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Review

Potentilla—A review of its phytochemical and pharmacological profile

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ABSTRACT

The genus *Potentilla* is a member of the family Rosaceae, subfamily Rosoideae, which is mainly distributed in temperate, arctic and Alpine zones of the Northern hemisphere. This genus has been known since ancient times for its curative properties. Extracts of the aerial and/or underground parts have been applied in traditional medicine for the treatment of inflammations, wounds, certain forms of cancer, infections due to bacteria, fungi and viruses, diarrhoea, diabetes mellitus and other ailments. This comprehensive review provides a botanical description of *Potentilla* species and their phytochemical constituents in the aerial and underground parts. *In vitro* and *in vivo* pharmacological studies are reviewed and discussed, focussing on antidiarrhoic, anti-ulcerogenic, anti-neoplastic, antiviral and antimicrobial, antihyperglycemic, anti-inflammatory, spasmolytic, hepatoprotective and antioxidative activities of *Potentilla* species. Most of the pharmacological effects can be explained by the high amount of tannins and to a lesser extent by triterpenes, present in all plant parts. However, future efforts should concentrate more on *in vitro* and *in vivo* studies and also on clinical trials in order to confirm traditional wisdom in the light of a rational phytotherapy. Especially the efficacy of *Potentilla erecta* rhizome extracts in the treatment of colitis ulcerosa and of viral infections should be further substantiated in clinical studies.

Contents

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1. Introduction

Potentilla species have been used for a long time in traditional medicine. In Greek and Latin language *Potentilla* species have been known under the names "Heptaphyllon" or "Pentaphyllon" and "Septifolium" sometimes as "Quinquefolium" (Fuchs, 1543). The Greek physician Pedanius Dioscurides recommended a condensed decoction of the underground parts of *Potentilla erecta* (L.) RAEUSCH. (tormentil) to bathe a purulent facial eczema and to rinse oral cavity ulceration. In the medieval ages the European physicians and botanists H. Bock, L. Fuchs, Paracelsus, Tabernaemontanus, C. Bauhin and others described and depicted *Potentilla* species in their herbal books. Fuchs, for example, mentioned five *Potentilla* species in his "New Kreüterbuch" (1543) comprising *Potentilla alba* L., *Potentilla reptans* L. and *Potentilla neumanniana* RCHB. (underground parts and leaves), *Potentilla anserina* L. (herbal part) and *Potentilla erecta* (underground parts and herbal parts). Extracts were prepared with water, milk, honey and alcoholic solutions and were applied for the treatment of tooth ache, inflammations of the throat, for wound-healing, jaundice, ulcers of the mouth, dysentery and as a homeostatic. In Chinese traditional medicine *Potentilla* extracts have been used to treat diarrhoea, hepatitis, rheuma and scabies and as a remedy for detoxification (Xue et al., 2005, 2006). In Tibetan traditional medicine *Potentilla anserina* root extracts have been applied for the treatment of certain viral infections (Zhao et al., 2008). Similarly the same or other (local) *Potentilla* species have been used in traditional medicine of different cultures in Asia, Europe and Northern America. Examples for the traditional use of *Potentilla* species in different regions of the world are given in Table 1.

Various monographs on *Potentilla* species have been published. Frohne (2004a,b), for example, described herbal parts of *Potentilla anserina* and rhizomes of *Potentilla erecta*. Hiller (1994) concentrated in his comprehensive review article in Hager's Handbuch der Pharmazeutischen Praxis on four *Potentilla* species comprising *Potentilla anserina*, *Potentilla erecta*, *Potentilla aurea* L. and *Potentilla reptans* L. Moreover, positive monographs were released by the German Commission E (1985/1990 and 1988/1990) for *Potentilla anserina* (herbal parts) *and Potentilla erecta* (rhizomes). The therapeutic indications of the herbal parts of *Potentilla anserina* and the rhizomes of *Potentilla erecta* include according to the Commission E simple forms of dysmenorrhoa, the supporting therapy of simple forms of unspecific, acute diarrhoea and also simple forms of mucosal inflammations of throat and mouth. The gynecological indication for silverweed (*Potentilla anserina*) is based on pharmacological studies showing that the herb increases the tonus of the isolated uterus in various animal species (Schulz et al., 1998). Several pharmacopoeias contain monographs on *Potentilla* species, e.g. the European Pharmacopoeia 6, 2007 and the Polish Pharmacopoeia VI, 2002. Tormentillae tinctura (*Potentilla erecta* rhizomes) is official in the Ph. Eur. (drug-to-extract ratio 1:5, solvent: ethanol 70% (v/v), contains a minimum 1.5% (m/m) of tannins, expressed as pyrogallol). Besides, several *Potentilla* species like *Potentilla erecta* (rhizomes), *Potentilla anserina* (aerial parts or the whole plant), *Potentilla aurea* (aerial part), *Potentilla reptans* (aerial part) are used in order to prepare homeopathic medications according to the homeopathic pharmacopoeias like HPUS, HAB and others (Hiller, 1994).

Although *Potentilla* species and their extracts, respectively, have been widely used in different cultures of the Northern hemisphere, little has been known about the phytochemistry and pharmacology of this genus. In 1811, C.H. Pfaff described for the first time the presence of tannins as main ingredients in *Potentilla erecta* rhizomes and concluded that these compounds are responsible for the astringent effects of this drug (Hermann and Enge, 1957). In the 1960s, investigations on the phytochemistry mainly of *Potentilla erecta* rhizomes were performed and published. Starting from the 1980s many more papers dealing with *Potentilla* species which are in part only locally important were published. In parallel pharmacological (*in vitro* and *in vivo*) evaluations of *Potentilla* species and their extracts were put forward especially since the 1980s. Within the last years first clinical studies were performed for *Potentilla erecta* rhizome extracts for the treatment of colitis ulcerosa (Huber et al., 2007) and also for the treatment of virus-induced diarrhoea in children (Subbotina et al., 2003).

However, a large phytochemical study comparing the metabolic pattern of important *Potentilla* species is missing, except for some ellagitannins from four *Potentilla* species (Okuda et al., 1992), for some flavonoids and some organic acids for a large number of species (Bate-Smith, 1961). Therefore, the results of the studies cannot be easily transferred from one *Potentilla* species to another. In addition the extracts used in the studies from one *Potentilla* species are generally obtained by different extraction methods which are sometimes insufficiently described. The aim of this contribution is to review the literature covering botanical, phytochemical and pharmacological aspects of *Potentilla* species and to discuss them.

2. Botanical description

Potentilla LINNAEUS (L.) (syn.: *Dasiphora* RAFINESQUE or *Pentaphylloides* DUHAMEL) is one of a hundred genera in the rose family (Rosaceae), subfamily Rosoideae, tribe Potentilleae (Chaoluan et al., 2003; USDA-ARS, 2008). The genus name *Potentilla* comes from the latin diminutive of *potens* meaning "powerful" in reference to the medicinal properties of some species. The genus *Potentilla* includes about 500 species of perennial, rarely biennial, and annual herbs and small shrubs with rhizomes. In their natural habitat they commonly occur in temperate, arctic and Alpine zones of the Northern hemisphere. A few species are also found in high mountain regions of the tropics and in South America. Species diversity is highest in Northern Eurasia (Fig. 1). Many species are even grown for their decorative values.

Table 1
Traditional use of *Potentilla* species in different regions of the world.

Regions	Plant species	Part used	Traditional use	References
Europe, e.g. central Europe, Italy, Sweden, Serbia and Montenegro, Russia, Bulgaria, Turkey	*Potentilla erecta*	Roots	Inflammations, treatment of wounds, bleeding, dysentery, diarrhoea, inflammatory bowel disease, bacterial, fungal and viral infections, certain forms of cancer, antiseptic for the mouth and throat	Enge and Hermann (1957) Tunón et al. (1995) Ivancheva and Stantcheva (2000) Langmead et al. (2002) Subbotina et al. (2003) Spiridonov et al. (2005) Latté (2006) Palombo (2006) Fuchs (1543)
	Potentilla fruticosa	Aerial parts	Viral infections, impairment of immune system	Evstropov et al. (2002)
	Potentilla anserina	Aerial parts	Acute, nonspecific diarrhoea with mild discomforts, mild inflammation of the oral and pharyngeal mucosa, tooth ache	Frohne (2004a) Fuchs (1543)
	Potentilla speciosa	Aerial parts, roots	Inflammations, anti-ulcer activity	Kovzačević and Ristić (2007)
	Potentilla recta	Aerial parts	Microbial infections	Tosun et al. (2006)
	Potentilla reptans	Aerial parts, leaves	Tooth ache, ulcers, inflammations of the throat	Fuchs (1543) De Natale and Pollio (2007)
Asia, e.g. China, Korea, Japan, Nepal, India	*Potentilla fulgens*	Roots	Stomach disorders, certain forms of cancer, diabetes mellitus	Manandhar, 1995 Syiem et al. (2002) Syiem et al. (2003) Rosangkima and Prasad (2004) Chhetri et al. (2005)
	Potentilla chinensis	Aerial parts	Certain forms of cancer	Liu et al. (2006)
	Potentilla multicaulis	Roots		Li et al. (2007)
	Potentilla atrosanguinea	Roots	Wound-healing	Sharma et al. (2004)
	Potentilla kleiniana	Aerial parts	Diarrhoea, bleeding, influenza, cough, parotitis, lymphadenitis, hepatitis, scare, numbness of limbs, dysmenorrhea, ulcer	Okuda et al. (1984) Long and Li (2004)
	Potentilla peduncularis	Leaves, buds	Fever, influenza, cough	Manandhar (1995)
	Potentilla freyniana	Roots	Viral infections	Chen et al. (2005)
	Potentilla discolor	Aerial parts, roots	Diarrhoea, hemorrhage, diabetes mellitus	Jang et al. (2007)
	Potentilla multifida	Aerial parts, roots	Hepatitis, enterobiasis, functional uterine hemorrhage, type 2 diabetes	Xue et al. (2005)
America, e.g. Canada	*Potentilla arguta*	Roots	Viral infections	McCutcheon et al. (1995)
	Potentilla simplex	Leaves, stems	Fungal infections	Webster et al. (2008)

The genus *Potentilla* L. representatives develop fully erect, rising or trailing stalks with pinnate and palmate compound leaves that can be attached to short petiols, or directly to the main stem, and their leaves create rosettes of basal leaves. Flowers are mounted individually or are gathered in cyme, and are usually bisexual. Perigons consist of calyx, corolla and an additional epicalyx, the leaves of which originate from converted bracts, occurring alternately with the calyx. Petals are usually yellow, rarely white or are of a purplish red. The flowers have five petals, sometimes four (*Potentilla erecta*). The *Potentilla* receptacle is slightly raised and covered with numerous free styles. Ten to 30 stamens occur and its fruits take the form of small nuts (Ball et al., 1968; Chaoluan et al., 2003).

Fig. 1. Main distribution areas of *Potentilla* species.

Table 2
Constituents isolated from the roots and rhizomes of *Potentilla* species.

