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Plant of interest – *Prunella vulgaris* L.

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Summary: Self-heal (*Prunella vulgaris* L.), known as a remedy traditionally used as Chinese medicine, was neglected in modern pharmacy until the 20th century. Although in the Middle Ages it was respected for its wound-healing effect, the usage of this medicinal plant was confined just to the conventional pharmacy. Nowadays, because of the great dislike of synthetic materials, however, self-heal has become one of the most important target plants again. Owing to its valuable active constituents, besides its wound-healing effect, the plant can also be used as hepato-protective, antioxidant, anti-HIV, anti-cancer remedy, and it is effective against *Herpes* virus, as well. Its taste – and odourless extracts are applied by the food industry as natural food preservatives. Taking into account the importance of self-heal our aim was to introduce this plant species more detailed with regard to its active agents, effects and cultivation methods.

Key words: self-heal, antioxidant, phenol, Chinese medicine

Introduction

Self-heal, belonging to the *Lamiaceae* family, is native to Eurasia, but it has been naturalized also in the temperate zone of America and Australia (*Kirtikar* et al., 1935; *Keville*, 1991). It is a herbaceous, slightly pubescent perennial plant. It has short rhizome and erect or ascending, 5–30 cm tall stems. These small stalks are creeping on the ground from which new roots are shooting. The leaves are opposite with a typical mintlike form. The flowers are found in whorls in dense terminal cylindrical or almost globular inflorescences. The fruit consisted of 4 smooth nutlets. In Hungary it is very common in meadows, pastures, and open forests. Its lilac flowers can be seen from June until October (*Culpeper*, 1604; *Keville*, 1991; *Laurent*, 1996; *Simon*, 2000) (*Figure 2*).

The Latin name of the plant – *Prunella* – seems to be originating from the old German name „*Brunella*". The expression „die Braüne" means sore throat indicating that basically self-heal was used to treat the inflammation of the throat (*Keville*, 1991). According to other authors the name of the plant comes from the brown (*Braun*) colour of the spikes bearing the fruits. In the Latin name we can also discover „prunun", with the meaning of lilac that is connected to the colour of the flowering spikes (*Rogers*, 2000).

The drug of the plant – *Prunellae herba* – is not official either in the European or in the Hungarian Pharmacopoeia (Ph. Eur. V., Ph. Hg. VIII.). Probably, owing to the lacking description of the drug the literature is very contradictory with relevance to the collected plant part. For example in China spikes holding fruits are recommended to collect (*Tien*, 1979), while in Japan just the flowering spikes are regarded to be the drug (Pharmacopoeia Japonica, 1981., *Tabba* et al., 1989). In Europe the flowering stems are used traditionally (*Grieve*, 1992; *Psotová* et al., 2005; *Bomme* et al., 2006). However, in some cases the leaves collected before flowering were the starting materials of the analysis (*Laurent*, 1986; *Kojima* et al., 1990). In many experiments the origin of the plant material is unknown, and it is very common that the researchers do not pay enough attention to the description of the quality of the drug (*Collins et* al., 2006; *Psotová* et al., 2006; *Zhang* et al., 2007).

Utilization of the plant has a huge historical background. It is traditionally applied by the Chinese (*Beusky Gamble*, 1986), the Japanese (*Kojima* et al., 1990) and the Indian pharmacy (*Kirtikar* et al., 1935). In the Medieval Times similarly to other medicinal plants it was considered to be an all-heal remedy (*Culpeper*, 1640). The possible usage of self-heal in the modern pharmacy was unreasonably neglected. However, at the end of the 20th century more and more experiments were focusing on the chemical components of *Prunella vulgaris* (*Kojima Ogura*, 1986; *Kojima* et al., 1987). According to the results today self-heal is tended to be one of the most perspective „rediscovered" plants among medicinal plant species (*Psotová* et al., 2005). Both pharmaceutical and nutraceutical utilization of the species has become more significant, recently.

