Chapter 8

Natural Products from Semi–Mangrove Plants in China

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Additional information is available at the end of the chapter

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1. Introduction

Mangroves are various kinds of trees up to medium height and shrubs that grow in saline coastal sediment habitats in the tropics and subtropics-mainly between latitudes 25° N and 25° S [1]. Mangrove plants were comprised of true-mangrove plants and semi-mangrove plants. The true-mangrove plants were woody plants, which only grew in the intertidal zone and couldn't survive in the land. Semi-mangroves were woody plants that could both grow in the intertidal zone and in the land. The differences between the two kinds of mangroves were the specificity of living habitats of the true-mangrove and the amphibiotic living habitats of the semi-mangrove as shown in Figure 1. Meanwhile, all of them were woody plants and could grow in the specific environment of intertidal zone, and the latter was the basis of the diversified chemical constituents and biological activities of the mangroves [2].

True-mangroves Semi-mangroves

Figure 1. Pictures of some true and semi-mangroves

The word's mangrove plants have 84 species (including 12 varieties) in 24 genera and 16 families. Of which, true mangrove plants have 70 species (including 12 varieties) in 16 genera and 11 families, and semi-mangrove plants 14 species in eight genera and five families [3]. 12 species of semi-mangroves were grown in China including *Barringtonia racemosa, Cerbera manghas*, *Dolichandrone spathacea*, *Pluchea indic, Hernandia nymphiifolia*, *Pongamia pinnata*, *Pemphis acidula*, *Hibiscus tiliaceus*, *Thespesia populnea*, *Premna obtusifolia*, *Clerodendrum inerme*, *Heritiera littoralis* [3]. Hainan province of China is most rich in semi-mangroves, where all of the 12 species were spread there. 8 species were grown in Guangxi province, 10 species were distributed in Taiwan province, 7 species were found in Fujian province, 7 species were grown in Hongkong, and 3 species were found in Macao [4].

Most semi-mangroves possessed medicinal usages were utilized as folk medicine in many provinces of China. For example, the seeds of *Cerbera manghas* were used as emetic and purgative medicine in Hainan province [1]. The leaves and branches of *Hibiscus tiliaceus* were used as the agents of clearing heat and reducing the swelling. The crude extract of *Pongamia pinnata* can effectively inhibit pathogen of the multiple evanescent white dot syndromes, and reduce mortality. The seeds of *Barringtonia racemosa* showed anti-cancer and anti-microbial activities. *Thespesia populnea* possessing relieving pain, anti-inflammatory, anti-microbial, and antioxidant activities can also protect the liver damage induced by carbon tetrachloride.

Chemical constituents isolated form semi-mangrove plants with various and unique structures including flavanoids, lignans, sesquiterpenoids, diterpenoids, triterpenoids, steroids, and alkaloids et al. For example, Abe and coworkers obtained cardiac glycosides from the seeds of *Cerbera manghas* [4]. Alis isolated some oxygenated sesquiterpenoids from the roots of *Hibiscus tiliaceus*. Some flavanoids as glabone were isolated from *Pongamia pinnata* and Wang obtained 5 thiophene derivatives from *Pluchea indic*.

Meanwhile, the biological activities of the isolated compounds were studied extensively. Some were found to have obvious biological activities. For example, cardiac glycosides showed obvious anti-cancer activity [11] and bartogenic acid can inhibit the activity of α-glycosidase and amylase [13].

In short, semi-mangrove plants played an important role in curing disease and finding new chemical entities. We highlight that it will become more and more significant to the research and development of new drugs. In this review, chemical constituents and biological activities of semi-mangrove plants were mainly regarded and they are as follows.

2. Chemical constituents

2.1. Flavanoids

Pongamia pinnata were rich in flavanoids compared with other semi-mangroves. Up to now, more than 50 flavaonoids have been isolated from *Pongamia pinnata* with the structural characteristic of furan or pyran ring parallelized with the skeleton of flavaonoids. Partial flavaonoids including flavone, flavonone, chalcone, dihydrochalcone were listed in Figure 3.

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Figure 2. Pictures of 12 semi-mangroves spread in China

