CHAPTER 1

INTRODUCTION

1.1 Introduction

Cerbera odollam Gaertner, a mangrove plant belonging to the Apocynaceae family, is distributed widely in the coastal areas of Southeast Asia and countries surrounding the Indian Ocean. The family Apocynaceae contain about 155 genera and 1700 species. In Thailand only 42 genera and 155 species are found, from *Cerbera* genera only 2 species are found, *C. odollam* and *C. manghas* (The Forest Herbarium, Royal Forest Department, 1999). *C. odollam* was found in Bangkok, Ranong, Surat Thani, Phangga, Krabi, Satun and Narathiwat while *C. manghas* was found in Prachuap Khiri Khan, Chonburi, Rayong, Phuket, Songkhla, Satun and Narathiwat.

Cerbera odollam is a tree, 12 m high. Leave: petiole 1.6-3.8 cm long; blade papery to coriaceous, obovate, 8.9-26 x 2.4-5.7 cm, apex acuminate, base cuneate; secondary veins 12-25 pairs anastomosing into an intramaginal nerve; globrous. Inflorescence few to many flowered, robust, lax; 8.8-35 cm long; glabrous; pedicels 1.2-4 cm long. Sepals linear, lanceolate or oblanceolate, 8.6-26 x 2.6-5 mm, apex acute or acuminate; glabrous. Corolla white with a yellow eye (in Thailand); tube 1.3-2.2 cm long, bulging in middle; lobes 1.2-3.8 cm long; glabrous outside, pubescent in upper half of tube inside. Stamens inserted around middle of corolla tube; anthers 2.2-2.4 x 1.3-1.5 mm. Ovary 1.2-1.7 mm long; style + pistil head 9.1-12 mm long. Fruit spherical to ovoid; green when mature; 4.7-7.7 cm long; 3.7-6.6 cm diameter.

In Thailand, *C. odollam* has various local names: tinpet thale (ตีนเป็ดทะเล) (Central), tinpet num (ตีนเป็ดน้ำ), tinpet (ตีนเป็ด), sang la (สั่งลา) (Krabi).

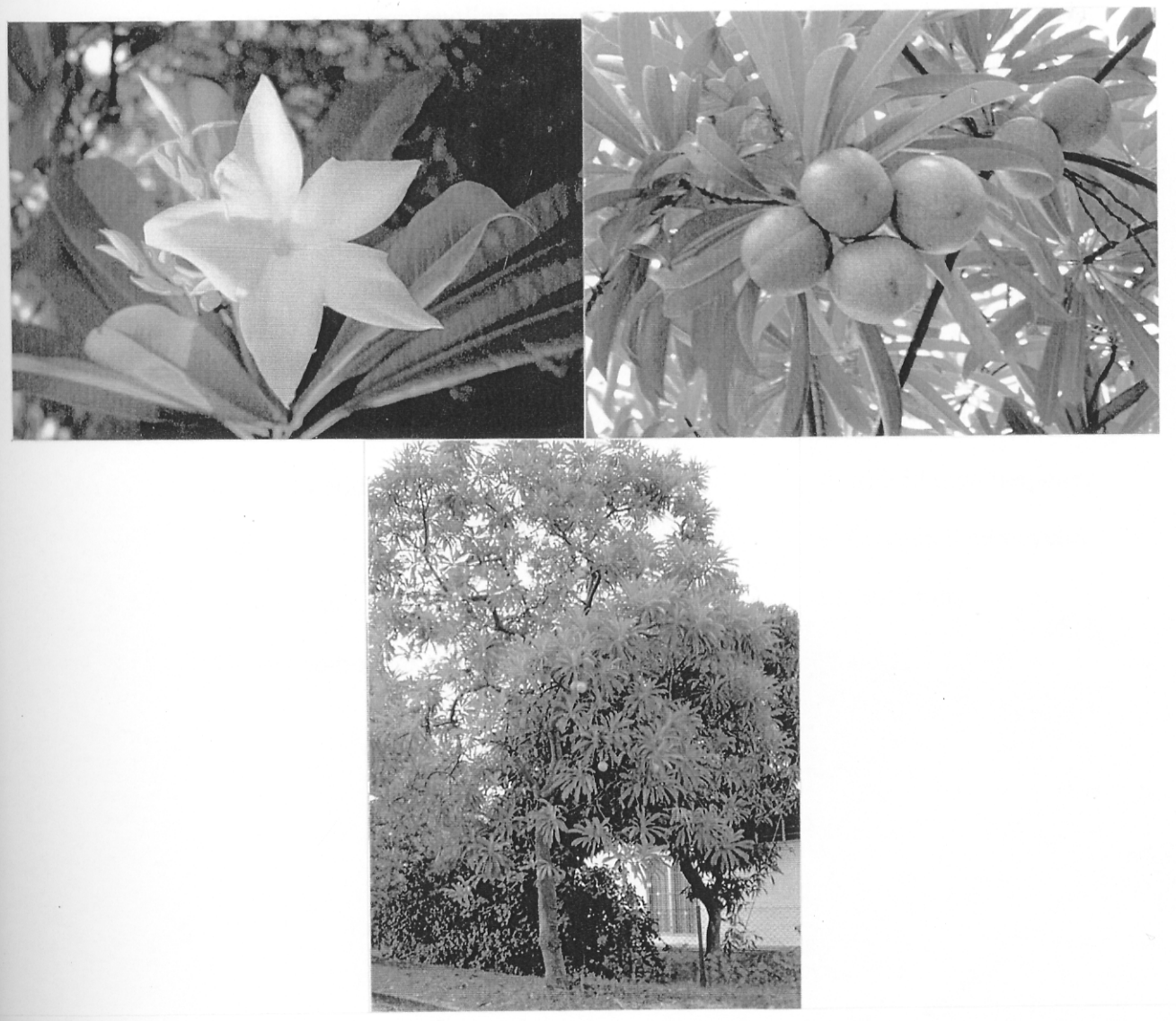


Figure 1. *Cerbera odollam* (Apocynaceae)

1.2 Review of Literatures

Plants in the *Cerbera* genus (Apocynaceae) are well known to be rich in a variety of compounds: cardenolide glycosides (Abe, *et.al.*, 1977; Yamauchi, 1987); lignan (Abe, *et.al.*, 1988; 1989); iridoid monoterpenes (Abe, *et.al.*, 1977; Yamauchi, *et.al.*,1990) normonoterpene glycosides (Abe, *et.al.*, 1988; 1996) and dinormonoterpeniod glycosides (Abe, *et.al.*, 1996) etc.

Information from NAPRALERT database developed by University of Illinois at Chicago reveal several types of compounds present in plants of *Cerbera* genus and they can be classified into groups as follows:

1. Alkanes	2. Benzenoids	3. Carbohydrates
4. Cardenolides	5. Flavonols	6. Iridoid monoterpenes
7. Lignans	8. Monoterpenes	9. Oxygen heterocycles
10. Steroids	11. Triterpenes	12. Vitamins

These compounds are presented in **Table 1**.

