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# *Pedicularis* L. genus: systematics, botany, phytochemistry, chemotaxonomy, ethnopharmacology and other

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## ABSTRACT

In this review, the relevance of plants belonging to the *Pedicularis* L. genus was explored from different points of view. Particular emphasys was given especially to the phytochemistry and the ethnopharmacology of the genus since several classes of natural compounds have been evidenced within it and several *Pedicularis* species are well known to be employed in the traditional medicine of many Asian countries. Nevertheless, some important conclusions on the chemotaxonomic and chemosystematic aspects of the genus were also provided for the first time. This work represents the first total comprehensive review on the genus *Pedicularis*.

**KEYWORDS:** *Pedicularis* L. genus, Orobanchaceae family, Phytochemistry, Chemotaxonomy, Ethnopharmacology.

## Abbreviations:

a.n. = accepted name
n.r. = none reported
n.s. = not specified
s.n. = synonym name
u.n. = unresolved name

## Systematics

*Pedicularis* L. is a genus of hemiparasitic plants, originally comprised in the Scrophulariaceae family but now belonging to the Orobanchaceae one [1]. The rest of the systematic classification is the following: order Scrophulariales, subclass Asteridae, class Magnoliopsida, division Magnoliophyta, superdivision Spermatophyta, subkingdom Tracheobionta. The genus comprises 568 accepted species, 335 synonyms species and 450 unresolved species [2].

## Etymology of the name

The etymology of the name is Latin with the term “pediculus”, meaning “louse”, which refers to the fact that, according to an ancient English belief, cattle which grazed on these plants, was found to be soon infested with lice [3].

## Botany

The plants of the genus *Pedicularis* are generally herbaceous and perennial with a height which can reach up to 50 cm. Annual or biennial species are quite rare. From the morphological standpoint, these species are characterized by big and fleshy roots, often taproots, which contain specific organs (haustoria) that serve for their feeding on the lymph of the near plants.The stem is erected and ascendant and may present itself as simple or branched (Figure 1). The leaves are basal and cauline. The former ones are disposed to form a rosette and are petiolate while the latter ones are opposite, alternated or verticillatedand sessile. Both of them have a lanceolate shape and dentate margins. These are rarely entire. Bracts are also present and are similar to the

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cauline leaves even if they are smaller (Figure 1). More or less dense terminal spikes generally constitute the inflorescence.The flowers are big, hermaphrodite, zigomorphic, tetrameric or pentameric. They can be sessile or pedunculated. The floreal formula is X, K(5), [C (2+3), A 2+2], G (2), (superior), capsule. The calyx is gamosepalous formed by five lobes that may be dentate or not. The corolla is gamopetalous and bilabiate with a cylindrical shape slightly compressed on its sides. Its color ranges from pink to white passing through red, purple and yellow. The androecium possesses four didinamous stamens with the filaments well included into the base of the corolla. The anthers are hidden among dense hairs and may be mucronate. The pollen maturation is contemporaneous to the stigma. The ovary is superior, is formed by two carpels and is bilocular. The stylus is inserted in the ovary apex and is filiform. The stigma is simple and protruded beyond the corolla hat in order to avoid self-pollination (Figure 1). The fruit is an acuminated bivalve capsule with an oval-lanceolate shape (Figure 1). The seeds are numerous or not and present an angular geometry. The reproduction occurs through pollination by insects or dispersion [4, 5].

Examples of the morphological features of *Pedicularis* species - stem (left), leaves (middle left), flowers (middle right), fruits (right) [source Wikipedia]

## Distribution and habitat

Two morphological features of the species belonging to the *Pedicularis* genus i.e. the presence of big flowers and the great color variability of the corolla [6]. They are distributed in Europe especially in the mountainous areas of the Mediterranean Basin and of Northern Asia and America (Figure 2). The highest biodiversity is present in Europe with about 70 species, India with about 83 species and China with about 350 species of which 271 are endemic [6-8]. Indeed, in North America the present species are 36 with two endemisms [9]. Nevertheless, these species have been reported in Africa and Australia only as imported plants. The preferred habitat is the temperate-mountain one at different quotes. The soil must be quite acidic and little

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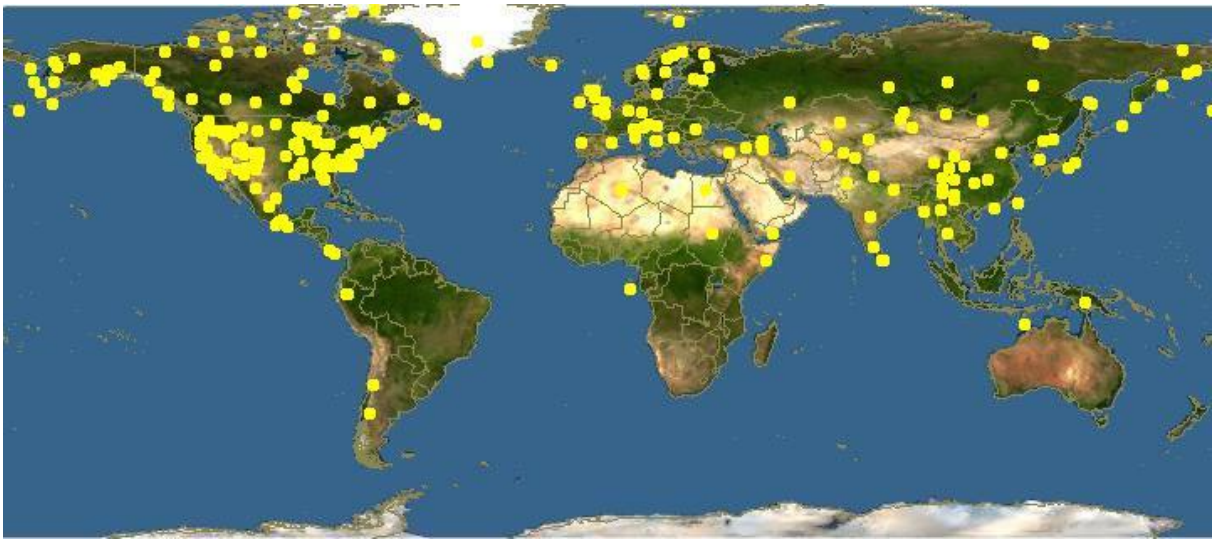
drained. The typical areas where these species can be found are meadows and lawns with little other vegetation [3].



Worldwide distribution of *Pedicularis* species [source Wikipedia]

## Phytochemistry

The genus *Pedicularis* is a rich source of different secondary metabolites mainly belonging to the polar fraction. In fact, *Pedicularis* species are poor essential oil producers. In particular, only three species have been investigated under this aspect i.e. *Pedicularis condensata* M.Bieb. (unresolved name), *P.sibthorpii* Boiss. and *P.wilhelmsiana* Fisch. ex M.Bieb. The first one was collected in Turkey and showed the presence of several typical components of the essential oils such as more or less oxidized hydrocarbon derivatives, and volatile terpenes [10]. The same was also observed in *P.wilhelmsiana* which was collected in Iran [11]. Indeed, an important difference was found in the two studied exemplars of *P.sibthorpii* both collected in Iran but in two different regions. In fact, if on one side, the work by Khodaie et al. [12] did not absolutely evidence the presence of sesquiterpenes, the work by Morteza-Semnani et al. [13] did and even in high amounts since they represented the 35.4% of all the identified components. This may be actually explained by the different environmental growth conditions of the two studied species and this, once again, highlights how the essential oil composition is greatly affected by external factors and does not only depend on the genetic factors [14]. Indeed, among the polar fraction metabolites, several classes of natural compounds were found i.e.fatty acids, alkaloids, steroids, lignans, *neo*-lignans, tannins, ionones, phenylpropanoid glycosides, phenylethanoid

glycosides, flavonoids, xanthones, iridoids, *seco*-iridoids, phenyl-glycosides, organic acids, polyols, saccharides and amino acids.

Table 1 reports on the exact components identified in all the studied *Pedicularis* species.

| *Pedicularis* spp. | Studied organs | Phytochemical compounds | References |
|---|---|---|---|
| *P. acmodonta* Boiss. (u.n.) | n.s. | leucosceptoside A, echinacoside | [15] |
| *P. alaschanica* Maxim. (a.n.) | aerial parts | alaschanioside A, alaschanioside C, citrusin A, syringaresinol-4-*O*-β-D-glucoside, verbascoside, leucosceptosideA, martynoside, boschnaloside, ixoroside, euphroside, geniposidic acid, mussaenosidic acid | [16, 17] |
| *P. armata* Maxim (a.n.) | whole plant | armaoside, citrusin B, euphroside, mussaenoside, geniposidic acid, 8-*epi*-loganic acid, aucubin | [18] |
| *P.artselaeri* Maxim. (a.n.) | whole plant | lariciresinol-4-*O*-β-D-glucoside, lariciresinol-4′-*O*-β-D-glucoside,alaschanioside A, citrusin A,artselaeroside A, artselaeroside B, isoverbascoside, martynoside, artselaenin I, artselaenin III, artselaenin A, artselaenin B, artselaenin C, 8-*epi*-loganic acid, 8-*epi*-loganin, 7-deoxy-8-*epi*-loganic acid, plantarenaloside, mussaenoside, aucubin, 6-*O*-methyl-aucubin, 6-*O*-methyl-*epi*-aucubin, ixoroside, 7-deoxy-gardoside, gardoside methyl ester, caryoptoside, shanzhiside methyl ester, 2-(*p*-hydroxyphenyl)-ethanol-1-*O*-β-D-glucopyranoside, 3-methoxy-4-primeverosyl-acetophenone | [19, 20] |
| *P. bicornuta* Klotzsch (u.n.) | whole plant | alkaloids, lignans glycosides, phenylpropanoid glycosides, flavonoids, iridoids **(exact compounds not specified)** | [21] |
| *P. bracteosa* Benth. (a.n.) | aerial parts | aucubin, mussaenoside | [22] |
| *P.bracteosa* subsp. *paysoniana* (Pennell) W.A. Weber (a.n.) | whole plant | alkaloids **(exact compounds not specified)** | [23] |
| *P. capitata* Adams (a.n.) | leaves | alkaloids **(exact compounds not specified)** | [24] |
| *P. cephalantha* Franch. ex Maxim. (a.n.) | whole plant | pinoresinol, kidjolanin, martynoside, isomartynoside, clerodenoside A, acacetin, luteolin, 7-deoxy-gardoside, plantarenaloside, mussaenosidic acid, euphroside, mussaenoside, aucubin | [25] |
| *P. chamissonis* Steven (a.n.) | leaves | verbascoside, luteolin-7-*O*-glucoside, luteolin-7-*O*-glucuronide | [26] |
| *P.chinensis* Maxim. (a.n.) | roots | syringaresinol-4-*O*-β-D-glucoside, martynoside, *cis*-martynoside, pedicularioside N, luteolin-7-*O*-glucoside, aucubin, 6-*O*-methyl-aucubin, 6-*O*-butyl-aucubin, 3β-butoxy-3,4-dihydro-aucubin, 6-*O*-butyl-*epi*-aucubin, iridolactone, bartsioside, pedicularislactone, pedicularislactone glucoside, *Rel*-(6*R*,5*R*,9*R*)-(2-oxa-bicyclo-[3,3,0]oct-3-one-8-en-9,8-diyl)-dimethanol, 1-*O*-β-D-(3-hydroxy-4-methoxy-phenyl)-ethyl-β-D-apiosyl-L-(1→3)-rhamnosyl-(1→6)-4-trans-feruloyl-glucopyranoside,1-*O*-β-D-(3-hydroxy-4-methoxy-phenyl)-ethyl-β-1-(1→3)-4-trans-feruloyl-glucopyranoside, 1-*O*-β-D-(3-hydroxy- | [27, 28] |