Compounds	*Potentilla* species	References
• Flavonoids		
Kaempferol	*Potentilla erecta*	Selenina et al. (1973)
Cyanidinglucoside		
Leucoanthocyanidin	*Potentilla erecta*	Seidl and Bednarska (1969)
• Hydrolysable tannins and related compounds		
Monomers		
Pentadigalloylglucose	*Potentilla erecta*	Schenck et al. (1957)
2,3-Hexahydroxydiphenoic acid β-D-glucoside		Lund (1986)
Casuarictin	*Potentilla discolor*	Feng et al. (1996)
Tellimagrandin II (eugenin)		
Pedunculagin	*Potentilla erecta*	Lund (1986)
	Potentilla discolor	Feng et al. (1996)
Dimers		
Agrimoniin	*Potentilla erecta*	Lund and Rimpler (1985)
	Potentilla discolor	Feng et al. (1996)
Laevigatin B	*Potentilla erecta*	Geiger and Rimpler (1990)
Laevigatin F (tormentillin)		Geiger et al. (1994)
Related compounds		
Ellagic acid	*Potentilla candidans*	Terashima et al. (1990)
3,3′,4-Tri-*O*-methylellagic acid 4′-sulfate Potassium salt		
4-0-Methylellagic acid 3-0-α-L-rhamnoside	*Potentilla discolor*	Jang et al. (2007)
• Condensed tannins (proanthocyanidins) and their precursors		
(+)-Catechin	*Potentilla erecta*,	Vennat et al. (1992)
	Potentilla anserina	Kombal and Glasl (1995)
	Potentilla alba	Gritsenko and Smik (1977)
	Potentilla viscosa	Zhang et al. (1988)
(+)-Catechin 3-*O*-glucoside	*Potentilla viscosa*	Zhang et al. (1988)
(−)-Epicatechin	*Potentilla erecta*	Vennat et al. (1992)
	Potentilla alba	Oszmiański et al. (2007)
(+)-Gallocatechin	*Potentilla erecta*,	Vennat et al. (1992)
	Potentilla chrysantha TREV.	Omurkamzinova and Erzhanova (1986)
	Potentilla anserina	Kombal and Glasl (1995)
(−)-Epigallocatechin	*Potentilla erecta*	Selenina et al. (1973)
(−)-Epigallocatechingallate		
Dimers		
[6′,6]-All-trans-bi-(+)-catechin	*Potentilla erecta*	Ahn (1974)
potentillanin	*Potentilla viscosa*	Zhang et al. (1988)
[4,8]-All-trans-bi-(+)-catechin (procyanidin B_3)	*Potentilla erecta*	Schleep et al. (1986)
	Potentilla viscosa	Zhang et al. (1988)
[4,6]-All-trans-bi-(+)-catechin (procyanidin B_6)	*Potentilla erecta*	Schleep et al. (1986)
[4,8]-All-trans-bi-(+)-catechin 3′-*O*-glucoside	*Potentilla viscosa*	Zhang et al. (1988)
[4,8]-2,3-trans-3,4-cis-bi-(+)-catechin	*Potentilla erecta*	Schleep et al. (1986)
Procyanidin B_1 (traces)	*Potentilla erecta*	Vennat et al. (1992)
Procyanidin B_2 (traces)		
Procyanidin B_5 (traces)		
Trimers		
(+)-Catechin-[6′,8]-(+)-catechin-[4,8]-(+)-catechin	*Potentilla erecta*	Ahn (1974)
(+)-Catechin-[4,8]-(+)-catechin-[4,8]-(+)-catechin		
Afzelechin-[4,8]-all-trans-bi-(+)-catechin	*Potentilla viscosa*	Zhang et al. (1988)
• Triterpenoids		
Ursolic acid	*Potentilla anserina*	Li et al. (2003)
Pomolic acid		
3-Epi-pomolic acid 28-*O*-β-D-glucoside	*Potentilla erecta*	Bilia et al. (1992)
Tormentic acid	*Potentilla erecta*	Potier et al. (1966)
	Potentilla anserina	Li et al. (2003)
Arjunetin	*Potentilla erecta*	Stachurski et al. (1995)
Euscaphic acid	*Potentilla anserina*	Li et al. (2003)
Euscaphic acid 28-*O*-β-D-glucoside (kaji-ichogoside F_1)	*Potentilla erecta*	Stachurski et al. (1995)
	Potentilla anserina	Li et al. (2003)
Chinovic acid	*Potentilla erecta*	Lund and Rimpler (1985)
	Potentilla erecta	Stachurski et al. (1995)
Tormentoside (rosamultin)	*Potentilla anserina*	Li et al. (2003)
	Potentilla discolor	Jang et al. (2007)
19-Hydroxy-2,3-secours-12-ene-2,3,28-trioic acid 3-methyl ester	*Potentilla multicaulis*	Li et al. (2007)
19-Hydroxy-1-oxo-2-nor-2,3-secours-12-ene-3,28-dioic acid		
(3β,18α,19α)-3,28-Dihydroxy-20,28-epoxyursan-24-oic acid		
3β,19α-Dihydroxyurs-12-en-28-oic acid β-D-glucopyranosyl ester	*Potentilla erecta*	Bilia et al. (1994)
2α,3β-Dihydroxyurs-12-en-28-oic acid β-D-glucopyranosyl ester		
3β,19α-Dihydroxyolean-12-en-28-oic acid β-D-glucopyranosyl ester		
2α,3β,19α-Trihydroxyurs-12-en-28-oic acid β-D-glucopyranosyl ester	*Potentilla anserina*	Zhao et al. (2008)

Table 2 (*Continued*)

Compounds	*Potentilla* species	References
2α,3β,19α-Trihydroxyurs-28-oic acid β-D-galactopyranosyl ester (anserinoside) 2α,3β,19α-Trihydroxy-oleanolic acid-28-β-D-glucopyranosyl ester (24-deoxy-sericoside) 2-Carbonyl-3β,19α-dihydroxyurs-28-β-D-glucopyranoside ester (2-oxo-pomolic acid β-D-glucopyranoside ester)	*Potentilla anserina*	Hong et al. (2006)
• Organic acids and phenol carboxylic acids		
3,4-Dihydroxy-benzoic acid[a] Gallic acid[a] *p*-Coumaric acid[a]	*Potentilla erecta*	Grujic-Vasic et al. (1982)
p-Hydroxy-benzoic acid Salicylic acid Gentisic acid Syringic acid β-Resorcylic acid	*Potentilla erecta*	Geszprych et al. (2003)
Caffeic acid[a]	*Potentilla erecta*	Grujic-Vasic et al. (1982)
• Others		
β-Sitosterol	*Potentilla anserina* *Potentilla palustris*	Li et al. (2003) Sokołowska-Woźniak et al. (2002)
Stigmasterol	*Potentilla palustris*	Sokołowska-Woźniak et al. (2002)
Daucosterol	*Potentilla anserina*	Li et al. (2003)
Fructose	*Potentilla erecta*	Schenck et al. (1957)
Amino acids	*Potentilla fruticosa* *Potentilla parviflora* FISH. ex LEHM.	Nikolaeva (2007)
Fatty acids	*Potentilla erecta*	Kas'yanov et al. (1977)

[a] After hydrolysis with acid or base.

Wolf (1908) listed 302 species and divided them into two sections – *Trichocarpae* and *Gymnocarpae* – and many subsections, series and tribes or groups of species (Wolf, 1908; Guillén et al., 2005). The genus *Potentilla* is well known for its difficulties in identifying species and the frequent synonymies (Nicolè et al., 2007). A common phenomenon within this genus is interspecies hybridization and apomixis. This has resulted in a great morphological variability of species. Hybridization has been mainly described in some taxa of subgenus *Potentilla* (Müntzing and Müntzing, 1941; Guillén et al., 2005). Members of the genus *Potentilla* represent an extensive polyploidal group with its chromosome number (*n*) being always a multiple of seven (Ball et al., 1968; Goswami and Matfield, 1975; Eriksson et al., 1998).

3. Chemical constituents of *Potentilla* species

Tannins have been known to be important constituents of *Potentilla* species and their extracts, respectively, and the cause for the astringent effects. Therefore thorough phytochemical studies on *Potentilla* species starting especially in the 1960s were primarily focussed on tannins (Hegnauer, 1990). More recent studies concentrated on triterpenoid structures. In former times European species like *Potentilla erecta*, *Potentilla anserina* and *Potentilla reptans* were investigated, but within the last years several more *Potentilla* species coming from other parts of the world, e.g. from Asia and Russia (*Potentilla chinensis* SER., *Potentilla discolor* BUNGE, *Potentilla fruticosa* L., *Potentilla palustris* (L.) SCOP.), were considered. In general most phytochemical studies have been performed with the aerial parts of *Potentilla* species. However, *Potentilla erecta* is still the *Potentilla* species for which the highest number of constituents have been described (i.e. for the aerial and the underground parts altogether 68 structures), followed by *Potentilla anserina* (aerial and the underground parts altogether 37 compounds).

3.1. Constituents of the roots and rhizomes

A total of 67 compounds present at least in 1 of the 11 investigated *Potentilla* species are known, belonging to only few groups of natural compounds (Table 2). For *Potentilla erecta* altogether 43 compounds have been identified and structurally elucidated. Due to the high amount of 17–22% of tannins in the rhizomes of *Potentilla erecta* (i.e. 15–20% condensed tannins, ca. 3.5% hydrolysable tannins; Hiller, 1994), this group of natural compounds has been in the focus of many phytochemical studies.

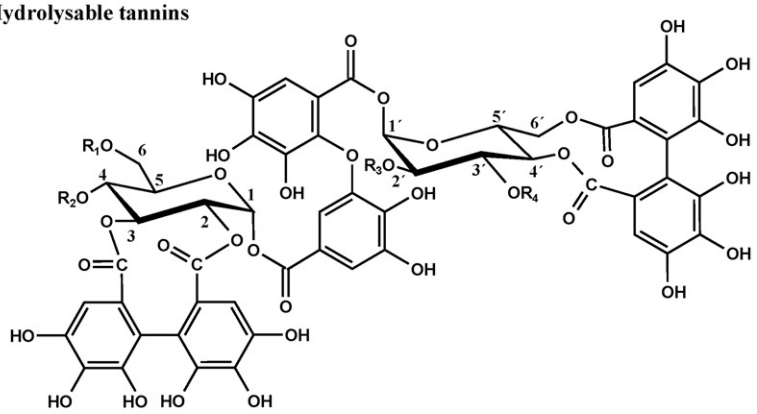
The condensed tannins of *Potentilla erecta* consist of dimeric and trimeric type B proanthocyanidins in which the catechin units are connected via 4,8-, 4,6-, 6,6′- or 6′,8-bonds (Fig. 2). The [4,8]-2,3-*trans*-3,4-*cis*-bi-(+)-catechin is a rare example of a *cis*-configurated dimeric proanthocyanidin (Schleep et al., 1986), found in *Potentilla erecta*. Several precursors for condensed tannins were identified for this plant source including (+)-catechin, (−)-epicatechin, (+)-gallocatechin and (−)-epigallocatechin. A few more condensed tannins have been reported to be present in *Potentilla viscosa* DONN ex LEHM. (Table 2).

Hydrolysable tannins have only been isolated from two *Potentilla* species, *Potentilla erecta* and *Potentilla discolor*. Apart from pentadigalloylglucose, four monomeric and three dimeric ellagitannins were isolated with agrimoniin being the most complex structure with altogether four hexahydroxydiphenoyl residues in one molecule. In addition, the degradation product of ellagitannins, ellagic acid and two of its derivatives, were found in the phytochemical analysis of *Potentilla candicans* HUMB. et BONPL. and *Potentilla discolor*.

