PHYTOCHEMICAL STUDY OF *PHLOMIS OLIVIERI* BENTH. AND *PHLOMIS PERSICA* BOISS.

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ABSTRACT

Ethyl acetate and *n*- butanol fractions obtained from the column chromatography of methanolic extract of aerial parts of *P. olivieri* gave chrysoeriol-7-O-β-D-glucoside (**I**) and verbascoside (**II**), respectively. In addition, two flavonoid glycosides as compound (**I**) and chrysoeriol-7-β-D- (3"-E-p-coumaroyl) glucoside (**III**) and one iridoid glycoside, namely, lamiide (**IV**) were isolated from the ethyl acetate, ether and *n*-butanol fractions of a methanolic extract of aerial parts of *Phlomis persica,* respectively. Isolation and structural elucidation of compounds were accomplished by PTLC, CC, HPLC and spectroscopic methods (UV, FTIR, EIMS, ^{1}H-NMR, ^{13}C-NMR, DEPT, ^{1}H- ^{1}H COSY, HMQC and HMBC).

Keywords: *Phlomis persica*, *Phlomis olivieri*, Flavonoid, Phenylpropanoid and Iridoid glycosids

INTRODUCTION

The genus *Phlomis* (Lamiaceae) consists of about 100 species in the world (1, 2). According to the last report, the genus of *Phlomis* (except hybrids and subspecies) is represented by 17 species in Iran, of which ten are endemic (3).

Phlomis species are described by Dioscorides as herbal drugs and used ethnopharmacologically in herbal medicine for the respiratory tract diseases or local treatment of wounds (4, 5). A number of *Phlomis* species are used in folk medicine as stimulant, tonic (6), analgesic (7) antidiarrheatic, and for treatment of ulcers and hemorrhoids (8).

There are a few reports about the pharmacological and biological effects of *Phlomis*. Some studies have shown various activities such as anti-inflammatory, immunosuppressive, antimutagenic, anti-nociceptive (9), antifibriel (10), free radical scavenging (2), anti-malarial (11) and anti-microbial effects (2, 4, 12).

Plants belonging to the genus *Phlomis* have been shown to contain different classes of glycosides comprising iridoids, flavonoids, phenyl-propanoids, phenylethanoids, monoterpene, lignans, neolignans, diterpenoids and alkaloids (13, 14). The iridoid glycosides are charachteristic in this genus. For example, lamiide, auroside and ipolamide, were found in the most species of *Phlomis* (6, 11, 12). Some flavonoids from this genus such as phlomisflavoside A and B (15) have been identified for the first time in this genus. The most common flavonoids reported are luteolin 7-*O*-*β*-D-glucopyranoside and chrysoeriol 7-*O*-*β*-D-glucopyranoside (11, 16). In regard to phenolic acids, a wide variety of caffeic acid derivatives, including verbascoside (acteoside) and forsythoside B from many species have been identified (2,6,11,12). Therefore, some of biological effects of this plant might be related to presence of iridoid glycosides, flavonoids and other phenolic compounds (11, 17- 19).

Pharmacological study has been previously performed on methanolic extracts of two endemic species, *P. olivieri* and *P. persica* which wildly grow in Iran, showed antinociceptive effect in writing test (9). In this article the phytochemical study of *P. persica* and *P. olivieri* is described. To the best of our knowledge, except of three reports about essential oils of *P. olivieri* and *P. persica* (20- 22) no study has been reported on the chemical constituents of *P. persica, P. olivieri* and this paper describes the phytochemical investigation of these species for the first time.

MATERIALS AND METHODS

General

Column Chromatography (CC) was performed with Silica gel 30- 70 (Merck) and/or Polyamide 6, bulk density: 0.25 g/ml, particle size 50-160 μm (Fluka); Analytical and preparative TLC were carried out on Silica gel 0.2 mm layer thickness of Schleicher & Schuell (F 1500/LS 254 20 × 20 cm) and Silica gel 60 F 254 (Merck). NMR spectra were recorded on a Varian 400 Unity plus spectrometer or ECA600 MHz with JEOL Soft-ware (TMS as the internal standard, DMSO- d_6

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and pyridine- d_5 as solvent) and FT-IR spectra were recorded on a Nicolet 550 spectrometer using KBr disks. UV spectra was obtained by Shimadzu 160 A spectrometer. Melting points were determined on a Reichert-jung apparatus. EIMS spectra were measured by a Finning Mat-EI-TSQ-70 eV; HPLC were performed on a Waters Prep LC ™ 4000 system, UV detector Waters ™ 486 (Tunable absorbance detector) with Kromasil 100 C 18 (10 µm, 25 cm × 0.7 cm, Teknokroma) as a semi-preparative column. Phenolic compounds were detected by UV fluorescence and spraying with KOH 5% or $AlCl_3$ 5% and for iridoid compounds HCl 5% was used as a reagent, followed by heating at 102 ˚C for 30 seconds on TLC.