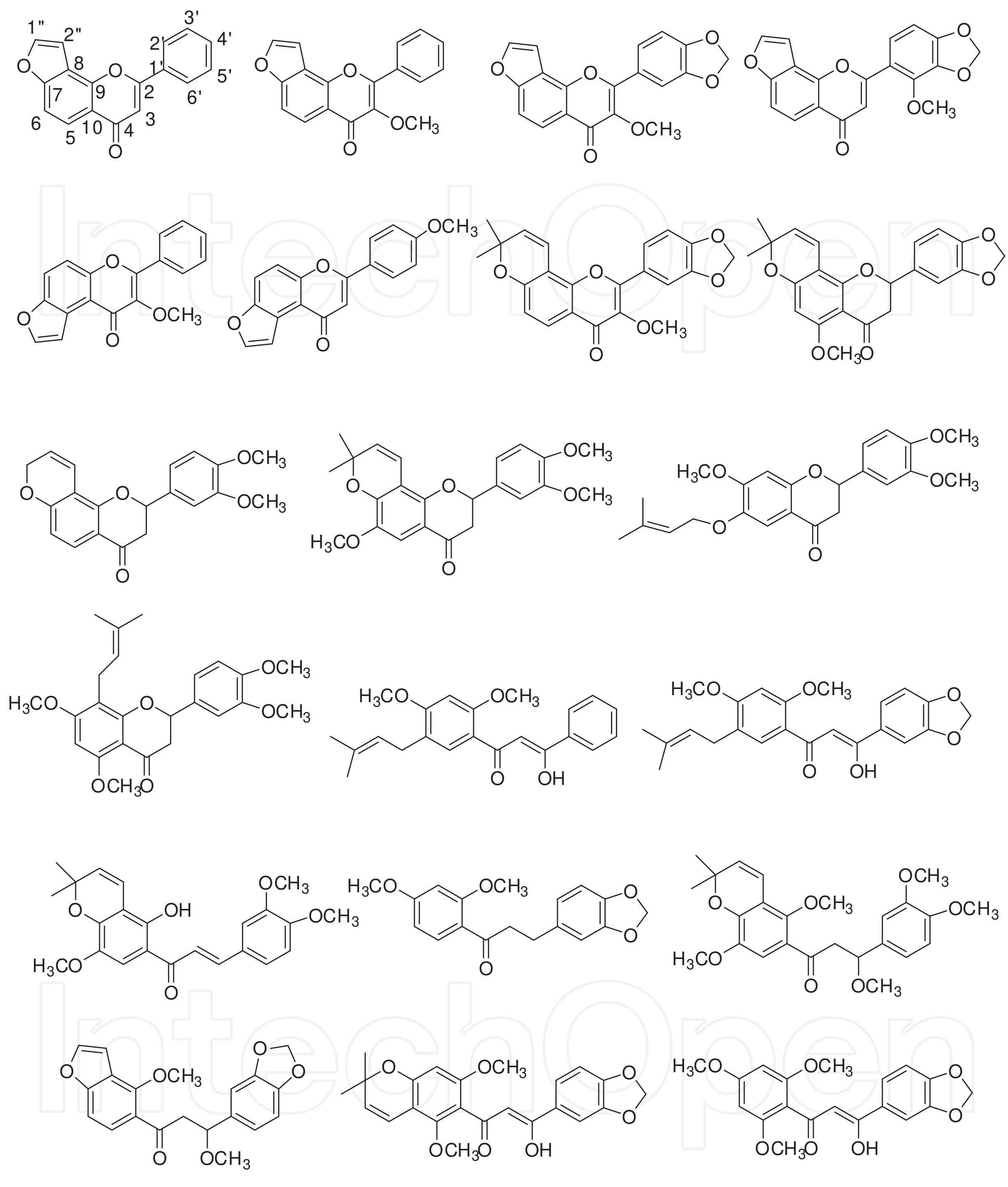


Figure 3. Flavonoids from *Pongamia pinnata*

2.2. Sesquiterpenoids

Sesquiterpenoids isolated form *Pluchea indic*, *Hibiscus tiliaceus*, and *Thespesia populnea* were given full attention. Most sesquiterpenoids isolated form *Pluchea indic* were eudesmane and eremophilane diterpenoid skeleton, For example, the compounds were depicted in Figure 4.

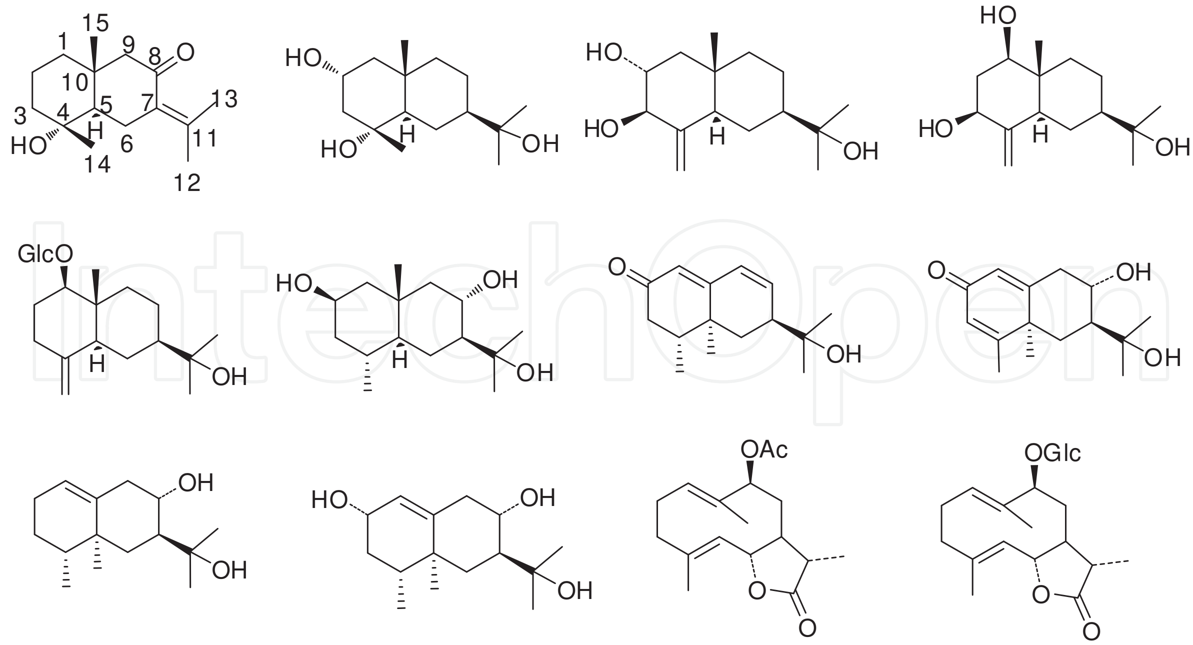


Figure 4. Structures of sesquiterpenoids from *Pluchea indica*

Sesquiterpenoids isolated form *Hibiscus tiliaceus* and *Thespesia populnea* with highly oxygenated structures attracted many scientists' attention. Nine oxygenated sesquiterpenoids were isolated from the heartwood of *Hibiscus tiliaceus* and they are shown in Figure 5.