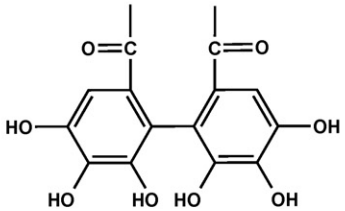
Several more phytochemical studies have concentrated on the isolation of triterpenoids. These compounds are generally based on an ursan or an olean skeleton and have been isolated from four *Potentilla* species, comprising *Potentilla erecta*, and recently also *Potentilla anserina*, *Potentilla discolor* and *Potentilla multicaulis* BUNGE. In these plant sources both aglycones and their 28-*O*-β-D-glycosyl esters have been found. A characteristic constituent is tormentoside (rosamultin), which has originally been isolated from *Potentilla erecta*, but has recently also been detected in *Potentilla anserina* and *Potentilla discolor*. Some typical terpenoid structures are depicted in Fig. 2.

A very limited number of flavonoids have only been reported for *Potentilla erecta*. Further ingredients include a series of organic acids and phenol carboxylic acids which were exclusively described for *Potentilla erecta*. Finally, sterols, a sugar, amino acids and fatty acids were detected in a few *Potentilla* species.

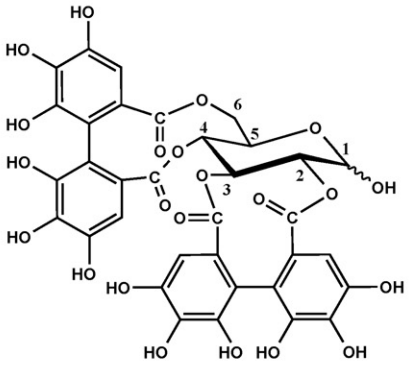
Hydrolysable tannins



	R_1	R_2	R_3	R_4
laevigatin B	H	H	HHDP	
laevigatin F	HHDP		H	H
agrimoniin	HHDP		HHDP	

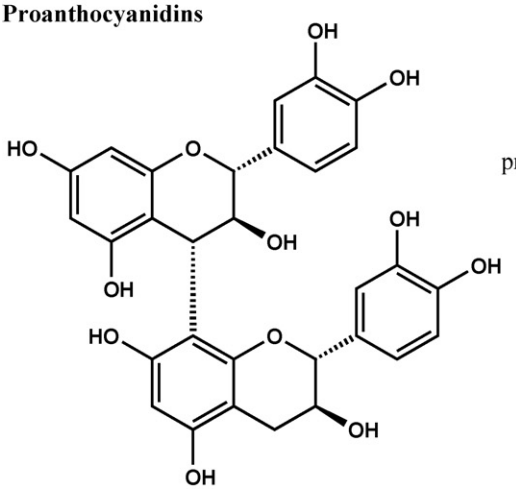


HHDP



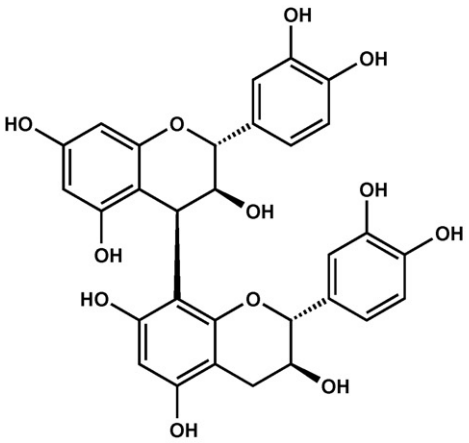
pedunculagin

Proanthocyanidins

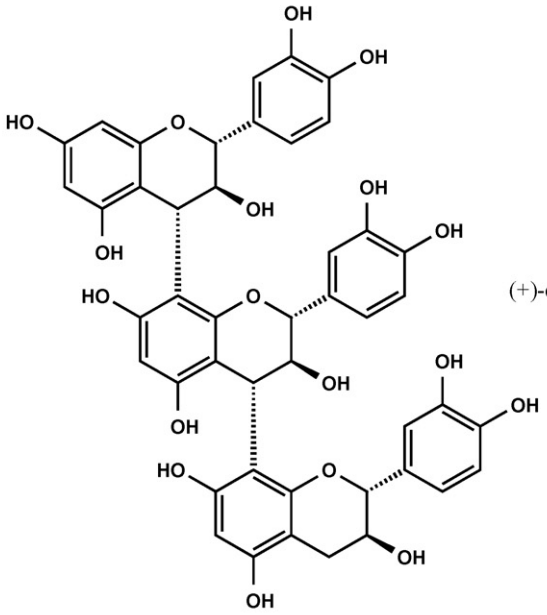


procyanidin B_3 = (+)-Catechin-[4,8]-(+)-catechin

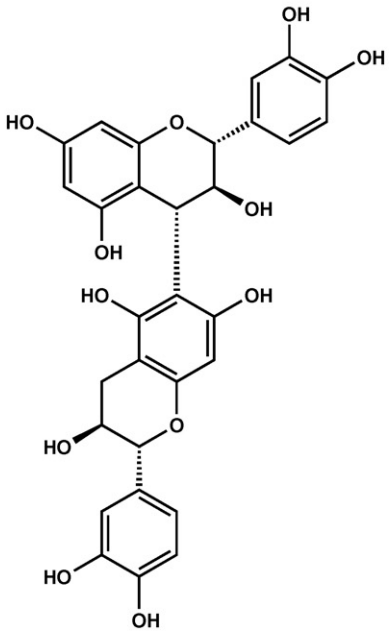
Fig. 2. Structures of constituents from *Potentilla* species.



[4,8]-2,3-trans-3,4-cis-bi-(+)-catechin



(+)-catechin-[4,8]-(+)-catechin-[4,8]-(+)-catechin



procyanidin B_6 = (+)-catechin-[4,6]-(+)-catechin

Fig. 2. (*Continued*)

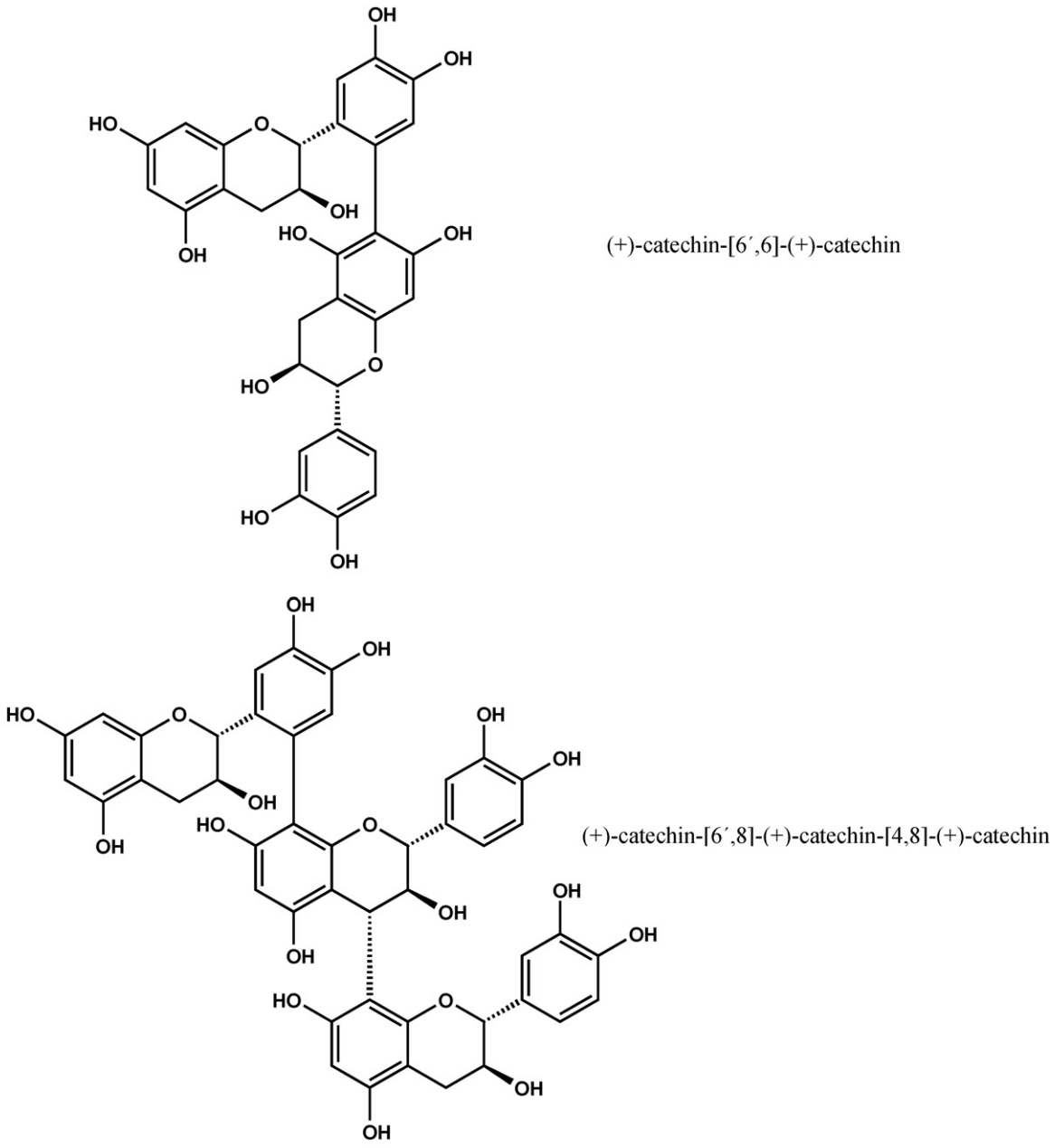


Fig. 2. (*Continued*)

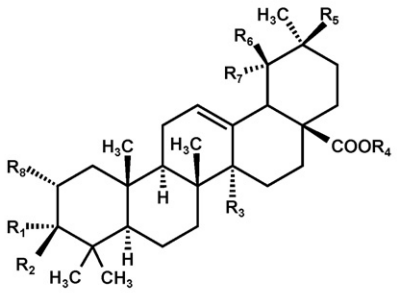
3.2. Constituents of the aerial parts

Altogether 134 compounds (Table 3) have been structurally identified. Compared to the underground parts the studies of the aerial parts include a large number of *Potentilla* species (far more than 20 species). In respect to the number of compounds elucidated important *Potentilla* species are *Potentilla anserina* (26 compounds) and *Potentilla erecta* (25 compounds), followed by *Potentilla fruticosa* (22 compounds), *Potentilla chinensis* (19 compounds), *Potentilla discolor* (14 compounds), *Potentilla palustris* (12 compounds) and *Potentilla reptans* (8 compounds).

Predominant in aerial parts of plants are generally flavonoids which were found in cinquefoils (more than 20 species) in a large number (57 compounds) and in a wide structural variety. A common feature is the mono-, di- and also tri-hydroxy substitution of ring B in the instances isolated. In 15 flavonoid aglycones one or more hydroxy groups in positions 7, 3′, 4′ and/or 5′ are methylated. Characteristic is also the presence of a large number of flavonoid *O*-glycosides (28 compounds) and *O*-glucuronides (6 compounds), again with a large structural variety of the aglycone.

