

Article

Cytotoxic Activity of Inositol Angelates and Tirucallane-Type Alkaloids from *Amoora Dasyclada*

Sheng-Xiang Yang ^{1,†}, Cheng-Gang Song ^{2,†}, Yi Kuang ^{1,†}, Bing Liu ², Yan-Xin Zhang ²,
Ming-Zhe Zhang ², Chun-Ying Zhang ³, Gang Ding ^{4,*} and Jian-Chun Qin ^{2,*}

¹ Zhejiang Provincial Key Laboratory of Chemical Utilization of Forestry Biomass, Zhejiang A&F University, Lin'an 311300, Zhejiang, China; shengxiangyang2000@163.com (S.-X.Y.); jlu_bio@163.com (Y.K.)

² College of Plant Science, Jilin University, Xi'an Road No. 5333, Changchun 130062, Jilin, China; songcg18@mail.jlu.edu.cn (C.-G.S.); liubing18@mail.jlu.edu.cn (B.L.); zhangyx17@mail.jlu.edu.cn (Y.-X.Z.); mzzhang@jlu.edu.cn (M.-Z.Z.)

³ The clinical medicine department of Changchun Medical College, Jilin Road No. 6177, Changchun 130013, Jilin, China; 15754305325@163.com

⁴ Institute of Medicinal Plant Department, Chinese Academy of medical Sciences and Peking Union Medical College, Beijing 100193, China

* Correspondence: gding@implad.ac.cn (G.D.); qinjc@jlu.edu.cn (J.-C.Q.); Tel./Fax: +86-431-87835722 (J.-C.Q.)

† These authors contributed equally to this paper.

Academic Editor: Laura De Martino

Received: 21 February 2020; Accepted: 6 March 2020; Published: 9 March 2020



Abstract: Three new inositol angelate compounds (1–3) and two new tirucallane-type alkaloids (4 and 5) were isolated from the *Amoora dasyclada*, and their structures were established mainly by means of combination of 1D and 2D nuclear magnetic resonance and HR-ESI-MS. Based on cytotoxicity testing, compounds 4 and 5 exhibited significant cytotoxic activity against human cancer cell line HepG2 with IC₅₀ value at 8.4 and 13.2 μM. In addition, compounds 4 and 5 also showed remarkable growth inhibitory activity to *Artemia salina* larvae.

Keywords: inositol angelate; tirucallane alkaloid; *Amoora dasyclada*; cytotoxicity

1. Introduction

The Meliaceae family comprises about 1400 species, mainly distributed in tropical and subtropical areas, with 62 among them being found in China. Plants of this family are rich sources of structurally diverse and biologically significant limonoids [1,2]. Some vegetative storage proteins in Meliaceae were investigated by Tian et al. [3]. *Amoora dasyclada*, a member of the Meliaceae family, yields varied kinds of terpenoids, including diterpenoid, triterpenoid and tetraterpenoid, with anticancer and cytotoxic activities [4–13]. We firstly isolated three new inositol angelates and two alkaloids (compounds 1–5, Figure 1) which have not been investigated previously in *Amoora dasyclada*. Angelate compounds were exhibited to have antitumor activity: 3-ingenyl angelate has significant inhibitory effects on skin cancer [14]; decursinol angelate caused a significant increase in the life span and a significant decrease in the tumor weight and volume of mice inoculated with Sarcoma-180 tumor cells [15]. Tirucallane derivatives with a pyrrole ring from Meliaceae family showed obvious cytotoxicity against five human cancer cell lines [7]. Compounds 1–5 were identified by 1D and 2D NMR method and HR-ESI-MS and structurally compared with similar compounds found previously.

