sciendo

herba polonica
International journal edited by the Institute of Natural Fibres and Medicinal Plants
Vol. 65 No. 3 2019

Received: 2019-08-01
Accepted: 2019-09-20
Available online: 2019-09-30

DOI: 10.2478/hepo-2019-0018

REVIEW PAPER

Fireweed (*Epilobium angustifolium* L.): botany, phytochemistry and traditional uses. A review

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Summary

Fireweed (*Epilobium angustifolium* L., *Onagraceae*) is one of important medicinal plants used especially in the treatment of urogenital disorders, including benign prostatic hyperplasia (BPH) and prostatitis. The therapeutic effects of *E. angustifolium* extracts comprise antiproliferative, anti-inflammatory, immunomodulatory, antioxidant, and also antimicrobial activities. The aim of the present review was to provide the information on the botany, phytochemistry and traditional uses of *E. angustifolium*. This plant is a widespread circumboreal species of North America and Eurasia, tolerant in terms of habitat conditions, and often occupying man-made open habitats. Phytochemical studies on *E. angustifolium* resulted in the identification of about 250 different metabolites, including about 170 substances found for the first time in this plant in the last six years (2014–2019). Fireweed has an abundance of polyphenolic compounds, particularly ellagitannins. Oenothein B and quercetin-*3*-*O*-glucuronide are proposed as markers for the identification and standardization of the plant raw material. *E. angustifolium* exhibits significant phytochemical variability in relation to the geographical origin, plant part and time of harvest/vegetation phase. Survey of the ethnobotanical literature showed that the above-mentioned species has been widely used not only as a medicinal, but also as an edible, honey and decorative plant.

Key words: ***rosebay willowherb, phytochemical composition and variability, ellagitannins, oenothein B, ethnobotany***

Słowa kluczowe: ***wierzbówka kiprzyca, skład i zmienność fitochemiczna, elagotaniny, oenoteina B, etnobotanika***

INTRODUCTION

Nowadays, the consumption of herbal products and the popularity of dietary supplements are growing throughout the world. Nutraceuticals or functional foods are intended to improve the state of health and well-being and to reduce the risk of nutrition-associated diseases, including cancer prevention. Fireweed (*Epilobium angustifolium* L.) is an important medicinal plant used in the pharmaceutical, food and cosmetic industries. It is particularly utilized in the treatment of benign prostatic hyperplasia (BPH) and prostatitis [1]. Today, dietary supplements or nutraceuticals containing *E. angustifolium* components are widely available in many countries in the form of tea, capsules, pills, water and alcohol extracts/tonics. Fireweed extracts are also utilized in creams, shampoos and other cosmetic products, especially for acne.

E. angustifolium is a rich source of phenolic compounds, especially hydrolysable tannins (ellagitannins), flavonoids, and phenolic acids [2-4]. Medicinal properties of fireweed extracts have been attributed to the synergic effect of polyphenols and the presence of the most abundant, compound – oenothein B. This substance shows various pharmacological activities, including anti-androgenic, antiproliferative, anticancer, antioxidant, anti-inflammatory, and immunomodulatory properties [5-10]. Additionally, *E. angustifolium* exhibits antimicrobial [11-15], analgesic [16] as well as photoprotective and antiaging [17] activities.

Recently, the number of publications concerning the above-mentioned species has increased significantly. Screening of the Scopus database with the keywords of '*Epilobium/Chamerion/Chamaenerion angustifolium*' found 416 document results, including 80 articles published in the years of 2014–2019. A new detailed summary is required not only for phytochemistry and pharmacology of *E. angustifolium*, but also in the case of scattered data on fireweed botany and ethnobotany.

The aim of the study was to provide an overview of information available on the botany, phytochemistry and traditional uses of *E. angustifolium*. In the botanical part, we described taxonomy, synonyms, and also morphology, ploidy, distribution and habitats of fireweed. The phytochemistry included the composition of the bioactive substances found in the plant raw material, with particular emphasis on the newly identified metabolites and with the description of the phytochemical variability of this species. In turn, the ethnobotanical characteristic aimed to present the traditional uses of *E. angustifolium* as a medicinal, edible, honey and decorative plant.

BOTANY

Taxonomy

Epilobium (*Chamerion*) *angustifolium* is classified to the *Onagraceae* family, which consists of 22 genera and approximately 650 species. The genus *Chamerion* (Raf.) Raf. ex Holub (syn. *Chamaenerion* Ség.) with eight species restricted to the northern hemisphere (mainly in Eurasia) belongs to the *Onagroideae* subfamily and *Epilobieae* tribe [18]. Relatively often, it is included in *Epilobium* L., which is the largest genus in the *Onagraceae* [19-22]. However, *Chamerion* clearly differs from *Epilobium* in terms of flower structure, leaf arrangement and other features [18, 23-25]. Molecular data also show that *Chamerion* is a separate monophyletic group of plants [26-28].

