Supporting Information

Phloroglucinol and its derivatives: Antimicrobial properties towards microbial pathogens

Fazlurrahman Khan[1]*, Nazia Tabassum[2], Nilushi Indika Bamunuarachchi[3], and Young-Mog Kim[1, 4*]

[1]*Research Center for Marine Integrated Bionics Technology, Pukyong National University, Busan 48513, Republic of Korea*

[2]*Industry 4.0 Convergence Bionics Engineering, Pukyong National University, Busan 48513, Republic of Korea*

[3]*Department of Fisheries and Marine Sciences, Ocean University of Sri Lanka, Tangalle 82200, Sri Lanka*

[4]*Department of Food Science and Technology, Pukyong National University, Busan 48513, Republic of Korea*

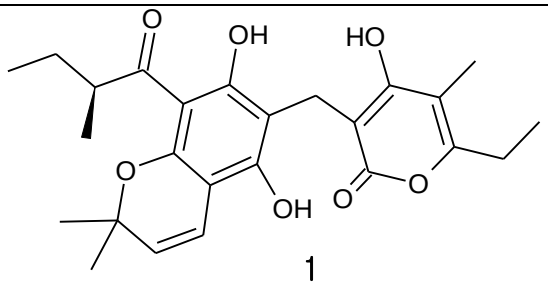
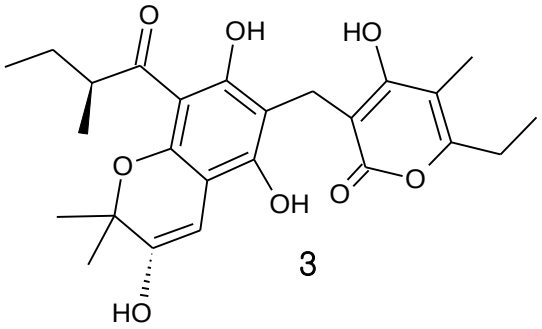
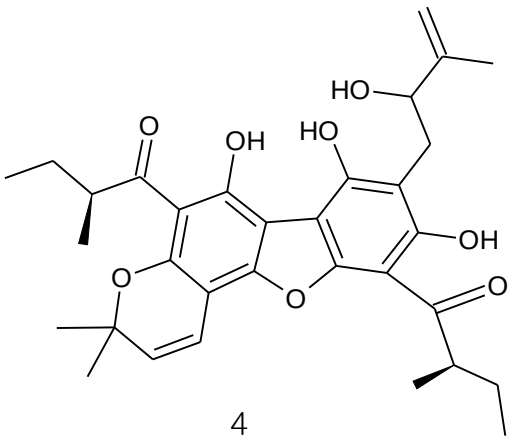
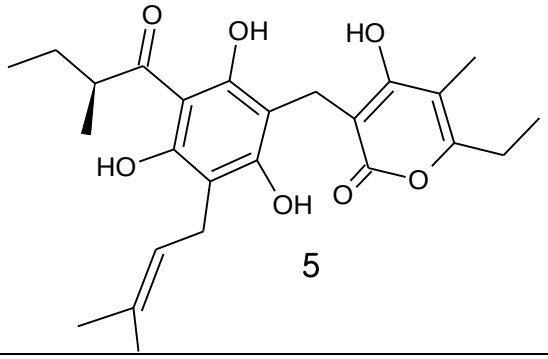
Running head: Antimicrobial properties of phloroglucinol and its derivatives

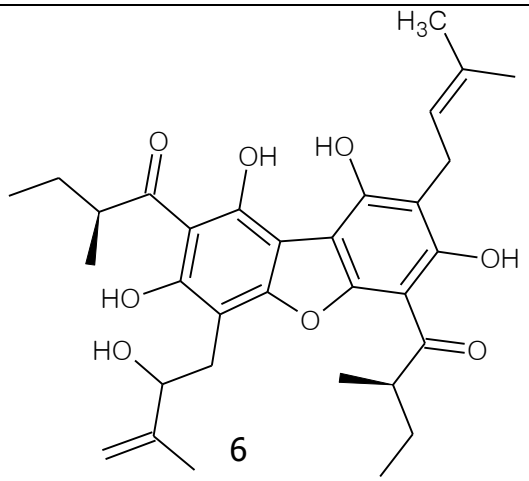
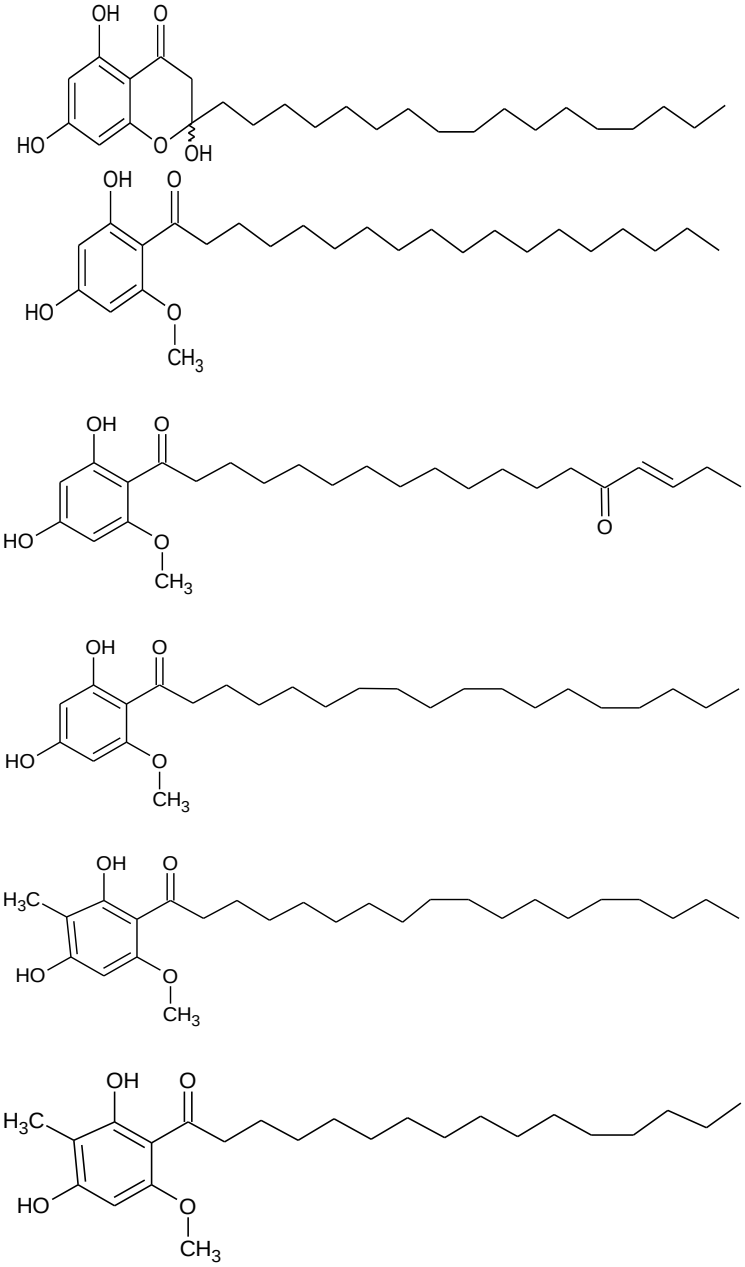
*Corresponding author: Fazlurrahman Khan and Young-Mog Kim

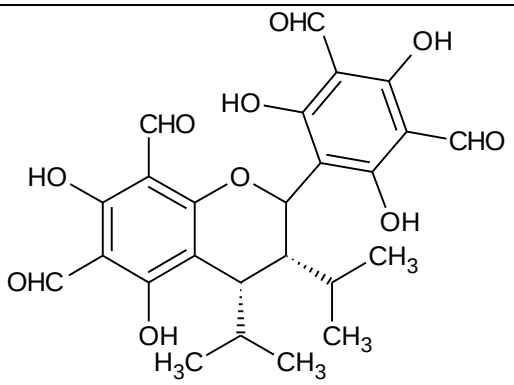
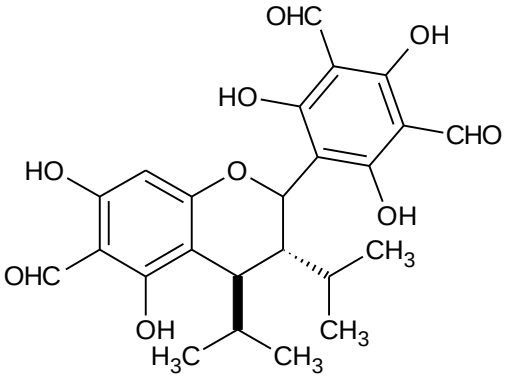
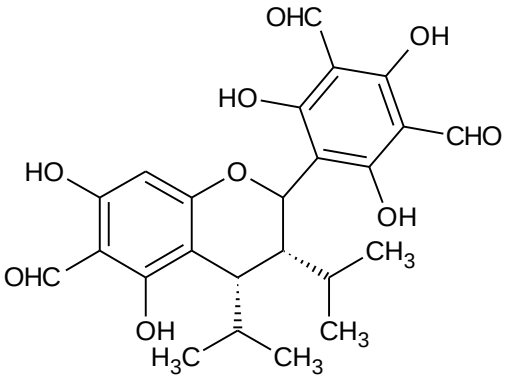
Phone: +82-51-629-5832; Fax: +82-51-629-5824

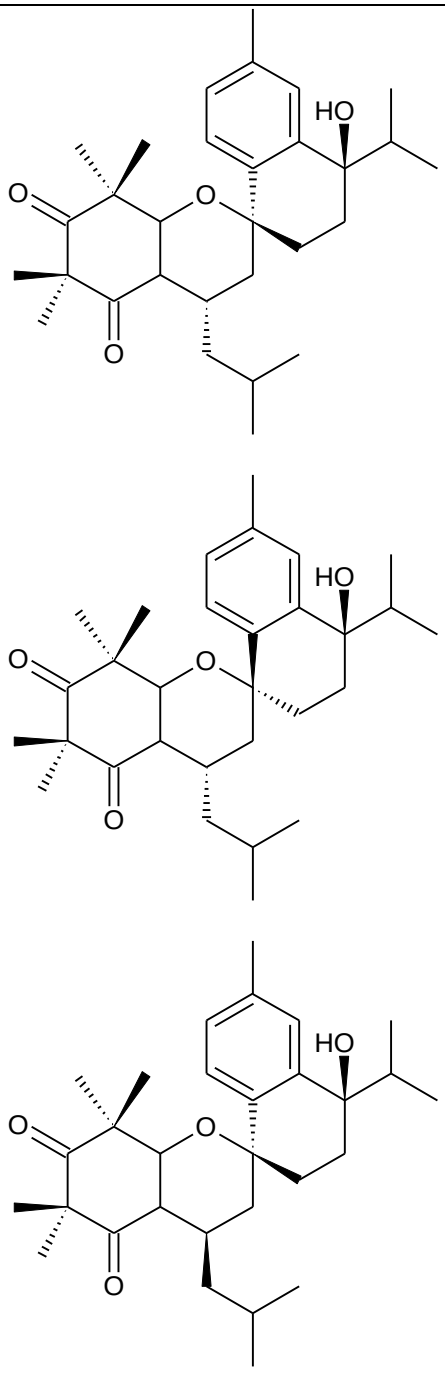
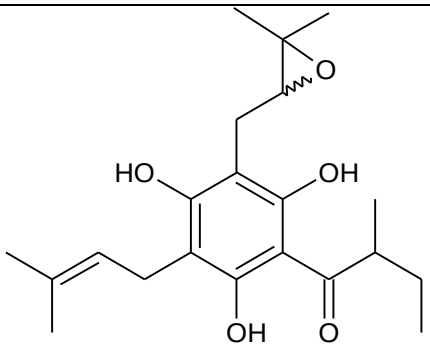
E-mail: fkhan055@pknu.ac.kr and ymkim@pknu.ac.kr

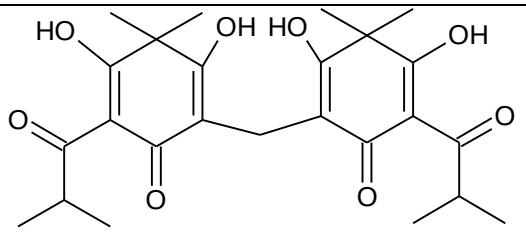
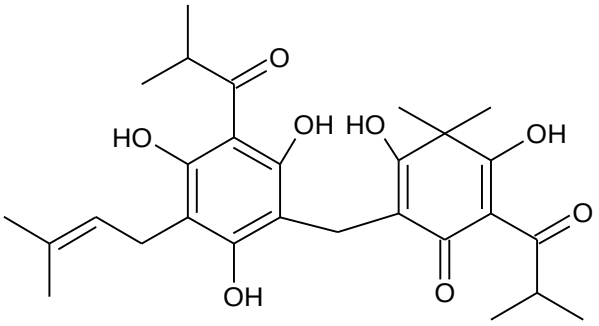
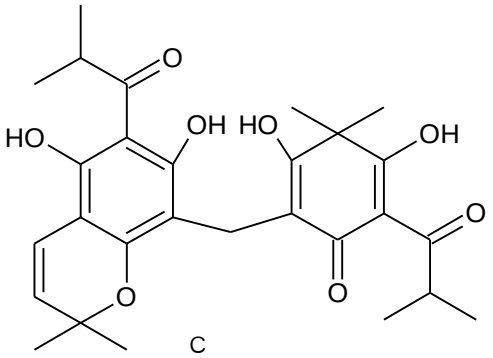
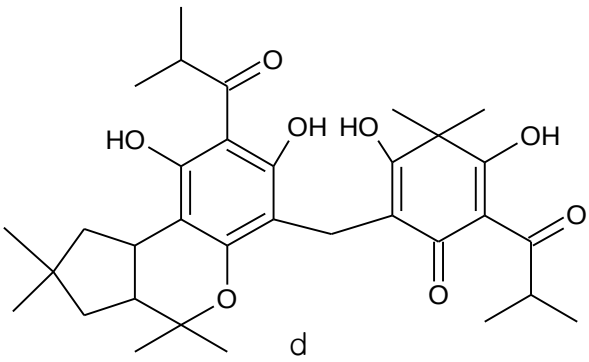
Table S1: Natural and synthetic phloroglucinol derivatives as antibacterial, antifungal, and antiviral activities

