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Lythrum salicaria L.- underestimated medicinal plant from European traditional medicine. A review.

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ABSTRACT

Ethnopharmacological relevance:

Purple loosestrife- *Lythrum salicaria* L. is an herbaceous perennial plant belonging to the Lythraceae family. It has been used for centuries in European traditional medicine. Despite Lythri herba being a pharmacopoeial plant material (Ph. Eur.), *Lythrum salicaria* popularity as a medicinal plant has recently declined. The aim of the paper is to recall a traditional and historical use of *Lythrum salicaria* and juxtapose it with comprehensive view on the current knowledge about its chemical composition and documented biological activities in order to bring back the interest into this valuable plant and indicate reasonable directions of future research and possible applications.

Materials and methods:

Systematic survey of historical and ethnopharmacological literature was carried out using sources of European and American libraries. Pharmacological and phytochemical literature research was performed using Scopus, PubMed, Web of Science and Reaxys databases.

Results:

The review of historical sources from ancient times till 20th century revealed an outstanding position of *Lythrum salicaria* in traditional medicine. The main applications indicated were gastrointestinal tract ailments (mainly dysentery and diarrhea) as well as different skin and mucosa affections. The current phytochemical studies have shown that polyphenols (*C*-glucosidic ellagitannins and *C*-glucosidic flavonoids) as well as heteropolysaccharides are dominating constituents, which probably determine the observed pharmacological effects. The extracts and some isolated compounds were shown to possess antidiarrheal, antimicrobial, anti-oxidant, anti-inflammatory and anti-diabetic activities.

Conclusions:

The intrinsic literature overview conclusively demonstrates that *Lythrum salicaria* L. used to be considered as an exceptionally effective remedy in European traditional medicine. Despite its unquestionable important position from unknown reasons its popularity has been weakened during the past few decades. Unfortunately the contemporary pharmacological research is still insufficient to support its thoroughly described traditional uses. The necessity of complex studies regarding modes of action, which would directly refer to *Lythrum salicaria* main traditional applications- gastrointestinal tract ailments, is strongly underlined.

Keywords:

Lythri herba, dysentery, diarrhea

Contents:

1. Introduction

European traditional medicine is currently in a state of decline. The traditional knowledge about European plants healing properties was eroded by the deep economical and social changes of the past few decades. Many of the medicinal plants being popular for centuries are today superseded by synthetic pharmaceuticals. Research into native medicinal plants that are presently underused in officinal medicine by physicians is a promising strategy, which may lead to the development of future innovative and sustainable pharmaceuticals (Quave et al., 2012).

Purple loosestrife- *Lythrum salicaria* L. is native to Europe, Asia and Northern Africa (Wichtl, 2004). Reportedly introduced to USA in the early 1800s via ships' ballast and livestock. Popularly cultivated for its ornamental and pharmacological values, *Lythrum salicaria* nowadays is a main invasive plant to North American wetlands. It is considered as one of the 100 worst invasive alien species in the world by the International Union for the Conservation of Nature (Invasive Species Specialist Group) (Lavoie, 2010).

Lythri herba monograph was taken from French Pharmacopoeia for introduction in European Pharmacopoeia. However, still is not listed by the European Medicines Agency's Committee (EMEA) on Herbal Medicinal Products as well as not included in European Scientific Cooperative on Phytotherapy (ESCOP) monographs. Despite important position in historic and folk medicine nowadays its preparations lost their previous popularity and are hardly available on the market.

The aim of the presented review is to bring back the interest into *Lythrum salicaria* as a valuable medicinal plant originating from European traditional medicine. Conducted survey could allow indicating potential applications and reasonable directions of future research, which would derive from documented empirical observations.

To accomplish the undertaken task, traditional and historical sources regarding use and research conducted on *Lythrum salicaria* were recalled and elaborated. Critical evaluation of documented biological activities, especially in terms of their relation to established traditional use and current pathophysiological knowledge was performed. In order to point out compounds potentially responsible for biological effects phytochemical studies review was conducted followed by discussion of standardization methods validity, compounds' metabolism and specificity of their biological activities.

2. Methods

The systematic survey of historical and ethnopharmacological literature was carried out using sources of European and American libraries. Pharmacological and phytochemical literature research was performed using Scopus, PubMed, Web of Science and Reaxys databases. The terms used in searches included the Latin synonyms according to the Plant List (See section 3.) as well as historical and current names listed in Table 1 and 2.

3. Botanical profile and taxonomy

Lythrum sp. is a one of the 32 genera in the Lythraceae family. Genus *Lythrum* comprises of 30 species of herbaceous annual or perennial flowering plants. *Lythrum salicaria* L. synonyms according to The Plant List (2015) are:

Chabraea vulgaris Bubani

Lythrum anceps (Koehne) Makino

Lythrum argyi H. Lév.

Lythrum intermedium Ledeb. ex Colla

Lythrum tomentosum Mill.

According to Flora Europea (2010) *Lythrum salicaria* is an erect perennial herb, 0.5-1.5 m high, subglabrous to densely grey pubescent. Stem with 4 or more raised lines, sparingly branched. Leaves mostly opposite or in whorls of 3 (but the upper ones sometimes alternate), ovate to lanceolate-oblong, acute, sessile, truncate and semi-amplexicaul at base. Flowers trimorphic, in whorl-like cymes in the axils of small bracts, forming long, terminal spikes. Hypanthium 4.5 × 1.5-2 mm, broadly tubular; epicalyx-segments 2.5-3 mm, subulate, longer and narrower than the deltate sepals. Petals *c.* 10 mm reddish-purple. Stamens 12, some or all exserted. Capsule 3-4 mm, ovoid.

Following Ph. Eur. 8.0 characteristic features of powdered herb are the thick-walled one- to two-celled trichomes of the lower leaf surface and the thin-walled hairs of the calyx tips; other features include the anomocytic stomata, calcium oxalate crystals, purple-violet fragments of the corolla and pollen grains with three pores.

4. Traditional uses

4.1. History of therapeutic uses and research

Historical and current traditional names of *Lythrum salicaria* and its preparations found in a cited literature are listed in Table 1. Historical Latin names are given in Table 2.

Table 1.

Historical and current common names of *Lythrum salicaria* and its preparations.

Country/region	Common names
Bosnia and Herzegovina	potočnjak
China	Qian Qu Cai
Czech Republic	kyprij obecný
Denmark	pilebladet kattehale
Finland	rantakukka
France	salicairé à épi, lysimachie rouge, salicaire officinale, salicaire commune
Germany:	Brauner Weiderich, Rother Weiderich, Großes/Gemeines Blutkraut, Blutweiderich, Gemeiner Weiderich, Stolzer Heinrich, Kattsteert
Great Britain	purple loosestrife, blooming sally, purple willow-herbe, rainbow weed, spiked lythrum, salicaire, purple spiked loosestrife, bouquet violet, purple spiked willowstrife
Hungary	füzény
Iran	farandal
Italy	acquarola, riparella, salcerella, salicaria, spergola, verga rossa, canestrell
Japan	ezo-misohagi
Kamchatka	kipri
Lithuania	raudoklé
Netherlands	partijke
Norway	kattehale
Poland	krwawnica pospolita, płaczek, biedrzeniec, sowia strzała, wodohlad, wilczy ogon, lisia ogonia, wierzbienica
Portugal	erva carapau, carapauzeiro
Romania	răchitan
Russia	плакунЬ, плакун- трава, чальчак, или дербенник
Spain	sumidad florida de salicaria, beherantzako bedarra, hierbas de la cagalera, salicaria, makilbelarra, herba de Sant Antoni, té de brazal
Sweden	fackelblomster, fackelros
Turkey	tibbi hevhulma

Table 2.

Historical Latin names of *Lythrum salicaria.*

Lysimachia purpurea (Pharm.)
Salicaria vulgaris purpurea (Tournefort)
Lysimachia spicata purpurea, forte Plinii (C.B.)
Lysimachia purpurea spicata (Ger. Park.)
Pseudolysimachium purpureum alterum (Dod.)
Lysimachia purpurea quibusdam spicata (J.B.Raii)
Lythrum foliis oppositis (Roven)

Salicaria spicata (Lamk.)
Salicaria vulgaris (Moench.)

