CHAPTER II

LITERATURE REVIEW

Lagerstroemia loudonii

1. Botanical studies

Lagerstroemia loudonii belongs to the family Lythraceae, other name is called "salao-bai-yai", "ta-baek-khon", "ta-kriap", "kriap" and "In-thara-chit" (Smitinand, 2001). This species can grow up to 15 m in height and has a vase shape crown. The bark's color varies from grey to dark brown, rough, hard, compacted, furrowed; over whole trunk. The leaves are opposite, simple, with entire margins, hair cover and vary from 3.5-11.5 x 9.0-21.0 cm. The flowers of this species are pink-purple turning white, slightly fragrant and bloom time is in March to April. The fruit is an oval, hair cover, round about 1.0-1.8 x 1.2-2.0 cm, which is dry at maturity and splits in 5-6 pieces to release the winged seeds. (Huanbutta, 1999)

2. Traditional uses

Lagerstroemia genus is used in folk medicine and garden tree. The traditional uses of this genus are shown in table 1 (Prasitpan, et al., 1988).

Table 1 Uses of the *Lagerstroemia* tree

Tree	Part of tree used	Uses
L. speciosa	bark	treating diarrhea and cold
	leaf	diuretic and reduces blood sugar levels
L. indica	bark	treating cold
	leaf	laxatives
L. floribunda	bark	treating diarrhea
L. tomentosa	bark	treating diarrhea
L. loudonii	bark	treating diarrhea

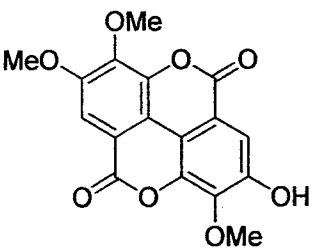
Chemical studies and biological activities

1. *L. Loudonii*

In 1988, Prasitpan, et al. studied the methanolic extract from leaves and stem bark of *Lagerstroemia* genus. The preliminary tests of four species showed that there were only trace amount of alkaloids in the leaf of *L. speciosa*, *L. macrocarpa*, *L. loudonii*, *L. duperreana* and in the bark of *L. duperreana*. Flavonoids were not found in the leaf and the bark of *L. duperreana*. Trace amounts of flavonoids were found in the leaf of *L. speciosa* but large amounts were discovered in the leaves of *L. macrocarpa* and *L. loudonii*. In addition steroids were found in leaf and bark every sample. (Prasitpan, et al., 1988)

In 2003, Boonphong, et al. reported that dichloromethane and methanol extracts from *L. loudonii* had antioxidant activity and bioactivity. The DCM extract of flower has an anti NCI-H187 (Small cell lung cancer) (IC_{50} 2.20 μg/mL), The DCM extract of root, stem, leaf, flower and fruit had an anti-TB (MIC 200, 50, 50, 200 and 100 μg/mL respectively). The DCM extract of leaf, flower and fruit have anti-malaria (EC_{50} 4.90, 7.60 and 2.20 μg/mL). Especially the dichloromethane extract from *L. loudonii* fruit has the anti-TB (MIC 100 μg/mL) and the anti-malarial activity (EC_{50} 2.20 μg/mL) which are more effective than the methanol extract from the same part of plant. (Boonphong, et al., 2003)

In 2006, Malaisree, et al. isolated compounds of the methanol extract and dichloromethane extract from flower of *L. loudonii*. Six compounds were identified as 3,4,3'-tri-*O*-methylellagic acid (1), 3-*O*-methylellagic acid (2), 4-*O*-methylellagic acid (3), 4-*O*-methylellagic acid 3'-(2",3"-di-*O*-acetyl)-α-L-rhamnoside (4), ellagic acid (5) and methyl gallate (6). Their antioxidant activities were determined *via* DPPH free radical scavenging assay. It was found that their antioxidant activities were 56.55%, 79.71%, 91.87%, 92.59%, 93.54% and 95.77%, respectively. (Malaisree, et al., 2006)



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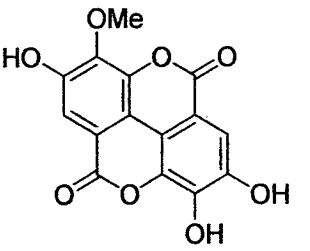

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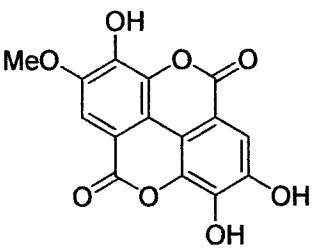

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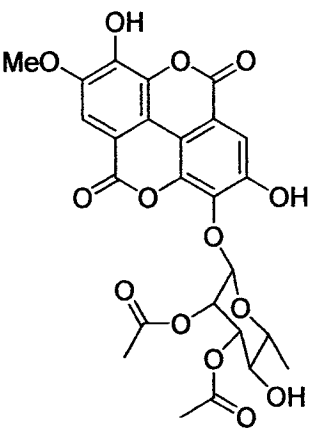

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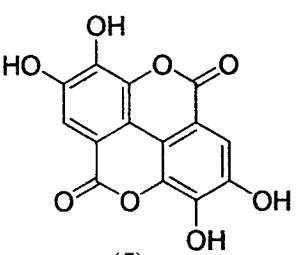

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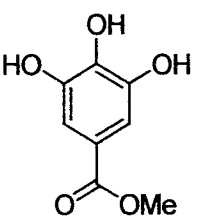

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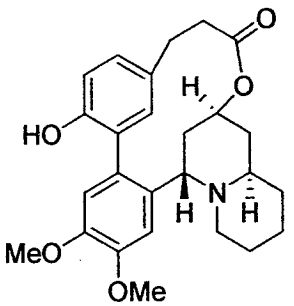
2. Other *Lagerstroemia* genus

In 1971, Ferris, et al. isolated compounds from *L. indica*. Six compounds were identified as decamine (7), decinin (8), decodine (9), dihydroverticillatine (10), lagerine (11) and lagerstroemin (12). (Ferris, et al., 1971)