Table 1 Compounds from plants of *Cerbera* genus

1 = Alkanes **2** = Benzenoids **3** = Carbohydrates

4 = Cardenolides **5** = Flavonols **6** = Iridoid monoterpenes

7 = Lignans **8** = Monoterpenes **9** = Oxygen heterocycles

10 = Steroids **11** = Triterpenes **12** = Vitamins

Scientific name	**Investigated Part**	**Compound**	**Bibliography**
C. dilatata	Kernels	Cerberin, **4l** Cerbertin, **4ae** Neriifolin, **4a**	Mahmoud, *et.al.*, 1979
	Seeds	Cerbertin, **4ae** Deacetyl cerbertin, **4ad** Neriifolin, **4a**	Cable, *et.al.*, 1964
C. floribunda	Kernels	Cerbertin, **4ae** Neriifolin, **4a** Deacetyl cerbertin, **4ad**	Mahmoud, *et.al.*, 1979 Cable, *et.al.*, 1964 Mahmoud, *et.al.*, 1979
	Seeds	Cerberin, **4l** Cerbertin, **4ae**	Mahmoud, *et.al.*, 1979 Cable, *et.al.*, 1964
C. manghas	Seeds Flowers	Deacetyl cerbertin, **4ad** Cerberin, **4l**	Cable, *et.al.*, 1964 Mahran, *et.al.*, 1972

Table 1 (Continued)

Scientific name	Investigated Part	Compound	Bibliography
C. manghas	Entire plants	Neriifolin, **4a**	Yen, *et.al.*, 1974
	Fruits	Theviridoside, **6f**	Inouye, *et.al.*, 1972
		Theviside, **6e**	
	Kernels	Cerberin, **4l**	Rao, *et.al.*, 1976
		Cerberin, **4l**	Chen, *et.al.*, 1942
		Sucrose, **3c**	
		Thevetin, **4m, 4n**	Mahmoud, *et.al.*, 1979
		Thevetin B, **4m**	Li, *et.al.*, 1981
	Leaves	2-Hydroxy-6-methoxy benzoic acid, **2a**	Danie, *et.al.*, 1978
		Bornesitol, **3a**	Mahmoud, *et.al.*, 1979
		Bornesitol, L:(+), **3b**	Sakushima, *et.al.*, 1976
		Cerbera manghas olivil dimer 5, **7s**	Abe, *et.al.*, 1988
		Cerbera manghas olivil dimer 6, **7t**	Abe, *et.al.*, 1988
		Cerbera manghas olivil dimer 7, **7u**	
		Cerberalignan A, **7a**	

Table 1 (Continued)

Scientific name	Investigated Part	Compound	Bibliography
C. manghas	Leaves	Cerberalignan B, **7c**	
		Cerberalignan C, **7e**	Abe, *et.al.*, 1988
		Cerberalignan D, **7g**	
		Cerberalignan E, **7h**	
		Cerberalignan F, **7i**	
		Cerberalignan G, 7**j**	
		Cerberalignan H, **7b**	
		Cerberalignan I, **7k**	
		Cerberalignan J, **7m**	Abe, *et.al.*, 1989
		Cerberalignan K, 7**n**	
		Cerberalignan L, 7**o**	
		Cerberalignan M, **7f**	
		Cerberalignan N, **7d**	
		Cerberidol, **7a**	
		Epoxy cerberidol, **8d**	
		Cerberidol, epoxy: 3-*O*-*β*-D-allopyranoside, **8e**	Abe, *et.al.*, 1989
		Epoxy cerberidol -3-*O*- *β* -D-glucoside, **8f**	Abe, *et.al.*, 1996
		Cerberidol-3-10-bis-*O*-*β*-D-allopyranoside, **8c**	Abe, *et.al.*, 1989
		Cerberin, **4l**	Mahran, *et.al.*, 1972

Table 1 (Continued)

Scientific name	Investigated Part	Compound	Bibliography
C.manghas		Cerleaside B, **4s**	
		Cyclocerberidol, **8g**	Abe, *et.al.*, 1989
		Cyclocerberidol-3-*O*-β-D-allopyranoside, **8h**	
		Cyclocerberidol-3-*O*-β-D-glucoside, **8i**	Abe, *et.al.*, 1996
		Digitoxigenin β-D-gentiobiosyl-(1-4)-alpha-L-thevetoside, **4u**	Yamauchi, *et.al.*, 1987
		Digitoxigenin β-D-gentiotriosyl-(1-4)-α-L-thevetoside, **4v**	
		17α-Digitoxigenin β-D-gluco-3-ulosyl- (1-4)-alpha-L- thevetoside, **4t**	Yamauchi, *et.al.*, 1987
		17β-Digitoxigenin β-D-glucosyl-(1-4)- α-L-thevetoside, **4w**	
		10-Dehydro geniposide, **6j**	Yamauchi, *et.al.*, 1990
		Kaempferol, **5a**	Daniel, *et.al.*, 1978

Table 1 (Continued)

Scientific name	Investigated Part	Compound	Bibliography
C. manghas	Leaves	Loganin, **6h**	Yamauchi, *et.al.*, 1990
		10-carboxy Loganin, **6i**	Yamauchi, *et.al.*, 1996
		Olivil-4-*O*-beta-D-glucopyranoside, **7p**	Abe, *et,al.* 1988
		Olivil-4′-*O*-beta-D-glucopyranoside, **7q**	
		(Z)-3-Isopropyl-3-penten-1,5-diol-1-*O*-β-D-glucoside, **8m**	Abe, *et,al.* 1996
		3-(Hydroxyisopropyl) -pentane-1-ol-*O*-β-D-glucoside, **8k**	Abe, *et,al.* 1996
		3-(Hydroxyisopropyl)-pentane-1,4-diol-*O*-β-D-glucoside, **8j**	
		(3ξ,4ξ)-3-Isopropyl-3,4-epoxypentane-1,5-diol-1-*O*-β-D-glucoside, **8l**	Abe, *et,al.* 1996
		Quercetin, **5b**	Daniel, *et.al.*, 1973

Table 1 (Continued)

Scientific name	Investigated Part	Compound	Bibliography
C. manghas	Leaves	Rutin, **5c**	Sakushima, *et.al.*, 1976
		Succinic acid, **1**	Sakushima, *et.al.*, 1976
		Succinic acid, **1**	Mahmoud, *et.al.*, 1979
		Syringic acid, **2c**	Daniel, *et.al.*, 1978
		Tanghinigenin β-D-gentiobiosyl-(1-4)-α-L-theevetoside, **4z**	Yamauchi, *et.al.*, 1987
		Deacetyl tanghinigenin, **4o**	Yamauchi, *et.al.*, 1987
		Gentiobiosyl 17α-Deacetyl tanghinigenin, **4p**	
		Glucosyl 17α- Deacetyl tanghinigenin, **4q**	
		Glucosyl 17β- Deacetyl tanghinigenin, **1r**	
		Deacetyl tanghenin, **4e**	
		Theveside, **6e**	Yamauchi, *et.al.*, 1990

Table 1 (Continued)