Plant material

Aerial parts of *Phlomis olivieri* Benth. (Chalme in Persian) and *Phlomis persica* Boiss. (Goosh bareh in Persian) were collected from northern part of Iran (Mazandaran province) in June 2001 and from the area near Bojnoord, north-east of Iran (Khorassan province) in June 2002, during the flowering stages. Voucher specimens (No. 6534 TEH for *P. olivieri* and No. 6532 TEH for *P. persica*) were deposited at Herbarium of Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran.

Extraction and Isolation

Isolation of compounds ***I*** *&* ***II*** *from P. olivieri*

The air-dried and powdered aerial parts of *P. olivieri* (500g) were extracted twice with MeOH 80% (2 × 2 l) at 45 ˚C in a percolator. The combined methanolic extracts were evaporated to dryness in vacuum (20 g, yield 4 %), suspended in H_2O and partitioned successively between ether, ethyl acetate, *n*- butanol, respectively.

EtOAc fraction (5 g) was chromatographed over silica gel 60 with a $CHCl_3$- EtOAc gradient (0-100% EtOAc). The fraction A2 was applied to PTLC over silica gel, using MeOH: EtOAc: $CHCl_3$ (1: 0.5: 0.5) as solvent system to give compound **I** (20 mg).

The *n*-BuOH fraction (6 g) which was fractionated over polyamide 6 (CC) and eluted with H_2O-MeOH gradient (0-100% MeOH) yielded four main fractions. Fraction B2 was subjected to silica gel (PTLC), solvent system MeOH: EtOAc: $CHCl_3$ (1: 0.5: 0.5) to give compound **II** (30 mg).

Compound I (chrysoeriol-7-O-β-D-glucoside)

Yellow crystal: mp 172-174 ˚C. UV λ_{max} nm (logε) MeOH: 335 (1.58), 301 (1.15), 265 (1.32), 254 (1.47); + NaOH: 387 (1.90), 295 (0.88), 270 (1.47); + $AlCl_3$: 380 (0.50), 343 (0.61), 276 (0.70); + $AlCl_3$/HCl: 380 (0.50), 343 (0.61), 277 (0.70); + NaOAc: 346 (1.42), 297 (1.00), 260 (1.48); + NaOAc/H_3BO_3: 346 (1.72)sh, 290 (1.00), 260 (1.67). FTIR ν_{max} (KBr) cm^{-1}: 3303 (OH); 1680 (flavone C=O); 1618 & 1521 (C=C). EIMS (70 eV) m/z (rel. int.): 300 (aglycone) (100), 270 (M^+-(glucose + OCH_2)) (30), 252 (M^+- (glucose + OCH_2 + H_2O)) (30), 153 (25), 148 (20), 121 (18). ^{1}H-NMR (400 MHz, DMSO - d_6): aglycone: 7.61 (1H, *dd*, *J*= 8.4, 2 Hz, H-6'), 7.58 (1H, *d*, *J*=2 Hz, H-2'), 6.97 (1H, *d*, *J*= 8.4 Hz, H-5'), δ 6.95 (1H, *s*, H-3), 6.90 (1H, *d*, *J*= 2 Hz, H-8), 6.46 (1H, *d*, *J*= 2 Hz, H-6), 3.89 (3H, *s*, OMe), glucose moiety: δ 5.05 (1H, *d*, *J*= 7.2 Hz, H-1"). ^{13}C-NMR (100 MHz, DMSO - d_6): aglycone: δ 164.1 (C-2), 103.4 (C-3), 182.0 (C-4), 161.1 (C-5), 99.5 (C-6), 163.0 (C-7), 95.0 (C-8), 156.9 (C-9), 105.3 (C-10), 121.3 (C-1'), 110.3 (C-2'), 148.0 (C-3'), 150.1 (C-4'), 115.8 (C-5'), 120.4 (C-6'), 60.6 (OCH_3), glucose moiety: δ 100 (C-1"), 73.1 (C-2"), 76.4 (C-3"), 69.6 (C-4"), 77.2 (C-5"), 62.8 (C-6").