Lythrum salicaria L. is a medicinal plant, which has been well known since ancient times. Its Latin name originated from Greek word lythron (λυθρον) meaning clotted blood referring probably to its hemostatic properties or to the color of the flowers and salicaria due to the shape of the leaves resembling those of willow species (*Salix* sp.) (Desmartis, 1857; Senning, 2007; Valmont de Bomare, 1775). Initially it was named *Lysimachia purpurea spicata* Bauh. Pinax.; then Tournefort first introduced the name *Salicaria vulgaris purpurea* Tourn.; finally Linne gave the plant name *Lythrum salicaria* L. which is used nowadays (Linnaei, 1737; Martin and Martin, 1850; Tournefort, 1694).

Its medicinal properties were described by Dioscorides in Materia Medica, Pliny the Elder in Naturalis Historia and Hildegard von Bingen in Causae Curae (Hildegard von Bingen, 1903; Pliny the Elder, 1906). However from ancient times till 17th century *Lysimachia* name referred both to present genus *Lysimachia* (Primulaceae) as well as *Lythrum* (Lythraceae). In Jacob Meyderbach's Hortus Sanitatis (Johann Pruss, 1499) and Hieronymus Bock's Krauterbuch (1546) still *Lysimachia* was treated as one species, but authors of later Renaissance herbals started to clearly distinguish these plants. Monographs dedicated to *Lysimachia* referring to therapeutic use of both species were included in main European 16th and 17th century herbals listed in Table 3.

Table 3.

European 16th and 17th century herbals containing monographs referring to *Lysimachia*.

Title	Author and year
De Historia Stirpium Commentarii Insignes	Leonhart Fuchs (1542)
Petri Andreae Matthioli senensis, serenissimi Principis Ferdinandi Auchiducis Austriae &c. Medici	Pietro Andrea Mattioli (1558)
A New Herball	William Turner (1568)
Stirpium Historiae Pemptades Sex	Rembert Dodoens (1583)
A New Herball or Historie of Plants	Rembert Dodoens (1586)
Kreutterbuch deß hochgelehrten unnd weitberühmten Herrn D. Petri Andreae Matthioli	Pietro Andrea Mattioli (1590)
Herbarz Polski	Marcin z Urzędowa (1595)
Zielnik	Syreniusz (1616).
The Herbal	John Gerard (1636)
Les Commentaires de M. P. André Matthiolus sur les six livres de Pedacius Dioscoride Anazarbeen, de la Matiere Medecinale	Pietro Andrea Mattioli (1627)
Theatrum Botanicum: The Theater of Plants	John Parkinson (1640)

Crvyd-boeck	Rembert Dodoens (1644)

The data about the medicinal use are generally consistent among the listed herbals. The authors' recommendations include treatment of hemorrhages (form gastrointestinal tract, nose, wounds as well as in menorrhagia), infected wounds and dysentery.

From 18th till early 20th century many theses and reports regarding *Lythrum salicaria* use by physicians accompanied by case studies descriptions were published in leading medical journals of that time: Bulletin General de Therapeutique Medicale et Chirurgicale; Journal de Médecine, Chirurgie, Pharmacie, etc.; Journal Universel des Sciences Medicinales; La Presse Medicale; Bulletin des Sciences Pharmacologiques; L'Union Pharmaceutique. Dysentery and diarrhea were the main applications traditionally attributed to *Lythrum salicaria* (Collin, 1903; Fouquet, 1793, 1828; Martin and Martin, 1850; Paluch, 1989; Sagar, 1762; Scherbius, 1791). Its medicinal use was authorized by many case reports of European physicians describing its exceptional effectiveness (Campardon, 1883; Murray, 1793; Sagar, 1762). Treatment of diarrhea in animals was also noted (Dufour, 1919b).

Campardon (1878) described the case of a woman who brought from her village the herb of *Lythrum salicaria*, which was traditionally used there by peasants in the treatment of gastrointestinal ailments. She cured herself using infusions from leaves and stems from dysentery towards which two month lasting conventional therapy occurred ineffective. Pharmacist M. Gigon on behalf of Campardon prepared standardized extract and tincture, determining large quantities of tannins and mucus in these preparations. Following traditional use and own experience Campardon recommended its application in the treatment of dysentery, chronic and acute diarrhea, especially with accompanying intestinal atony emphasizing effectiveness in the case of enhanced secretion of inflamed mucosa. He stated that the astringency and the increase of muscle tone caused by tannins and soothing effect of mucus as factors responsible for therapeutic effect (Campardon, 1878). Preparations prescribed in the gastrointestinal tract ailments: powdered herb (3-5 g/day), infusion (30-40 g of herb/1L of water), tincture (20 drops on sugar, 4-5 times a day); syrup for children (1g of extract/ 30g of syrup). Campardon underlined the importance of *Lythrum salicaria* in the folk medicine in French rural areas and justified the need of standardized formulations development allowing its introduction to officinal medicine. The author supported his claims by the detailed descriptions of many cases of acute and chronic dysentery and diarrhea towards which classical therapy occurred to be ineffective, while the treatment with *Lythrum salicaria* powder and infusions gave very positive outcomes. The necessity of applying

preparations in the form of infusion or macerate to prevent decomposition of active principles was emphasized. Interestingly in contrast to conventional treatment of diarrhea with bismuth salts or rathania, the *Lythrum salicaria* therapy did not caused adverse effects such as constipation (Campardon, 1883).

Early experiments

Between 1915-1916 Caille and Viel (1919) isolated glucoside (unknown structure) from *Lythrum salicaria*- salicairine. In experiments conducted using *in vitro* models as well as animal trials and people suffering from chronic and acute diseases of gastrointestinal tract, several therapeutic activities of salicairine were determined: astringent properties expressed as stool consistency normalization; hemostatic activity observed as disappearance of blood from feces; decrease of pain and disappearance of pathogenic bacilli. No adverse effects, even at high doses were observed. Dumont (1920) taking into account the above properties recommended preparation containing salicairine (under the same name) in the treatment of diarrheas in children, non-specific enteritis, bacterial enteritis, dysentery caused by bacilli as well as combined with emetine in amoebiasis. Recommended doses of preparation salicairine: children: acute affections: 10-20 drops (equivalent 10-20 mg of glucoside- salicairine), chronic affections 4-10 drops; adults: acute affections 40-100 drops, chronic affections 20-50 drops. Dufour used *Lythrum salicaria* liquid extract (salicairine) at a dose of 0.5-0.6 g/day in the treatment of diarrhea in infants and in 2/3 from 100 cases observed significant recovery. In adults therapy with *Lythrum salicaria* liquid extract at a dose of 3-4 g/day occurred to be very effective in the therapy of diarrhea, acute and chronic dysentery with accompanying diarrhea and in *Shigella* sp.-caused dysentery. The author claimed that the changes in intestine mucosa caused by tannins and/or other constituents were responsible for the therapeutic effects (Dufour, 1919a; Dufour, 1917). Dedieu (1921) reported the use of salicairine in children's clinic in Toulouse in the treatment of gastrointestinal tract disorders in infants. Seventeen patients (aged 2-20 months) with acute and sub-acute gastroenteritis accompanied by fever, with infantile colic or with diarrhea caused by the overeating. The standard therapy-hydration plus calomel (mercury (I) chloride) gave no positive results towards diarrhea. When infants were given salicairine 3 drops/3 times/day the amount of stools significantly decreased as well as water content in feces. Maurin (1922) stated the effectiveness of *Lythrum salicaria* in the dysentery observed as amelioration of stool consistency and its smell followed by the general patient condition improvement. Interestingly the positive impact on gut microbiota composition was observed accompanied by disappearance of pathogenic strains. He

recommended the use in acute and chronic diarrhea, dysentery caused by *Shigella* sp., enteritis, intestine infections, gastroenteritis and green stools in children in the form of powdered herb (1 g 3-4 times/day), infusion (3-6 g/day) and aqueous extract (0.5-1 g/day).

