

Chemical Constituents Isolated from *Lycium shawii* and their Chemotaxonomic Significance

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Abstract: Phytochemical investigation of *Lycium shawii* Roem. & Schult provided fourteen compounds, including lyciumate (**1**), dehydrocostus lactone (**2**), costunolide (**3**), catechin (**4**), lyciumaside (**5**), emodin (**6**), emodin-8-*O*- β -D-glucoside (**7**), aloe-emodin (**8**), aloe-emodin-8-*O*- β -D-glucoside (**9**), aloe emodin-11-*O*-rhamnoside (**10**), chrysophanol-8-*O*- β -D-glucoside (**11**), nonacosane-10-ol (**12**), betulinic acid (**13**) and β -sitosterol glucopyranoside (**14**). The compounds may be classified as three sesquiterpene lactones (**1-3**), two phenolic compounds (**4** and **5**), six anthraquinones (**6-11**), one long chain alcohol (**12**), one lupane-type triterpenoid (**13**) and a steroid (**14**). Compounds **2**, **3**, **7** and **9-12** are reported here for the first time as isolated from any species of *Lycium* as well as from the Solanaceae family while compounds **8**, **13** and **14** are reported to be found for the first time in the genus *Lycium*. All structural assignments were made by comparing the NMR spectral data of the pure isolates with that published in the quoted literature.

Keywords: *Lycium shawii*; Solanaceae; anthraquinone; sesquiterpene. © 2018 ACG Publications. All rights reserved.

1. Plant source

Lycium (Solanaceae) comprises of ca. 90 species of thorny shrubs distributed throughout the tropical regions of the world. *L. shawii* Roem & Schult is a thorny shrub which is locally known as "Ghasad" and is found in the Sultanate of Oman. The stem bark, *L. shawii*, was purchased from Nizwa Souq (May, 2015) and identified through a plant taxonomist (Department of Biological Sciences and Chemistry, University of Nizwa, the Sultanate of Oman), where a voucher specimen (BSHR-05/2015) is deposited.

2. Previous studies

A previous report by Baghdadi *et al.* described the presence of rutin, diosgenin, and β -sitosterol [1], while the current author described the presence of one diacylglycoside and one sesquiterpene lactone from *L. shawii* [2].

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3. Present Study

Due to the increasing importance in the use of active agents in plants for medicinal purposes, a more comprehensive phytochemical investigation of *L. shawii* was of paramount importance. The air-dried powder material (640 g) of the stem bark (*L. shawii*) was extracted with methanol for a couple of weeks. The obtained methanol extract (304 g) was suspended in water and successively partitioned to provide the following fractions viz., *n*-hexane (26 g), CH₂Cl₂ (11 g), EtOAc (25 g), *n*-BuOH (26 g) and aqueous (44.5 g). The *n*-hexane fraction was loaded on silica gel column chromatography (CC) and eluted with *n*-hexane, followed by increasing concentrations of EtOAc in *n*-hexane (10, 20, 30, and 100%) to give four fractions H_{A-D}. Fraction H_B (0.5 g) was further purified by CC using *n*-hexane:EtOAc (80:20 to 60:40) to provide lyciumate (**1**, 5 mg) [2], dehydrocostus lactone (**2**, 60 mg) and costunolide (**3**, 45 mg) [3], while fraction H_A (0.3 g) on further CC purification with *n*-hexane:EtOAc (90:10) as eluent provided nonacosane-10-ol (**12**, 12 mg) [4].

Similarly, the EtOAc fraction (25 g) was loaded over CC and eluted with a solvent system of increasing polarity, viz., *n*-hexane–EtOAc, EtOAc, EtOAc–MeOH and pure MeOH to obtained four fractions (E_{A-D}). Fraction E_B was further subjected to CC purification using the eluent system of *n*-hexane:EtOAc (80:20 to 40:60) and afforded catechin (**4**, 85 mg) [5], emodin (**6**, 16 mg) [6], aloemodin (**8**, 60 mg) [7], and aloemodin-11-*O*-rhamnoside (**10**, 25 mg) [8], chrysophanol-8-*O*- β -D-glucoside (**11**, 9 mg) [9], betulinic acid (**13**, 30 mg) [10] and β -sitosterol glucopyranoside (**14**, 30 mg) [11]. Similarly fraction E_C was further subjected to silica gel CC eluting with MeOH:EtOAc (10:90) to afford lyciumaside (**5**, 12 mg) [2] while fraction E_D was loaded directly onto a recycling HPLC system using MeOH:EtOAc (50:50) at a flow rate of 4 mL/min and using a UV detector to indicate the active compounds, provided emodin-8-*O*- β -D-glucoside (**7**, 12 mg) [7] and aloemodin-8-*O*- β -D-glucoside (**9**, 9 mg).