Scientific name	Investigated Part	Compound	Bibliography
C. manghas	Leaves	Theveside, 10-*O*-benzoyl, **6g**	
		Theviridoside, **6f**	Inouye, *et.al.*, 1972
		Theviridoside, **6f**	Abe, *et.al.*, 1996
		Theviridoside, **6f**	Yamauchi, *et.al.*, 1990
		Theviridoside, **6f**	Mahmoud, *et.al.*, 1979
		Theviside, **6e**	Inouye, *et.al.*, 1972
		Theviside, **6e**	Mahmoud, *et.al.*, 1979
	Roots	Cerberin, **4l**	Mahran, *et.al.*, 1972
		Neriifolin, **4a**	Chang, *et.al.*, 2000
		Olivil, **7r**	Lee, *et.al.*, 1998
	Root barks	Cerberic acid, **6c**	Abe, *et.al.*, 1989
		Cerberic acid, **6c**	Mahmoud, *et.al.*, 1979
		Cerbinal, **6a**	Abe, *et.al.*, 1977

Table 1 (Continued)

Scientific name	Investigated Part	Compound	Bibliography
C. manghas	Root barks + Stem barks	Deacetyl tanghenin, **4e**	Mahmoud, *et.al.*, 1979
	Seeds	Fucosterol, **10c**	Riaensuwan, *et.al.*, 1979
		Cerberin, **4l**	Mahmoud, *et.al.*, 1979
		Cerdoloside, **4j**	Yamauchi, *et.al.*, 1987
		17α-Cerdoloside, **4k**	
		Cerleaside A, **4i**	
		Neriifolin, **4a**	Rangaswami, *et.al.*, 1957
		Neriifolin, **4a**	Abe, *et.al.*, 1977
		17α-Neriifolin, **4b**	Yamauchi, *et.al.*, 1987
		Neriifolin, **4a**	Rangaswami, *et.al.*, 1957
		Neriifolin, **4a**	Mahmoud, *et.al.*, 1972
		17β-Solanoside, **4c**	Yamauchi, *et.al.*, 1987
		17α-Solanoside, **4e**	

Table 1 (Continued)

Scientific name	Investigated Part	Compound	Bibliography
C. manghas	Seeds	β-Sitosterol, **10d**	Riaensuwan, *et.al.*, 1979
		Stigmast-7-en-3β-ol, **10f**	
		Stigmasterol, **10e**	
		17α-Deacetyl tanghenin, **4e**	Abe, *et.al.*, 1977
		Thevetin B, **4m**	Chen, *et.al.*, 1942
		Thevetin B, **4m**	Rao, *et.al.*, 1974
		Thevetin B, **4m**	Mahmoud, *et.al.*, 1979
		Thevetin B, **4m**	Abe, *et.al.*, 1977
		2′-*O*-Acetyl thevetin B **4n**	
		2′-*O*-Acetyl thevetin B **4n**	Mahmoud, *et.al.*, 1979
		α-Tocopherol, **9**	Daniel, *et.al.*, 1978
		Vitamin A, **12**	Riaensuwan, *et.al.*, 1979
	Stems	Cerapioside, **4aa**	Yamauchi, *et.al.*, 1987

Table 1 (Continued)

Scientific name	Investigated Part	Compound	Bibliography
C. manghas	Stems	17α-Digitoxigenin β-D-glucosyl-(1-4)- α-L-thevetoside, **4x**	
		Cerberoside B, **4s**	Mahran, *et.al.*, 1972
		(-)-Olivil, **7l**	Abe, *et,al.* 1988
		Thevetin B, **4m**	Yamauchi, *et.al.*, 1987
	Stem barks	3α-Amyrin acetate, **11**	Mahmoud, *et.al.*, 1979
		Cerberidol-3-*O*-β-D-allopyranoside, **8b**	Abe, *et.al.*, 1989
		Cerbinal, **6a**	Abe, *et.al.*, 1977
		17α-Digitoxigenin β-cellonbiosyl-(1-4)-α-L-thevetoside, **4ab**	Yamauchi, *et.al.*, 1987
		17α-Digitoxigenin β-gentiobiosyl-(1-4)-α-L-thevetoside, **4ac**	
	Stem barks	Stigmasterol, **10e**	Mahmoud, *et.al.*, 1979
	Stem woods	Cerberin, **4l**	Mahran, *et.al.*, 1972

Table 1 (Continued)

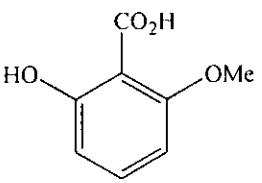
Scientific name	**Investigated Part**	**Compound**	**Bibliography**
C. odollam	Seeds	Thevetin B, **4m**	Rao, *et.al.*, 1974
C. tanghinia	Kernels	Tanghinin, **4h**	Mahmoud, *et.al.*, 1979
	Seeds	Tanghigenin, **4af** 17α-Tanghigenin, **4ag**	Cable, *et.al.*, 1964

Structures

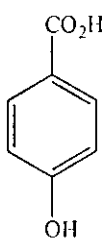
1. Alkane

$HOOCH_2CH_2COOH$ **1**: Succinic acid

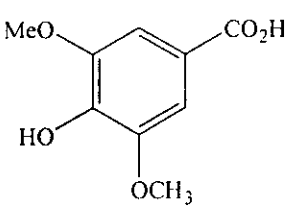
2. Benzenoids



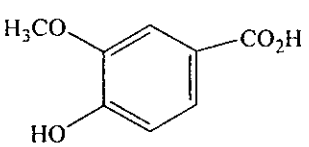
2a; 2-Hydroxy-6-methoxy benzoic acid



2b: 4-Hydroxy benzoic acid

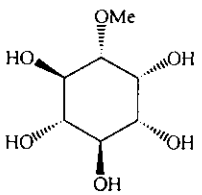


2c: Syringic acid

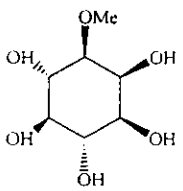


2d: Vanillic acid

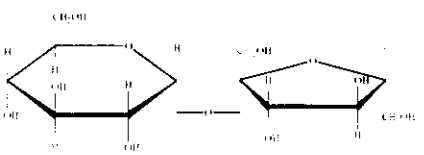
3. Carbohydrates



3a: (-)-Bornesitol

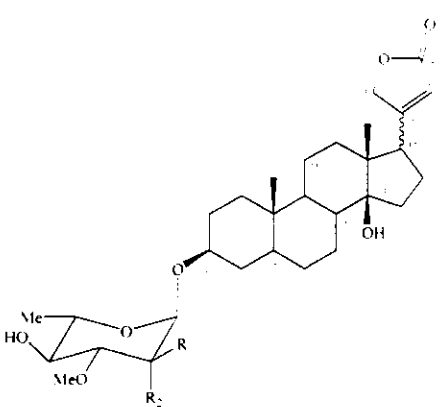


3b: (+)-Bornesitol



3c: Sucrose

4. Cardenolide glycosides

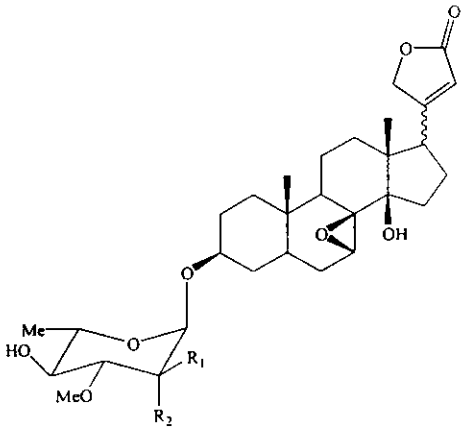


4a: R_1=OH, R_2=H; 17β-Neriifolin

4b: R_1=OH, R_2=H; 17α-Neriifolin

4c: R_1=H, R_2=OH; 17β-Solanoside

4d: R_1=H, R_2=OH; 17α-Solanoside



4e: R_1= OH, R_2= H;