Compound II (verbascoside)

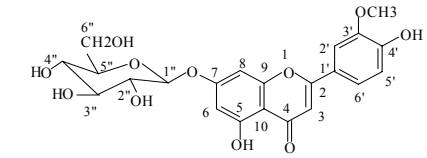
Yellow amorphous powder: mp 149-151˚C. UV λ_{max} nm (logε) MeOH: 340 (0.67), 330 (0.72), 290 (0.54); + NaOH: 380 (0.91), 300 (0.35), 260 (0.24); + $AlCl_3$: 361 (0.53), 320 (0.37), 268 (0.42); + $AlCl_3$/HCl: 330 (0.53), 243 (0.35), 220 (0.62). FTIR ν_{max} (KBr) cm^{-1}: 3391 (OH); 1701 (C=O); 1598 and 1516 (C=C and aromatic rings). EIMS (70 eV) m/z (rel. int.): 359 (glucose + caffeic acid) (100), 315 (glucose + aglycone) (95), 154 (aglycone) (18). ^{1}H-NMR and ^{13}C-NMR spectral data (400 MHz, DMSO - d_6), are reported in Table1.

Isolation of compounds ***I, III, and IV*** *from P. persica*

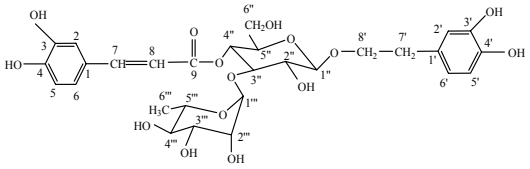
The air dried powdered (750g) of *P. persica* were extracted twice with MeOH 80% (2 × 2 l) at 45 ˚C in a percolator. The combined methanolic extracts were evaporated to dryness under reduced pressure to give solid residue (24.5 g, yield 3.3%). The crude extract was suspended in H_2O and partioned successively with ether, ethyl acetate and *n*- butanol. The ether extract (10 g) after evaporation, was washed with *n*-hexane to remove lipids. The residue which was subjected to silica gel CC and eluted by increase in the percent of EtOAc in $CHCl_3$ (0→ 100%), gave a fraction rich in **III.** This fraction rechromatographed on silica gel (PTLC) using solvent system $CHCl_3$: MeOH (3: 1) to yield compound **III** (15 mg).

The ethyl acetate extract (4 g) was twice chromatographed over silica gel (PTLC) using solvent system MeOH: EtOAc: $CHCl_3$ (1: 0.5: 0.5) to give compound **I** (10 mg).

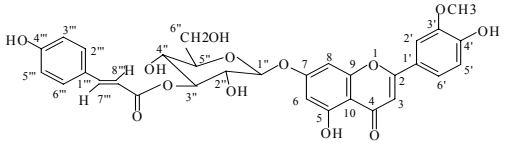
The *n*-BuOH extract (5 g) was chromatographed over polyamide 6 (CC) with H_2O-MeOH gradiant (100%→25% H_2O). Fraction C1 (semi- solid red gum, 150 mg) was applied to semi-prep. HPLC on Kromasil 100 C_{18} column and elution program was MeOH- H_2O gradients (20- 100%) at 225 nm to separate compound **IV** (4 mg).



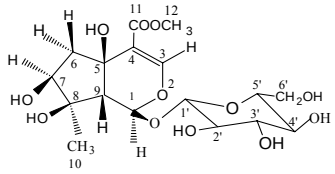
chrysoeriol-7- O- *β*- D - glucoside (**I**)



verbascoside or acteoside (**II**)



chrysoeriol-7-β-D-(3"-E-p-coumaroyl)glucoside (**III**)



lamiide (**IV**)

Figure 1. Isolated compounds from *P. olivieri* (**I** & **II**) and *P. persica* (**I**, **III** & **IV**)