4. Chemotaxonomic Significance

More than 200 natural products have been reported to be present in the genus *Lycium*, including the alkaloids viz., cyclopentapyrrolidine, imidazole, piperidine, nortropane, tropane, pyrrole, spermine, in addition to peptides, flavonoids, ceramides, anthraquinones, coumarins, steroids, terpenoids (monoterpenes, diterpenes and triterpenes), organic acids, polysaccharides, carotenoids, cinnamic acid amides, lignans, neo-lignanamides, and lignanamides [12]. In the current investigation, a total of fourteen compounds viz., three sesquiterpene lactones [(lyciumate (**1**), dehydrocostus lactone (**2**) and costunolide (**3**)], two phenolic compounds [(catechin (**4**) and lyciumaside (**5**)], six anthraquinones/anthraquinone glycosides [(emodin (**6**), emodin-8-*O*- β -D-glucoside (**7**), aloemodin (**8**), aloemodin-8-*O*- β -D-glucoside (**9**), aloemodin-11-*O*-rhamnoside (**10**), chrysophanol-8-*O*- β -D-glucoside (**11**)], one long chain alcohol (nonacosane-10-ol, **12**), one lupane-type triterpenoid (betulinic acid, **13**), and the steroid (β -sitosterol glucopyranoside, **14**) have been isolated and identified (Figure 1). Moreover lyciumate (**1**) and lyciumaside (**5**) have earlier been identified in *L. shawii* while compounds **2-4**, and **6-14** are reported here for the first time as being isolated from the title plant.

Although the sesquiterpene lactone viz., lyciumate (**1**) has been identified in the extract of the title plant [2], the sesquiterpene lactones viz., dehydrocostus lactone (**2**) and costunolide (**3**) are reported here for the first time to be identified from any species of *Lycium* as well as from the Solanaceae family. Moreover, no sesquiterpene lactone, to our best knowledge, has been reported from genus *Lycium*. Our search of the literature revealed that only four sesquiterpenes were reported from *L. chinense* and *L. halimifolium* [12]. It is well known that sesquiterpene lactones are common in families' viz., Euphorbiaceae, Cactaceae, Solanaceae and Araceae as well as being quite prevalent in the Asteraceae [13]. A further interesting feature of plants of the Solanaceae family is that they produce a distinctive collection of sesquiterpenes described as the phytoalexins [14]. Previously dehydrocostus lactone (**2**) and costunolide (**3**) were reported to be isolated from *Saussurea lappa* Clarke (Compositae) [15], *Cichorium intybus* L. (Asteraceae) [16]. On the other hand the occurrence of catechin (**4**) in the title plant is in agreement with similar types of compounds previously reported

from other *Lycium* species i.e from *L. chinense* [17]. Importantly, compound **4** is now reported for the first time as being isolated from the genus *Lycium* while it has previously been reported to be present in various plants of Solanaceae viz., potato (*Solanum tuberosum*) [18], *Amanaga capsicum*, *Lycopersicon esculentum* Mill, *Capsicum annuum* [19], and *Alchemilla barbatiflora* Juz [20]. The diester lyciumaside (**5**) has previously been reported from the title plant [2].