17β-Deacetyltanghinin

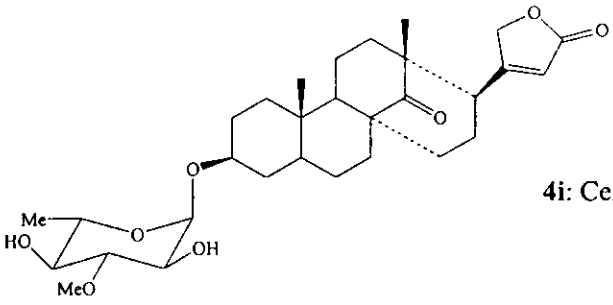
4f: R_1= OH, R_2= H;

17α-Deacetyltanghinin

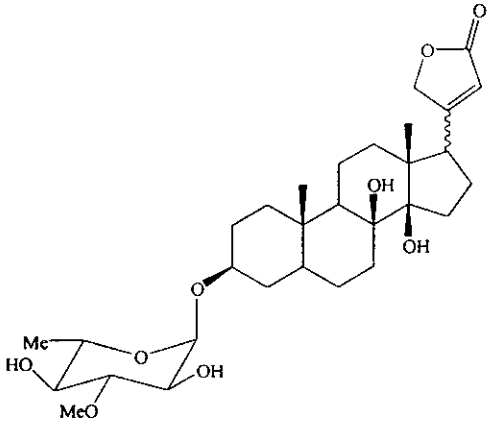
4g: R_1= H, R_2= OH;

17β-Tanghigenin α-L-acofriose

4h: R_1= OAc, R_2= H; Tanghinin

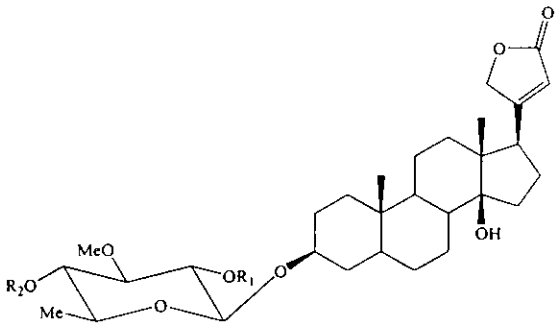


4i: Cerleaside A



4j: 17β-Cerdollaside

4k: 17α- Cerdollaside



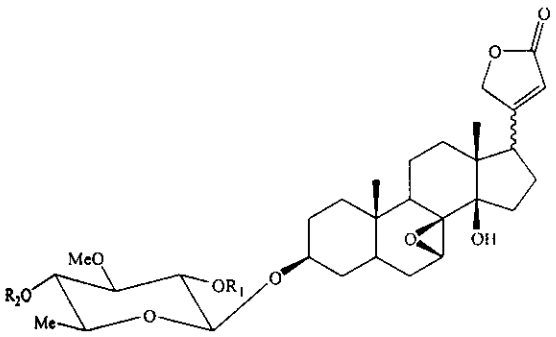
4l: R_1= Ac, R_2= H; Cerberin

4m: R_1= H, R_2= β-gentiobiosyl;

Thevetin B

4n: R_1= Ac, R_2= β-gentiobiosyl;

2′-*O*-Acetyl thevetin B



4o: R_1= R_2= H; 17β-deacetyltanghigenin

4p: R_1= H, R_2= β-gentiobiosyl;

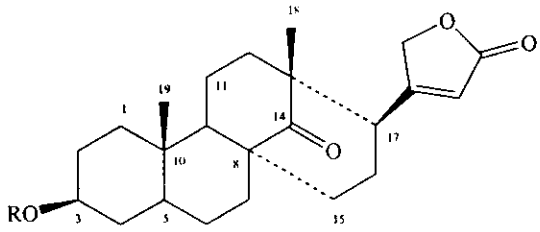
Gentiobiosyl-17α-deacetyltanghigenin

4q: R_1= H, R_2= β-D-glucosyl;

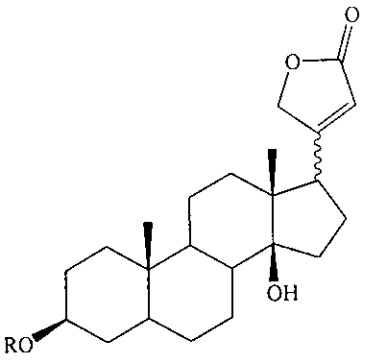
Glucosyl -17α-deacetyltanghigenin

4r: R_1= H, R_2= β-D-glucosyl;

Glucosyl -17β-deacetyltanghigenin



4s: R = b; Cerleaside B



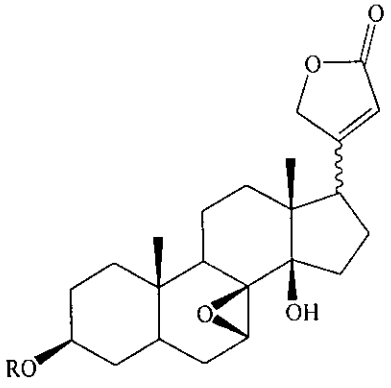
4t: R = a; 17α-Digitoxigenin β-D-glucosyl-3-ulosyl(1$\rightarrow$4)-α-thevetoside

4u: R = d; 17β- Digitoxigenin gentiobio(1$\rightarrow$4)-α-thevetoside

4v: R = c; 17β- Digitoxigenin β-D-gentiotriosyl(1$\rightarrow$4)-α-thevetoside

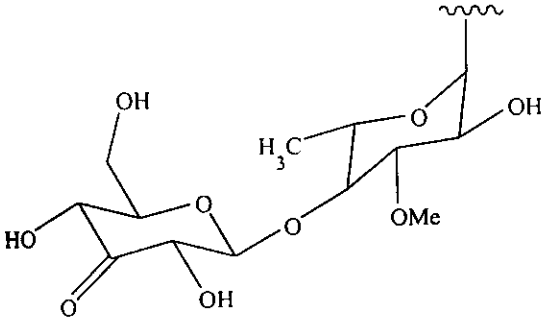
4w: R = b; 17β- Digitoxigenin β-D-glucosyl(1$\rightarrow$4)-α-thevetoside

4x: R = b; 17α- Digitoxigenin β-D-glucosyl(1$\rightarrow$4)-α-thevetoside



4y: R = a; 17α-Tanghigenin β-D-glucos-3-urosyl-(1$\rightarrow$4)-α-L-thevetoside

4z: R = d; 17β- Tanghigenin gentiobiosyl-(1$\rightarrow$4)-α-L-thevetoside



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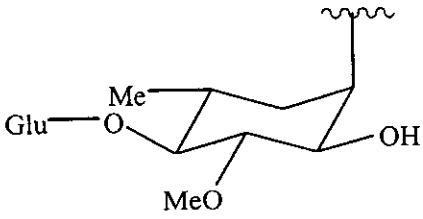