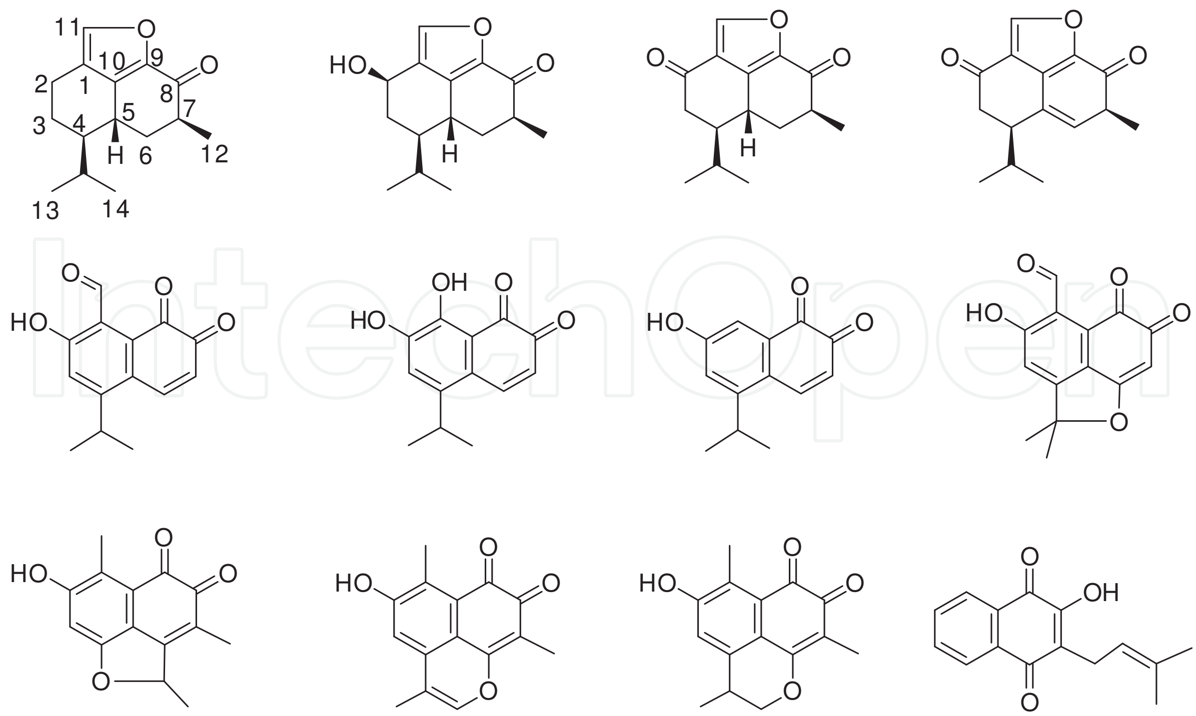


Figure 5. Structures of mansonones from *Hibiscus tiliaceus*

2.3. Triterpenoids

Some oleanane type triterpenoids with highly oxygenated were isolated form *Barringtonia racemosa* as shown in Fig 6. Six friedelane type triterpenoids were isolated from bark of *Hibiscus tiliaceus* collected from Hainan province as shown in Figure 7.

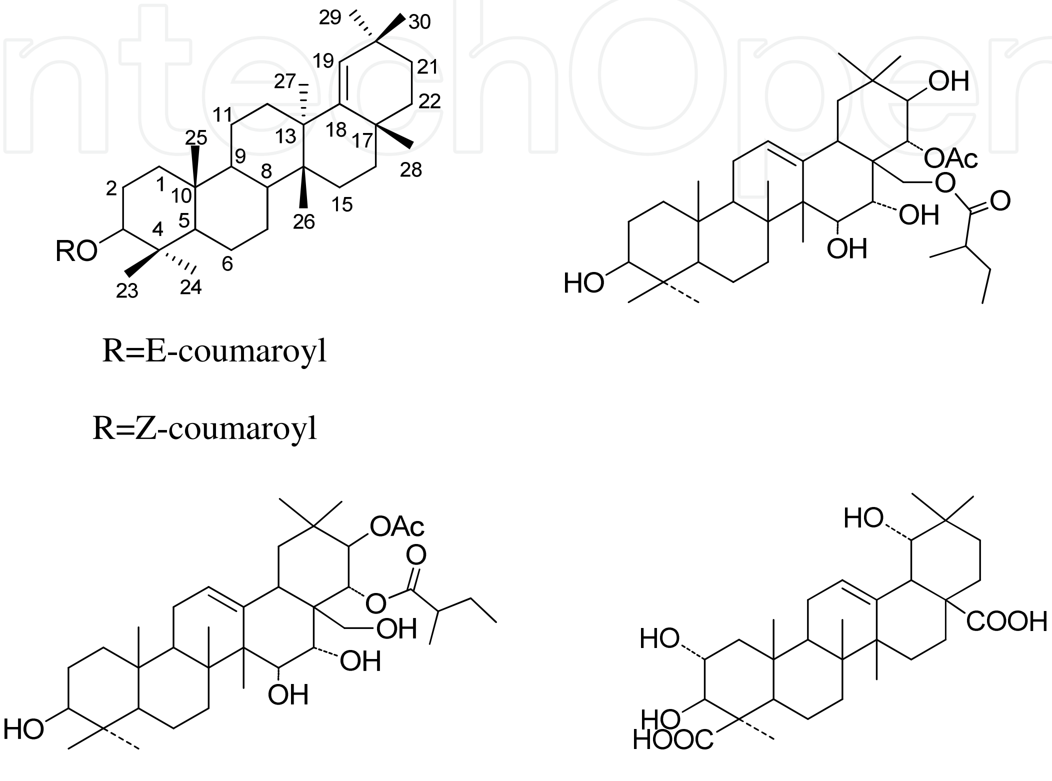
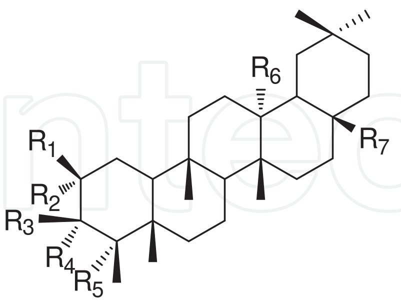