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|---|---|---|---|
| | | 4-methoxy-phenyl)-ethyl-α-L-rhamnosyl(1→3)-4-*cis*-feruloyl-gulopyranoside | |
| *P. comosa* L. (a.n.) | aerial parts | verbascoside, forsythoside B | [15] |
| *P. condensata* M.Bieb. (u.n.) | aerial parts | verbascoside, echinacoside, aucubin, 6-*O*-acetyl-aucubin, 8-*epi*-loganin, mussaenoside, shanzhiside methyl ester, gardoside methyl ester | [29] |
| *P. crenulata* Benth. (a.n.) | aerial parts | anagyrine, aucubin, euphroside, plantarenaloside | [22, 30] |
| *P. decora* Franch. (a.n.) | whole plant | β-sitosterol, β-daucosterol, *iso*-verbascoside, kaempferol, aucubin, lamalbid, pedicularislactone glucoside, ningpogoside B, D-mannitol, β-(3',4'-dihydroxyphenyl-*O*-a-L-rhamnopyranosyl-(1–3)-β-D-glucopyranoside, salicylic acid, 2,5-dihydroxybenzoic acid, 3-hydroxy-4-methoxybenzoic acid, 3-methoxy-4-hydroxybenzoic acid, aspartic acid, threonine, serine, glutamic acid, glycine, alanine, cysteine, methionine, isoleucine, phenylalanine, alanine, valine, arginine, proline, leucine, tyrosine | [31-36] |
| *P. densispica* Franch. ex Maxim. (a.n.) | whole plant | (+)-isolariciresinol 3a-*O*-β-D-glucopyranoside, pinoresinol-4-*O*-β-D-glucoside, syringaresinol4-*O*-β-D-glucoside, longifloroside B, densispicoside, pedicutricone A, verbascoside, martynoside, *iso*-martynoside, 2''-*O*-acetyl-verbascoside, *cis*-martynoside, dearabinosyl-pneumonanthoside, salidroside, darendoside B, 4-*O*-β-D-glucopyranosyl-sinapic acid methyl ester, 3-(4-hydroxy-3-methoxyphenyl)-1,2,3-propantriol, citrusin C, robustaside B, acacetin, kaempferol, apigenin-7-*O*-glucoside, kaempferol-3,7-*O*-α-di-rhamnopyranoside, scutellarein-7-*O*-glucoside, chrysoeriol-7-*O*-glucoside,mussaenin A, argyol, densispicnin A, densispicnin B, densispicnin C, densispicnin D shanzhiside methyl ester, 8-*epi*-loganin, maltol-β-D-glucoside | [37, 38] |
| *P. dolichocymba* Hand.-Mazz. (a.n.) | whole plant | lariciresinol-4'-*O*-β-D-glucoside, plantagonine, indicaine, pediculidine, pediculine, verbascoside, 2'''-*O*-acetyl-martynoside, leucosceptoside A, jionoside D,apigenin, dolichocymboside A,dolichocymboside B, dolichocymbosideC,dolichocymbosideD, gardoside methyl ester, 7-*O*-acetyl-gardosidemethyl ester, uridine, 2-phenylethyl-*O*-β-D-xylopyranosyl-(1→2)-β-D-glucopyranoside | [30, 39-41] |
| *P. dolichorrhiza* Schrenk (a.n.) | n.s. | plantagonine, indicaine, pediculidine, pediculine | [41] |
| *P. gracilis* Wall. ex Benth. (a.n.) | whole plant | tannins, terpenoids, flavonoids, glycosides **(exact compounds not specified)** | [42] |
| *P. grayi* A. Nelson (a.n.) | roots | *N*-methyl-cytisine | [30] |
| *P. groenlandica* Retz. (a.n.) | aerial parts | senecionine, aucubin, euphroside, mussaenoside | [22, 30] |
| *P. integrifolia* Hook. f. (a.n.) | aerial parts | alkaloids, tannins **(exact compounds not specified)** | [43] |
| *P. kanei* Durand (s.n.) | leaves | alkaloids **(exact compounds not specified)** | [24] |
| *P. kansuensis* Maxim. (a.n.) | whole plant | β-sitosterol, β-daucosterol, 1,2,3,16,19,20-hexahydroxyolean-12-en-28-oic acid, alaschanioside A, alaschanioside C, kansuenin, | [44-49] |

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|---|---|---|---|
| | | kansuenin B, kansuenoside, verbascoside, leucosceptoside A, martynoside, *iso*-martynoside, *cis*-*iso*-martynoside, 2''',3'''-*O*-diacetyl-martynoside, jionoside B1, pedicularioside A, pedicularioside M, echinacoside, forsythoside B, 4'methyl-chrysoeriol, luteolin, luteolin-7-*O*--glucoside, lagotiside,tricin-7-*O*-glucuronide, gardosidemethylester, geniposidic acid, euphroside, (*E*)-2-hexenyl β-sophoroside, phenethylalcohol β-sophoroside, 1-(2,3,4-trihydroxy-phenyl)ethyl-3-*O*-rhamnose-4-[(2*E*)-3-(3,4-dihydroxy-phenyl)-2-propenoate]-glucopyranoside,1-(2,3,4-trihydroxy-phenyl)ethyl-3-*O*-rhamnose-4-[(2*E*)-3-(3,4-dihydroxy-phenyl)-2-propenoate]-6-[(2*E*)-3-(3,4-dihydroxy-phenyl)-2-propenoate]-glucopyranoside, 3-methoxy-4-hydroxybenzoic acid | |
| *P.kerneri* Dalla Torre (a.n.) | aerial parts | verbascoside, leucosceptoside A, echinacoside, aucubin, monomelittoside, plantarenaloside, euphroside, mussaenosidic acid, 8-*epi*-loganic acid, D-mannitol | [50] |
| *P.langsdorffii* Fisch. ex Steven (a.n.) | leaves | alkaloids, tannins **(exact compounds not specified)** | [24] |
| *P. lapponica* L. (a.n.) | aerial parts | alkaloids **(exact compounds not specified)**, euphroside, aucubin, mussaenoside | [24, 51] |
| *P. lasiophrys* Maxim. (a.n.) | whole plant | verbascoside, leucosceptoside A, cistanoside D, pedicularioside E, pedicularioside F, 8-*epi*-loganin | [52] |
| *P. longiflora* Rudolph (a.n.) | whole plant | longifloroside A, longifloroside B, longifloroside C, longifloroside D, scopoletin, 7(*R*)-dehydro-diconiferyl alcohol-4-*O*-β-D-glucoside, longiflor A, longiflor B, tortoside D, tortoside E, verbascoside, *iso*-verbascoside, leucosceptoside A, pedicularioside A, pedicularoside I, pedicularoside M, cistanoside D, echinacoside, geniposidic acid, mussaenoside, loganic acid, longifloroside, adenosine, 6-(1'',3''-dihydroxy-2''-propoxyl)-inosine | [46, 53-55] |
| *P. longiflora* var. *tubiformis* (Klotzsch) Tsoong (a.n.) | whole plant | hexatriacontanol, nonatriacontanol, β-daucosterol, martynoside, 1-hydroxy-xanthone, apigenin, chrysoeriol, luteolin, tricin, acacetin, orientin, morelosin, apigenin 7-*O*-glucuronide, luteolin 7-*O*-glucoside, luteolin-5-*O*-glucoside, chrysoeriol 7-*O*-glucuronide luteolin 7-*O*-glucuronide, tricin 7-*O*-glucuronide, 7-deoxy-8-*epi*-loganic acid, mussaenosidic acid, boschnaloside, aucubin, muconic acid, cinnamic acid, *p*-formyl cinnamic acid | [56-58] |
| *P. muscicola* Maxim. (a.n.) | whole plant | hentriacontane, arachidic acid, syringaresinol-4-*O*-β-D-glucoside, β-daucosterol, verbascoside, martynoside, *cis*-martynoside, pedicularioside A, mussaenoside, euphroside, geniposidic acid, aucubin, mussaenosidic acid, shanzhiside methyl ester, penstemonoside, pedicularoside, gardoside methyl ester, sesamoside, phloyoside II, caryoptoside, D-mannitol | [59-61] |

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|---|---|---|---|
| *P. nordmanniana* Bunge (u.n.) | aerial parts | verbascoside, martynoside, leucosceptoside A, forsythoside B, iridolactone, geniposidic acid, aucubin, euphroside, mussaenoside | [62] |
| *P. palustris* L. | aerial parts | aucubin, euphroside, ixoroside, shanzhiside methyl ester, gardoside methyl ester, plantarenaloside, mussaenoside, pedicularioside, penstemonoside, boschnaloside, 8-*epi*-loganin, 7-deoxy-8-*epi*-loganin, 8-*epi*-loganic acid. | [51] |
| *P. pectinata* Wall. ex Benn. (a.n.) | flowers | phenolics **(exact compounds not specified)** | [21] |
| *P. peduncularis* Popov (a.n.) | aerial parts | plantagonine, indicainine, plantagonin, indicine, peducularine, *N*-methyl-cytisine | [63] |
| *P. plicata* Maxim.(a.n.) | whole plant | verbascoside, martynoside, *iso*-martynoside, *cis*-leucosceptoside A, boschnaloside, plicatoside A, plicatoside B, 3,4-dihydroxy-phenethyl alcohol, 1-*O*-β-D-(3,4-dihydroxy-β-phenylethyl)-glucopyranoside | [64] |
| *P. procera* A.Gray (u.n.) | aerial parts | aucubin, mussaenoside, 6-deoxy-catalpol, shanzhiside methyl ester, 8-*epi*-loganic acid, gardoside, proceroside | [22, 65] |
| *P. punctata* Decne. (a.n.) | flowers, leaves | phenolics **(exact compounds not specified)**, verbascoside, aucubin | [8, 66] |
| *P. pycnantha* Boiss. (u.n.) | whole plant | alkaloids, tannins **(exact compounds not specified)** | [67] |
| *P. racemosa* Douglas ex Benth. (a.n.) | aerial parts | lupanine, tetrahydrorhombifoline, aucubin, euphroside | [22, 30] |
| *P. resupinata* L. (a.n.) | whole plant | alaschanioside A, alaschanioside C, syringaresinol-4"-*O*-β-D-glucoside, verbascoside, 2"',3"'-*O*-diacetyl-martynoside, leucosceptoside A, plantarenaloside, euphroside, boschnaloside, gardoside methyl ester, geniposidic acid | [16, 48] |
| *P. rex* C.B. Clarke ex Maxim. (a.n.) | whole plant | pedicurexoside, verbascoside, martynoside, *iso*-martynoside, 4-hydroxy-phenylpropenyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-feruloyl-β-D-glucopyranoside,apigenin, chrysoeriol, luteolin, luteolin-7-*O*-glucoside, 5,4'-di-hydroxy-3'-methoxy-flavone-7-*O*-6"-*n*-butyryl-β-D-glucopyranoside, aucubin, 6-*O*-ethyl-aucubin, euphroside, 6-*O*-ethyl-*epi*-aucubin, mussaenoside, plantarenaloside | [68] |
| *P. rostratocapitata* Crantz (a.n.) | aerial parts | verbascoside, echinacoside, campneoside II, cistantubuloside $C_1$, aucubin, euphroside, monomelittoside, mussaenosidic acid, 8-*epi*-loganic acid | [69] |
| *P. sarawschanica* Regel (u.n.) | fruits | plantagonine, peducularine | [70] |
| *P. semibarbata* A. Gray (a.n.) | whole plant | α-*iso*-lupanine, **17-oxo-*iso*-lupanine or isomer** | [71] |
| *P. semitorta* Maxim. (a.n.) | whole plant | syringaresinol-4"-*O*-β-D-glucoside, semitortoside A, semitortoside B, *cis*-*iso*-verbascoside, shanzhiside methyl ester, mussaenoside | [72] |
| *P. sibthorpii* Boiss. (a.n.) | aerial parts | verbascoside, martynoside, *iso*-martynoside, luteolin 7-*O*-glucoside, aucubin, D-mannitol | [73] |
| *P. siphonantha* D.Don (a.n.) | whole plant | (+)-dehydro-vomifoliol, vomifoliol, ω-hydroxy-propioguaiacone, 3-hydroxy-1-(4-hydroxy-3,5-dimethoxyphenyl)-1-propanone | [25] |
| *P. spicata* Pall. (a.n.) | whole plant | verbascoside, permethyl-verbascoside, pedicularioside A, pedicularioside G, | [74, 75] |

