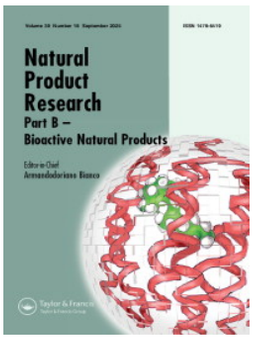


การอ้างอิงอยู่ในหน้า 8

Natural Product Research

Formerly Natural Product Letters

ISSN: 1478-6419 (Print) 1478-6427 (Online) Journal homepage: www.tandfonline.com/journals/gnpl20

Secondary metabolites from the twigs and stems of *dasymaschalon filipes* (ridl.) ban. and their biological activities

Tanapol Bunpan, Phansuang Udomputtimekakul, Wilart Pompimon, Wipanoot Baison, Yaowares Chusiri, Saranya Wattananon, Narong Nuntasaen, Kanoknetr Suksen, Arthit Chairoungdua, Jitra Limthongkul, Chanita Naparswad, Suttiporn Pikulthong & Anan Athipornchai

To cite this article: Tanapol Bunpan, Phansuang Udomputtimekakul, Wilart Pompimon, Wipanoot Baison, Yaowares Chusiri, Saranya Wattananon, Narong Nuntasaen, Kanoknetr Suksen, Arthit Chairoungdua, Jitra Limthongkul, Chanita Naparswad, Suttiporn Pikulthong & Anan Athipornchai (14 May 2025): Secondary metabolites from the twigs and stems of *dasymaschalon filipes* (ridl.) ban. and their biological activities, Natural Product Research, DOI: 10.1080/14786419.2025.2503016

To link to this article: https://doi.org/10.1080/14786419.2025.2503016

View supplementary material

Published online: 14 May 2025.

Submit your article to this journal

Article views: 129

View related articles

View Crossmark data

Full Terms & Conditions of access and use can be found at
https://www.tandfonline.com/action/journalInformation?journalCode=gnpl20

NATURAL PRODUCT RESEARCH
https://doi.org/10.1080/14786419.2025.2503016

Taylor & Francis
Taylor & Francis Group

Check for updates

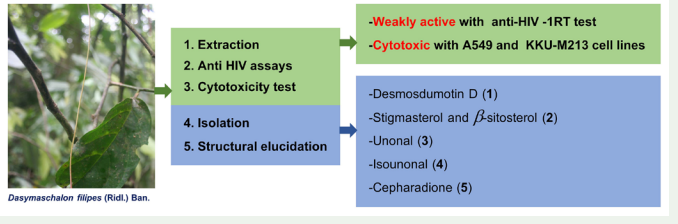
Secondary metabolites from the twigs and stems of *dasymaschalon filipes* (ridl.) ban. and their biological activities

Tanapol Bunpan[a], Phansuang Udomputtimekakul[a], Wilart Pompimon[a], Wipanoot Baison[a], Yaowares Chusiri[a], Saranya Wattananon[b], Narong Nuntasaen[c], Kanoknetr Suksen[d], Arthit Chairoungdua[d], Jitra Limthongkul[e], Chanita Naparswad[e], Suttiporn Pikulthong[f] and Anan Athipornchai[g]

[a]Department of Chemistry and Center of Excellence for Innovation in Chemistry, Faculty of Science, Lampang Rajabhat University, Lampang, Thailand; [b]Department of Food Science, Faculty of Agricultural Technology, Lampang Rajabhat University, Lampang, Thailand; [c]Department of Chemistry, Faculty of Science and Center of Excellence for Innovation in Chemistry, Mahidol University, Bangkok, Thailand; [d]Department of Physiology, Faculty of Science, Mahidol University, Bangkok, Thailand; [e]Department of Microbiology, Faculty of Science, Mahidol University, Bangkok, Thailand; [f]Department of Chemistry, Faculty of Science, Mahidol University, Bangkok, Thailand; [g]Department of Chemistry and Center of Excellence for Innovation in Chemistry, Faculty of Science, Burapha University, Bangsaen, Chonburi, Thailand

