



Alkaloids from Mongolian species of *Peganum multisectum* (Maxim) Bobrov

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Abstract: Alkaloids of the aerial parts of *P. multisectum* (Maxim) Bobrov (Zygophyllaceae) growing in Mongolia have been studied by capillary Gas Chromatography-Mass Spectrometry (GC-MS) and Column Chromatography (CC). Four compounds comprising of 2-methylquinoline (**1**), 9-amino-2, 3,5,6,7,8-hexahydro-1H-cyclopenta [b] quinoline (**2**), vasicinone (**3**) and harmine (**4**) have been determined by GC-MS, while harmine (**4**), peganine (**5**), deoxypeganine (**6**), deoxyvasicinone (**7**) and harmine (**8**) were isolated as pure compounds by the CC. The structures of the five alkaloids **4**, **5**, **6**, **7** and **8** were elucidated by the MS and ¹H and ¹³C NMR analysis. The alkaloids **1**, **2** and **8** were identified for the first time from this species.

Keywords: *Peganum multisectum* (Maxim) Bobrov, quinoline, quinazoline and indole alkaloids, GC-MS

INTRODUCTION

The family of Zygophyllaceae can be considered as Zygophyllales, which contains more than 285 species within 22 genera. The genus of *Peganum* has six species such as *Peganum harmala* L., *Peganum mexicanum* Gray, *Peganum nigelalastrum* Bunge, *Peganum rothschildianum* F.Buxbaum, *Peganum texanum* M.E.Jones and *Peganum multisectum* (Maxim) Bobrov, which occur in the regions of warm and subtropical temperatures in the world. These species were widely distributed across North Africa, Pakistan, India and Southern part of Iran and have been introduced in Southern and Northern America, Australia, Mexico, Tunisia, China and Mongolia [1-3]. *Peganum nigelalastrum* Bunge, *Peganum harmala* L. and *Peganum multisectum* (Maxim) Bobrov are common plants in Mongolia. In particular, *Peganum multisectum* recently found for the first time in the Eastern and Alashan Gobi part of Mongolia [4, 5].

In 1994, Cai and his coworkers identified total 34 volatile components from the stem and leaves of *P.nigellastrum*, *P.multisectum* and *P.harmala* by GC-MS analysis. The alkaloid fractions of these three plant species showed anti-tumor activities [6-8]. In previous studies, the alkaloids harmine, evodiamine, vasicine, vasicinone, deoxyvasicinone and fagomine were reported from *Peganum multisectum* [9]. Currently, no results have been found on phytochemical study of *P.multisectum* grown in Mongolia. This is the first report of the alkaloids study of this species.

EXPERIMENTAL

Gas Chromatography-Mass Spectrometry (GC-MS):

The GC-MS which is equipped with fused silica capil-

lary column 30m×0.25mm×0.25µm, has been used for the identification of 2-methylquinoline (**1**), 9-amino-2,3,5,6,7,8-hexahydro-1H-cyclopenta[b]quinolone (**2**), vasicinone (**3**) and harmine (**4**).

Moreover, the HP-5 MS phase coupled with Hewlett Packard 6890/MSD 5793A E were also applied in this study. Flow rate of the helium with 0.8 ml/min was used to carry a gas. A detailed program of the GC-MS as follows: temperature 50-300°C at 6°/min, isotherma 0-10 min, solvent delay 2.0 min and mass range 50-750. In addition, the flame ionization detector was used at T_{int} 260°C, T_{aux} 280°C. The molecular weight and structure of compounds from the total alkaloids were ascertained by interpretation of GC-MS using the database of the National Institute of Standard and Technology (NIST) of the US Department of Commerce.

Column chromatography (CC): Neutral alumina (Merck, Aluminum oxide 90, act. II-III Brockmann, 70 (230 mesh). Preparative Thin Layer Chromatography (PTLC) and Thin Layer Chromatography (TLC): Kieselgel 60: GF 254. Mobile phases (Mph) used for PTLC are acetone, acetone-methanol and acetone-methanol-ammonia (2:0.3:1 drop, 2:0.3:2 drops). Visualization for TLC: *Dragendorff* reagent.