Figure 6. Triterpenoids from *Barringtonia racemosa*



R_1=R_2=O, R_3=R_5=H, R_4=OH, R_6=R_7=CH_3 (1)
R_1=R_2=H, R_3=R_4=O, R_5=OH, R_6=R_7=CH_3 (2)
R_1=R_2=R_5=H, R_3=R_4=O, R_6=R_7=CH_3 (3)
R_1=R_2=R_4=R_5=H, R_3=OH, R_6=R_7=CH_3 (4)
R_1=R_4=R_5=H, R_2=R_3=OH, R_6=R_7=CH_3 (5)
R_1=R_2=R_5=H, R_3=R_4=O, R_6=R_7=COOH (6)

Figure 7. Structures of friedelane type triterpenoids from *Hibiscus tiliaceus*

2.4. Cardiac glycosides

More than 30 cardiac glycosides were isolated from the seeds of *Cerbera manghas* and the skeleton of the obtained compounds were calssified into three classess including digitoxigenin (A), Oleandrin (B), and tanghinin (C) as shown in Fig 8.

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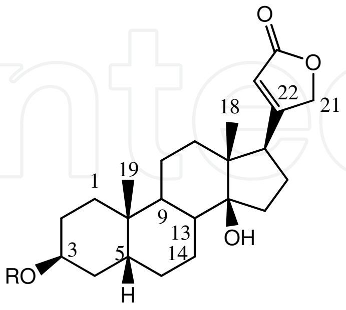
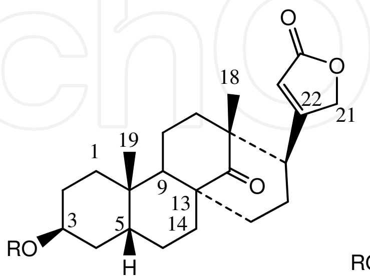
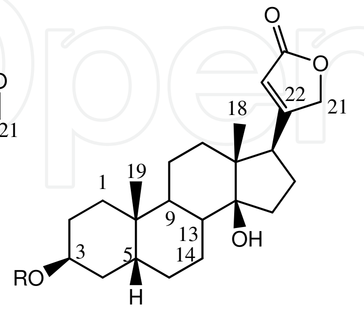


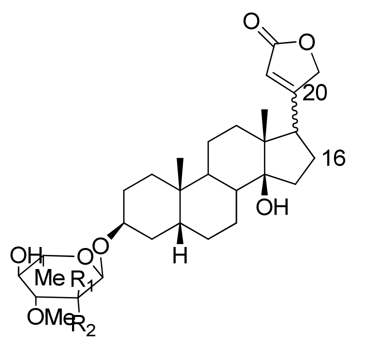
A



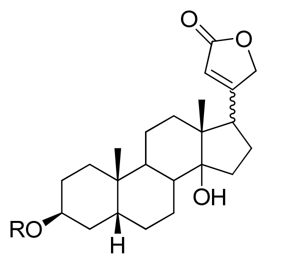
B



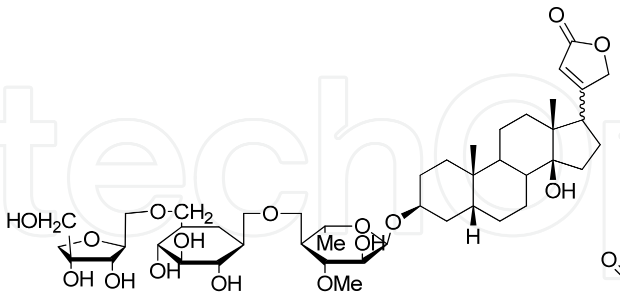
C

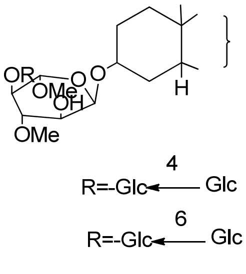


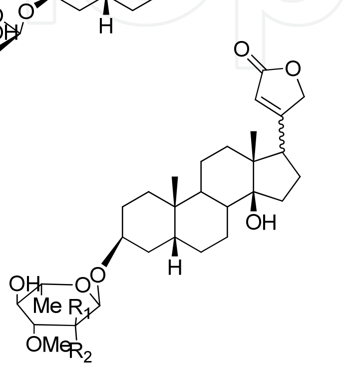
17β R$_1$=OH;R$_2$=H neriiforlin
17α R$_1$=OH;R$_2$=H 17α neriiforlin
17β R$_1$=H;R$_2$=OH
17α R$_1$=H;R$_2$=OH