At least two preparations of *Lythrum salicaria* were available on the French market since 1920s' Salicairine (standardized extract in the form of fluid or tablets produced by Laboratoires Legras, France) and Salitol (the liquid extract). These formulations basing on research cited above were recommended in the treatment of chronic and acute dysentery and diarrhea of different etiologies in adults and children.

In 1960' *Lythrum salicaria* was still popular as a remedy for diarrhea, especially in children and applied even in diarrheas of bacterial etiology. It was used in the form of decoction, powdered herb or standardized liquid extract. Lafon (1962) in qualitative reports on plant-derived drugs to French Pharmacopoeia enumerates astringent, cicatrizing and antidiarrheal properties of *Lythrum salicaria* flowering tops. These times amount of *Lythrum salicaria* herb used for production of galenic preparations in France reached 3-4 tones per year (Paris and Moyse, 1967).

The important position of *Lyhrum salicaria* in the therapy of gastrointestinal tract inflammation-associated ailments (especially dysentery of different etiologies) can be deduced basing on its descriptions in many 18th, 19th and early 20th century medicinal dictionaries, manuals and guidebooks listed in Table 4.

Table 4.

18th, 19th and early 20th century medicinal dictionaries, manuals and guidebooks containing information about *Lythrum salicaria* use in therapy of gastrointestinal tract ailments.

Title	Ref.
Materia Medica et Chirurgica Juxta Systema Naturae Digesta	Cranz (1762)
Dictionnaire Raisonné Universel des Plantes	Buc'hoz (1770)
Dictionnaire Raisonné Universel d'Histoire Naturelle	Valmont de Bomare (1775)
Opisanie roślin litewskich według układu Linneusza	Jundziłł (1791)
The Edinburgh New Dispensatory	Duncan (1818)
Dictionnaire des Sciences Médicales	Une Société de Médecins et de Chirurgiens (1820)
Codex Medicamentarius Europaeus	Niemann (1824)

Farmacopea Ferrarese	Campana (1825)
Handbuch für Praktische Aerzte	Richter (1826)
Encyclopédie Méthodique Médecine	Vicq-d'Azyr and Moreau (1827)
Handbuch der Medicinisch-Pharmaceutischen Botanik. Nach den Natürlichen Familien des Gewächsreiches	Nees von Esenbeck and Ebermaier (1830-1832)
Lexicon Medicum	Blancard and Kühn (1832)
Handbuch der Pharmakologie als Erläuterung Aller in der Österr. Pharmakopöe vom Jahre 1834 Enthaltenen Arzneymittel	Meyer (1835)
De Dysenteria	Zadej (1841)
Materiae Medicae Compendium	Folchi (1841)
Medizinisch-Pharmazeutische Botanik	Bischoff (1843)
L'Officine, ou Répertoire Général de Pharmacie Pratique	Dorvault (1844-1910)
Dictionnaire de Médecine de Chirurgie de Pharmacie des Sciences Accessoires et de l'Art Vétérinaire	Littre (1873-1908); Nysten (1833-1865)
American Eclectic Dyspensatory	King (1856)
Formulaire Raisonné des Médicaments Nouveaux	Reveil (1864)
Exposition Universelle de 1867 à Paris. Rapports du Jury International. L'histoire Naturelle Médicale à l'Exposition Universelle	Chatin (1867)
Dictionnaire Encyclopédique des Sciences Médicales	Dechambre (1878)
Deutsche Flora. Pharmaceutisch-medicinische Botanik	Karsten (1880-1883)
Dictionnaire Usuel des Sciences Médicales	Dechambre et al. (1885)
Commentaires Thérapeutiques du Codex Medicamentarius	Gubler (1885)
Formulaire Pratique de Thérapeutique et de Pharmacologie	Dujardin-Beaumetz and Yvon (1887)
Flore Médicale Usuelle et Industrielle du XIXe Siècle	Dupuis and Reveil (1887)
Dictionnaire de Thérapeutique, de Matière Médicale, de Pharmacologie, de Toxicologie et des Eaux Minérales. Tome Quatrième	Dujardin-Beaumetz (1889)
Les Plantes Médicinales Indigènes et Exotiques, Leurs Usages Thérapeutiques, Pharmaceutiques et Industriels	Dujardin-Beaumetz and Egasse (1889)
Plantes Remèdes et Maladies, ou la Médecine Simple et Facile à la Portée de Tous	Lehamau (1894)
Die Heilpflanzen der Verschiedenen Völker und Zeiten	Dragendorff (1898)
Précis de Matière Médicale	Collin (1903)
Les Plantes médicinales de la Picardie	Caussin (1907)

Larousse Médical Illustré	Burnier (1924)
Neues Illustriertes Kräuterbuch	Marzell (1935)
Lehrbuch der Biologischen Heilmittel	Madaus (1938)
Ziołolecznictwo i Leki Roślinne	Muszyński (1949)

***Lythrum salicaria* in epidemics**

Lythrum salicaria was effectively used in dysentery epidemics in Sweden (Murray, 1793), Boulogne (Cazin, 1858) and around Lyon (Gardane, 1773). Doctor Henri Leclerc, adjutant in army of general Ferdinand Foch during First Battle of the Marne (1914) recalled therapy of diarrheas among soldiers (which were not responding to classical therapy) with *Lythrum salicaria* infusion. He intentionally used infusion, not decoction to prevent decomposition of active ingredients (Leclerc, 1916). Dr. Gougeon documented successful treatment of dysentery in soldiers in a hospital on the military front in Rennes during World War I (Gougeon and Laumonier, 1918).

External use of *Lythrum salicaria*

The external use of *Lythrum salicaria* due to its detersive, astringent, hemostypic, wound healing and refreshing properties was recommended especially in treatment of eyes inflammation, sinusitis (rinsing nose with diluted tincture), varicose veins, hemorrhoids, menorrhagia, hemorrhages, leucorrhoea and ulcerations (Alexandre, 1829; Buc'hoz, 1770; Campardon, 1878, 1883; Collin, 1903; Kluk, 1786; Lemery, 1733; Losch, 1908; Martin and Martin, 1850; Scherbius, 1791). Moreover, Campardon (1878) recommended *Lythrum salicaria* in the treatment of chronic and acute vaginitis (decoction 30-60g herb/1L) and pruritus of different etiology as well as in the dermatitis and eczema.

Other historical uses

Single reports about *Lythrum salicaria* use in rheumatism (Kuźnicka, 1993), benign prostate hyperplasia, infections and irritations of urinary tract mucosa (Thompson, 1874), rabies (powdered root) (Kasperowski, 1858) and as a tonic and febrifuge agent (Desmarest, 1829) can be found.

4.2. Current traditional uses

Because of an overall trend of decline in local medicinal plant use especially in urban areas of northern Europe (Quave et al., 2012), the majority of reports concerning *Lythrum salicaria* current traditional use come from ethnopharmacological studies conducted in southern Europe and Near East regions. Reports about contemporary use of *Lythrum salicaria* in folk medicine are summarized in Table 5.

Table 5.

Contemporary traditional uses of *Lythrum salicaria*.