ABSTRACT

Investigation of the crude hexane and ethyl acetate extracts of the twigs and stems of *D. filipes* (Annonaceae) led to the discovery of five compounds: desmosdumotin D (**1**), a mixture of stigmasterol and *β*-sitosterol (**2**), unonal (**3**), isounonal (**4**), and cepharadione B (**5**). The structural elucidation of the compounds was accomplished using ^{1}H,^{13}C, and 2D NMR techniques. The three crude extracts of *D. filipes* showed weak activity versus the HIV-1 virus. The cytotoxicity assays showed that the crude hexane extract was particularly effective against A549 cell lines, with an ED_{50} of 15.24 mg/mL. Meanwhile, the crude ethyl acetate and methanol extracts inhibited KKU-M213 cell lines, demonstrating ED_{50} values of 13.42 and 10.92 mg/mL, respectively. *D. filipes* is a rich source of potential compounds with anti-HIV-1RT or cytotoxicity activities. This is the first report on the phytochemistry and bioactivity study of *D. filipes*.



ARTICLE HISTORY

Received 18 November 2024
Accepted 4 May 2025

KEYWORDS

Dasymaschalon filipes (ridl.) ban; anti-HIV assays; cytotoxicity assays

CONTACT Phansuang Udomputtimekakul phansuang@g.lpru.ac.th
Supplemental data for this article can be accessed online at https://doi.org/10.1080/14786419.2025.2503016.
© 2025 Informa UK Limited, trading as Taylor & Francis Group

1. Introduction

The genus *Dasymaschalon* (Annonaceae) comprises approximately 30 species of small trees indigenous to the tropical and subtropical regions worldwide. In Thailand, 12 different species have been identified (Wang et al. 2009). Previous phytochemical studies on the *Dasymaschalon* genus have reported various classes of chemical compounds, including acetogenins (Sinz et al. 1998), alkaloids (Chanakul et al. 2011; Hongthong et al. 2014; Jaidee et al. 2015), cyclohexene derivatives (Hongthong et al. 2015; Jaidee et al. 2015), flavonoids (Sinz et al. 1998; Prawat et al. 2013; Chokchaisiri et al. 2015), neolignans (Hongthong et al. 2016), oxygenated phenylpropanoids (Yu et al. 2017), and triterpenoids (Prawat et al. 2013). Some of these compounds have significant biological activities with anti-HIV (Hongthong et al. 2016; Yu et al. 2017); Bunteang et al. 2018), anti-inflammatory (Hongthong et al. 2015), anti-malarial (Jaidee et al. 2015), and cytotoxicity properties (Chanakul et al. 2011; Hongthong et al. 2014; Jaidee et al. 2015; Hongthong et al. 2016). A preliminary screening of the crude extracts from the twigs and stems of *Dasymaschalon filipes* (Wang et al. 2009) (Figure 1) demonstrated cytotoxicity against human cholangiocarcinoma (KKU-M213), human colon adenocarcinoma (MDA-MB-231), and human lung carcinoma (A549) cell lines. An investigation into the chemical compounds in these extracts was initiated. This paper outlines the isolation and structural elucidation of the phytochemicals derived from this plant.

2. Results and discussion

The air-dried, milled, and mixed twigs and stems of *D. filipes* (1.8 kg) were extracted using hexane (15 litres × 3 days × 4 times), ethyl acetate (23 litres × 3 days × 4 times), and methanol (23 litres × 3 days × 4 times), yielding crude extracts of hexane (7.43 g), ethyl acetate (25.28 g), and methanol (46.55 g), respectively. Biological activity tests revealed that the three crude extracts of the twigs and stems of *D. filipes* are weakly active in the anti-HIV-1RT test at a range value of 30.33–47.52% inhibition (Table 1).

Figure 1. The leaves, twigs, stems, flowers, and fruits of *D. filipes* (ridl.) ban.

Table 1. Anti-HIV-1RT Study of three crude extracts from twigs and stems of *D. filipes*.

	Anti-HIV-1RT[a]
Crude extracts	% inhibition (Activity results)
Hexane extract	47.52 (Weakly active)
Ethyl acetate extract	42.42 (Weakly active)
Methanol extract	30.33 (Weakly active)

[a]Anti-HIV-1RT activity express as % inhibition at 200 μg/mL: very active *(VA)* = >70% inhibition, moderately active *(MA)* = 50% to 69% inhibition, weakly active *(WA)* = 30% to 50% inhibition and inactive *(I)* = <30% inhibition; For determination of IC_{50} in the HIV-1 RT assay, the coefficients of determination, R^2, were 0.98 – 0.99 in all assays for 50% end point.

Table 2. Cytotoxicity study of crude extracts of twigs and stems of *D. filipes*.