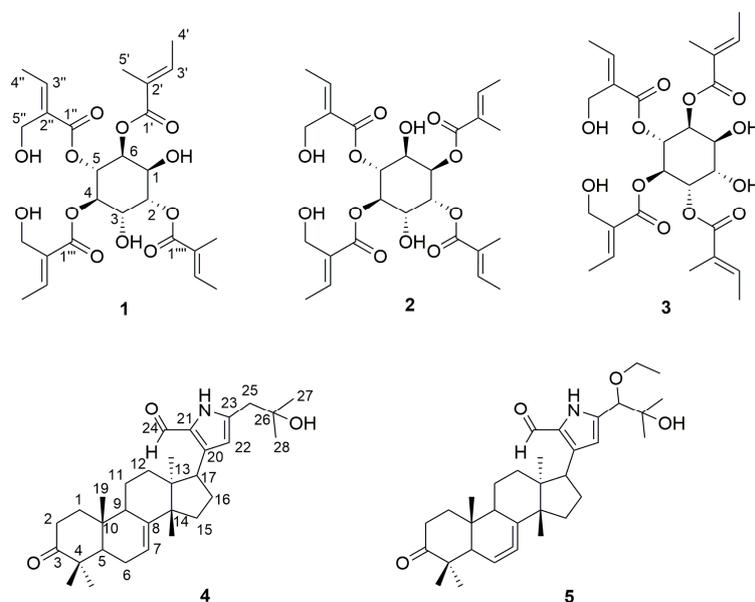


Figure 1. Compounds 1–5 isolated from *Amoora dasyclada*.

2. Results and Discussion

2.1. Identification of Compounds

Compounds 1–3 were identified as inositol angelates. According to the structure of the previously isolated compound from *Inula cappa*, it is similar to *cis*-1,2,3,5-*trans*-4,6-inositol-2,3,6-triangelate and *L*-inositol-1,2,3,5-tetraangelate [16,17]. The inositol angelates isolated from *Amoora dasyclada* have hydroxyl groups attached to two of its side chains. The chemical shifts of carbon and hydrogen at the same position are changed due to the strong electron-withdrawing ability of the hydroxyl group.

Molecular formula of compound 1 was determined to be $C_{26}H_{36}O_{12}$ on the basis of its HR-ESI-MS data (m/z 563.2109 $[M + Na]^+$, calcd for $C_{26}H_{36}NaO_{12}$: 563.2106), requiring nine degrees of unsaturation. The IR and UV spectrum exhibited absorption bands for -OH, C=O, and C=C groups. Analysis of ^{13}C -NMR and DEPT data indicate 26 carbon resonances including six methyl, two methylene, ten methine and eight quaternary carbons (Table 1). 1H -NMR data show four hydroxyl and four carbon–carbon double-bonds, which revealed four ester groups and four olefinic bonds. Furthermore, the remaining unsaturation demonstrates a six-carbon skeleton established by COSY data. Two meta hydroxyls were elucidated by HMBC correlations between δ_C 66.3 (1-OH), δ_C 66.4 (3-OH) and δ_C 72.5 (C-2); moreover, relationships between 2-H and 1'-C, 4-H and 1''-C, 5-H and 1'''-C, 6-H and 1''''-C revealed the four esterification substituent groups of inositol. According to the data comparison, the overall structure of compound 1 is almost similar to the known compound angelate from *Inula cappa*. The difference is that HMBC correlations from δ_C 4.01 (5''-2H) and δ_H 4.06/4.09 (5'''-2H) to δ_C 165.9 (C-1'', C-1''') show the interaction from extra hydroxyls to carbonyl, indicated that two side chains on the carbon ring each connected to a hydroxyl group, which does not exist in the previously identified compound (Figure 2).

Compounds 2 and 3 are isomers of compound 1; their chemical shifts are basically the same. The differences between them are embodied in the relative position of two hydroxyls on the ring (adjacent in compound 2 and para in compound 3) which were proved by HMBC and COSY data. The relative stereochemistry of 1–3 was determined by circular dichroism spectrum recorded in MeOH. According to the ECD data (Figure S32, supplementary information) and quantum-chemical calculation using time-dependent density functional theory, the absolute configuration of compound 3 is indicated to be (1*S*,2*S*,3*R*,4*R*,5*S*,6*S*). Considering the location of hydroxyls and comparing to the CD data of 3, we establish the absolute configurations of compound 1 (1*S*,2*S*,3*S*,4*R*,5*R*,6*S*) and 2 (1*R*,2*R*,3*S*,4*R*,5*R*,6*S*).

Table 1. ^1H - and ^{13}C -NMR spectra data of 1–5.