General: Mass Spectrometer (MS) Hewlett Packard MSD 5973, 70 eV. ¹H and ¹³C NMR: 219 Bruker DRX-250, in CDCl₃, with TMS as an internal standard. GC-MS, ¹H, ¹³CNMR and MS methods were used to determine and describe the structure of alkaloids.

Plant material: Aerial parts of *P.multisectum* (Maxim) Bobrov were collected in June from Sevrei sum of Umnugobi province, Eastern Mongolia. The plant was identified by Prof. N.Amartuvshin, Institute of General Experimental Biology, MAS, where a voucher specimen was deposited.

Extraction: The air-dried aerial parts of *P.multisectum* (223.0 g) were extracted three times with 90% of

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ethanol and combined extracts were concentrated under vacuum to afford a viscous residue (20.6 g). The residue was treated three times with 300.0 mL of 5% HCl and filtrated. Then the acidic solution was basified with concentrated ammonia solution up to pH 10-11 and extracted three times with chloroform (CHCl₃). The chloroform extracts were combined and dried over anhydrous Na₂SO₄, and then evaporated under reduced pressure to give 0.41 g of crude alkaloid mixtures (CAMs). Two µl of CAMs from aerial parts of *P. multisectum* were dissolved in methanol and employed for GC-MS analysis. Although GC-MS was applied to isolate the total of alkaloids and determine four alkaloids the rest of the alkaloids were isolated by CC. The pure alkaloids were prepared after CC of CAMs on silica gel 60 Merck (0.2-0.6 mm) with the mobile phases acetone, methanol, acetone-methanol and methanol gradient. PTLC on mixed fractions was carried out on plates (20×20 cm silica gel GF₂₅₄ Merck, 1 mm thickness) and acetone-methanol in vapours of NH₃ (2:0.1), acetone-methanol-ammonia (2:0.1:1 drop) and (2:0.3:2 drops) of mph were used. The bands were detected under UV light and or visualization by Dragendorff reagent.

Isolation of pure compounds: The alkaloids were eluted with acetone and acetone-methanol mixtures, with increasing methanol concentration (1 to 15%), to give fractions PM-1 to PM-32. According to TLC analysis of all fractions with a mobile phase acetone-methanol (2:0.1) and acetone-methanol-ammonia (2:0.1:1 drop, 2:0.3:2 drops) they were combined to give 5 fractions. PTLC with mph (2:0.1:1 drop) was applied to isolate compound **5** (Pm-4¹ 1.04 mg, and Pm-4² 0.62 mg), compounds **8**, **3**, **4** and **7** (Pm-5¹ 1.07 mg, **8**, Pm-5³ 0.79 mg, **3**, Pm-5⁴ 0.97 mg, **4**, Pm-5⁵ 2.32 mg, and Pm-6² 0.59 g, **7**). Then with mph (2:0.3:2 drops) was used to isolate the compounds **7** (0.74 mg) and **8** (0.98

mg) from Pm-8-9 and Pm-10-15 fractions, respectively. The structures of the compounds harmine (**4**, 0.97 mg), peganine (**5**, 1.66 mg), deoxypeganine (**6**, 0.74 mg), deoxyvasicinone (**7**, 2.91 mg), harmane (**8**, 0.98 mg) were elucidated by MS and NMR spectroscopy.

RESULTS AND DISCUSSION

The phytochemical investigation of the aerial parts *P. multisectum* grown in Mongolia afforded 8 alkaloids of the quinolone-, quinazoline- and indole-type, respectively. Two of the alkaloids are quinolines as 2-methylquinoline (**1**) and 9-amino-2,3,5,6,7,8-hexahydro-1H-cyclopenta[b] quinoline (**2**), four are quinazolines as vasicinone (**3**), peganine (**5**), deoxypeganine (**6**) and deoxyvasicinone (**7**), and two are the indole-type as harmine (**4**) and harmane (**8**), have been identified by GC-MS, MS and ¹H, ¹³C NMR analysis. Alkaloids **1**, **2** and **8** were determined for the first time from this species.

Amongst them, 9-amino-2,3,5,6,7,8-hexahydro-1H-cyclopenta[b]quinolone **2** (11.501%) was identified as the major alkaloid in the alkaloid extract, while compounds **1** (0.791%), **3** (4.785%) and **4** (0.909%) were detected as the minor (Figure 1 and Table 1) by GC-MS.