Active constituents and effects of *Prunella vulgaris* L.

Prunella vulgaris contains many types of active agents having important biological effects on the human body. Several scientists managed to detect one of the most important phenol components, the rosmarinic acid in the

plant tissues (*Psotová* et al., 2005; *Psotová* et al, 2006; *Park* et al., 2007), however the proper percentage of this constituent was given only one time by Lamaison and co-workers in 1991 (6.1%). During the examination of Hungarian wild populations of self-heal in 2005 the results regarding to the rosmarinic acid content, however, were between 1.84–0.13% (*Sárosi & Bernáth*, unpublished). Its related component, caffeic acid can also be found in the extracts. Other types of phenols, such as flavonoids (rutin, hyperoside) and colouring antocyanidins (delphinidin, cyanidin) were also detected. The strong astringent activity is due to the high content of tannins (*Sendra*, 1963). The amount of the above mentioned components are not given in the publications. Dmitruk and co-workers were the first in 1985, who managed to find coumarins in the plant in the amount of 0.26–0.4%. Phenol compounds are considered to be "multifunctional antioxidants" (*Laughton* et al., 1989; *Aruoma* et al., 1990). They are able to scavenge singlet oxygen, and thus lower the local oxygen concentration (*Beutner* et al., 2001). They take part in chelating metal ions (*Brown* et al., 1998), and can also block the activity of some enzymes responsible for oxidation (*Cos* et al., 1998).

Prunella vulgaris contains essential oil (0.4–0.6%) too, in which the main components are d-camphor and d-fenchone (bicyclic monoterpenes) (*Gildemeister Hoffmann*, 1961). Essential-oil glands formed by 2–4 bunched cells were discovered by *Dmitruk* et al. (1985) during the microscopic examination of the leaf surface. From the group of triterpenoids ursolic and oleanolic acid, and among tetraterpenoids carotinoid type constituents were also described in the plant without giving the proper percentage of these active agents (*Sendra*, 1963). Triterpenoids are effective against high blood-pressure (*Sokovnová* et al., 2003), as well as they are antibacterial (*Braca* et al., 2000) and cytotoxic to tumour cells (*Ukiya* et al., 2002). Moreover, these chemical substances also have antiviral and anti-HIV effects (*Serra* et al., 1994), they can be used against hyperglycaemia (*Taniguchi* et al., 2002) and gastric-ulcer (*Farina* et al., 1998) and they protect the liver by scavenging the free radicals (*Lin* et al., 1994).

Ursolic acid was first detected by Shimano and co-workers, and it was assumed that also the glycoside form of this compound was also accumulated by the plant. This new active agent later was called as „prunellin" (*Tabba* et al., 1989).

Therapeutic application of *Prunella vulgaris* L.

In China, the herb "clears the liver and brightens the eyes…Clears heat and dissipates nodules" (*Beusky Gamble*, 1986). In the Indian traditional medicine self-heal is used as an antipyretic, tonic, diuretic remedy. It is also applied against inflammations, diseases of the heart, difficult breathing, lung problems, bronchitis, muscular pain, diseases of the liver. *Prunella vulgaris* is also used by the Indians in North-America. Traditionally, it is applied for cleansing wounds, or as a gargle for sore and inflamed throats. The plant's extracts are considered to be a tonic against stomach problems (*Rogers*, 2000). In the Middle Ages according to Culpeper it was used "either inwardly or outwardly, for all inward wounds or ulcers whatsoever within the body, for bruises or falls, and such like hurts" (*Culpeper*, 1640).

