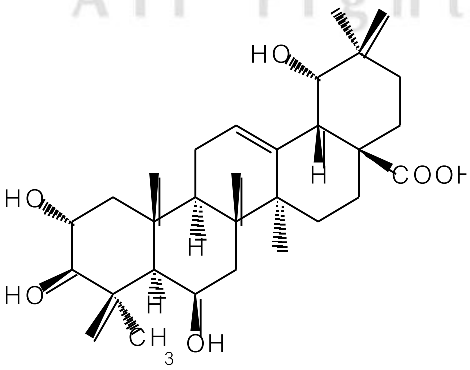
Plant and chemical compound	Plant part	Reference
Glucosyl 2*α*,3*β*-23-trihydroxyurs-12,18-dien-28-oate [109]	seeds	[Adnyana, 2001b]
		
Glucosyl 2*α*,3*β*-23-trihydroxyurs-12,19-dien-28-oate [110]	seeds	[Adnyana, 2001b]
		
6*β*-Hydroxyarjunic acid [111]	seeds	[Adnyana, 2001b]
		

Table 2.3 (continued)

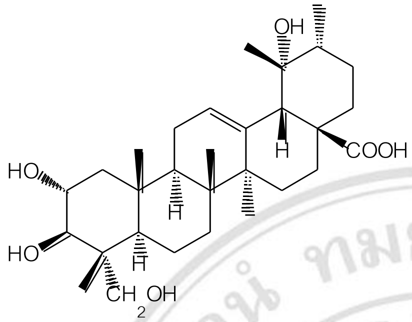
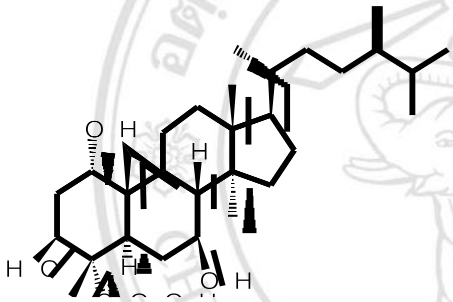
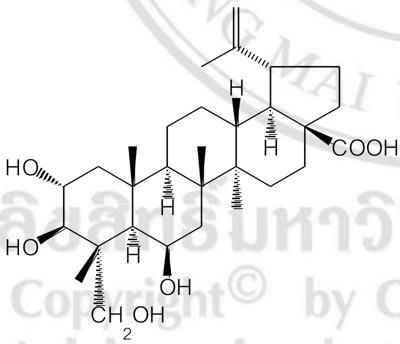
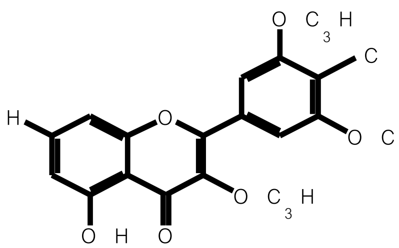
Plant and chemical compound	Plant part	Reference
19α-Hydroxyasiatic acid [112] 	seeds	[Adnyana, 2000b]
7β-Hydroxy-23-deoxojessic acid [113] 	leaves	[Banskota, 2003]
6β-Hydroxyhovenic acid [114] 	seeds	[Adnyana, 2001b]
5-Hydroxy-2-(4'-hydroxy-3,5'-dimethoxyphenyl)-3,7-dimenthoxy-4*H*-1-benzopyran-4-one [115] 	flowers	[Castledol, 1985]

Table 2.3 (continued)

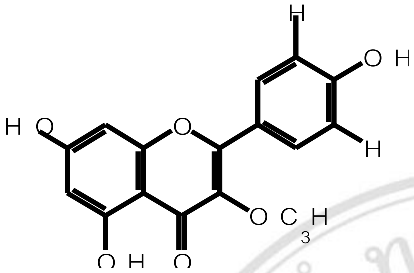
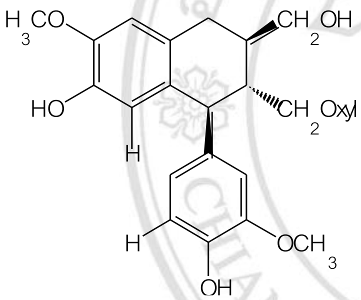
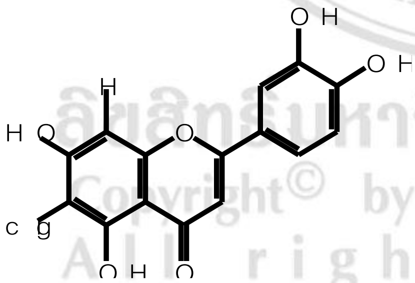
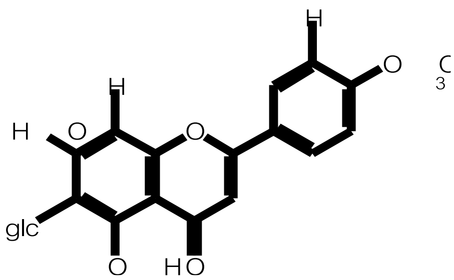
Plant and chemical compound	Plant part	Reference
Isokaempferide [116] 	leaves	[Banskota, 2000b]
(-)-Isolariciresinol-2*α*-*O*-*β*-xylopyranoside [117] 	seeds	[Banskota, 2003]
Isoorientin [118] 	leaves	[Banskota, 2000a]
Isovitexin 4'-methyl ether [119] 	leaves	[Banskota, 2000a]

Table 2.3 (continued)

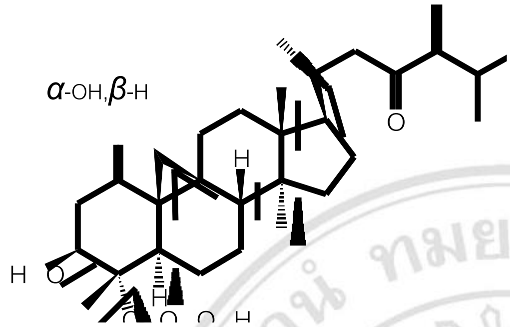
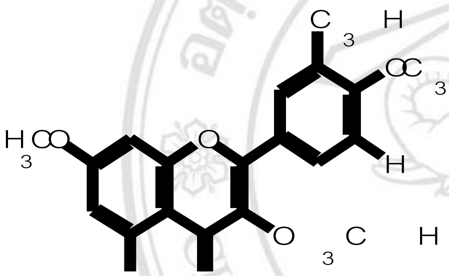
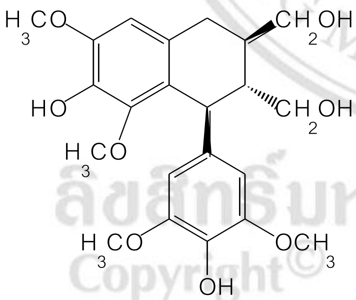
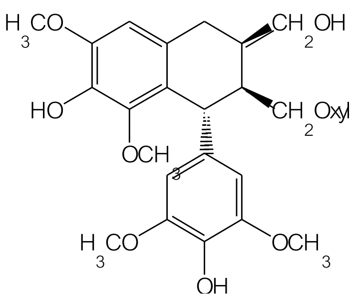
Plant and chemical compound	Plant part	Reference
Jessic acid [27] 	leaves	[Banskota, 2000b]
Kamatakenin [120] 	leaves	[Banskota, 2000a]
(-)-Lyoniresinol [121] 	seeds	[Banskota, 2003]
(+)-Lyoniresinol-2*α*-*O*-*β*-xylopyranoside [122] 	seeds	[Banskota, 2000a]

Table 2.3 (continued)

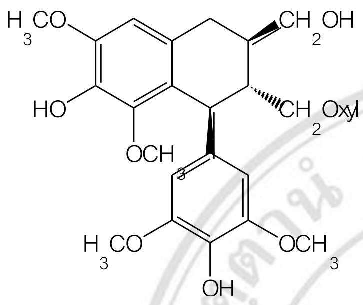
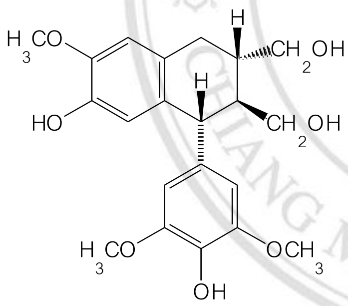
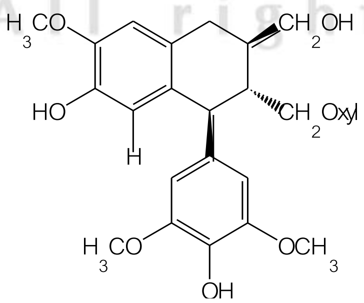
Plant and chemical compound	Plant part	Reference
(-)-Lyoniresinol-2*α*-*O*-*β*-xylopyranoside [123] 	seeds	[Banskota, 2000a]
5-Methoxy-(-)-isolariciresinol [124] 	seeds	[Adnyana, 2000b]
5-Methoxyisolariciresinol-2*α*-*O*-*β*-xylopyranoside [125] 	seeds	[Banskota, 2003]