Synonyms

The Plant List [22] provides more than 40 synonyms of the species described, with three of these being the most commonly used: *Epilobium angustifolium* L., *Chamerion angustifolium* (L.) Holub and *Chamaenerion angustifolium* (L.) Scop. According to Holub [23], *Chamerion* should be considered the correct Latin name of this genus, while *Chamaenerion* is an illegitimate name. On the other hand, Sennikov [25] recently presented arguments for the restoration of the older name *Chamaenerion*. However, in

this review, the name appearing most frequently in the references will be used: *Epilobium angustifolium*.

E. angustifolium is commonly known as fireweed in the United States and rosebay willowherb in Britain [25]. Other names mentioned include: perennial fireweed, narrow-leaved fireweed, great willowherb, willow herb, flowering willow, French willow, etc. [29, 30].

Morphology and ploidy

Fireweed is an herbaceous perennial with long branched rhizomes and fleshy stolons. Green stems, frequently reddish, glabrous below and pubescent above, are erect up to 2 m high. The willow-like leaves are alternate, 3–20 cm long. *E. angustifolium* blooms from June to September, developing large raceme inflorescences consist of a number of pink (rarely white) flowers (figure 1). They are up to 3 cm in diameter, zygomorphic, epigynous with a small nectar-secreting disc, markedly protandrous. The capsules, 4–8 cm long, contain small light brown seeds (1.0–1.3 mm in length) with greyish white hairs up to 13 mm long. One plant could produce 76 000 wind-dispersed seeds per year [31-33]. The weight of 1 000 seeds is about 0.07 g [34] and without the pappus reaches about 0.05 g [35].

E. angustifolium is a variable species diverse in terms of morphology and ploidy. The diploid representing subsp. *angustifolium* (n=18) has subsessile leaves with an obtuse or subrounded base, subentire margin, and glabrous abaxial midribs, as well as subglabrous stems and usually triporate pollen. The polyploid plants of subsp. *circumvagum* (n=36, 54) are generally luxuriant with taller stems, larger leaves, flowers and pollen. They have leaves with petioles 2–7 mm long, a cuneate base, denticulate margin, glabrous to very pubescent midribs, as well as strigillose stems, at least in the upper section, while pollen is usually a mixture of triporate and quadriporate grains [36, 37].

Distribution and habitats

E. angustifolium is a widespread circumboreal species occurring in the temperate zone of North America and Eurasia at a latitude from 25° to 70° north. It grows both in the lowlands and in the mountains: in Switzerland to 2530 m, in North America to 3960 m, and in the Himalayas to an altitude of 4850 m a.s.l. Diploid populations occur in colder climates: in Greenland, Canada, Alaska, Siberia and northern Europe, and also tend to develop at higher altitudes. Tetraploids grow in warmer and drier habitats occupying the southern part of the range in Eurasia and North America [18, 38, 39]. In turn, triploids (n=27) appear in mixed-ploidy populations of border areas [40]. The hexaploid cytotype was reported only in central Japan and the Yunnan province of China [36, 41].

Fireweed is a common plant occupying man-made open habitats, such as deforested or burned

Figure 1

Epilobium angustifolium in the blooming phase (Krajewice, Poland)

areas, roadsides and railway embankments. This species also occurs on the edge of forests and thickets, along streams, on rocky and scree slopes, as well as in mountain meadows. *E. angustifolium* prefers nutrient-rich and mesic-moist soils, but it is tolerant in terms of habitat conditions [31-33, 36].

PHYTOCHEMISTRY

Chemical composition

Phytochemical studies on *E. angustifolium* resulted in the identification of about 250 different metabolites, of which about 170 substances have been found for the first time in this plant in the last six years [2, 3, 8, 42-50] (table 1). Polyphenols are the most abundant and are represented by flavonoids, phenolic acids, and hydrolysable tannins (ellagitannins). Other constituents such as lignans, steroids, triterpenoids, fatty acids, and essential oils, have also been identified. The structures of some bioactive compounds are given in figures 2 and 3.

Flavonoids

About 50 different flavonoids and their derivatives have been identified in fireweed extracts. They include flavonol aglycones: kaempferol, quercetin and myricetin, which contain a single sugar moiety of glucuronic acid, rhamnose, glucose, arabinose or galactose. Quercetin-*3*-*O*-glucuronide is the most dominant and characteristic flavonoid of *E. angustifolium*, contrary to myricetin-*3*-*O*-rhamnoside (myricitrin), which is the main flavonoid of the other *Epilobium* species [51]. Recently, flavonol glycoconjugates acylated with hydroxycinnamic acids were also detected [50].