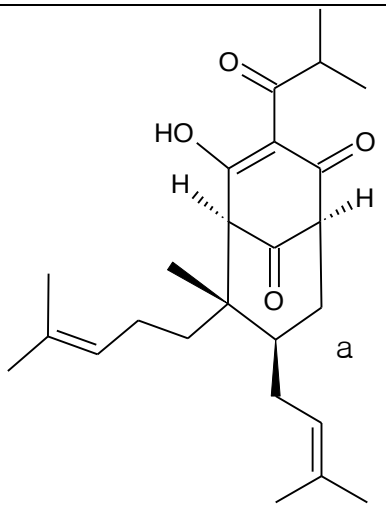
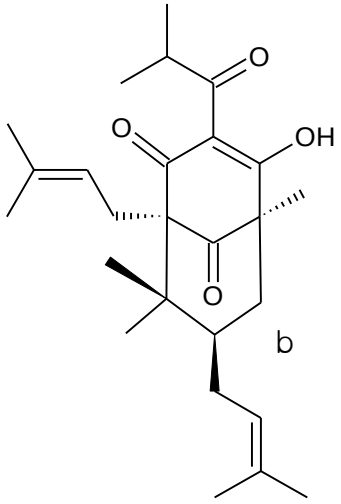
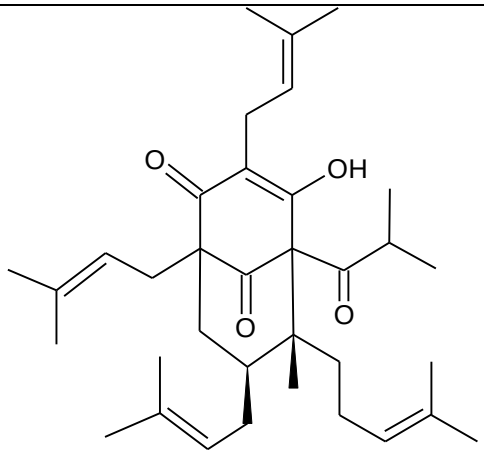
Phloroglucinol and its derivatives	**Sources**	**Chemical Structures**	**References**
• Phloroglucinol α-pyrones (1-3) • Dibenzofuran (4) • 23-methyl-6-o-demethylauricepyrone (5) • Achyrofuran (6)	*Achyrocline satureioides*	 1  3  4  5	[1]

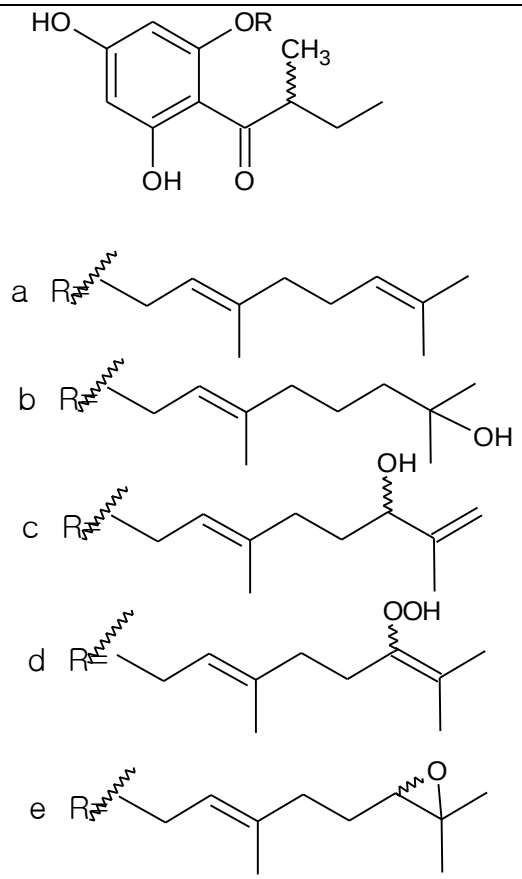
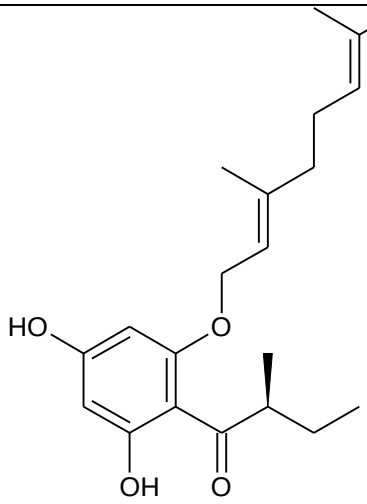
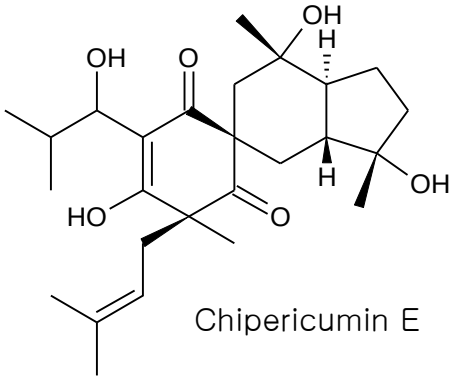
		 6	
Acylphlorogluci nol derivative	*Syzygim oblatum*		2

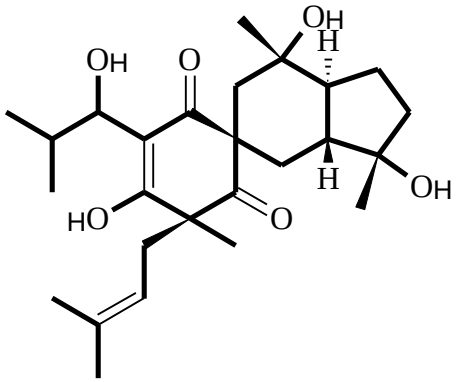
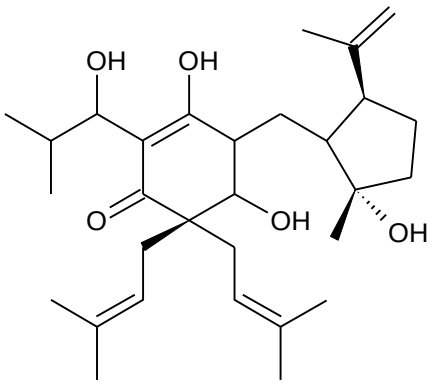
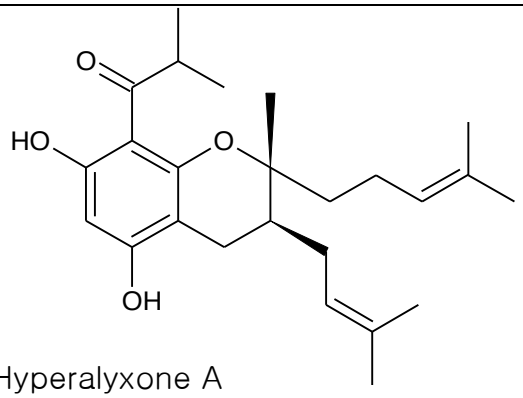
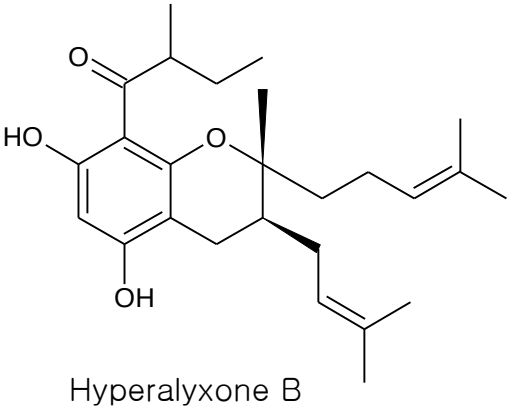
Sideroxylonal A, C, and loxophlebal A	*Eucalyptus loxophleba foliage*	 Sideroxylonal A  Sideroxylonal C  Loxophlebal A	3

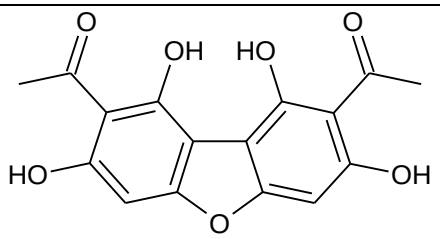
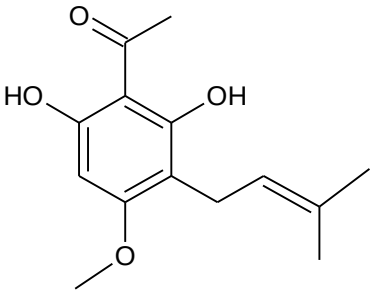
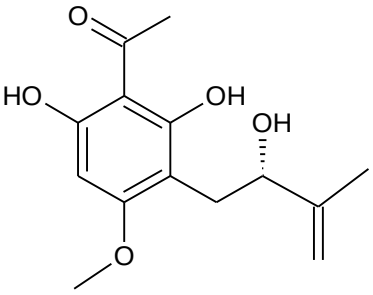
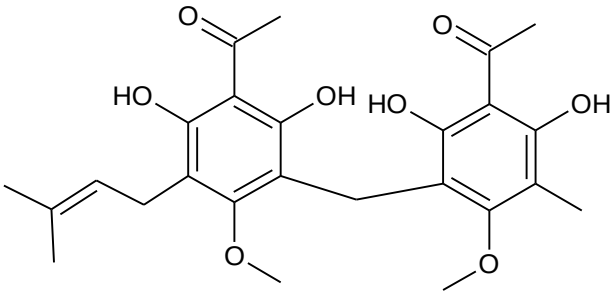
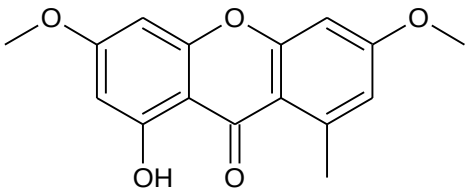
Rhotomentodiones (polymethylated phloroglucinol meroterpenoids)	*Rhodomyrtus tomentosa*		4
Acylphlorolucinol	*Hypericum foliosum*		5

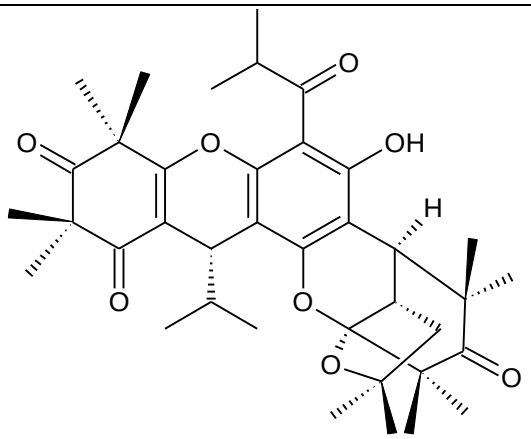
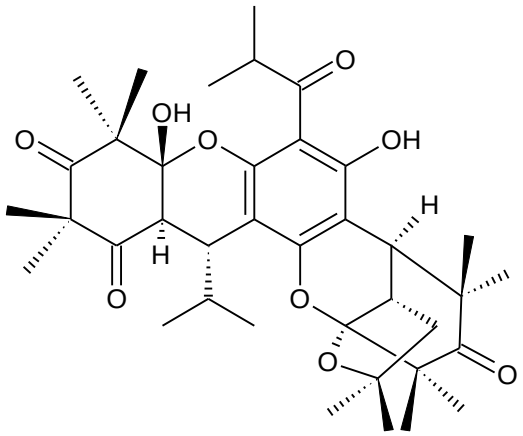
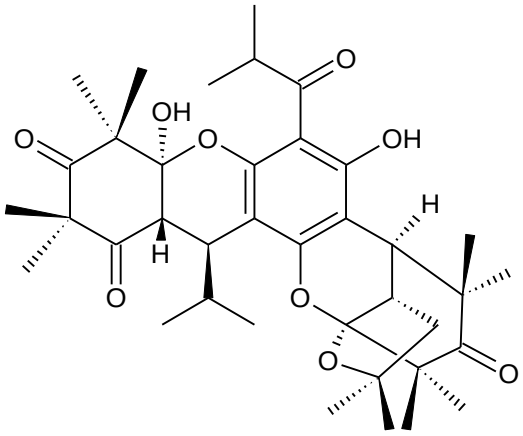
• Japonicine A (a) • Uliginosin A (b) • Isouliginosin B (c) • Hyperbrasilol A (d)	*Hypericum brasiliense*	 a  b  c  d	6

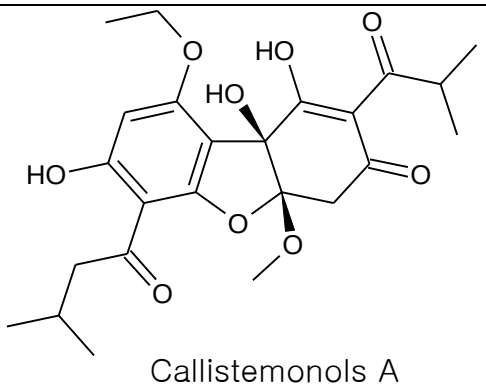
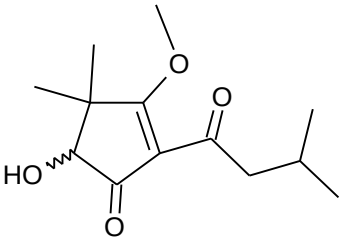
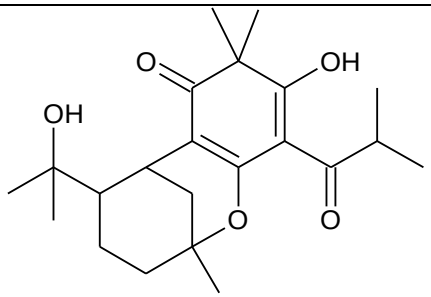
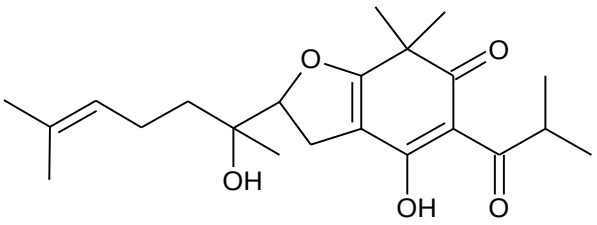
Hyperatomarin	*Hypericum atomarium* ssp. *degenii*	 	7
Hyperforin (acylphloroglucinol)	*Hypericum perforatum*		8

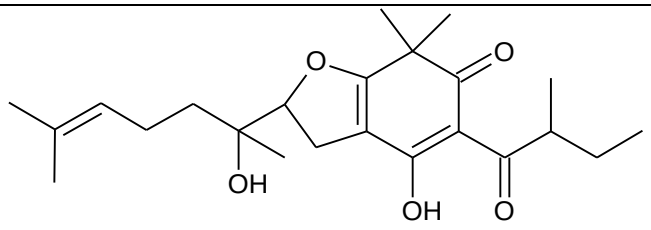
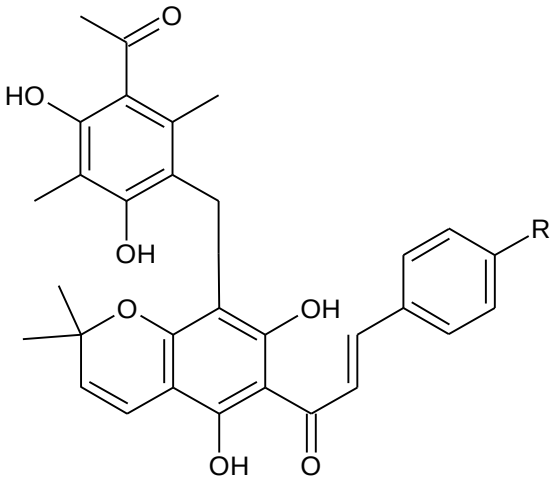
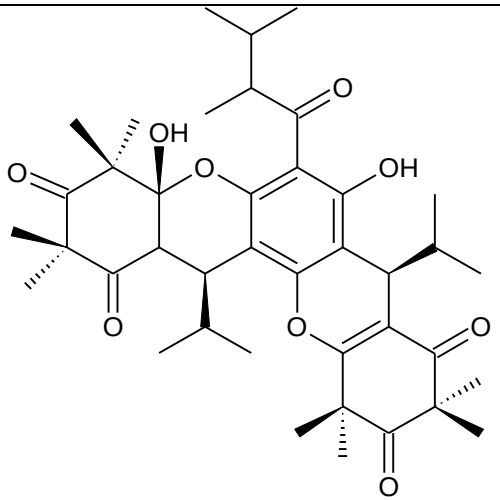
Olympicin A	*Hypericum olympicum* L.cf. *uniflorum*		9
Acylphlorogluci nol compound	*Hypericum olympicum* L.cf. *uniflorum*		10
Chipericumin E Hypercalin C	*Hypericum riparium*		11