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|---|---|---|---|
| | | pedicularioside H, *cis*-pedicularioside H, shanzhiside methyl ester, gardoside methyl ester, 5-deoxy-puchelloside I | |
| *P. striata* | whole plant | ecdysterone 3-*O*-β-D-galactoside, striatoside A, striatoside B, verbascoside, *iso*-verbascoside, decaffeoyl-verbascoside, echinacoside, pedicularioside A, pedicularioside G, pedicularioside H, 1'-*O*-β-D-(3-methoxy-4-hydroxy-phenyl)-ethyl-α-L-apiosyl-(1→3')-α-L-rhamnosyl-(1→6')-4'-*cis*-feruloyl-glucopyranoside, 8-*O*-acetyl-harpagide, dihydro-catalpolgenin | [76-78] |
| *P. striata* subsp. *aracnoidea* (Franch.) Tsoong | whole plant | eremophila-10,11-dien-7a,13-diol, pedicularioside M, pedicularioside N, dihydro-catalpolgenin | [79-81] |
| *P. sudetica* Willd. (a.n.) | leaves | alkaloids **(exact compounds not specified)** | [24] |
| *P. sylvatica* L. (a.n.) | aerial parts | luteolin-7-O-glucoside, euphroside, plantarenaloside, 8-*epi*-loganin | [11, 51] |
| *P. tenuirostris* Benth. (a.n.) | flowers and leaves | phenolics **(exact compounds not specified)** | [8] |
| *P.torta* Maxim. (a.n.) | whole plant | longiflor A,longiflor B,tortoside A, tortoside B, tortoside C, tortoside D, tortoside E, tortoside F, dihydro-dehydro-diconiferylalcohol-4-*O*-α-L-rhamnoside, dihydro-dehydro-diconiferyl alcohol-4-*O*-β-D-glucoside, dihydro-dehydro-diconiferyl alcohol-9-*O*-β-D-glucoside, (7*R*)-dehydro-diconiferyl alcohol-4-*O*-β-D-glucoside, (7*S*)-dehydro-diconiferyl alcohol-4-*O*-β-D-glucoside, verbascoside, leucosceptoside A, cistanoside D, shanzhiside methyl ester, gardoside methyl ester, 8-*epi*-loganin, loganic acid | [82, 83] |
| *P. tricolor* Hand.-Mazz. (a.n.) | whole plant | 3β,19α-dihydroxy-12-ursen-28-oic acid, β-sitosterol, β-daucosterol, verbascoside, martynoside, pedicutricone A, quercetin-7-*O*-galactoside, apigenin, luteolin, chryoseriol, 3, 3'-di-*O*-methyl-quercetin, 3,5,4'-trihydroxy-3',5'-dimethoxy-flavone-7-*O*-β-D-glucopyranoside, 3,5,4',5'-tetrahydroxy-3'-methoxy-flavone-7-*O*-β-D-glucopyranoside, 3,5,3',4'-tetrahydroxy-flavone-7-*O*-β-gluopyranoside, myricetin 3'-methyl ester 7-*O*-glucopyranoside, pedicutricoside A, viburtinal, 3-methoxy-4-hydroxybenzoic acid | [84] |
| *P. uliginosa* Bunge (a.n.) | whole plant | (*rel*-4a*S*,7*R*,7a*R*)-1,4a,5,6,7,7a-hexahydro-7-hydroxyl-7-methyl-cyclopenta[c]pyran-4-carboxaldehyde, 1,3,5,6-tetrahydro-1-methoxyl-7-methyl-cyclopenta[c]pyran-4-carboxaldehyde, (*rel*-1*R*,4*S*,4a*S*,7*R*,7a*R*)-7-methyl-hexahydro-1,4-(epoxymethano)-cyclopenta[c]pyran-3(1*H*)-one, 4-*epi*-alyxialactone, alyxialactone, artselaenin A, artselaenin B, boschnarol, (4*R*)-4-hydroxymethyl-boschnialactone, densispicnin B | [85] |
| *P. verticillata* L. (a.n.) | whole plant | verticillatoside A, verticillatosideB, verbascoside, leucosceptoside A, cistanoside D, echinacoside, angoroside A, cistantubuloside $B_1$, wiedemannioside C, excelside B, aucubin, euphroside, monomelittoside, mussaenosidic acid, 7-deoxy-8-*epi*-loganic acid, 8-*epi*- | [69, 86, 87] |

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| | | | |
|---|---|---|---|
| | | loganicacid, plantarenaloside, geniposidic acid, boschnaloside, caryoptoside, pediverticilatasin A, pediverticilatasin B, pediverticilatasin C, kansuenin B, densispicnins B, euphrasin, scyphiphin A1, scyphiphin A2, ligustroside, | |
| *P. wilhelmsiana* Fisch. ex M.Bieb. (a.n.) | aerial parts | phenolics **(exact compounds not specified)** | [12] |

Table 1: Phytochemical compounds reported in the studied *Pedicularis* species

As the table clearly shows only 59 species have been studied for their phytochemical profiles and, out of these, 12 have been studied only preliminarly evidencing the presence of some classes of natural compounds but not the specific compounds. The highest amounts of identified compounds have been recorded in 14 species i.e. *P. artselaeri*, *P. chinensis*, *P. decora*, *P. densispica*, *P. dolichocymba*, *P. kansuensis*, *P. longiflora*, *P. longiflora* var. *tubiformis*, *P. muscicola*, *P. rex*, *P. striata*, *P. torta*, *P. tricolor* and *P. verticillata* whilst the lowest amounts have been recored in 6 species i.e. *P. acmodonta*, *P. bracteosa*, *P. comosa*, *P. grayi*, *P. sarawchanica* and *P. semibarbata*. All the other species have shown to biosynthesize metabolites in medium amounts. Only in two cases, the data reported in literature have not specified the organs of the plant species which have been studied i.e. *P. acmodonta* and *P.dolichorrhiza*. In general, the studied organs of the plants have been the aerial parts, the leaves, the flowers or the whole plant beside a few exceptions such as *P. chinensis* and *P. grayi* where the roots have been analyzed and *P. sarawchanica* where the fruits have been analyzed. Indeed, for what concerns the other accepted, synonym and unresolved named speciesno phytochemical data or even no total data are reported in literature. The structures of the majority ofthe identified compounds in *Pedicularis* species are reported in the figures below (Figures 3-13).

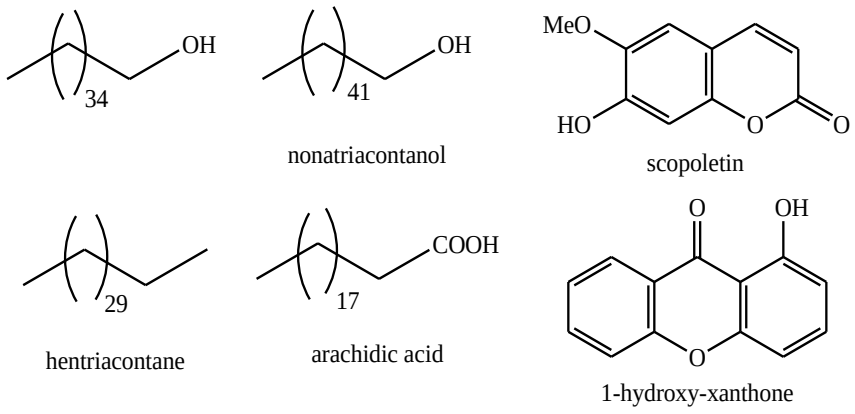


Figure 3: Fatty acids, lactones and xanthones identified in *Pedicularis* species

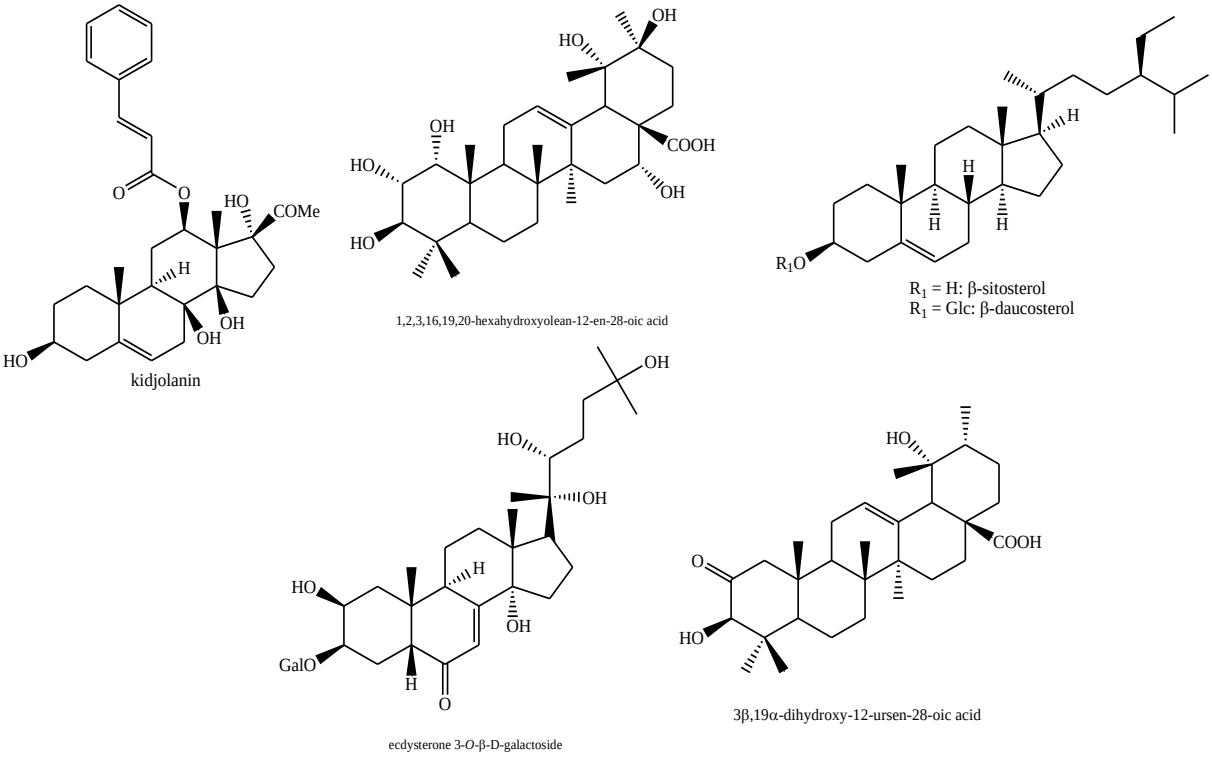


Figure 4: Terpenoids identified in *Pedicularis* species

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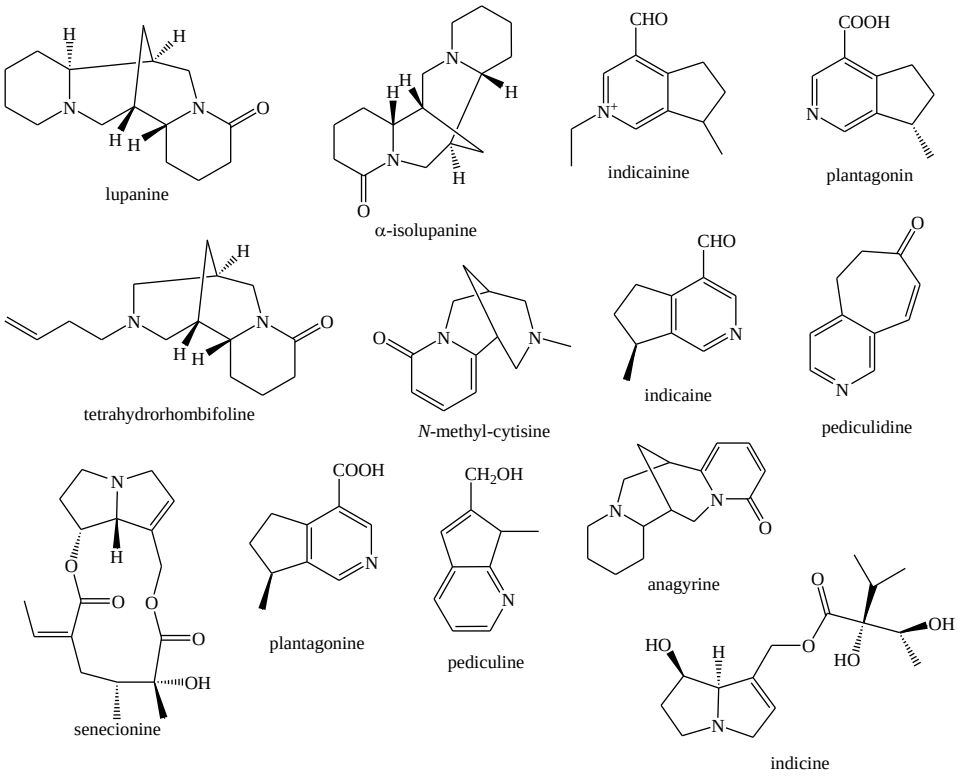