Country	Part used	Formulation	Medicinal use/disease treated	Ref.
Iran	Flower	Decoction	Astringent, antihaemorragic, tonic, cleansing. Dysentery, diarrhea, intestinal inflammation, haematuria, leucorrhoea, epistaxis, dysmenorrhea, lupus, eczema, impetigo, female urogenital inflammation	Miraldi et al. (2001)
Jordan	Leaf, seed		Haemorrhoids and internal bleeding	Al-Qura'n (2007)
Portugal	Aerial part	Decoction	Digestive, carminative. Indisposition of intestines, colic, diarrhea	Gaspar et al. (2002)
Spain	Aerial part	Decoction	Antidiarrheal	Gonzalez et al. (2010)
	Inflorescence	Infusion or decoction	Diarrhea, stomach disorders	Menendez-Baceta et al. (2014)
	Herb	Infusion	Lowering blood pressure	Pardo de Santayana et al. (2005)
	Aerial part	Infusion	Diarrhea, vomiting, gastroenteritis (in animals)	Akerreta et al. (2010)
	Aerial part	Infusion	Diarrhoea in calves	Bonet and Valles (2007)
Bosnia and Herzegovina	Root		Diarrhea, gastrointestinal tract ailments, blood circulation disorders, skin ailments	Saric-Kundalic et al. (2011)
Romania	Aerial parts	Infusion	Astringent Diarrhoea, dysentery, gastrointestinal disorders, uterine haemorrhages	Tita et al. (2009)
Italy	Fresh aerial parts		Topically as a vulnerary plaster	Di Novella et al. (2013)
Russia (southeast)	Herb	Decoction and infusion	Colitis and stomatitis	Moskalenko (1986)

5. Chemical composition

Lythrum salicaria is a rich source of polyphenols including ellagitannins, tannin related compounds, flavonoids, flavan-3-ols, phenolic acids and antocyanins. Apart from phenolics the presence of some unpolar compounds belonging to different chemical groups such as steroids, triterpenes, phthalates, coumarines was confirmed in extracts prepared form *Lythrum salicaria*. The presence of nitrogen containing constituents classified as alkaloids was also determined. Based on conducted literature research it must be noted that in all published reports only aerial parts or flowers of *Lythrum salicaria* were investigated. Up-to-date studies concerning sub-aerial parts of this plant, despite mentions of its therapeutic use, are lacking. Table 5 summarizes the key phytochemicals that were found in *Lytrum salicaria* including chemical name of constituent, its molecular weight, investigated part of the plant and proper citations. Only those chemicals that were properly identified, either by isolation and structure determination with spectroscopic methods or by chromatographic methods using chemical standards are cited in the present review. Each chemical is numbered from **1** to **70**. The chemical structures of all mentioned compounds are depicted in Fig. 1 to Fig. 10. In the case of compound **32** described in the literature as isochlorogenic acid, which corresponds to one of isomers of di-*O*-caffeoylquinic acid the sample structure was in shown in Fig. 4. The molecular masses of all depicted compounds are given in Table 6 together with their chemical structures and were rounded down to the nearest integer.

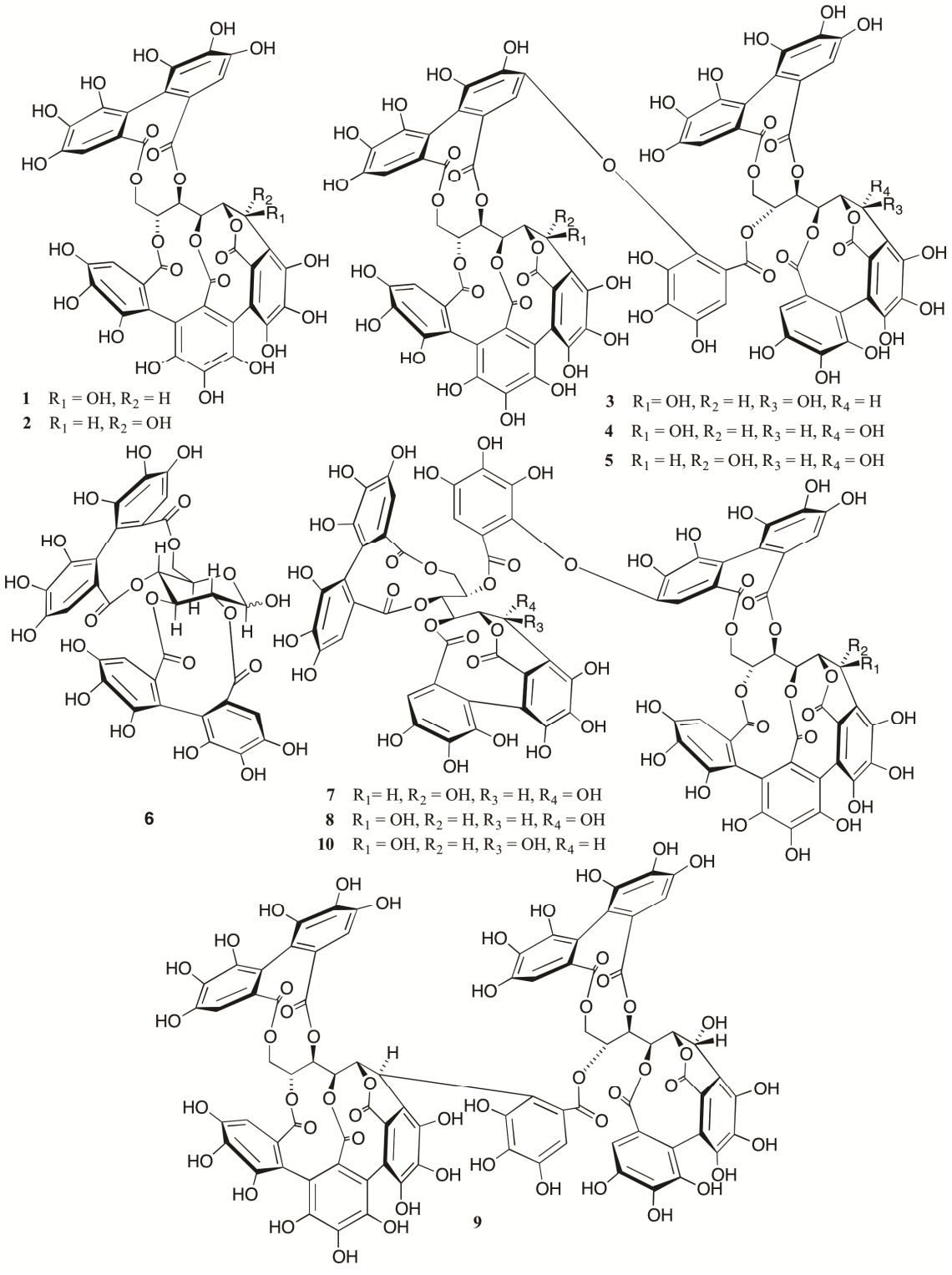
5.1. Ellagitannins

Lythri herba is known as tannin-rich plant material, but first study dealing with chemical structures of purple loosestrife ellagitannins comes from middle 1990's. Ma (1996) described for the first time five main compounds isolated from aerial parts of *Lythrum salicaria*. Four of them identified as dimeric ellagitanninns (lythrines A-D, **7-10**) turned out to be new natural products. Apart from dimeric compounds Ma (1996) isolated one monomeric constituent – castalagin (**2**). Further studies confirmed the presence of monomeric ellagitannins such as castalagin (**2**), vescalagin (**1**) and pedunculagin (**6**) in aerial parts of *Lythrum salicaria* (Granica et al., 2014; Ma, 1996; Piwowarski and Kiss, 2013; Rauha et al., 2001). In depth phytochemical investigation of *Lythri herba* recently carried out by Piwowarski and Kiss (2013) proved that it contains significant amounts of three new dimeric

compounds named salicarinins A-C (**3**-**5**), which structurally differ from those identified previously by Ma (1996) by valoneoyl interunit orientation. Chemical structures of ellagitannins described in *Lythrum salicaria* are given in Fig. 1.

According to The European Pharmacopoeia *Lythri herba* is standardized on total tannin content (quantified as pyrogallol equivalents) without taking into consideration the structural differences of dominating ellagitannins. Following this approach papers regarding quantitative analysis of *Lythrum salicaria* exstracts were usually based on total tannin/polyphenol content determination (Humadi and Istudor, 2009; Moller et al., 2009). The first qualitative analysis, which complied with the structural differences between dominating ellagitannins was performed by Granica et al. (2014) using UHPLC-CAD method. Taking into consideration the specificity of *C*-glucosidic ellagitannins' biological effects discussed in Section 7, the analytics of *Lythrum salicaria* extracts should include the structural differences between the dominating compounds, rather than only quantify their total content.

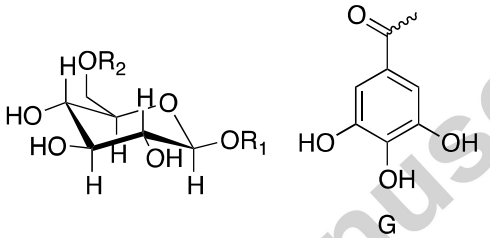
Figure 1. Chemical structures of ellagitannins compounds **1-10**.