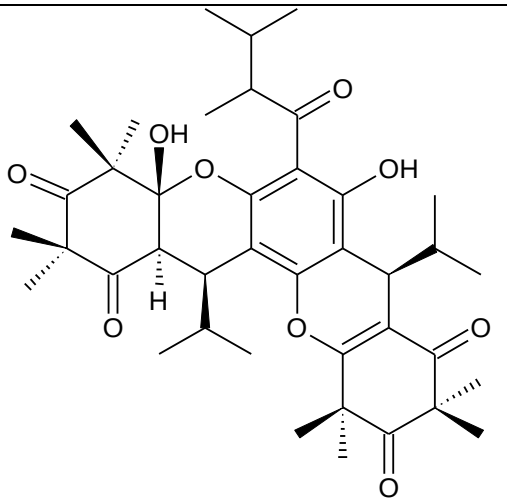
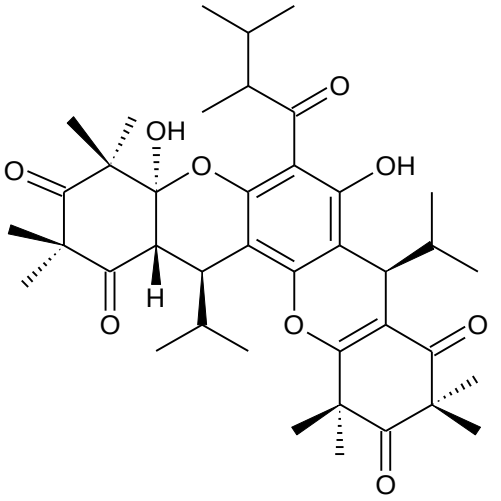
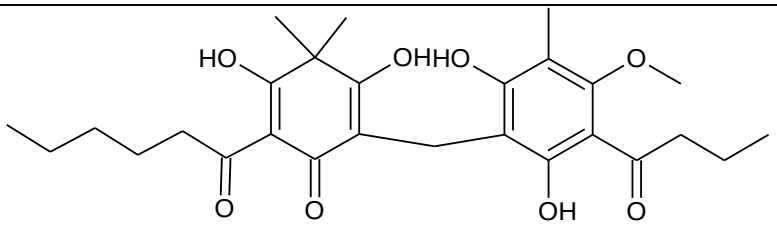
		  Hypercalin C	
Hypercalyxone A and Hypercalyxone B	*Hypericum amblycalyx*	 Hyperalyxone A  Hyperalyxone B	12

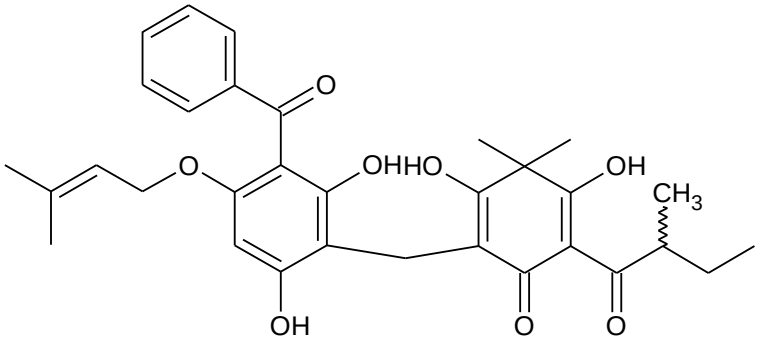
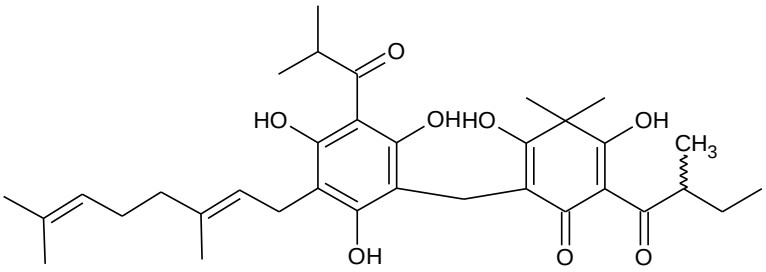
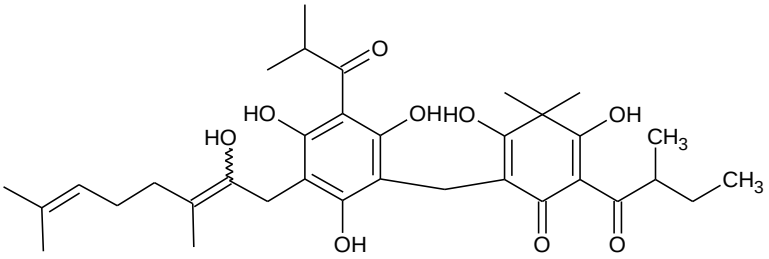
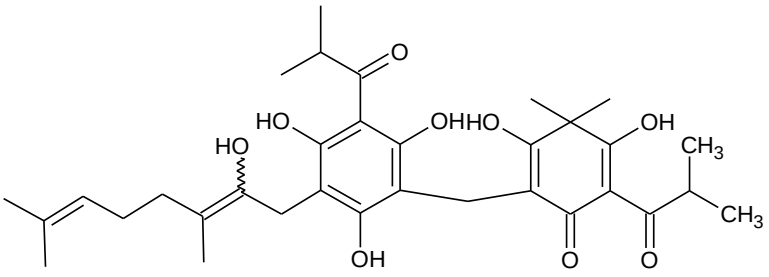
Dibenzifuran type Phloroglucinol	*Myrtus communis* Linn.		13
Acylphlorogluci nol compounds	*Mallotus oppositifolius (Geisler) Mull. Arg.*	 Acronyculatin S  Acronyculatin T  Acronyculatin T 	14

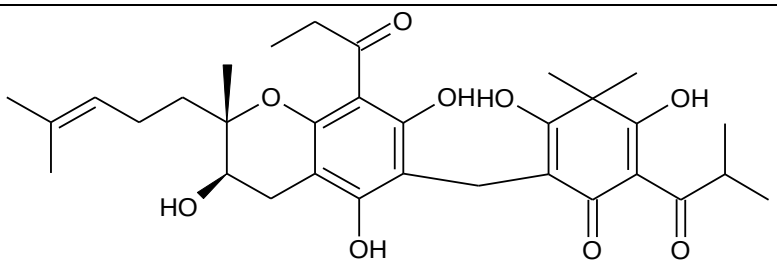
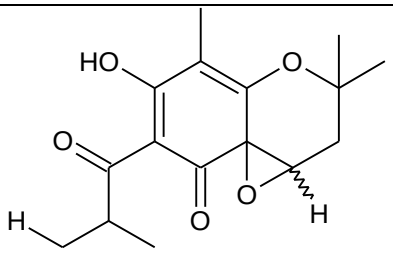
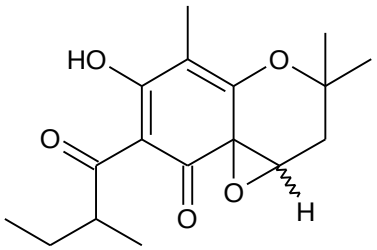
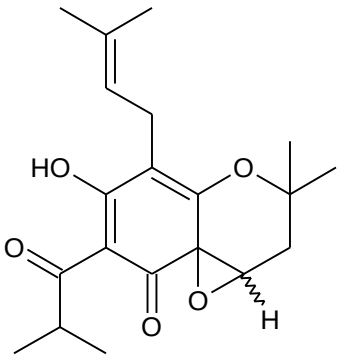
Triketone-phloroglucinol-triketone	*Myrtus communis*	 Myrtucyclitones A  Myrtucyclitones B  Myrtucyclitones C	15

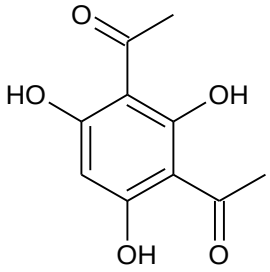
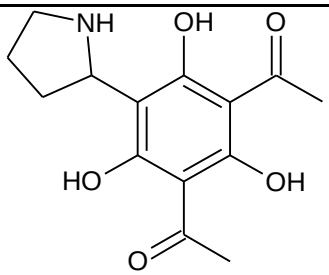
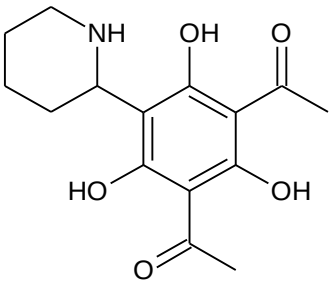
Acylphlorogluc inol derivatives	*Callistemon viminalis*	 Callistemonols A  Callistemonols B	16
Dimethylated acylphlorogluci nol meroterpenoids	*Hypericm elodeoides*	 Elodeoidols E  Elodeoidols H	17

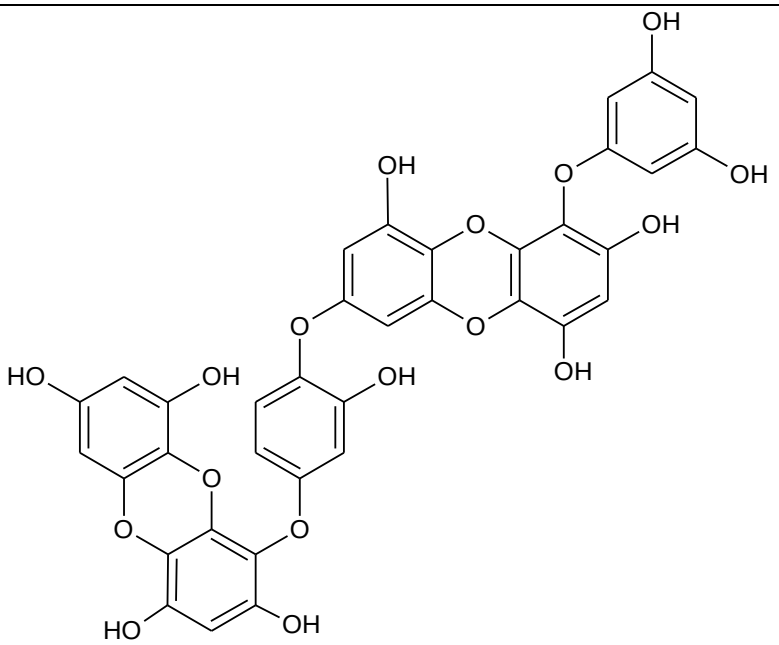
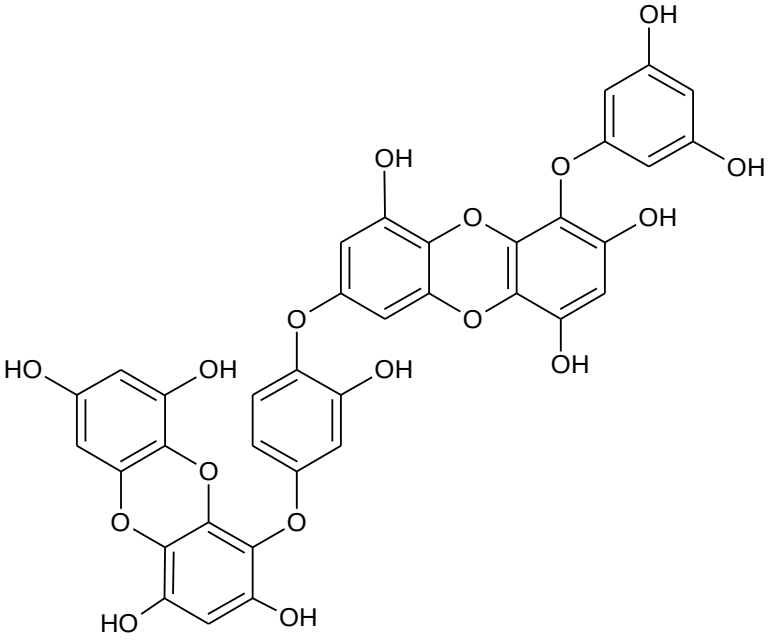
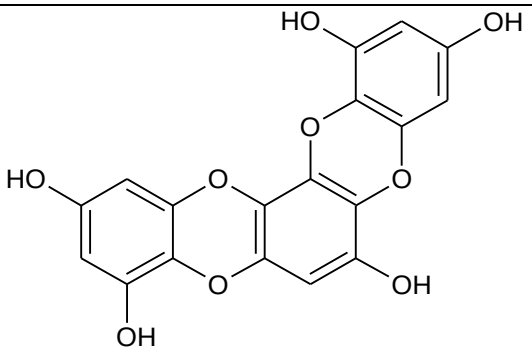
		 Elodeoidols I	
• Rottlerin • 4-Hydroxyrottlerin	*Mallotus philippensis*	 R= H, OH	18
• Myrtucomvalone F • Myrtucommulone D • Callistenone D	*Myrtus communis*	 Myrtucomvalone F	19

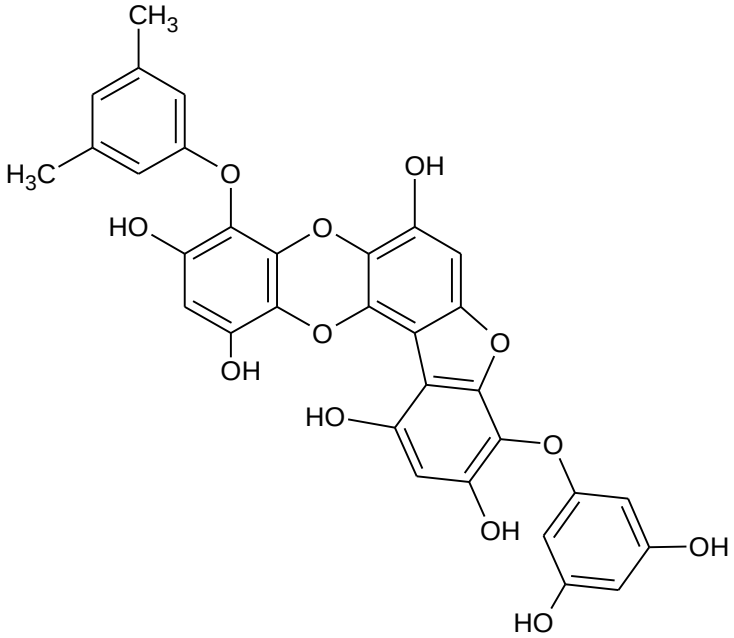
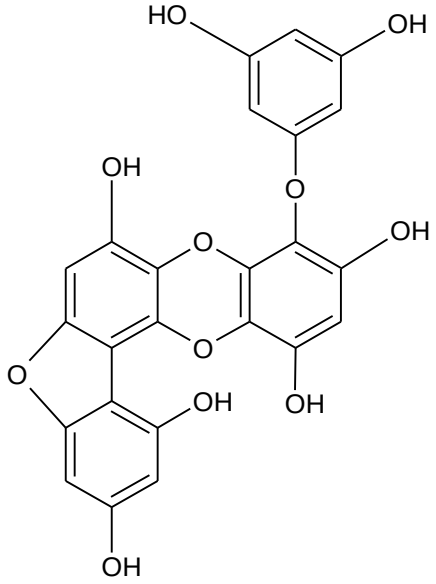
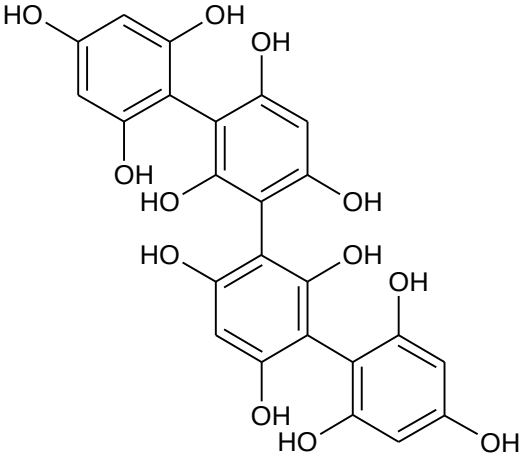
		 Myrtucommulone D  Callistenone D	
Aspidin VB	*Psiloxylon mauritianum*		20