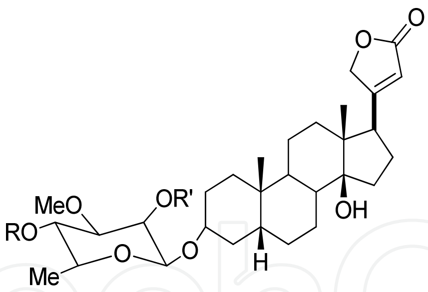


17β ,R=a
17β ,R=c
17β ,R=b
17α ,R=b
17β ,R=d

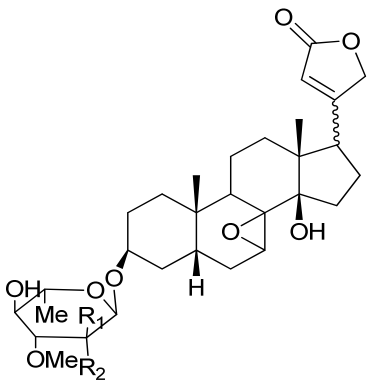




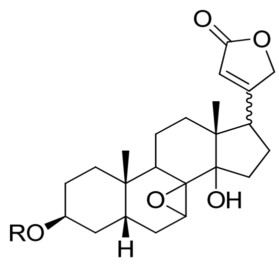




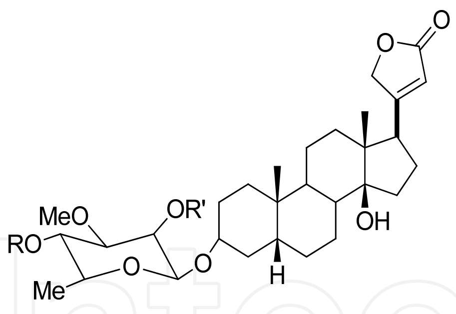
thevetin B R=β -gentiobiosyl R'=H
2'-O-Ac-thevetin B R=β -gentiobiosyl R'=OAc
cerberin R=H R'=OAc



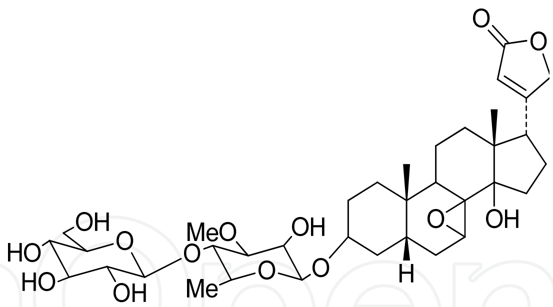
17β ;R1=OH;R2=H deacetyltanghinin
17α ;R1=H;R2=OH 17α -deacetyltanghinin
17β ;R1=H;R2=OH

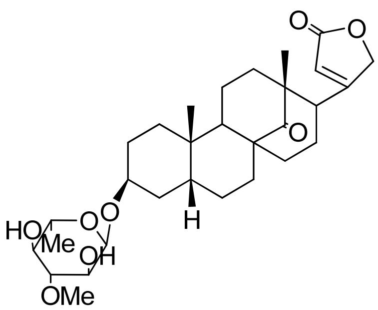


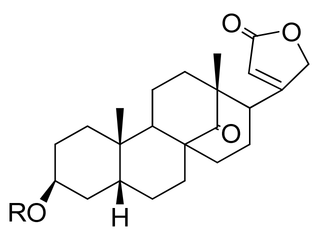
17α ,R=a
17β ,R=b
17α ,R=b
17β ,R=d



R=β -gentiobiosyl R'=OAc $C_{7,8}$β β -epxoy
R=β -gentiobiosyl R'=H $C_{7,8}$β β -epxoy







17α ,R=b

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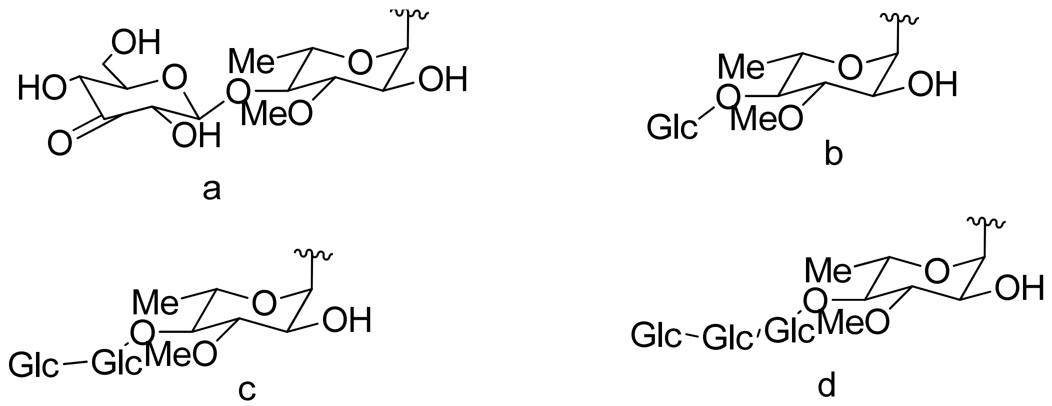
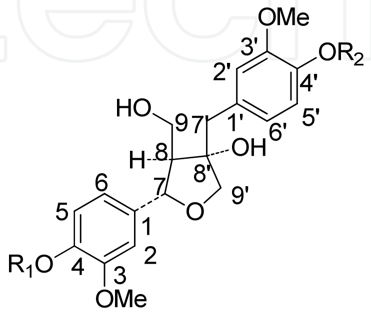


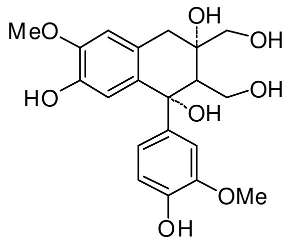
Figure 8. Cardenolides from *Cerbera manghas*

2.5. Lignans

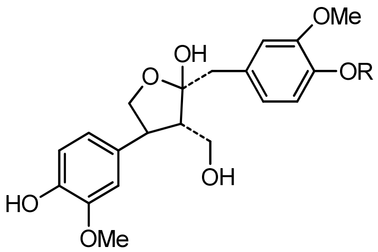
Many lignans were isolated from the semi-mangroves, and lignans obtained from *Cerbera manghas* with unique structures have attracted more attention. These lignans were classified to be monomerlignans (1-4), sesquilignans (5-7), dilignans (8-16), sesterlignans (17) and trilignans (19). They are listed as belows.