Compound III (chrysoeriol -7-β-D-(3"-E-p-coumaroyl) glucoside

Yellow amorphous powder: UV λ_{max} nm (logε) MeOH: 316 (0.83), 280 (0.71), 266 (0.60), 235 (1.80); + NaOH: 368 (1.04), 300 (0.46), 245 (0.75); + $AlCl_3$: 380 (0.50), 320 (0.85), 297 (0.95), 278 (0.82); + $AlCl_3$/HCl: 380 (0.50), 320 (0.85), 297 (0.95), 278 (0.82); + NaOAc: 316 (0.80), 280 (0.73), 260 (0.64); + NaOAc/H_3BO_3: 317 (0.42), 280 (0.70), 260 (0.64). FTIR ν_{max} (KBr) cm^{-1}: 3430 (OH); 1706 (C=O ester); 1630 (C=O flavone); 1603 (C=C). EIMS (70 eV) m/z (rel. int.): 300 (flavone) (90), 164 (aglycone) (35), 147 (aglycone -OH) (100), 119 (aglycone- COOH) (22), 91 (20). ^{1}H-NMR (400 MHz, DMSO - d_6): flavone: δ 7.61 (1H, overlapped, H-6'), 7.60 (1H, overlapped, H-2'), 7.01 (1H, *s*, H-3), 6.95 (1H, *d*, *J*= 8.4 Hz, H-5'), 6.91 (1H, *d*, *J*=1.2 Hz, H-8), 6.49 (1H, d, *J*= 2 Hz, H-6), 3.90 (3H, *s*, OMe); glucose moiety: δ 5.28 (1H, *d*, *J*= 7.6 Hz, H-1"), 5.07 (1H, *t*, *J*= 9.6 Hz, H-3"), coumaric acid (aglycone): 7.59 (1H, *d*, *J*= 16 Hz, H-7'"), δ 7.58 (2H, *d*, *J*= 8.8 Hz, H-2'", 6'"), 6.81 (2H, *d*, *J*= 8.8 Hz, H-3'", 5'"), 6.45 (1H, *d*, *J*= 16 Hz, H-8'").

Compound IV (lamiide)

White amorphous powder: mp 184-186 ˚C. UV λ_{max} nm: 225 (MeOH). ^{1}H-NMR & ^{13}C-NMR, DEPT, HMBC (600 MHz, pyridine- d_5) spectral data, are reported in Table2.

RESULT AND DISCUSSION

The crude methanolic extract of the plants were suspended in H_2O and partitioned successively between ether, ethyl acetate, *n*- butanol, respectively. Chromatographic separations (CC and PTLC) of EtOAc and *n*-BuOH extract from the aerial parts of *P. olivier*i gave Compounds **I** and **II**, respectively. Compounds **I, III** and **IV** were respectively isolated from the ethyl acetate, ether and *n*- butanol fractions of a methanolic extract of aerial parts of *P. persica*, using PTLC, CC or semi- prep. HPLC. Compounds **I-IV** were identified by comparing their physical and spectroscopic data with those reported in the literature. Compound **I** was obtained as a yellow crystal and its structure was confirmed as chrysoeriol-7-O-β-D-glucoside by EIMS, NMR, UV and IR (23). Fragmentation in EIMS showed the presence of chrysoeriol as a major peak. ^{1}H-NMR also allowed identification of characteristic H-1" of glucose moiety at 5.05 (*d*, *J* = 7.2). The $J_{1", 2"}$ value is compatible with a β- linked glucose. The ^{13}C-NMR spectral data showed twenty two signals. The peak at 182.0 ppm shows a characteristic carbonyl peak in γ keton ring and the peak at 60.6 ppm is related to methoxy group. The position of phenolic hydroxyl groups were proved by classical UV techniques. The IR spectrum was characterized by a strong carbonyl group (flavone) at 1680 cm^{-1}.

Comparing spectral data of **I** with the reported data for chrysoeriol-7-O-β-D-glucoside (23), which has been identified in *P. brunneogaleata* (11), *P. lunariifolia* (24), *P. capitata* (25), *P. integrifolia* (26), *P. aurea* (27, 28) and *P. floccosa* (28), confirmed its assignment as chrysoeriol -7-0-B-D glucoside.

Compound **II** was a yellow, amorphous powder. In its ^{1}H-NMR spectrum, aromatic protons were resolved as two ABX systems, one belonging to the caffeic acid substitution, and the other to 3', 4' - dihydroxyphenylethyl group. A multiplet at 2.70 ppm had signal due to 2H-7' in β-phenyl- ethanol

Table 1. ^{1}H-NMR and ^{13}C-NMR data of verbascoside (**II**) in DMSO- d_6. TMS

