ORIGINAL ARTICLE

Thaliporphine from *Berberis lycium* Royle

[1]Syed Fazal Hussain, [2]Lajbar Khan, [1]Shaukat Khalid, [1]Kaneez Fatimaand [1]Rana Asif Hussain
[1]Baqai Institute of Pharmaceutical Sciences, Baqai Medical University, Karachi.
[2]PCSIR Laboratories, Jamrud Road, Peshawar.

ABSTRACT
Chemical studies on the aerial part of *Berberis lycium* Royle belonging to the family Berberidaceae resulted in the isolation of the aporphine alkaloid 'Thaliporphine', the structure of which was elucidated by using spectroscopic techniques such as ^{1}H NMR, ^{13}C NMR, DEPT-90, DEPT-135 and Mass spectrometry. Although only nine aporphines have been isolated from different *Berberis* species, this is the first report of the isolation of thaliporphine from *Berberis lycium.*

Keywords: *Berberis lycium*, Isoquinoline Alkaloids, Thaliporphine, ^{1}H, ^{13}C and Mass Spectra

1. INTRODUCTION

Berberis is the largest genus of the family Berberidaceae. It is comprised of over 450 species in the world out of which 29 species are found in Pakistan[1]. The most abundant and common species found in the northern part of Pakistan at an altitude of over 1100 meters is *Berberis lycium* Royle. Locally the plant is known as 'kashmal' or 'sumlu'. *Berberis* is one plant whose medicinal value has been acknowledged in many countries of the world. *B. lycium* is known to possess antidiabetic, antihyperlipidemic, hepatoprotective, antibacterial, antifungal, anticoccidial, pesticidal, antimutagenic and wound healing properties, supporting its traditional uses[2].It is an anti-inflammatory agent which is specially used as a remedy for enlargement of liver and spleen[3]. Decoction of fruit is also used in typhoid and fever[4]. *B.lycium* has shown hypoglycemic activity in steptozotocin-nicotinamide induced Type II diabetic rats by an extra pancreatic mechanism[5]. *B. lycium* significantly helps in lowering the LDL, serum total cholesterol and triglycerides and helps in increasing HDL level[6]. A more recent review on *B. lycium* provides information on medicinal uses of the drug[7].

Berberis species are rich repositories of isoquinoline alkaloids. About 200 isoquinoline alkaloids of diverse chemical structures have been isolated from various species of Berberis throughout the world. *B. lycium* has yielded the protoberberine alkaloids berberine[8], the bisbenzylisoquinolines berbamine[8], palmitine[9] and berbamunine[10], the novel seco-bisbenzyl-isoquinoline alkloids sindamine, punjabine, gilgitine[11], chenabine, jhelumine, and karakoramine[10]. Though several aporphine-benzylisoquinoline dimers have been isolated from different *Berberis* species, occurrence of aporphines is rare in *Berberis.* Only nine aporphine alkaloids have been isolated from *Berberis* species namely, amurenine, corydine, glaucine, isoboldine, isocorydine, isocorydine-N-oxide, magnoflorine, thaliporphine(thalicmidine) and thalicmidine-N-oxide from 25 different species namely *B. amurensis*[11], *B.actinacantha*[12],*B. turcberinica*[13], *B. densiflora*[14], *B. integerrima*[15], *B. heteropoda*[16], *B. turcomanica*[17], *B. oblongata*[18], *B. iliensis*[19], *B. nummalaria*[20], *B. mingetsensis*[21], *B. thunbergii*[22], *B. morrisonensis*[23], *B. julianae*[24], *B. microphylla*[25], *B.heterobotrys*[26], *B. crataegina*[27], *B. brandisiana*[28], *B. interbrinine and B. intebrimine*[29], *B.*

* Corresponding Author Email:*sfhkosvi@gmail.com*

polymorpha[30], *B. cretica*[31],*B. koreana*[32], *B. kawakamii*[33],*B. tschonoskyana* and *B. vulgaris*[34], *B. montana*[3].