	Cytotoxicity ED_{50} (μg/mL)[a]						
Crude extracts	KKU-M213	FaDu	HT-29	MDA-MB-231	A549	SH-SY5Y	MMNK-1
Hexane extract	16.30	–	–	18.61	15.24	–	–
Ethyl acetate extract	13.42	–	–	18.99	–	–	–
Methanol extract	10.92	–	–	–	–	–	–
Ellipticine (Control)	0.51	0.49	0.54	0.48	0.39	0.48	0.51

[a]Cytotoxic assay: ED_{50} less than 20 μg/mL were considered active for extracts and ED_{50} less than 4 μg/mL were considered active for pure compounds. Cancer cell lines: KKU-M213 *(*Human cholangiocarcinoma*)*, FaDu *(*Human squamous cell carcinoma*)*, HT-29 *(*Human colon adenocarcinoma*)*, MDA-MB-231 *(*Human mammary gland/breast adenocarcinoma*)*, A549 *(*Human lung adenocarcinoma*)*, SH-SY5Y *(*Human neuroblastoma*)*, MMNK-1 *(*highly differentiated immortalised human cholangiocyte cell line*)*.

Moreover, the crude hexane extracts of the twigs and stems of *D. filipes* are active against KKU-M213, MDA-MB-231, and A549 cell lines with an ED_{50} of 16.30, 18.61, and 15.24 mg/mL, respectively, and the crude ethyl acetate extract is active against KKU-M213 and MDA-MB-231 cell lines with an ED_{50} of 13.42 and 18.99 mg/mL, respectively, while the crude methanol extract was only active against KKU-M213 cell lines with an ED_{50} of 10.92 mg/mL (Table 2). The separation and purification of the crude extracts were accomplished using column chromatography techniques with gradient systems of hexane, ethyl acetate, and methanol. The hexane extract was separated, purified, and recrystallized with ethanol to give desmosdumotin D (**1**) (5 mg) (Wu et al. 1989) as a light yellow-white solid. Similarly, the crude ethyl acetate extract gave a mixture of stigmasterol and *β*-sitosterol (**2)** (0.2 g) (Forgo and Kövér 2004; Kamal et al. 2016; Karim et al. 2021) as a white solid, unonal (**3**) (8 mg) (Ju and Yu 1999; Rittiwong 2010) as a yellow-white solid, isounonal (**4**) (15 mg) (Ju and Yu 1999; Rittiwong 2010), as a yellow-white solid, and cepharadione B (**5**) (12 mg) (Kim et al. 2001) as a yellow-white solid. Unfortunately, the separation of the crude methanol extract did not give any interesting compound. The structures of compounds **1–5** are illustrated in Figure 2. The material and methods, bioactivities test, extraction, isolation, and structural characterisation of all compounds are described in the supplemental material.

Although not all compounds were evaluated for anti-HIV-1 RT activity and cytotoxicity tests, the previous report indicates that desmosdomutin B (Nakagawa-Goto et al. 2005) and desmosdomutin C (Nakagawa-Goto et al. 2007) showed cytotoxicity against A549 (human lung carcinoma) with ED_{50} values of 28 and 3.5 μg/mL, while desmosdomutin D demonstrated anti-HIV activity with an IC_{50} value of 13.6 μg/mL