Figure 5: Alkaloids identified in *Pedicularis* species

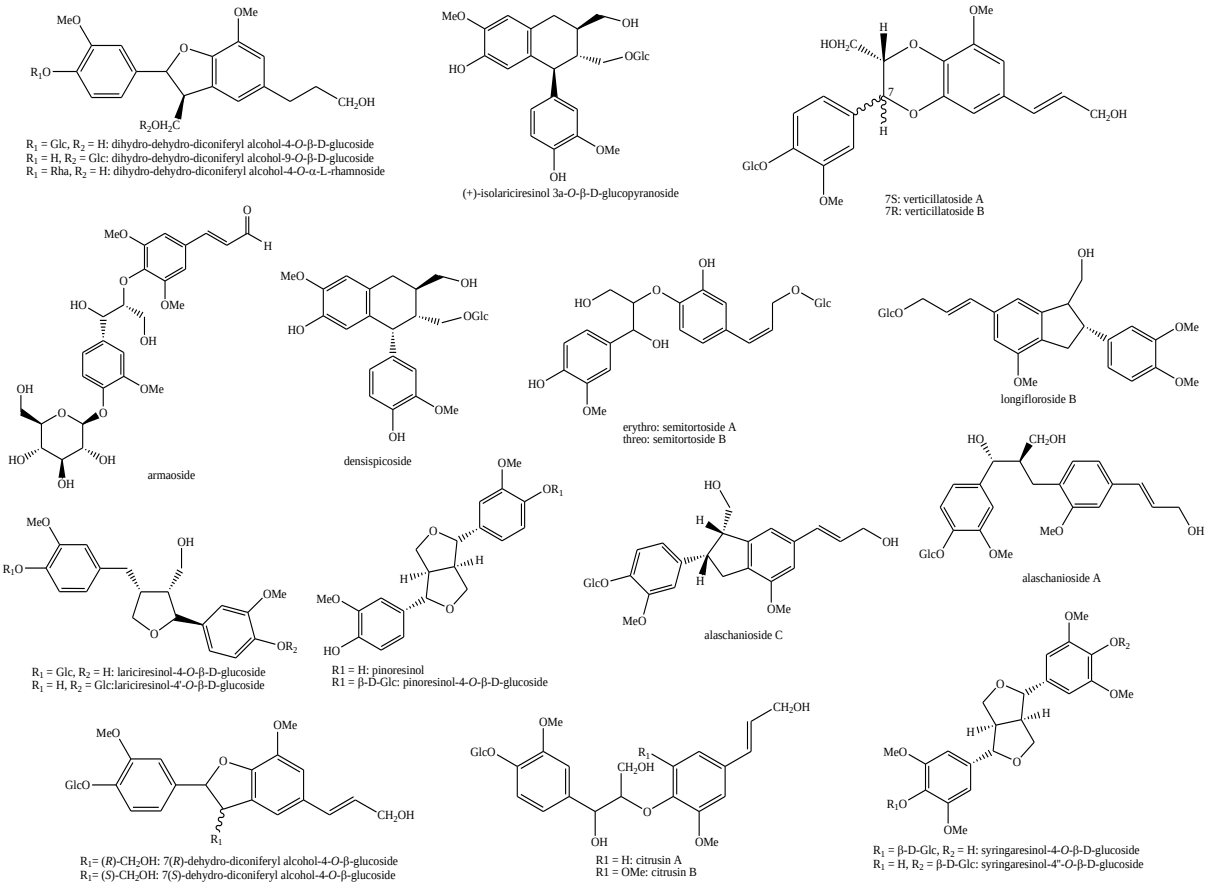


Figure 6: Lignans and *neo*-lignans identified in *Pedicularis* species

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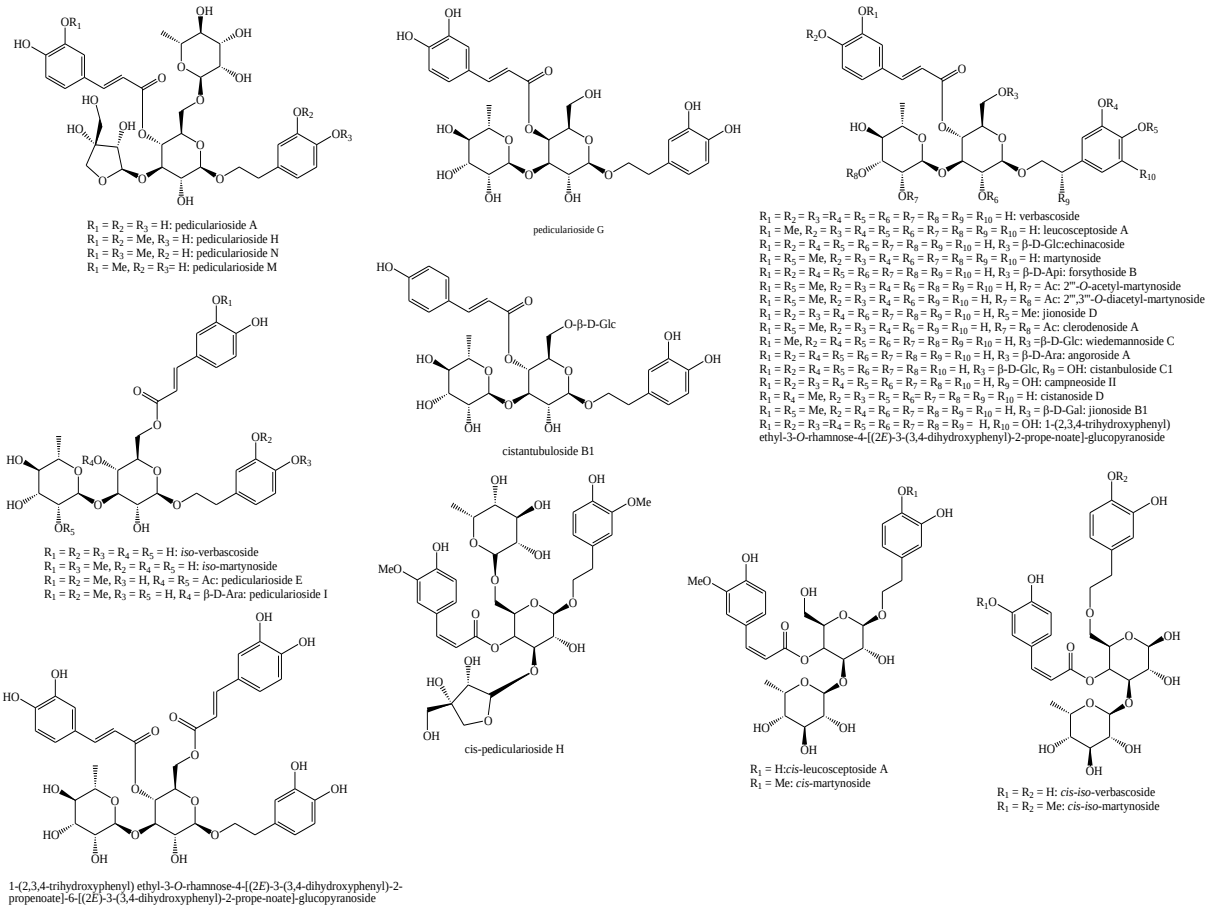


Figure 7: Phenylethanoid glycosides identified in *Pedicularis* species

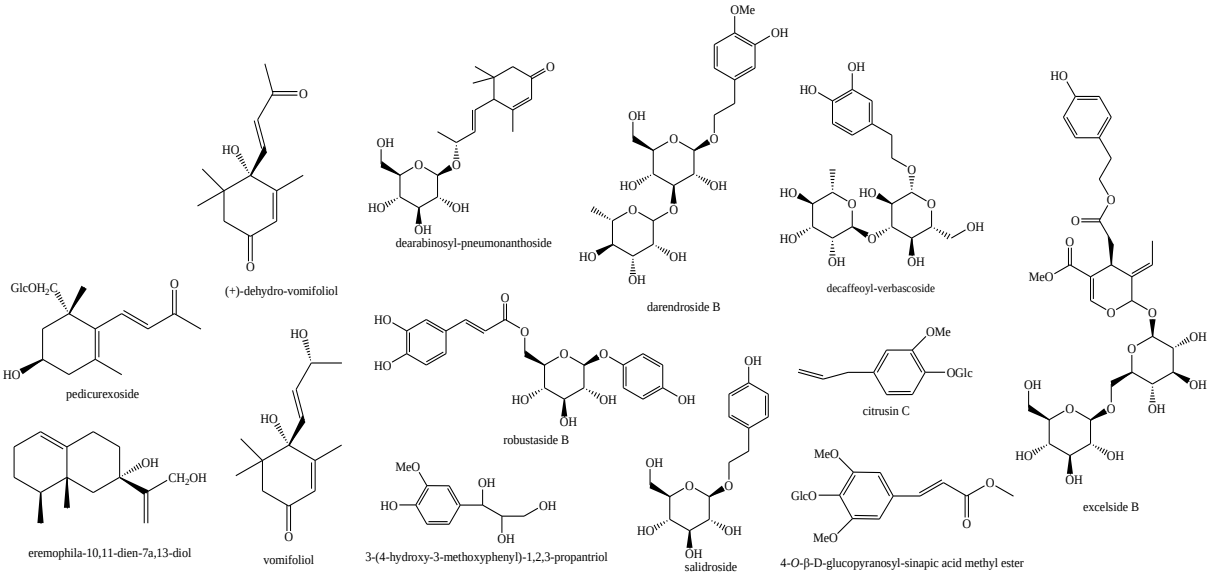


Figure 8: Miscellaneous glycosides identified in *Pedicularis* species

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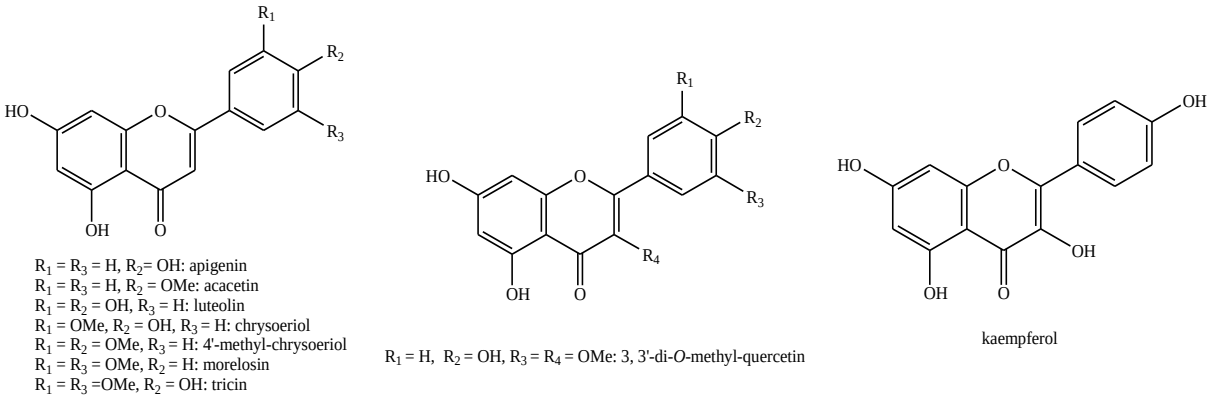