Table 2.3 (continued)

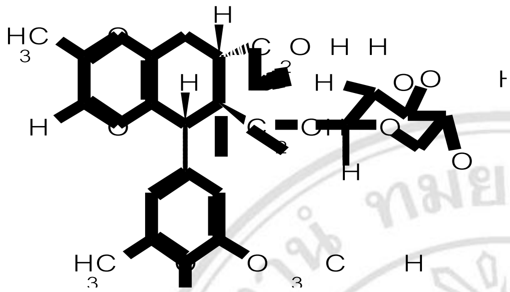
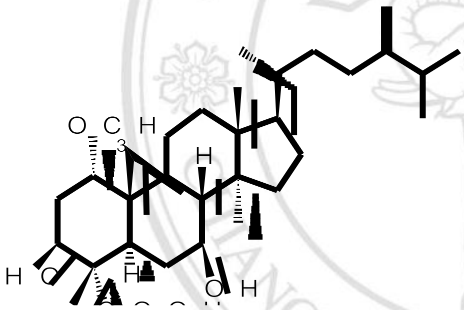
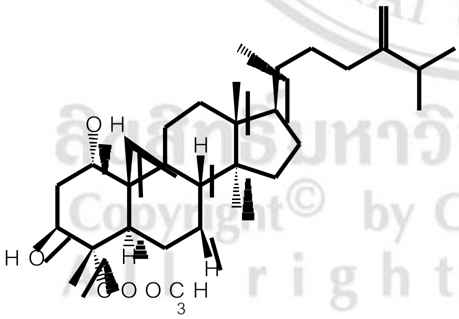
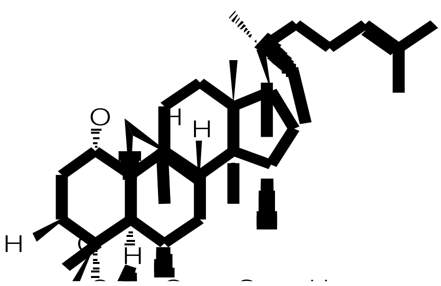
Plant and chemical compound	Plant part	Reference
5-Methoxy-9-*β*-xylopyranosyl-(-)-isolariciresinol [126] 	seeds	[Adnyana, 2000b]
Methyl-*O*'-acetyl-23-deoxojessic acid [127] 	leaves	[Banskota, 1998]
Methyl 23-deoxojessate [128] 	leaves	[Banskota, 2000b]
Mollic acid [24] 	leaves	[Banskota, 2000b]

Table 2.3 (continued)

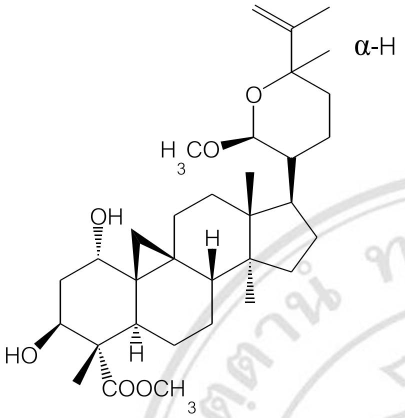
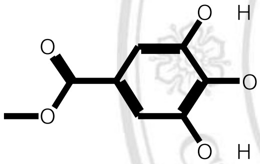
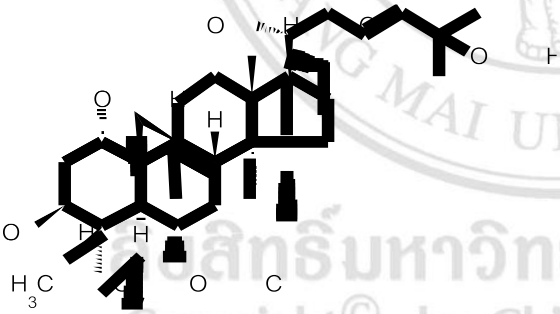
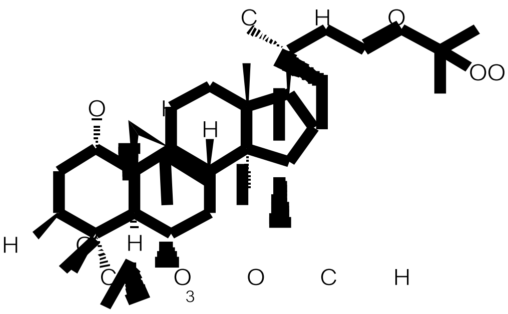
Plant and chemical compound	Plant part	Reference
Methyl 24-epiquadrangularate C [129] 	leaves	[Banskota, 2000b]
Methyl gallate [130] 	seeds	[Adnyana, 2000b]
Methyl guadrangularate A [131] 	leaves	[Banskota, 1998 ; 2000b]
Methyl quarangularates B [132] 	leaves	[Banskota, 1998 ; 2000b]

Table 2.3 (continued)

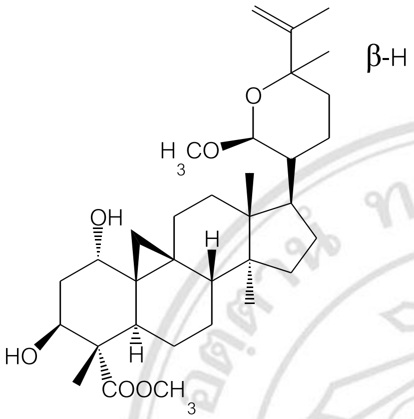
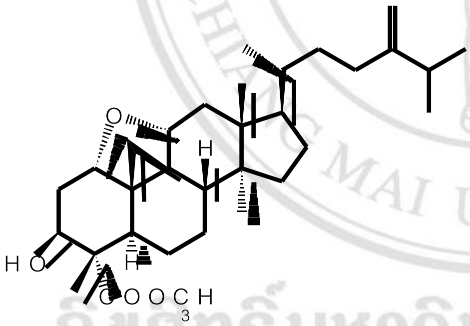
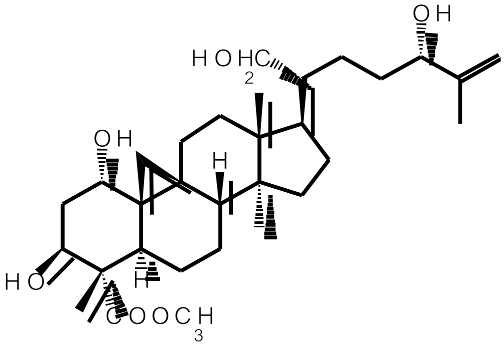
Plant and chemical compound	Plant part	Reference
Methyl quarangularates C [133] 	leaves	[Banskota, 1998 ; 2000b]
Methyl quarangularates D [134] 	leaves	[Banskota, 1998 ; 2000b]
Methyl quarangularates I [135] 	leaves	[Banskota, 2000a]

Table 2.3 (continued)

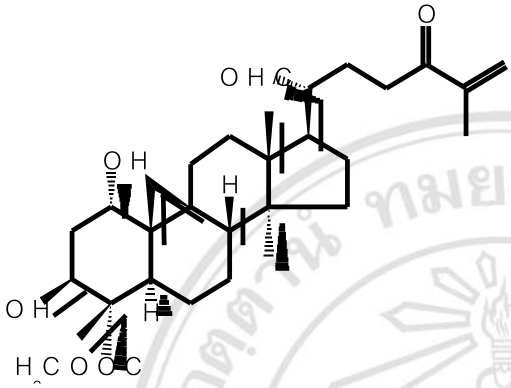
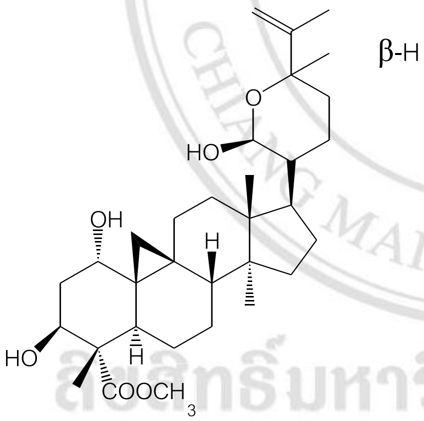
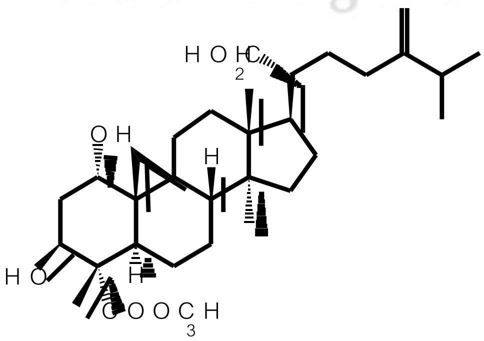
Plant and chemical compound	Plant part	Reference
Methyl quarangularates N [136]	leaves	[Banskota, 2000b]
		