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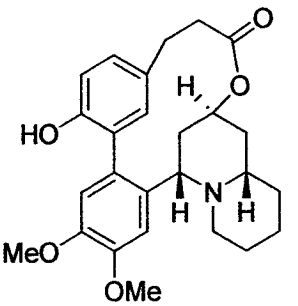

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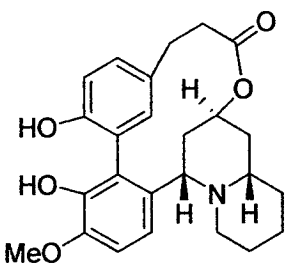

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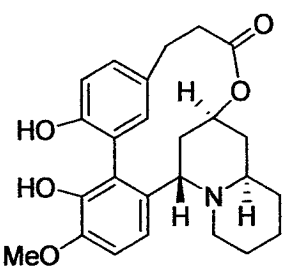

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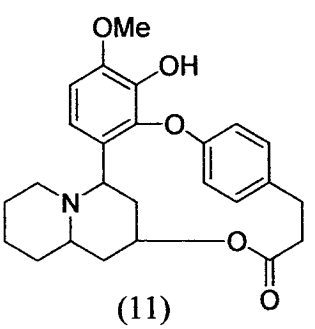

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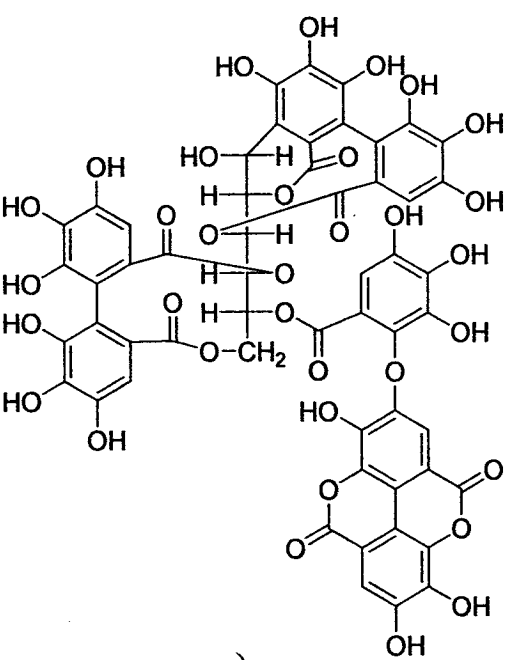

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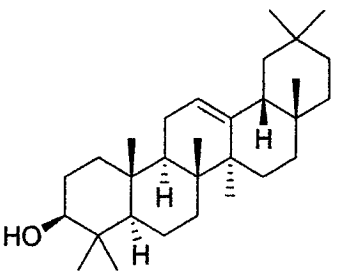
In 1990, Sato and Ueda studied the aerial parts of *L. indica* (except flower). The constituents of the aerial parts were *β*-amyrin (13), *β*-sitosterol (14), ethyl palmitate (15), 2,6,10,15,19,23-hexamethyl-2,6,10,14,18,22-tetracosahexene (16) and ellagic acid (2). (Sato and Ueda, 1990)



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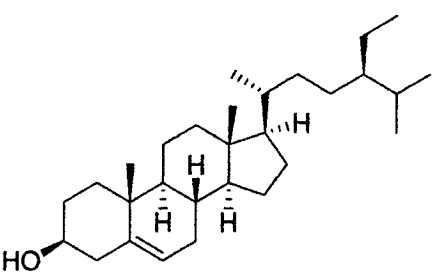

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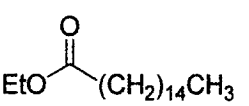

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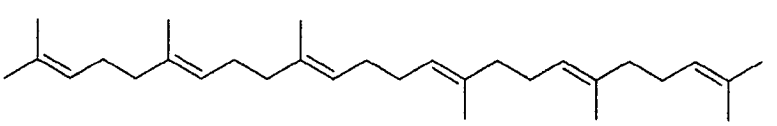

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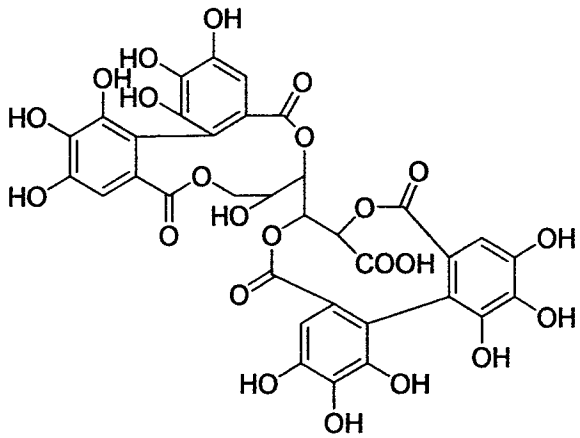
In 1992, three ellagitannins, lagerstannins A (17), lagerstannin B (18) and lagerstannin C (19) having a gluconic acid core, have been isolated from the fruits and leaves of *L. speciosa.* (Tanaka, et al., 1992)



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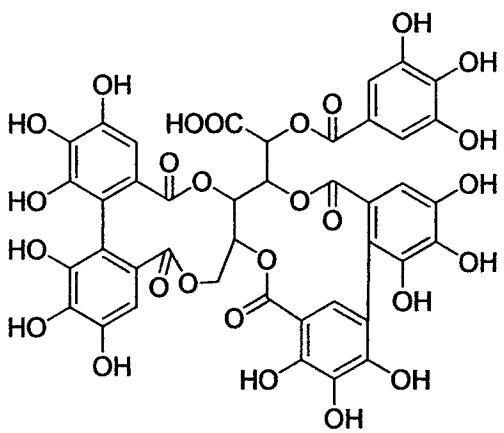