C/H Atoms	δC (ppm)	DEPT	δH (ppm)
Caffeic acid			
1	125.65	C	-
2	114.59	CH	7.01 (*d*, *J* = 2 Hz)
3	145.68	C	-
4	148.38	C	-
5	113.70	CH	6.72 (*d*, *J* = 8 Hz)
6	121.63	CH	6.94 (*dd*, *J* = 2, 8 Hz)
7	145.50	CH	7.45 (*d*, *J* = 16 Hz)
8	115.85	CH	6.17 (*d*, *J* = 16 Hz)
9	165.86	C	-
Aglycone			
1'	129.34	C	-
2'	116.35	CH	6.62 (*d*, *J* = 2 Hz)
3'	144.88	C	-
4'	143.44	C	-
5'	115.52	CH	6.64 (*d*, *J* = 8 Hz)
6'	119.71	CH	6.50 (*dd*, *J* = 2, 8 Hz)
7'	35.11	CH_2	2.70 (*m*, *J* = 8.4 Hz)
8'	70.38	CH_2	a: 3.88 (*m*, *J* = 9.2 Hz), b: *
Glucose			
1"	102.38	CH	4.34 (*d*, *J* = 8 Hz)
2"	74.56	CH	3.20 (*m*, *J* = 8.4 Hz)
3"	79.32	CH	*
4"	69.27	CH	4.70 (*t*, *J* = 9.2 Hz)
5"	74.56	CH	*
6"	60.72	CH_2	*
Rhamnose			
1"'	101.30	CH	5.00 (*bs*)
2"'	70.49	CH	*
3"'	70.38	CH	3.27
4"'	71.68	CH	3.10 (*t*, *J* = 9.6 Hz)
5"'	68.82	CH	*
6"'	18.25	CH_3	0.95 (*d*, *J* = 6.4 Hz)

* It was not detected because of the presence of DMSO signal between δ_H 3.30 & 3.80 ppm

and the two protons of the CH_2 -8', gave a multiplet between δ_H 3.60- 3.92 ppm. In addition, the anomeric proton H-1"' and methyl group (CH_3-6"') of rhamnose were easily recognized: the former at 5.00 ppm with a broad singlet, and the latter at 0.95 ppm as a doublet with J = 6.4 Hz. The other values were in good agreement only with the α-configuration of the rhamnopyranose, (Table 1). The coupling constant ($J_{H1"-H2"}$ = 8 Hz) of the glucose anomeric proton resonating at 4.34 ppm is in accordance with a β-configuration. Its diglycosidic nature was also confirmed by the ^{13}C-NMR spectrum in which two anomeric carbons appeared at δc 102.38 (β- glucose) and 101.30 (α- rhamnose). Consequently, the structure of compound **II** was established as β- (3', 4'-dihydroxyphenyl) ethyl- O- α- L- rhamnopyranosyl (1→3)- β- D- (4- O- caffeoyl)- glucopyranoside (verbascoside) by comparing its spectral charactristics with the literatures data (29 –31). This compound has been found in many of *Phlomis* species such as *P. samia* (2), *P. brunneogaleata* (11), *P. integrifolia* (13), *P. lunariifolia* (24), *P. nissolii* and *P. capitata* (25).

Compound **III** was isolated as a yellow, amorphous powder and its structure was confirmed as chrysoeriol -7-β-D-(3"-E-p-coumaroyl) glucoside by ^{1}H-NMR, UV and EIMS (13, 28, 32). The complete structure of this naturally occurring glycoside was clear from the ^{1}H-NMR spectrum. The signals at δ 7.59 and 6.45 with large olefinic J value, ($H_{7"'-8"'}$, J = 16 Hz) correspond to trans isomer of coumaric acid. The UV values were similar to those reported for acylated derivatives of flavonoids in which the acyl group was p- coumaric acid. EIMS spectrum showed ion peak due to the loss of coumaroyl moiety + glucose (m/z 300). In addition, ion peaks were observed at m/z 147 and m/z 119 due to the loss of hydroxyl and carbonyl groups from coumaroyl part and other fragmentations were similar to fragmentation pattern for the chrysoeriol. The other data were in good agreement with chrysoeriol derivative substituted at the 7 position (13, 16, 28), namely, chrysoeriol-7-β-D-(3"-E-p-coumaroyl) glucoside which has been detected in *P. integrifolia* (13), *P. lychnitys* (16), *P. aurea, P. floccosa* (28) and *P. crinita* (32).