Figure 9: Aglycone flavonoids identified in *Pedicularis* species

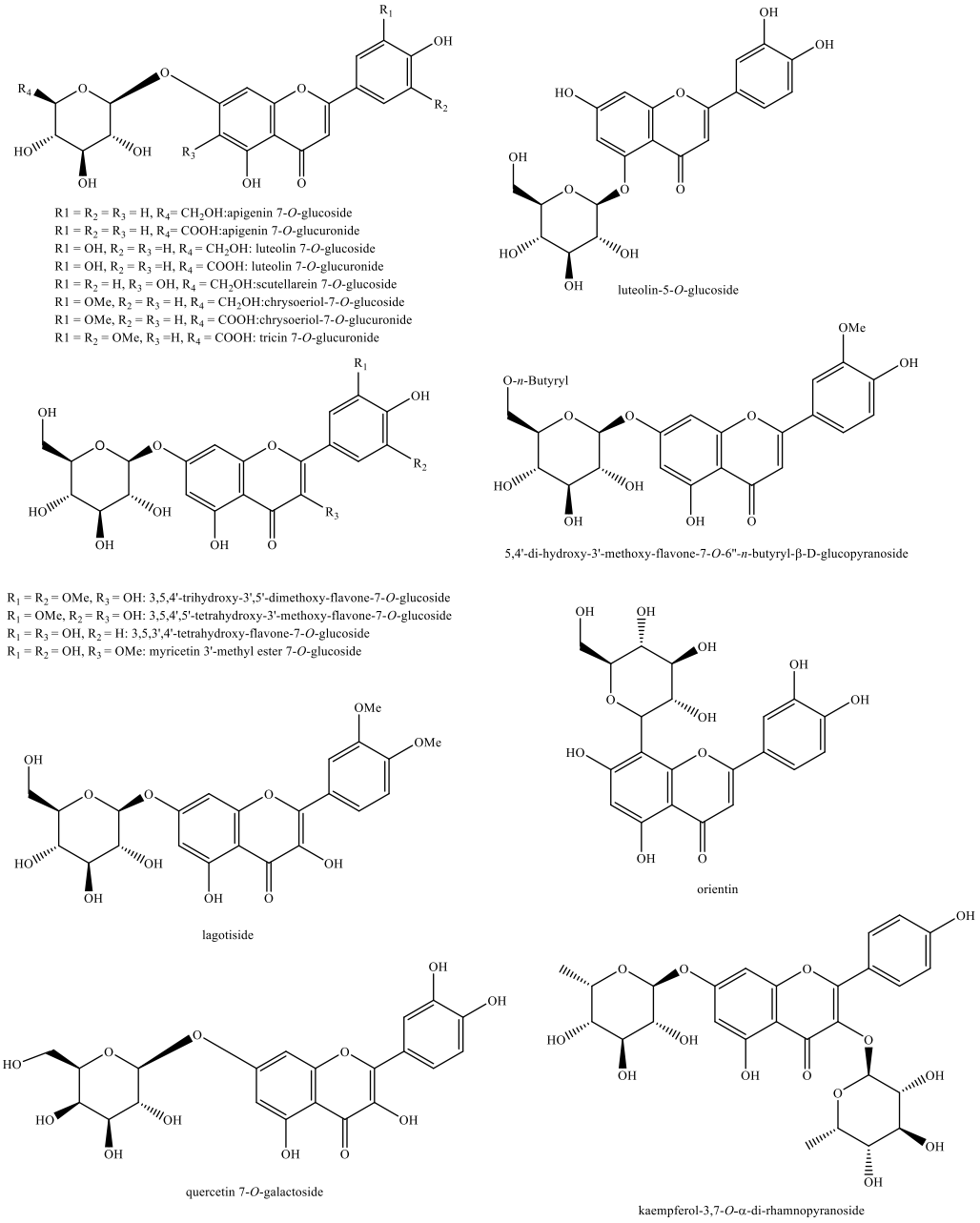


Figure 10: Glysosidic flavonoids identified in *Pedicularis* species

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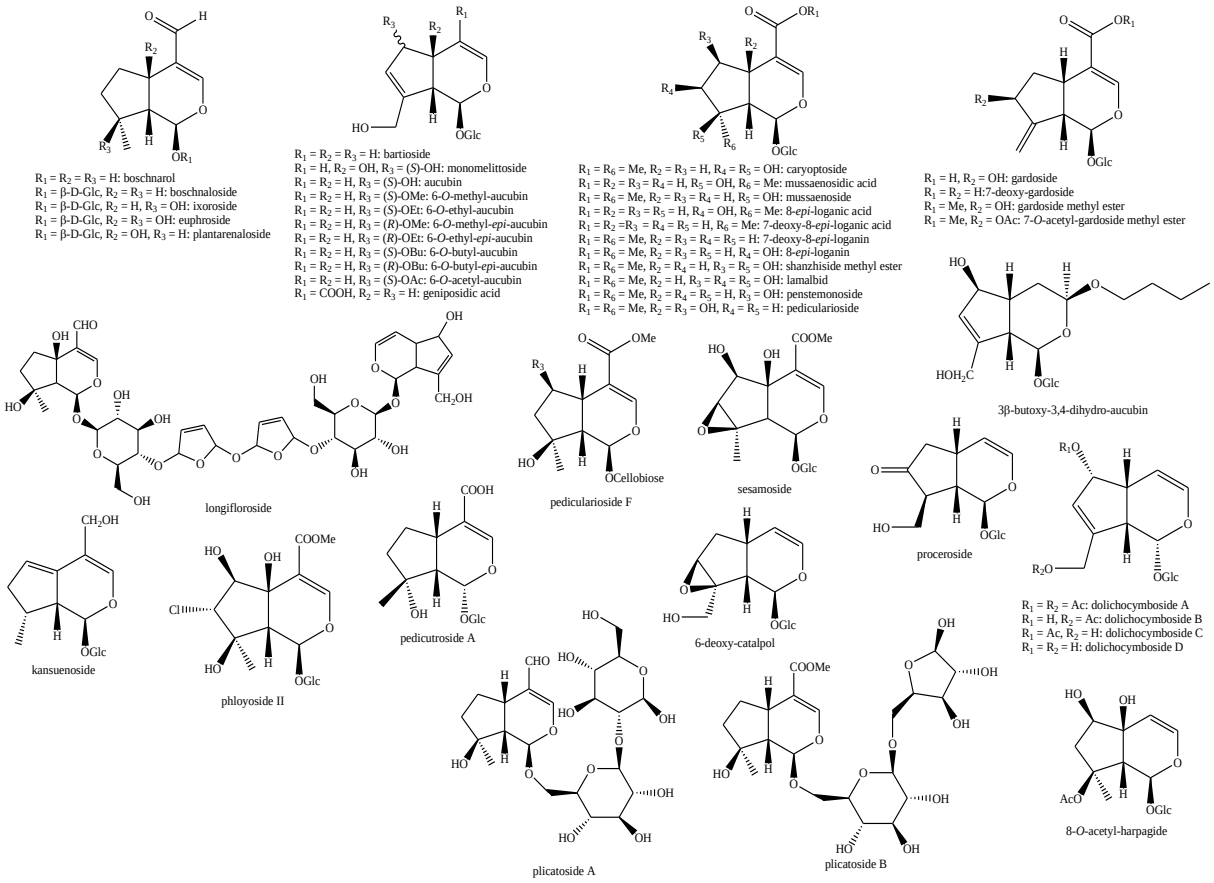