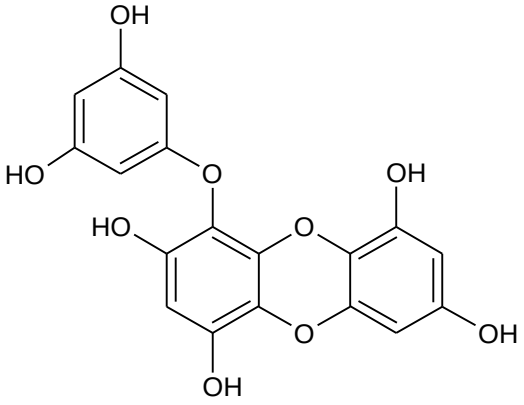
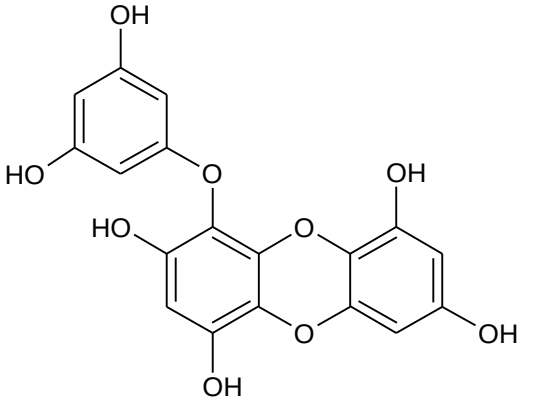
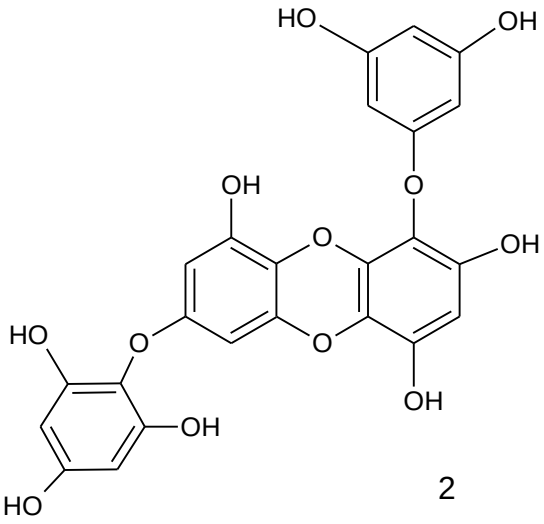
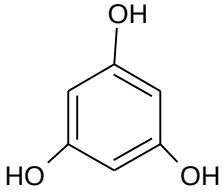
Dimeric acylphlorogluci nol	*Hypericum japonicum*	 Hyperjaponicols A  Hyperjaponicols B  Hyperjaponicols C  Hyperjaponicols D	21

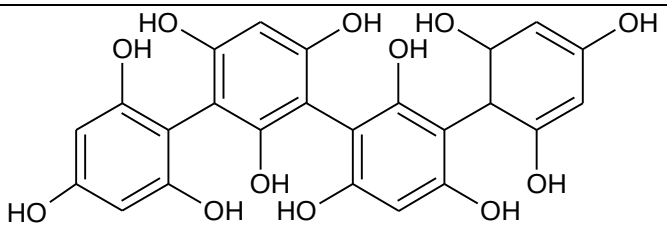
		 Sarothralen C	
Prenyolated acylphlorogluci nols	*Psorothamnu s fremontii*	 Psorothatins A  Psorothatins B  Psorothatins C	22

2,4-Diacetylphloroglucinol	*Pseudomonas fluorescens, Pseudomonas* sp. AMSN, and *Pseudomonas protegens*		23-25
Pyrrolidinyl and piperidinyl substituted 2,4-diacetylphloroglucinol	*Pseudomnas protegens* UP46	 (Pyrrolidin-2-yl)DAP  6-(piperidin-2-yl)DA	26

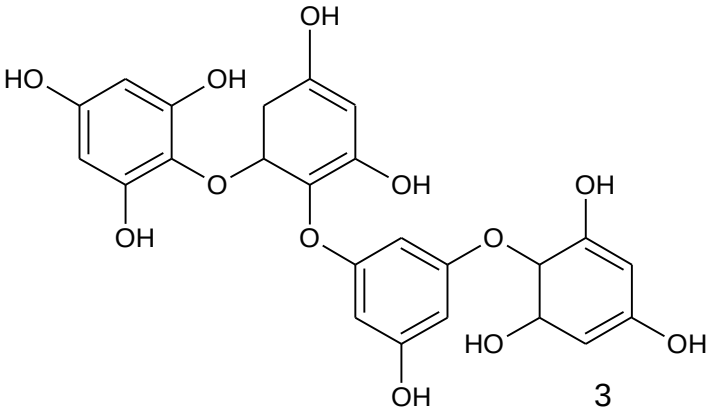
Dieckol	*Ecklonia stolonifera*		27
Dieckol	*E. bicyclis*		28
Dioxinodehydroeckol	*E. bicyclis*		28

Phlorofucofuroeckol-A	*E. bicyclis*		28
Fucofuroeckol-A	*Eisenia bicyclis*		29
Phlorotannin	*Sargassum thunbergii*		30

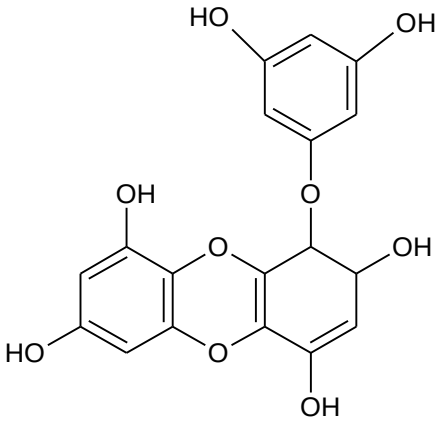
Eckol	*Ecklonia cava*		31
Eckol 1, 7-Phloroeckol **2**	*E. bicyclis*	 1  2	28
Phlorotannin extraction Phloroglucinol (1) Tetrafucol A(2) Tetraphlortol B (3) Eckol (4)	*Laminaria digitata*	 1	32


HO
OH
HO
OH
OH
OH
OH
HO
OH
HO
OH
OH
OH

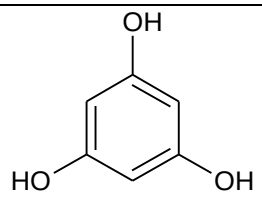
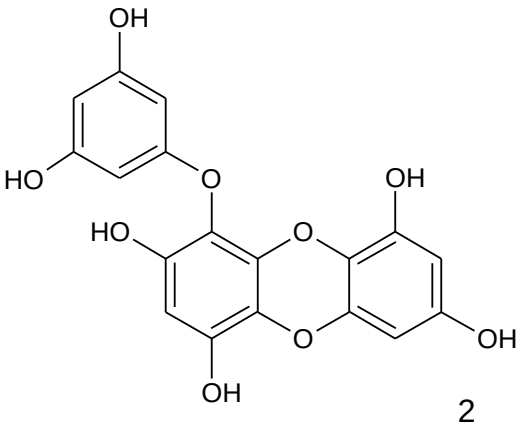
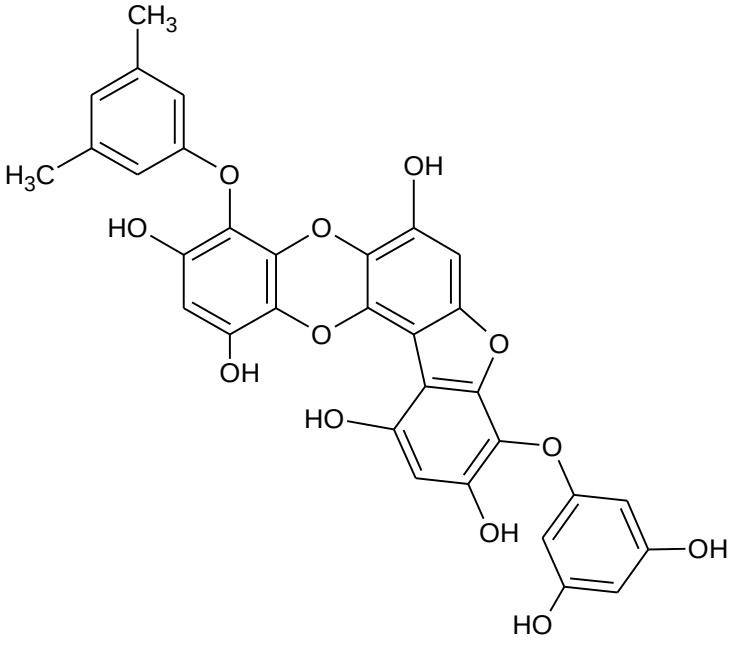
2

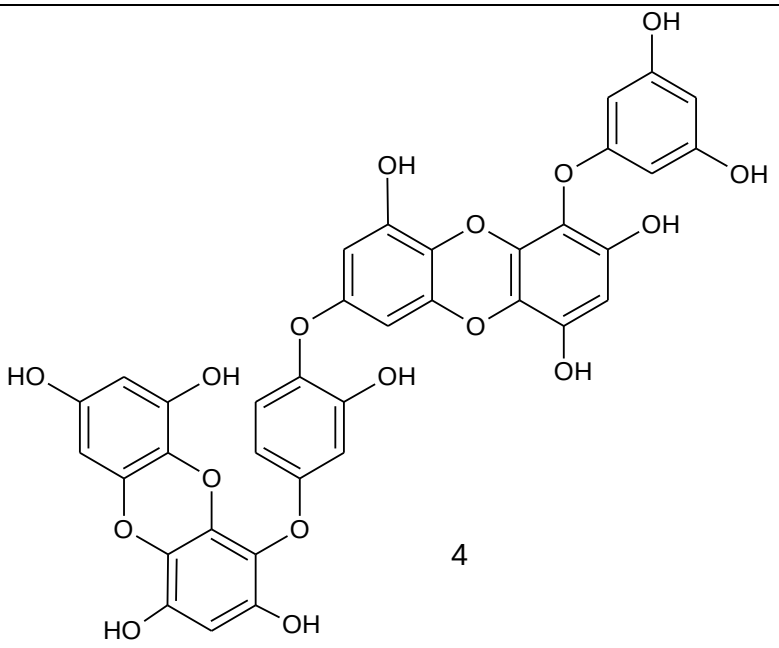
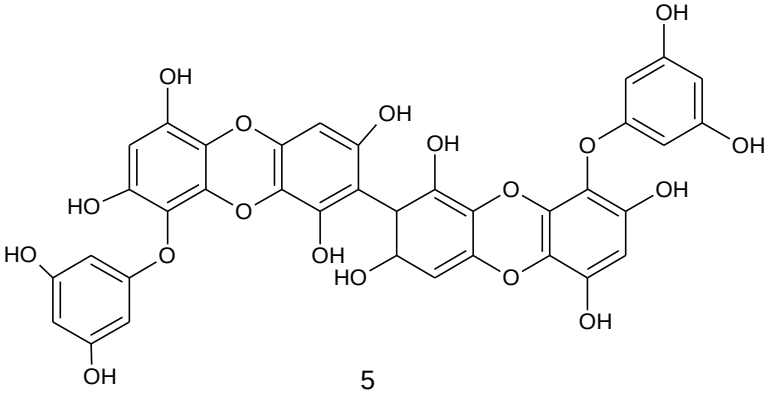
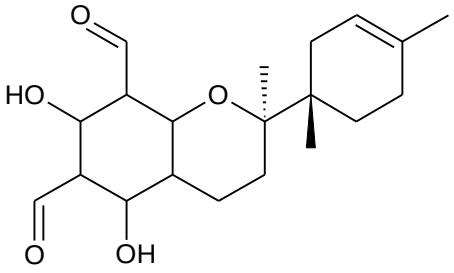
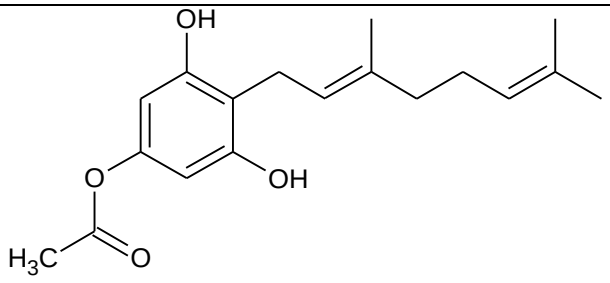

OH
HO
OH
O
OH
OH
O
O
OH
HO
OH
OH

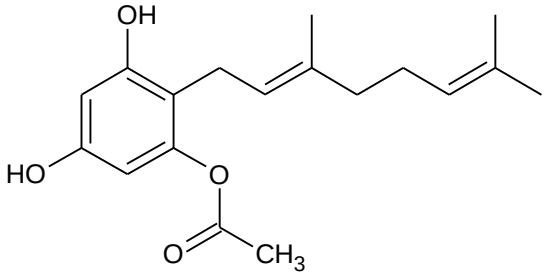
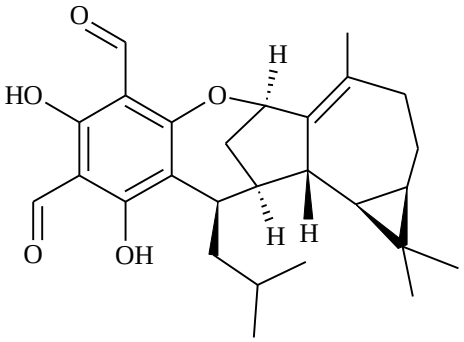
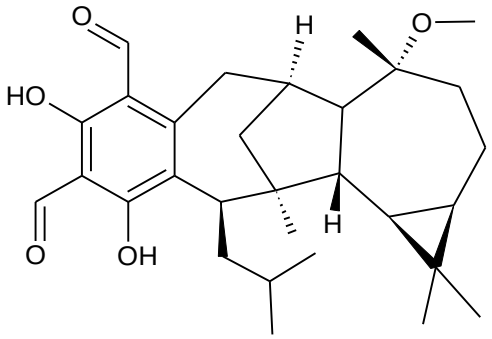
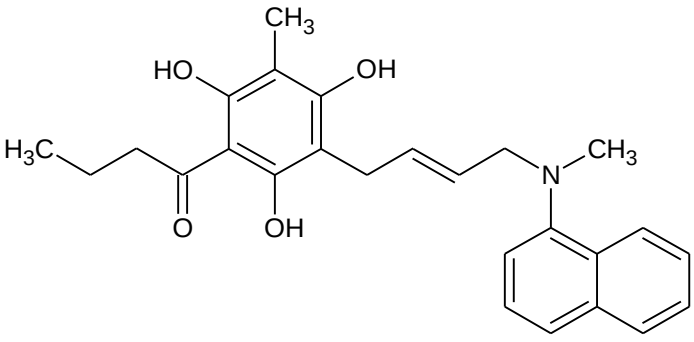
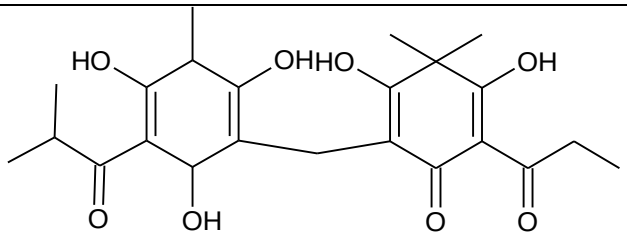
3