5–10% of the constituents in *Potentilla anserina* are tannins (Hiller, 1994), especially hydrolysable tannins. Interestingly, no distinct hydrolysable tannin has ever been isolated from this plant, in contrast to several other *Potentilla* species. Altogether four monomeric hydrolysable tannins (potentillin, pedunculagin, tellimagrandin I, casuarictin) were detected at least in one species. Only one dimer, agrimoniin, has been described for *Potentilla kleiniana* WIGHT et ARNOTT (Okuda et al., 1984). Several degradation products of hydrolysable tannins, namely ellagic acid and six of its derivatives and methyl brevifolincarboxylate, were isolated at least from one *Potentilla* species, indicating the presence of ellagitannins in several more species. Interestingly, no condensed

Triterpenoids



	R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8
ursolic acid	H	OH	CH_3	H	H	CH_3	H	H
pomolic acid	H	OH	CH_3	H	H	CH_3	OH	H
3-epi-pomolic acid 28-O-β-D-glucopyranosyl ester	OH	H	CH_3	β-D-glc	H	CH_3	OH	H
tormentic acid	H	OH	CH_3	H	H	CH_3	OH	OH
tormentoside	H	OH	CH_3	β-D-glc	H	CH_3	OH	OH
arjunetin	H	OH	CH_3	β-D-glc	CH_3	H	OH	OH
euscaphic acid	OH	H	CH_3	H	H	CH_3	OH	OH
euscaphic acid 28-O-β-D-glucopyranosyl ester (kaji-ichigosid F_1)	OH	H	CH_3	β-D-glc	H	CH_3	OH	OH
chinovic acid	H	OH	COOH	H	H	CH_3	H	H

Fig. 2. (*Continued*).

tannins were elucidated, whereas their precursors, e.g. (+)-catechin, (+)-gallocatechin, (−)-epigallocatechin, were detected mainly in *Potentilla erecta*.

A high number of triperpenoid compounds (27 structures) with similar or even the same structures as in the underground parts were described within the last few years. A common feature of these structures is again the ursan or olean skeleton. Most triterpenoids occur as a free form, only four 28-*O*-β-D-glycosides have been elucidated.

Furthermore several other constituents were described for *Potentilla* species, comprising coumarins (four compounds from *Potentilla erecta*, *Potentilla anserina* and *Potentilla argentea* L.), organic acids and phenolic carboxylic acids (14 compounds from several species), sterols, megastigmanes (from *Potentilla multifida* L.), essential oils (from *Potentilla palustris*, *Potentilla speciosa* WILLD.) and a pectin (coumaruman from *Potentilla palustris*) along with polyprenols with 19–45 units (various species) and 2-pyrone-4,6-dicarboxylic acid (various *Potentilla* species).

4. Pharmacological profile (*in vivo*, *in vitro*, clinical studies)

The scientific world's particular interest in the genus *Potentilla* and their curative properties originated from the realm of traditional medicine. Ethnic medicine has come to be an irreplaceable source of knowledge of medicinal plants and their curative qualities, as well as creating clues for scientific research, which usually confirms the legitimacy of their usage (Fabricant and Farnsworth, 2001). An overview on the main ethnopharmacological uses of *Potentilla* species and the current status of modern pharmacological evaluations are summarized in Table 4.

4.1. Anti-ulcerogenic (colitis ulcerosa) activity

A variety of herbal products have been reported to possess anti-ulcer activity, but the documented literature has focussed primarily on pharmacological effects in animals. It should be noted that especially polyphenolics such as tannins are of particular therapeutic importance as gastroprotective agents (Borrelli and Izzo, 2000).

4.1.1. In vitro experiment

Langmead et al. (2002) investigated the antioxidant effect of a tormentil (*Potentilla erecta*) rhizome extract in cell-free-oxidant-generating systems (luminol-enhanced chemiluminescence in a xanthine/xanthine-oxidase system and a fluorimetric phycoerythrin degradation assay) and inflamed human colorectal biopsies (chemiluminescence test). Tormentil scavenged superoxide and peroxyl radicals dose-dependently. Oxygen radical release from biopsies was reduced after incubation with a tormentil extract. This finding is of significance because reactive oxygen metabolites are present in excess in inflamed colonic mucosa and might play a pathogenic role in inflammatory bowel disease (colitis ulcerosa).

4.1.2. In vivo experiment

Inhabitants of the Turkish Kayseri province use *Potentilla reptans* leaves in congenital disease therapy and for treatment of heartburn and accompanying abdominal pain symptoms. Recent pharmaco-

Table 3
Constituents isolated from the aerial parts of *Potentilla* species.

Compounds	*Potentilla* species	References
• Flavonoids		
Flavonoid aglycones		
Apigenin	*Potentilla multifida; Potentilla chinensis; Potentilla viscosa*[a]	Xue et al. (2005) Shen et al. (2006) Xue et al. (2007) Gao et al. (2007) Wollenweber and Dörr (2008)
Luteolin	*Potentilla multifida; Potentilla viscosa*[a]	Xue et al. (2005) Wollenweber and Dörr (2008)
Kaempferol	*Potentilla erecta*; *Potentilla palustris*; *Potentilla argentea*; *Potentilla discolor; Potentilla recta*; *Potentilla reptans*; *Potentilla aurea* L.; *Potentilla fruticosa; Potentilla salesoviana* L., *Potentilla palustris; Potentilla bifurca* L.; *Potentilla biflora* WILLD. ex SCHLTDL.; *Potentilla multifida; Potentilla viscosa*[a] and more than 20 other *Potentilla* species[b]	Bate-Smith (1961) Chaika and Minaeva (1973) Fedoseeva (1979) Liu et al. (1984) Xue et al. (2005) Tomczyk (2006) Wollenweber and Dörr (2008)
Quercetin	*Potentilla erecta*; *Potentilla palustris*; *Potentilla areata* L.; *Potentilla argentea*; *Potentilla recta*; *Potentilla reptans*; *Potentilla discolor; Potentilla aurea; Potentilla alba*[c]*; Potentilla multifida; Potentilla chinensis; Potentilla viscosa*[a] and more than 20 other *Potentilla* species[b]	Bate-Smith (1961) Chaika and Minaeva (1973) Liu et al. (1984) Klyshev and Pershukova (1989) Xue et al. (2005) Tomczyk (2006) Świąder et al. (2006) Xue et al. (2007) Gao et al. (2007) Wollenweber and Dörr (2008)
Myricetin	*Potentilla anserina*[b]	Bate-Smith (1961) Chaika and Minaeva (1973)
Naringenin	*Potentilla discolor*	Liu et al. (1984)
cyanidin	*Potentilla erecta*; *Potentilla argentea*; *Potentilla aurea* and more than 20 other *Potentilla* species[b]	Bate-Smith (1961)
Leucodelphinidin	*Potentilla anserina*[b]	Bate-Smith (1961)
Apigenin-7-methyl ether (genkwanin) Apigenin-7,4′-dimethyl ether Luteolin-7-methyl ether Luteolin-7,3′-dimethyl ether (velutin) Luteolin-7,3′,4′-trimethyl ether Tricetin-3′,5′-dimethyl ether (tricin) Tricetin-7,3′,4′-trimethyl ether (lethedocin) 6-Methoxy-luteolin (nepetin) Kaempferol-7-methyl ether (rhamnocitrin) Quercetin-7,3′-dimethyl ether (rhamnazin) Naringenin-7-methyl ether (sankuranetin) Eriodictyol Eriod-7-methyl ether	*Potentilla viscosa*[a]	Wollenweber and Dörr (2008)
Quercetin-7,3′,4′-trimethyl ether	*Potentilla fruticosa*	Ganenko et al. (1991)
Luteolin-3′-methyl ether (chrysoeriol)	*Potentilla multifida; Potentilla viscosa*[a]	Xue et al. (2005) Wollenweber and Dörr (2008)
Flavonoid O-glycosides and O-glucuronides		
Apigenin-7-*O*-β-D-glucuronide Luteolin-7-*O*-β-D-glucuronide	*Potentilla multifida*	Xue et al. (2007)
Apigenin-7-*O*-(*p*-coumaroyl)- O-β-D-glucoside (terniflorin)	*Potentilla fruticosa*	Ganenko et al. (1988)
Kaempferol-3-*O*-β-D-glucoside (astragalin)	*Potentilla anserina; Potentilla areata*	Klyshev and Pershukova (1989) Kombal and Glasl (1995)
Kaempferol-3-*O*-β-D-(6″-*O*-(*E*)-p-coumaroyl)-glucoside (tiliroside)	*Potentilla anserina*; *Potentilla argentea; Potentilla fruticosa*[d]; *Potentilla discolor*	Kombal and Glasl (1995) Miliauskas et al. (2004) Tomczyk (2006) Xue et al. (2006)
Kaempferol-3-*O*-β-D-rutinoside	*Potentilla fruticosa*[d]	Miliauskas et al. (2004)
Kaempferol-3-*O*-rutinoside-7-*O*-glucoside Kaempferol-3-*O*-sophoroside-7-*O*-glucoside	*Potentilla* spp.	Harborne and Baxter (1999)
8-Methoxykaempferol-3-*O*-β-D-sophoroside (herbacetin 8-metyl ether-3-*O*-β-D-sophoroside)	*Potentilla anserina*[d]	Kombal and Glasl (1995)
Quercetin-3-*O*-β-D-glucoside (isoquercitrin)	*Potentilla anserina*; *Potentilla areata; Potentilla fragarioides; Potentilla fruticosa*[d]; *Potentilla multifida*	Kombal and Glasl (1995) Klyshev and Pershukova (1989) Choi et al. (1998) Miliauskas et al. (2004) Xue et al. (2007)

Table 3 (*Continued*)