Phenolic acids

Phenolic acids and their derivatives are one of the dominant groups of phenolics found in *E. angustifolium*, and are important contributors to the antioxidant [48] and therapeutic potential against BPH of this species [49]. A great variety of these compounds, including 39 substances (e.g., caffeic, ellagic, ferulic, gallic, protocatechuic acids and caffeoylquinic acid isomers), has been found in the fireweed [8, 43, 48-50].

Hydrolysable tannins

E. angustifolium contains a high level of ellagitannins, which represent about 15% of the dry mass of the herb [2]. Ellagitannins are bioactive polyphenols belonging to the class of hydrolysable tannins, characterized as hexahydroxydiphenoyl (HHDP) esters of sugar, mainly glucose. Both monomeric (e.g., tellimagrandin I, gemin D) and macrocyclic ellagitannins have been isolated from *E. angustifolium* herb [2, 3]. Oenothein B is a dimer which includes two molecules of tellimagrandin I monomers. Other macrocyclic ellagitannins – oenothein A (trimer) and larger ellagitannins up to heptamers – were also detected and characterized using the UPLC-MS/MS method [2]. Oenothein B is a principal bioactive compound and the most abundant ellagitannin, whose content ranges up to 50% of the total mass of oligomeric ellagitannins in the extract [2]. Depending on the plant origin and harvest time, oenothein B concentration in the raw material varies from 2 to 4.5% [50, 52, 53]. This compound has been considered to be the main contributor to the anti-androgenic, antiproliferative and anticancer, antioxidant, anti-inflammatory as well as antimicrobial effects of *E. angustifolium* extracts [4]. Therefore, analysis of oenothein B and quercetin-*3*-*O*-glucuronide contents is recommended to provide markers and a basis for the plant raw material standardization [4, 6, 43, 51].

Lignans

Recently, phytochemical analyses of ethyl acetate and *n*-butanol extracts obtained from the aerial parts of *E. angustifolium* resulted in the identification of five lignans, including pinoresinol and its derivatives, and salicifoliol. However, these compounds did not show the anti-BPH activity [49].

Steroids, terpenoids and fatty acids

Besides polyphenols, the aerial parts of *E. angustifolium* contain a lipophilic fraction rich in steroids, terpenoids and fatty acids. The presence of campesterol, cholesterol, stigmasterol as well as β-sitosterol and its derivatives was reported [49, 50, 54-56]. Fatty acids (41 identified compounds) as well as triterpenes (e.g., oleanolic, pomolic and ursolic acids) are the main components of the lipophilic fraction of *E. angustifolium* extracts [42].