5.2. Tannin related compounds

The only study concerning tannin related compounds occurring in aerial parts of purple loosestrife was carried out by Rauha et al. (2001). The HPLC-UV-ESI-MS analysis of 80% aqueous-methanol extract revealed that it contains several compounds classified as galloylglucose derivatives (**11**-**13**). Some HHDP-glucose and galloyl-HHDP-glucose were also detected and but only partially identified due to the lack of proper HPLC standards. This is the only report confirming the presence of this group of constituents. None of mentioned compound was isolated as a pure chemical. The chemical structures of tannin related constituents are depicted in Fig. 2.

Figure 2. Chemical structures of tannin related compounds **11-13**.



compound	R_1	R_2
11	G	H
12	H	G
13	G	G

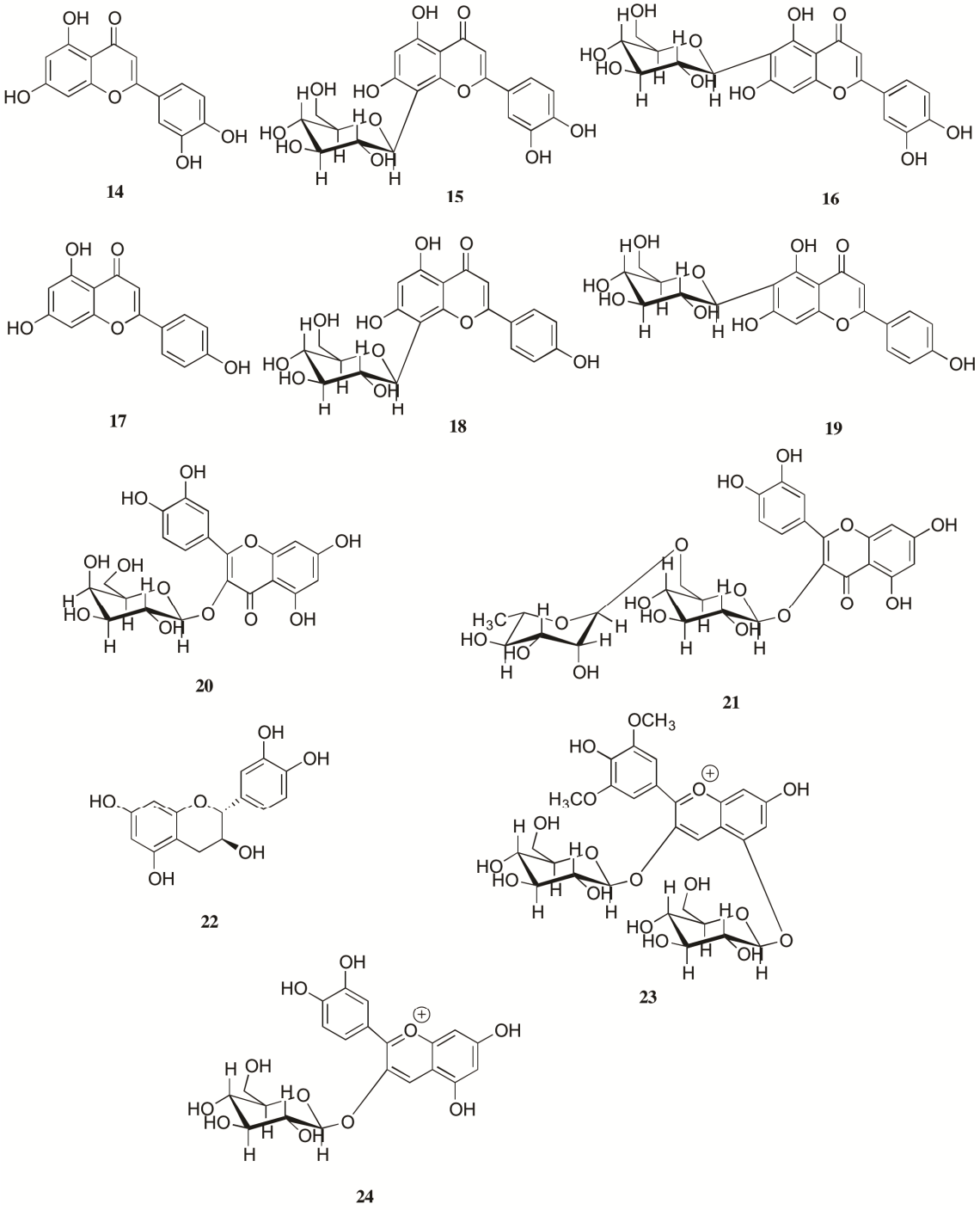
5.3. Flavonoids

Flavonoids are the most common and the best-analyzed group of polyphenols occurring in aerial parts of many plant materials. There are several reports concerning the occurrence of these constituents in purple loosestrife. It was established that Lythri herba contains mainly *C*-glycosides of flavon: luteolin and apigenin (Becker et al., 2005; Bencsik et al., 2013; Paris and Paris, 1964; Piwowarski and Kiss, 2013; Rauha et al., 2001; Tunalier et al., 2007). Isomeric luteolin *C*-glucosides – orientin (**15**) and isoorientin (**16**) as well as apigenin derivatives – vitexin (**18**) and isovitexin (**19**) were identified in most of conducted studies. The presence of free aglycones luteolin (**14**) and apigenin (**15**) in the raw plant material was also confirmed. In one report the presence of flavonol derivatives such as hyperoside (**20**) and rutin (**21**) were mentioned as minor constituents. Catechin as the only representative of flavan-3-ols was detected in raw plant material by Bencsik et al. (2013). The chemical structures of flavonoids and catechin found in *Lythum salicaria* are presented in Fig. 3.

5.4. Anthocyanins

One study focused on water-soluble vacuolar pigments occurring in flowers of purple loosestrife was carried by Paris and Paris (1964). It was shown that two dominating dyes – malvidin 3,5-di-*O*-glucoside (**23**) and cyaniding 3-*O*-glucoside (**24**) were found and characterized in analyzed material. Their chemical structures are given in Fig. 3.