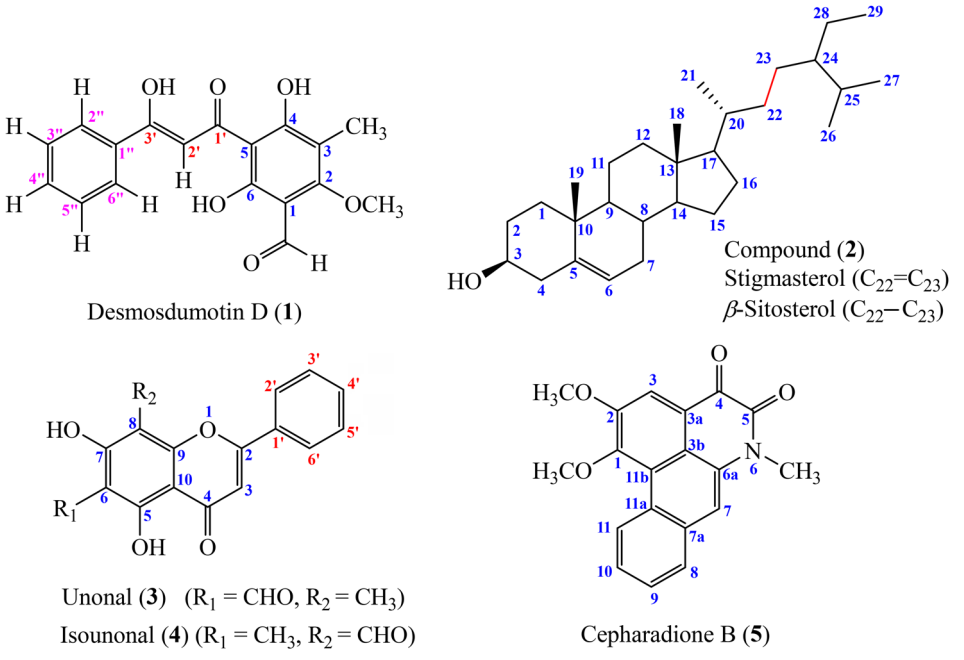


Figure 2. Chemical structure of compounds **1–5**.

(Deng et al. 2024). Isounonal and unonal exhibited NO inhibition in RAW 264.7 cells, with IC_{50} values ranging from 69.1 to 89.8 µg/mL (Kuo et al. 2015). Moreover, their compounds also showed antifungal activities against P. oryzae, R. solani, and S. rolfsii, with MIC/MBC ranges of 15.6/15.6 to 125/250 µg/mL (Tuntipaleepun et al. 2012). Cepharadione B demonstrates significant cytotoxicity against five human tumour cell lines, including A549, SK-OV-3, SK-MEL-2, XF-489, and HCT-15, with identical EC_{50} values of 40 µg/mL (Kim et al. 2001). It also exhibits anti-tyrosinase activities on HSV-1 virus cells, with an inhibition percentage of 3.24 (Chou et al. 2009). Cepharadione B demonstrates significant cytotoxicity against five human tumour cell lines, including A549, SK-OV-3, SK-MEL-2, XF-489, and HCT-15, with identical EC_{50} values of 40 µg/mL (Kim et al. 2001). It also exhibits anti-tyrosinase activities on HSV-1 virus cells, with an inhibition percentage of 3.24 (Chou et al. 2009). Moreover, stigmasterol and *β*-sitosterol were studied and exhibited a wide range of bioactivities, including anti-cancer, anti-osteoarthritis, anti-inflammatory, anti-viral, and anti-diabetic effects (Patel et al. 2017; Bakrim et al. 2022; Zhang et al. 2022; Nandi et al. 2024). Exploring these compounds in twigs and stems of *D. filipes* is consistent with this study's anti-viral and antitumor activity tests. Additional research into the phytochemical investigation and biological activity of other parts of this plant is particularly fascinating. The significant findings of the study could inspire future research in natural product chemistry and modern pharmacology.

3. Conclusions

In this work, five known compounds, including desmosdumotin D (**1**), a mixture of stigmasterol and *β*-sitosterol (**2**), unonal (**3**), isounonal (**4**), and cepharadione B (**5**),

were found in the twigs and stems of *D. filipes*. In the anti-HIV-1RT testing, the three crude extracts showed weak activity versus the HIV-1 virus. The cytotoxicity assay showed that the crude hexane extract is quite specifically active against A549 cell lines, while the crude ethyl acetate and methanol extracts are quite active against KKU-M213 cell lines. However, the cytotoxicity properties of the three crude extracts were not as effective as those of ellipticine, which served as the standard compound in the experiment.

Disclosure statement

No potential conflict of interest was reported by the authors.

Funding

The Centre of Excellence for Innovation in Chemistry (PERCH-CIC), part of the Ministry of Higher Education, Science, Research, and Innovation, supports this research project. The authors express their gratitude to Prof. Dr. Banchob Sripa from the Liver Fluke and Cholangiocarcinoma Research Centre, Department of Pathology, Faculty of Medicine, Khon Kaen University, for the KKU-M213 cells. We would also like to express our gratitude to the Department of Microbiology for the AIDs examination, the Department of Chemistry at Mahidol University, Thailand, for the NMR measurement, and Dr. Narong Nantasean for correcting the plant material.

ORCID

Phansuang Udomputtimekakul http://orcid.org/0000-0002-6664-3055

References

Bakrim S, Benkhaira N, Bourais I, Benali T, Lee L-H, El Omari N, Sheikh RA, Goh KW, Ming LC, Bouyahya A, et al. 2022. Health benefits and pharmacological properties of stigmasterol. Antioxidants. 11(10):1912. doi:10.3390/antiox11101912.