Table 2. ^{1}H-NMR, ^{13}C-NMR, DEPT & HMBC data of lamiide (**IV**) in pyridine- d_5.TMS

C/H Atoms	HMQC		DEPT	COSY	HMBC (C →H)
	δC (ppm)	δH (ppm)			
1	95.31	6.41 (*s*)	CH	-	H3, H9, H1′
3	151.08	7.68 (*s*)	CH	-	H1
4	115.58	-	C	-	H3, H9, H6 α
5	68.75	-	C	-	H1, H7*, H6α & β, H9, H3
6	46.57	α: 2.79 (*dd*, *J* = 3.2, 8.8 Hz)	CH_2	H7, H6β	H7*
		β: 2.86 (*dd*, *J* = 2.3, 8.8 Hz)		H7, H6α	
7	78.61	3.92- 3.93 (*m*)	CH	H6α & β	H6α & β, H9, H10
8	78.27	-	C	-	H1*, H7, H9, H10
9	58.08	3.64 (*s*)	CH	H6β, H10	H10
10	21.56	1.34 (*s*)	CH_3	H9	H9
11	166.74	-	C	-	H3, H12
12	50.53	3.48 (*s*)	CH_3	-	-
Glucose					
1′	100.34	5.31 (*d*, *J* = 4.7 Hz)	CH	H2′	H1, H2′, H5′
2′	74.22	3.92- 3.93 (*m*)	CH	H1′, H3′	H3′
3′	78.27	4.20 (*m*)	CH	H2′, H4′	H2′, H4′
4′	70.89	4.22 (*m*)	CH	H3′, H5′	H3′
5′	77.09	3.92- 3.93 (*m*)	CH	H6′, H4′	-
6′	62.05	α: 4.33 (*dd*, *J* = 4.8, 11.9 Hz)	CH_2	H5′, H4′	H5′
		β: 4.43 (*dd*, *J* = 1.8, 11.7 Hz)			

* It shows weak correlation
The ^{13}C and ^{1}H assignments were based on 2D-NMR (DQF-COSY, HMQC and HMBC) experiments.

Compound **IV** was obtained as a white, amorphous powder and its structure was determined based on ^{1}H-NMR, ^{13}C-NMR, DEPT, DQF-Cosy, HMQC and HMBC experiments. The ^{1}H-NMR spectrum of compound **IV** showed signals at 7.68 (1H, *s*) and 5.31 (1H, *d*) which are characteristic of iridoid glycosides having either carboxy or carbomethoxy group at C-4 and glucose at C-1, respectively. DEPT 135 analysis showed resonance for two CH_2 at 46.57 (C-6), 62.05 (C-6') ppm and resonance due to four quaternary carbons, two of which attached to ring and hydroxyl group (68.75; C-5, and 78.27; C-8) ppm, one carbonyl group (C=O, 166.74 ppm) and a quaternary double bond (C=CH, 115.58 ppm). By the complete analysis of the NMR data (see Table 2) and a comparison with the reported data in the literatures (33), compound **IV** was identified as lamiide which has been found in many *Phlomis* species , such as *P. integrifolia* (13), *P. nissolii* (25), *P. capitata* (25), *P. aurea* (27, 28) and *P. floccosa* (28), *P. physocalyx* (34) and *P. lycia* (35).

Isolated Compounds from *Phlomis olivieri* and *P. persica* were similar to those obtained from *P. integrifolia* (13, 26). However, additional compounds such as two phenylethanoid glycoside, integrifoliosides A and B, are present in *P. integrifolia* (26). Among isolated compounds, verbascoside has shown a variety of pharmacological activities such as antioxidant, antiinflamatory, immunosuppressive, cytotoxic, cytostatic and anti-allergic (18, 36). There are only a few reports about the pharmacological effects of other isolated compounds. Chrysoeriol-7-O-β-D-glucoside has found as a anti-malaria (11) and anti-obesity compound (37) and chrysoeriol-7-O-beta-(3"-E-p-coumaroyl)-glucoside has shown to inhibit the release of PGE2, but this effect is not statistically significant (38). Lamiide as an iridoide glycoside has shown anti-inflammatory activity and lipid peroxidation inhibition (19).

CONCLUSION

In this investigation, isolation of Chrysoeriol-7-O-β-D-glucoside **I** (flavonoid) and verbascoside **II** (phenylpropanoid glycoside) from *P. olivieri*, and, two flavonoid glycosides, namely, chrysoeriol-7-β-D-(3"-E-p-coumaroyl) glucoside **III** and chrysoeriol-7-O-β-D-glucoside **I** and one iridoid glycoside, namely, lamiide **IV** from *P. persica* for the first time has been reported. On the basis of antinociceptive activities of *P. olivieri* and *P. persica* reported previously (9) it may be concluded that, this effect could be possibly related to the presence of some isolated compounds such as verbascoside and lamiide (18, 19).

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