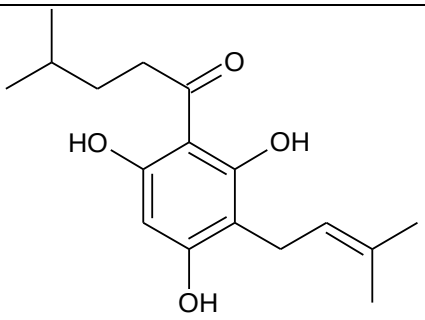
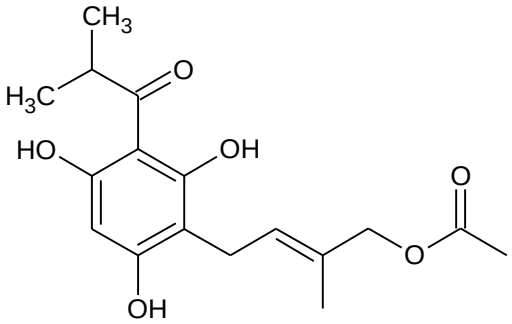
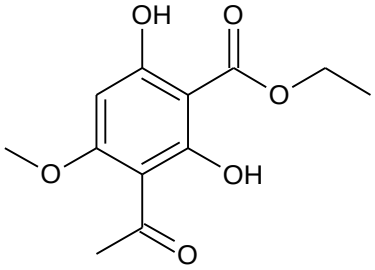
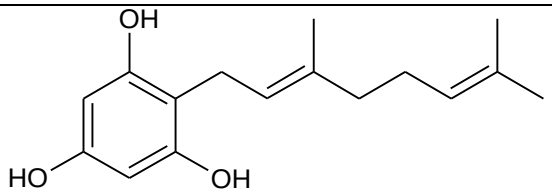
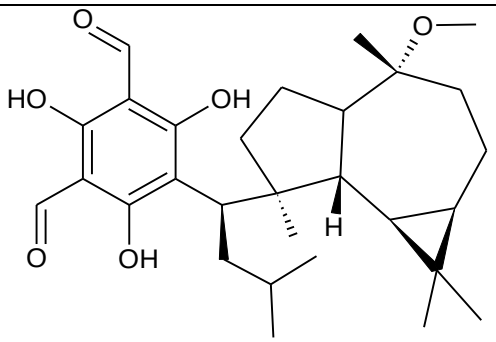

HO
OH
OH
O
O
OH
HO
O
OH

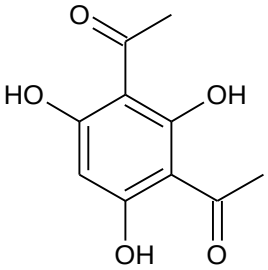
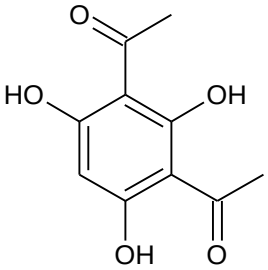
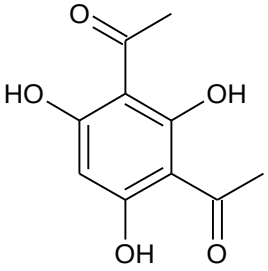
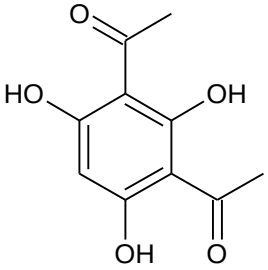
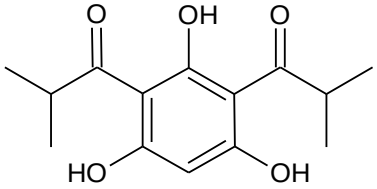
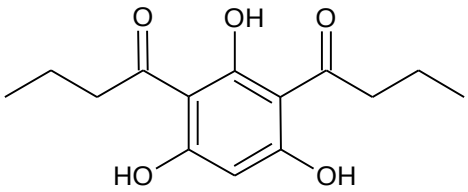
4

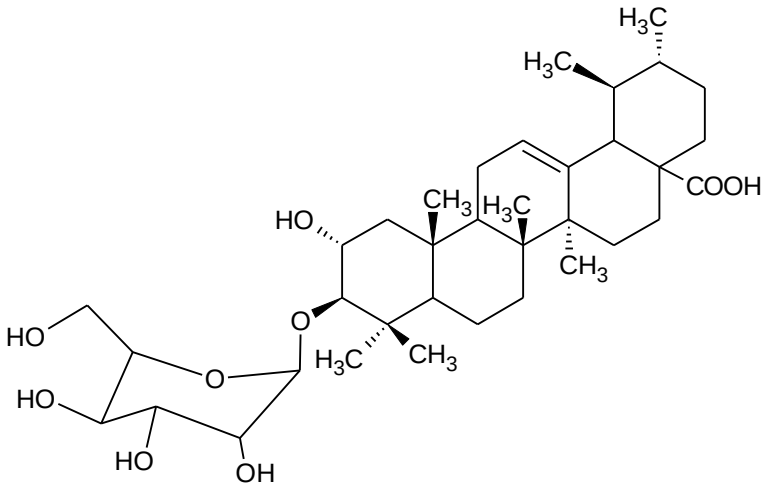
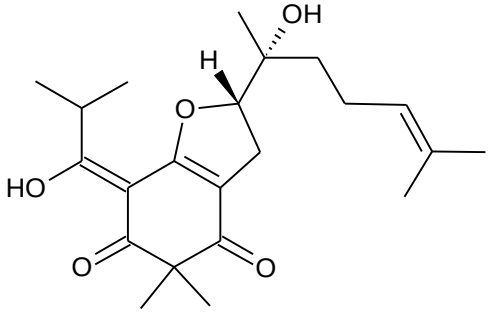
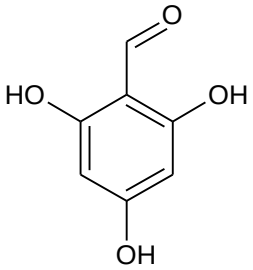
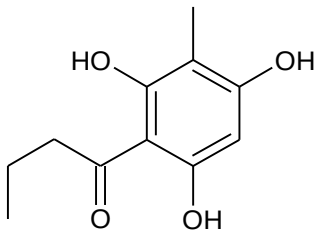
Phlorotannins Phloroglucinol (1), Eckol (2), Phlorofucifuroeckol A (3), Dieckol (4), and 8,8'-bieckol (5)	*Ecklonia kurome*	 1  2  3	33

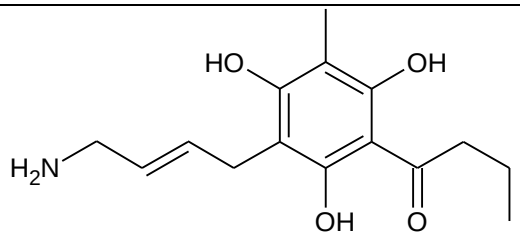
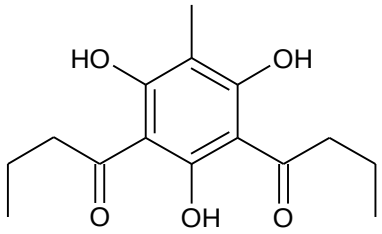
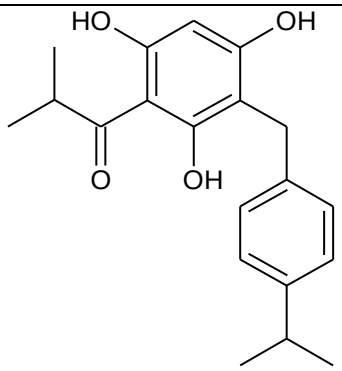
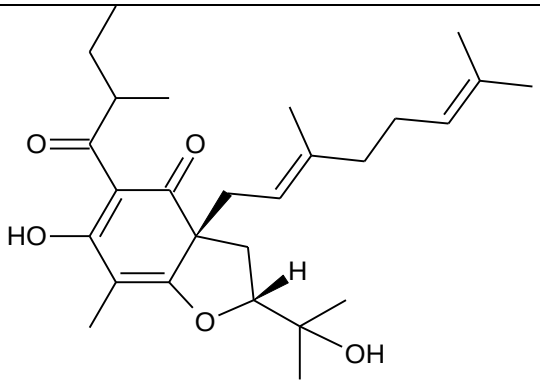
		 4  5	
Anti-fungal			
Formyl-phlorog lucinol meroterpenoids	Essential oil of *Eucalyptus*		34
Acetylated phloroglucinol	*Gibberella fujikuroi*		35

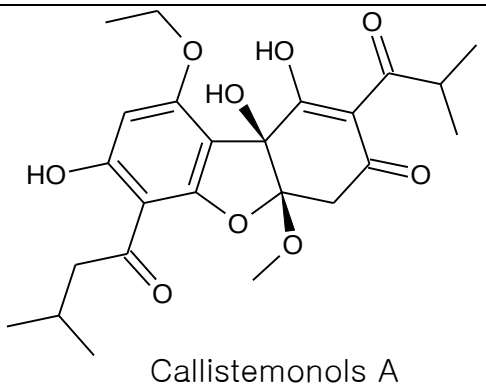
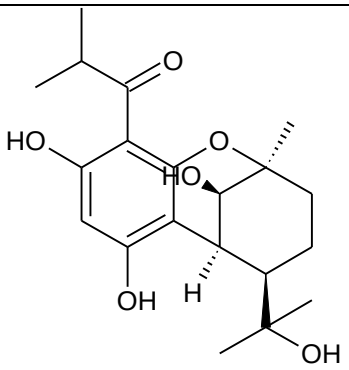
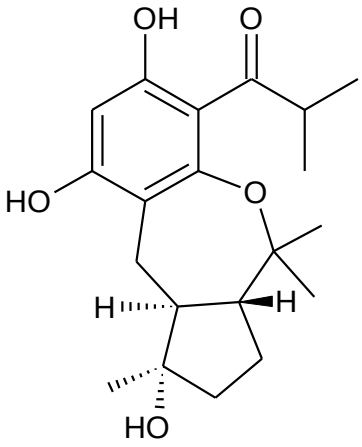
			
• Formyl-phlorog lucinol meroterpenoid • Eucalyptal D	*E. robusta*	 	36
Pseudoaspidinol	*Dryopteris fragrans*		37
Isoflavaspidic acid PB	*Dryopteris fragrans* (L.) Schott		38

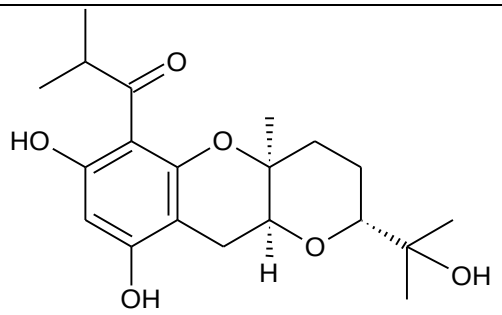
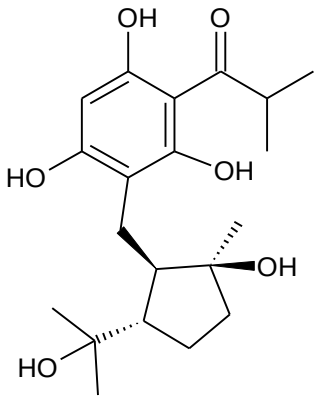
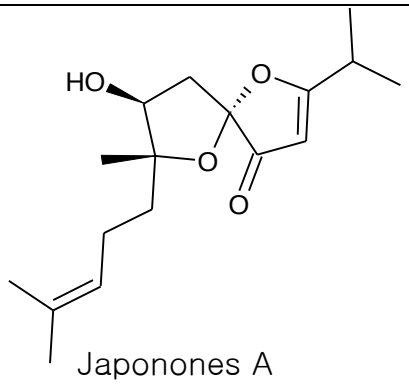
Acyl phloroglucinol	*Helichrysum caespititium*	 Caespitin  2-methyl-4-[2',4'6'-trihydroxy-3'-{2-m panoyl)-phenyl]but-2-enyl acetate	39
Phloroglucinol derivative	*Artemisia annua*		40
Mono-geranyl phloglucinol	*Gibberella fujikuroi*		35
Eucarobustol E	*Eucalyptus robusta*		41

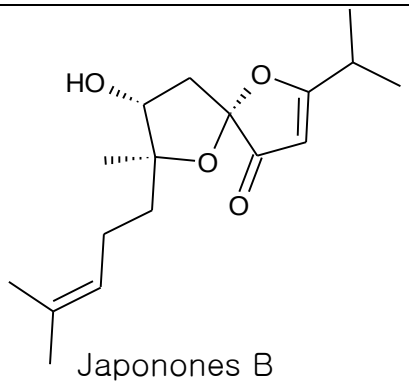
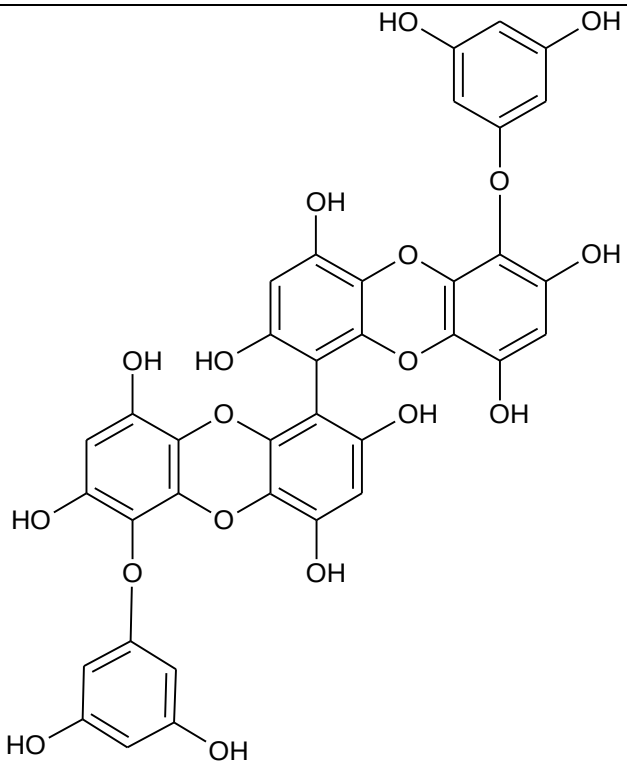
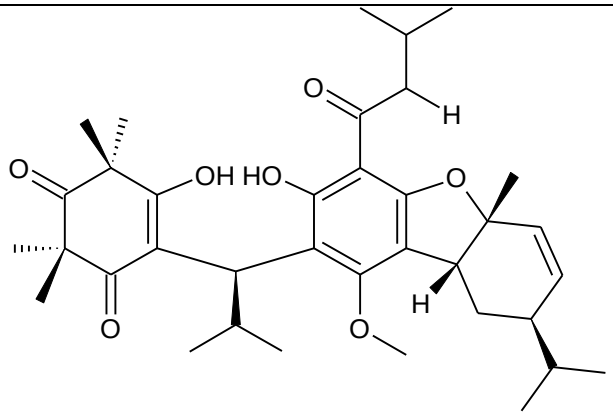
2,4-Diacetylphloroglucinol	Synthetic		42
2,4-Diacetylphloroglucinol	Synthetic		43
2,4-Diacetylphloroglucinol	*Lysobacter gummosus* (AB161361)		44
2,4-Diacetylphloroglucinol	*Pseudomonas fluorescens*		45
2,4-Diacetylphloroglucinol analogues	Synthetic	 A  B	46