Methyl quarangularates O [137]	leaves	[Banskota, 2000b]
		
Methyl quarangularates P [138]	leaves	[Banskota, 2000b]
		

Table 2.3 (continued)

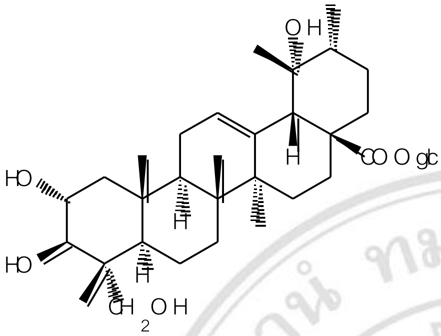
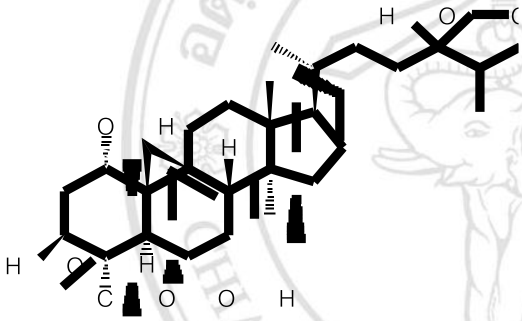
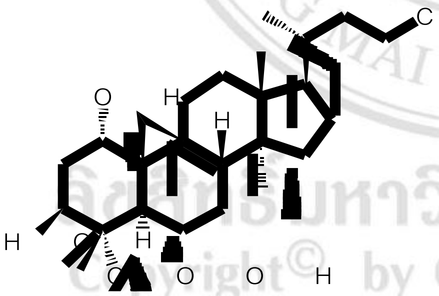
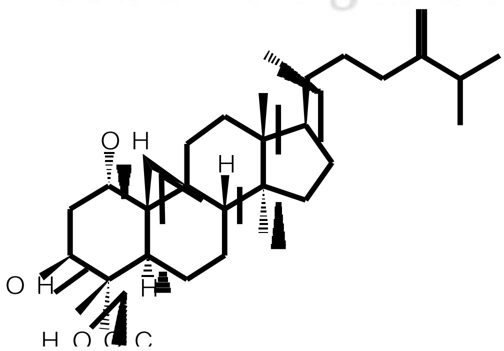
Plant and chemical compound	Plant part	Reference
Nigaichigoside F1 [139] 	seeds	[Adnyana, 2000b ; 2001b]
29-Norcycloartanes [140] 	leaves	[Banskota, 2000a]
Norquadrangularic acids A [141] 	leaves	[Banskota, 2000a]
Norquadrangularic acids B [142] 	leaves	[Banskota, 2000a ; 2000b]

Table 2.3 (continued)

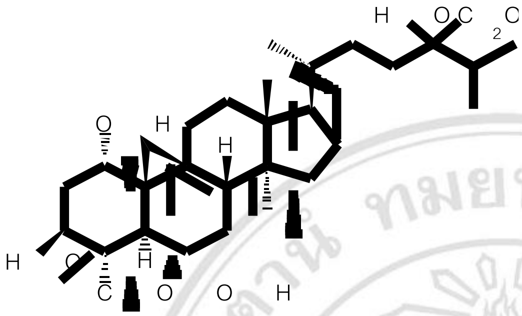
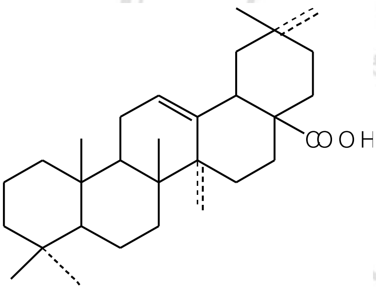
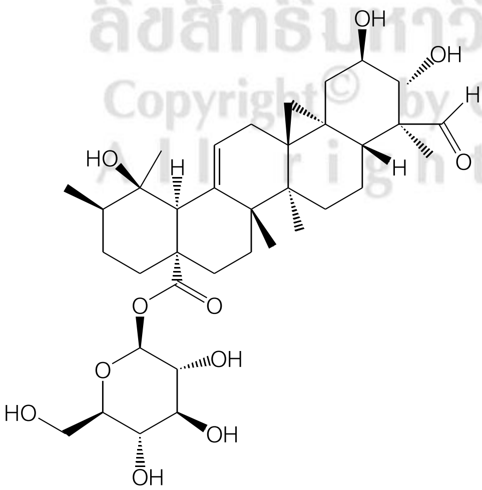
Plant and chemical compound	Plant part	Reference
Norquadrangularic acids C [143]	leaves	[Banskota, 2000b]
		
Olean-12-en-28-oic acid [144]	roots and seeds	[Wungchinda, 1979]
		
Pinfaensin [145]	seeds	[Adnyana, 2000b]
		

Table 2.3 (continued)

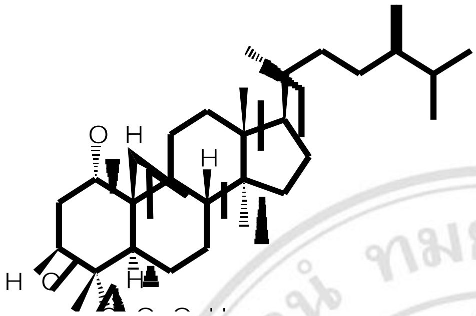
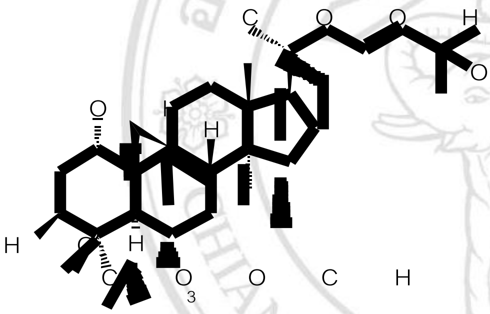
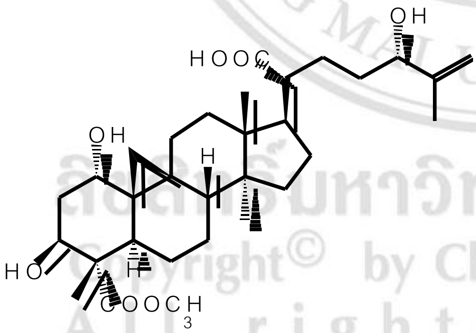
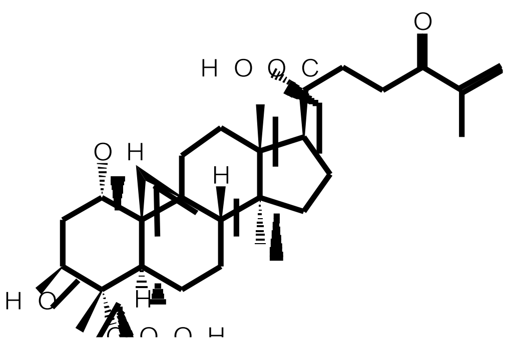
Plant and chemical compound	Plant part	Reference
Quadrangularic acids E [146] 	leaves	[Banskota, 2000b]
Quadrangularic acids F [147] 	leaves	[Banskota, 2000c]
Quadrangularic acids G [148] 	leaves	[Banskota, 2000c]
Quadrangularic acids H [149] 	leaves	[Banskota, 2000c]

Table 2.3 (continued)