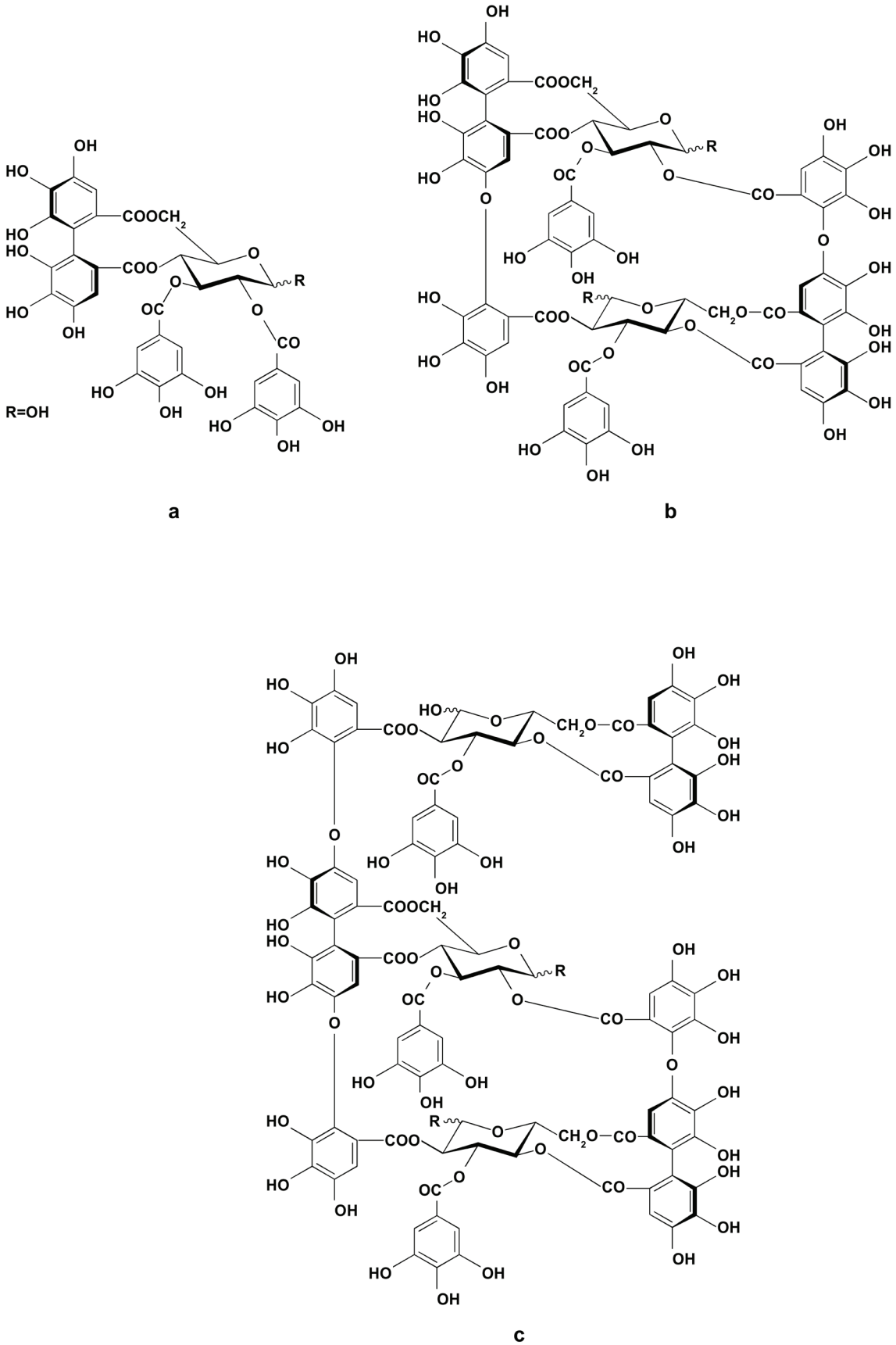

Figure 2

Chemical structures of tellimagrandin I (a), oenothein B (b), and oenothein A (c)