No.	1		2		3		No.	4		5	
	δ_{C}	δ_{H}	δ_{C}	δ_{H}	δ_{C}	δ_{H}		δ_{C}	δ_{H}	δ_{C}	δ_{H}
1	66.3	4.00, m	69.4	4.19, m	70	4.34, m	1	38.4	1.97, m	39.6	1.94, m
2	73.7	5.11, dd (4.2, 3.2)	72.9	5.36, dd (9.6, 6.9)	70	4.34, m	2	34.8	1.43, m	35.8	1.42, m
3	66.4	4.10, dd (10.2, 3.2)	72.9	5.36, dd (9.6, 6.9)	71.4	5.54, dd (5.5, 3.8)	2	34.8	2.75, m	35.8	2.83, m
4	72.3	5.27, t (10.2, 6.5)	69.4	4.19, m	70.5	5.79, dd (5.5, 3.8)	3	216.9	2.23, m	219.1	2.14, m
5	69.4	5.52, t (10.0, 6.5)	70.3	5.42, t (5.5, 3.8)	70.5	5.79, t (10.0, 6.5)	3	216.9		219.1	
6	71.9	4.91, dd (10.5, 2.9)	70.3	5.42, t (5.5, 3.8)	71.4	5.54, dd (5.5, 3.8)	4	47.9		48.8	
1'	166.1		167.6		167		5	52.4	1.89, m	53.9	1.88, m
2'	127.9		131.3		127.7		6	24.4	1.97, m 2.05, m	24.3	1.97, m 2.05, m
3'	138.3	6.86, brq (7.3)	143.2	7.02, q (7.0)	13.9	6.84, brq (7.2)	7	118.2	5.36, br m	115.4	5.39, br m
4'	14.4	1.83, d (7.3)	14.4	1.89, s	14.5	1.74, d (7.3)	8	145.5		146.9	
5'	12.1	1.83, s	56.3	4.36, d (12.6)	12	1.75, s	9	48.2	2.34, m	49.7	2.38, m
1''	165.9		167.6		166.8	-	10	35.2		36.4	
2''	132.5		131.3		131.3	-	11	17.3	1.60, m	18.3	1.63, m
3''	140.7	6.75, q (7.2)	143.2	7.02, q (7.0)	143	6.91, q (7.2)	12	30.1	1.39, m 1.45, m	31.3	1.39, m 1.46, m
4''	14.2	1.81, d (7.2)	14.4	1.89, s	14.4	1.84, d (7.2)	13	45.2		46.5	
5''	54.6	4.06, d (12.0)	56.3	4.36, d (12.6)	56	4.20, d (12.0)	14	50.9		52.1	
1'''	165.9		166.8		166.8		15	34.2	1.66, m	35.8	1.66, m
2'''	132.5		127.5		131.3		16	28.2	1.73, m	24.9	1.74, m
3'''	140.5	6.61, q (7.2)	140	6.96, brq (7.2)	143	6.91, q (7.2)	17	43.3	1.97, m	44.4	1.98, m
4'''	14.1	1.76, d (7.2)	12.2	1.86, s	14.4	1.84, d (7.2)	18	23.1	2.18, m	21.7	2.17, m
5'''	54.4	4.01, 2H, s	14.7	1.88, s	56	4.20, s 4.24, s	19	12.6	3.41, dd (9.3, 9.4)	44.4	3.57, dd (9.4, 9.4)
1''''	166.6		166.8		167		20	138.6	0.73, s	23.8	0.76, s
2''''	127.5		127.5		127.7		21	130	1.03, s	13.0	1.07, s
3''''	138.2	6.69, brq (7.3)	140	6.96, brq (7.2)	13.9	6.84, dd (10.0, 6.9)	22	112.4		131.1	
4''''	14.3	1.70, d (7.2)	12.2	1.86, s	14.5	1.74, d (7.2)	23	112.4	6.02, s	113.2	6.24, s
5''''	11.8	1.65, s	14.7	1.88, s	12	1.75, s	24	176.7	9.48, s	179.1	9.49, s
							25	41.3	2H, 2.76, s	83.6	4.13, s
							26	70.9		73.5	
							27	29.6	1.25, s	29.8	1.25, s
							28	29.5	1.24, s	29.5	1.23, s
							29	21.5	1.12, s	22.0	1.13, s
							30	25.5	1.04, s	25.0	1.02, s
							31	27.5	1.13, s	28.0	1.18, s
							32			66.5	3.33–3.48, m
							33			15.5	1.17, m

Compound 4 and 5 were identified to be tirucallane-type alkaloids; common to these alkaloids is the attachment of a pyrrole ring having small groups such as aldehyde or alkyl groups to the C-17 of the main structure of the tirucallane [7]. Structures of compound 4 and 5 were elucidated based on known scaffold data of compounds from *Dysoxylum laxiracemosum*.