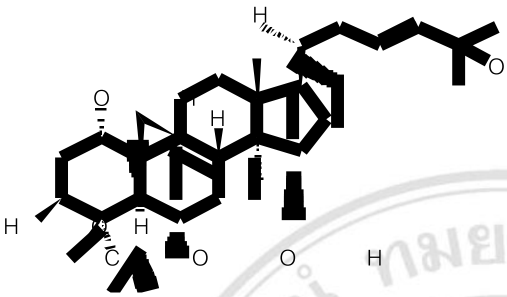
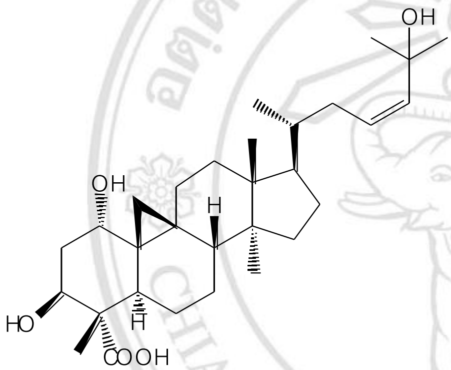
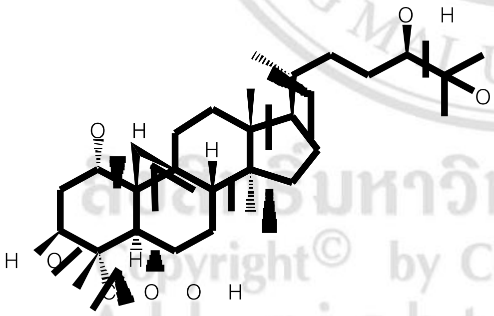
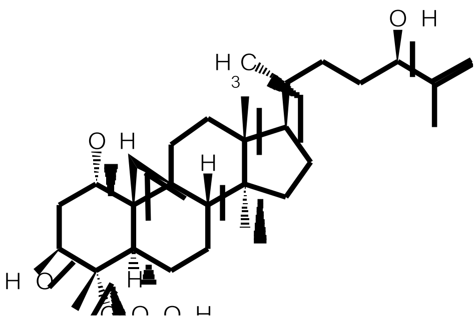
Plant and chemical compound	Plant part	Reference
Quadrangularic acids J [150] 	leaves	[Banskota, 2000c]
Quadrangularic acids K [151] 	leaves	[Banskot, 2000c]
Quadrangularic acids L [152] 	leaves	[Banskota, 2000c]
Quadrangularic acids M [153] 	leaves	[Banskota, 2000c]

Table 2.3 (continued)

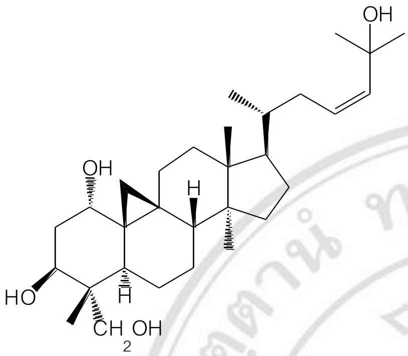
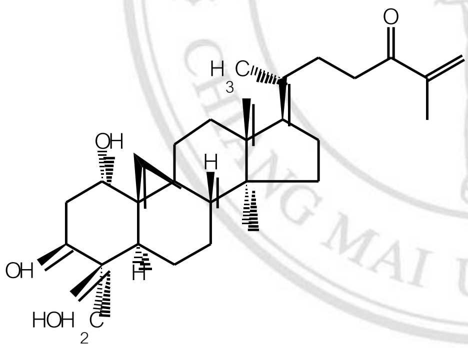
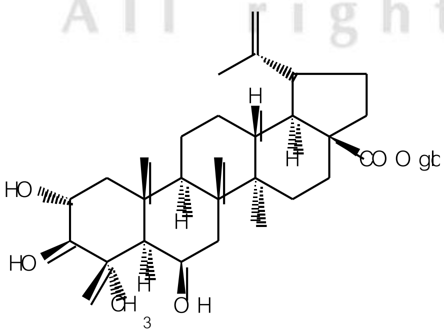
Plant and chemical compound	Plant part	Reference
Quadrangularols A [154] 	leaves	[Banskota, 2000b)]
Quadrangularols B [155] 	leaves	[Banskota, 2000a ; 2000b]
Quadranoside I [72] 	seeds	[Adnyana, 2000b]

Table 2.3 (continued)

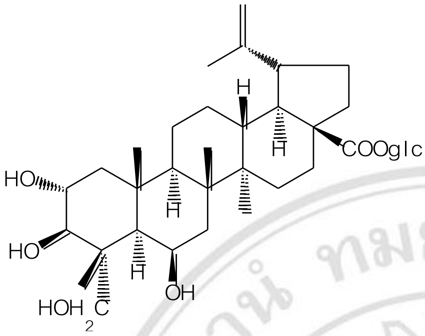
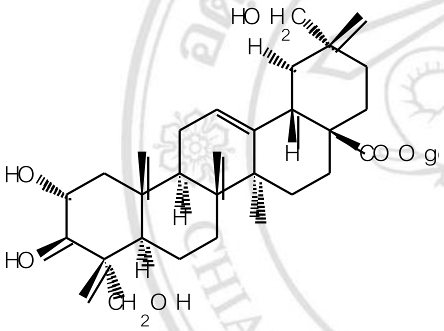
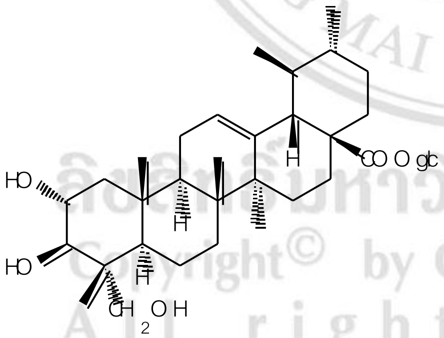
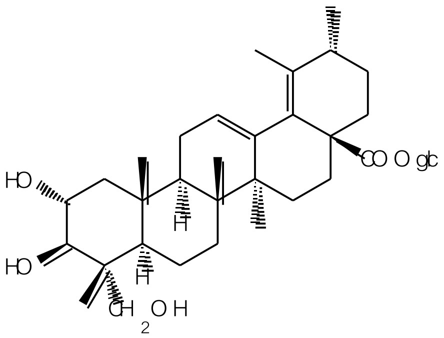
Plant and chemical compound	Plant part	Reference
Quadranoside II [156] 	seeds	[Adnyana, 2000b ; 2001b]
Quadranoside III [157] 	seeds	[Adnyana, 2000b]
Quadranoside IV [69] 	seeds	[Adnyana, 2000b ; 2001b]
Quadranoside V [158] 	seeds	[Adnyana, 2000b]

Table 2.3 (continued)

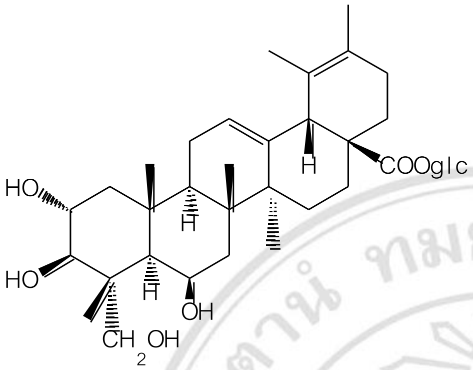
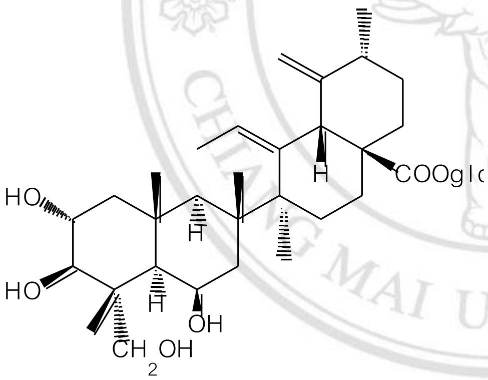
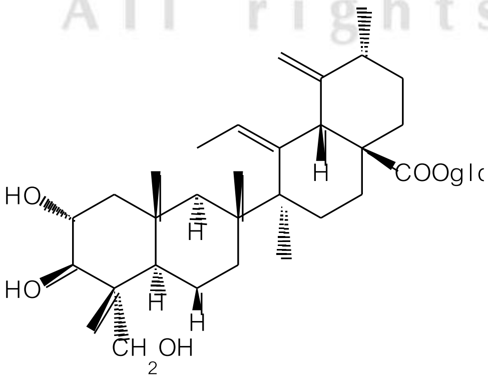
Plant and chemical compound	Plant part	Reference
Quadrannosides VI [159] 	seeds	[Adnyana, 2000a]
Quadrannosides VII [160] 	seeds	[Adnyana, 2000a]
Quadrannosides VIII [161] 	seeds	[Adnyana, 2000a]

Table 2.3 (continued)