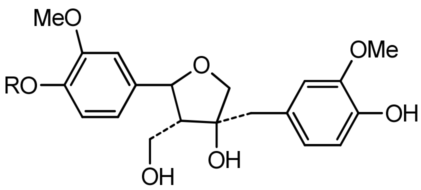
R_1=R_2=H
R_1=glucosyl,R_2=H
R_1=H,R_2=glucosyl



cycloolivil



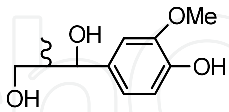
R=X(erythro) cerberalignan F
R=X(threo) cerberalignan G

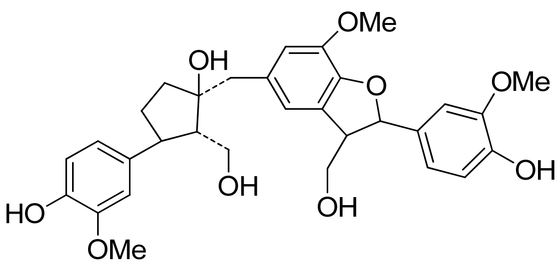


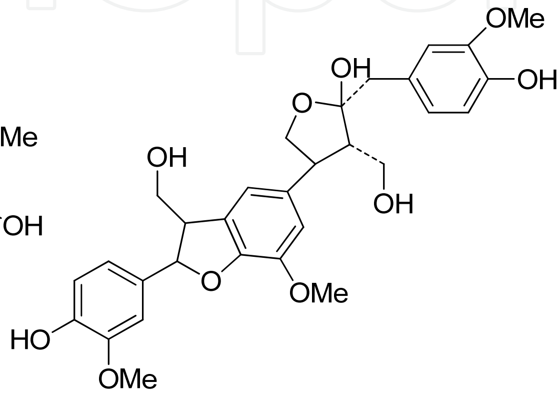
R=X(threo)