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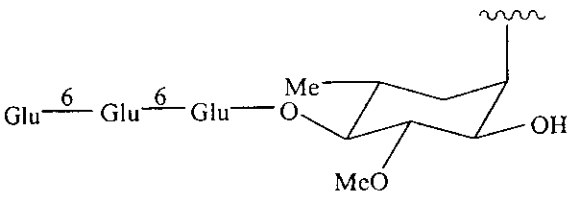

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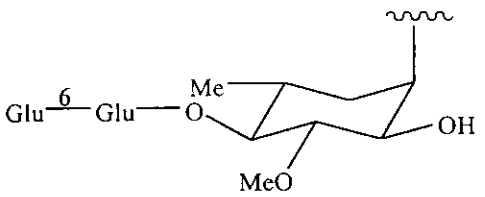
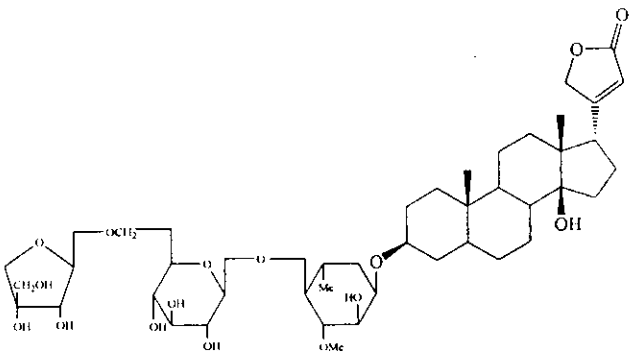
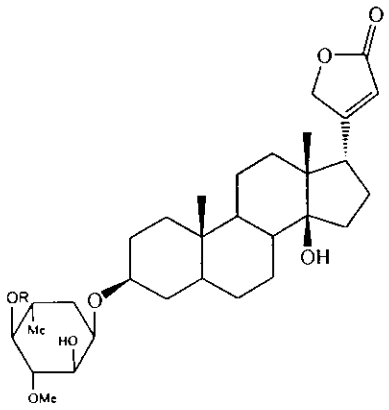


d; 4s-4z



4aa: 17α-Digitoxigenin β-D-apiosyl-(1⟶6)- β-D-glucosyl-(1⟶6)- α-L-thevetoside (Cerapioside)

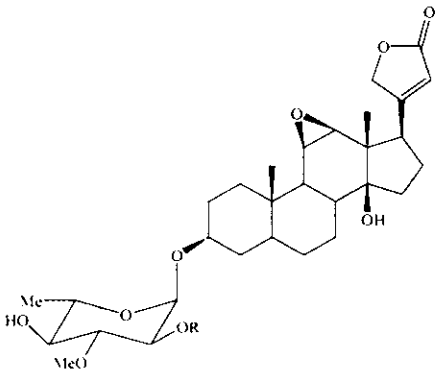


$^{4\beta}$

4ab: R = Glc ← Glc; 17α-Digitoxigenin β-cellobiosyl-(1⟶4)- α-L-thevetoside

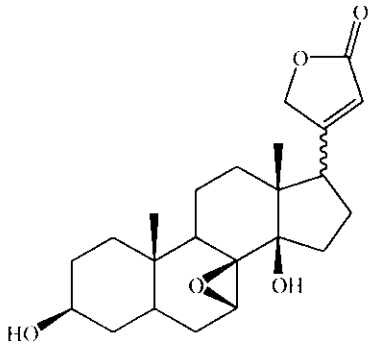
$^{6\beta}$

4ac:R = Glc ← Glc; 17α-Digitoxigenin β-gentiobiosyl-(1⟶4)- α-L-thevetoside



4ad: R = H: Deacetyl cerbertin

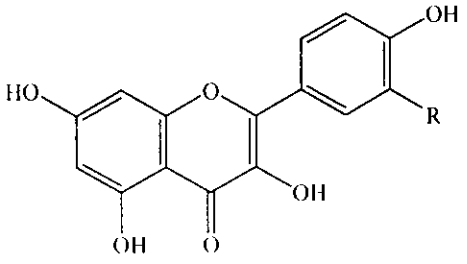
4ae: R = Ac; Cerbertin



4af: 17β-Tanghinigenin

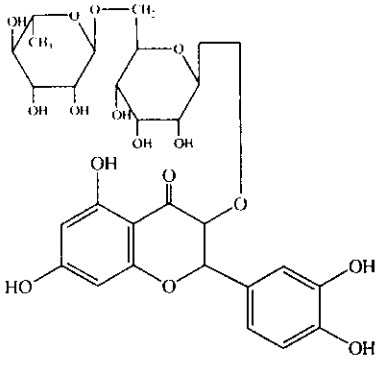
4ag: 17α-Tanghinigenin

5. Flavonols



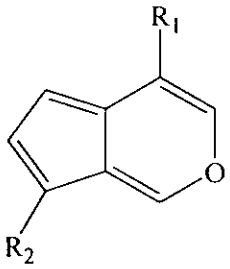
5a: R = H; Kaempferol

5b: R = OH: Quercetin



5c: Rutin

6. Iridoid monoterpenes

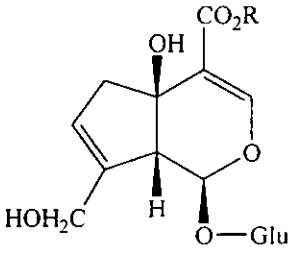


6a: $R_1 = CO_2CH_3$, $R_2 = CHO$; Cerbinal

6b: $R_1 = CO_2CH_3$, $R_2 = CO_2CH_3$; Cerberic acid

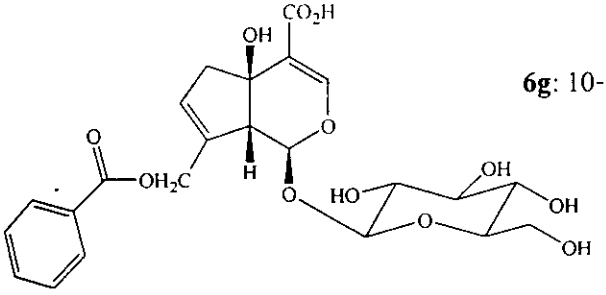
6c: $R_1 = CO_2H$, $R_2 = CHO$; Cerberinic acid