Compound 4 was determined to be $\text{C}_{31}\text{H}_{45}\text{NO}_3$ on the basis of HR-ESI-MS data (m/z 480.3475 $[\text{M} + \text{H}]^+$, calcd for $\text{C}_{31}\text{H}_{46}\text{NO}_3$: 480.3478), requiring nineteen degrees of unsaturation. The δ_{H} 7.26 and 9.48 indicate an extra hydroxyl and aldehyde. Further analysis by the correlations from δ_{H} 7.26 to δ_{C} 129.9 (C-21) and 138.6 (C-20) confirmed the aldehyde attached to the C-21 of pyrrole ring. HMBC

correlations from δ_H 1.25, 1.24 (6H, H-27/28) to δ_C 70.9 (C-26) and 41.3 (C-25) indicated an isopropyl group attached to C-25.

The molecular formula of compound **5** was $C_{33}H_{49}NO_4$ (m/z 524.3731 $[M + H]^+$, calcd for $C_{33}H_{50}NO_4$: 524.3740), whose structure was basically the same as compound **4** but with one more oxygen atom than compound **4** from the chemical formula. An extra ethoxy was pointed to from δ_H 3.33 and 1.17, while the obvious signal in HMBC data between δ_H 3.33 and δ_C 83.6 (C-25) showed an oxyethyl attached on C-25.

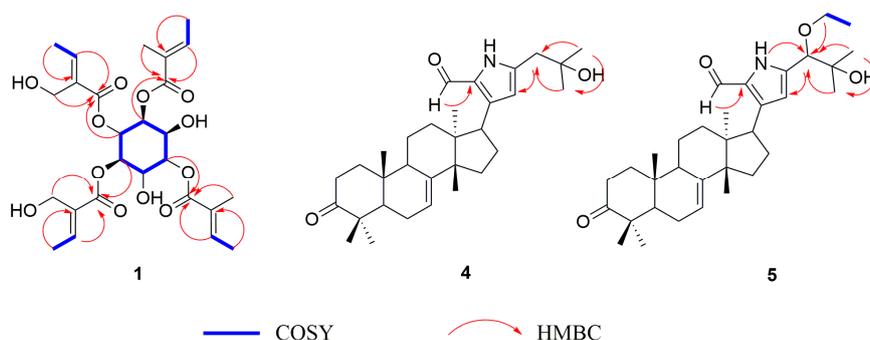


Figure 2. 1H - 1H COSY and HMBC correlations of **1**, **4** and **5**.

2.2. Bioactive Assay

Compounds **1–5** were evaluated for their cytotoxicity against human cancer cell line hepatoblastoma (HepG2) by the MTT method. Compounds **1–3** showed moderate toxicity, with IC_{50} values of 40.3, 48.9 and > 50 μM , respectively. Compounds **4** and **5** exhibited significant activity with the IC_{50} values of 8.4 and 13.2 μM , respectively, compared to camptothecin (32.3 μM) (Figure 3a). In addition, compounds **1–5** were evaluated by brine shrimp bioassay, and the mortality rates to *Artemia salina* were 32.6%, 37.5%, 25.3%, 98.2% and 87.4%, respectively, at a concentration of 10 $\mu g/mL$, in contrast to actinomycin D (100%) (Figure 3b).