Compounds	*Potentilla* species	References
Quercetin-3-*O*-β-D-galactoside (hyperoside)	*Potentilla fruticosa*[d]; *Potentilla multifida*	Ganenko et al. (1988) Miliauskas et al. (2004) Xue et al. (2005, 2007)
Quercetin-6″-gallate-3-*O*-β-D-galactoside	*Potentilla fruticosa*	Ganenko et al. (1991)
Quercetin-3-*O*-β-D-xyloside	*Potentilla anserina*	Kombal and Glasl (1995)
Quercetin-3-*O*-α-L-rhamnoside (quercitrin)	*Potentilla anserina; Potentilla fruticosa; Potentilla fragarioides*	Fedoseeva (1979) Kombal and Glasl (1995) Choi et al. (1998)
Quercetin-3-*O*-α-L-arabinofuranoside	*Potentilla areata; Potentilla fruticosa*[d]; *Potentilla discolor*	Klyshev and Pershukova (1989) Miliauskas et al. (2004) Xue et al. (2006)
Quercetin-3-*O*-α-L-arabinopyranoside	*Potentilla fruticosa*	Ganenko et al. (1988)
Quercetin-3′-glucoside	*Potentilla erecta*; *Potentilla reptans*	Harborne and Nash (1984)
Quercetin-3-*O*-β-D-sambubioside	*Potentilla anserina*	Kombal and Glasl (1995)
Quercetin-3-*O*-β-D-rutinoside (rutin)	*Potentilla fruticosa*[d]; *Potentilla argentea*	Miliauskas et al. (2004) Tomczyk (2006)
Quercetin-3-*O*-β-D-glucuronide	*Potentilla anserina*; *Potentilla fruticosa*[d]	Harborne and Nash (1984) Kombal and Glasl (1995) Miliauskas et al. (2004)
Quercetin-3,7-diglucuronide	*Potentilla reptans*	Harborne (1965) Harborne and Baxter (1999)
Quercetin-3-*O*-β-D-glucosyl- β-D-xyloside	*Potentilla fragarioides*	Choi et al. (1998)
Myricetin-3-*O*-α-L-rhamnoside	*Potentilla anserina*	Kombal and Glasl (1995)
Myricetin-3-*O*-β-D-glucuronide		
Naringenin-7-*O*-β-D-glucoside	*Potentilla* spp.	Harborne and Nash (1984)
Cyanidin-3-*O*-β-D-glucoside	*Potentilla nepalensis; Potentilla atrosanguinea*	
Cyanidin-3-*O*-β-D-rutinoside		
Rhamnetin-3-*O*-β-D-glucoside	*Potentilla fruticosa*[d]	Miliauskas et al. (2004)
Rhamnetin-3-*O*-β-D-galactoside		
Isorhamnetin-3-*O*-β-D-glycoside-7-*O*-α-L-rhamnoside (antosid)	*Potentilla erecta*	Goncharov et al. (1989)
Isorhamnetin-3-*O*-β-D-rutinoside (narcissin)		
Isorhamnetin-3-*O*-β-D-glucuronide	*Potentilla anserina*	Kombal and Glasl (1995)
2′,4′,6′,4-Tetrahydroxychalkon-2′-*O*- β-D-glucoside (isosalipurposide)	*Potentilla erecta*; *Potentilla reptans*	Harborne and Nash (1984)
Acacetin-7-*O*-α-L-rhamnosyl-β-D-glucoside	*Potentilla multifida*	Xue et al. (2005)
• Hydrolysable tannins and related compounds		
Monomers		
Potentillin	*Potentilla kleiniana*[e]	Okuda et al. (1982) Okuda et al. (1984)
Pedunculagin	*Potentilla anemonefolia* LEHM.[c]; *Potentilla cryptotaeniae* MAXIM.; *Potentilla freyniana*	Okuda et al. (1992)
Tellimagrandin I	*Potentilla anemonefolia*[c]	Okuda et al. (1992)
Casuarictin	*Potentilla centrigrana* MAXIM.[c]	Okuda et al. (1992)
Dimers		
Agrimoniin	*Potentilla kleiniana*[e]	Okuda et al. (1982) Okuda et al. (1984)
Related compounds		
Ellagic acid	*Potentilla erecta; Potentilla anserina; Potentilla fruticosa; Potentilla palustris; Potentilla argentea; Potentilla recta; Potentilla reptans* and more than 20 other *Potentilla* species[b]	Bate-Smith (1961) Krzaczek (1984)
Ellagic acid-3,3′-dimethyl ether	*Potentilla multifida; Potentilla discolor*	Xue et al. (2005), Xue et al. (2006)
Ellagic acid-3,3′,4-trimethyl ether		
Ellagic acid-3,3′-di-*O*-methyl ether-4-*O*-β-D-glucoside		
Ellagic acid-3,3′-di-*O*-methyl ether-4-*O*-β-D-xyloside	*Potentilla multifida; Potentilla argentea*	Xue et al. (2005) Tomczyk (2006)
Ellagic acid-3-*O*-methyl ether-4′-*O*-α-D-rhamnoside	*Potentilla discolor*	Xue et al. (2006)
Ellagic acid-3,3′4-tri-*O*-methyl ether-4′-*O*-β-D-glucoside		
Methyl brevifolincarboxylate	*Potentilla argentea*	Tomczyk (2006)
• Precursors of condensed tannins		
(+)-Catechin	*Potentilla erecta*; *Potentilla fruticosa*[d], *Potentilla fragarioides*	Goncharov et al. (1989a) Kombal and Glasl (1995) Choi et al. (1998) Miliauskas et al. (2004)
(+)-Gallocatechin	*Potentilla erecta*	Goncharov et al. (1989a) Kombal and Glasl (1995)
(−)-Epigallocatechin	*Potentilla erecta*	Goncharov et al. (1989a)
(−)-Epigallocatechingallate	*Potentilla erecta*	Goncharov et al. (1989a)

Table 3 (*Continued*)

Compounds	*Potentilla* species	References
• Triterpenoids		
Ursolic acid	*Potentilla chinensis*	Xue et al. (2005a)
Corosolic acid	*Potentilla discolor*	Liu et al. (2006) Jang et al. (2006)
Epiursolic acid	*Potentilla fruticosa*	Ganenko and Semenov (1989)
2α-Hydroxyursolic acid	*Potentilla fruticosa; Potentilla chinensis*	Ganenko and Semenov (1989) Shen et al. (2006)
23-Hydroxyursolic acid	*Potentilla discolor*	Jang et al. (2006)
2α,3α-Dihydroxyurs-12-en-28-oic acid	*Potentilla chinensis*	Liu et al. (2006)
2α,3β-Dihydroxyurs-12-en-28-oic acid	*Potentilla discolor*	Xue et al. (2005a)
2β,3β,19α-Trihydroxyurs-12-en-28-oic acid	*Potentilla chinensis*	Liu et al. (2006)
2α,3β,19α-Trihydroxyurs-12-en-28-oic acid β-D-glucopyranosyl ester	*Potentilla anserina*	Zhao et al. (2008)
3α,30-Dihydroxylup-20(29)-en-27-oic acid (20S)-3α,29-dihydroxylupan-27-oic acid	*Potentilla discolor*	Yang et al. (2008)
Tormentic acid	*Potentilla fruticosa* *Potentilla griffithii* var. *velutina* HOOK.f.[e] *Potentilla chinensis* *Potentilla discolor*	Ganenko and Semenov (1989) Zhong et al. (2000) Xue et al. (2005a) Liu et al. (2006) Jang et al. (2006)
Euscaphic acid	*Potentilla griffithii* var. *velutina*[e] *Potentilla discolor* *Potentilla chinensis*	Zhong et al. (2000) Xue et al. (2005a) Liu et al. (2006)
Tormentoside (rosamultin)	*Potentilla griffithii* var. *velutina*[e]	Zhong et al. (2000)
Euscaphic acid 28-*O*-β-D-glucoside (kaji-ichogoside F_1)		
2α,3β,19α-Trihydroxy-oleanolic acid-28-β-D-glucopyranosyl ester (24-deoxy-sericoside)		
2α-Hydroxyoleanolic acid	*Potentilla chinensis*	Shen et al. (2006)
Pomolic acid	*Potentilla chinensis*	Liu et al. (2006)
24-Hydroxy-tormentic acid		
Asiatic acid		
Myrianthic acid		
Oleanolic acid		
2α,3α-Dihydroxyolean-12-en-28-oic acid		
Maslinic acid		
α-Amyrin		
β-Amyrin		
• Organic acids and phenol carboxylic acids		
Benzoic acid	*Potentilla chinensis*	Gao et al. (2007)
p-Hydroxy-benzoic acid	*Potentilla anserine* *Potentilla erecta*	Krzaczek (1984) Geszprych et al. (2003)
Protocatechuic acid	*Potentilla discolor*	Liu et al. (1984)
Gallic acid	*Potentilla anserina; Potentilla erecta; Potentilla discolor; Potentilla chinensis*	Krzaczek (1984) Liu et al. (1984) Goncharov et al. (1989a) Xue et al. (2006) Gao et al. (2007)
Vanillic acid	*Potentilla anserina*	Krzaczek (1984)
Gentisic acid	*Potentilla anserina*	Krzaczek (1984)
p-Hydroxy-phenylacetic acid	*Potentilla anserina*	Krzaczek (1984)
p-Coumaric acid	*Potentilla erecta; Potentilla anserina; Potentilla palustris; Potentilla argentea; Potentilla recta; Potentilla reptans* and more than 20 other *Potentilla* species[b]	Bate-Smith (1961) Krzaczek (1984) Geszprych et al. (2003)
Caffeic acid	*Potentilla erecta; Potentilla anserina; Potentilla fruticosa; Potentilla palustris; Potentilla argentea; Potentilla recta; Potentilla reptans* and more than 20 other *Potentilla* species[b]; *Potentilla fragarioides*	Bate-Smith (1961) Krzaczek (1984) Choi et al. (1998)
Ferulic acid	*Potentilla erecta; Potentilla fruticosa; Potentilla palustris; Potentilla argentea; Potentilla recta; Potentilla reptans* and more than 20 other *Potentilla* species[b]	Bate-Smith (1961)
Sinapic acid	*Potentilla erecta; Potentilla fruticosa; Potentilla palustris* and more than 5 other *Potentilla* species	Bate-Smith (1961)
4-*O*-caffeoyl-L-threonic acid	*Potentilla fragarioides*	Choi et al. (1998)
Chlorogenic acid	*Potentilla erecta; Potentilla anemonefolia*[c]; *Potentilla centrigrana*; *Potentilla cryptotaeniae*; *Potentilla freyniana*	Goncharov et al. (1989a) Okuda et al. (1992)
Fumaric acid	*Potentilla discolor*	Liu et al. (1984)

Table 3 (*Continued*)

Compounds	*Potentilla* species	References
Coumarins		
Coumarin	*Potentilla erecta*	Goncharov et al. (1987)
Umbelliferon	*Potentilla erecta*; *Potentilla anserina; Potentilla argentea*	Goncharov et al. (1987) Goncharov and Kotov (1991)
Esculetin	*Potentilla erecta*	Goncharov and Kotov (1991)
Scopoletin	*Potentilla erecta*; *Potentilla anserina; Potentilla argentea*	Goncharov et al. (1987) Goncharov and Kotov (1991)
Carotenoids		
α-Carotene β-Carotene	*Potentilla argentea; Potentilla erecta*	Goncharov and Kotov (1991)
Sterols		
β-Sitosterol	*Potentilla erecta; Potentilla argentea; Potentilla discolor; Potentilla freyniana; Potentilla palustris*	Goncharov and Kotov (1991) Sokołowska-Woźniak et al. (2002) Cai et al. (2005) Xue et al. (2005a)
Stigmasterol	*Potentilla palustris*	Sokołowska-Woźniak et al. (2002)
β-Sitosterol-3-*O*-β-D-glucoside	*Potentilla discolor*	Xue et al. (2005a) Jang et al. (2006)
Daucosterol	*Potentilla freyniana*	Cai et al. (2005)
Campesterol Ergosterol	*Potentilla palustris*	Sokołowska-Woźniak et al. (2002)
Megastigmanes		
Citroside A Icariside B1 (6S,7E,9R)-roseoside (6S,7E,9R)-vomifoliol-9-*O*-β-D-xylosyl-β-D-glucoside	*Potentilla multifida*	Xue et al. (2005b)
• Others		
Essential oil	*Potentilla palustris, Potentilla speciosa,*	Naumchik and Rozentsveig (1963) Kovzačević and Ristić (2007)
Polyprenols with 19–45 units	*Potentilla anserina; Potentilla argentea, Potentilla alba, Potentilla ambiqua* CAMB., *Potentilla argyrophylla* WALL., *Potentilla atrosanguinea, Potentilla chrysantha, Potentilla crantzii* BECK et FITSCH (Crantz); *Potentilla fruticosa, Potentilla gracilis* DOUGLAS ex HOOK, *Potentilla megalantha* TAKEDA., *Potentilla rupestris*[c]	Świeżewska and Chojnacki (1989)
2-Pyrone-4,6-dicarboxylic acid	*Potentilla anserina*; *Potentilla erecta*; *Potentilla recta; Potentilla argentea; Potentilla aurea; Potentilla calycina* BOISS.*; Potentilla crantzii Potentilla grandiflora;*	Wilkes and Glasl (2001)
Coumaruman (pectin)	*Potentilla palustris*	Popov et al. (2005a)

[a] Surface flavonoid aglycones to be present in the lipophilic exudates.
[b] Hydrolysates of leaves.
[c] Leaves.
[d] Blossoms.
[e] Whole plant.

logical and histopathological studies confirmed the effectiveness of an orally administered extract of the leaves of this species for ethanol-induced peptic ulcers in rats (Gürbüz et al., 2005). Russian authors (Popov et al., 2006) obtained interesting results when testing the influence of comaruman, a pectin isolated from aerial parts of *Comarum palustre* (syn. *Potentilla palustris*), on acetic acid-induced colitis in mice. They could prove the protective properties of this pectin. A considerable reduction of injury areas, increased myxiosis within the colon area, and limited neutrophil infiltration were observed. Moreover, decreased blood vessels permeability and tissue myeloperoxidase activity were found (Popov et al., 2006).