Nowadays self-heal has been the target plant of several researches. In 1987, Lee and co-workers examined the cytotoxic principles of the ursolic acid, extracted from self-heal, since this agent is regarded as one of the main active constituents having antileukemic effect. It was proved, that the plant extract had a cytotoxic effect against mammary tumour cells, too (*Lee* et al., 1987). Chang and Yeung, in 1988, proved first that the aqueous extract of *Prunella vulgaris* – mainly its polysaccharide, the prunellin – inhibited the in vitro growth of human immunodeficiency virus (HIV). Then, in 2002 Liu and co-workers managed to describe the whole anti-HIV process initiated by the extracts of self-heal. In 2000, Liu and Ng examined the antioxidant, superoxide- and hydroxyl scavenging activities and prooxidant effect of twelve selected medicinal plants. According to the authors mainly polyphenols, flavonoids and terpenes are responsible for the antioxidant activity. As the aqueous extract of *Prunella vulgaris* is rich in phenolic compounds it was characterised by strong activity with slight prooxidant effect. *Škottová* et al. (2004) studied the effect of the phenolics-rich extracts of self-heal on blood and liver antioxidant status and lipoprotein metabolism. According to the results the plant improved the antioxidant status both in blood and liver. It was found that the extract of the plant (consisting of a mixture of triterpenoids, flavonoids, tannins and polysaccharide) had an immunosuppressive effect (*Sun* et al., 2005) while in the same year Fang and co-workers ascertained that self-heal (mainly its polysaccharides) was immune stimulatory. *Psotová* et al. (2005) analyzed the cardio-protective effect of the plant. The ethylacetate fraction (rich in rosmarinic acid) of self-heal was more effective than the medicine Dexrazoxan, applied as a control. In the latest research, *Psotová* et al. (2006) examined the photoprotective properties of self-heal on human keratinocytes. According to the results *Prunella vulgaris* can be used in skin care cometics owing to the high rosmarinic acid content. The extract protects against UVA-induced oxidative-stress.

Today, self-heal is one of the basic materials of several modern and very effective products too. Among these one of the most important was developed by a Hungarian research group. The name of the product is ROSMOL, a natural food-preservative that contains the extracts of rosemary, hyssop, lemon balm and self-heal. It was proved to have strong antioxidant activity in vitro during the storage of products containing lipid (*Lugasi* et al., 2006). Another well-known product – RUHEXIAO capsule – was developed by Chinese scientists. It is consisted of the following materials: *Prunella vulgaris*, *Ligusticum wallichii*, *Bupleurum chinense*, *Paeonia lactiflora* and tortoise-shell. In clinical trials it was effective against mammary gland proliferation with little toxic side-effects (*Lu* et al., 2002).

In 2002 a new natural herbal product – SKI 306 (extracted from *Clematis mandshurica*, *Trichosante*

kirilowii and *Prunella vulgaris*) – was examined against osteoarthritis. The results indicated that this product inhibited the proteoglycan degeneration and significantly protected the knee joint of rabbits (*Choi* et al., 2002).

Cultivation of *Prunella vulgaris* L.

There is just a very few data in the literature concerning to the cultivation of self-heal. In her preview, *Keville* (1991) writes that the plant can be propagated by sowing, cuttings or division. For the appropriate growing it needs 20–30 cm spacing, well-drained soil (soil temperature must be above 21 °C) with the pH 6-7. The germination of the seeds can take 1–3 weeks. It prefers sunny position. The seeds of the plant are drafted by the wind, so it can easily become a weed.

Macek Leps (2003) noticed that self-heal, in its natural habitat prefers vegetative reproduction. Similarly to mint species the plant grows stolons and in adventitious conditions it develops more stolons and shorter internodes.

In Germany, in 1999 new research projects were started focusing on the possibility of cultivation of several Chinese medicinal plants. According to the results in the case of self-heal Central-Europe was signed to be the most appropriate place for cultivation (*Blaszczyk*, 1999). In 2002, continuing the research work on selected Chinese medicinal plants it was ascertained, that in two-year periods good drug yields of self-heal can be achieved. Nevertheless, they have pointed out that drug production is highly affected by the growing year (*Bomme* et al. 2006).