The structures of the alkaloids were determined based on a comparison of their retention time and mass spectral fragmentation (NIST) with those of reference data in the literature [10].

The other five alkaloids were isolated from the aerial parts of *P. multisectum* by CC. They were analyzed by NMR spectroscopy and their molecular structures were determined as harmine (**4**), peganine (**5**), deoxypeganine (**6**), deoxyvasicinone (**7**) and harmane (**8**) (Figure 2). The assignment of the protons and carbons is described in Table 2-3 and is consistent with the data reported in the previous literature [11, 12].

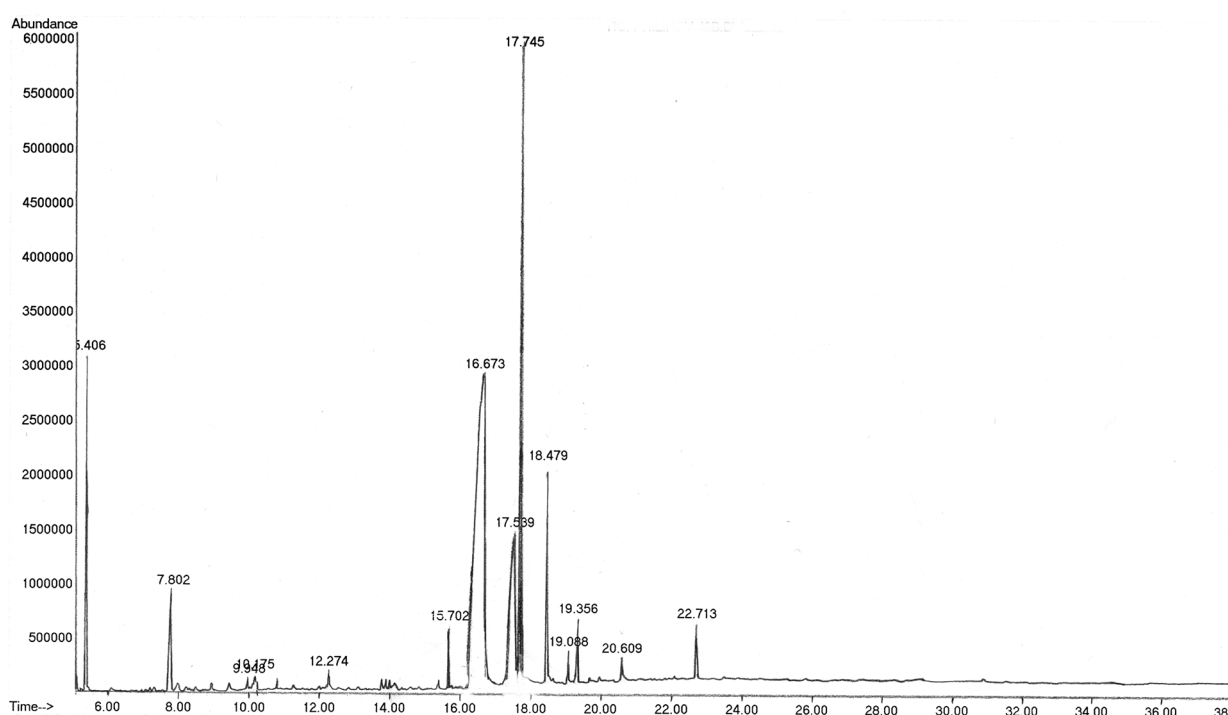


Fig. 1. GC-MS data of aerial parts of *P. multisectum*

Table 1. Alkaloids from aerial parts of *P. multisectum* (Maxim) Bobrov determined by GC-MS analysis

Alkaloids	Retention time	Molecular formula	Amount of the alkaloid, %	M ⁺ , base peak, %
2-methylquinoline (1)	18.47	C ₁₀ H ₉ N	0.791	143(100), 128(14), 115(16), 36(22)
9-amino-2,3,5,6,7,8-hexahydro-1H-cyclopenta[b]quinolone (2)	17.52	C ₁₂ H ₁₆ N ₂	11.501	187(100), 159(12), 131(16), 77(6)
Vasicinone (3)	18.49	C ₁₁ H ₁₀ N ₂ O ₂	4.785	202(100), 146(70), 119(40), 90(12)
Harmine (4)	20.60	C ₁₀ H ₉ N ₂ O	0.909	212(100), 197(25), 169(43.7), 106(6.25)