4.1.3. Clinical study

Recently, the efficacy of a tormentil (*Potentilla erecta*) rhizome extract in the treatment of active colitis ulcerosa in 16 patients has been demonstrated in an open-label, dose-escalating study. During treatment with the tormentil extract, the colitis activity index (CAI) significantly declined from a mean value of 8.3–3.9 ($p > 0.001$) when a dosage of 2.400 mg/day was administered. Lower doses (1.200 and 1.800 mg/day) proved to be not as beneficial as the 2.400 mg/day dose. Also a higher dose (3.000 mg/day) provided no additional efficacy. The observed adverse effects were mild gastrointestinal symptoms (mild upper abdominal discomfort by six patients) and were not a reason for the discontinuation of the medication. The tormentil rhizome extract appeared safe up to 3.000 mg/day. A reduction of the concomitant steroidal medication was possible. The authors (Huber et al., 2007) suggest that the addition of the tormentil extract to conventional therapy in active ulcerative colitis may help to reduce some of the troublesome symptoms. Interestingly, no unchanged or metabolized tannins could be detected in patient sera, indicating that the tannins in the tormentil rhizome extract were not systemically absorbed (Huber et al., 2007).

4.2. Antidiarrhoic activity

The oligomeric and polymeric flavan-3-ols also known as condensed tannins or proanthocyanidins (PAs) showed therapeutic properties to treat diarrhoea (Santos-Buelga and Scalbert, 2000; Palombo, 2006). The antidiarrhoeal effect of tannins is commonly attributed to the unspecific complexation of mucosal proteins in the gut with formation of a protective layer. The antidiarrhoeal effects of tannins may therefore be explained by the complexation of secre-

Table 4
Overview on the main ethnopharmacological uses of *Potentilla* species and the current status of modern pharmacological evaluations.

Ethnopharmacological use	*In vitro*	*In vivo*	Clinical trials	References
Ulcer		Ethanol-induced peptic ulcers (*Potentilla reptans*)		Gürbüz et al. (2005)
Diarrhoea	Antisecretory activity (*Potentilla erecta*)		Antidiarrhoic and antiviral activities against *Rotavirus*-induced diarrhoea (*Potentilla erecta*); prevention of travel-associated diarrhoea	Lund and Rimpler (1985) Geiger et al. (1994) Raedsch et al. (1991) Subbotina et al. (2003)
Inflammations	Strong inhibition of cyclooxygenase, i.e. anti-inflammatory activity (*Potentilla erecta*)	Anti-inflammatory activity in mouse ear (*Potentilla alba*, *Potentilla erecta* and *Potentilla malýana*); formalin-induced paw pad in mice: anti-inflammatory effects (for comaruman from *Potentilla palustris*)		Tunón et al. (1995) Pilipović et al. (2005, 2007) Popov et al. (2005, 2005a)
Colitis ulcerosa	Antimicrobial, anti-inflammatory, antioxidant (*Potentilla erecta*)	Acetic-induced colitis in mice: reduction of injury areas (for comaruman from *Potentilla palustris*)	Efficacy in treatment of colitis ulcerosa (*Potentilla erecta*)	Langmead et al. (2002) Popov et al. (2006) Huber et al. (2007)
Cancer	Inhibition of the growth of lymphoma cells; anti-cancer activity of single compounds (triterpenoids, from *Potentilla chinensis* and *Potentilla multicaulis*); anti-cancer activity of flavonoids and tannin-like compounds (*Potentilla argentea*)	Activity against neoplastic tumours in mice (*Potentilla fulgens*)		Syiem et al. (2003) Rosangkima and Prasad (2004) Spiridonov et al. (2005) Liu et al. (2006) Li et al. (2007) Tomczyk et al. (2008)
Viral infections	Prophylactic and therapeutic activity against *Coxsackie* virus B 1-6 in Hep-2 cells (*Potentilla fruticosa*); antiviral activity against *Respiratory Syncytial* virus (*Potentilla arguta*); antiviral effect against *Herpes* virus (*Potentilla erecta*, *Potentilla anserina*) and *Vaccine* virus (*Potentilla anserina*); antiviral activity against *Hepatitis B* virus for single triterpenoid (*Potentilla anserina*)	Prophylactic and therapeutic activity against *Coxsackie* virus B 1-6 in mice (*Potentilla fruticosa*); antiviral effects in mice against *Vaccine* virus (*Potentilla erecta*); inhibitory effect on duck *Hepatitis B* virus DNA replication for single triterpenoid (*Potentilla anserina*)	Antiviral activity against *Rotavirus* infection in children (*Potentilla erecta*)	May and Willuhn (1978) Lund and Rimpler (1985) McCutcheon et al. (1995) Evstropov et al. (2002, 2004, 2005) Subbotina et al. (2003) Zhao et al. (2008)
Bacterial infections	Suppression of glucotransferase activity in *Streptococcus mutans* and *Streptococcus sobrinus*; inhibition of synthesis of water soluble glucans and anulation of mutan adherence to hard surfaces (*Potentilla erecta*); moderate antibacterial activity against *Staphylococcus aureus*, *Bacillus substilis*; no or very low activity against *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*; high activity against *Campylobacter pylori* (various *Potentilla* species)			Pleszczyńska et al. (2003) Tomczyk et al. (2007) Tosun et al. (2006)
Antioxidants	Antioxidant activity against DPPH, $ABTS^{+}$ (*Potentilla alba*, *Potentilla fruticosa*, *Potentilla freyniana*, *Potentilla chinensis*, *Potentilla fragarioides*, *Potentilla viscosa*), FRAP assay (*Potentilla fruticosa*); antioxidative properties of polyphenols from *Potentilla erecta*, *Potentilla anserina*, *Potentilla argentea*, *Potentilla aurea*, *Potentilla fruticosa*, *Potentilla palustris*, *Potentilla reptans*, *Potentilla tabernaemontani*	Strong antioxidant activity in albino rats (*Potentilla erecta*); antioxidant activity in mice (*Potentilla reptans*, *Potentilla anserina*)		Lamaison et al. (1990) Kirby and Schmidt (1997) Choi et al. (1998) Teftyuyeva (2004) Chen et al. (2004) Miliauskas et al. (2004, 2004a) Chen et al. (2005) Chen et al. (2005) Świąder et al. (2006) Avci et al. (2006) Li et al. (2006) Oszmiański et al. (2007) Kalia et al. (2008)

Table 4 (*Continued*)

Ethnopharmacological use	*In vitro*	*In vivo*	Clinical trials	References
Fungal infections	Moderate antifungal activity against *Candida albicans*, *Candida krusei* and *Cryptococcus neoformans* (various *Potentilla* species); potent antifungal activity against *Candida glabrata* (*Potentilla simplex*); only weak activity against dermatophytes and moulds (*Potentilla simplex*)			Tosun et al. (2006) Tomczyk et al. (2007) Webster et al. (2008)
Impairment of immune system	Immunomodulating activity in Hep-2 cells (*Potentilla fruticosa*)	Immunomodulating activity in mice (*Potentilla fruticosa*); induction of interferon synthesis in mice (*Potentilla erecta*)		Evstropov et al. (2004, 2005)
Diabetes mellitus	Inhibition of aldose reductase, i.e. prevention of diabetes induced damages (*Potentilla recta*, tannins from *Potentilla candicans and Potentilla discolor*)	Healthy and alloxan-induced diabetes in mice: lowering of blood glucose levels (*Potentilla fulgens*); increase of insulin secretion (*Potentilla erecta*)		Terashima et al. (1990) Syiem et al. (2002) Enomoto et al. (2004) Jang et al. (2007)
Spasms	Spasmolytic effects at the isolated guinea-pig ileum and the rat uterus (*Potentilla anserina*)			Youngken et al. (1949)
Liver complaints		Hepatoprotective effect (*Potentilla erecta* and *Potentilla fruticosa*)		Youngken et al. (1949) Kolpakov et al. (2001)

togogue compounds such as cholera toxin (Hör et al., 1995), rhein (Verhaeren and Lemli, 1986) or the inhibition of intestinal motility (Galvez et al., 1991).

4.2.1. *In vitro experiment*

The antisecretory activity of a lyophilized hot water extract (3 g/150 ml, 10 min) of *Tormentillae rhizoma* was examined with the isolated rabbit colon mounted in an Ussing chamber. Mucosal application of 200–800 μg/ml of the Tormentillae extract showed a dose-dependent increase in the prostaglandin E_2 (PGE_2) stimulated Cl^- secretion of 4–32% (Geiger et al., 1994).

4.2.2. *Clinical study*

In a randomized, double blinded, placebo-controlled clinical trial Russian authors (Subbotina et al., 2003) have shown a high efficacy of a *Potentilla erecta* rhizome dry extract (one part of dried root with 10 parts of 40% ethanol, 30–40% of tannins, saponin and other components) in child diarrhoea therapy due to a *Rotavirus* infection (Subbotina et al., 2003). Forty children (20 verum- and 20 placebo-treated) were enrolled. The children received either three drops of the tormentil extract or placebo per year of life, three times a day until discontinuation of diarrhoea, or a maximum of five days. In the verum group the dose corresponded to a tannin dose of 1.0–1.5 mg/kg and day. The placebo dry extract consisted of an Indian black tea (10–20% of tannins) with identical appearance and taste as the tormentil extract. The primary endpoint was the duration of diarrhoea, measured by the volume of stool, a secondary endpoint was the physical examination in order to assess the degree of dehydration in the subjects. The duration of diarrhoea in the verum group was significantly shorter than in the placebo group (3 days vs. 5 days, $p < 0.0001$). In the verum group 8 of 20 children (40%) were free of diarrhoea within 48 h after admission to hospital compared to 1 of 20 (5%) in the placebo-treated group (highly significant, $p < 0.0001$). Tormentil-treated patients received smaller volumes of parenteral fluids than the children in the placebo group. In the tormentil rhizome extract treatment group no clinical side effects including increased vomiting were detected during the study. The extract had a high tannin content, making water penetration through intestinal walls and loss of water and electrolytes from the body difficult. Therefore, the tormentil extract also decreased the demand for hydrating fluids during treatment. The authors assume that an interaction of the tannins with *Rotavirus* proteins might contribute to the high efficacy of this extract, but other unknown ingredients might also be involved in the antidiarrhoic effects of the tormentil rhizome extract (Subbotina et al., 2003).

Tormentil was shown to be also effective in the prevention of travel-associated diarrhoea (Raedsch et al., 1991).

4.3. *Anti-neoplastic activity*

4.3.1. *In vitro experiment*

Chinese authors (Liu et al., 2006; Li et al., 2007) have attributed a significant anti-cancer activity to a number of triterpenoid compounds isolated from the aerial parts of *Potentilla chinensis* and the roots of *Potentilla multicaulis* which were evaluated for their *in vitro* cytotoxic activities against SMMC-7221 (human hepatoma) and HL-60 (human promyelocytic leukemia) cells. *Potentilla erecta*, a traditional plant in Russian medicine, was used to alleviate disease symptoms in patients with cancer. The ethanol extract of the rhizomes may inhibit the growth of lymphoma cells as concluded from *in vitro* data. The crude ethanol (40%) extract from *Potentilla erecta* displayed the highest cytotoxicity, completely suppressing the cell growth of the cells at concentrations of 10 and 50 μg/ml (Spiridonov et al., 2005).