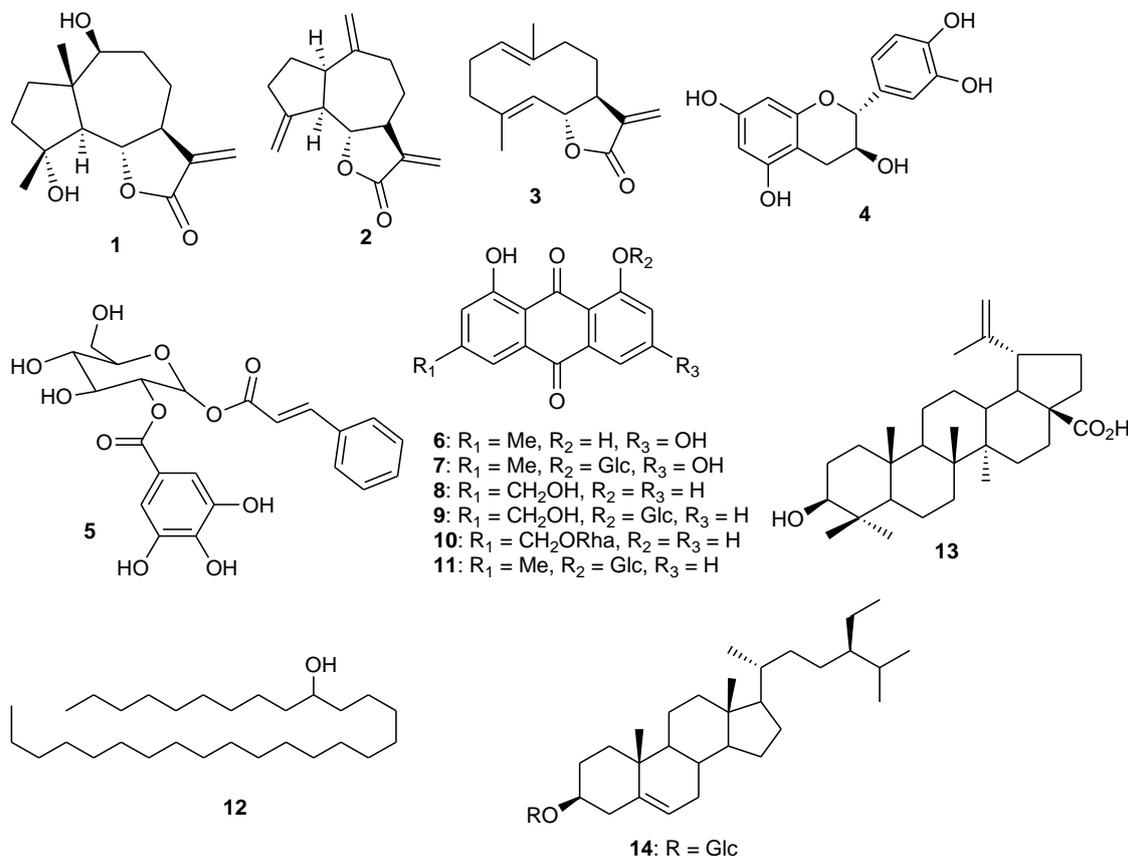


Figure 1. Compounds **1-14** isolated from *L. shawii*

Emodin (**6**) has to the best of our knowledge been reported to be present in only one species of the genus *Lycium* viz., root bark *L. chinense* [12]. However, the presence of emodin (**6**) has been found in numerous other plant families; Actinidiaceae, Amaranthaceae, Asteraceae, Bignoniaceae, Clusiaceae, Cupressaceae, Fabaceae, Liliaceae, Myrsinaceae, Plantaginaceae, Poaceae, Polygonaceae, Rhamnaceae, Rosaceae, Saxifragaceae, Simaroubaceae and Vitaceae [21]. Furthermore, the presence of the anthraquinones emodin-8-*O*- β -D-glucoside (**7**), aloe-emodin (**8**), aloe-emodin-8-*O*- β -D-glucoside (**9**), emodin-11-*O*-rhamnoside (**10**) and chrysophanol-8-*O*- β -D-glucoside (**11**) were reported, for the first time, from the genus *Lycium* and family Solanaceae except aloe-emodin (**8**) which was previously reported from Solanaceae [22]. Interestingly, aloe-emodin (**8**) has been found to be present in various *Cassia* species (family Fabaceae) viz., *C. absus*, *C. alata*, *C. angustifolia*, *C. didymobotrya*, *C. fistula*, *C. grandis*, *C. italica*, *C. javanica* and *C. obtusifolia* [23]. Four additional anthraquinones (other than **6-11**) have previously been reported from only one species of the genus *Lycium* viz., *L. chinense* [12]. The substitution patterns in anthraquinones isolated from *L. shawii* and *L. chinense* have some common structural feature viz., most of the anthraquinones are 1, 3-oxygenated with a methyl group at the C-2 position. Finally, the presence of nonacosane-10-ol (**12**), betulinic acid (**13**) and β -sitosterol glucopyranoside (**14**) is reported here for the first time being isolated from *L. shawii*. The authors have noted that the latter compound (**14**) has previously been reported from *L. chinense* and *L. barbarum* [12] and *Embelia schimperi* [24]. Moreover, a number of triterpenoids have been reported as being isolated from the genus *Lycium* [12]. However, only one lupane-type triterpenoid (lupeol) has been reported from the said genus [12] and betulinic acid (**13**)