Bunteang S, Chanakul W, Hongthong S, Kuhakarn C, Chintakovid W, Sungchawek N, et al. 2018. Anti-HIV activity of alkaloids from *Dasymaschalon echinatum*. Nat Prod Commun. 13(1):29–32. doi:10.1177/1934578X1801300110.

Chanakul W, Tuchinda P, Anantachoke N, Pohmakotr M, Piyachaturawat P, Jariyawat S, Suksen K, Jaipetch T, Nuntasaen N, Reutrakul V, et al. 2011. Cytotoxic alkaloids from stems, leaves and twigs of *Dasymaschalon blumei*. Fitoterapia. 82(7):964–968. – doi:10.1016/j.fitote.2011.05.012.

Chokchaisiri R, Chaichompoo W, Chalermglin R, Suksamrarn A. 2015. Potent antiplasmodial alkaloids and flavonoids from *Dasymaschalon acuminatum*. Rec Nat Prod. 9(2):243–246.

Chou SC, Su CR, Ku YC, Wu TS. 2009. The constituents and their bioactivities of *Houttuynia cordata*. Chem Pharm Bull (Tokyo). 57(11):1227–1230. doi:10.1248/cpb.57.1227.

Deng Y, Song X, Yun T, Xiang Z, Wang G, Li G, Zhang Y, Song Y, Liu Q. 2024. Total synthesis and anti-HIV activity evaluation of desmosdumotin D and Analogues. DDC. 3(1):33–51. doi:10.3390/ddc3010003.

Forgo P, Kövér KE. 2004. Gradient enhanced selective experiments in the ^{1}H NMR chemical shift assignment of the skeleton and side-chain resonances of stigmasterol, a phytosterol derivative. Steroids. 69(1):43–50. doi:10.1016/j.steroids.2003.09.012.

Hongthong S, Kuhakarn C, Jaipetch T, Piyachaturawat P, Jariyawat S, Suksen K, et al. 2016. A new neolignan, and the cytotoxic and anti-HIV-1 activities of constituents from the roots

of *Dasymaschalon sootepense*. Nat Prod Commun. 11(6):809–813. doi:10.1177/1934578X1601100628.

Hongthong S, Kuhakarn C, Jaipetch T, Prabpai S, Kongsaeree P, Piyachaturawat P, Jariyawat S, Suksen K, Limthongkul J, Panthong A, et al. 2015. Polyoxygenated cyclohexene derivatives isolated from *Dasymaschalon sootepense* and their biological activities. Fitoterapia. 106:158–166. – doi:10.1016/j.fitote.2015.09.001.

Hongthong S, Kuhakarn C, Reutrakul V, Jariyawat S, Piyachaturawat P, Nuntasaen N, Jaipetch T.,. 2014. Cytotoxic alkaloids from leaves and twigs of *Dasymaschalon sootepense*. Nat Prod Commun. 9(7):929–932. doi:10.1177/1934578X1400900711.

Jaidee A, Promchai T, Trisuwan K, Laphookhieo S, Rattanajak R, Kamchonwongpaisan S, Pyne SG, Ritthiwigrom T. 2015. Cytotoxic and antimalarial alkaloids from the twigs of *Dasymaschalon obtusipetalum*. Nat Prod Commun. 10(7):1175–1177. doi:10.1177/1934578X1501000709.

Ju J, Yu J. 1999. Zhongguo Zhong yao za zhi = Zhongguo zhongyao zazhi =. Zhongguo Zhong Yao Za Zhi. 24(7):418–421, 446.

Kamal N, Clements C, Gray AI, Edrada-Ebel R. 2016. Anti-infective activities of secondary metabolites from *Vitex pinnata*. J App Pharm Sci. 6(1):102–106. doi:10.7324/JAPS.2016.600117.

Karim N, Khan I, Abdelhalim A, Halim SA, Khan A, Al-Harrasi A. 2021. Stigmasterol can be new steroidal drug for neurological disorders: evidence of the GABAergic mechanism via receptor modulation. Phytomedicine. 90:153646. doi:10.1016/j.phymed.2021.153646.

Kim SK, Ryu SY, No J, Choi SU, Kim YS. 2001. Cytotoxic alkaloids from *Houttuynia cordate*. Arch Pharm Res. 24(6):518–521. doi:10.1007/BF02975156.