Polyphenolics, i.e. kaempferol 3-*O*-β-D-(6″-*E*-p-coumaroyl)-glucopyranoside (tiliroside) and methyl brevifolincarboxylate isolated from aerial parts of *Potentilla argentea* L., were evaluated for their cytotoxicities against human breast carcinoma cell line (MCF-7) and their DNA-binding ability. The DNA-binding ability of these compounds were studied employing the human DNA topoisomerases I and II inhibition assay and ethidium displacement assay using calf thymus DNA, poly(dA-dT)$_2$ and poly(dG-dC)$_2$. Methyl brevifolincarboxylate was much more active and showed higher cytotoxic potency than tiliroside. In DNA topoisomerase I and II inhibition assays *in vitro* both investigated compounds were more effective against topoisomerase II than I. The results of DNA-binding studies revealed that methyl brevifolincarboxylate has a greater DNA-binding affinity than tiliroside, which correlates with its greater potency as a topoisomerase I/II inhibitor (Tomczyk et al., 2008).

Wall et al. (1996) found out that tannin-containing topoisomerase I and II inhibitory plant extracts which were subjected to tannin removal procedures lost their activity in this test assay. Thus tannins play an important role in inhibitory effects on topoisomerases I or II (Bastow et al., 1993).

4.3.2. In vivo experiment

Herbal medicine was also applied by the Meghalay tribes in India. A preliminary study revealed that the methanolic extract of the roots of *Potentilla fulgens* L. was found active against certain tumors in a dose-dependent manner. Approximately 1×10^6 Dalton's lymphoma cells were transplanted intraperitoneally into swiss-albino mice. Data indicate the high antitumor activity of the methanolic extract on DL cells. The treated/control value was 154% (250 mg/kg) when the animals were treated on the 1st, 3rd, 5th and 7th day after transplantation. The data obtained in this study are quite promising and open a way for further investigation (Syiem et al., 2003).

The herb and the underground parts of the same plant were also used by them to treat various ailments, including neoplastic diseases. Further studies showed that the aqueous root extracts of the herb of *Potentilla fulgens* are active against neoplastic tumours murine ascites Dalton's lyphoma (DL), depending on the method of administration (Rosangkima and Prasad, 2004).

4.4. Antiviral and antimicrobial activity

4.4.1. In vitro experiment

May and Willuhn (1978) found out that extracts of *Potentilla erecta* rhizomes and also of the herbal part of *Potentilla anserina* had moderate antiviral effects against the *Herpes* virus *in vitro*. In addition this *Potentilla anserina* extract showed some activity against the *Vaccine* virus. Earlier, other authors had also shown the suppressive effect of a *Potentilla arguta* PURSH methanol root extract against bovine respiratory syncytial virus proliferation (McCutcheon et al., 1995).

On several occasions, the antiviral characteristics of isolated hydrolysable and condensed tannins from *Potentilla erecta* rhizome against *Herpes* virus types I and II have also been reported, as well as its cytotoxic activity against *Influenza* virus type A_2 and *Cowpox* (May and Willuhn, 1978; Tackechi et al., 1985; Fukuchi et al., 1989; De Bruyne et al., 1999; Latté, 2006). Nakanishi et al. (1993) reported that 70% aqueous ethanol extract of underground parts of *Potentilla gracilis* DOUGL. ex HOOK. showed more than 20% inhibition effects on HIV-1 reverse transcriptase at 0.5 μg/ml concentration in this *in vitro* screening test.

Great results were observed in benign oral and pharynx mucosa. Russian authors (Volodina et al., 1997) showed that rinsing of the throat with a tormentil tincture was helpful in the treatment of lichen planus of oral mucosa, whereas the study results of Polish authors (Pleszczyńska et al., 2003) show the suppressive effect of tormentil's aqueous rhizome extract on glucotransferase (GTF) activity – enzymes being a vital virulence factor of the variable streptococci *Streptococcus mutans* and *Streptococcus sobrinus*. Furthermore, aqueous and ethanol extracts of tormentil rhizome inhibit the synthesis of water insoluble glucans and annuls mutan adherence to hard surfaces. As a result, both extracts effectively prevent dental caries. Diluted tinctures and decoctions from tormentil rhizome are also used in dentistry where they are great agents against bleeding gums and stomatitis (Volodina et al., 1997; Pleszczyńska et al., 2003; Latté, 2006). Generally, the antibacterial activities from aerial parts of nine *Potentilla* aqueous extracts (*Potentilla argentea, Potentilla fruticosa, Potentilla recta* L., *Potentilla rupestris* L., *Potentilla erecta, Potentilla anserina, Potentilla nepalensis* HOOK. var. 'Miss Willmott', *Potentilla thuringiaca* BERNH. ex LINK, *Potentilla grandiflora* L.) against Gram-positive bacteria (*Staphylococcus aureus*, *Bacillus subtilis*) were moderate. Nearly no activity was observed against Gram-negative bacteria (*Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*) with the exception of high activity against *Helicobacter pylori*. Moderate antifungal effects of *Potentilla* extracts against *Candida albicans* were determined (Tomczyk et al., 2007).

A series of altogether 27 tannins (hydrolysable tannins and related compounds and proanthocyanidins of type A and B including some proanthocyanidins also occurring in *Potentilla* species) were tested for their activity against two Gram-positive and four Gram-negative bacteria and also two yeasts. The compounds showed only weak to moderate antibacterial activity, but fairly high anticryptococcal activities (Kołodziej et al., 1999). Also, the methanol extract from the aerial parts of *Potentilla recta* showed moderate antibacterial and antifungal activities against *Staphylococcus aureus, Escherichia coli, Candida albicans* and *Candida krusei*, respectively (Tosun et al., 2006). Recently, Webster et al. (2008) analyzed antifungal activities of an aqueous plant extract from stems and leaves of *Potentilla simplex* MICHX. The extract showed weak to moderate antifungal activities against various yeasts (*Candida* species and *Cryptococcus neoformans*) whereas very potent antifungal activities against *Candida glabrata* have been observed. Only weak antifungal activities were determined against dermatophytes (*Trichophyton* sp., *Epidermophyton floccosum*, *Microsporum canis*) while no or only very weak effects were observed against moulds (*Aspergillus* sp., *Fusarium* sp., *Rhizopus* sp.). In a study on antifungal effects of some tannins from *Pelargonium reniforme* CURT no activity was observed against filamentous fungi (dermatophytes, mould fungi). Prominent activity was found for these tannins against *Candida glabrata, Candida brusei, Cryptococcus neoformans*. Less potent activity was determined against *Candida albicans* (Latté and Kołodziej, 2000).

The whole plant of *Potentilla sericea* L. (syn. *Potentilla pensylvanica* L.) is also used in the general treatment of tuberculous lupus as an adjuvant drug, along with tuberculocidal and tuberculostatic agents (Gautam et al., 2007). These results support the use of *Potentilla* plants and some tannin-containing preparations as antimicrobial and antifungal agents, which may act as pharmaceuticals and preservatives.

4.4.2. In vivo experiment

Based on studies conducted on Hep-2 cell cultures and newborn BALB/c mice, a team of Russian scientists proved the prophylactic and therapeutic activity of aqueous *Potentilla fruticosa* extracts from aerial parts, with reference to *Coxsackie B 1-6* enterovirus types. The scientists showed for this extract a reduction of the virus concentration in the infected Hep-2 cell cultures (Evstropov et al., 2002). Interestingly, two hydrolysable tannins, namely geraniin and its galloylated derivative, were active *in vitro* against the *Coxsackie B2* virus (Corthout et al., 1991). Also a dose-dependant effect on

average survival time and body mass dynamics in the mice was reported. Additionally, they observed a reduction in the degree of virus accumulation in the brain, the liver and myocardium in the studied animals. The same studies demonstrated the extract's immunomodulating properties and its ability to induce interferon (IFN) synthesis (Evstropov et al., 2002; Evstropov et al., 2004; Evstropov et al., 2005).

Interestingly, Lund and Rimpler (1985) observed antiviral effects of a *Potentilla erecta* rhizome extract against the *Vaccine* virus in mice and also the induction of interferon synthesis in this test model.

2α, 3β, 19α-trihydroxyurs-12-en-28-oic acid β-D-glucopyranosyl ester isolated from rhizomes of *Potentilla anserina* was tested for its effect on *Hepatitis* B virus (HBV) antigene expression and anti-HBV activities *in vitro*. The compound showed inhibitory effects on duck *HBV* DNA replication *in vivo* (Zhao et al., 2008).

4.5. Antihyperglycemic activity

4.5.1. In vitro experiment

Japanese authors (Terashima et al., 1990) noticed that an ellagic acid derivative isolated from *Potentilla candicans* inhibited aldose reductase activity—an enzyme catalyzing glucose transition into sorbitol. Blocking of this metabolic path prevents fructose and sorbitol accumulations in the organs, as well as in the eyes, therefore decreasing the likelihood of complications in the future (Terashima et al., 1990). Similarly, a methanolic extract of *Potentilla recta* (aerial parts) exhibited potent inhibitory activity exceeding 60% on human aldose reductase (h-AR) (Enomoto et al., 2004). Recently, 4-*O*-methylellagic acid 3-*O*-α-L-rhamnoside obtained from ethyl acetate fraction of an ethanolic extract from the roots of *Potentilla discolor* was subjected to *in vitro* bioassays to evaluate advanced glycation end products (AGEs) and rat lens aldose reductase (RLAR) inhibitory activities. This compound showed a significant inhibitory activity with observed IC_{50} values of 79.5 and 8.03 μM against AGEs formation and RLAR, respectively (Jang et al., 2007).

4.5.2. In vivo experiment

Diabetological studies performed in India showed the hypoglycemic activity of pure methanol *Potentilla fulgens* root extracts. In both healthy and alloxan-induced diabetes mice, the blood glucose level was lowered. Alloxan-induced diabetic mice were administered intraperitoneally (i.p.) the extract at varying doses (150–450 mg/kg b.w.) and the blood glucose levels were measured at varying time intervals up to a period of 5 days. Toxicity studies carried out on mice up to a dose of 450 mg/kg b.w. did not show any adverse effects during the 4 weeks of observation (Syiem et al., 2002). An extract of *Potentilla erecta* rhizome showed similar effects, probably due to the presence of tormentoside. An increase of insulin secretion was also proven during oral administration of this compound preparation. In the initial diabetic stages, both extracts could be used as subsidiaries and the genus *Potentilla* may be helpful in diabetic complications such as neuropathy and retinopathy (Stachurski and Strzelecka, 1994; Strzelecka and Kowalski, 2000).

4.6. Anti-inflammatory, spasmolytic, hepatoprotective activity

4.6.1. In vitro experiment

Based on the available literature and observation of traditional, native methods of inflammatory process prevention, Swedish authors selected 52 plant species and studied their aqueous extracts *in vitro* with regard to prostaglandin and exocytosis biosynthesis inhibition induced by platelet activating factors (PAF). It was observed that some of them, including *Potentilla erecta* (rhizome extract), have very strong cyclooxygenase inhibiting properties, and therefore show anti-inflammatory activity (Tunón et al., 1995).

Externally, the extracts of *Potentilla* species are also used for bathing (dermatoses, mycoses, excessive perspiration), irrigation (white leucorrhea, vulvovaginitis conditions), compresses (burns, frostbite, skin injuries), enemas (large bowel and rectal ulcerative inflammation), and ointments (purulent and allergic dermatitis). Analogous activity has also been shown for the *Potentilla anserina* herb.