Peganine (5): The proton NMR chemical shift values for peganine are shown in Table 2. The ¹H NMR spectrum of **5** in CDCl₃ shows the presence of four doublets at δ, 6.92 (1H, d, J=8.8 H-2), 7.02 (1H, d, J=2.7, H-3), 7.19 (1H, m, J=2.7, H-4) and 7.78 (1H, d, J=8.8, H-1), which were attributed to the four aromatic protons. A multiplet of the hydroxyl group was found at δ 3.27. The

alkaloids **5** and **6** were similar, the difference of these two alkaloids was the absence of hydroxyl group in **6**. Instead of the hydroxyl group, in **6** appeared signal of methylene group at δ 3.72 (2H, m, H-9). Based on the good agreement between our NMR data with literature [11, 12], **6** was identified as deoxypeganine.

Deoxyvasicinone (7): Compound **7** was obtained as



Fig. 2. Molecular structure of the **quinazoline-type alkaloids** (A): peganine (7,8,9,5-tetrahydro-pyrrolo[8,7-b] quinazoline-9-ol; R=OH, R₁=R₂=R₃=H, **5**), deoxypeganine (7,8,9,5-tetrahydro-pyrrolo [8,7-b] quinazoline; R= R₁=R₂=R₃=H, **6**), deoxyvasicinone (7,8,9-trihydro-5-oxo-pyrrolo[8,7-b]-quinazoline; R= R₁=H, R₂=R₃=O, **7**) and **indole-type alkaloids** (B): harmine (1-methyl-7-methoxy-β-carboline; R=OCH₃, **4**) and harmane (1-methyl-β-carboline; R=H, **8**)

chemical shift value at δ 4.18 (1H, t, H-1) confirms the proton which attached to the carbon with OH group. Two multiplets were identified at δ 2.15 (1H, m, H-7) and 2.37 (1H, m, H-8) and are resulting from methylene groups. In addition, one multiplet indicated at δ, 3.27 (1H, m H-9), and a singlet assigned to methylene group appeared at δ, 4.62 (2H, s, H-5).

In the carbon spectrum of **5** (Table 2) signals of 11 carbons were determined. A quaternary carbon signals (C-4a, C-9a and C-10a) appeared at δ 118.9, 163.9 and 142.4. The signals at δ 134.19, 128.37, 124.13 and 125.77 were assigned to other aromatic methine carbons of the A-formula.

The signals at δ 29.67, 47.10 and 48.38 were attributed to methylene carbons, signal at δ 70.02 were attributed to methine carbon (C-9) of the A-formula.

In the MS of **5**, the molecular ion peak was determined at *m/z* 189.5 [M+H]⁺. Interpretation of the results of ¹H and ¹³C NMR spectral data, and MS let to conclude that the compound is the alkaloid peganine (Figure 2) [11, 12].

Deoxypeganine (6): It was obtained as a pale white powder, which gives an orange-red color with *Dragendorff's* reagent on a TLC plate. A molecular formula was determined as C₁₁H₁₂N₂ from the positive-ion molecular peak at *m/z* 173 [M+H]⁺.

The ¹H and ¹³C NMR spectroscopic data of the

a white powder, with the molecular formula C₁₁H₁₀N₂O, which resulted from the high-resolution MS analysis *m/z* [M+1]⁺ 187. The ¹H NMR spectrum of **7** in CDCl₃ shows the presence of four multiplets at δ, 7.48 (1H, m, H-1), 7.63-7.75 (2H, m, H-2, H-3) and 7.19 (2H, m, H-4) which were attributed to the four aromatic protons. One multiplet at δ, 2.30-2.36 (2H, m, J=7.90, 7.22 Hz, H-7), and two triplets 3.20 (2H, t, J=7.90, 7.22 Hz, H-8) and 4.21(2H, t, J=7.21, H-9). The ¹H and ¹³C NMR spectroscopic data of the alkaloids **6** and **7** were similar, the difference of these two alkaloids was the absence of a methylene group in **7**. Instead of the methylene group in **7** appeared carbonyl group. In the carbon spectrum (Table 2) the signals of 11 carbons were determined. Four quaternary carbon signals appeared at δ 126.17, 32.48, 159.38 and 160.95 in the 4a, 5, 9a and 10a positions. The signals at δ 149.11, 134.10, 126.76 and 126.35 were assigned to other aromatic methine carbons of the A formula (Figure 2). Three methylene carbon signals appeared at δ 46.44, 19.48 and 120.46 positions of the A formula (Figure 2). All evidence confirmed the structure of **7** which was identified as deoxyvasicinone [9].