Results of cultivation trials in Hungary

In our own research work we have established populations by using German seed in the experimental field of the Department, in Soroksár. Seeds were sown into propagation trays in February 2005 and 2006. The seedlings were planted into the open field in May, with the spacing of 20 x 20 cm. The plants were often watered by spraying irrigation during summer. In the first year only a few individuals flowered,

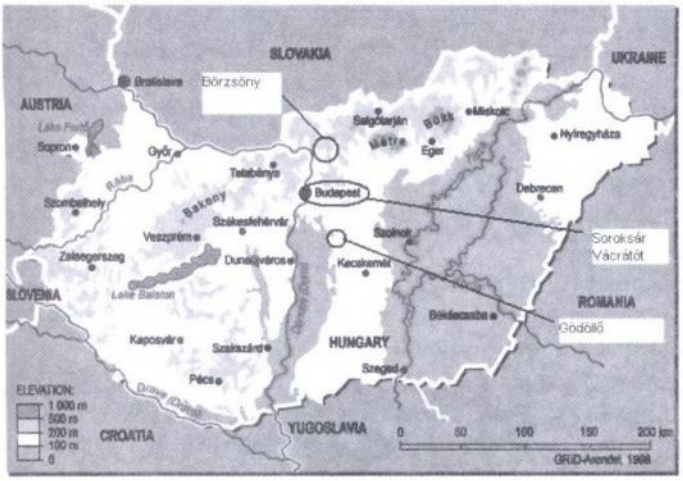

Figure 1 Natural habitats of the collected *Prunella vulgaris* L. in Hungary

Table 1 Morphological characteristics of the examined *Prunella vulgaris* L. populations Values are expressed in mean±standard deviation

Population/ Locations	Length of flowering stems (cm)	Length of spikes (cm)	Number of nodes
K	20.50±5.47	1.70±0.75	2.50±0.71
B	16.5±4.00	1.90±0.74	2.2±0.45
KR	26.1±7.48	2.58±1.04	2.80±0.63
G	15.45±4.29	1.47±0.42	2.60±0.52
SB	10.70±2.47	1.12±0.47	3.30±0.48
V	17.05±3.89	1.75±0.35	3.10±0.88
SV1	9.67±2.89	2.50±0.87	1.33±0.58
SV2	33.80±6.37	2.60±0.84	4.50±0.53

(K: Katalinvölgy, B: Börzsönyliget, KR: Királyrét, G: Botanical garden-Gödöllő, SB: Botanical garden-Soroksár, V: Vácrátót, SV1: one-year-old cultivated population-Soroksár, SV2: two-year-old cultivated population-Soroksár)

however, in the second year we observed very long flowering stems comparing to those of the wild populations. The wild self-heal herbage collection was done from June to August, 2006, from the following Hungarian habitats: Katalinvölgy, Börzsöny Hills (K); Börzsönyliget, Börzsöny Hills (B);

Figure 2 Prunella vulgaris L. in its natural habitat, Grassalkovich Castle Park, Gödöllő, Hungary

Figure 3 Flowering two-year-old Prunella vulgaris L. under cultivation. Soroksár, Hungary

Királyrét, Börzsöny Hills (KR); Grassalkovich Castle Park, Gödöllő (G); Soroksár, Botanical Garden (SB); Vácrátót, Botanical Garden (V) (*Figure 1*). The identification of the appropriate plant species was carried out by following the botanical description of SIMON (2000). For morphological observations, the length of the blooming sprouts and spikes, and number of nodes were determined on 20 randomly chosen plants. As in the wild habitats plants are growing diffusely drug yields were impossible to measure. For the characterization of growing – strength the above mentioned morphological features are given.

Among experimental circumstances the average flowering stem length of the two-year-old plants was 33.80 cm, while in the natural habitats it was between 10.70–26.10 cm (*Table 1*, *Figures 2–3*). The cultivated two-year-old plants were also characterised by longer flowers (average length 2.60 cm, in the wild populations the length of the flowers varied between 1.12–2.58 cm) (*Table 1*). According to these results self-heal can be easily cultivated; and the flowering sprouts should be harvested in the second year.

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