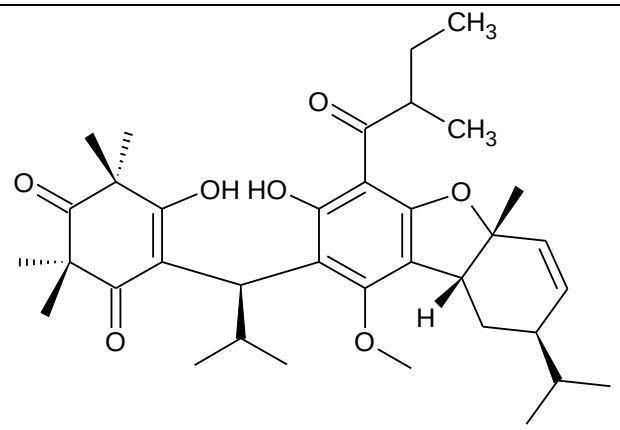
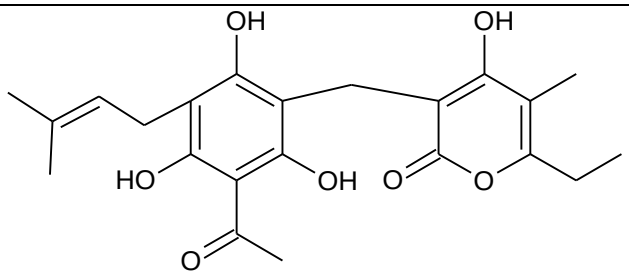
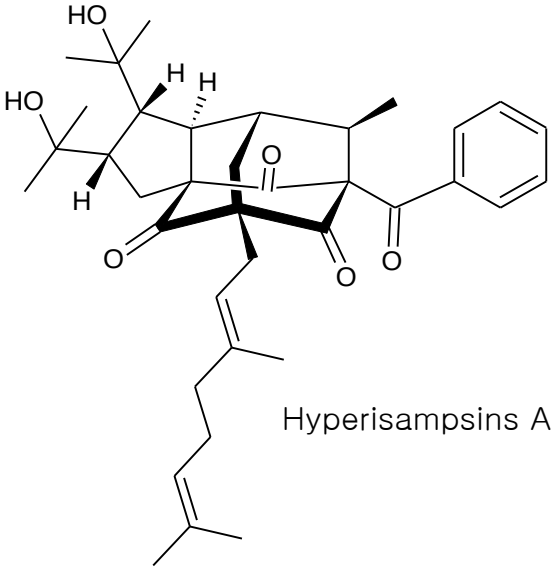
Phloroglucinol glucosides	*Syzygium szemaoense*		47
Petiolins C	*Hypericum pseudopetiolatum* var. *kiusianum*		48
Methylphloroglucinol derivatives	*Dryopteris fragrans*	 	49

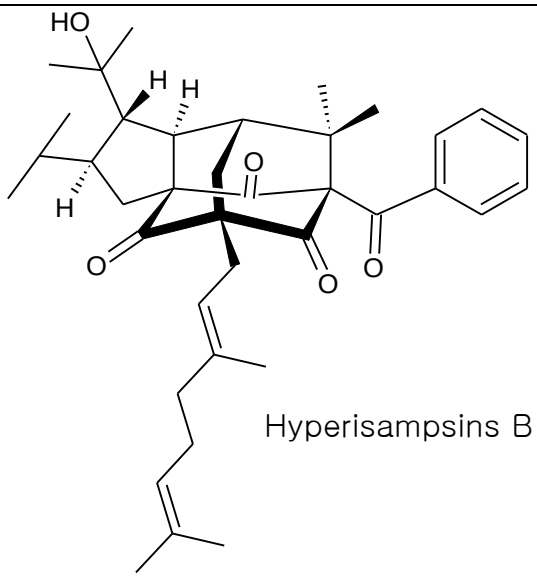
		 	
Acylphlorogluci nol derivatives	*Helichrysum kraussii*		50
Yojironins E	*Hypericum yojiroanum*		51
Anti-viral			

Callistemonols A	*Cleistocalyx operculatus*	 Callistemonols A	52
Japonicols A,B,C, and D	*Hypericum japoinicum*	 Japonicols A  Japonicols	53

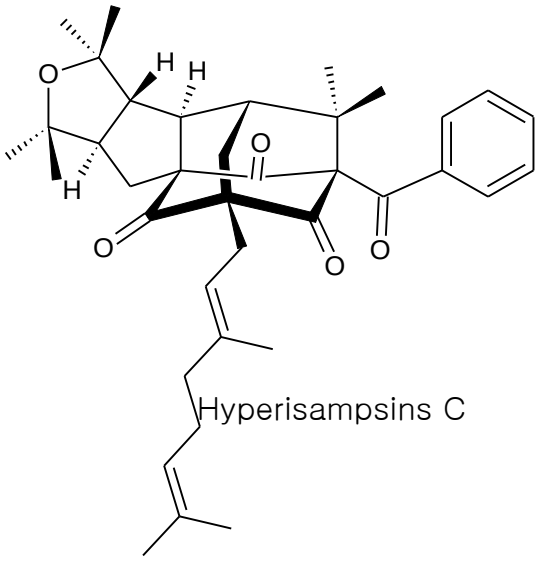
		 Japonicols C  Japonicols D	
Japonones A and B	*Hypericum japoinicum*	 Japonones A	54

		 Japonones B	
6,6'-Bieckol	*Ecklonia cava*		55
Callistrilones H and I	*Callistemon rigidus*	 Callistrilone H	56

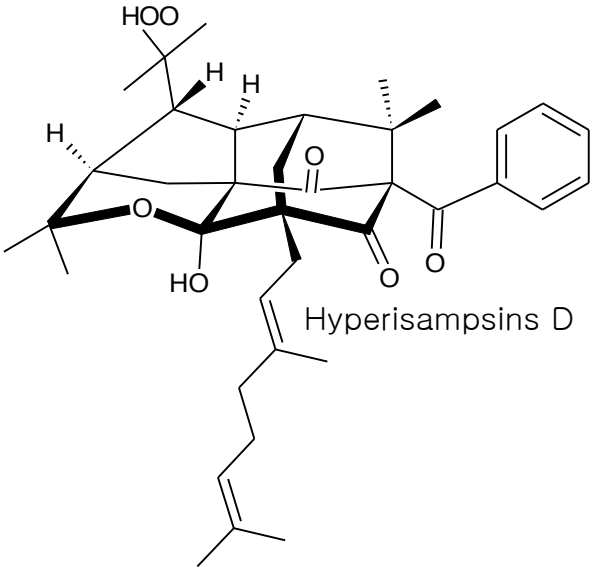
		 Callistrilone I	
α-Pyrone arzanol	*Helichrysum italicum* ssp. *microphyllum*		57
Hyperisampsins A and D	*Hypericum sampsonii*	 Hyperisampsins A	58



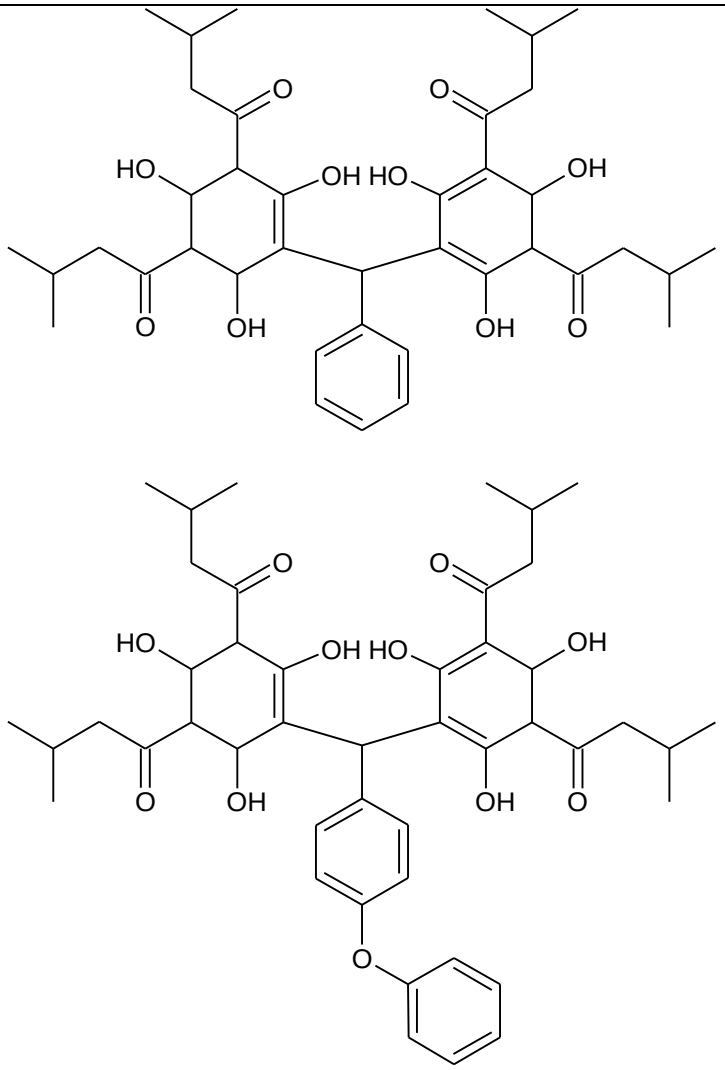
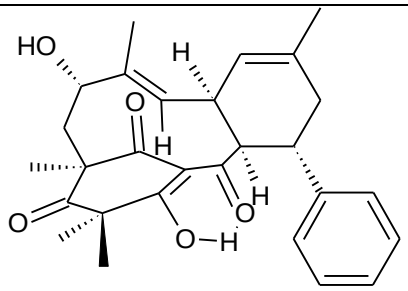
Hyperisampsins B

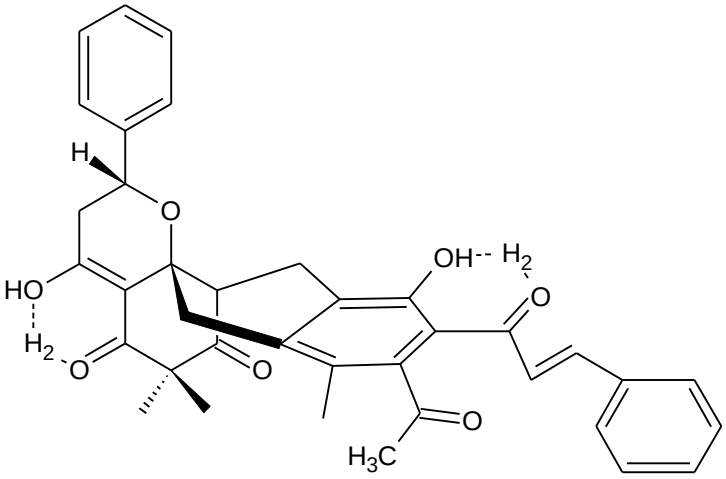
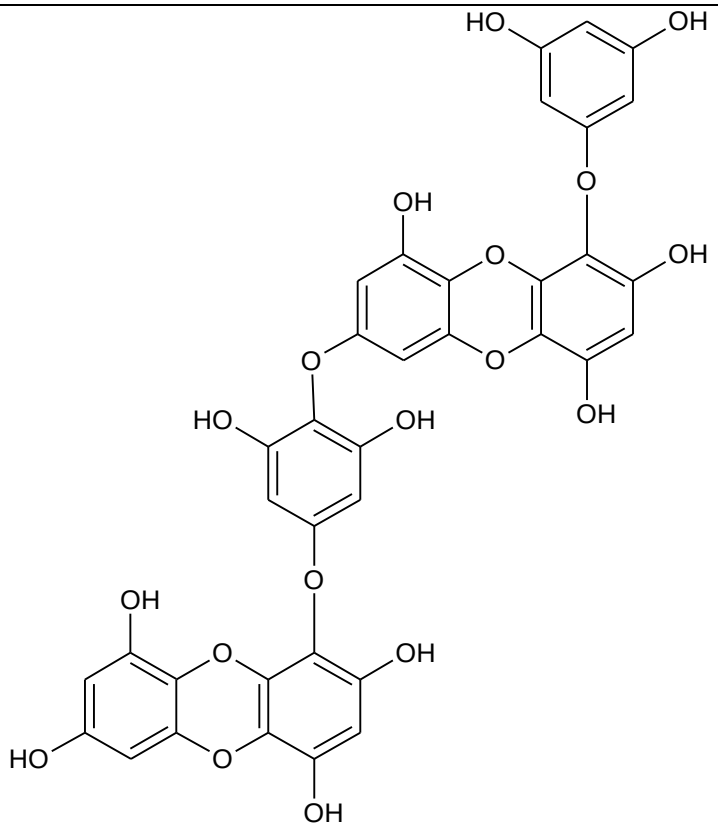
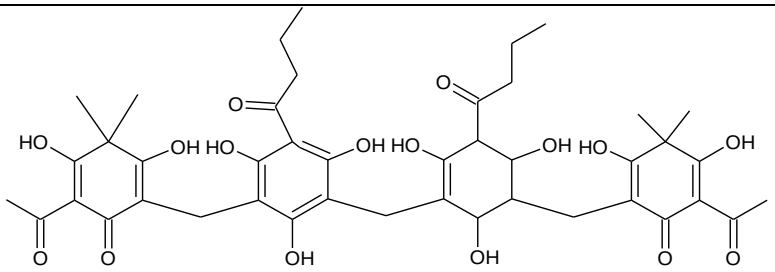