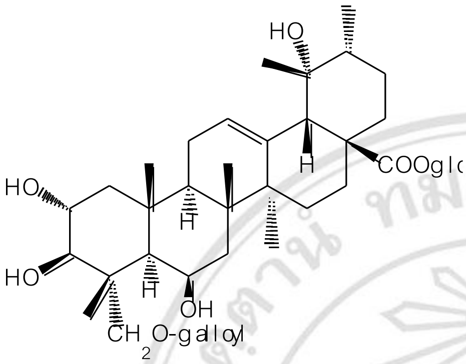
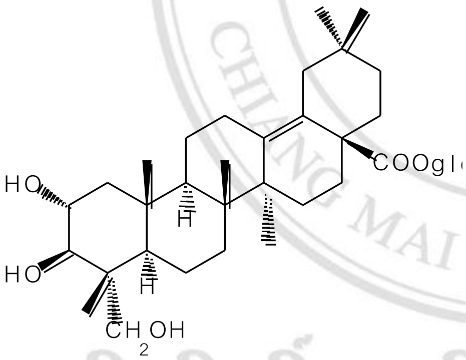
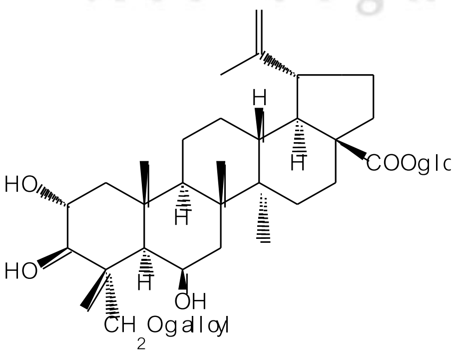
Plant and chemical compound	Plant part	Reference
Quadrannosides IX [162]	seeds	[Adnyana, 2000a]
		
Quadrannosides X [163]	seeds	[Adnyana, 2000a]
		
Quadrannosides XI [164]	seeds	[Adnyana, 2000a]
		

Table 2.3 (continued)

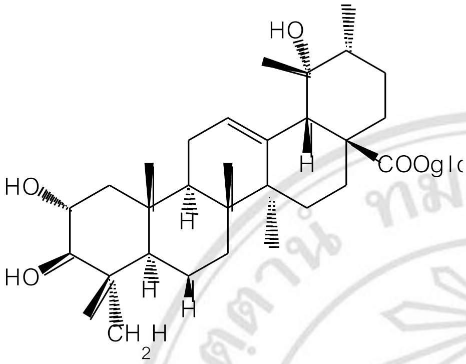
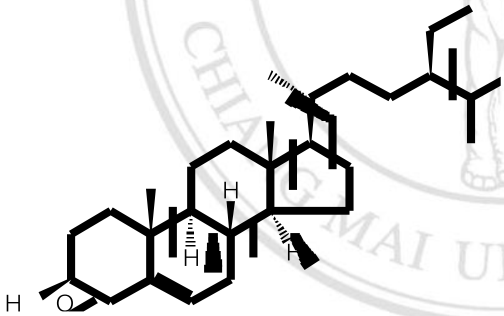
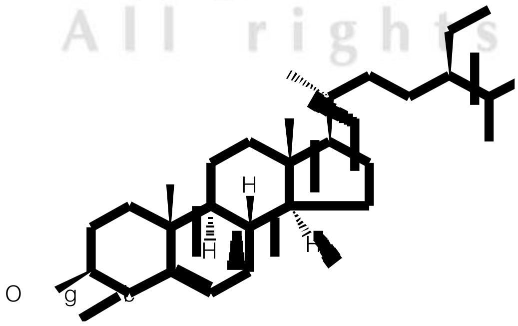
Plant and chemical compound	Plant part	Reference
Rosamutin [165] 	seeds	[Adnyana, 2000a]
β-Sitosterol [166] 	seeds leaves roots and seeds	[Adnyana, 2000b ; 2001b] [Banskota, 2000a] [Wungchinda, 1979]
β-Sitosterol glucoside [167] 	seeds leaves roots and seeds	[Adnyana, 2000b ; 2001b] [Banskota, 2000a] [Wungchinda, 1979]

Table 2.3 (continued)

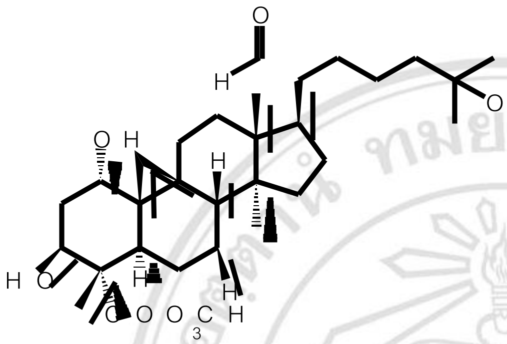
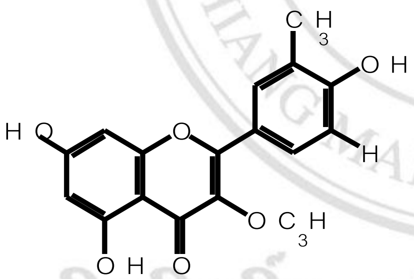
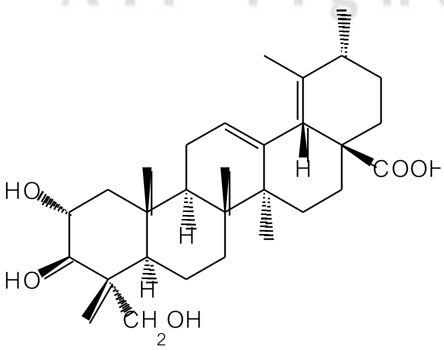
Plant and chemical compound	Plant part	Reference
(20*ξ*)-1*α*,3*β*-25-Trihydroxy-cycloart-21-al-23-ene-30-carboxylic acid methyl ester [168] 	leaves	[Ganzera, 1998]
5,7,4’-Trihydroxy-3,3’-dimethoxyflavone [169] 	leaves	[Banskota, 2000a]
2*α*,3*β*-23-Trihydroxyurs-12,18-dien-28-oic acid [170] 	seeds	[Adnyana, 2001b]

Table 2.3 (continued)

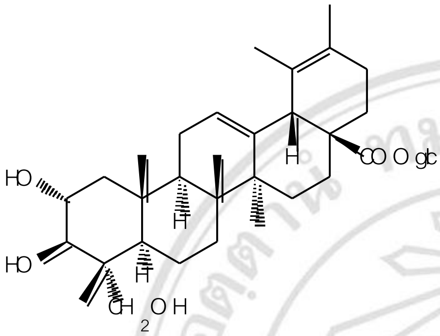
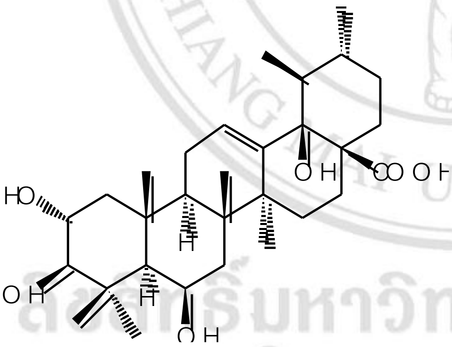
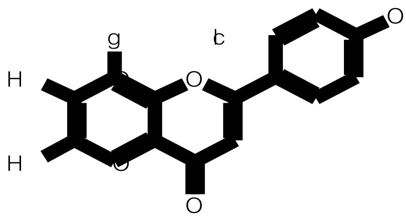
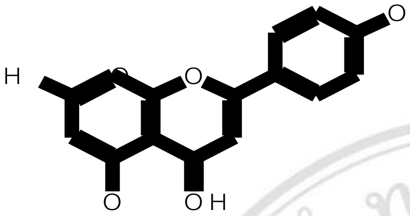
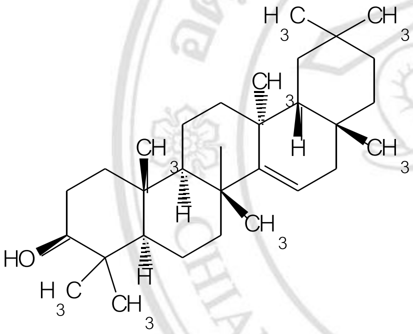
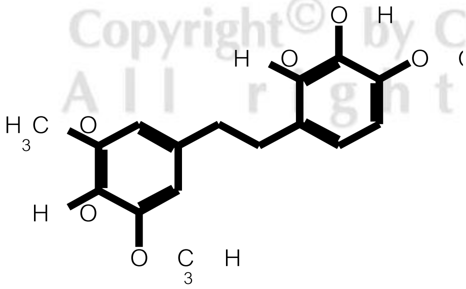
Plant and chemical compound	Plant part	Reference
2*α*,3*β*,23-Trihydroxyurs-12,19-dien-28-oic acid *β*-*D*-glucopyranosyl ester [171] 	seeds	[Adnyana, 2000b]
3*β*,6*β*,18*β*-Trihydroxy-urs-12-en-30-oic acid [172] 	seeds	[Banskota, 2003]
Vitexin [173] 	seeds	[Adnyana, 2000a]

Table 2.3 (continued)

Plant and chemical compound	Plant part	Reference
Combretum vendae A.E. van Wyk		
Apigenin [31] 	leaves	[Eloff, 2008]
Taraxerol [174] 	leaves	[Eloff, 2008]
Combretum woodii Dümmer		
Combretastatin B5 [175] 	leaves	[Eloff, 2005b ; 2008]

2.5 Biological activities of the Genus *Combretum*

In contrast to the enormous amount of phytochemical works, were known about the biological activities of extracts and pure compounds of genus *Combretum*.