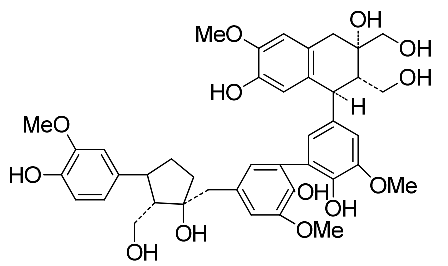
cerberalignan J

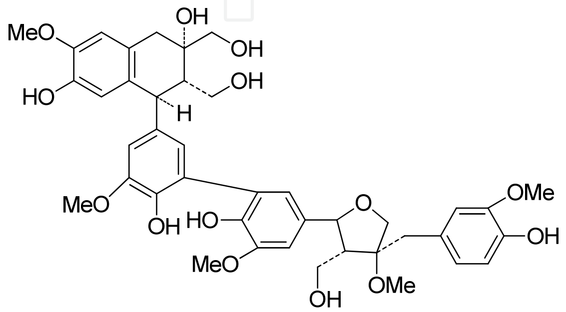
X=

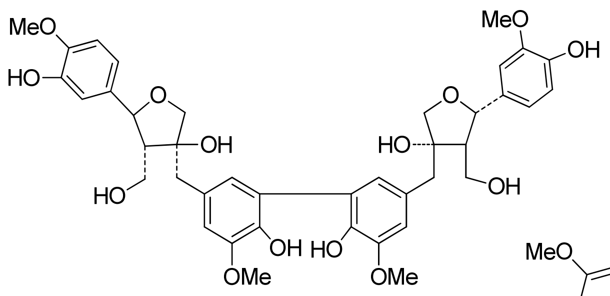


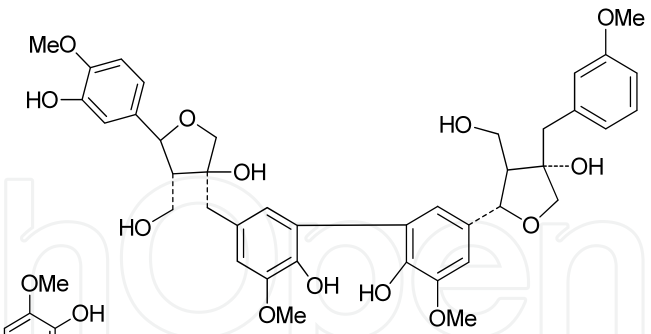


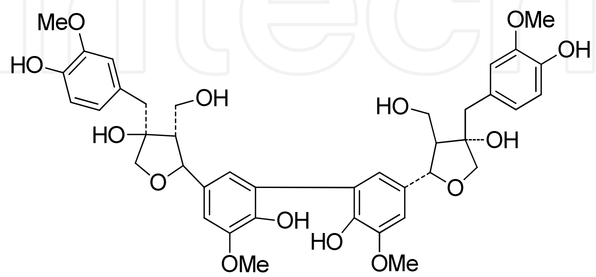












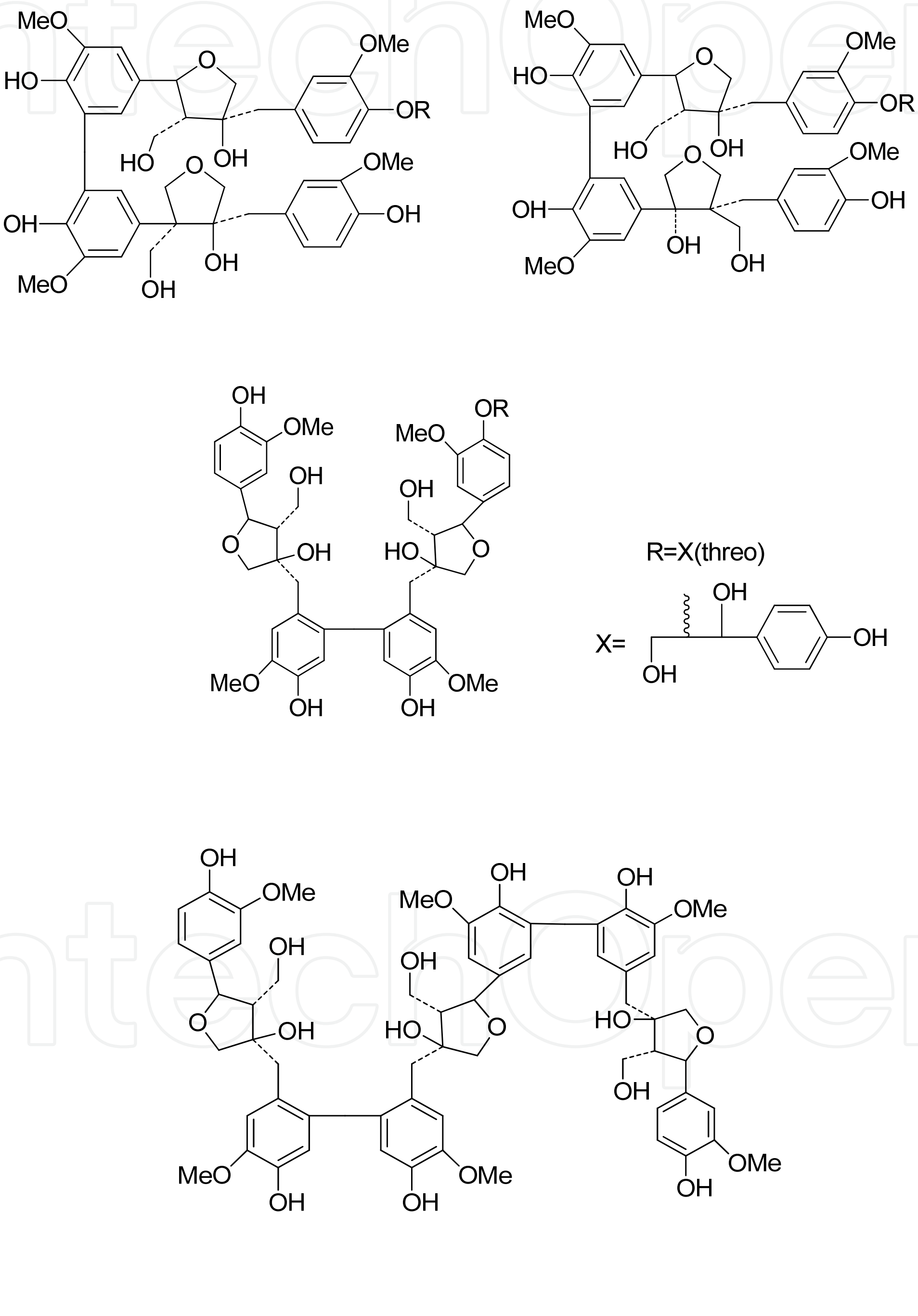


Figure 9. Structures of lignans from *Cerbera manghas*

2.6. Others

Apart from these above mentioned compounds, courmains, iridoids, and alkaloids have also been obtained from semi-mangroves distributed in China. For example, cerbinal, p-hydroxy-benzaldehyde, benzamide, n-hexadecane acid monoglyceride, loliolide, β-sitosterol, *et al*.

3. Biological activities

3.1. Antitumor activities

The seeds extract of *Cerbera manghas* were found possessing obvious cytotoxic activity against some human cancer cell lines by MTT methods. Feng and coworkers obtained two cardiac glycosides named GHSC-73 and GHSC-74. Further study suggested GHSC-73 and GHSC-74 can significantly inhibited growth and proliferation of HepG2 cells in dose-dependent manner. GHSC-73 inhibited the growth and proliferation of HepG2 cells through blocking S phase and inducing apoptosis, while GHSC-74 through blocking S and G2 phases and inducing apoptosis.Wang and coworkers tested 24 compounds isolated from *Pluchea indic* and found that valenc-l (10)-ene-8α, 13-diol showed inhibiting activity against Bel-7402 and A2780 cells. Lanceolatin B purified from *Pongamia pinnata* can prevent the development of cancer [20]. The cytotoxic activities of mansonone D, mansonone H, thespesone, and thespone were tested against MCF-7 cells by Johnson using the MTT methods. The results indicated that they all showed certain cytotoxic activities [21]. Ethnomedical survey has shown that the seeds of *Barringtonia racemosa* are traditionally used in certain remote villages of Kerala (India) to treat cancer like diseases. Thomas [22] tested the seed extracts for their anti-tumor activity and toxicity. Intraperitoneal (i.p.) daily administration of 50% methanol extract of this seed to mice challenged with 1 million Dalton's Lymphoma Ascitic (DLA) cells resulted in remarkable dose dependent anti-DLA activity in mice. The optimum dose was found to be 6 mg/kg. This dose protected all the animals challenged with the tumor cells. The efficacy of the drug was found to be better than that of a standard drug, vincristine in this tumor model. However, the oral administration showed only marginal activity compared to i.p. administration. The extract was found to be devoid of conspicuous acute and short-term toxicity to mice, when administered daily, (i.p.) for 14 days up to a dose of 12 mg/kg (which was double the concentration of optimum therapeutic dose). The treated mice showed conspicuous toxic symptoms only at 24 mg/kg. The LD (50) to male mice for a single i.p. dose was found to be 36 mg/kg. Consequently, they found that the seed extract is an attractive material for further studies leading to drug development. Anbu and coworkers [23] evaluated anti-tumor activity of the roots of *Hibiscus tiliaceus* against Dalton's Ascitic Lymphoma (DAL) in Swiss albino mice. A significant enhancement of mean survival time (MST) of *H. tiliaceus* treated tumor bearing mice was found with respect to control group. *H. tiliaceus* treatment was found to enhance peritoneal cell counts. When these *H. tiliaceus* treated animals under-went intraperitoneal (i.p.) inoculation with DAL cells, tumor cell growth was found to be inhibited. The results indicated that, *H. tiliaceus* treated group were able to reverse the haematological parameters, protein and Packed