6d: $R_1 = CH_2OAc$, $R_2 = CHO$; Baldrinal

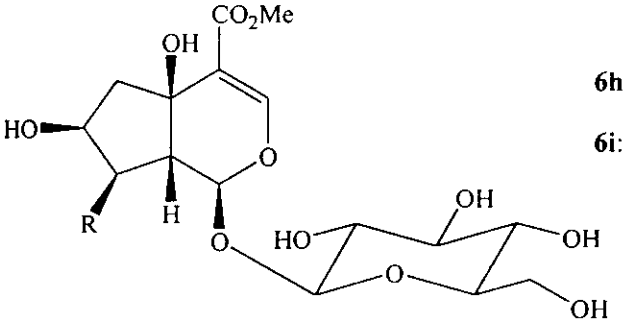


6e: R = H; Theveside

6f: R = Me; Theviridoside

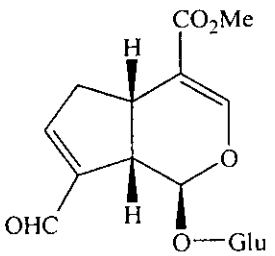


6g: 10-*O*-Benzoyltheveside



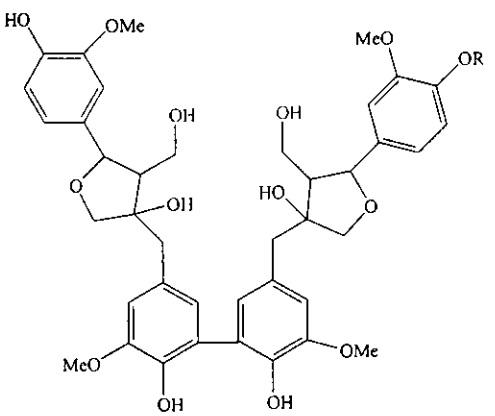
6h: R = CH_3; Loganin

6i: R = CO_2H; 10-Carboxyloganin



6j: Dehydrogeniposide

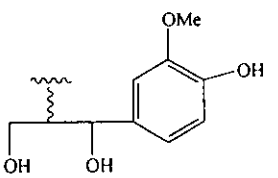
7. Lignans

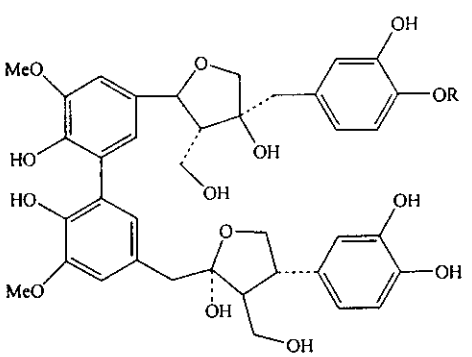


7a: R = H; Cerberalignan A

7b: R = X; (*erythro*) Cerberalignan H

X =

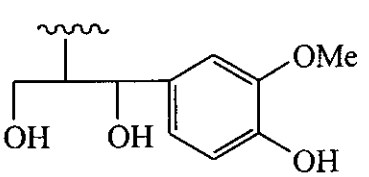


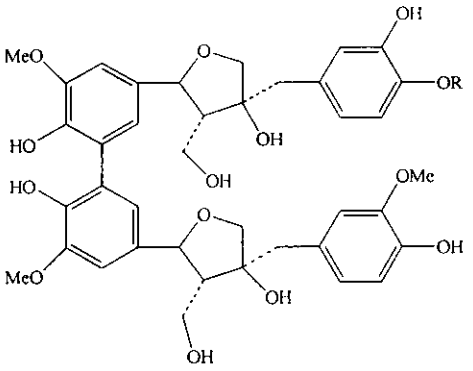


7c: R = H; Cerberalignan B

7d: R = X; Cerberalignan N

X =

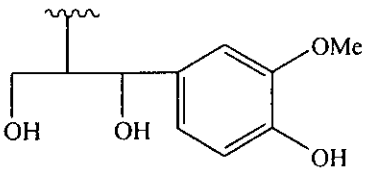


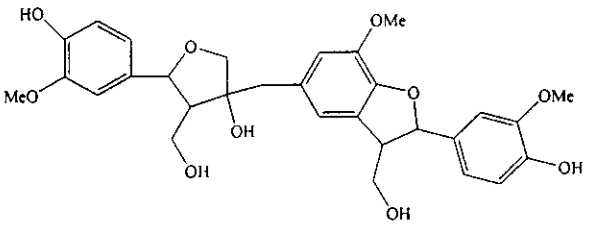


7e: R = H; Cerberalignan C

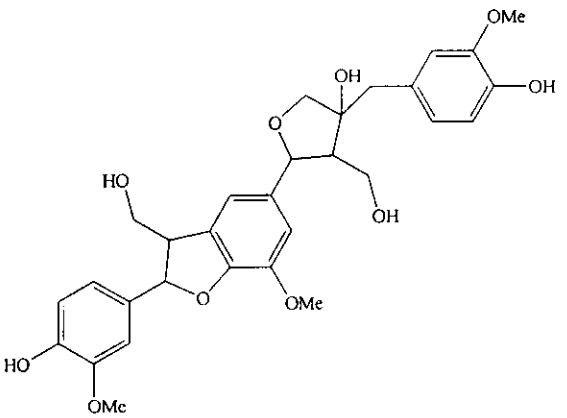
7f: R = X; Cerberalignan M

X =

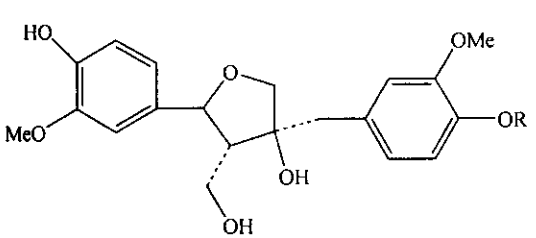




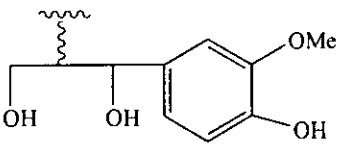
7g: Cerberalignan D



7h: Cerberalignan E

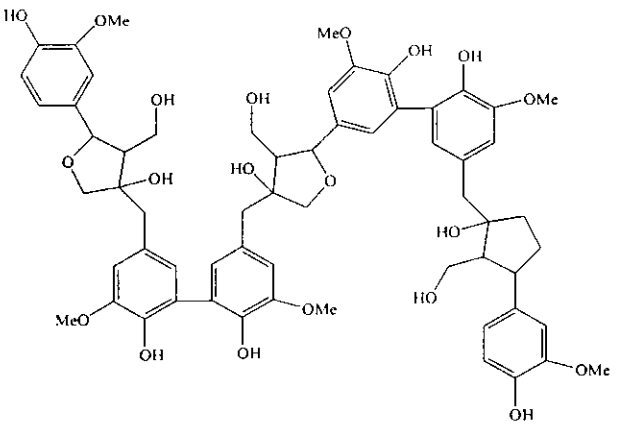


X =

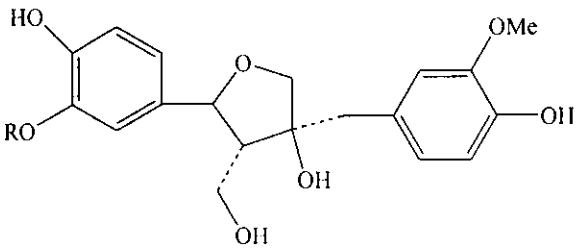


7i: R = X (*erythro*) Cerberalignan F

7j: R = X (*threo*) Cerberalignan G

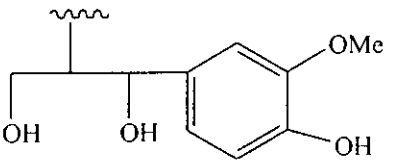