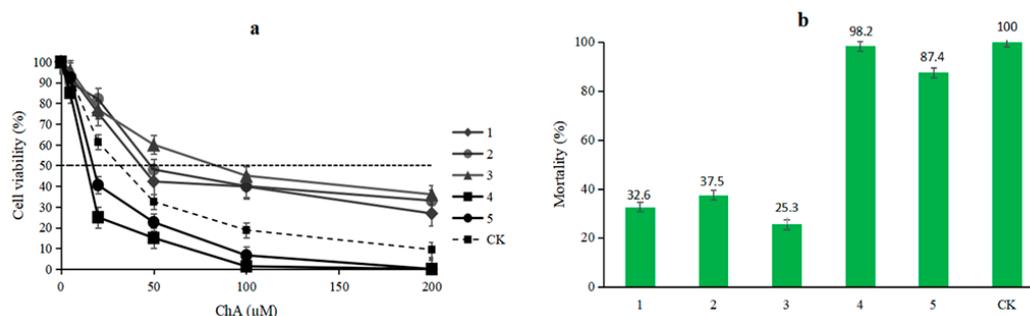


Figure 3. Bioactive assay of compounds **1–5**: **(a)** Cell viability inhibition of HepG2 cell, CK: camptothecin; **(b)** mortality rates to *Artemia salina*, CK: actinomycin D.

3. Materials and Methods

3.1. General Experimental Procedures

Optical rotations were taken on a Perkin-Elmer 241 polarimeter (PerkinElmer, Waltham, MA, USA). The 1D and 2D NMR spectra were measured in acetone- d_6 and DMSO- d_6 (δ_H 2.09/ δ_C 206.0) on a Bruker 600 spectrometer (1H : 500MHz; ^{13}C : 125MHz) (Bruker, Rheinstetten, Germany). HR-ESI-MS were obtained using an ESI-MS (Electrospray Ionization Mass Spectrometer) (Waters Synapt G2, Milford, MA, USA). Semipreparative HPLC separation was performed on a Shimadzu LC-6AD instrument packed with a YMC-Pack ODS-A column (5 μm , 250 mm \times 10 mm). Column chromatographies

(CC) were carried out on Sephadex LH-20 (Amersham Biosciences, Uppsala, Sweden) and silica gel (Qingdao Haiyang Chemical Co., Ltd., Qingdao, China).

3.2. Plant Material

Amoora dasyclada (How et T. Chen) C. Y. Wu, whole plant collected from Xiao-Meng-Lun, Yunnan province, China in August 2013 was used as plant material.

3.3. Extraction and Isolation

The dry branches (16 kg) was smashed directly with ultrasonic extraction by ethanol three times successively, then the extract (820 g) was separated by silica gel CC, eluting with petroleum-ether-acetone step-gradient (100:1, 80:1, 60:1, 40:1, 20:1, 10:1, 5:1, 1:1, 0:1, MeOH) to get the fractions 1–10. Fraction 7 (60:1) was subjected to silica gel (CH₂Cl₂-MeOH, 300:1 to 80:1) to yield fraction 7.3 and fraction 7.4. Fraction 7.3 was chromatographed on silica gel (petroleum-ether-EtOAc, 50:1 to 10:1), sephadex LH-20 (CH₂Cl₂-MeOH) and silica gel (CH₂Cl₂-MeOH, 200:1) to give compound 4. Fraction 7.4 was subjected to MPLC (speed 20 mL/min, 80% MeOH to 100% MeOH), sephadex LH-20 (CH₂Cl₂-MeOH) and silica gel CC (petroleum-ether-EtOAc, 10:1) to give compound 5. Fraction 10 was applied with silica gel CC (CH₂Cl₂-MeOH, 100:1 to 5:1) to obtain fraction 10.2 (50:1) and fraction 10.3 (40:1). Fraction 10.2 was chromatographed on MPLC (70% MeOH), sephadex LH-20 (MeOH) and then silica gel (CH₂Cl₂-MeOH, 50:1) to give compound 3. Fraction 10.3 was chromatographed MPLC (70% MeOH to 40% MeOH). Then, 33% methanol part and 35% methanol part were chromatographed on silica gel CC (CH₂Cl₂-MeOH, 100:1 to 20:1) to give compounds 1 and 2, respectively.

3.4. Cytotoxic Evaluation

Compounds 1–5 were evaluated for their cytotoxic activities to HepG2 tumor cell line and the growth inhibitory activity towards brine shrimp by using the colorimetric assay and small modified microtiter-plate method, respectively as previously described in the literature [18,19].