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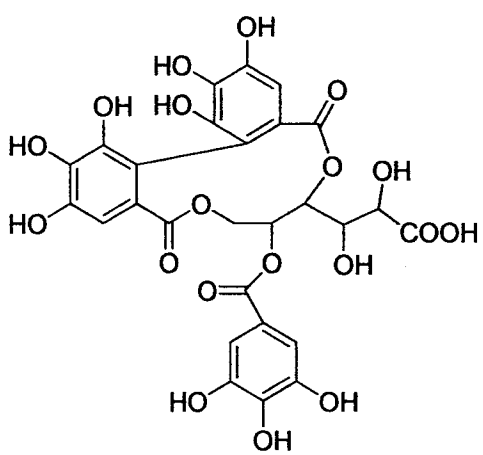

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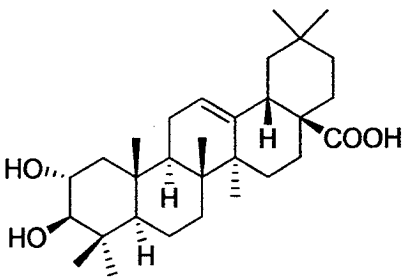
In 1993, two triterpenoids, maslinic acid (20) and corosolic acid (21) were isolated from *L. speciosa*. Corosolic acid was shown to be a glucose transport activator. (Murakami, et al., 1993)



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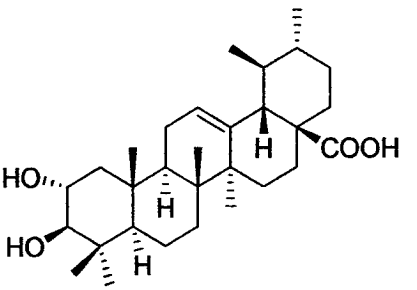

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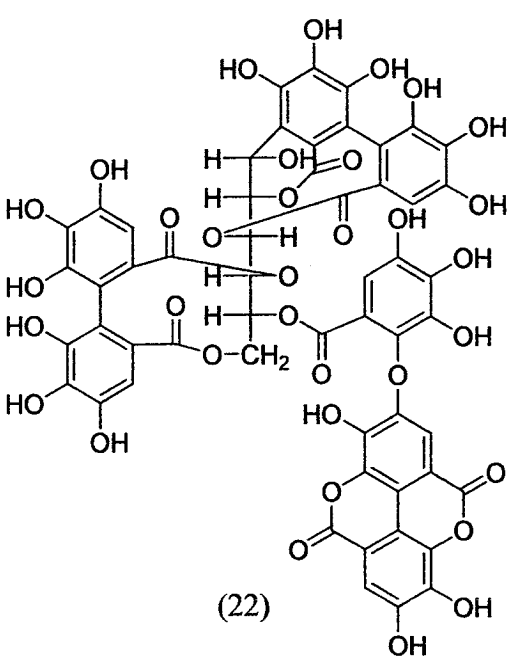
In 2000, Sato, et al. reported the hot water extract and the methanol extract of *L. speciosa* were measured for their antifungal activity against *Arthrinium sacchari* M001 and *Chaetomium funicola* M002 strains. The extracts showed high activity. (Sato, et al., 2000)

In 2002, Hayashi, et al. studied *L. speciosa* extract. Bioassay-guided fractionation of the aqueous acetone extract of the leaves afforded three active ellagitannins, lagerstroemin (12), flosin B (22) and reginin A (23). These compounds increased glucose uptake of rat adipocytes, and could be responsible for lowering the blood glucose level. (Hayashi, et al., 2002)



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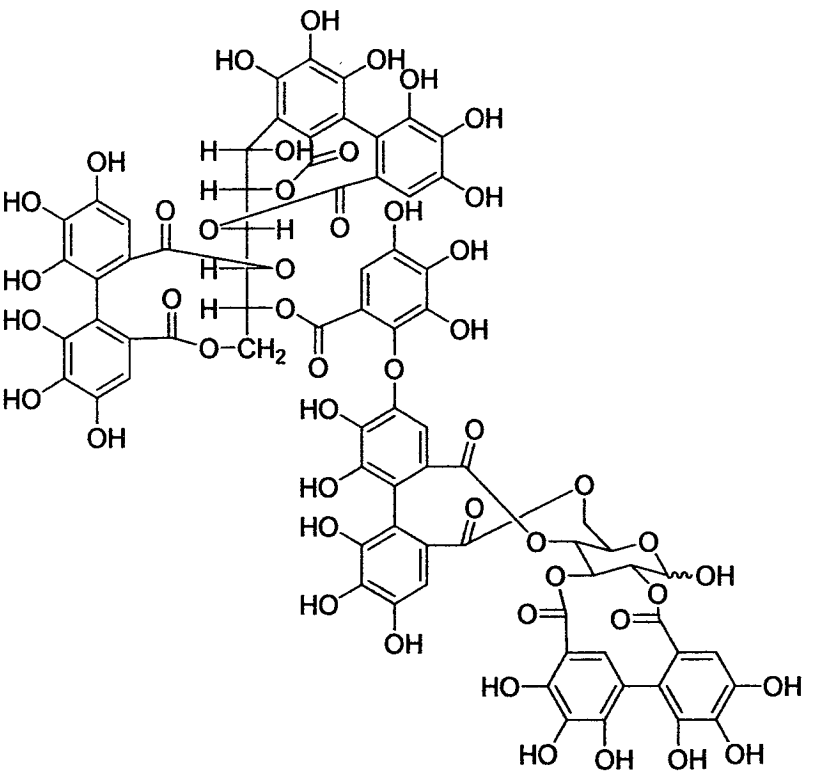