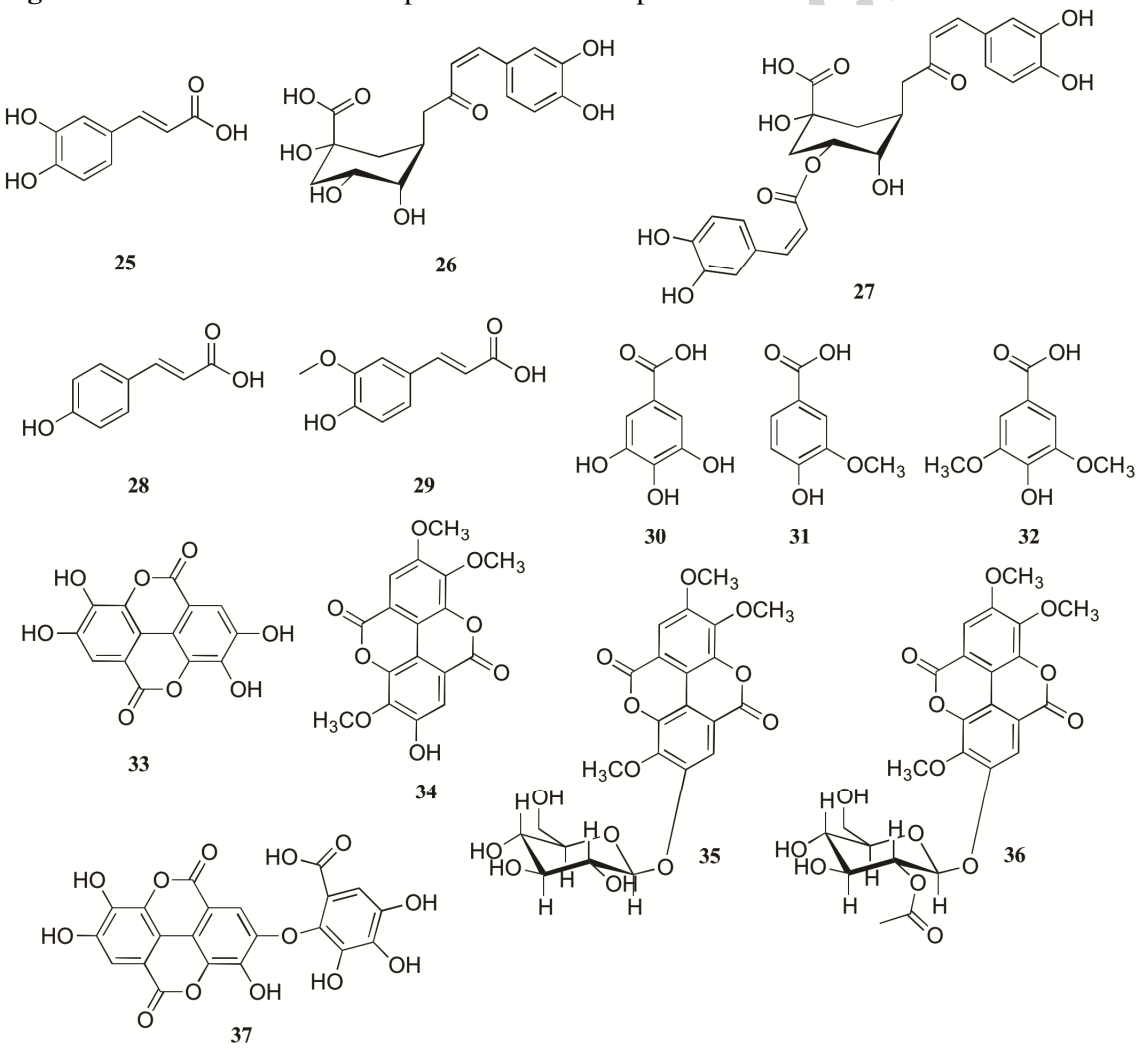
Figure 3. Chemical structures of flavonoids, catechin and anthocyanins compounds **14-24**.



5.5. Phenolic acids and ellagic acid derivatives

Phenolic acids belonging to three structural groups were detected in extracts from aerial parts of *Lythrum salicaria*. The first group comprises of cinnamic acid derivatives such as caffeic acid (**25**), chlorogenic acid (**26**), isochlorogenic acid (**27**), *p*-coumaric acid (**28**) and ferulic acid (**29**) (Bencsik et al., 2013; Rauha et al., 2001; Tokar, 2007; Torrent Marti, 1975). The second group consists of compounds classified as simple derivatives of benzoic acid including gallic acid (**30**), syringic acid (**31**) and vanilic acid (**32**) (Rauha et al., 2001; Tokar, 2007). As a third separate group of compounds we distinguished ellagic acid (**33**) and its derivatives including 3,3',4'-tri-*O*-methylellagic acid (**34**), its glycosides (**35-36**) and valoneic acid dilactone (**37**) (Manayi et al., 2013b; Manayi et al., 2013c; Rauha et al., 2001). Chemical structures of phenolic acids determined in *Lythrum salicaria* are presented in Fig. 4.

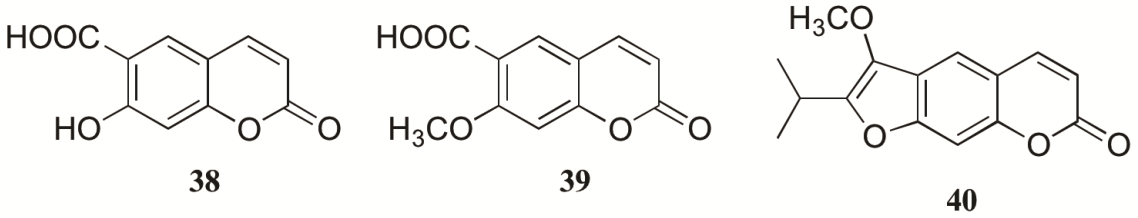
Figure 4. Chemical structures of phenolic acids compounds **25-37**.



5.6. Coumarins

In the literature there is only one report describing the occurrence of coumarins in aerial parts of purple loosestrife. Three compounds (**38-40**) were isolated and identified as umbeliferone-6-carboxylic acid (**38**) and buntansin (**39**) representing simple coumarins and peucedanin (**40**) belonging to the group of furocoumarins (Manayi et al., 2013c). Their chemical structures are depicted in Fig. 5.

Figure 5. Chemical structures of coumarins compounds **38-40**.



5.7. Triterpenes and steroids

The presence of triterpenes and steroids in aerial parts of *Lythrum salicaria* was revealed in four reports (Becker et al., 2005; Fujita et al., 1972; Kim et al., 2011; Manayi et al., 2013c). Total of six triterpenes were isolated and characterized comprising oleanolic acid (**41**), corsolic acid (**42**), ursolic acid (**43**), betulinic acid (**44**) and its methyl ester (**45**) and erythrodiol (**46**). Among two detected steroids ß-sitosterol (**47**) and its glucoside - daucosterol (**48**) were identified. Chemical triterpenes and steroids found in *Lythrum salicaria* are given in Fig. 6 and 7.

Figure 6. Chemical structures of triterpenes compounds **41-46**.

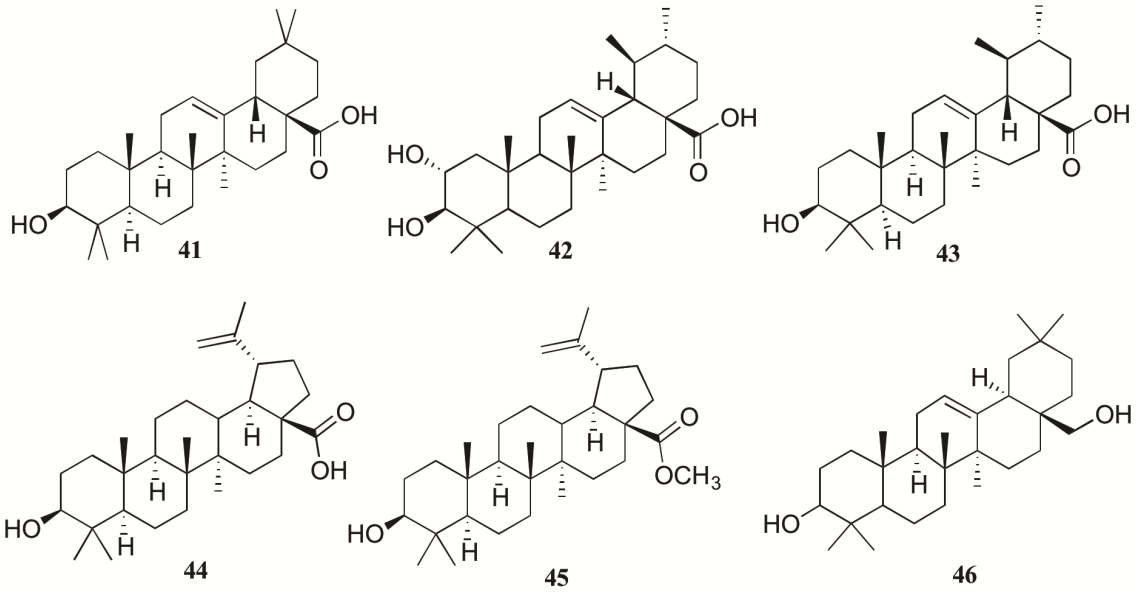
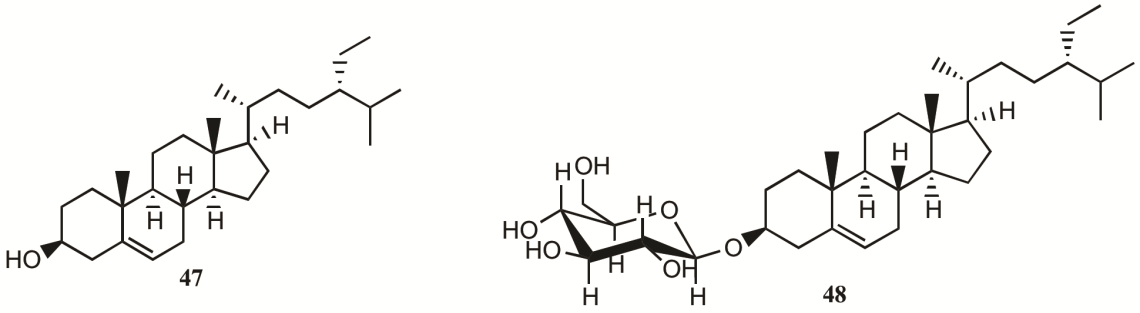


Figure 7. Chemical structures of steroids compounds **47-48**.