In 1979, Wungchinda reported the chemical constituents of *Combretum quadrangulare* Kurz that found the crude ethanolic extract from seeds possess antimicrobial activity, which was most effective in inhibiting *Shigella dysenteriae* and *Pseudumonas aeruginosa* respectively, but was not effective against *Bacillus subtilis*, *Escherichia coli* and *Salmonella typhi*. Then Banskota *et al*. [1998 ; 2000a ; 2000c] and Adnyana *et al*. [2000a ; 2000b ; 2000c ; 2001b] found that the seeds and leaves extract of *C. quadrangulare* Kurz showed strong cell proliferative activity against murine colon 26-L5 carcinoma cells and cytotoxicity, and also showed significant hepatoprotective effect on *D*-galactosamine or tumor necrosis factor alpha-induced cell death in primary cultured mouse hepatocytes in a concentration-dependent manner due to the presence of phenolic constituents, triterpene glucosides and triterpene saponins. And Nantachit *et al*. [2006] found crude methanolic extract of the seeds of *C. quadrangulare* Kurz, and the purified samples from column chromatography and from PTLC showed antibacterial activity against gram-positive cocci and non-fermentative gram-negative bacilli better than the activity shown against fermentative gram-negative bacilli.

Pettit *et al*. [1986 ; 1987 ; 1995] found three 9, 10-dihydrophenanthrenes (6,7-dihydroxy-2,3,4-trimethoxy ; 7-hydroxy-2,3,4,6-tetramethoxy ; and 2,7-dihydroxy-3,4,6-trimethoxy) from *Combretum caffrum* (Eckl. & Zeyh.) Kuntze that inhibit (ED_{50} 2.20, 2.80 and 2.6 μg/ml) growth of the murine lymphocytic leukemia cell line. Then they found antineoplastic constituent (combretastatin [8]) from this plant to display significant (71-90% astrocyte reversal at 1-100 μg/ml dose levels) astrocyte reversal and murine P-388 lymphocytic leukemia (PS) cell growth inhibition (ED_{50} 0.01 μg/ml). Other prominent, albeit PS-inactive, constituents were found to be 3,3',4'-tri-*O*-meyhylellagic acid [23] and acacetin [5]. They also investigated more antineoplastic constituents from *C. caffrum* (Eckl. & Zeyh.) Kuntze, aseries of closely related bibenzyls, stilbenes and phenanthrenes. Some of the stilbenes proved to be potent antimitotic agents which inhibited both tubulin polymerization and the binding of colchicine to tubulin. And they found combretastatin A-4 [10], combretastatin A-5 [11] and combretastatin A-6 [12] inhibited growth of *Neisseria gonorrhoeae*. And Masika and Afolayan [2002] studied the antimicrobial activity of some plants used for the treatment of livestock disease in the Eastern Cape, South Africa. *C. caffrum* (Eckl. & Zeyh.) Kuntze was screened with water, methanolic, and acetonic bark extracts as well as decoctions of the three plants against 10 bacteria. They found antibacterial activity against all the gram-positive bacteria tested with the minimum inhibitory concentrations ranging from 0.10 to 0.50 mg/mL.

Martini and Eloff [1998] found that acetone extracts consisting of 14 different antimicrobial components in the ground leaves of *Combretum erythrophyllum* (Burch.) Sond., inhibited the growth of *Staphyllococcus aureus*. The lowest minimum inhibitory concentration of purification for *S. aureus* was 0.05 mg/mL, compared to the MIC values of 0.08 and 0.16 mg/mL for ampicillin and chloramphenicol. And Eloff [1999] studied the antibacterial activity of herbarium specimens of *C. erythrophyllum* (Burch.) Sond. growing in the Pretoria area by comparing those originally collected between 12 and 92 years ago to freshly collected leaves. He found that there were no differences in the minimal inhibitory concentration of the different samples with *S. aureus*, *E. faecalis*, *E. coli*, *P. aeruginosa* as test organisms. And Martini *et al*. [2004] isolated 7 antibacterial flavonoids of *C. erythrophyllum* (Burch.) Sond. leaves subsequently by bioassay-guided fractionation. These showed good activity against *Vibrio cholerae* and *Enterococcus faecalis*, with MIC values in the range of 25-50 μg/mL. Rhamnocitrin [40] and quercetin-5,3’-dimethylether [38] also inhibited *Micrococcus luteus* and *Shigella sonei* at 25 μg/mL. Also, Eloff *et al*. [2001] studied the stability and the relationship between anti-inflammatory activity and antibacterial properties of Southern African *Combretum* species. They found that extracts of 20 *Combretum* species growing under the same environmental conditions displayed anti-inflammatory activity with an average 65% inhibition of cyclooxygenase activity. The inhibition was remarkably stable, with a slight increase in average activity to 78% after storage for three months at room temperature. This was a fair to moderate correlation between total anti-inflammatory activity and total antibacterial activity of the same taxa studied earlier. Some *Combretum* species show antibacterial activity. There are at least 14 antibacterial compounds present in acetone extracts of *C. erythrophyllum* (Burch.)

Sond. leaves. All 27 taxa of the Combretaceae investigated yielded substantial antibacterial activity.

McGaw *et al*. [2000] screened for antibacterial, anthelmintic and anti-amoebic activities from *n*-hexane, ethanol and water extracts of *Combretum apiculatum* Sond. used by South African traditional healers for treating the stomachache. They evaluated antibacterial activity by using the disc-diffusion assay against several gram-positive and gram-negative species. Minimal inhibitory concentration values were determined with a microdilution assay. *C. apiculatum* Sond. showed the best activities with MIC < 200 μg/ml and could provide useful leads for the discovery of antibacterial compounds.

Smith *et al*. [2000] screened 8 plants from Belize for antibacterial activity. By using the influences of medium type, inoculum density, and a cold incubation, antimicrobial assay sensitivity was tested. The largest and most distinct zones were produced using nutrient agar and the $1/10^4$ inoculum density for *S. aureus* and *Proteus mirabilis* but a $1/10^{12}$ inoculum density for *P. aeruginosa* and *E. coli*. They found that *C. fruticosum* (Leofl.) Stuntz. showed activity against organisms tested.

Katerere *et al*. [2003] isolated 4 pentacyclic triterpenes from *Combretum imberbe* Engl. & Diels. leaves. Several of the compounds had antibacterial activity, and 1*α*,3*β*-hydroxyimberbic acid [51] showed particularly potent activity against *Mycobacterium fortuitum* and *S. aureus*.

Eloff *et al*. [2005a ; 2005b] isolated an antibacterial stilbene from *Combretum woodii* Dümmer (Combretaceae) leaves. Acetone extracts of this plant were separated by solvent-solvent partition into 6 fractions. The highest total activity was in the chloroform fraction, which contained mainly a compound active against *S. aureus*, and was identified as combretastatin B5 (2’,3’,4-trihydroxyl-3,5,4’-trimethoxybibenzyl) [175]. They also extracted *C. woodii* Dümmer with 10 different solvents (*n*-hexane, diisopropyl ether, diethyl ether, methylene dichloride, ethyl acetate, tetrahydrofuran, acetone, ethanol, methanol and water) to determine the best extractant for subsequent isolation and characterization of antibacterial compounds. The extracts (except the water extract) were bioactive, with at least one of them exhibiting minimum inhibitory concentration (MIC) values of 0.04 mg/mL against *S. aureus*, *P. aeruginosa*, *E. coli* or

E. faecalis. Ethyl acetate was the best extractant with an average MIC value of 0.08 mg/mL for 4 pathogens followed by acetone and methylene dichloride with values of 0.14 mg/mL. The average MIC values for the positive controls were 0.13 mg/mL (ampicillin) and 0.12 mg/mL (chloramphenicol).