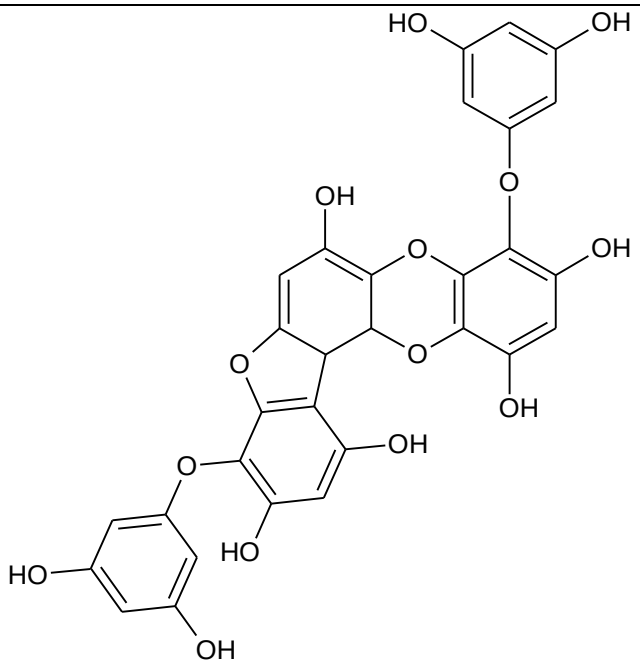
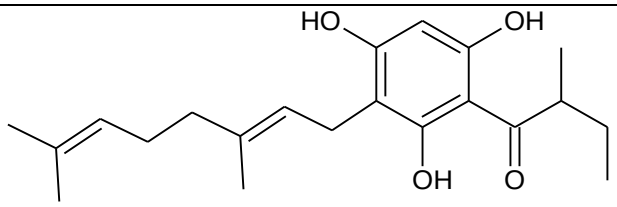
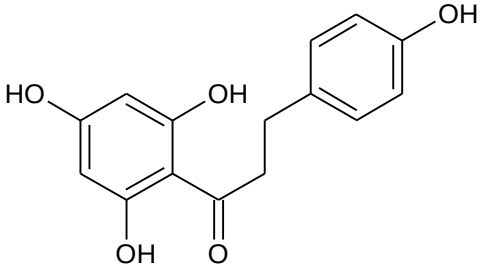
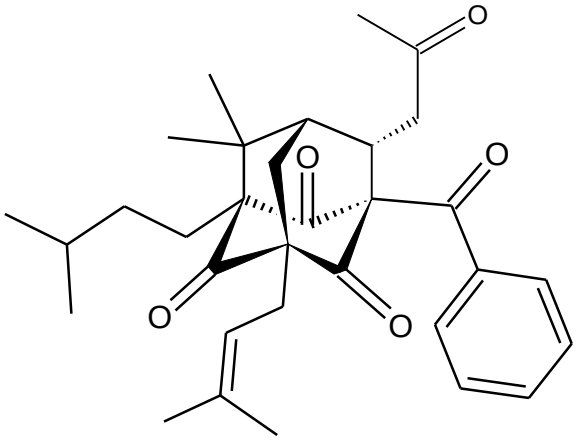
Hyperisampsins C

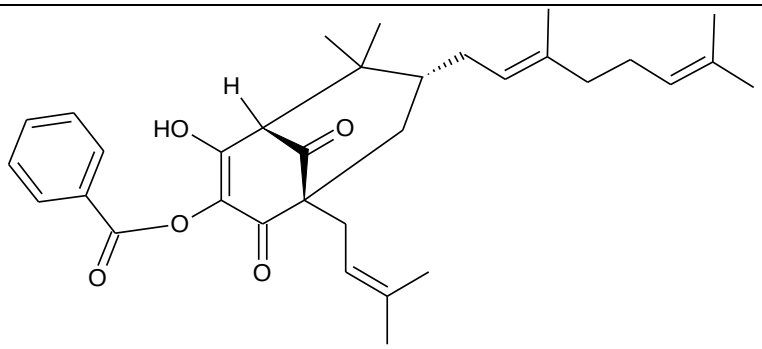
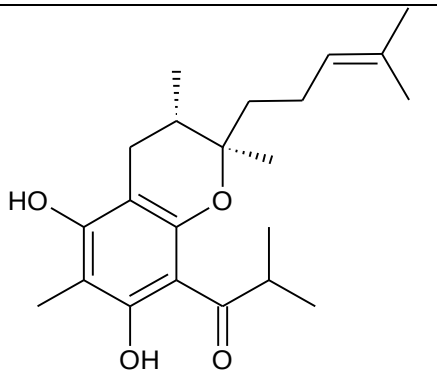
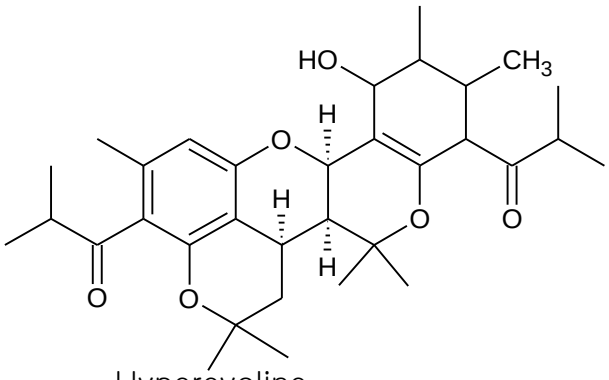
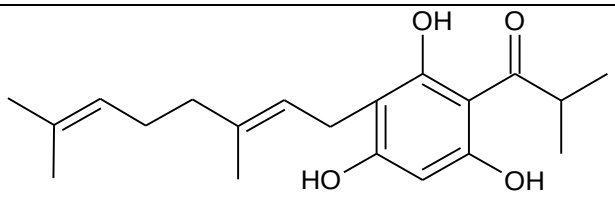


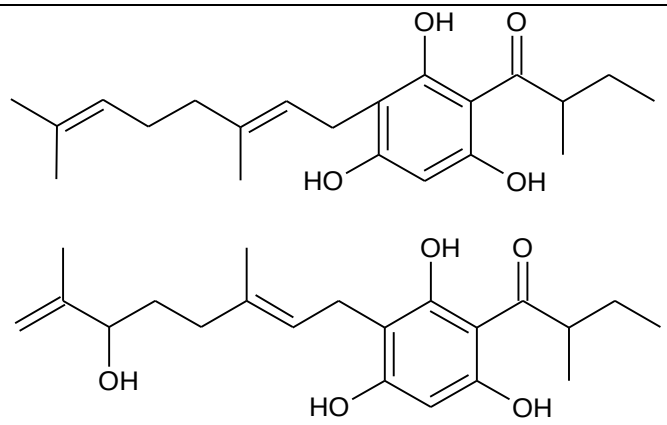
Hyperisampsins D

Dimeric phloroglucinol	Biogenetic synthesis		59
Cleistocaltones A and B	*Cleistocalyx operculatus*	 Cleistocaltones A	52

2,4-Dimethyl-cinnamyl-phlorog lucinol moiety derivative	*Cleistocalyx operculatus*		60
Dieckol	*Ecklonia cava*		61
Dryocrassin ABBA	*Rhizoma Dryopteridis crassirhizomatis*		62

Phlorofucofuroeckol	*Ecklonia cava*		63
Acylphlorogluci nol	*Hypericum roeperianum*		64
Phloretin	*Malus pumila*		65
Prenylated benzoylphlorogl ucinol	*Garcinia oblongifolia*	 Oblongifolin J	66

		 Oblongifolin M	
Acylphlorogluci nol	*Hypericum peplidifolium*	 Petiolin J  Hyperevoline	67
Prenylated phloroglucinol	*Hypericum scruglii*		68

References

1. Casero, C.; Machín, F.; Méndez-Álvarez, S.; Demo, M.; Ravelo, Á. G.; Pérez-Hernández, N.; Joseph-Nathan, P.; Estévez-Braun, A., Structure and Antimicrobial Activity of Phloroglucinol Derivatives from Achyrocline satureioides. *Journal of Natural Products* **2015,** *78* (1), 93-102.
2. Huang, J.-C.; Liu, Y.-N.; Tao, Y.-H.; Chen, B.-Y.; Lei, C.; Fu, W.; Li, J.-Y.; Hu, X.; Hou, A.-J., Acylphloroglucinol derivatives with ATP citrate lyase inhibitory activities from Syzygium oblatum Wall. *Phytochemistry* **2021,** *187*, 112765.
3. Sidana, J.; Rohilla, R. K.; Roy, N.; Barrow, R. A.; Foley, W. J.; Singh, I. P., Antibacterial sideroxylonals and loxophlebal A from Eucalyptus loxophleba foliage. *Fitoterapia* **2010,** *81* (7), 878-883.
4. Liu, H.; Li, P.; Bi, L.-S.; Wu, W.-J.; Yan, H.; He, L.; Qin, X.-J.; Liu, H.-Y., Polymethylated Phloroglucinol Meroterpenoids from Rhodomyrtus tomentosa and Their Antibacterial and Acetylcholinesterase Inhibitory Effects. *Chemistry & Biodiversity* **2020,** *17* (10), e2000489.
5. Gibbons, S.; Moser, E.; Hausmann, S.; Stavri, M.; Smith, E.; Clennett, C., An anti-staphylococcal acylphloroglucinol from Hypericum foliosum. *Phytochemistry* **2005,** *66* (12), 1472-1475.
6. Rocha, L.; Marston, A.; Potterat, O.; Kaplan, M. A. C.; Stoeckli-Evans, H.; Hostettmann, K., Antibacterial phloroglucinols and flavonoids from Hypericum brasiliense. *Phytochemistry* **1995,** *40* (5), 1447-1452.
7. Šavikin-Fodulović, K.; Aljančić, I.; Vajs, V.; Menković, N.; Macura, S.; Gojgić, G.; Milosavljević, S., Hyperatomarin, an Antibacterial Prenylated Phloroglucinol from Hypericum atomarium ssp. degenii. *Journal of Natural Products* **2003,** *66* (9), 1236-1238.
8. Schempp, C. M.; Pelz, K.; Wittmer, A.; Schöpf, E.; Simon, J. C., Antibacterial activity of hyperforin from St John's wort, against multiresistant Staphylococcus aureus and gram-positive bacteria. *The Lancet* **1999,** *353* (9170), 2129.
9. Shiu, W. K. P.; Rahman, M. M.; Curry, J.; Stapleton, P.; Zloh, M.; Malkinson, J. P.; Gibbons, S., Antibacterial Acylphloroglucinols from Hypericum olympicum. *Journal of Natural Products* **2012,** *75* (3), 336-343.
10. Shiu, W. K. P.; Malkinson, J. P.; Rahman, M. M.; Curry, J.; Stapleton, P.; Gunaratnam, M.; Neidle, S.; Mushtaq, S.; Warner, M.; Livermore, D. M.; Evangelopoulos, D.; Basavannacharya, C.; Bhakta, S.; Schindler, B. D.; Seo, S. M.; Coleman, D.; Kaatz, G. W.; Gibbons, S., A new plant-derived antibacterial is an inhibitor of efflux pumps in Staphylococcus aureus. *International Journal of Antimicrobial Agents* **2013,** *42* (6), 513-518.
11. Tala, M. F.; Talontsi, F. M.; Zeng, G.-Z.; Wabo, H. K.; Tan, N.-H.; Spiteller, M.; Tane, P., Antimicrobial and cytotoxic constituents from native Cameroonian medicinal plant Hypericum riparium. *Fitoterapia* **2015,** *102*, 149-155.
12. Winkelmann, K.; San, M.; Kypriotakis, Z.; Skaltsa, H.; Bosilij, B.; Heilmann, J., Antibacterial and Cytotoxic Activity of Prenylated Bicyclic Acylphloroglucinol Derivatives from Hypericum amblycalyx. *Zeitschrift für Naturforschung C* **2003,** *58* (7-8), 527-532.
13. Khan, N.; Rasool, S.; Ali Khan, S.; Bahadar Khan, S., A new antibacterial dibenzofuran-type phloroglucinol from myrtus communis linn. *Natural Product Research* **2020,** *34* (22), 3199-3204.
14. Tchangoue, Y. A. N.; Tchamgoue, J.; Lunga, P. K.; Knepper, J.; Paltinean, R.; Ibrom, K.; Crișan, G.; Kouam, S. F.; Ali, M. S.; Schulz, S., Antibacterial

phloroglucinols derivatives from the leaves of Mallotus oppositifolius (Geisler) Müll. Arg. (Euphorbiaceae). *Fitoterapia* **2020,** *142*, 104527.
15. Wu, Y.; Liu, J.-W.; Liu, C.; Huang, X.-J.; Li, N.-P.; Ye, W.-C.; Wang, L., Antibacterial Triketone-Phloroglucinol-Triketone Adducts from Myrtus communis. *Chemistry & Biodiversity* **2020,** *17* (11), e2000708.
16. Wu, J.-W.; Li, B.-L.; Tang, C.; Ke, C.-Q.; Zhu, N.-L.; Qiu, S.-X.; Ye, Y., Callistemonols A and B, Potent Antimicrobial Acylphloroglucinol Derivatives with Unusual Carbon Skeletons from Callistemon viminalis. *Journal of Natural Products* **2019,** *82* (7), 1917-1922.
17. Li, Q.-J.; Tang, P.-F.; Zhou, X.; Lu, W.-J.; Xu, W.-J.; Luo, J.; Kong, L.-Y., Dimethylated acylphloroglucinol meroterpenoids with anti-oral-bacterial and anti-inflammatory activities from Hypericum elodeoides. *Bioorganic Chemistry* **2020,** *104*, 104275.
18. Cheenpracha, S.; Pyne, S. G.; Patrick, B. O.; Andersen, R. J.; Maneerat, W.; Laphookhieo, S., Mallopenins A–E, Antibacterial Phenolic Derivatives from the Fruits of Mallotus philippensis. *Journal of Natural Products* **2019,** *82* (8), 2174-2180.
19. Wu, Y.; Chen, M.; Wang, W.-J.; Li, N.-P.; Ye, W.-C.; Wang, L., Phloroglucinol Derivatives from Myrtus communis 'Variegata' and Their Antibacterial Activities. *Chemistry & Biodiversity* **2020,** *17* (8), e2000292.
20. Sorres, J.; André, A.; Elslande, E. V.; Stien, D.; Eparvier, V., Potent and Non-Cytotoxic Antibacterial Compounds Against Methicillin-Resistant Staphylococcus aureus Isolated from Psiloxylon mauritianum, A Medicinal Plant from Reunion Island. *Molecules (Basel, Switzerland)* **2020,** *25* (16), 3565.
21. Li, Y.-P.; Hu, K.; Yang, X.-W.; Xu, G., Antibacterial Dimeric Acylphloroglucinols from Hypericum japonicum. *Journal of Natural Products* **2018,** *81* (4), 1098-1102.
22. Yu, Q.; Ravu, R. R.; Xu, Q. M.; Ganji, S.; Jacob, M. R.; Khan, S. I.; Yu, B. Y.; Li, X. C., Antibacterial Prenylated Acylphloroglucinols from Psorothamnus fremontii. *J Nat Prod* **2015,** *78* (11), 2748-53.
23. Suresh, P.; Varathraju, G.; Shanmugaiah, V.; Almaary, K. S.; Elbadawi, Y. B.; Mubarak, A., Partial purification and characterization of 2, 4-diacetylphloroglucinol producing Pseudomonas fluorescens VSMKU3054 against bacterial wilt disease of tomato. *Saudi Journal of Biological Sciences* **2021,** *28* (4), 2155-2167.
24. Julian, W. T.; Vasilchenko, A. V.; Shpindyuk, D. D.; Poshvina, D. V.; Vasilchenko, A. S., Bacterial-Derived Plant Protection Metabolite 2,4-Diacetylphloroglucinol: Effects on Bacterial Cells at Inhibitory and Subinhibitory Concentrations. *Biomolecules* **2020,** *11* (1).
25. Isnansetyo, A.; Cui, L.; Hiramatsu, K.; Kamei, Y., Antibacterial activity of 2,4-diacetylphloroglucinol produced by Pseudomonas sp. AMSN isolated from a marine alga, against vancomycin-resistant Staphylococcus aureus. *International Journal of Antimicrobial Agents* **2003,** *22* (5), 545-547.
26. Levenfors, J. J.; Nord, C.; Bjerketorp, J.; Ståhlberg, J.; Larsson, R.; Guss, B.; Ö berg, B.; Broberg, A., Antibacterial pyrrolidinyl and piperidinyl substituted 2,4-diacetylphloroglucinols from Pseudomonas protegens UP46. *The Journal of Antibiotics* **2020,** *73* (11), 739-747.
27. Lee, D.-S.; Kang, M.-S.; Hwang, H.-J.; Eom, S.-H.; Yang, J.-Y.; Lee, M.-S.; Lee, W.-J.; Jeon, Y.-J.; Choi, J.-S.; Kim, Y.-M., Synergistic effect between dieckol from Ecklonia stolonifera and β-lactams against methicillin-resistant Staphylococcus aureus. *Biotechnology and Bioprocess Engineering* **2008,** *13* (6), 758-764.