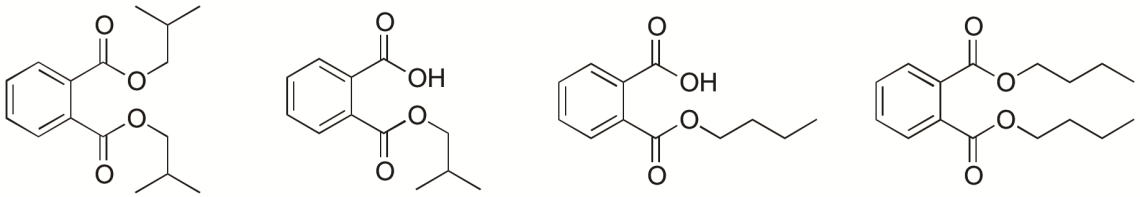


47 48

5.8. Phtalates

In the literature there is one study focused on neutral constituents occurring in the herb of *Lythrum salicaria* (Fujita et al., 1972). Four phthalates were fully characterized in analyzed extract including di-isobutyl phthalate (**52**), isobutyl phthalate (**50**), *n*-butyl phthalate (**51**) and di-*n*-butyl phthalate (**52**). Using GC-MS method the authors also detected dioctyl phthalate, four isomeric diheptyl phthalates and two isomers of dinonyl phthalate but their exact structure is not described. The question appears if all identified compounds are actual natural products occurring in the raw material or they were detected and/or isolated as contaminations of solvents used in the extraction and chromatography procedures. Chemical structures of phthalates found in *Lythrum salicaria* are given in Fig. 8.

Figure 8. Chemical structures of phthalates compounds **49-52**.



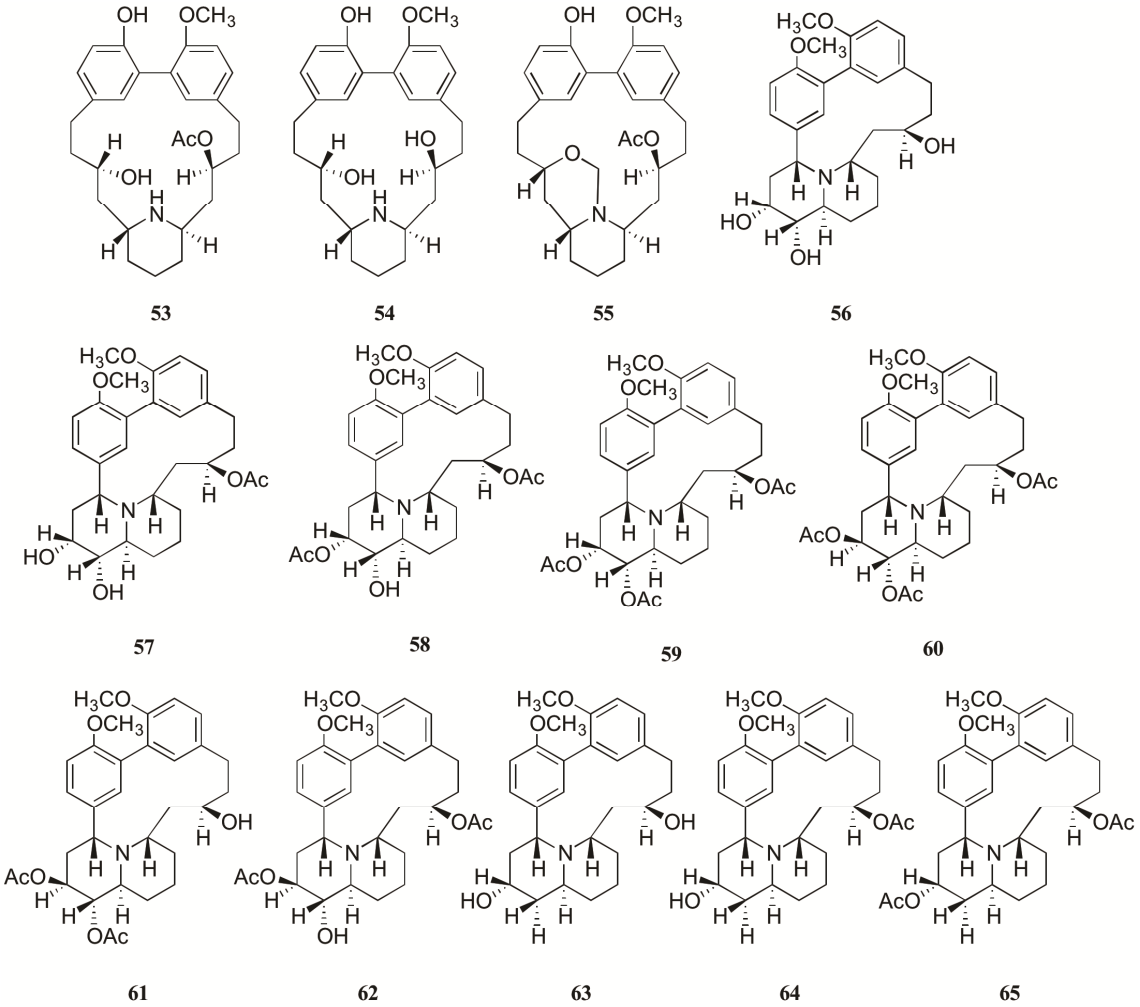
49 50 51 52

5.9. Alkaloids

Starting in 1960's the group of Fujita and coworkers isolated the total of thirteen nitrogen-containing compounds, which were chemically characterized as alkaloids (Fujita et al., 1970; Fujita et al., 1971a; Fujita et al., 1967). The chemical structure of those compounds was later resolved using chemical methods and using X-ray experiments. Isolated alkaloids were classified as piperidine and quinolizidine derivatives and were named lythranine (**53**), lythranidine (**54**), lythramine (**55**), lythrancine I-VII (**56-62**) and lythrancepine I-III (**63-65**). As the total synthesis and chemical transformations of nitrogen-containing compounds, especially naturally occurring alkaloids, is challenging task for chemists thus several papers

dealing with chemistry of alkaloids from *Lythrum salicaria* and other lythraceous plants were developed (Carruthers et al., 1991; Ferris et al., 1971; Fuji et al., 1980; Fujita et al., 1971b; Fujita and Saeki, 1973a). It must be noted that the presence of identified alkaloids in *Lythrum salicaria* has not been confirmed in any later studies investigating this plant material. However some of the authors state that none or only traces of alkaloids are present in raw material (Gougeon and Laumonier, 1918; Rauha, 2001; Steinfeld, 1968). The chemical structures of alkaloids are depicted in Fig. 9.

Figure 9. Chemical structures of alkaloids compounds **53-65**.