Cytotoxic activities of compounds 1–5 were examined with the MTT colorimetric method. The HepG2 cells (2×10^4) were grown in Eagle's Minimum Essential Medium, then seeded and attached in 96-well plates for 24 h at 37 °C in 5% CO₂. Then, the cells were treated with 1–5 using different concentrations and incubated for 72 h. Then, the cells were fixed for 1 h at 4 °C with 50% trichloroacetic acid (TCA). Subsequently, the cells were washed with distilled water and dried. Then, 100 µL of SRB was added to each well, and the plate was incubated for 30 min at RT. To remove the excess dye, the cells were washed using 1% acetic acid. Absorption at 540 nm was measured with an ELISA plate reader, and the IC₅₀ value was defined as the concentration at which 50% survival of cells was discerned. All experiments were performed in duplicate and were repeated three times.

Brine shrimp toxicity was assayed by small modified microtiter-plate method using brine shrimp *Artemia salina* as a test organism. Briefly, approximately 30 nuclei larvae hatched from eggs of *A. salina* in 0.2 mL of artificial sea water were incubated with a sample (5 mL in DMSO solution) in a deep-well microtiter plate at room temperature. After 24 h, the dead larvae were determined by counting the number of the dead animals in each well under microscope. To each test row, positive sample was accompanied by adding actinomycin D.

4. Conclusions

Three new inositol angelate compounds (1–3) and two new tirucallane-type alkaloids (4 and 5) were isolated from the *Amoora dasyclada* and their structures were established. Compounds 4 and 5 exhibited significant cytotoxic activity against human cancer cell line HepG2 with IC₅₀ values at 8.4 and 13.2 µM. In addition, compounds 4 and 5 also showed remarkable toxicity to the larvae of *Artemia salina*.

Amoora dasyclada, together with *Amoora ouangliensis* and *Amoora stellato-spuamosa*, belongs to the terpenoid-rich genus *Amoora* Roxb. (Meliaceae), which is followed with interest in the studies on

the chemicals with antitumor properties [8–12]. Two novel tirucallane triterpenoids (4 and 5) with cytotoxicity identified in this research can provide evidence of chemotaxonomy and medicinal value for this species. Additionally, the rarely studied inositol angelates had only been isolated from the Chinese traditional medicine herb *Inula cappa* before, which is an ingredient of a famous Chinese formula against fever, abdominal distention and menoxenia [16,17]. Identification and evaluation of three new inositol angelates (1–3) from *Amoora dasyclada* in this work suggest the further definition of the roles of *Amoora dasyclada* in phytochemistry research and medicinal application.

Supplementary Materials: The supplementary materials are available online.

Author Contributions: Isolation and identification, S.-X.Y., Y.K. and G.D.; bioassay performance, B.L. and Y.-X.Z.; writing—original draft preparation, C.-G.S.; writing—review and editing, J.-C.Q.; project administration, M.-Z.Z. and C.Z. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by The Ability Establishment of Sustainable Use for Valuable Chinese Medicine resources (2060302); the Fundamental Research Funds for the Central Universities; National Science & Technology Fundamental Resources Investigation Program of China (2018FY100800); National Natural Science Foundation of China (21702187, 31870332, 31470414).