Figure 11: Iridoids identified in *Pedicularis* species – part 1

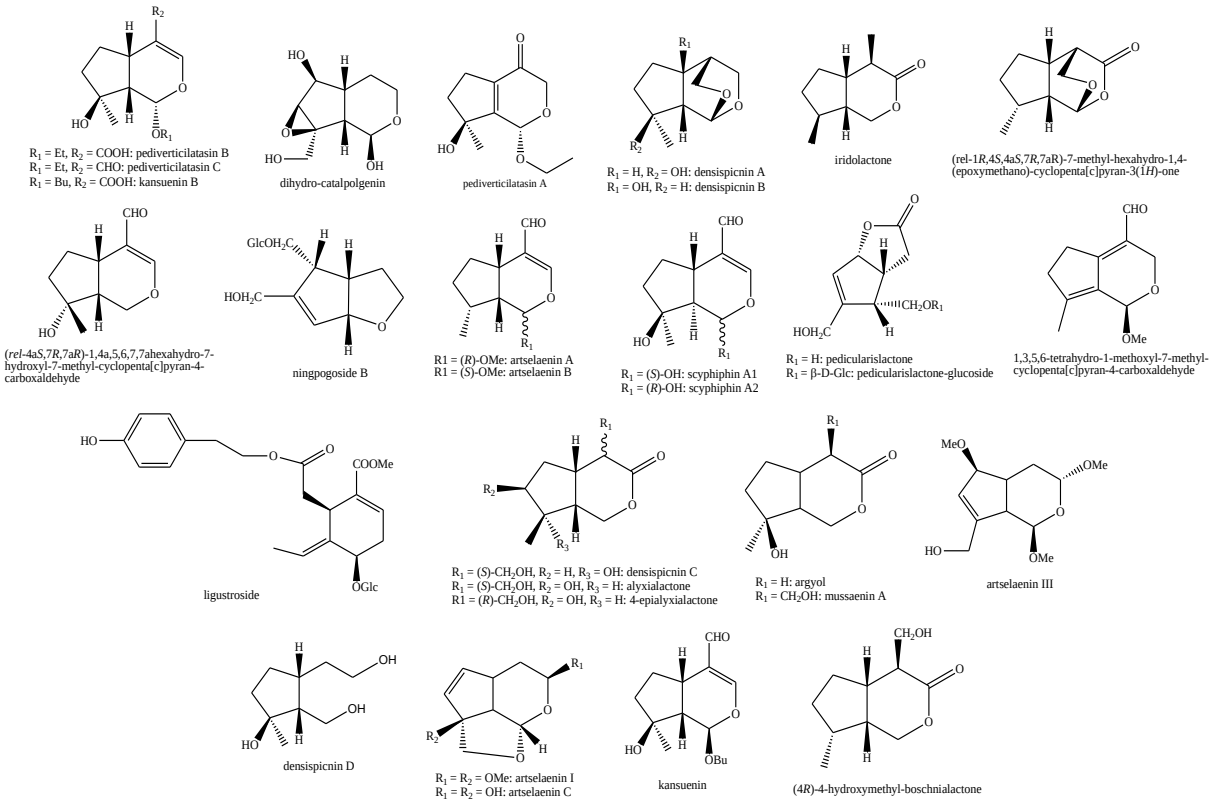


Figure 12: Iridoids identified in *Pedicularis* species – part 2

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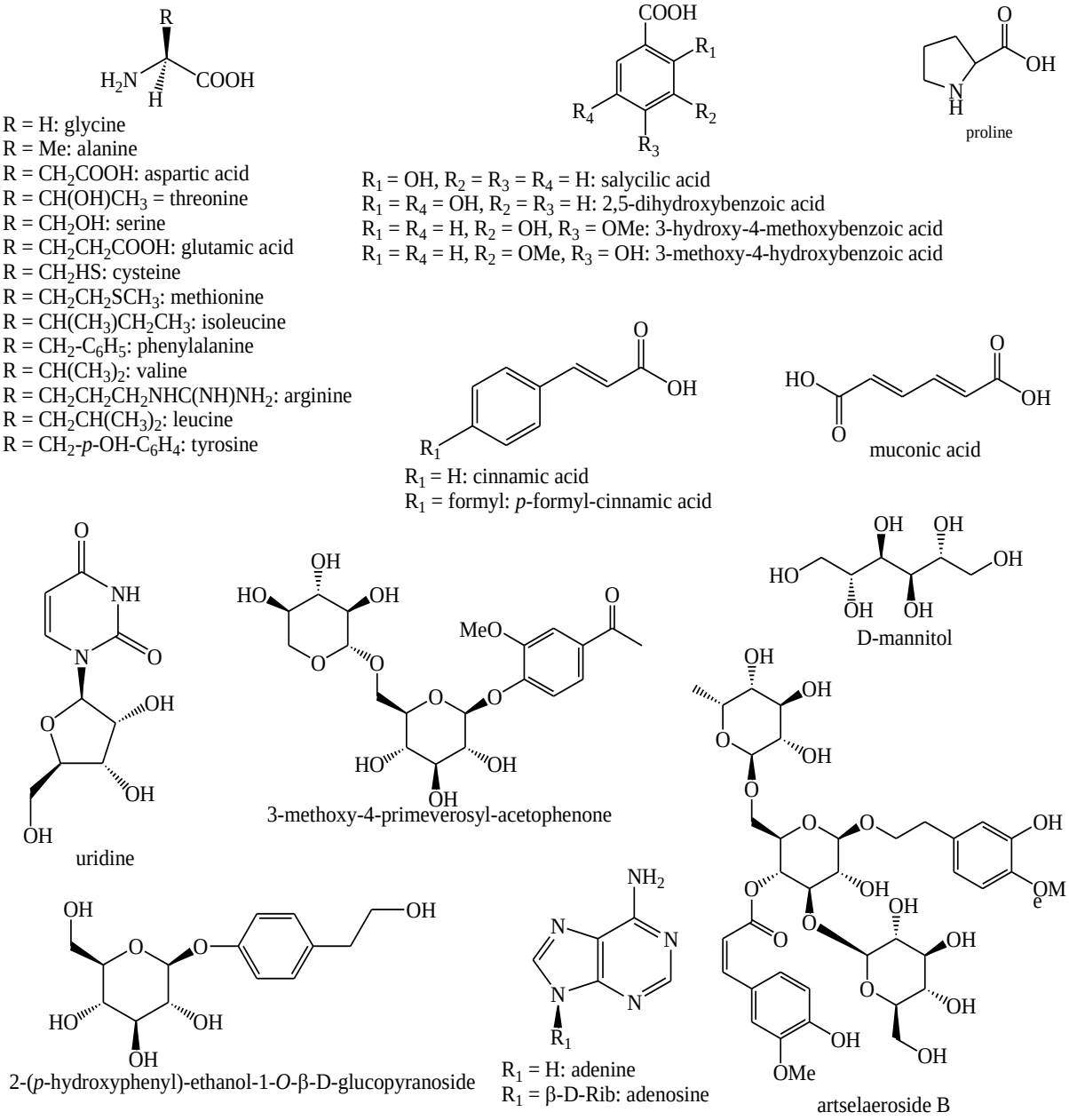


Figure 13: Other compounds identified in *Pedicularis* species

## Corollary to phytochemistry

After visualization of the relative structures of the identified compounds in *Pedicularis* spp., two important elements must be observed and highlighted.

The first one concerns the compound found in *P. kansuensis* by Zhang et al. [49]. According to the structure, the compound should not be named as 1,2,3,16,19,20-hexahydroxyolean-12-en-28-oic acid but rather as 1,2,3,16,19,20-hexahydroxy-12-ursen-28-oic acidon the basis of the

vicinal dimethyl functionalization in positions 19,20 of the pentacyclic triterpene skeleton which indicates it as anursaneand not an oleane.

Moreover, for what concerns iridoids, some of those identified in *Pedicularis* spp. may indeed be artifacts due to the applied procedures during the phytochemical analysis. In particular, the two new iridoid glycosides 6-*O*-ethyl-aucubin and 6-*O*-ethyl-*epi*-aucubin, recognized from *P. rex* [68] and the three pediverticilatasin A-C isolated from *P. verticillata* [86] are much likely due to the extraction with ethanol. The same has very likely happened for 6-*O*-methyl-*epi*-aucubin, artselaenin III and artselaenin I [19, 20], all isolated from *P. artselaeri* after extraction with boiling methanol (at reflux). The possibility to generate this kind of artifacts from iridoids was one of the arguments of a recent review and editorial article [88, 89] which reported about the reactivity of hydroxyl substituent in allylic configuration, a functionalization very often present in several iridoid structure, as well as the possibility of addition of short-chain alcohols used as extractive solvents to the double bond in 3,4-positions of the iridane skeleton. Unfortunately, the presence of such iridoid derivatives was not confirmed in the studied species by avoiding the possible cause of artefact formation. Therefore, the presence of these compounds remain doubtful without any further confirmation.

## Chemotaxonomy

The chemotaxonomy of the *Pedicularis* genus is quite complex and involves several classes of natural compounds. In particular, its main chemotaxonomic marker is aucubin and, in fact, it has been recognized in 25 of the studied species (Table 1). From the biogenetic standpoint, aucubin, like the other decarboxylated C-10 iridoids observed in species comprised in the Lamiales Order, derives from geranyl pyrophosphate. In particular, these follow the biosynthetic *Route II*, which involves *epi*-iridotrial and 8-*epi*-deoxy-loganic acid among the precursors, and lead to the biosynthesis of iridoids characterized by the α-configuration for the methyl function linked in the 8 position of the iridane skeleton. Yet, its cyclization reaction occurs through a hydride nucleophillic attack on C1 that leads to the 1-*O*-carbonyl atom attack on C3 and then to the lcyclicacetale [90]. Considering the biogenesis of iridoids in this genus, it is doubtful the presence of loganic acid recognized among the phytoconstituents of *P. torta* and *P. longiflora* (see table for references). We are instead of the advice that, without a further reconfirmation, it was mistakenly reported instead of the *epi*-loganic acid. Actually, minor chemotaxonomic markers of the genus are also euphroside and mussaneoside, even if in several

species the content of euphroside resulted to be higher than those of aucubin itself [22, 50] and the level of mussaenosidic acid resulted comparable with those of other iridoidic constituents [59]. Conversely, some iridoids are considered to be chemotaxonomic markers at the species level since their presence has been reported only in them. The main example of this are pedicularioside for *P. muscicola*, kansuenin, kansuenin B and kansuenoside for *P. kansuensis*, pliatosides A-B for *P. plicata* and densispicnin A for *P. densispica*. In contrast with what written in the previous paragraph concerning artefact iridoids, the presence of proceroside in *P. procera* [65], even if it presents a β-configuration in C-8 and therefore it would seem to be derived from the *Route I* biogenetic pathway, is not an artefact and is not due to an erroneous interpretation of experimental data. In fact, the inversion of configuration at C-8 in proceroside is favored by the presence of a ketone function on the adjacent carbon (C-7) which is involved in a keto-enol equilibrium and this may perfectly justify the β-configuration of the hydroxymethyl group at the position 8.

Phenylethanoid glycosides (i.e. verbascoside and its derivatives) are considered to be other chemotaxonomic markers of the genus since their presence has been evidenced in most of the studied species. Yet, these compounds are very common in all the Asteridae class and, in fact, they have been identified also in other families such as Asteraceae [91], Caprifoliaceae [92], Lamiaceae [14], Oleaceae [93], Plantaginaceae [94], Scrophulariaceae [95] and Verbenaceae [96]. More specifically, the phenylethanoid glycosided have a chemotaxonomical relevance when in co-occurrence with iridoids [97]. This was already observed in several species comprised in the Lamiales order [98-103] as well as in the case of several *Pedicularis* spp.Also within the same family which *Pedicularis* genus belong to (Orobanchaceae), these compounds are extremely common and, in fact, they have been already reported in several genera such as *Orobanche* L., *Cistanche* L. and *Orthocarpus* Nutt. [104]. For these reasons, phenylethanoid glycosides can not be actually taken as general chemotaxonomic markers of the *Pedicularis* genus. Nevertheless, specific compounds can be useful cheotaxonomic markers such as pedicullariosides A, E, G, H, I, M, N for the entire genus, permethyl-verbascoside for *P. spicata*, *cis*-*iso*-martynoside for *P. kansuensis*, *cis*-pedicularioside H for *P. spicata* andartselaeroside B for *P. artselaeri*.

For what concerns lignans and derivatives, they are quite widespread in the genus but also in the family Orobanchaceae and in many others [105]. Yet, semitortosides A-B can serve as chemotaxonomic markers for *P. semitorta*, striatosides A-B for *P. striata* and longiflor B, longiflorides C-D for *P. longiflora*.

Also flavones and, in particular, flavonols and glycosidic flavonoids presenting an apigenin, scutellarein and isoscutellarein base moiety, are considered to be chemotaxonomic markers of the genus. Yet, they are very common compounds in the plant kingdom and for this reason they are notso useful as chemotaxonomic markers. In particular, their presence can be easily evidenced in Lamiaceae species [14] as well as in many other families such as Euphorbiaceae, Asteraceae, Compositae and Hypericaceae [106-112].

For what concerns alkaloids, pediculidine, pedicularidine, pediculine and pediculinine have been evidenced only in *Pedicularis* species and they can serve as chemotaxonomic markers at the genus level.

As for other compounds belonging to different classes of natural metabolites from the ones already described, there is no report on them as chemotaxonomic markers of the *Pedicularis* genus or in general, since they are extremely common. Nevertheless, pedicurexoside, a sesquiterpene, may be suggested as a specific marker for *P. rex* since it has been only evidenced in that species so far while the polyol D-mannitol seems to be highly represented in hemiparasitic entities previously comprised in Scrophulariaceae and now classified as Orobanchaceae [50, 69, 100, 113].

In this context, concerning the phytochemistry and the chemotaxonomy, it is of primary importance also to consider other aspects, together with the markers metabolite biogenesis, such as the ecology and the hemiparasitic behaviour of the plant species when the scope of the study is related to the chemosystematic. In fact, in several cases it was observed the transfer of metabolites from the hosts to the hemiparasitic species, such in the cases of *Euphrasia stricta* D. Wolff [114], *Euphrasia rostkoviana* Hayne [115] and *Odontites luteus* Steven [116]. Therefore, it is auspicable that the results from the phytochemical analysis of hemiparasites should be carefully checked with the required criticism.