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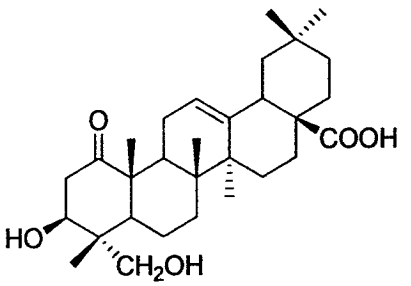
In 2003, Judy, et al. studied the antidiabetic activity of an extract from the leaves of *L. speciosa* standardized to 1% corosolic acid (20) (GlucosolTM). GlucosolTM showed a significant reduction in the blood glucose levels. (Judy, et al., 2003)

In 2003, a new triterpenoid along with four known compounds were isolated from the leaves of *L. speciosa*. The new compound was established as 3*β*, 23-dihydroxy-1-oxo-olean-12-en-28-oic acid (24). Four known compounds were 3*β*-hydroxy-1-oxo-olean-12-en-28-oic acid (virgatic acid) (25), corosolic acid (20), ursolic acid (26) and *β*-sitosterol glucoside (27). (Okada, et al., 2003)



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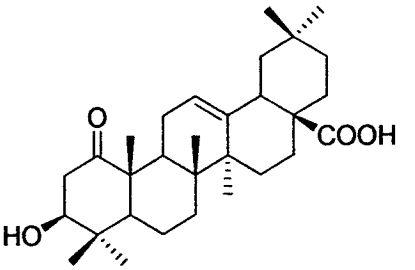

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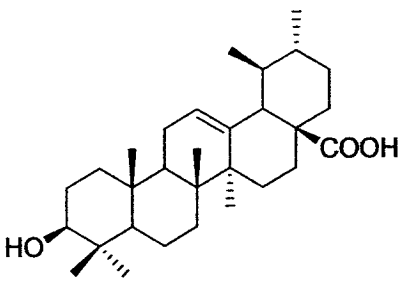

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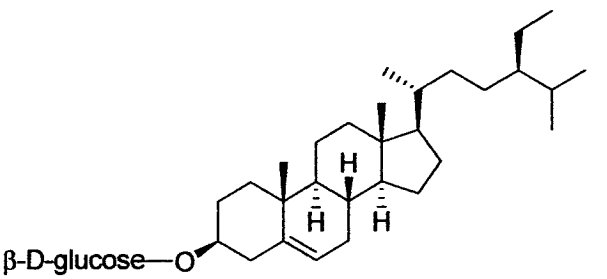
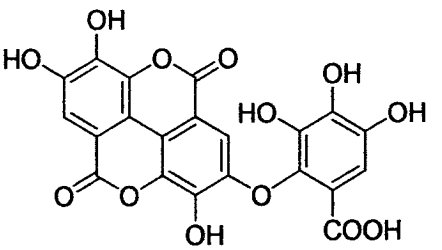


(27)

In 2003, lagerstroemin (12), an ellagitannin isolated from the leaves of *L. speciosa*, was examined for its biological activities. The compound increased the rate of glucose uptake and decreased the isoproterenol-induced glycerol released in rat adipocytes. It increased the Erk activity in Chinese hamster ovary cells expressing human insulin receptors. (Hattori, et al., 2003)

In 2004, Unno, et al. reported valoneic acid dilactone (VAD) (28) and ellagic acid (EA) (2) isolated from the aqueous extracts of the *L. speciosa* leaves. The result demonstrated that the XOD-inhibitory effect of VAD (IC_{50} VAD = 2.5μM, IC_{50} EA = 71.5μM) was stronger than that of allopurinol, a clinical drug used for XOD inhibitor, with a non-competitive mode for the enzyme with respect to xanthine as the substrate. These results may explain and support the dietary use of the aqueous extracts from *L. speciosa* leaves for the prevention and treatment of hyperuricemia. (Unno, et al., 2004)



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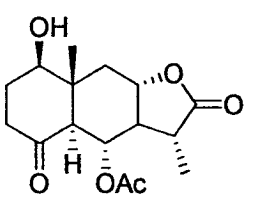
In 2005, Dou, et al. studied the air-dried and powdered branches of *L. calyculata*, *L. floribunda*, and *L. tomentosa* extracted with 95% EtOH. A sesquiterpene, dihydro-β-cyclopyrethrosin (29), a triterpene, betulinic acid (2) and a coumarin, clauslactone-K (31) were isolated from EtOAc extract of *L. calyculata*. Two lignans, lingueresinol (32) and ent-isolariciresinol (33), and four triterpenes, alphitolic acid (34), 3β,29-dihydroxy-olean-12-en-28-oic acid (35), ursolic acid (26) and 2β,3α urs-12-en-28-oic acid (36) were isolated from EtOAc extract of *L. floribunda*. In addition, a norsesquiterpene, (6S,7E,9R)-blumenol A (37) , as well as a triterpene, arjunolic acid (38) were characterized from EtOAc extract of *L. tomentosa*. (Dou, et al., 2005)



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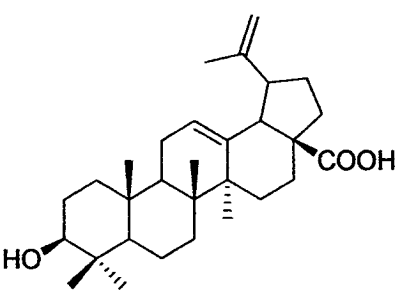

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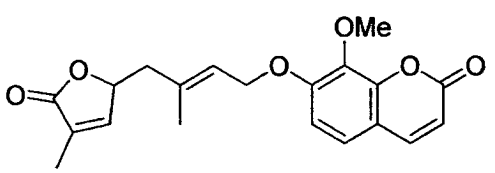

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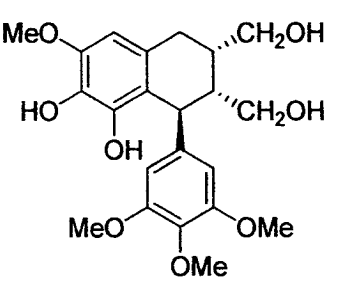