The most common aporphine in *Berberis* is magnoflorine which has been reported from 16 different species. Thaliporphine, the synonym of which is thalicmidine, has been reported only from six *Berberis* species, *B. densiflora*, *B. heterobotrys*, *B. heteropoda*, *B. integerrima*, *B. oblonga* and *B. turcomanica*. We report here the isolation and structure elucidation of thaliporphine from the aerial part of *Berberis lycium* Royle.

Aporphines have been shown to possess antioxidant to antiproliferative properties[35] and are also potent vasoconstrictor[36]. In another study thaliporphine possessing antioxidant and alpha-1 adrenoceptor antagonistic activity improves acute lung injury after traumatic brain injury[37]. It has also been observed that pretreatment with thaliporphine before ischemia afords cardioprotective efects against reperfusion injury via antioxidant activity[38].

2. EXPERIMENTAL

2.1. General Methods

The ^{1}H and ^{13}C NMR spectra were recorded in Bruker 400 MHz instrument in acetone-d^{6} while the mass spectrum was obtained on a JEOL instrument.

2.2. Plant Material

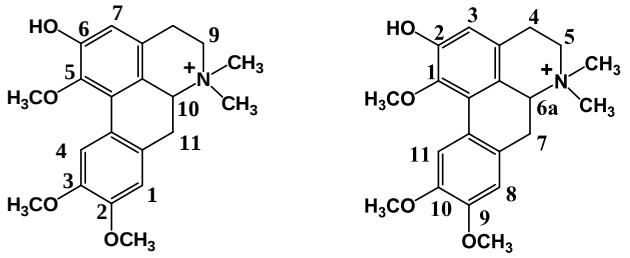
Aerial parts of *Berberis lycium* werecollected from the Murree hills in June 2014, and deposited at PCSIR Peshawar Herbarium (Voucher specimen No. PES-9015).

2.3. Extraction and Isolation

The air-dried leaves and stems (19 kg) were powdered and extracted with ethanol. The removal of solvent, extraction of base with 5% hydrochloric acid and making it alkaline with ammonium hydroxide yielded the basic fraction C(105 g) which was passed through a column of silica gel and eluted with 2% methanol in dichloromethylene. A total of 147 fractions were obtained by combining several fractions and designated as sub fraction C(A). It was packed in a small silica column and eluted with 5% acetone in hexane with ten drops of diethylamine (DEA) and the polarity was increased up to 10% acetone in hexane and DEA. By using preparative TLC on silica gel GF-250 on the fraction 71 obtained from the column by eluting with a solvent system (hexane and acetone, 8:2, *v/v* + 10 drops of DEA), a pure alkaloid was isolated which was identified as thaliporphine.

3. RESULTS AND DISCUSSION

Thaliporphine was originally isolated from *Fagara tinguassoiba* as quaternary salt and was assigned the structure, 6-hydroxy-2,3,5-trimethoxy-N,N-dimethylaporphinium salt (according to old system of numbering for aporphines)[39].

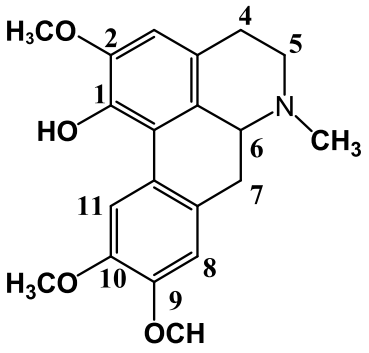


Old system of numbering: 6-hydroxy-2,3,5-trimethoxy-N,N-dimethylaporphinium ion

New system of umbering: 2-Hydroxy-2,9,10-trimethoxy-N,N-dimethylaporphinium ion

Figure 1. Old and New systems of numbering of Aporphines

The structure of quaternary salt of *Fagara tinguassoiba* was revised by synthesizing the alkaloid and the new structure was assigned as 1-hydroxy-2,9,10-trimethoxy-aporphine with the new system of numbering as follows[40].