Then Ahmed *et al*. [2004] isolated two new lanosteriod type triterpenes from the aerial parts of *Combretum molle* R.Br. *ex* G. Don, were combretene-A [79] and combretene-B [80], and the other isolated compounds were mollic acid [24], 3α-*L*-arabinoside, 3β-*D*-xyloside and 3β-*D*-glucoside. Geyid *et al*. [2005] screened some medicinal plants of Ethiopia for their antimicrobial properties and chemical profiles. They found that the extracts belonging to 44 species (66%) exhibited activity against one or more bacterial strains. The alcoholic (methanolic/ethanolic) extracts showed higher antibacterial effects than the corresponding petroleum ether and aqueous extracts. Twenty three species inhibited or regarded growth of one or more organisms at dilution as low as 250 µg/mL. The most potent of these was *C. molle* R.Br. *ex* G. Don, which showed activity against 2 organisms (*Bacillus cereus* and *N. gonorrhoea*). Steenkamp *et al*. [2007] screened antibacterial activity from crude methanol and water extracts of 36 plants, employed in the treatment of diseases of probable bacterial etiology by the Venda people. They found that *C. molle* R.Br. *ex* G. Don showed the most active and presented MIC values $\leq$ 1.00 mg/ml. And Mamidou Kone *et al*. [2007] studied the activity of 20 crude ethanol extracts from 17 plants of Northern Cote d' Ivoire was evaluated in vitro against *Streptococcus pneumoniae*. The results demonstrated a link between the usage of some of those plants in traditional healing and the effect of their antipneumococcal activity. Active plants, such as *C. molle* R.Br. *ex* G. Don, were reported by healers to show a curative effect on pneumonia, an infection often caused by *S. pneumoniae*. After that, Gronhaug *et al*. [2008] surveyed the ethnopharmacology of 6 medicinal plants from Mali, West-Africa. One of these plants is *C. molle* R.Br. *ex* G. Don, which was used as a remedy to cure several diseases such as malaria, diarrhoea, yellow fever, and bronchial affections. *C. molle* R.Br. *ex* G. Don was used in wound healing procedures in the Bamako region of Mali. Some studies have been performed on the biological activities of *C. molle* R.Br. *ex* G. Don, which include analgesic, anti-inflammatory and antiprotozoal activity, along with cardiovascular effects. Ojewole [2008] studied the *C. molle* R.Br. *ex* G. Don leaf extractive (mollic acid glucoside, a 1α-hydroxycycloartenoid) possesses analgesic and anti-inflammatory properties, and thus lend pharmacological credence to the folkoric, ethanomedical uses of the plant's leaf in the management, control and/or treatment of painful, arthritic and other inflammatory conditions in some rural communities of southern African. And Yeo *et al*. [2012] showed the aqueous leaf extract of *C. molle* R.Br. *ex* G. Don is moderately toxic when given intraperitoneally.

Karou *et al*. [2005] screened polyphenols from 4 medicinal plants of Burkina Faso include, *Combretum micranthum* G. Don leaves for their antioxidant and antimicrobial activities against pathogenic bacteria. Some microorganirms were susceptible to polyphenol extracts with minimal bactericidal concentration values between 20 and 2,000 μg/mL, while other microorganisms appeared to be resistant to the extracts. In 2012, Udoh *et al*. found the methanolic and aqueous of leaves, root bark and stem bark extracts of *C. micranthum* G. Don exhibited antimicrobial activities against both gram-negative and gram-positive isolated including *P. aeruginosa* and *S. aureus*. And in the same year, Akeem *et al*. found ethanolic extract of the stem bark of *C. micranthum* G. Don exhibited potent antimicrobial activities against two gram-positive organisms (*S. aureus* and *B. subtilis*) and two gram-negative organisms (*E. coli* and *P. aeruginosa*). Then Osonwa *et al*. [2012] showed phytochemical analyses on the aqueous extract of the fresh leaves. The absence of alkaloids, anthraquinones and flavonoids, saponins (cardiac glycosides and steroids) were present in moderate amounts and there was abundance of tannins. The extract had similar effect on both *S. aureus* and *E. coli* cultures but activity was very low with *B. subtilis*. When *S. aureus* activity increased with time of storage up to 48 h. The activity of *E. coli* continued to increase with time. It appears reasonable to store the extract for at least 48 h before the use for enhanced activity.

Pietrovski *et al*. [2006] examined the antinociceptive effects of the methanolic extract and of the triterpene, $3\beta,6\beta,16\beta$-trihidroxilup-20(29)-ene [74] obtained from the flowers of *Combretum leprosum* Mart. in chemical and thermal behavioural models of pain in mice. The study provide convincing evidence that ethanolic extract exert a rapid onset, relatively long-lasting and pronounced systemic antinociception in chemical (acetic acid-, formalin-, capsaicin- and glutamate-induced pain) and thermal (hot-plate at 50°C) models of nociception in the mouse at a dose that dose not interfere with the motor performance.

Angeh *et al*. [2007] found the dichloromethane extract of *Combretum padoides* Engl. & Diels leaves was subjected to antibacterial activity guided fractionation against *S. aureus* to afford a new oleanene-type triterpenoid glycoside identified as $1\alpha,23\beta$-dihydroxy-12-oleanen-29-oic-acid-23β-*O*-α-4-acetylrhamnopyranoside [84], along with known compounds 1,22-dihydroxy-12-oleanen-30-oic acid [83]. Compounds [83] and [84] had a reasonable antibacterial activity (MIC of 0.03 and 0.06 mg/mL) against *S. aureus* and *E. coli*.

Eldeen and van Staden [2007] screened extracts from 7 tree species used in Sudanese traditional medicine for antibacterial activity, by using micro-dilution assay. The extracts were tested against gram-positive: *B. subtilis* and *S. aureus* and gram-negative: *E. coli* and *Klebsiella pneumoniae.* Of the plant extracts investigated, 75% showed MIC values less than or around 1.50 mg/mL. Extracts obtained from *Combretum hartmannianum* Schweinf. (ethanolic leaf and root extracts), inhibited bacterial growth of both gram-positive and gram-negative bacteria at concentration less than or around 0.39 mg/mL.

Maregesi *et al*. [2007] surveyed the ethnopharmacology of 6 villages in the Bunda district, Mara Region, Tanzania, where the use of plants still has special meaning to the society in the treatment of various diseases. Information was obtained from traditional healers and other experienced persons having some knowledge on medicinal plants. Fifty-two plants were reported for use in the treatment of various infectious diseases. The Combretaceae is a large family with at least 600 species, and its commonly occurring genera, *Terminalia* and *Combretum*, with 250 species each are widely used in African traditional medicine. Previous studies had confirmed antimicrobial activity from extracts or isolated compounds of some species belonging to this family, such as *Combretum adenogonium* Steud *ex* A. Rich. The leaves, stem bark and roots were noted as common medicinal plants in the studied area, which is in the evergreens of the Savannah grassland. In 2012, Mushi *et al*. found root, stem bark and leaf aqueous ethanolic extracts from *C. adenogonium* exhibited antibacterial activity to at least one of the test bacteria with MIC values ranging from 0.31-5.00 mg/ml. And root and stem bark extracts exhibited anti-HIV-1 PR activity with IC_{50} values of 24.70 and 26.50 μg/ml, respectively. Stem bark and leaf extracts showed mild toxicity with LC_{50} values of 65.77 μg/ml and 76.96 μg/ml, respectively, whereas roots were relatively non-toxic (LC_{50} = 110.04 μg/ml).

Bisoli *et al*. [2008] isolated two new triterpene glucosides, β-*D*-glucopyranosyl-2α,3β,24-trihydroxyolean-12-en-28-oate [62] and β-*D*-glucopyranosyl-2α,3β,23,24-tetrahydroxyurs-12-en-28-oate [70], in addition to nine known compounds belonging to three different triterpene classes (oleanane-, ursane- and lupane-type) from the stem of a specimen of *Combretum laxum* growing in the Pantanal of the central-western region of Brazil. Their *in vitro* antifungal activities against standard strains of *Candida albicans*, *Candida krusei* and *Cryptococcus neoformans* were also evaluated.

Odda *et al*. [2008] found the crude extract of *Combretum collinum* Fresen effective against IV instar larvae of *Aedes aegypti* and its larvicidal activity is located in the shoot bark.

Rahman *et al*. [2008] studied the antibacterial activity of methanol extracts of 17 plant species of Bangladesh, evaluated by the agar disc diffusion method. *Combretum glandifolium* extract exhibited potent antimicrobial activity against *E. coli*, *P. aeruginosa* and *Vibrio mimicus* at a concentration of 400 μg/disc.

Sini *et al*. [2008] showed the water extract of *Combretum sericeum* G. Don roots may be active against diarrhea and this may be the basis for its use traditionally for gastrointestinal disorders.

Coulidiati *et al*. [2009] studied the acetone extract and various fractions from leaf acetone extract of *Combretum nioroense* Aubrev. *ex* keay, which showed antioxidant and antibacterial activities at different levels. The extracts had shown effectiveness against microorganisms responsible of infectious diseases, thus justifying the successful use of *C. nioroense* Aubrev. *ex* keay for the treatment of diarrhea and dysenteries in traditional medicine.