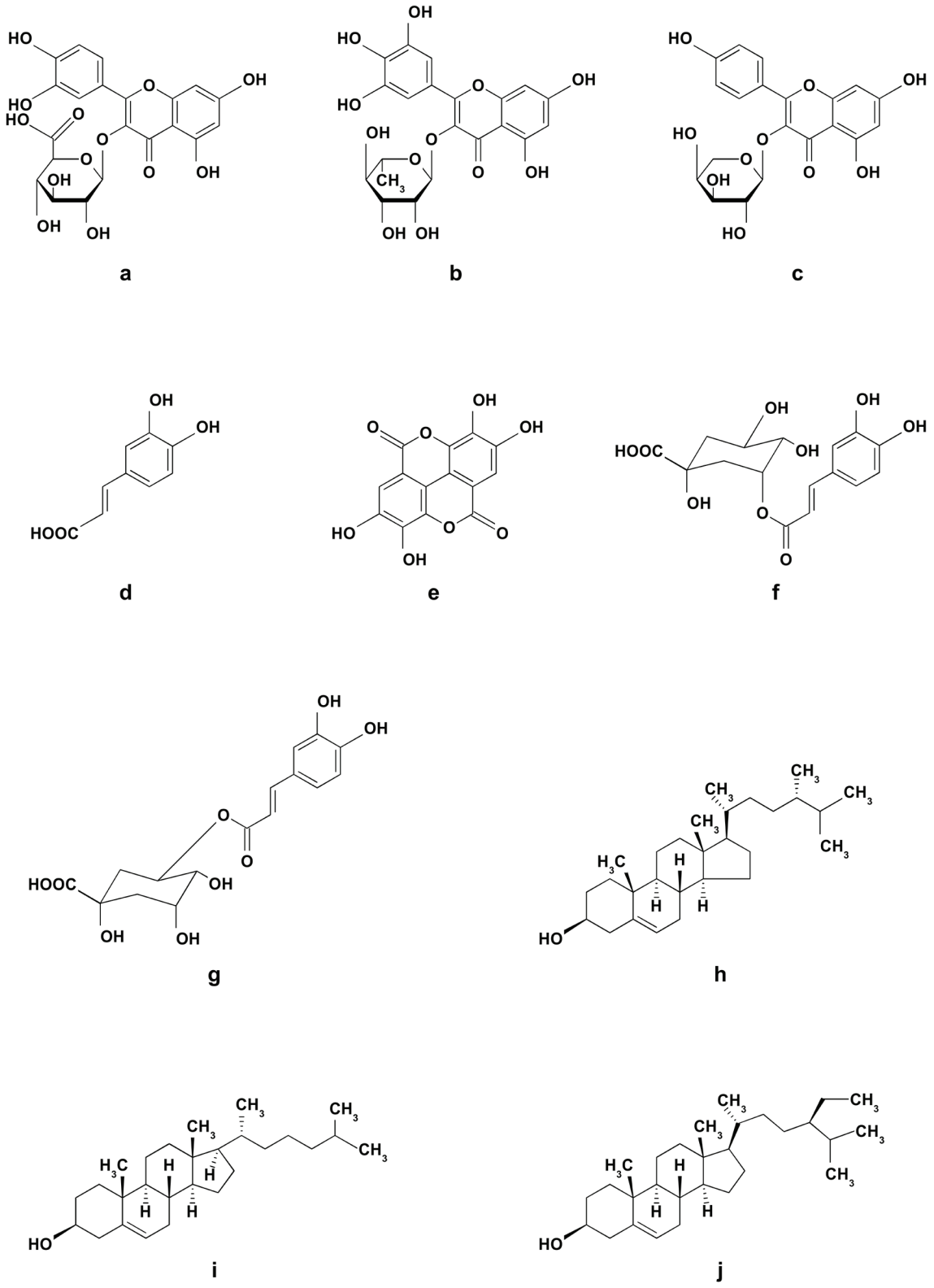

Figure 3

Chemical structures of quercetin-3-*O*-glucuronide (a), myricetin-3-*O*-rhamnoside (b), kaempherol-3-*O*-arabinoside (c), caffeic acid (d), ellagic acid (e), 3-*O*-caffeoylquinic acid (f), 5-*O*-caffeoylquinic acid (g), campesterol (h) cholesterol (i), and *β*-sitosterol (j)