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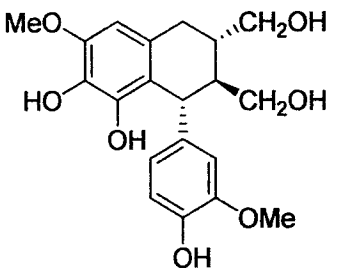

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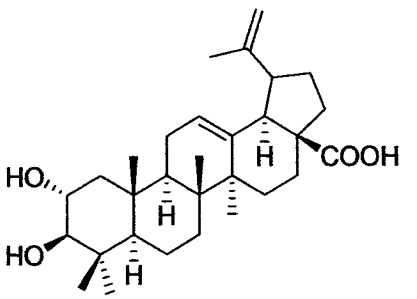

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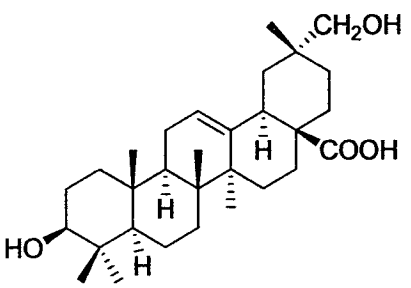

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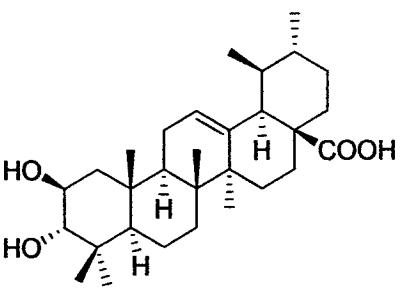

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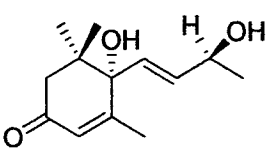

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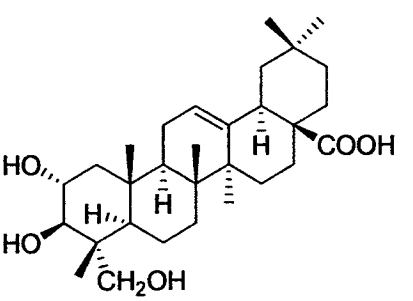

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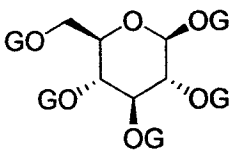
Afterwards, Liu, et al. reported that an extract from *L. speciosa* (banaba) possessed activities both stimulating glucose transport and inhibiting adipocyte differentiation in 3T3-L1 cells. Those two activities were not found in the banaba extract with tannin removed. Tannic acid (39), a major component of tannins, had the same 2 activities as banaba extract. (Liu, et al., 2005)



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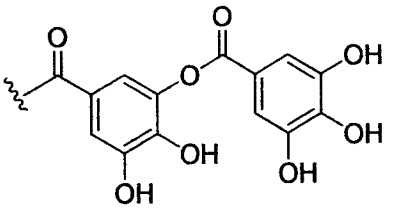
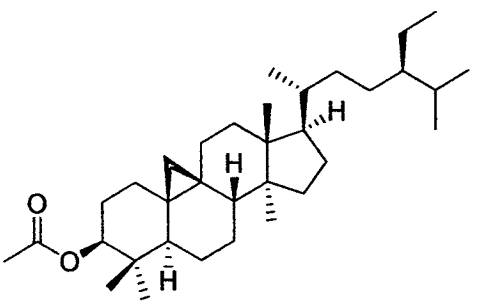


A new compound, 31-norlargerenol acetate (4) was isolated from $CHCl_3$ extract of *L. speciosa* leaves, along with known compounds 24-methylenecycloartanol acetate (40), cycloeucalenol acetate (41), largerenol acetate (42), 31-norlargerenol acetate (43), tinotufolin C (44), tinotufolin D (45), sitosterol acetate (46), phytol (47), lutein (48) and β-sitosterol (14). (Ragasa, et al., 2005)



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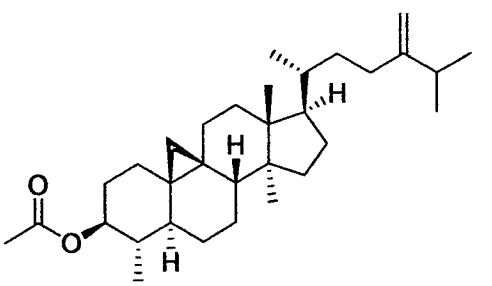

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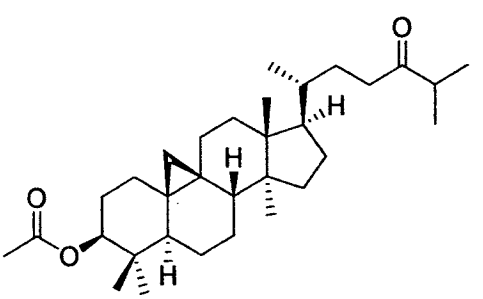

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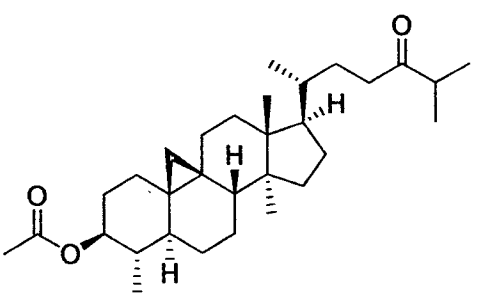

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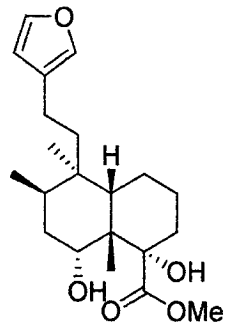

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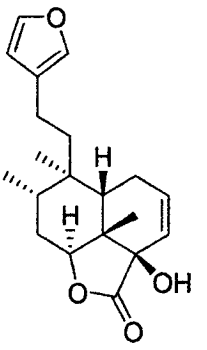