Harmane (8): Compound **8** was obtained as a white powder, with the molecular formula C₁₁H₁₀N₂O, which resulted from the high-resolution MS analysis *m/z* 182. It gave positive *Dragendorff's* test for alkaloids. The ¹H

Table 2. ¹H and ¹³C NMR chemical shift assignment for peganine (5) and deoxypeganine (6) (in CDCl₃, δ ppm, J Hz)

Protons	5	6	Peganine [11,12]
H-1	7.78(1H, d, J=8.8)	7.43(1H, d, J=8.7)	
H-2	6.92(1H, d, J=8.8)	7.16(1H, d, J=8.7)	
H-3	7.02(1H, d, J=2.7)	7.07(1H, d, J=2.8)	7.03
H-4	7.19(1H, d, J=2.7)	6.96(1H, d, J=2.8)	6.84-7.25
H-5	2.37	3.27	2.43
H-7	2.15	2.27	2.12
H-8	4.83(2H, m, J= 7.90Hz)	4.62(2H, m, J= 7.91Hz)	4.83
H-9	3.27(2H, d, J=5.7, H-9, -OH)	3.72(2H, m, J= 7.20Hz H-9)	3.33
Carbons			
C-1	134.19	129.48	123.6
C-2	128.37	126.87	128.3
C-3	124.13	126.14	124.0
C-4	125.77	118.58	125.7
C-4a	118.99	115.47	119
C-5	47.10	29.67	47.0
C-7	48.38	46.60	48.1
C-8	29.67	18.74	28.8
C-9	70.02	53.40	70.2
C-9a	163.96	162.90	163.9
C-10a	142.40	131.24	142.3

NMR spectrum of **8** in CDCl₃ showed signals for ortho-disubstituted phenyl ring at δ, 8.35(1H, d, J=5.2Hz, H-3), 8.05(1H, d, J=5.6Hz, H-4), 8.15(1H, d, J=8.0Hz, H-5) in addition to an at δ, 7.30(1H, ddd, J=6.8Hz, H-6), 7.60(1H, ddd, J=7.2Hz, H-7) and 7.65(1H, d, J=8.0Hz, H-8) and other proton that appear upfield at δ, 2.96 (3H, s, -CH₃) was assigned to a methyl proton. The ¹³C NMR spectrum displayed resonances for 12 carbons; including one methyl, six methines, and four quaternary carbons. Quaternary carbon signals appeared at δ 141.6, 137.2, 112.5 and 122.0 and correspond to the 8a, 4b, 4a and 9a positions. The signals at δ 139.4, 115.0, 122.3, 120.2, 128.8 and 112.5 were assigned to other aromatic methine carbons of the B-formula

(Figure 2). The ¹H and ¹³C NMR spectra combined with the MS data established the presence of indole system [13]. On reviewing the literature, the spectroscopic data of **8** were found to be identical with these of harmine [13] (Figure 2).

Harmine (4): Compound **4** was obtained as pale white crystals, showed a positive response with the *Dragendorff's* reagent. A molecular formula was determined as C₁₃H₁₂N₂O from the positive-ion molecular peak at *m/z* 212. The ¹H NMR spectrum of **4** exhibited five aromatic protons at δ 6.90 (1H, dd, J=8.6, 2Hz, H-6), 6.98 (1H, d, J=2, Hz, H-5), 7.72(1H, d, J=5.4Hz, H-3), 7.97 (1H, d, J=6.8Hz, H-5) and 8.33 (1H, d, J=5.4Hz, H-4) of the B formula. In addition, the

Table 3. ¹H and ¹³C NMR chemical shift assignment for deoxyvasicinone (7) (in CDCl₃, δ ppm, J Hz)