Table 1

Chemical compounds identified in *Epilobium angustifolium*

Group of compounds	Compounds
Flavonoids	Annulatin-*O*-arabinoside*, annulatin-*O*-glucoside*, annulatin-*O*-rhamnoside*
	Kaempferol, kaempferol-3-*O*-arabinoside (juglalin), kaempferol-3-*O*-glucoside*, kaempferol-7-*O*-*p*-coumaroylglucoside*, kaempferol-3-*O*-(6"-*p*-coumaroyl)-glucoside, kaempferol-3-*O*-glucuronide, kaempferol-7-*O*-glucuronide*, kaempferol-3-*O*-rhamnoside, kaempferol-7-*O*-rhamnoside*, kaempferol-3-*O*-rhamnopyranoside*, kaempferol-3-*O*-galloylhexoside*, kaempferol 8-*O*-methyl ether, kaempferol-3-*O*-[6"-(E)-*p*-coumaroyl]-mannopyranoside*
	Myricetin, myricetin-3-*O*-arabinoside, myricetin-3-*O*-galactoside, myricetin-3-*O*-galactopyranoside*, myricetin-3-*O*-glucoside (isomyricitrin), myricetin-7-*O*-glucoside*, myricetin-3,5-*O*-diglucoside*, myricetin-3-*O*-caffeoylglucoside*, myricetin-3-*O*-glucuronide, myricetin-3-*O*-rhamnoside (myricitrin), myricetin-3-*O*-pentoside*, myricetin-3-*O*-hexoside*, myricetin-3-*O*-galloylhexoside*
	Quercetin, quercetin-3-*O*-arabinoside (guajaverin), 3-*O*-methylquercetin-*O*-arabinoside*, quercetin-3-*O*-arabinofuranoside (avicularin)*, quercetin-3-*O*-galactoside (hyperoside), quercetin-3-*O*-(6"-galloyl)-galactoside, quercetin-3-*O*-glucoside (isoquercetin), quercetin-7-*O*-glucoside*, quercetin-7-*O*-caffeoylglucoside*, quercetin-caffeoylhexoside*, quercetin-7-*O*-*p*-coumaroylglucoside*, quercetin-3-*O*-*p*-coumaroylhexoside*, quercetin-3-*O*-feruloylglucoside*, quercetin-7-*O*-[galloyl]-glucoside*, quercetin-*O*-[digalloyl]-glucoside*, quercetin-3-*O*-galloylhexoside*, quercetin-3-*O*-glucuronide (miquelianin), quercetin-3-*O*-glucuronide-6"-methyl ester*, quercetin 3-*O*-(6"-*n*-butyl glucuronide)*, quercetin-3-*O*-rhamnoside (quercitrin), quercetin-7-*O*-rhamnoside*, quercetin-3-*O*-rutinoside (rutin)*
Phenolic acids and their derivatives	Benzoic acid*, 3-hydroxy-4-methoxybenzoic acid*, 3,4-dihydroxybenzoic acid (protocatechuic acid), protocatechuic acid methyl ester*, 4-glucosyloxy-3-hydroxybenzoic acid*, *p*-hydroxybenzaldehyde*, methyl *p*-hydroxy benzeneacetate*, benzyl 1-*O*-glucopyranoside*, caffeic acid, digalloyl caffeic acid*, cinnamic acid, *p*-hydroxycinnamic acid (*p*-coumaric acid)*, *p*-hydroxycinnamic methyl ester*, ellagic acid, ferulic acid, gallic acid, digallic acid*, methyl gallate*, octyl gallate, gentisic acid, 3-*O*-caffeoylquinic acid (chlorogenic acid), 4-*O*-caffeoylquinic acid (cryptochlorogenic acid)*, 5-*O*-caffeoylquinic acid (neochlorogenic acid), 4-*O*-caffeoylquinic acid methyl ester*, ethyl 4-*O*-caffeoylquinate*, methyl chlorogenat*, 3-*O*-*p*-coumaroylquinic acid, 4-*O*-*p*-coumaroylquinic acid, 5-*O*-*p*-coumaroylquinic acid, 5-*O*-coumaroylquinic acid methyl ester*, 3-*O*-feruloylquinic acid, 5-*O*-feruloylquinic acid, 3-*O*-feruloylquinic acid methyl ester*, galloylshikimic acid*, syringoylquinic acid*, valoneic acid dilactone, valoneic acid dilactone methyl ester*, 1'-monodecarboxyvaloneic acid dilactone*, vanillic aldehyde*
Hydrolysable tannins	1,6-di-*O*-Galloylglucose*, 1,2,6-tri-*O*-galloylglucose, 1,4,6-tri-*O*-galloylglucose*, 1,2,3,6-tetra-*O*-galloylglucose, 1,2,3,4,6-penta-*O*-galloylglucose, 1,2,6-tri-*O*-galloyl-4,6-HHDP-glucose, 2,3-di-*O*-galloyl-4,6-HHDP-glucose, β-glucogallin*, digalloylglucose* and its isomer*, galloylconiferolglucose*, digalloylrhamnoside*, gemin D* and its isomer*, isostrictinin*, oenothein A* and B, oxidized oenothein A derivative*, pedunculagin*, tellimagrandin I* and II*, tellimagrandin I oligomers* from tetramer to heptamer
Lignans*	Pinoresinol, pinoresinol-4-*O*-glucopyranoside, 4-ketopinoresinol, salicifoliol, (7R, 8S)-3,5'-dimethoxy-4',7-epoxy-8,3'-neolignane-5,9,9'-triol
Steroids	Campesterol, cholesterol, *β*-sitosterol, *β*-sitosterol caprate, *β*-sitosterol capronate, *β*-sitosterol caprylate, *β*-sitosterol glucoside (daucosterol), *β*-sitosterol (6"-*O*-acetyl)-glucoside, *β*-sitosterol palmitate, *β*-sitosterol propionate, stigmasterol
Triterpenes	Betulinic acid*, corosolic acid, maslinic acid, oleanolic acid, acetyl oleanolic acid*, oleanonic acid*, pomolic acid*, ursolic acid, acetyl ursolic acid*, ursonic acid*, urs-12-ene-2α,3-diol*
Fatty acids	Arachic acid*, arachidic acid, behenic acid, capric acid, caproic acid, caprylic acid, cerotic acid, tricosanic acid*, tetracosanic acid*, pentacosanic acid*, hexacosanic acid*, heptacosanic acid*, octacosanic acid*, nonacosanic acid*, heneicosanic acid*, 2-hydroxytricosanic acid*, 2-hydroxytetracosanic acid*, 2-hydroxyhexacosanic acid*, 2-hydroxyoctacosanic acid*, pentadecanoic acid*, nonadecanoic acid*, hexadecanedioic acid*, octadecanedioic acid*, pentadecenic acid*, triacontanic acid*, 2-hydroxytriacontanic acid*, eicosenoic acid, eicosandioic acid*, lauric acid, lignoceric acid, linoleic acid, α-linolenic acid, γ-linolenic acid*, margaric acid*, melissic acid, montanic acid, myristic acid, oleic acid, palmitic acid, palmitoleic acid*, stearic acid
Essential oil*	*ε*-Amorphene, anethole, *cis*-anethole, *trans*-anethole, dihydroapofarnesal, *cis*-arbusculone, benzyl alcohol, *β*-bisabolene, *β*-bourbonene, *γ*-cadinene, *δ*-cadinene, *α*-caryophyllene, *β*-caryophyllene, *α*-copaene, *β*-cubebene, decanal, tridecane, tetradecane, *n*-decane, 2,6-dimethyl-7-octen-4-one, *n*-dodecane, *γ*-elemene, estragole, eugenol, trans-*α*-farnesene, *n*-hexadecanol, *trans*-2-hexenal, *cis*-3-hexenol, *cis*-3-hexenyl hexanoate, *cis*-3-hexenyl pentanoate, *β*-ionone, isogermacrene D, isopentyl butyrate, 3-methylbutyl-2-methylbutyrate, 2-methyl-*cis*-3-hexenylbutanoate, *cis*-3-hexenyl isobutanoate, *cis*-3-hexenyl butyrate, linalool, pelargol, menthol, nonanal, *cis*-3-hexenol propanoate, *cis*-3-hexen-1-yl-2-methylcrotonate, phenethyl alcohol, phenylacetaldehyde, dihydromyrcenol, tetrahydrofurfuryl propionate, *γ*-terpinen-7-al, vomifoliol
Others	Abscisic acid*, L-ascorbic acid, 2-hydroxybenzothiazole*, 1H-indole-3-carboxylic acid methyl ester*, ceryl alcohol, chamaenerolide A*, charenol, chanerozan, choline, excavatine B*, benzofuran-2-carboxaldehyde*, 5-hydroxymethyl-2-furancarboxaldehyde*, (E)-4-(5-(hydroxymethyl) furan-2-yl)but-3-en-2-one*, methyl 1-(2-oxo-4-quinolyl) formate*, hematinic acid methyl ester*, loliolide*, *n*-nonacosan, *n*-butyl pyroglutamate*, serine, threonine

* – chemical compounds identified in *E. angustifolium* for the first time in the last six years (2014–2019) [2, 3, 8, 42-50].