Cell Volume (PCV) consequent to tumor inoculation with in fourteen days after the transplantation.

3.2. Antibacterial activity

Khan and coworkers [24] used disc diffusion methods to test antibacterial activity of the ethanol extract of *Barringtonia racemosa* roots, its chloroform soluble fraction, and a there from an isolated clerodane diterpenoid (Nasimalun A). The results presented that they all showed potent activity in inhibiting the growth of 19 strains of bacterial with the ethanol extract as the most activity part. A marble cup method was used by Goyal [25] to test the antimicrobial activities of the crude methanolic extract of *Barringtonia asiatica* (leaves, fruits, seeds, stem and root barks) and the fractions (petrol, dichloromethane, ethyl acetate, and butanol) and all the extract exhibited a very good level of broad spectrum antibacterial activity. Baswa [26] evaluated the antibacterial activity of *Pongamia pinnata* seed oil *in vitro* against fourteen strains of pathogenic bacteria. Using the tube dilution technique, it was observed that 57.14 and 21.42% of the pathogens were inhibited at 500 μl/ml, 14.28 and 71.42% at 125 μl/ml, and 28.57 and 7.14% at 250 μl/ml of *Pongamia pinnata* oils. The activity with both the oils was bactericidal and independent of temperature and energy. Most of the pathogens were killed more rapidly at 4°C than 37°C. The activity was mainly due to the inhibition of cell-membrane synthesis in the bacteria.

3.3. Anti–inflammatory analgesic activity

Srinivasan and coworkers studied the anti-inflammatory activity of 70% ethanolic extract of *Pongamia pinnata* leaves (PLE) in acute, subacute and chronic models of inflammation in rats. *Per os* (p.o.) administration of PLE (300, 1000 mg/kg) exhibited significant anti-inflammatory activity in acute (carrageenin, histamine, 5-hydroxytryptamine and prostaglandin E_2-induced hind paw edema), subcute (kaolin-carrageenin and formaldehyde-induced hind paw edema) and chronic (cotton pellet granuloma) models of inflammation. These results indicate that PLE possesses significant anti-inflammatory activity without ulcerogenic activity suggesting its potential as an anti-inflammatory agent for use in the treatment of various inflammatory diseases. The antinociceptive activity of a 70% ethanol extract of *Pongamia pinnata* leaves (PLE) was also investigated by Srinivasan [28] in different models of pain in mice and rats. Per os (p.o.) administration of the PLE (100-1000 mg/kg) produced significant antinociceptive activity in the hotplate and tail flick (central) as well as in acetic acid writhing and Randall-Selitto (peripheral) nociceptive tests. Narender[29] evaluated the antinociceptive and anti-inflammatory activities of different extracts of *Hibiscus tiliaceus* (Malvaceae). The antinociceptive investigations were carried out against two types of noxious stimuli, chemical (acetic acid-induced writhing) and thermal (hotplate and tail immersion tests). The different leaves extracts of *Hibiscus tiliaceus* (250 and 500 mg/kg, orally) possessed a significant anti-inflammatory activity on carragennan-induced paw edema in rat at the second and third hour. All the extracts significantly inhibited the acetic acid induced abdominal contractions in mice in order methanolic>chloroform>petroleum ether extract. The extracts showed the significant antinociceptive activity at dose of 250 mg/kg and 500 mg/kg ($p<0.01$) at 60 min after extracts administration.

3.4. Others

Chakraborty reported the bark, seeds of *Barringtonia acutangula* could be used as a fish poison. Pongamia pinnata was evaluated by Elanchezhiya [31] for antiviral properties against herpes simplex virus type-1 (HSV-1) and type-2 (HSV-2) by *in vitro* studies in Vero cells. A crude aqueous seed extract of *P. pinnata* completely inhibited the growth of HSV-1 and HSV-2 at concentrations of 1 and 20 mg/ml (w/v), respectively.

4. Conclusions

Among the 12 mangroves, *Pongamia pinnata*, *Cerbera manghas*, *Barringtonia racemosa* have been carried on deep researches concerning their chemical constituents, biological activities. Some compounds isolated from the semi-mangroves were proved to have obvious activities as the two cardenolides of GHSC-73 and GHSC-74. However, as proposed by Shao Changlun "Some semi-mangrove plants have not yet been analyzed and interpreted on their chemical constituents and pharmacological effects", the further researches of the semi-mangrove plants will make an important contribution to for the finding of new drugs.

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