Protons	7	Deoxyvasicinone [9]
H-1	7.48 (1H, m, H-1)	7.40-7.48 (m, 1H, H-1),
H-2, H-4	7.63-7.75 (2H, m)	7.62-7.77 (m, 2H, H-2, H-4),
H-3	7.63-7.75 (2H, m, H-3),	8.26 (2H, m, H-3)
H-7	2.30-2.36(2H, m, J=7.90, 7.22Hz)	2.21-2.36 (2H m, J= 7.94, 7.21 Hz, H-7)
H-8	3.20(2H, t, J=7.90, 7.22Hz)	3.18 (2H t, J= 7.94 Hz, H-8)
H-9	4.21(2H, t, J= 7.21 Hz, H-9)	4.21 (2H, t, J= 7.21 Hz, H-9)
Carbons		
C-1	149.1	123.6
C-2	134.1	128.3
C-3	126.7	124.0
C-4	126.3	125.7
C-4a	126.1	119.0
C-5	32.48	47.0
C-7	46.44	48.1
C-8	19.48	28.8
C-9	120.4	70.2

Table 4. Biological and pharmacological activities of alkaloids found from *Peganum multisectum* (Maxim) Bobrov

Compounds	Structure of compounds	Biological and pharmacological activities	Ref.
2-methylquinoline (1)		For use in drugs	13
9-amino-2,3,5,6,7,8-hexahydro-1H-cyclopenta[b]quinoline (2)		Acetylcholinesterase inhibitors; cholinomimetic drug	15, 16, 17,
Vasicinone (3)		Bactericidal activity; AchE inhibition -1μg	4, 16
Harmine (4)		neurological diseases; AchE inhibition -0.1μg; cytotoxicity and antimicrobial activities; antileishmanial activity	8, 9, 12, 13, 18, 19, 20
Peganine (5)		cardiac-depressant effect; uterine stimulant effect; acetylcholinesterase inhibition (AchE inhibition -0.1μg)	2, 3, 12, 13, 18
Deoxypeganine (6)		cardiac stimulant; the effect can be normalized by combining the peganine and vasicinone; AchE inhibition -1μg	2, 3, 11, 18
Deoxyvasicinone (7)		Chondrogenic and chondroprotective effects; AchE inhibition -0.1μg; cytotoxicity and antimicrobial activities; anti-tumor effects; antileishmanial activity	6, 7, 9, 13, 18,
Harmame (8)		AChE inhibition; central nervous system stimulant; cytotoxicity and antimicrobial activities; antileishmanial activity; anti-tumor effects.	9, 12, 13, 17, 20, 21

signals at δ 2.81 (3H, s, -CH₃) and 3.81 (3H, s, -OCH₃) were attributed to -CH₃ and -OCH₃ groups, respectively. The -CH₃ group is located at C-1 (carbon signal δ 134.9) and the -OCH₃ group is located at C-7 (carbon signal δ 160.8). The ¹³C NMR spectrum exhibited signals of 13 carbons at δ 142.0 (C-1), 137.80 (C-3), 115.0 (C-4), 122.73 (C-5), 109.03 (C-6), 160.8 (C-7), 94.90 (C-8), 141.30 (C-10), 111.20 (C-11), 127.5 (C-12), 134.40 (C-13), 20.4 (-CH₃), and 55.43 (-OCH₃). These data unequivocally support the molecular structure of the compound **4** as a harmine, described in Figure 2 [14]. Alkaloids genus *Peganum* well studied, literature data biological activity of determined us alkaloids shown in Table 4.

The following alkaloids have been studied previously, however, as it can be seen from this research, these compounds can be applied for medical purposes. The alkaloid composition of Mongolian *P. multisectum*, differs little from *P. multisectum* other regions. The above-mentioned alkaloids have been studied before, however, as can be seen from these studies (Table 4), the compounds can be applied for medical purposes.

CONCLUSION

By the CC and GC-MS, we have determined eight alkaloids from the aerial parts of *P. multisectum*

growing in Mongolia. The alkaloids 2-methylquinoline (**1**), 9-amino-2,3,5,6,7,8-hexahydro-1H-cyclopenta [b] quinoline (**2**), and harmame were found for the first time from this species. As shown in previous biologicaly studie, the compounds **4**, **5**, **6**, **7** and **8** are active against tumor, bacteria, chondrogenic and chondroprotective effects, leishmania and so on. Therefore, it is important to seek a chance to cultivate this plant and to introduce it in medicinal practice.

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