## Ethnopharmacology

*Pedicularis* species are widely used in the traditional medicine of several countries around the world especially Asiatic ones. The pharmacological activites exerted by these species are numerous and interesting and often, one species is employed to treat more maladies as well as the opposite. Table 2 reports on the specific ethnopharmacological properties associated to every studied plant in this field. In addition, the organs of the plant species capable to show that

medicinalactivity are described as well as the areas of the world where the indigenous people employ these species in traditional medicine.

| *Pedicularis* species | Ethnopharmacological uses | Organ /Form | Area of the world | References |
|---|---|---|---|---|
| *P. artselaeri* Maxim. (a.n.) | to treat diuresis, exhaustion, collapse, senility | aerial parts/ n.r. | Northwestern China | [117] |
| *P. bicornuta* Klotzsch. (u.n.) | - to treat vaginal and seminal discharges<br>- to treat burns, rheumatism, gout, general inflammation, acidity | - inflorescence/ paste<br>- whole plant/ decoction | - Nepal (Central Himalaya)<br>- China, India | - [118]<br>- [8, 119] |
| *P. bifida* (Buch.-Ham.) Pennell (u.n.) | - to treat stomachache<br>- to relieve joint paints | roots/ liquid and powder | Nepal (Newar community of Pharping Village, Kathmandu District) | [120] |
| *P. capitata* Adams (a.n.) | - to sedate and relax<br>- to stop bleeding in minor injuries | whole plant/ infusion | Canada (Inuit people of Kugluktuk, Nunavut regions) | [121] |
| *P. cheilanthifolia* Schrenk (a.n.) | - to cure stomachache, vaginal discharge, leucorrhoea, menorrhagia | whole plant, wood/ ethanolic extract, powder | India/Kashmir (Ladakh region) | [122, 123] |
| *P. chenocephala* Diels (a.n.) | - to relieve pain<br>- to treat oedema, oliguria, asthma, malnutrition, pains induced by osteomyelitis | flowers/ decoction | China | [8] |
| *P. chinensis* Maxim. (a.n.) | - to nourish yin<br>- to invigorate kidney<br>- to strengthen spleen and stomach | roots/ decoction | China | [8] |
| *P. comosa* L. | - to be used as food stuff | flowers/ nectar | Turkey | [124] |
| *P. cranolopha* Maxim. (a.n.) | - to clear away heat evil<br>- to expel superficial evils<br>- to treat fever, urinary tract infections, hepatitis, pneumonia, sore pain due to external injury | whole plant/ decoction | China | [8] |
| *P. davidii* Franch. (a.n.) | - to strengthen spleen and stomach<br>- to nourish yin<br>- to relieve pain<br>- to treat inanition, kidney deficiency, osteopyrexia, fever, joint pain, anorexia | rhizomes/ decoction | China | [8] |
| *P. decora* Franch. (a.n.) | - to treat general debility, collapse, exhaustion, seminal emission, spontaneous sweating and senility<br>- to invigorate the mind and the circulation of blood | roots/ decoction | China | [8, 125] |

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| | | | | |
|---|---|---|---|---|
| | - to strengthen spleen and stomach | | | |
| *P. decorissima* Diels (a.n.) | - to clear away heat evil<br>- to expel superficial evils<br>- to treat acute gastroenteritis and food poisoning | wholeplant, flowers/ decoction | China | [8] |
| *P. dissecta* (Bonati) Pennell & H.L. Li (a.n.) | - to supplement qi<br>- to nourish yin<br>- to detoxificate<br>- to relieve pain<br>- to treat asthenia due to disease, yin deficiency, sore, joint pains | roots/ decoction | China | [8] |
| *P. dunniana* Bonati (a.n.) | - to nourish yin<br>- to relieve pain<br>- to treat inanition, kidney deficiency, osteopyrexia, fever, joint pains, anorexia | rhizomes/decoction | China | [8] |
| *P. flagellaris* Benth. (u.n.) | - to treat excessive diuresis and wounds<br>-to treat excessive diuresis, wounds, rheumatisms<br>- to regulate menstruation | - aerial parts/ infusion, decoction<br>- aerial parts/ infusion, decoction | - Himalaya<br>- Buthan | - [126]<br>- [126] |
| *P. flava* Pall. (a.n.) | to treat general body pains,stomachaches<br>- to be used as sedative | leaves/ decoction | Pakistan | [127] |
| *P. gracilis* Wall. ex Benth. (a.n.) | to treat stomachache | roots/ liquid | Nepal (Newar community of Pharping Village, Kathmandu District;Western regions) | [120, 128] |
| *P. gracilis* subsp. *gracilis* (s.n.) | to relieve joint pain | roots/ powder | Nepal (Central Himalaya) | [120] |
| *P. henryi* Maxim. (a.n.) | - to nourish yin and qi<br>- to strengthen tendonsand bones with vital essence<br>- to activate collaterals<br>- to treathemiplegia and arthralgia due to blood stagnation | roots/ decoction | China | [8] |
| *P. hoffmeisteri* Klotzsch (a.n.) | - to cure food poisoning<br>- to cure flatulence and stomach disorders in animals | whole plant/ n.r.<br>whole plant/ n.r. | India (Western Himalaya)<br>India (Uttaranchal State) | [129, 130] |
| *P. integrifolia* Hook. f. (a.n.) | - to treat dropsy, excessive diuresis, asthma, rheumatisms<br>- to heal wounds and oedema<br>- to nourish body | aerial parts/ ethanolic extract | Bhutan | [43] |
| *P. kansuensis* Maxim. (a.n) | - to treat collapse, exhaustion, senility, edema and boils<br>- to relieve heat and toxicity<br>-to treatedema, inflammation,urinary | aerial parts/ n.r.<br><br>flowers/ n.r. | China<br><br>Tibet, China | - [49, 117]<br><br>- [8] |

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| | | | | |
|---|---|---|---|---|
| | obstructions. | | | |
| *P. lanata* Willd. ex Cham. & Schltdl. (a.n.) | to treat headache, migraine | n.r./ n.r. | Canada (Aborigens of the Boreal forest) | [131] |
| *P. longicaulis* Franch. ex Maxim. (a.n.) | to nourish yin and qi<br>- to activate collaterals<br>- to treat dizziness tinnitus, bones and muscles pain, deficiency heat | roots/decoction | China | [8] |
| *P. longiflora* Rudolph (a.n.) | - to cure hepatic, pancreatic, kidney, urinary diseases, vaginal discharge, leucorrhoea, menorrhagia | - whole plant, wood/ decoction, powder | - Himalaya (Ladakh region) | - [7, 123] |
| | - to treat rheumatisms, excessive diuresis and coagulation, wounds, hypertension, dehydration | - aerial parts/ ethanolic extract | - Buthan | - [43] |
| | - to treat edema, tinnitus, carbuncles wollen, hepatitis, spermatorrhea, cholecystitis, urine with pus and blood, dry mouth, carbuncle swollen | - whole plant, flowers/ decoction | - China | - [8] |
| | - to treat vertigo, dry tongue, excessive seminaldischarge,edema, diuretic, liver and gall bladder problems | - leaves, stems/ decoctions | - India | - [119] |
| *P. longiflora* var. *tubiformis* (Klotzsch) Tsoong (a.n.) | - to treat cough, sore throats, hepatitis, lymphatic disorders, poisioning, seminal and vaginal discharges, dropsy, spermatorrhoea, tinnitus, carbuncle disorders associated with alcoholism | whole plant/ raw food | Nepal (Central Himalaya) | [56, 132] |
| *P. megalantha* D.Don (a.n.) | - to soothe meat poisoning, intestinal disorders, acidity | aerial parts/ decoction | Buthan, Tibet | [133] |
| *P. megalochila* H.L. Li | to treat dysentery, diarrhea, hepatitis, urinary tract infections | wholeplant/ decoction | China | [8] |
| *P. muscicola* Maxim. (a.n.) | - to nourish qi<br>- to treat consumption diseases, blood deficiency, hidrosis, hypotension | roots/decoction | China | [8] |
| *P. oederi* Vahl (a.n.) | - to treat rheumatic arthritis, lithangiuria, scabies, micturition difficulties | - roots/ decoction | - China | - [8] |
| | - to treat food poisoning, headache, backache, bodyache<br>- to use as sedative | - whole plant/ raw vegetable | - India (Trans Himalaya region) | - [119, 134] |

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| | | | | |
|---|---|---|---|---|
| *P. oederi* var. *sinensis* (Maxim.) Hurus. (a.n.) | to treat urinary obstructions and edema in animals | flowers/ n.r. | Tibet, China | [135] |
| *P. oliveriana* Prain (a.n.) | - to reduce inflammation<br>- to ease gastric pains or disorders<br>- to treat poisoning, micturition difficulties | - inflorescence/ extract | - Nepal (Central Himalaya) | - [136] |
| | - to cure food poisoning, stomach ulcer, duodenalulcer, diarrhea, rheumatic joint pains, lithangiuria, abnormal leucorrhea, scabies | - flowers, whole plant/ decoctions | - China | -[8] |
| *P. pectinata* Wall. ex Benn. (a.n.) | - to increase urine flow<br>- to cure swelling and stomach pains due to intestinalinfections | - aerial parts/ powdered raw food in cold water | - Kashmir | - [137] |
| | - to alleviate stomach pain, flatulence, intestinal infections, intestinal swelling, high blood pressure, backache, bodyache, fever<br>- to increase urine flow<br>- to cure haemoptysis, alopecia | - flowers/ powdered raw food in cold water<br>- flowers/ decoction | - Western Himalaya (Lahaul-Spititribe)<br>- India, Kashmir | - [138]<br>- [139-141] |
| *P. pectinatiformis* Bonati (a.n.) | - to relieve pain<br>- to relax | leaves/ infusion | Pakistan (Gilgit-Baltistan region) | [142] |
| *P. peduncularis* Popov (a.n.) | - to treat uterine bleeding<br>- to favour diuresis<br>- to treat various skin diseases | - aerial parts/ decoction<br>- flowers/ decoction<br>- aerial parts/ baths | Tagikistan | [63] |
| *P. punctata* Decne. (a.n.) | - to treat fever, cancer and premature graying of hair<br>- to improve digestion and to control blood pressure<br>- to treat hypertension, fever, gastrointestinal disorders<br>- to relax skeletal muscles | - inflorescenze/ extract<br>- aerial parts/ powdered raw food in cold water<br>- flowers/ powder in cold water | - Nepal (Central Himalaya)<br>- Western Himalaya (Lahaul-Spititribe)<br>- Pakistan | - [136]<br>- [138, 143]<br>- [144, 145] |
| *P. pyramidata* Royle ex Benth. (a.n.) | to treat fluid retention, headache, bone inflammations, serous fluids accumulation | whole plant/ raw food | Nepal (Central Himalaya), India | [136, 141] |
| *P. resupinata* L. (a.n.) | - to treat malignant abscesses<br>- to treat rheumatoid arthritis, rheumatic pains, joint pains, scabies, *micturition difficulties*<br>- to cure lithangiuria abnormal leukorrhea, acute gastroenteritis, food poisoning | - aerial parts/ n.r.<br>- roots, stem/ powder, decoctions | - South Korea<br>- China | - [146]<br>- [8] |

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| | | | | |
|---|---|---|---|---|
| *P. rex* C.B. Clarke ex Maxim. (a.n.) | - to invigorate qi and blood<br>- to strengthenspleen<br>- to treat yin deficiency, hectic fever, rheumatism, cirrhosis, ascites<br>- to cure smallpox, measles, seasonal prevalent diseases | roots, whole plant/ decoctions | China | [8] |
| *P. rhinanthoides* Schrenk (a.n.) | - to treat cough, sore throat, hepatitis, lymphatic disorders, poisoning<br>- to treat diabetes | whole plant/ raw food<br>- whole plant/ decoction | - Nepal (Central Himalaya)<br>- India | - [136]<br>- [147] |
| *P. rudis* Maxim. (a.n.) | - to nourish yin<br>- to relieve pain<br>- to treat inanition, kidney deficiency,osteopyrexia, fever, joint pain, anorexia | rhizomes/decoction | China | [8] |
| *P. scullyana* Prain ex Maxim. (u.n.) | to remove pimples | wholeplant/ paste | Nepal (Western regions) | [128] |
| *P. siphonantha* D.Don (a.n.) | to treat cough, sore throat, hepatitis, lymphatic disorders, poisoning | whole plant/ raw food | Nepal (Central Himalaya) | [132, 148] |
| *P. spicata* Pall. (a.n.) | - to nourish qi<br>- to treat consumption diseases, blood deficiency, hidrosis, hypotension | roots/decoction | China | [8] |
| *P. striata* Pall. (a.n.) | to treat kidney-yang deficiency, edema, micturition difficulties | wholeplant/ decoction | China | [8] |
| *P. tenuirostris* Benth. (a.n.) | to cure swelling and stomach pain due to intestinalinfections | flowers/ powdered raw food in cold water | Western Himalaya (Lahaul-Spititribe) | [138] |
| *P. torta* Maxim. (a.n.) | to treat inflammations and urinary obstructions in animals | flowers/ n.r. | Tibet, China | [135] |
| *P. verticillata* L. (a.n.) | - to nourish qi<br>- to treat consumption diseases, blood deficiency, hidrosis, hypotension | roots/decoction | China | [8] |

Table 2: Ethnopharmacological employments of *Pedicularis* species as reported in literature

## Corollary for ethnopharmacology

Some *Pedicularis* species are also reported to have ethnopharmacological employments in certain areas of the world but no specific properties are reported in literature. In particular, this

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concerns *P. koengboensis* Tsoong var. *kongboensis* (a.n.) in Nepal [149], *P. heydei* Prain (u.n.), *P. nodosa* Pennell (u.n.) and *P. scullyana* Prain ex Maxim. (u.n.) in Tibet [150], and, lastly, *P. tristis* L. (a.n.) in Mongolia [151]. The absence of specific informations in literatue makes them quite doubtful but not totally false since their employment may be only on a traditional local basis and favoured by specialized people who may not be interested in sharing their knowledge. Anyway, the phytochemical analysis of also these species is strongly auspicable in future.