Essential oils

Kaškonienė *et al.* [8, 45] identified nearly 50 different compounds in essential oils of fireweed (table 1). Anethole and caryophyllenes were the most frequent constituents of the essential oil obtained from plants growing in Lithuania, and they divided specimens into two chemotypes [45].

Phytochemical variability

Fireweed is characterized by significant inter-population variability. Investigations of Kaškonienė *et al.* [8, 45] showed that the total content of phenolics and flavonoids in *E. angustifolium* herb harvested in the massive blooming phase from different Lithuanian populations varies from 70.6 to 144.5 mg/g and from 14.3 to 41.0 mg/g, respectively. In turn, the levels of these compounds in the samples consisting of leaves and flowers, and obtained from 10 Finnish populations, were 151–206 mg/g and 5.8–16.6 mg/g. Additionally, the inter-population variability was strongly expressed in the ratio of oenothein B and A as well as in flavonoid abundance, especially myricetin-3-*O*-glucoside and myricetin-3-*O*-glucuronide [3]. The phytochemical variation of *E. angustifolium* increases when different plant parts are analyzed, and the raw material is collected in various development phases (table 2). Generally, the highest polyphenol content was recorded in the massive flowering phase [3, 44, 47, 50, 57]. Flowers and inflorescences are distinguished by high amounts of flavonoids [3, 44, 47]. It was found that flavonoids and ellagitannins exhibit the most specific distribution pattern within the whole plant [3]. Flowers contained 10% more oenothein B and half as much oenothein A as leaves.

TRADITIONAL USES

E. angustifolium is an interesting medicinal and wild edible plant of the Northern Hemisphere. Its aerial parts (herb and leaves) have been used in European folk medicine to treat stomach disorders, liver and prostate gland inflammation as well as kidney and urinary tract diseases [58, 59]. Traditional application of this plant in phytotherapy also includes migraine headaches, insomnia, anaemia, delirium tremens, infections, colds, etc. Externally, fireweed is used as antiphlogistic and antiseptic agent for treating mycoses, minor burns, skin rashes, ulcers, wounds as well as inflammation of the ear, nose, and throat [4, 12].

In the USA, usage of *E. angustifolium* is recommended by herbalists in the case of colic with chronic, non-inflammatory diarrhea, gastroenteritis, vomiting, dysentery, and prostatitis [60]. In Russia, fireweed tea is often consumed as a remedy for stomach ulceration, gastritis, and sleeping disorders [61, 62]. In the 19th century, an infusion prepared from fermented leaves of *E. angustifolium*, called Ivan or Koporye tea, was popular in England and other Western European countries, and it constituted a very important export commodity of the Russian Empire. In turn, fireweed roots and stems are used in Chinese medicine for treatment of traumatic injury, subduing inflammation, and menstrual disorders [49].

A survey of ethnobotanical literature shows that medicinal properties of *E. angustifolium* have been well known by the North American indigenous peoples, especially in Canada and Alaska. The First Nations in northern Ontario used it to treat inflammation, burns, boils, sores, rashes, mouth ulcers, and yeast infections [63]. Among the Cree, macerated roots were applied to boils or infections, and leaves of this species were plastered on bruises. A tea from the whole plant was prepared by the Woods Cree of Saskatchewan against intestinal parasites, and crushed roots were used to boils, abscesses, and wounds. A decoction of fireweed herb was made in parts of Alaska and throughout the Arctic to initiate secretion of breast milk. In turn, the Cheyenne of Montana applied a tea from roots and leaves to rectal haemorrhage [64].

E. angustifolium has been widely utilized as a vegetable. Its young shoots, harvested in spring before blooming, were the source of the sweet and succulent raw pith or after cooking they were eaten like asparagus [30]. The unopened buds were added to salads, or pickled like capers [64], whereas the petals were used for jelly [65]. The Inuit consumed underground plant parts, after boiling [64]. In turn, the Saami occasionally collected the leaves of fireweed, mainly for mixing it with reindeer milk. In famine years, this plant has been eaten by the settlers in northern Sweden. Fireweed was also reported in the 19th century among emergency bread additives [66].