Interestingly, the new synthetic compound 1-hydroxy-2,9,10-trimethoxyaporphine corresponded to the aporphine alkaloid thaliporphine (thalicmidine) isolated from *Thalictrum fendleri*[41]. The alkaloid isolated from the ethanolic extract of *B. lycium* by using preparative thin-layer chromatography (TLC) as described above was identified as thaliporphine (thalicmidine) by NMR and mass spectrometry. The comparative spectral data of ^{1}H and ^{13}C NMR are as follows:

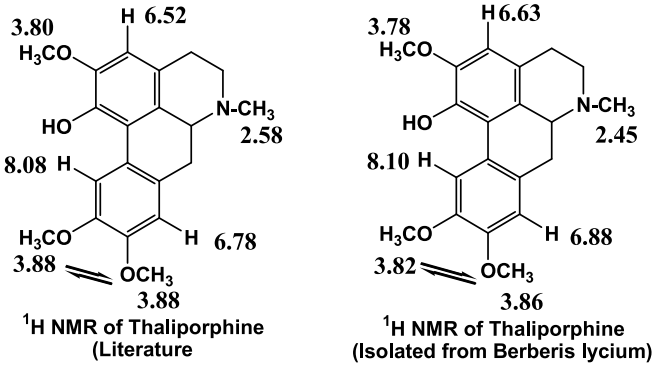


Figure 2: ^{1}H NMR Spectrum of Thaliporphine

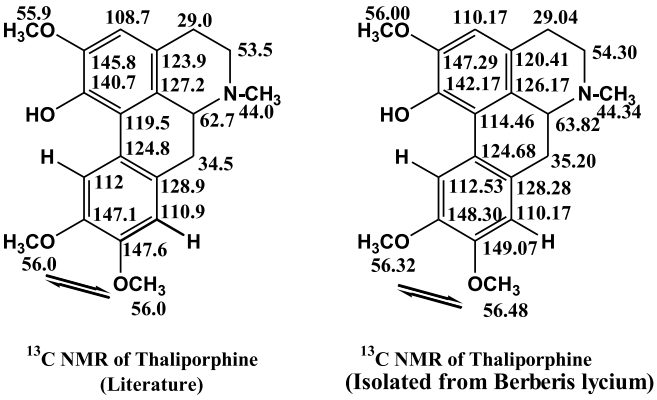


Figure 3. ^{13}C NMR Spectrum of Thaliporphine

The spectral data of the alkaloid was in conformity with that reported in the literature for thaliporphine (thalicmidine)[41]. This is the first report of the isolation of thaliporphine from *B. lycium*.

Conflict of Interest

The authors indicate that there is no conflict of interest regarding the contents in the paper.

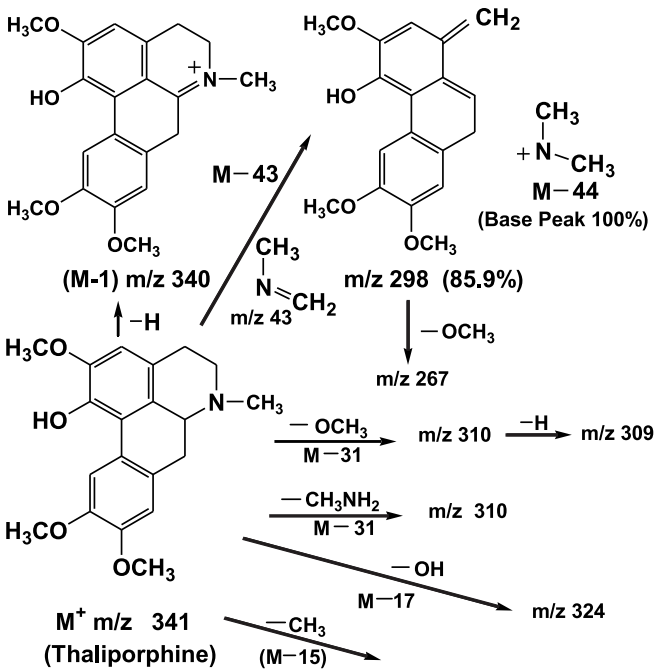


Figure 4. Mass spectral fragmentation of Thaliporphine

Acknowledgment

The authors are grateful to Prof. Dr. Iqbal Choudhary of HEJ Reseach Institute of Chemistry, University of Karachi for NMR and Mass spectra.

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