## Pharmacology

In spite of all the results reported in the previous section, for some *Pedicularis* species, only a few initial pharmacological properties have been assessed and for this, their ethnopharmacological employments have not been reported, yet. This concerns also the species already used in the ethnopharmacological field but that have been studied for other possible employments. Table 3 reports on these species and their relative pharmacological properties.

| *Pedicularis* species | Pharmacological properties | Organs/Forms | Collection area | References |
|---|---|---|---|---|
| *P. artselaeri* Maxim. (a.n.) | - strong antioxidant | aerial parts/ butanol and water extracts | China | - [152] |
| | - hepatoprotective | - water and ethanolic extracts | | - [153] |
| *P. cadmea* Boiss. (u.n.) | weak antibacterial | aerial parts/ methanolic extract | Turkey | [154] |
| *P. condensata* M.Bieb. (u.n.) | antibacterial, weak antioxidant, antifungal | aerial parts/ essential oil | Turkey | [10] |
| *P. davidii* Franch. (a.n.) | - strong antioxidant | - rhizomes/ butanol and water extracts | China | - [152] |
| | - hepatoprotective | - water and ethanolic extracts | | - [153] |
| *P. decora* Franch. (a.n.) | antioxidant, antidiabetic, hepatoprotective, anti-inflammatory | roots/ethanolic, n-butanol and water extracts | China | [7, 155, 156] |
| *P. flava* Pall. (a.n.) | medium antimicrobial | whole plant/ ethanolic extract | Mongolia | [157] |
| *P. longiflora* Rudolph (a.n.) | antidiabetic, antioxidant, radical scavenging | whole plant/ ethanolic extract | Himalaya (Ladakh region), China | [7, 55] |
| *P. olympica* Boiss. (u.n.) | weak antimicrobial | aerial parts/ methanolic extract | Turkey | [154] |
| *P. mexicana* Zucc. ex Bunge | antioxidant, medium cytotoxic | whole plant/ methanolic extract | Mexico | [158] |
| *P. sibthorpii* Boiss. (a.n.) | strong antioxidant, free-radical scavenging, antibacterial | aerial parts/ methanolic extract | Iran | [73] |

| | | | | |
|---|---|---|---|---|
| *P. wilhelmsiana* Fisch. ex M.Bieb. (a.n.) | strong antioxidant, antibacterial | aerial parts/ methanolic extract | Iran | [12] |

Table 3: Pharmacological activities of *Pedicularis* species as reported in literature

## Relation among pharmacology, ethnopharmacology and phytochemistry

Tables 2 and 3 clearly showed how fundamental *Pedicularis* species are in the ethnopharmacological and pharmacological fields. Yet, what is very interesting, if not essential, to underline is that many *Pedicularis*s pecies present ethnopharmacological and/or pharmacological uses but no phytochemical analysis has ever been conducted on them, yet. Thus, their employment is strictly related to the traditional uses which are established on the basis of previous experiences. Conversely, for those species presenting also a well established phytochemical profile, the ethnopharmacological and/or pharmacological uses can be obviously explained by their phytochemical compositions. In fact, phytochemical compounds (singularly or as a phytocomplex) are the major responsible for the pharmacological properties associated to every single species and may justify their use in that sense from the phytochemical standpoint.

Several classes of natural compounds have been evidenced within the *Pedicularis* genus and each of them exerts specific pharmacological activities. In particular, alkaloids have antimalarial, antitumor, antibacterial and stimulant activities among the others [152, 159]. Lignans exert mainly antioxidant and anti-inflammatory properties [160]. Tannins are widely known for their astringent and antioxidant effects [161]. Phenylethanoid glycosides are good antioxidant, antibacterial, antiviral, antitumor, neuroprotective and hepatoprotective compounds [104, 162]. Flavonoids display especially antioxidant, anti-inflammatory, anti-mutagenic and anti-carcinogenic properties [163]. Xanthones are mainly insecticidal compounds [164]. Iridoids are widely used as antiviral, anti-inflammatory, hepatoprotective, antimicrobial and antitumoral agents [165]. *Seco*-iridoids are mainly anti-inflammatory and antifungal compounds [166]. Lastly, fatty acids, organic acids, polyols, saccharides, nucleobases and amino acids have several nutraceutical properties.

## Other uses

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Some *Pedicularis* species are better known to have other uses different from ethnopharmacology and pharmacology.

These uses all are reported in the table below (Table 4).

| *Pedicularis* species | Other uses | Organs/ Forms | Area of employment | References |
|---|---|---|---|---|
| *P. atuntsiensis* Bonati (a.n.) | purely ornamental | - | China (Northwestern Yunnan) | [167] |
| *P. capitata* Adams (a.n.) | to make an olive green dye | flowerstalkes | Canada (Inuit people of Kugluktuk, Nunavut regions) | [121] |
| *P. crenularis* H.L. Li (a.n.) | purely ornamental | - | China (Northwestern Yunnan) | [167] |
| *P. cyclorhyncha* H.L. Li (a.n.) | purely ornamental | - | China (Northwestern Yunnan) | [167] |
| *P. dichrocephala* Hand.-Mazz. (a.n.) | purely ornamental | - | China (Northwestern Yunnan) | [167] |
| *P. fastigiata* Franch. (a.n.) | purely ornamental | - | China (Northwestern Yunnan) | [167] |
| *P. filicula* Franch. ex Maxim. (a.n.) | purely ornamental | - | China (Northwestern Yunnan) | [167] |
| *P. flava* Pall. (a.n.) | forage | - | Pakistan | [127] |
| *P. gracilicaulis* H.L. Li (a.n.) | purely ornamental | - | China (Northwestern Yunnan) | [167] |
| *P. groenlandica* Retz. (a.n.) | edible plant | whole plant/ tea | Canada (Inuit people, Kangiqsualujjuaq community) | [168] |
| *P. habachanensis* Bonati (a.n.) | purely ornamental | - | China (Northwestern Yunnan) | [167] |
| *P. humilis* Bonati (a.n.) | purely ornamental | - | China (Northwestern Yunnan) | [167] |
| *P. kariensis* Bonati (a.n.) | purely ornamental | - | China (Northwestern Yunnan) | [167] |
| *P. labradorica* Wirsing (a.n.) | edible plant | roots | Canada (Inuit people, Nain community) | [168] |
| *P. lamioides* Hand.-Mazz. (a.n.) | purely ornamental | - | China (Northwestern Yunnan) | [167] |
| *P. lanpingensis* H.P. Yang (a.n.) | purely ornamental | - | China (Northwestern Yunnan) | [167] |
| *P. lecomtei* Bonati (a.n.) | purely ornamental | - | China (Northwestern Yunnan) | [167] |
| *P. macrorhyncha* H.L. Li (a.n.) | purely ornamental | - | China (Northwestern Yunnan) | [167] |
| *P. maxonii* Bonati(a.n.) | purely ornamental | - | China (Northwestern Yunnan) | [167] |
| *P. mayana* Hand.-Mazz. (a.n.) | purely ornamental | - | China (Northwestern Yunnan) | [167] |
| *P. meteororhyncha* H.L. Li (a.n.) | purely ornamental | - | China (Northwestern Yunnan) | [167] |
| *P. micrantha* H.L. Li (a.n.) | purely ornamental | - | China (Northwestern Yunnan) | [167] |
| *P. mussotii* Franch. (a.n.) | purely ornamental | - | China (Northwestern Yunnan) | [167] |
| *P. obscura* Bonati (a.n.) | purely ornamental | - | China (Northwestern Yunnan) | [167] |

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| | | | | |
|---|---|---|---|---|
| *P. oederi* Vahl (a.n.) | fodder | whole plant/ raw food | Nepal (Central Himalaya) | [136] |
| *P. oligantha* Franch. ex Maxim. (a.n.) | purely ornamental | - | China (Northwestern Yunnan) | [167] |
| *P. orthocoryne* H.L. Li (a.n.) | purely ornamental | - | China (Northwestern Yunnan) | [167] |
| *P. pinetorum* Hand.-Mazz. (a.n.) | purely ornamental | - | China (Northwestern Yunnan) | [167] |
| *P. praeruptorum* Bonati (a.n.) | purely ornamental | - | China (Northwestern Yunnan) | [167] |
| *P. pseudoversicolor* Hand.-Mazz. (a.n.) | purely ornamental | - | China (Northwestern Yunnan) | [167] |
| *P. remotiloba* Hand.-Mazz. (a.n.) | purely ornamental | - | China (Northwestern Yunnan) | [167] |
| *P. salicifolia* Bonati (a.n.) | purely ornamental | - | China (Northwestern Yunnan) | [167] |
| *P. schizocalyx* (Lange) Steininger (a.n.) | edible | flowers/ rawplant | Spain (Cantabria region) | [169] |
| *P. sigmoidea* Franch. ex Maxim. (a.n.) | purely ornamental | - | China (Northwestern Yunnan) | [167] |
| *P. sylvatica* L. (a.n.) | edible | flowers/ rawplant | Spain (Galiciaregion) | [167] |
| *P. tomentosa* H.L. Li (a.n.) | purely ornamental | - | China (Northwestern Yunnan) | [167] |
| *P. tsaii* H.L. Li (a.n.) | purely ornamental | - | China (Northwestern Yunnan) | [167] |
| *P. umbelliformis* H.L. Li (a.n.) | purely ornamental | - | China (Northwestern Yunnan) | [167] |
| *P. weixiensis* H.P. Yang (a.n.) | purely ornamental | - | China (Northwestern Yunnan) | [167] |
| *P. yui* H.L. Li (a.n.) | purely ornamental | - | China (Northwestern Yunnan) | [167] |
| *P. zhongdianensis* H.P. Yang (a.n.) | purely ornamental | - | China (Northwestern Yunnan) | [167] |

Table 4: Other uses *Pedicularis* species as reported in literature

## Curiosities

Some *Pedicularis* species present strange but interesting curiosities concerning themselves.In particular, although *Pedicularis* species are considered to be strong hemiparasitic plant, *P. friderici-augusti* Tomm. (a.n.) *P. furbishiae* S. Watson (a.n.), *P. ishidoyana* Koidz. &Ohwi(u.n.), *P. kashmiriana* Pennell (a.n.), *P. petiolaris* Ten. (a.n.), *P. rainierensis* Pennel& Warren (a.n.), *P. rostratospicata* Crantz (a.n.), *P. siamensis*P.C.Tsoong (u.n.) and *P. thailandica* T.Yamaz. (u.n.) are endangered species in their growth areas [170-176]. Moreover, *P. porrecta* Wall. (u.n.) grows only in arid areas [177] and the name *P. stenantha* Franch. (u.n.)

is often used to identify also *P. stenocorys* Franch. (a.n.) but these are two different species [178].

## Conclusions

The previous lines of this review clearly evidenced and highlighted the importance of the plant species belong to the *Pedicularis* genus from different points of view.

Anyway, as it can be easily deduced, there is still so much to discover and study since the informations about this genus are quite scarce in many specific arguments.

We really hope that this review may be the starting base for future works in this field, renewing the interest in the studies of these interesting species.

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## Conflicts of interest

The authors declare no potential conflict of interests in this work.

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