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Mulholland, D.A.; Parel, B.; Coombes, P.H. The Chemistry of the Meliaceae and Ptaeroxylaceae of Southern and Eastern Africa and Madagascar. *Curr. Org. Chem.* **2000**, *4*, 1011–1054. [[CrossRef](#)]
2. Koul, O.; Singh, G.; Singh, R.; Daniewski, W.M.; Berlozecki, S.J. Bioefficacy and mode-of-action of some limonoids of salannin group from *Azadirachta indica* A. Juss and their role in a multicomponent system against lepidopteran larvae. *J. Biosci.* **2004**, *29*, 409–416. [[CrossRef](#)] [[PubMed](#)]
3. Tian, W.M.; Wu, J.L.; Hao, B.Z. Vegetative Storage Proteins in Meliaceae. *Acta. Bot. Sin.* **2002**, *44*, 242–245.
4. Ma, Y.Y.; Zhao, D.G.; Li, Y. Cytotoxic triterpenes with diverse skeletons from *Amoora tsangii*. *Phytochem. Lett.* **2016**, *15*, 251–255. [[CrossRef](#)]
5. Zhang, Y.; Wang, J.S.; Luo, J. Novel Nortriterpenoids from *Aphanamixis grandifolia*. *Chem. Pharm. Bull.* **2011**, *59*, 282–286. [[CrossRef](#)] [[PubMed](#)]
6. Zhang, Y.; Wang, J.; Wei, D. Cytotoxic tirucallane C26 triterpenoids from the stem barks of *Aphanamixis grandifolia*. *Phytochemistry* **2010**, *71*, 2199–2204. [[CrossRef](#)] [[PubMed](#)]
7. Zhang, X.Y.; Li, Y.; Wang, Y.Y.; Cai, X.H.; Feng, T.; Luo, X.D. Tirucallane-Type Alkaloids from the Bark of *Dysoxylum laxiracemosum*. *J. Nat. Prod.* **2010**, *73*, 1385–1388. [[CrossRef](#)] [[PubMed](#)]
8. Yang, S.M.; Wu, D.G.; Liu, X.K. Anticancer Activity of Diterpenoids from *Amoora ouangliensis* and *Amoora stellatosquamosa*. *Z. Naturforsch. C* **2010**, *65*, 39–42. [[CrossRef](#)] [[PubMed](#)]
9. Yang, S.M.; Song, Q.S.; Qing, C. Anticancer activity of tirucallane triterpenoids from *amoora dasyclada*. *Z. Naturforsch. C* **2006**, *61*, 193–195. [[CrossRef](#)] [[PubMed](#)]
10. Wang, H.; Zhang, X.F.; Yang, S.M. A new triterpenoid from *Amoora dasyclada*. *Acta. Bot. Sin.* **2004**, *46*, 256–260.
11. Yang, S.M.; Ma, Y.B.; Luo, X.D. Two new tetranortriterpenoids from *Amoora dasyclada*. *Chinese Chem. Lett.* **2004**, *15*, 1187–1190.
12. Yang, S.M.; Ding, L.; Wu, S.H. Two new tirucallane triterpenes with six-membered hemiacetal from *Amoora dasyclada*. *Z. Naturforsch. C* **2004**, *59*, 1067–1069. [[CrossRef](#)]
13. Huang, H.L.; Wang, C.M.; Wang, Z.H. Tirucallane-Type Triterpenoids from *Dysoxylum lenticellatum*. *J. Nat. Prod.* **2011**, *74*, 2235–2242. [[CrossRef](#)] [[PubMed](#)]
14. Ogbourne, S.M.; Suhrbier, A.; Jones, B.; Cozzi, S.J.; Boyle, G.M.; Morris, M.; McAlpine, D.; Johns, J.; Scott, T.M.; Sutherland, K.P.; et al. Antitumor Activity of 3-ingenyl Angelate. *Cancer Res.* **2004**, *64*, 2833–2839. [[CrossRef](#)] [[PubMed](#)]
15. Lee, S.; Lee, Y.S.; Jung, S.H.; Hyun, K.; Kim, S.K.; Kang, S.S. Anti-tumor activities of decursinol angelate and decursin from *Angelica gigas*. *Arch. Pharm. Res.* **2003**, *26*, 727–730. [[CrossRef](#)] [[PubMed](#)]
16. Zou, Z.M.; Xie, H.G.; Zhang, H.W.; Xu, L.Z. Inositol angelates from the whole herb of *Inula cappa*. *Fitoterapia* **2008**, *79*, 393–394. [[CrossRef](#)] [[PubMed](#)]

17. Bohlmann, F.; Ahmed, M.; Jakupovic, J. Inositol angelates from *Inula cappa*. *Phytochemistry* **1982**, *21*, 780–782. [[CrossRef](#)]
18. Li, X.; Tian, Y.; Yang, S.X.; Zhang, Y.M.; Qin, J.C. Cytotoxic azaphilone alkaloids from *Chaetomium globosum* TY1. *Bioorg. Med. Chem. Lett.* **2013**, *23*, 2945–2947. [[CrossRef](#)] [[PubMed](#)]
19. Qin, J.C.; Zhang, Y.M.; Gao, J.M.; Bai, M.S.; Yang, S.X.; Laatsch, H.; Zhang, A.L. Bioactive metabolites produced by *Chaetomium globosum*, an endophytic fungus isolated from *Ginkgo biloba*. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 1572–1574. [[CrossRef](#)] [[PubMed](#)]

Sample Availability: Not available.



© 2020 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<http://creativecommons.org/licenses/by/4.0/>).