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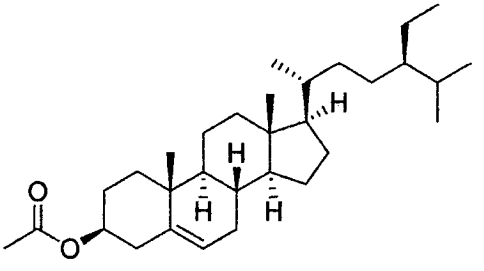

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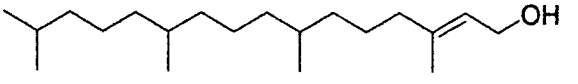

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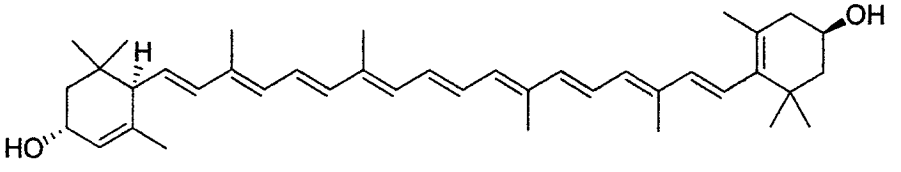
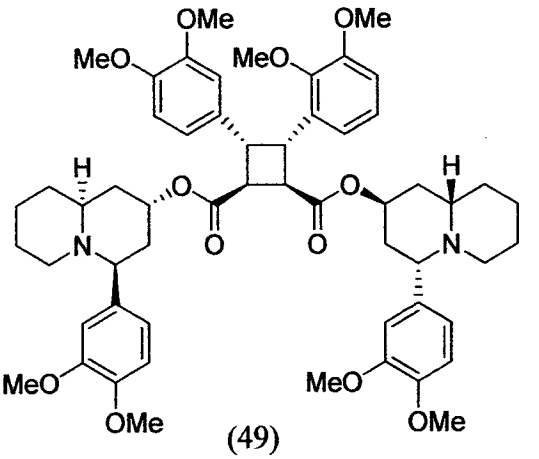


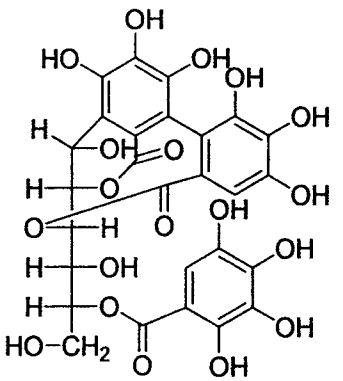
(48)

In 2007, Watanabe, et al. reported a new dimeric Lythraceae alkaloid with a cyclobutane ring, sarusubine A (49), isolated from the leaves of *L. subcostata.* (Watanabe, et al., 2007)



(49)

In 2008, Bai, et al. reported seven ellagitannins, lagerstroemin (12), flosin B (22), epipunicacortein A (50), stachyurin (51), 2,3-(*S*)-hexahydroxydiphenoyl-α/β-D-glucose (52), casuarinin (53) and casuariin (54) together with one ellagic acid sulfate, 3-*O*-methyl-ellagic acid 4'-sulfate (55), ellagic acid (2) and four methyl ellagic acid derivatives, 3-*O*-methylellagic acid (56), 3,3'-di-*O*-methyl ellagic acid (57), 3,3',4-tri-*O*-methyl ellagic acid (58) and 3,4,8,9,10-pentahydroxydibenzo[b,d]pyran-6-one (59), isolated from the leaves of *L. speciosa.* Other known compounds, including corosolic acid (20), isoquercitrin (60), gallic acid (61), caffeic acid (62), *p*-coumaric acid (63), kaempferol (64), quercetin (65) and 4-hydroxybenzoic acid (66), were also isolated from the same plant. This study was the first to report an inhibitory effect for methyl ellagic acid derivatives. The obtained ellagitannins exhibited strong activities in both stimulating insulin-like glucose uptake (12, 42 and 44) and inhibiting adipocyte differentiation (12 and 51) in 3T3-L1 cells. Meanwhile, ellagic acid derivatives (56-59) showed an inhibitory effect on glucose transport assay. (Bai, et al., 2008)



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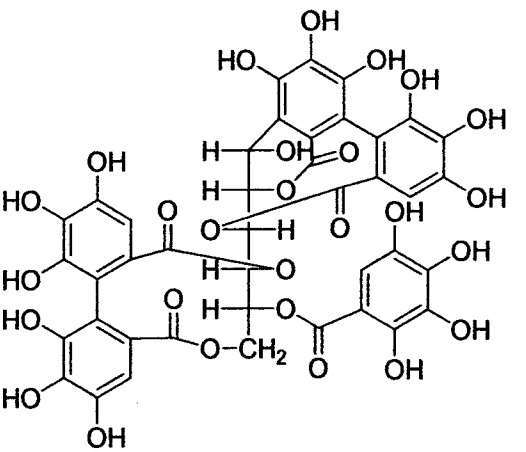

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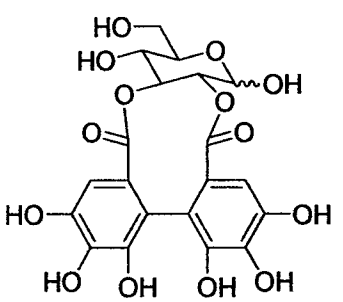
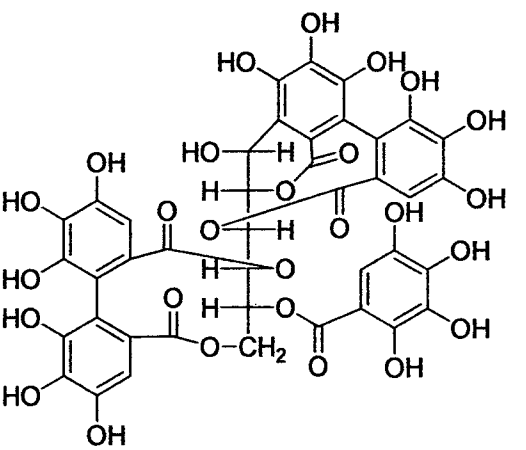
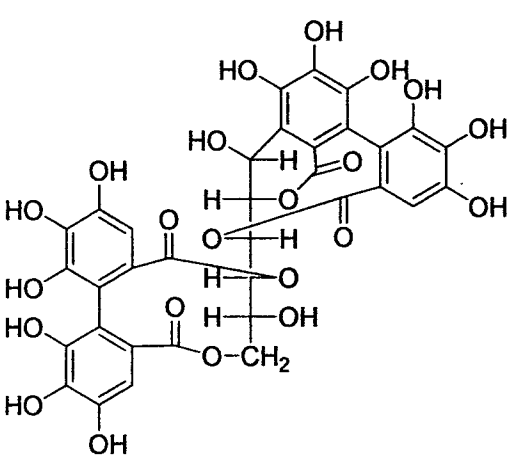