represents a second example of a lupane-type triterpenoid from the genus *Lycium* and *Calophyllum* [25].

The current investigation has shown that the main secondary metabolites identified in *L. shawii* were anthraquinones and sesquiterpenoids, in addition to one flavanol, triterpene and steroid. Interestingly, anthraquinones, sesquiterpenoids, flavanols and steroids, as a collective group have only been reported from one species of *Lycium* i.e. *L. chinense* [12]. Of further interest to the authors is the fact that only four additional anthraquinones (other than **6-11**) have previously been reported from only one species of the genus *Lycium* viz., *L. chinense* [12] and that six anthraquinones **6-11** (major class of compound) have been isolated in the current investigation from *L. shawii*. The authors are of the opinion that isolation of anthraquinones sesquiterpenoids, flavanols and steroids in the current study strongly suggests that *L. shawii* has a similar inherent biosynthetic system to and shares a close genetic relationship with *L. chinense* which might have a collective chemotaxonomic value.

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Supporting Information

Supporting information accompanies this paper on <http://www.acgpubs.org/RNP>

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References

- [1] H.H. Baghdadi, S.H. El-Sayed, G. A. Salem and A. M Metwally (1988). A comparative chemical study of *Lycium* species growing in Egypt, *Alexandria J. Pharm. Sci.* **2**, 73–76.
- [2] N. Rehman, H. Hussain, S.A. Al-Riyami, R. Csuk, M. Khiat, G. Abbas, A. Al-Rawahi, I.R. Green, I. Ahmed and A. Al-Harrasi (2016). Lyciumaside and Lyciumate: A new diacylglycoside and sesquiterpene lactone from *Lycium shawii*, *Hel. Chim. Acta.* **99**, 632–635.
- [3] A. Li, A. Sun and R. Liu (2005). Preparative isolation and purification of costunolide and dehydrocostuslactone from *Aucklandia lappa* Decne by high-speed counter-current chromatography, *J. Chromatogr. A.* **1076**, 193–197.
- [4] I. Naz, Saifullah and M.R. Khan (2013). Nematicidal activity of nonacosane-10-ol and 23a-homostigmast-5-en-3 β -ol isolated from the roots of *Fumaria parviflora* (Fumariaceae), *J. Agric. Food Chem.* **61**, 5689–5695.
- [5] Q. Shu-Hua, W. Da-Gang, M. Yun-Bao and L. Xiao-Dong (2003). A novel flavane from *Carapa guianensis*, *Acta Bot. Sin.* **45**, 1129–1133.
- [6] R.T. Dewi, Minarti, A. Darmawan and H. Mulyani (2008). *Proceeding of The International Seminar on Chemistry* 731.
- [7] A.M. Abd El-Kader, A.M.A. Abd El-Mawla, M.H. Mohamed and Z.Z. Ibraheim (2006). Phytochemical and biological studies of *Emex spinosa* (L.) campd. growing in Egypt, *Bull. Pharm. Sci., Assiut University* **29**, 328–347.
- [8] J.M. Conner, A.I. Gray, T. Reynolds and P.G. Waterman (1989). Anthracene and chromone derivatives in the exudate of *Aloe rabiansis*, *Phytochemistry* **28**, 3551–3553.
- [9] D.H. Kim, E.K. Park, E.A. Bae and M.J. Han (2000). Metabolism of rhaponticin and chrysophanol 8-*O*-beta-D-glucopyranoside from the rhizome of *Rheum undulatum* by human intestinal bacteria and their anti-allergic actions, *Biol Pharm. Bull.* **23**, 830–833.