Due to the mass occurrence and blooming, *E. angustifolium* belongs to the important honey plants in Canada and Russia (especially Siberia). In Alaska, a sugar syrup prepared with boiled clover and fireweed blossoms is also known under the same name of fireweed honey [67]. In this

Table 2

Phytochemical variability of *Epilobium angustifolium* (mg/g) in relation to the plant part and time of harvest/vegetation phase

Source of variability	Content of			Plant part	Harvest time	Reference: [57]
	Polyphenols	Tannins	Flavonoids			
Plant part and harvest time	40.6–85.0	77.2–162.8	0.05–0.19	Roots	From May to October (Estonia)	Conclusion: Summer (July-August) is the optimal time of harvest of the plant raw material.
	55.9–83.3	27.3–149.9	0.06–0.21	Stems		
	27.6–63.8	160.6–414.2	1.63–2.35	Leaves		
	34.1–34.7	279.0–361.5	1.55–2.09	Flowers		
	35.4–46.7	175.4–202.1	0.68–1.22	Fruits		

Source of variability	Content in herb during vegetation		Content in different parts of plants			Reference: [44]
	Flavonoids	Vegetation phase	Flavonoids	Plant part	Vegetation phase	
Vegetation phase and plant part	3.39	Intensive growing	12.57	Flowers	Massive blooming phase	Conclusion: Flowers and the herb in the massive blooming phase are the most valuable raw material.
	9.03	Flower buds	6.27	Leaves		
	11.12	Massive blooming	2.26	Stems		
	9.10	Ripening of fruits				
	7.56	End of vegetation				

Plant part	Content of individual flavonoids during the massive blooming phase					Plant part	
	Hyperoside	Myricetin	Quercitrin	Quercetin	Kaempferol		
	2.34	8.75	1.45	0.02	0.02	Flowers	Conclusion: Myricetin is the dominant flavonoid in flowers.
	4.43	0.65	1.14	0.04	0.02	Leaves	
	1.76	0.12	0.37	0.01	0.01	Stems	

Source of Variability	Content of				Plant part	Reference: [3]
	Oenothein B	Oenothein A	Neochlorogenic acid	Quercetin-3-*O*-GlcA		
Plant part	83.37	25.12	1.11	1.61	Flowers	Conclusion: The inflorescence apex exhibits the highest content of oenothein B and A, while the leaves are the richest in neochlorogenic acid and quercetin-3-*O*-glucuronide.
	75.44	22.83	1.10	1.49	Flower buds	
	66.09	43.18	4.71	5.23	Leaves	
	148.28	52.14	1.36	1.48	Apex of inflorescence	
	51.32	24.32	0.47	0.81	Bottom of inflorescence	
	17.01–26.61	11.50–16.34	0.02–0.29	0.09–0.34	Vegetative part of stem	

Quercetin-3-*O*-GlcA – quercetin-3-*O*-glucuronide.

region, rhubarb candy with fireweed vodka, jelly from fireweed blossoms and ice cream with its petals are made, too.

The stem fibres of *E. angustifolium* were used to weave of fishing nets [30]. The fresh leaves were utilized for preserving of bowstrings, whereas flowers for waterproofing of mittens and rawhide thongs [64].

Among the plants occurring in the North, *E. angustifolium* is one of the most attractive species. Because of its easy cultivation, large and numerous purple flowers and deep red autumn foliage, it occasionally grows as an ornamental. Fireweed was also chosen as the floral emblem of Yukon, and it is on the flag of this territory of Canada [65].

CONCLUSIONS

E. angustifolium is a valuable medicinal plant, used especially in the treatment of urogenital disorders: benign prostatic hyperplasia (BPH) and prostatitis. In the North (Canada, Alaska, Scandinavia, and Siberia), it has been traditionally used as an edible, honey and decorative species, too. *E. angustifolium* is a rich source of polyphenols: flavonoids, phenolic acids and ellagitannins. Phytochemical analyses resulted in the identification of about 250 metabolites, including about 170 substances found for the first time in this plant in the last six years. Two bioactive compounds: oenothein B and quercetin-*3*-*O*-glucuronide are proposed for the identification and standardization of the fireweed raw material. *E. angustifolium* is characterized by

significant phytochemical variability in relation to the geographical origin, plant part and time of harvest/vegetation phase. Flowers and the herb in the massive blooming phase are the most valuable plant raw material. The inflorescence apex exhibits the highest content of oenothein B and A, while the leaves are the richest in neochlorogenic acid and quercetin-3-*O*-glucuronide.

ACKNOWLEDGEMENTS

This work was funded by the Polish National Centre of Research and Development (grant no. PBS2/A8/23/2013) and the Polish Ministry of Science and Higher Education (contract number 205710/E-198/SPUB/2016/1).

Ethical approval: The conducted research is not related to either human or animal use.

Conflict of interest: Authors declare no conflict of interest.

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