(52)



(53)



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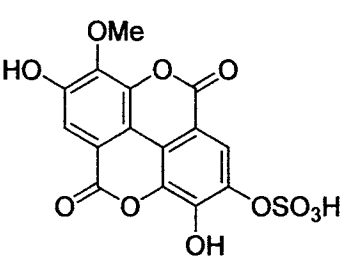

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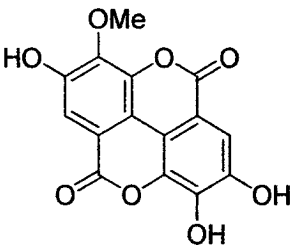
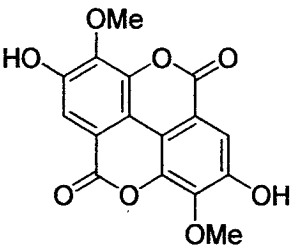


(56)



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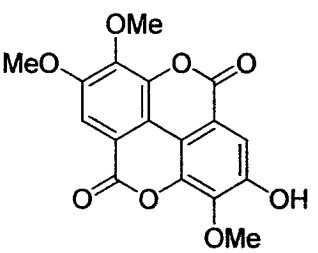
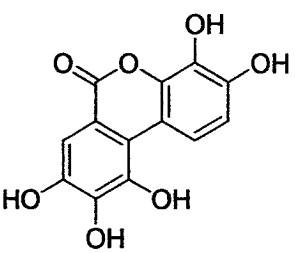
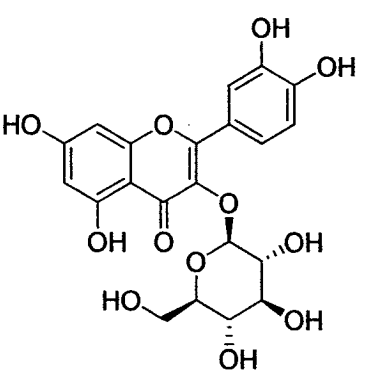


(58)



(59)



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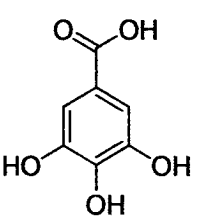
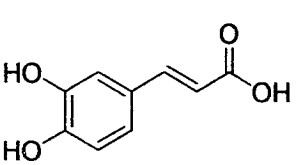


(61)



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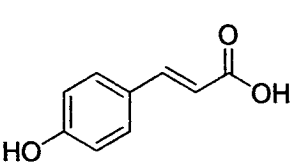
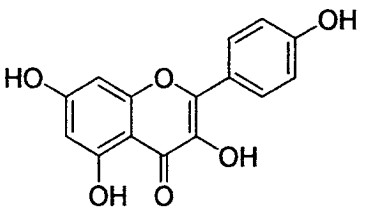
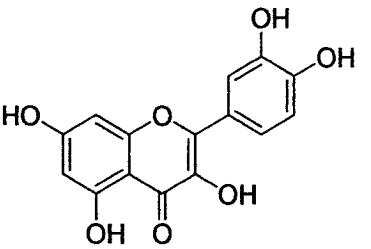


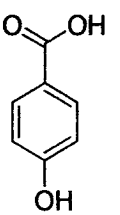
(63)



(64)

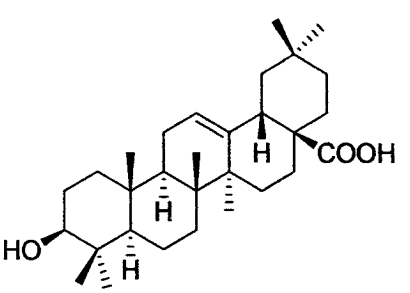


(65)



(66)

In 2009, Hou, et al. studied the potential antidiabetic activity of ethyl acetate extract of the leaves of *L. speciosa* (LSL) using alpha-amylase and alpha-glucosidase inhibition assay. Six pentacyclic triterpenes, oleanolic acid (67), arjunolic acid (38), asiatic acid (68), maslinic acid (69), 23-hydroxyursolic acid (70) and corosolic acid (20) were isolated from LSL. They exhibited no or weak inhibitory activity against alpha-amylase and middle alpha-glucosidase inhibitory activities. Corosolic acid showed the best bioactivity against alpha-glucosidase (IC_{50} = 3.53 μg/mL). (Hou, et al., 2009)



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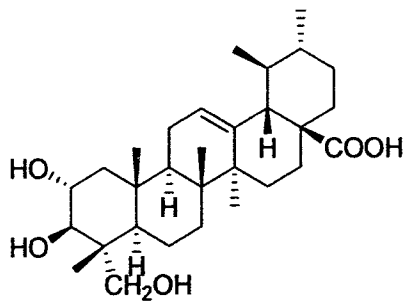
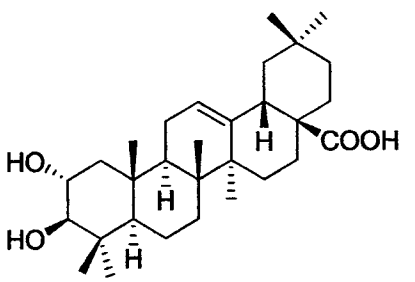