- [10] M.E. Haque, H.U. Shekhar, A.U. Mohamad, H. Rahman, A.M. Islam and M.S. Hossain (2006). Triterpenoids from the stem bark of *Avicennia officinalis*, *Dhaka Univ. J. Pharm. Sci.* **5**, 53–57.
- [11] N.M.M.U. Khan and M.S. Hossain (2015). Scopoletin and β -sitosterol glucoside from roots of *Ipomoea digitata*, *J. Pharmacog. Phytochem.* **4**, 5–7.
- [12] X. Yao, Y. Peng, L.J. Xu, L. Li, Q.L. Wu and P.G. Xiao (2011). Phytochemical and biological studies of *Lycium* medicinal plants, *Chem. Biodiver.* **8**, 976–1010.
- [13] M. Chadwick, H. Trewin, F. Gawthrop and C. Wagstaff (2013). Sesquiterpenoids lactones: Benefits to Plants and People, *Int. J. Mol. Sci.* **14**, 12780–12805.
- [14] B.A. Hess, L. Smentek, J.P. Noel and P.E.O. Maille (2011). Physical constraints on sesquiterpene diversity arising from cyclization of the eudesm-5-yl carbocation, *J. Am. Chem. Soc.* **133**, 12632–12641.
- [15] A. Robinson, T.V. Kumar, E. Sreedhar, V.G.M. Naidu, S.R. Krishna, K.S. Babu, P.V. Srinivas and J.M. Rao (2008). A new sesquiterpene lactone from the roots of *Saussurea lappa*: Structure-anticancer activity study, *Bioorg. Med. Chem. Lett.* **18**, 4015–4017.
- [16] J.W. de Kraker (2002). PhD Thesis; *The Biosynthesis of Sesquiterpene Lactones in Chicory (Cichorium intybus L.) Roots*, Wageningen University, Netherlands.
- [17] S.H. Bok, E.E. Kim, J.Y. Yoo and M.S. Choi (2014). Anti-obesity composition comprising *Lycium chinense* leaf extract and betaine as active ingredient, US 201400508104.
- [18] K. Helmja, M. Vahter, J. Gorbatšova and M. Kaljurand (2007). Characterization of bioactive compounds contained in vegetables of the Solanaceae family by capillary electrophoresis, *Proc. Estonian Acad. Sci. Chem.* **56**, 172–186.
- [19] Y. Ishioka, M. Yagi, M. Ogura and M.Y. Yonei (2015). Polyphenol content of various vegetables: Relationship to antiglycation activity, *Glycative Stress Res.* **2**, 41–45.
- [20] G. Renda, A. Ozel, B. Barut, B. Korkmaz, M. Soral, U. Kandemir and T. Liptaj (2018). Bioassay guided isolation of active compounds from *Alchemilla barbatiflora* Juz, *Rec. Nat. Prod.* **12**, 76–85.
- [21] I. Izhaki (2002). Emodin – a secondary metabolite with multiple ecological functions in higher plants. *New Phytologist.* **155**, 205–217.
- [22] Q. Chang, Y. Peng, C. Dan, Q. Shuai and S. Hu (2015). Rapid in situ identification of bioactive compounds in plants by in vivo nanospray high-resolution mass spectrometry, *J. Agric. Food Chem.* **63**, 2911–2918.
- [23] H. Dave and L. Ledwani (2012). A review on anthraquinones isolated from *Cassia* species and their applications, *Ind. J. Nat. Prod. Res.* **3**, 291–319.
- [24] K. Wabo, G. Zeng, N.H. Tan and P. Tane (2013). A New cytotoxic alkenylresorcinol from *Embelia schimperi*, *Rec. Nat. Prod.* **8**, 37–40.
- [25] N.I. Aminudin, F. Ahmad, M. Taher and R. Mohamed Zulkifli (2016). Cytotoxic and antibacterial activities of constituents from *Calophyllum ferrugineum* Ridley, *Rec. Nat. Prod.* **10**, 649–653.

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