In 2011, Gouveia *et al*. assessed the antioxidant, antinociceptive and anti-inflammatory activities of the ethanolic extract from leaves of *Combretum duarteanum* Cambess. in rodents through *in vitro* test. *C. duarteanum* Cambess. leaf ethanolic extract possesses a strong antioxidant potential according to the thiobarbituric acid reactive species, nitric oxide and hydroxyl radical-scavenging assays; it also presented scavenger activity in all *in vitro* tests. After intraperitoneal injection, ethanolic extract from leaves of *C. duarteanum* Cambess. significantly reduced the number of writhes in a writhing test and the number of paw licks during phase 1 and phase 2 of a formalin test. Ethanolic extract from leaves of *C. duarteanum* Cambess. exhibited an anti-inflammatory activity in the carrageenin test, which was based on interference with prostaglandin synthesis.

Kanwal and Karim [2011] reported that *Combretum* genus has many valuable plants, which can help the humanity suffering from microbial diseases. The scientific investigation of *Combretum pincianum* Hook provides a basic support to promote its use in antibacterial drug formation. They said, its extracts could inhibit the bacterial growth at different concentration depending upon the bacterium tested. And its extracts have tannins, saponins and alkaloids, which might be responsible for its antibacterial properties. Then Adejuwon *et al*. [2011] found the cold extraction of *C. pincianum* Hook powdered dry leaves in a mixture of methanol and water (3:2) was inhibition of growth of *Bacillus anthracis*, *Bacillus cereus*, *Clostridium sporogenes*, *E. coli*, *K. pneumonia*, *P. aeruginosa*, *Pseudomonas flurescens*, *Staphylococcus epidermidis* and *Streptococcus faecalis*.

Moosophon *et al*. [2011] isolated 3 new diarylpropanes, a new arylpropyl quinine and one known compound from a methanolic extract of stem of *Combretum grifftii* Van Heur & M. A. The compounds showed cytotoxicity against one or more cancer cell line and one known compound : 1-(2-hydroxy-4-methoxyphenyl)-3-(4-hydroxy-3-methoxyphenyl)propane [48] exhibited activity against *Mycobacterium tuberculosis* with MIC value = 3.13 µg/mL.

Bhatnagar *et al*. [2012] studied phytochemical analysis of *Combretum roxburghii* Spreng. Leaf and bark samples revealed presence of tannins, saponins and flavonoids. Acetone extracts of leaf showed 100 percent cytotoxic activity and was also rich in antioxidant properties, so same was fractionated and a pure antioxidant fraction was isolated which showed good antioxidant activity and moderate amount of cytotoxic activity in live cell assay using Jurkat cells (tumor cell line).

Yahaya *et al*. [2012] determined the antibacterial effects of *C. glutinosum* Perr. *ex* DC. extract on some clinically isolated bacteria species (*S. typhi*, *P. aeruginosa*, *S. aureus* and *E. coli*.).

Dechandt *et al*. [2013] evaluated the antidiabetic activity of the *Combretum lanceolatum* Pohl ex Eichler, Combretaceae, flowers extract in diabetic rats. The antihyperglycemic effect of this extract was similar to that of metformin and appears to be through inhibition of gluconeogenesis, since urinary urea was reduced and skeletal muscle mass was increased. These data indicate that antidiabetic activity of the *Combretum lanceolatum* Pohl ex Eichler extract could be mediated, at least in part, through activation of adenosine monophosphate-activated protein kinase by quercetin.

And Sahu *et al*. [2014] studies synergistic activity of the combination of crude leaf extract of *Combretum albidum* G. Don with ceftriaxone against MDR *P. aeruginosa*. And the leaf extract was non-toxic to human lymphocytes.

Furthermore, Eloff *et al*. [2001] found Combretaceae extracts have high anti-inflammatory activity and the compounds responsible for this property are apparently relatively stable. These plants include *Combretum nelsonii* Dümmer, *Combretum petrophilum* Retief, *Combretum mossambicense* (Klotzsch) Engl., *C. apiculatum* subsp. apiculatum and *Combretum hereroense* Schinz for anti-inflammatory activity, and *C. molle* R.Br. *ex* G. Don, *C. petrophilum* Retief, *Combretum moggii* Exell, *C. erythrophyllum* (Burch.) Sond. and *C. padoides* Engl. & Diels for antibacterial properties.

Fyhrquist *et al*. [2002] investigated ethnobotanical on the medicinal uses of some species of *Terminalia* and *Combretum*, which was carried out in Mbeya, Tanzania during a 5-weeks field expedition. Of the 16 species collected, *Combretum fragrans* F. Hoffm., *Combretum molle* R.Br. *ex* G. Don, *Combretum psidioides* Welw., *Combretum zeyheri* Sond., *Terminalia kaiserana* F. Hoffm. and *Terminalia sericea* Burch *ex* DC can be used as medical applications against various bacterial infections such as gonorrhoea, syphilis, symptoms like diarrhea, hypertension and even cancer. Antimicrobial screenings of the crude extracts of methanolic extracts of the roots of *C. fragrans* F. Hoffm. and *C. padoides* Engl. & Diels showed inhibition against gram-positive bacteria and were also good inhibitors of *Enterobacter aerogenes.*

Inngjerdingen *et al*. [2004] studied 73 species belonging to 34 plant families, such as *Combretum ghasalense* Engl. & Diels, *Combretum glutinosum* Perr. *ex* DC. And *Combretum micranthum* G. Don, that were used as wound healing remedies in Dogonland, Mali, West Africa. Plants used for the treatment of wounds also showed different properties like anti-inflammatory, anti-microbial, healing, analgesic, haemostatic and immuno-modulating activities.

Elegami *et al*. [2007] investigated a total of 48 extracts belonging to 4 Sudanese medicinal plant species from genus *Combretum* (namely : *Combretum adenogonium* Steud *ex* A. Rich., *Combretum glutinosum* Perr. *ex* DC., *Combretum aculeatum* Vent. and *Combretum sp. Aff. obovatum*) for their antibacterial activity against 2 gram-positive (*S. aureus* and *B. subtilis*) and 3 gram-negative (*E. coli* and *P. aeruginosa*) standard bacterial organisms.

Masoko and Eloff [2007] found the acetone and metanolic extracts leaves of twenty-four south African *Combretum* and six *Terminalia* species displayed the presence of antioxidant activity after spraying the chromatogram with DPPH.

Mangoyi *et al*. [2012] studied the *in vitro* antifungal activities of six *Combretum* species (*C. zeyheri* Sond., *C. apiculatum* Sond., *C. molle* R.Br. *ex* G. Don, *C. kraussii* Hochst., *Combretum elaegnoides* and *C. imberbe* Engl. & Diels.) were investigated against *C. albicans* and *C. krusei* using agar disc diffusion. All extracts from the *Combretum* species showed antifungal activity and had MIC values ranging from 0.31-0.63 mg/ml for both *Candida* species. *C. zeyheri* Sond. extract had the highest antifungal activity in all case with MIC values of 0.08-0.16 mg/ml.

And Ahmed *et al*. [2014] obtained phenolic-enriched leaf extracts of *Combretum bracteosum* (Hochst.) Brandis ex Engl., *C. padoides* Engl. & Diels, *C. vendae* A.E. van

Wyk and *C. woodii* Dümmer by extracting with a mixture of 70% acetone acidified with 1% HCl and *n*-hexane. Some of fraction had much higher antioxidant activity than the positive control. The everage EC_{50} values of the extracts for the DPPH and ABTS antioxidant assays were 0.21-12.00, 0.25-16.00, 0.33-9.41 and 4.97-85.00 μg/ml, respectively, while the mean EC_{50} values for the positive control ascorbic acid and Trolox were 1.28-1.51 and 1.02-1.19 μg/ml, respectively. All crude extracts inhibited lipid peroxidation of linoleic acid by more than 80% at a concentration of 64 μg/ml. *C. padoides* Engl. & Diels had the highest antibacterial activity with MIC ranging between 19-2500 μg/ml, followed by *C. vendae* A.E. van Wyk with MIC ranging between 39-625 μg/ml ; *C. woodii* Dümmer and *C. bracteosum* (Hochst.) Brandis ex Engl. had similar MIC ranging between 39-2500 μg/ml. *C. padoides* Engl. & Diels had the highest antifungal activity with MIC ranging between 19-625 μg/ml. *C. woodii* Dümmer and *C. vendae* A.E. van Wyk ranged from 19 to 1250 μg/ml. And *C. bracteosum* (Hochst.) Brandis ex Engl. had the lowest antifungal activity with MIC ranged from 139 to 625 μg/ml.