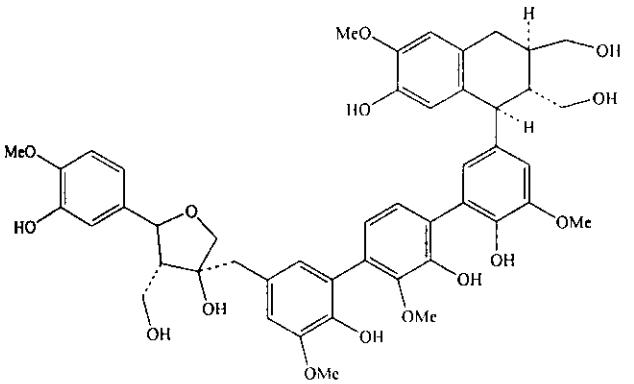
7k: Cerberalignan I



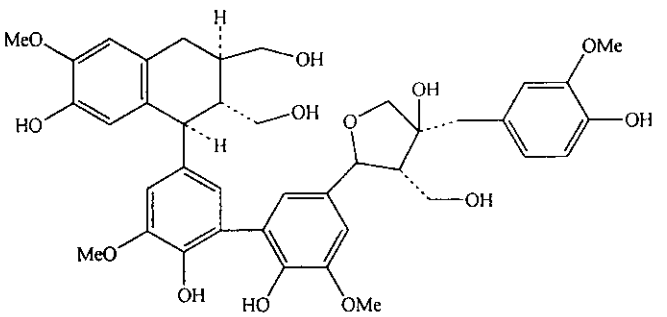
7l: R = H; (-)-Olivil

7m: R = X; Cerberalignan J

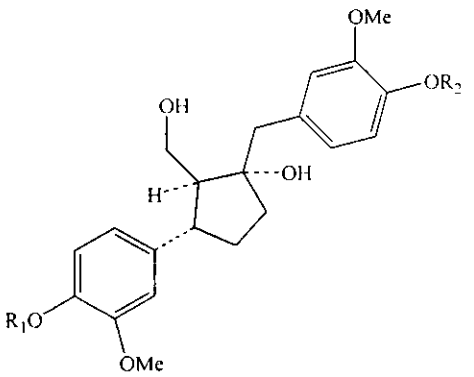
X = 



7n: Cerberalignan K



7o: Cerberalignan L

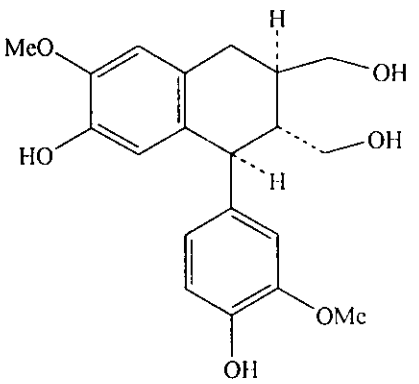


7p: R_1 = β-D-glucosyl; R_2= H;

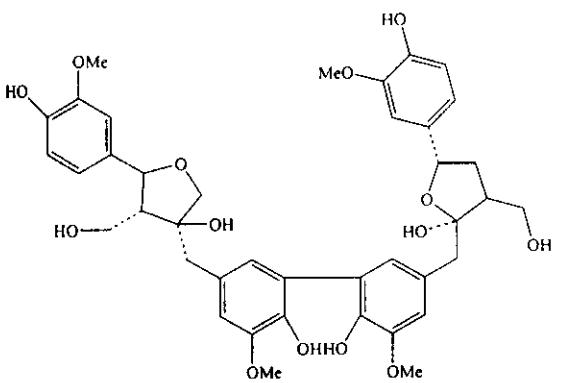
Olivil 4-*O*-β-D-glucoside

7q: R_1 = H; R_2 = β-D-glucosyl;

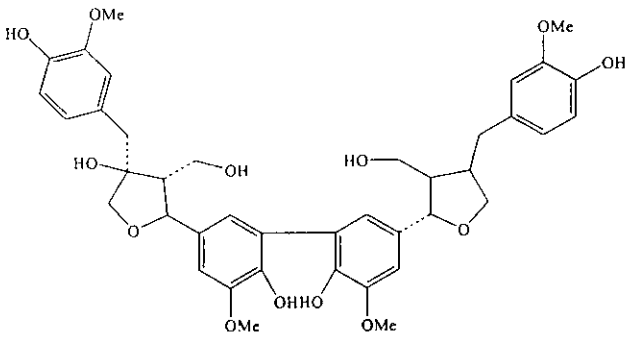
Olivil 4′-*O*-β-D-glucoside



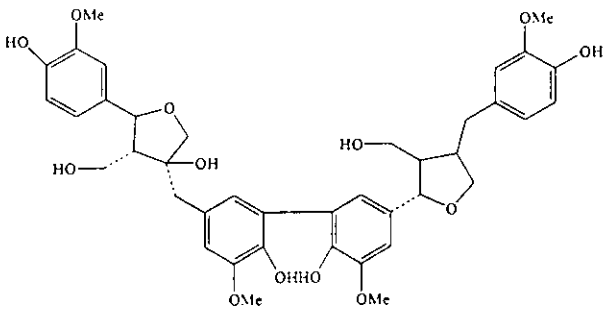
7r: (+)-Olivil



7s: Cerbera manghas olivil dimmer 5 (Lignan 5)

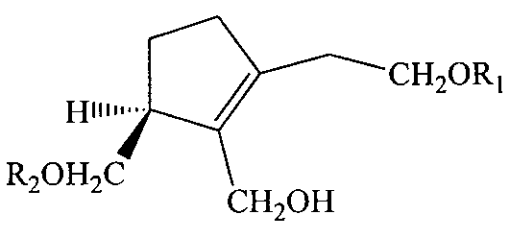


7t: Cerbera manghas olivil dimmer 6 (Lignan 6)



7u: Cerbera manghas olivil dimmer 7 (Lignan 7)

8. Monoterpenes



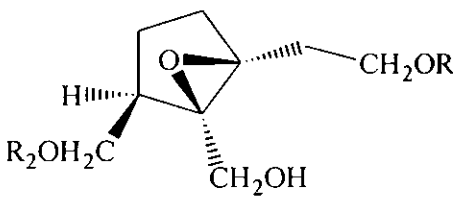
8a: $R_1 = R_2 = H$; Cerberidol

8b: $R_1 = \beta$-D-allose, $R_2 = H$;

Cerberidol-3-*O*-β-D-allopyranoside

8c: $R_1 = R_2 = \beta$-D-allose;

Cerberidol-3,10-*O*-bis-β-D-allopyranoside



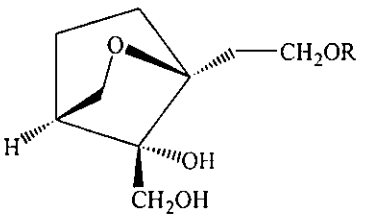
8d: R = H; Epoxycerberidol

8e: R = *β*-D-allose;

Epoxycerberidol-3-*O*-*β*-D-allopyranoside

8f: R = *β*-D-glucose;