Ethyl acetate extracts from the aerial part of *Potentilla anserina* have a significant spasmolytic activity in abnormal smooth muscle tones of the intestines and uterus. It appears then, that spasmolytic activity is comparable with papaverine hydrochloride. Moreover, it has been proven that spasmolytic properties do not include blood vessels and the urinary system, so this activity may be used in oligomenorrhea alleviation. Additionally, the *Potentilla anserina* herb has a good influence on liver functions and increases bile secretion. As a cataplasm, it is used in alleviation of rheumatic and arthritic pains and neuralgia (Youngken et al., 1949).

4.6.2. In vivo experiment

In vivo local anti-inflammatory effects of rhizomes and roots of *Potentilla alba* and *Potentilla erecta* acetone and ethanol extracts have been observed in the test model of mouse ear. Local anti-inflammatory effect of these extracts were tested on a modified model of a mouse ear. For the purpose of provoking inflammation, both mouse ears were applied 3% oleum crotonis acetone solution. The strongest pharmacological reaction was found with acetone extract of rhizome of *Potentilla alba*, the pharmacological reaction of which was similar to a hydrocortisone ointment. Acetone and ethanol extracts of the tested plant species *Potentilla* have significantly reduced inflammation in time for 30–50% in relation to control ear. Similarly, the acetone extract of the rhizome and root of *Potentilla malýana* BORBÁS has been evaluated for anti-inflammatory potential using the mouse ear edema model (Pilipović et al., 2005; Pilipović et al., 2007).

Previous studies by the afore-mentioned Russian authors, conducted on mice with formalin-induced paw pad edema, demonstrated high – comparable to 50 mg/kg indometacine – anti-inflammatory activity for the discussed compound. This activity is a result of comaruman inhibition and its neutrophil adhesion fragments to fibronectin (Popov et al., 2005, 2005a).

An aqueous extract derived from flowers and young shoots of *Potentilla fruticosa* had a protective effect on the liver. Studies performed in rats with chronic and toxic hepatitis showed the hepatoprotective influence of that extract on the microsomal liver system, as well as a protective effect on the xenobiotic metabolism and plasma lipids' peroxidation. Moreover, it normalised the alanine aminotransferase activity and bilirubin levels in plasma (Kolpakov et al., 2001).

4.7. Antioxidative activity

The antioxidative properties of the plants and their preparations are of particular importance. Currently, polyphenolic compounds are of great interest in nutrition and medicine for their potent antioxidant capacity and protective effects on human health and diseases with free radical ethiologies, including cardiovascular diseases, neoplastic diseases and blood clotting diseases. As a result, a number of works on antioxidative substances, isolated from aerial and underground parts of various genus *Potentilla* species, have been published.

4.7.1. In vitro experiment

Polish authors investigated the antioxidant effect of isolated polyphenolic compounds and the methanolic extract from

Potentilla alba roots against organic radicals such as 1,1-diphenyl-2-picrylhydrazyl (DPPH) and 2,2-azinobis (3-ethylbenzothiazoline-6-sulfonic) acid ($ABTS^+$) (Świąder et al., 2006; Oszmiański et al., 2007). In another study, the contents of polyphenols and flavonoids in 50% aqueous ethanol extracts from aerial parts of *Potentilla atrosanguinea* LODD. exhibited strong antioxidant activity measured in terms of Trolox equivalent antioxidant capacity (TEAC) with $ABTS^+$, DPPH and ferric reducing antioxidant potential FRAP assay (Kalia et al., 2008). Similar antioxidant activity was reported on different extracts (methanol, acetone, ethyl acetate) and isolated compounds obtained from the flowers of *Potentilla fruticosa* (Miliauskas et al., 2004, 2004a).

The ability to sweep free radicals results in the multidirectional activity of the active compounds present in plant extracts. Polyphenol compounds react very easily with oxidants and in this way prevent peroxidation of fats and LDL oxidation which would otherwise damage the vessels' endothelium. Moreover, an increase of endothelial permeability is prevented by *Potentilla* extracts. A decrease of NO release is observed and the dilatation of blood vessels is impaired. Studies with *Potentilla* extracts containing condensed tannins and their monomers show that the antioxidative properties of these extracts are determined not only by their qualitative composition but also by the degree of polymerization of their compounds. It was observed that procyanidin oligomers and dimers isolated from the *Potentilla erecta* rhizome had much higher activity in that direction compared to their monomers, whereas pentamers and hexamers had an elastase inhibiting capacity (Vennat et al., 1994; Bos et al., 1996). It is worth mentioning that these activities are also displayed by tannins studied by French authors, that were isolated from other plants from the *Potentilla* species such as *Potentilla anserina*, *Potentilla argentea*, *Potentilla aurea*, *Potentilla fruticosa*, *Potentilla palustris*, *Potentilla reptans* and *Potentilla tabernaemontani* ASCH (Lamaison et al., 1990).

The radical scavenging properties have been verified for individual tannins and related polyphenols characteristic for *Potentilla* species: for tellimagrandin I, epigallocatechin, epicatechin, catechin, pedunculagin and casuarictin the radical scavenging effects on superoxide anion radical and on 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical have been demonstrated in several experiments. The scavenging effects of all of the tannins and related polyphenols tested in the experiments on DPPH radical were stronger than that of dl-α-tocopherol (Hatano et al., 1989; Yoshida et al., 1989). The antioxidant activity of an extract (70% EtOH) of rhizome and roots of *Potentilla freyniana* BORNM. has been investigated using both enzymatic and non-enzymatic *in vitro* antioxidant assays. An extract from *Potentilla freyniana* showed stronger antioxidant activity than grape seed extract (Chen et al., 2005). Similar activity has also been observed for *Potentilla alba*, *Potentilla chinensis*, *Potentilla fragarioides* L. and *Potentilla viscosa* LEHM. extracts (Kirby and Schmidt, 1997; Choi et al., 1998; Chen et al., 2004; Chen et al., 2005).

4.7.2. In vivo experiment

The effect of different doses of the spirituous tincture from the *Potentilla erecta* rhizome (TPTR; 1:5) on malonaldehyde content, lipid peroxidation and on the biochemical indices of lipid metabolism in the blood of albino rats under normal physiological conditions was studied. The tincture was administered intragastrically for 14 days at 0.05 and 0.1 ml per 100 g of the animals' body weight. There was a decrease in malonaldehyde and endogenic lipids after three administrations of the *Potentilla erecta* tincture. Strong antioxidant effects of *Potentilla erecta* tincture were also observed (Teftyuyeva, 2004). Two kinds of extracts with ethanol and water from aerial parts of *Potentilla reptans* were evaluated for *in vivo* hypercholesterolaemic and antioxidant activities (Avci et al., 2006). Li et al. (2006) investigated the antioxidation effects of petroleum fraction from *Potentilla anserina* roots. The analyzed fraction obviously prolonged the survival time of mice in normobaric hypoxia and decreased the oxygen consumption of the mice.

4.8. Other effects

Potentilla species and their extracts are rarely used *per se*, but generally as components in ready-made herbal mixtures. An example of such a formulary is a drug used in Korean folk medicine which contains leave extracts of *Potentilla discolor* and *Potentilla chinensis*. The drug, "Jin Hae Cho lp", alleviates neuralgic pain and shows a muscle toning effect after childbirth (Park et al., 2004). In other preparations a mixture of *Potentilla* extracts with other tannin-containing plant extracts or essential oils is used (e.g. antimicrobial effect, acceleration of wound-healing).

The effects of ethanol (70%) extract of *Potentilla erecta* roots were observed in various concentrations on *trans*-sialidase activity in human blood plasma. The inhibition of the *trans*-sialidase can decrease the rate of LDL modification and prevent cholesterol accumulation in vascular cells. An extract from *Potentilla erecta* rhizomes had no effect on enzyme activity (Aksenov et al., 2007).

5. Toxicity

Only few studies have addressed potential toxicity of *Potentilla* species and their extracts. No signs of acute toxicity could be observed after intraperitoneal and oral application of a *Potentilla erecta* rhizome extract (prepared with a water–acetone mixture) in doses up to 200 and 300 mg/kg body weight, respectively (Lund and Rimpler, 1985). Earlier studies (Rodewald, 1950) revealed that a continuous infusion of a *Potentilla anserina* extract (herbal part, decoction, concentration 2–10%) into the vena juglaris led to systolic heart death in guinea-pigs after 14–18 min (7–9 ml of the decoct). A decoction of *Potentilla erecta* (rhizomes) in the same test model also led to heart death. A 3–4-fold doses of the above-mentioned *Potentilla anserina* decoct was needed in cats to lead to cardiac arrest.

Neither toxic effects nor side-effects of clinical significance have been reported in clinical trials for *Potentilla erecta* (Subbotina et al., 2003; Huber et al., 2007). This is in line with the fact that during the long time of administration of *Potentilla* species and their extracts in the traditional medicine no reports of toxic effects have been known.

It is also worth considering the antimutagen activity demonstrated by the aqueous and ethanol extracts and tincture of the *Potentilla anserina* herb. Studies conducted using Ames' test with 2-nitrofluorene as standard mutagen showed an insignificant or moderate decrease in *Salmonella typhimurium* strains TA99 and TA100 revertants' numbers under the influence of tannoid fractions of those preparations (Schimmer et al., 1993; Schimmer and Lindenbaum, 1995).

6. Conclusions

Modern pharmacological studies have generally confirmed the traditional use of *Potentilla* species and their extracts from aerial and/or underground parts as an ailment for inflammations, colitis ulcerosa, certain forms of cancer, viral and microbial infections, an impaired immune system, diabetes mellitus, spasms and liver complaints. Most of the biological effects of *Potentilla* species can be explained by the high amount of condensed and hydrolysable tannins present in the aerial and the underground parts, e.g. the antiviral and antimicrobial activities, immunomodulating effects, hepatoprotective and anti-inflammatory effects.

A high number of constituents have been elucidated both for the aerial and the underground part. However, these compounds

were often only described for one or a limited number of *Potentilla* species. Therefore, a large comparison of the metabolic patterns of therapeutically important *Potentilla* species would be desirable in order to see whether the chemical constituents and also their quantities are more or less the same. In addition the different types of extracts (e.g. prepared with water, ethanol, water–ethanol mixtures, etc.) and their phytochemical profile should be investigated. This would be of high value in order to answer the question whether the pharmacological results for one *Potentilla* species can be transferred to another *Potentilla* species and also for one extract within the same *Potentilla* species to another kind of extract.

The pharmacological studies so far have mostly been performed *in vitro* and *in vivo* with animals. Therefore clinical studies are urgently needed in order to confirm traditional wisdom in the light of a rational phytotherapy. The rhizome extracts of *Potentilla erecta* have recently been tested in first clinical trials for the treatment of *Rotavirus*-induced diarrhoea in children and for the treatment of colitis ulcerosa. These promising results should be further substantiated by more clinical studies with a higher number of patients enrolled. Thus, the rhizome extracts of *Potentilla erecta* might become an alternative to chemically defined drugs in certain viral infections and in the therapy of colitis ulcerosa, for which only a limited number of medications exist.

Even today, plants are the almost exclusive source of drugs for a majority of the world's population (Hamburger and Hostettmann, 1991). Therefore, it remains a challenge for scientists to provide efficient, safe and cheap medications especially for rural areas. *Potentilla* species are distributed and used in traditional medicine of different cultures in Asia, Europe and Northern America. These local *Potentilla* species and their quantification of individual *Potentilla* phytoconstituents as well as pharmacological profile based on *in vitro*, *in vivo* studies and on clinical trials should be further investigated.

Conflict of interests

K.P. Latté is a scientific employee at Axxonis Pharma AG company which does not intend to develop a *Potentilla*-based product.

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