Kuo P-C, Thang TD, Huang G-J, Huang B-S, Hoa LTM, Yang M-L, Wu T-S. 2015. Flavonoids from the fruits of *Desmos cochinchinesis* var. fulvecens and their inhibitory effects on No production. Chem Nat Compd. 51(1):152–155. doi:10.1007/s10600-015-1226-7.

Nakagawa-Goto K, Bastow KF, Wu JH, Tokuda H, Lee KH. 2005. Total synthesis and bioactivity of unique flavone desmosdumotin B and its analogs. Bioorg Med Chem Lett. 15(12):3016–3019. doi:10.1016/j.bmcl.2005.04.070.

Nakagawa-Goto K, Chen TH, Peng CY, Bastow KF, Wu JH, Lee KH. 2007. Antitumor agents 259. Design, syntheses, and structure – activity relationship study of desmosdumotin C analogs. J Med Chem. 50(14):3354–3358. doi:10.1021/jm0702534.

Nandi S, Nag A, Khatua S, Sen S, Chakraborty N, Naskar A, Acharya K, Calina D, Sharifi-Rad J. 2024. Anticancer activity and other biomedical properties of β-sitosterol: bridging phytochemistry and current pharmacological evidence for future translational approaches. Phytother Res. 38(2):592–619. doi:10.1002/ptr.8061.

Patel K, Kumar V, Verma A, Rahman M, Patel DK. 2017. β-sitosterol: bioactive compounds in foods, their role in health promotion and disease prevention "a concise report of its phytopharmaceutical importance". Curr Tradit Med. 3(3):168–177. doi:10.2174/2215083803666170615111759.

Prawat U, Chairerk O, Lenthas R, Salae A-W, Tuntiwachwuttikul P. 2013. Two new cycloartane-type triterpenoids and one new flavanone from the leaves of *Dasymaschalon dasymaschalum* and their biological activity. Phytochem Lett. 6(2):286–290. doi:10.1016/j.phytol.2013.03.002.

Rittiwong T. 2010. *Chemical constituents from the leaves of Desmos chinensis Lour* [Doctoral dissertation, MS thesis]. Thailand: Prince of Songkla University, Hat Yai.

Sinz A, Matusch R, Kämpchen T, Fiedler W, Schmidt J, Santisuk T, Wangcharoentrakul S, Chaichana S, Reutrakul V. 1998. Novel acetogenins from the leaves of *Dasymaschalon sootepense*. HCA. 81(9):1608–1615. doi:10.1002/(SICI)1522-2675(19980909)81:9%3C1608::AID-HLCA1608%3E3.0.CO;2-F.

Sinz A, Matusch R, Santisuk T, Chaichana S, Reutrakul V. 1998. Flavonol glycosides from *Dasymaschalon sootepense*. Phytochemistry. 47(7):1393–1396. doi:10.1016/S0031-9422(97)00719-X.

Tuntipaleepun M, Chakthong S, Ponglimanont C, Plodpai P, Voravuthikunchai SP. 2012. Antifungal and cytotoxic substances from the stem barks of *Desmos chinensis*. Chin Chem Lett. 23(5):587–590. doi:10.1016/j.cclet.2012.03.019.

Wang J, Chalermglin P, Saunders RMK. 2009. The genus *Dasymaschalon* (Annonaceae) in Thailand. Syst Bot. 34(2):252–265. – doi:10.1600/036364409788606271.

Wu J, Shi N, Pan M, Wang X, Yi Y. 1989. 2005. Studies on the structure and activity of anti-HIV compounds in {\sl Desmos dumosus}. Zhongguo Yao Xue Za Zhi. 40(7):495–497.

Yu Z-X, Niu Z-G, Li X-B, Zheng C-J, Song X-M, Chen G-Y, Song X-P, Han C-R, Wu S-X. 2017. New phenylpropanoid and 6H-dibenzo[*b*,*d*]pyran-6-one derivatives from the stems of *Dasymaschalon rostratum*. Fitoterapia. 118:27–31. doi:10.1016/j.fitote.2017.02.003.

Zhang X, Wang J, Zhu L, Wang X, Meng F, Xia L, Zhang H. 2022. Advances in stigmasterol on its anti-tumor effect and mechanism of action. Front Oncol. 12:1101289. doi:10.3389/fonc.2022.1101289.