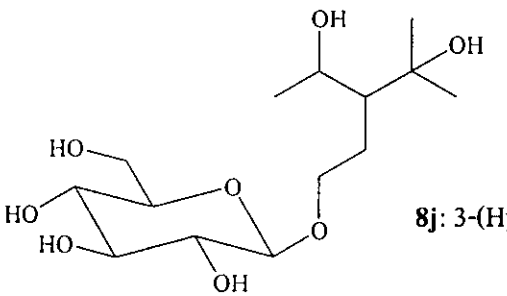
Epoxycerberidol-3-*O*-*β*-D-glucoside



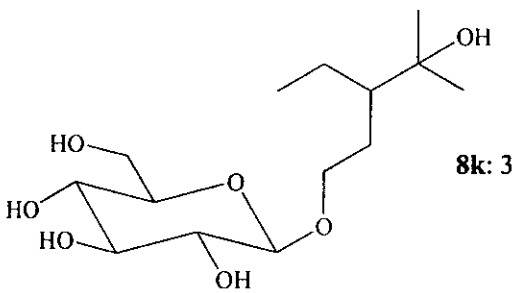
8g: R = H; Cyclocerberidol

8h: R = *β*-D-allose; Cyclocerberidol-3-*O*-*β*-D-allopyranoside

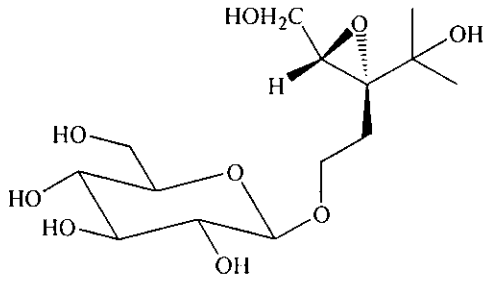
8i: R = *β*-D-glucose; Cyclocerberidol -3-*O*-*β*-D-glucoside



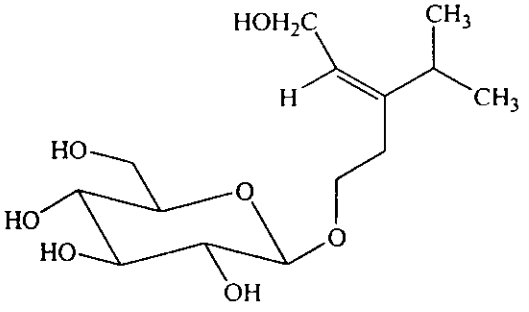
8j: 3-(Hydroxyisopropyl)-pentane-1,4-diol-*O*-*β*-D-glucoside



8k: 3-(Hydroxyisopropyl)pentane-1-ol-*O*-*β*-D-glucoside

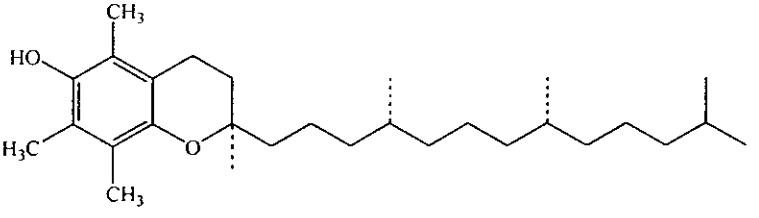


8l: (3ξ,4ξ)-3-Isopropyl-3,4-epoxypentane-1,5-diol-1-*O*-β-D-glucoside



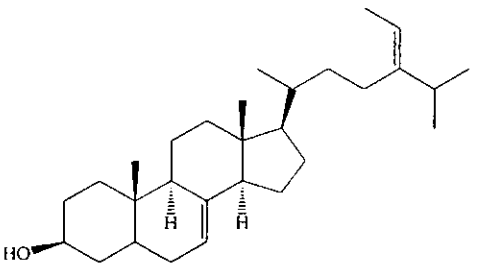
8m: (Z)-3-Isopropyl-3-penten-1,5-diol-1-*O*-β-D-glucoside

9. Oxygen heterocycle

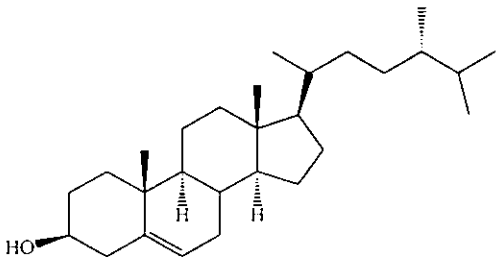


9: α-Tocopherol

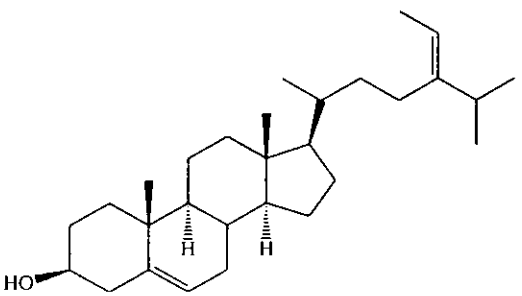
10. Steroids



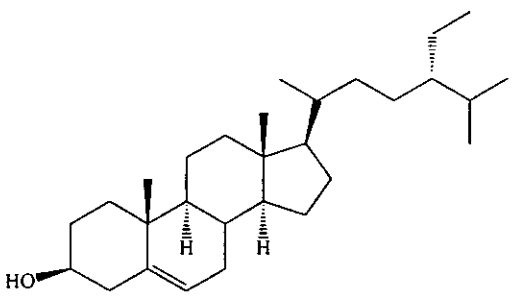
10a: Avenast-7-en-3β--ol



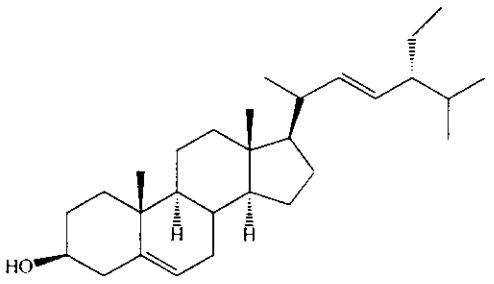
10b: Campesterol



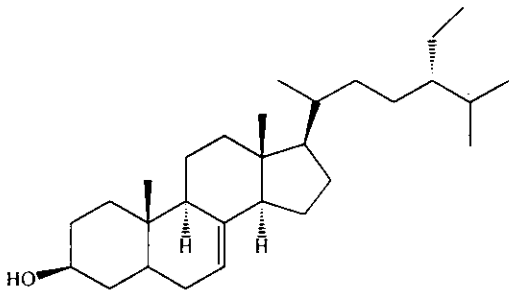
10d **10c**: Fucosterol



10d: Sitosterol

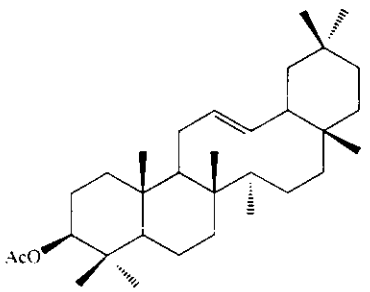


10e: Stigmaserol



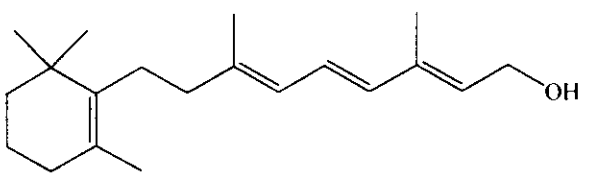
10f: Stigmast-7-en-3β-ol

11. Triterpene



11: α-Amyrin-3-acetate

12.Vitamin



12: Vitamin A

This research involved isolation, purification and structure elucidation of chemical constituents were isolated from the seeds, barks and latex of *C. odollam.*