28. Lee, J.-H.; Eom, S.-H.; Lee, E.-H.; Jung, Y.-J.; Kim, H.-J.; Jo, M.-R.; Son, K.-T.; Lee, H.-J.; Kim, J. H.; Lee, M.-S.; Kim, Y.-M., In vitro antibacterial and synergistic effect of phlorotannins isolated from edible Brown seaweed Eisenia bicyclis against acne-related bacteria. *ALGAE* **2014,** *29*, 47-55.
29. Kim, H.-J.; Dasagrandhi, C.; Kim, S.-H.; Kim, B.-G.; Eom, S.-H.; Kim, Y.-M., In Vitro Antibacterial Activity of Phlorotannins from Edible Brown Algae, Eisenia bicyclis Against Streptomycin-Resistant Listeria monocytogenes. *Indian journal of microbiology* **2018,** *58* (1), 105-108.
30. Wei, Y.; Liu, Q.; Xu, C.; Yu, J.; Zhao, L.; Guo, Q., Damage to the Membrane Permeability and Cell Death of Vibrio parahaemolyticus Caused by Phlorotannins with Low Molecular Weight from Sargassum thunbergii. *Journal of Aquatic Food Product Technology* **2016,** *25* (3), 323-333.
31. Choi, J. G.; Kang, O. H.; Brice, O. O.; Lee, Y. S.; Chae, H. S.; Oh, Y. C.; Sohn, D. H.; Park, H.; Choi, H. G.; Kim, S. G.; Shin, D. W.; Kwon, D. Y., Antibacterial activity of Ecklonia cava against methicillin-resistant Staphylococcus aureus and Salmonella spp. *Foodborne Pathog Dis* **2010,** *7* (4), 435-41.
32. Hierholtzer, A.; Chatellard, L.; Kierans, M.; Akunna, J. C.; Collier, P. J., The impact and mode of action of phenolic compounds extracted from brown seaweed on mixed anaerobic microbial cultures. *J Appl Microbiol* **2013,** *114* (4), 964-73.
33. Nagayama, K.; Iwamura, Y.; Shibata, T.; Hirayama, I.; Nakamura, T., Bactericidal activity of phlorotannins from the brown alga Ecklonia kurome. *J Antimicrob Chemother* **2002,** *50* (6), 889-93.
34. Zhong, L. F.; Shang, Z. C.; Sun, F. J.; Zhu, P. H.; Yin, Y.; Kong, L. Y.; Yang, M. H., Anticandidal formyl phloroglucinol meroterpenoids: Biomimetic synthesis and in vitro evaluation. *Bioorganic Chemistry* **2020,** *104*, 104248.
35. Carvajal, M.; Vergara, A.; Contreras, J.; Osorio, M.; Seeger, M., Biotransformation of geranylated- and acetylated-phloroglucinols by Gibberella fujikuroi into molecules with increased antifungal activity against Botrytis cinerea. *Fungal Biology* **2018,** *122* (8), 752-760.
36. Xu, J.; Liu, R.; Sun, F.; An, L.; Shang, Z.; Kong, L.; Yang, M., Eucalyptal D Enhances the Antifungal Effect of Fluconazole on Fluconazole-Resistant Candida albicans by Competitively Inhibiting Efflux Pump. *Frontiers in cellular and infection microbiology* **2019,** *9*, 211-211.
37. Teng, X.; Wang, Y.; Gu, J.; Shi, P.; Shen, Z.; Ye, L., Antifungal Agents: Design, Synthesis, Antifungal Activity and Molecular Docking of Phloroglucinol Derivatives. *Molecules* **2018,** *23* (12), 3116.
38. Lin, H.; Liu, X.; Shen, Z.; Cheng, W.; Zeng, Z.; Chen, Y.; Tang, C.; Jiang, T., The effect of isoflavaspidic acid PB extracted from Dryopteris fragrans (L.) Schott on planktonic and biofilm growth of dermatophytes and the possible mechanism of antibiofilm. *J Ethnopharmacol* **2019,** *241*, 111956.
39. Mathekga, A. D.; Meyer, J. J.; Horn, M. M.; Drewes, S. E., An acylated phloroglucinol with antimicrobial properties from Helichrysum caespititium. *Phytochemistry* **2000,** *53* (1), 93-6.
40. Li, K. M.; Dong, X.; Ma, Y. N.; Wu, Z. H.; Yan, Y. M.; Cheng, Y. X., Antifungal coumarins and lignans from Artemisia annua. *Fitoterapia* **2019,** *134*, 323-328.
41. Liu, R.-H.; Shang, Z.-C.; Li, T.-X.; Yang, M.-H.; Kong, L.-Y., In Vitro Antibiofilm Activity of Eucarobustol E against Candida albicans. *Antimicrobial agents and chemotherapy* **2017,** *61* (8), e02707-16.
42. Troppens, D. M.; Dmitriev, R. I.; Papkovsky, D. B.; O'Gara, F.; Morrissey, J. P., Genome-wide investigation of cellular targets and mode of action of the antifungal

bacterial metabolite 2,4-diacetylphloroglucinol in Saccharomyces cerevisiae. *FEMS Yeast Research* **2013,** *13* (3), 322-334.
43. Troppens, D. M.; Chu, M.; Holcombe, L. J.; Gleeson, O.; O'Gara, F.; Read, N. D.; Morrissey, J. P., The bacterial secondary metabolite 2,4-diacetylphloroglucinol impairs mitochondrial function and affects calcium homeostasis in Neurospora crassa. *Fungal Genet Biol* **2013,** *56*, 135-46.
44. Brucker, R. M.; Baylor, C. M.; Walters, R. L.; Lauer, A.; Harris, R. N.; Minbiole, K. P., The identification of 2,4-diacetylphloroglucinol as an antifungal metabolite produced by cutaneous bacteria of the salamander Plethodon cinereus. *J Chem Ecol* **2008,** *34* (1), 39-43.
45. Gleeson, O.; O'Gara, F.; Morrissey, J. P., The Pseudomonas fluorescens secondary metabolite 2,4 diacetylphloroglucinol impairs mitochondrial function in Saccharomyces cerevisiae. *Antonie Van Leeuwenhoek* **2010,** *97* (3), 261-73.
46. Gong, L.; Tan, H.; Chen, F.; Li, T.; Zhu, J.; Jian, Q.; Yuan, D.; Xu, L.; Hu, W.; Jiang, Y., Novel synthesized 2, 4-DAPG analogues: antifungal activity, mechanism and toxicology. *Scientific reports* **2016,** *6* (1), 1-9.
47. Xu, W.; Tan, J.; Mu, Y.; Zheng, D.; Huang, X.; Li, L., New antimicrobial terpenoids and phloroglucinol glucosides from Syzygium szemaoense. *Bioorg Chem* **2020,** *103*, 104242.
48. Tanaka, N.; Kubota, T.; Ishiyama, H.; Araki, A.; Kashiwada, Y.; Takaishi, Y.; Mikami, Y.; Kobayashi, J., Petiolins A-C, phloroglucinol derivatives from Hypericum pseudopetiolatum var. kiusianum. *Bioorg Med Chem* **2008,** *16* (10), 5619-23.
49. Ye, L.; Lin, P.; Du, W.; Wang, Y.; Tang, C.; Shen, Z., Preparation, Antidermatophyte Activity, and Mechanism of Methylphloroglucinol Derivatives. *Frontiers in Microbiology* **2018,** *9* (2262).
50. Yu, Q.; Ravu, R. R.; Jacob, M. R.; Khan, S. I.; Agarwal, A. K.; Yu, B. Y.; Li, X. C., Synthesis of Natural Acylphloroglucinol-Based Antifungal Compounds against Cryptococcus Species. *J Nat Prod* **2016,** *79* (9), 2195-201.
51. Tanaka, N.; Mamemura, T.; Shibazaki, A.; Gonoi, T.; Kobayashi, J. i., Yojironins E–I, prenylated acylphloroglucinols from Hypericum yojiroanum. *Bioorganic & Medicinal Chemistry Letters* **2011,** *21* (18), 5393-5397.
52. Song, J.-G.; Su, J.-C.; Song, Q.-Y.; Huang, R.-L.; Tang, W.; Hu, L.-J.; Huang, X.-J.; Jiang, R.-W.; Li, Y.-L.; Ye, W.-C.; Wang, Y., Cleistocaltones A and B, Antiviral Phloroglucinol–Terpenoid Adducts from Cleistocalyx operculatus. *Organic Letters* **2019,** *21* (23), 9579-9583.
53. Hu, L.; Xue, Y.; Zhang, J.; Zhu, H.; Chen, C.; Li, X.-N.; Liu, J.; Wang, Z.; Zhang, Y.; Zhang, Y., (±)-Japonicols A–D, Acylphloroglucinol-Based Meroterpenoid Enantiomers with Anti-KSHV Activities from Hypericum japonicum. *Journal of Natural Products* **2016,** *79* (5), 1322-1328.
54. Hu, L.; Zhu, H.; Li, L.; Huang, J.; Sun, W.; Liu, J.; Li, H.; Luo, Z.; Wang, J.; Xue, Y.; Zhang, Y.; Zhang, Y., (±)-Japonones A and B, two pairs of new enantiomers with anti-KSHV activities from Hypericum japonicum. *Sci Rep* **2016,** *6*, 27588.
55. Artan, M.; Li, Y.; Karadeniz, F.; Lee, S. H.; Kim, M. M.; Kim, S. K., Anti-HIV-1 activity of phloroglucinol derivative, 6,6'-bieckol, from Ecklonia cava. *Bioorg Med Chem* **2008,** *16* (17), 7921-6.
56. Cao, J. Q.; Wu, Y.; Zhong, Y. L.; Li, N. P.; Chen, M.; Li, M. M.; Ye, W. C.; Wang, L., Antiviral Triketone-Phloroglucinol-Monoterpene Adducts from Callistemon rigidus. *Chem Biodivers* **2018,** *15* (7), e1800172.
57. Appendino, G.; Ottino, M.; Marquez, N.; Bianchi, F.; Giana, A.; Ballero, M.; Sterner, O.; Fiebich, B. L.; Munoz, E., Arzanol, an anti-inflammatory and anti-HIV-1

phloroglucinol alpha-Pyrone from Helichrysum italicum ssp. microphyllum. *J Nat Prod* **2007,** *70* (4), 608-12.
58. Zhu, H.; Chen, C.; Yang, J.; Li, X.-N.; Liu, J.; Sun, B.; Huang, S.-X.; Li, D.; Yao, G.; Luo, Z.; Li, Y.; Zhang, J.; Xue, Y.; Zhang, Y., Bioactive Acylphloroglucinols with Adamantyl Skeleton from Hypericum sampsonii. *Organic Letters* **2014,** *16* (24), 6322-6325.
59. Chauthe, S. K.; Bharate, S. B.; Sabde, S.; Mitra, D.; Bhutani, K. K.; Singh, I. P., Biomimetic synthesis and anti-HIV activity of dimeric phloroglucinols. *Bioorg Med Chem* **2010,** *18* (5), 2029-36.
60. Su, J.-C.; Wang, S.; Cheng, W.; Huang, X.-J.; Li, M.-M.; Jiang, R.-W.; Li, Y.-L.; Wang, L.; Ye, W.-C.; Wang, Y., Phloroglucinol Derivatives with Unusual Skeletons from Cleistocalyx operculatus and Their in Vitro Antiviral Activity. *The Journal of Organic Chemistry* **2018,** *83* (15), 8522-8532.
61. Park, J. Y.; Kim, J. H.; Kwon, J. M.; Kwon, H. J.; Jeong, H. J.; Kim, Y. M.; Kim, D.; Lee, W. S.; Ryu, Y. B., Dieckol, a SARS-CoV 3CL(pro) inhibitor, isolated from the edible brown algae Ecklonia cava. *Bioorg Med Chem* **2013,** *21* (13), 3730-7.
62. Ou, C.; Zhang, Q.; Wang, J.; Wu, G.; Shi, N.; He, C.; Gao, Z., Dryocrassin ABBA, a novel active substance for use against amantadine-resistant H5N1 avian influenza virus. *Frontiers in Microbiology* **2015,** *6* (592).
63. Ryu, Y. B.; Jeong, H. J.; Yoon, S. Y.; Park, J.-Y.; Kim, Y. M.; Park, S.-J.; Rho, M.-C.; Kim, S.-J.; Lee, W. S., Influenza virus neuraminidase inhibitory activity of phlorotannins from the edible brown alga Ecklonia cava. *Journal of agricultural and food chemistry* **2011,** *59* (12), 6467-6473.
64. Fobofou, S. A.; Franke, K.; Sanna, G.; Porzel, A.; Bullita, E.; La Colla, P.; Wessjohann, L. A., Isolation and anticancer, anthelminthic, and antiviral (HIV) activity of acylphloroglucinols, and regioselective synthesis of empetrifranzinans from Hypericum roeperianum. *Bioorg Med Chem* **2015,** *23* (19), 6327-34.
65. Lin, S.-C.; Chen, M.-C.; Liu, S.; Callahan, V. M.; Bracci, N. R.; Lehman, C. W.; Dahal, B.; de la Fuente, C. L.; Lin, C.-C.; Wang, T. T.; Kehn-Hall, K., Phloretin inhibits Zika virus infection by interfering with cellular glucose utilisation. *International journal of antimicrobial agents* **2019,** *54* (1), 80-84.
66. Zhang, H.; Tao, L.; Fu, W.-W.; Liang, S.; Yang, Y.-F.; Yuan, Q.-H.; Yang, D.-J.; Lu, A.-P.; Xu, H.-X., Prenylated Benzoylphloroglucinols and Xanthones from the Leaves of Garcinia oblongifolia with Antienteroviral Activity. *Journal of Natural Products* **2014,** *77* (4), 1037-1046.
67. Fobofou, S. A.; Harmon, C. R.; Lonfouo, A. H.; Franke, K.; Wright, S. M.; Wessjohann, L. A., Prenylated phenyl polyketides and acylphloroglucinols from Hypericum peplidifolium. *Phytochemistry* **2016,** *124*, 108-13.
68. Sanna, C.; Scognamiglio, M.; Fiorentino, A.; Corona, A.; Graziani, V.; Caredda, A.; Cortis, P.; Montisci, M.; Ceresola, E. R.; Canducci, F.; Poli, F.; Tramontano, E.; Esposito, F., Prenylated phloroglucinols from Hypericum scruglii, an endemic species of Sardinia (Italy), as new dual HIV-1 inhibitors effective on HIV-1 replication. *PLoS One* **2018,** *13* (3), e0195168.