(68)



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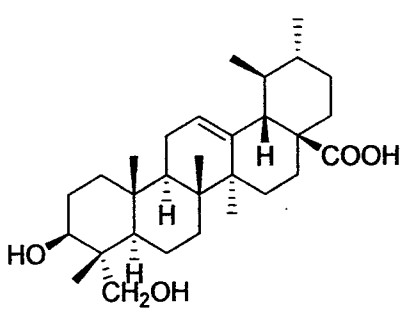
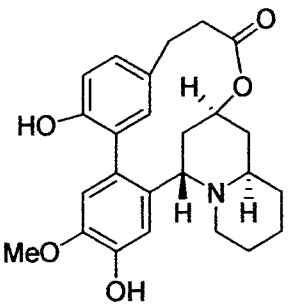
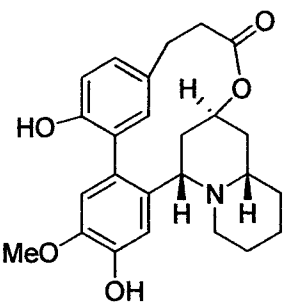


(70)

In 2009, Kim, et al. reported two new biphenylquinolizidine alkaloids, 5-epi-dihydrolyfoline (71) and its stereoisomer, dihydrolyfoline (72) isolated from the aerial parts of *L. indica*. (Kim, et al., 2009)

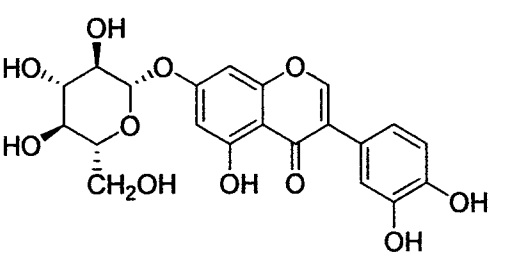


(71)



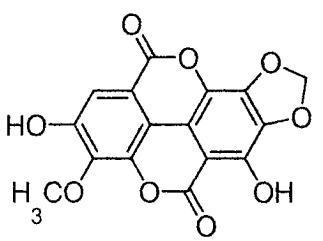
(72)

In 2010, Choi, et al. reported orobol 7-*O*-D-glucoside (73) from *L. speciosa* which was a novel drug class with broad spectrum antiviral activity against an anti-human rhinovirus (HRV) species A (HRV1B, HRV2, HRV15 and HRV40) and species B (HRV3, HRV6 and HRV14), as well as pleconaril-resistant virus (HRV5). (Choi, et al., 2010)

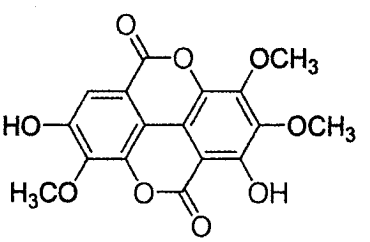


(73)

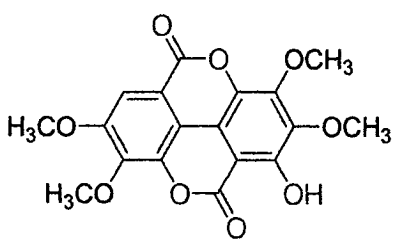
In 2013, Huang, et al. reported fourteen compounds from *Lagerstroemia speciosa*, including four triterpenes; ursolic acid (26), corosolic acid (20), asiatic acid (68) alphitolic acid (68), eight ellagic acids; ellagic acid (2),3-*O*-methyl ellagic acid (56),3,3'-di-*O*-methyl ellagic acid (57), 3,3',4-tri-*O*-methyl ellagic acid (58), 3'-*O*-methyl-3,4-methylenedioxy ellagic acid (74), 3,4,3'-tri-*O*-methyl flavellagic acid (75), 3,4,3',4'-tetra-*O*-methyl flavellagic acid (76), 3',4'-di-*O*-methyl-3,4-methylenedioxy flavellagic acid (77), one coumarin; 6,7-dihydroxy coumarin (78) and one neolignan; (+)-dihydrodehydro diconiferyl alcohol 9'-*O*-sulfate (79). It was the first report of (+)-dihydrodehydro diconiferyl alcohol 9'-*O*-sulfate from the genus *Lagerstroemia* and the first report of compounds (74) - (77) from the family Lythraceae. (Huang, et al., 2013)



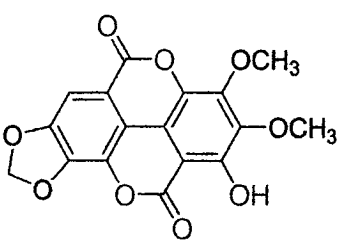
(74)



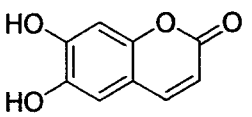
(75)



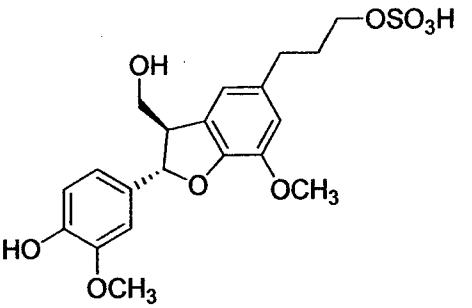
(76)



(77)



(78)



(79)

In 2013, Nutan, et al. studied the anti-HIV activity of the extracts from the leaves and stems of *L. speciosa* (banaba). The aqueous and ethanolic extracts showed inhibition of HIV-1 (IC_{50} = 1 to 25 μg/mL). The active components responsible for anti-HIV activity were gallic acid and ellagic acid, through inhibition of reverse transcriptase and HIV protease, respectively. (Nutan, et al., 2013)