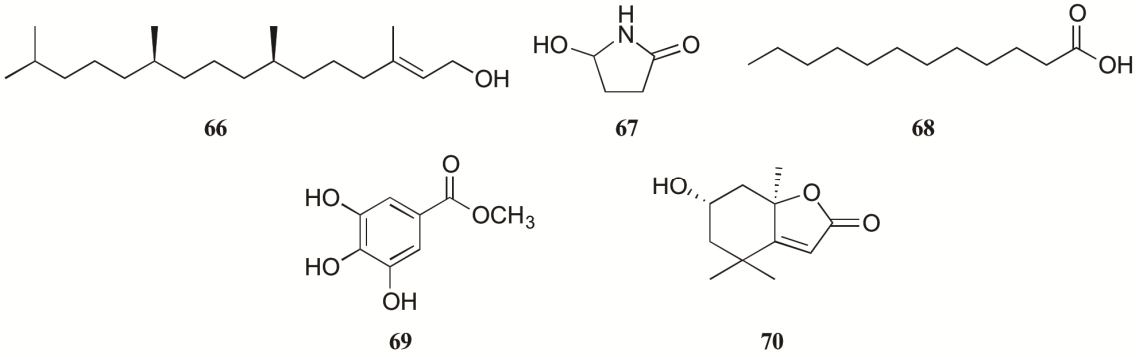
5.10. Other compounds

Five constituents classified in the present review as other compounds were isolated and characterized from aerial parts of purple loosestrife. Those compounds are: long chain terpene alcohol phytol (**66**), 5-hydroxypyrrolidin-2-one (**67**), dodecanoic acid (**68**), methyl gallate

(**69**) that most probably is an artifact produced during the extraction of raw material with hydrated methanol and terpenic compound loliolide (**70**). Their structures are given in Fig. 10.

One study using GC-MS was conducted for the detection volatile compounds in flowering aerial parts of purple loosestrife (Manayi et al., 2014). Forty-three constituents were detected, characterized based on MS spectrum and Kovats index and quantified. The presence of analyzed compounds should be confirmed by their isolation and spectroscopic identification from raw plant material to support these findings.

Figure 10. Chemical structures of other compounds **66-70**.



66 **67** **68**

69 **70**

5.11. Glycoconjugates

The research group of Gancarz investigated the alkaline extract from aerial parts of *Lythrum salicaria* (Pawlaczyk et al., 2011; Pawlaczyk et al., 2010; Sutovska et al., 2012). It has been shown that the crude isolate is a conjugate of carbohydrates – especially neutral sugars, uronic acids and phenolics. The chemical composition of obtained fraction was analyzed using FT-IR and NMR methods. The separation of obtained mixture using ion-exchange chromatography led to identification of some macromolecular substances characterized as polymeric saccharides giving only the proportions of individual sugars (Pawlaczyk et al., 2011; Pawlaczyk et al., 2010). The exact structure of compounds present in analyzed mixture was not established.

Table 6. The summary of chemical compounds found in *Lythrum salicaria*, their chemical names and molecular weights.

Phytochemical classification	No.	Constituent name	molecular weight	Part of plant	References
Ellagitannins					
	1	vescalagin	934	aerial parts	Becker et al. (2005); Rauha et al. (2001); Piwowarski and Kiss (2013); Granica et al. (2014)
	2	castalagin	934	aerial parts	Ma (1996); Rauha et al. (2001); Piwowarski and Kiss (2013); Granica et al. (2014)
	3	salicarinin A	1883	aerial parts	Piwowarski and Kiss (2013); Granica et al. (2014)
	4	salicarinin B	1883	aerial parts	Piwowarski and Kiss (2013); Granica et al. (2014)
	5	salicarinin C	1883	aerial parts	Piwowarski and Kiss (2013)
	6	pedunculagin	784	aerial parts	Rauha et al. (2001)
	7	lythrine A	1883	aerial parts	Ma (1996)
	8	lythrine B	1883	aerial parts	Ma (1996)
	9	lythrine C	1883	aerial parts	Ma (1996)
	10	lythrine D	1883	aerial parts	Ma (1996)
Tannin related compounds					
	11	1-*O*-galloylglucose	332	aerial parts	Rauha et al. (2001)
	12	6-*O*-galloylglucose	332	aerial parts	Rauha et al. (2001)
	13	1,6-di-*O*-galloylglucose	484	aerial parts	Rauha et al. (2001)
Flavonoids					
	14	luteolin	286	aerial parts	Bencsik et al. (2013)
	15	orientin	448	aerial parts	Paris and Moyse (1967); Rauha et al. (2001); Becker et al. (2005); Bencsik et al. (2013); Piwowarski and Kiss (2013)
	16	isoorientin	448	aerial parts	Rauha et al. (2001); Becker et al. (2005); Tunalier et al. (2007); Bencsik et al. (2013); Piwowarski and Kiss (2013)
	17	apigenin	270	aerial parts	Bencsik et al. (2013)
	18	vitexin	432	aerial parts	Paris and Moyse (1967); Rauha et al. (2001); Becker et al. (2005); Bencsik et al. (2013); Piwowarski and Kiss (2013)
	19	isovitexin	432	aerial parts	Rauha et al. (2001); Becker et al. (2005); Tunalier et al. (2007); Bencsik et al. (2013)
	20	hyperoside	464	aerial	Bencsik et al. (2013)

Phytochemical classification	No.	Constituent name	molecular weight	Part of plant	References
				parts	
	21	rutin	610	aerial parts	Bencsik et al. (2013)
Flavan-3-ols					
	22	catechin	290	aerial parts	Bencsik et al. (2013)
Anthocyanins					
	23	malvidin 3,5-di-*O*-glucoside	655	flowers	Paris and Paris (1964); Paris and Moyse (1967)
	24	cyanidin 3-*O*-glucoside	449	flowers	Paris and Paris (1964); Paris and Moyse (1967)
Phenolic acids					
	25	caffeic acid	180	aerial parts	Torrent Marti (1975); Bencsik et al. (2013)
	26	chlorogenic acid	354	aerial parts	Torrent Marti (1975); Rauha et al. (2001); Tokar (2007); Bencsik et al. (2013)
	27	isochlorogenic acid	516	aerial parts	Tokar (2007); Bencsik et al. (2013)
	28	*p*-coumaric acid	164	aerial parts	Torrent Marti (1975); Tokar (2007)
	29	ferulic acid	194	aerial parts	Tokar (2007)
	30	gallic acid	170	aerial parts	Torrent Marti (1975); Rauha et al. (2001); Tokar (2007); Bencsik et al. (2013); Manayi et al. (2013b)
	31	syringic acid	198	aerial parts	Tokar (2007)
	32	vanilic acid	168	aerial parts	Tokar (2007)
Ellagic acid derivatives					
	33	ellagic acid	302	aerial parts	Torrent Marti (1975); Rauha et al. (2001); Tokar (2007); Piwowarski et al. (2011); Bencsik et al. (2013); Piwowarski and Kiss (2013)
	34	3,3',4'-tri-*O*-methylellagic acid	344	aerial parts	Manayi et al. (2013c)
	35	3,3',4'-tri-*O*-methylellagic acid-4-*O*-β-D-(2''-acetyl)-glucopyranoside	506	aerial parts	Manayi et al. (2013c)
	36	3,3',4'-tri-*O*-methylellagic acid-4-*O*-β-D-glucopyranoside	548	aerial parts	Manayi et al. (2013b); Manayi et al. (2013c)
	37	valoneic acid dilactone	470	aerial parts	Rauha et al. (2001)
Coumarins					
	38	umbeliferone-6-carboxylic acid	206	aerial parts	Manayi et al. (2013c)
	39	buntansin	220	aerial	Manayi et al. (2013c)

Phytochemical classification	No.	Constituent name	molecular weight	Part of plant	References
				parts	
	40	peucedanin	258	aerial parts	Manayi et al. (2013c)
Triterpenes					
	41	oleanolic acid	456	aerial parts	Becker et al. (2005); Manayi et al. (2013c)
	42	corosolic acid	472	aerial parts	Manayi et al. (2013c)
	43	ursolic acid	456	aerial parts	Becker et al. (2005)
	44	betulinic acid	456	aerial parts	Kim et al. (2011)
	45	betulinic acid methyl ester	470	aerial parts	Kim et al. (2011)
	46	erythrodiol	442	aerial parts	Manayi et al. (2013c)
Steroids					
	47	β-sitosterol	414	aerial parts	Fujita et al. (1972); Kim et al. (2011); Manayi et al. (2013c)
	48	daucosterol	576	aerial parts	Manayi et al. (2013c)
Phtalates					
	49	di-isobutyl phthalate	278	aerial parts	Fujita et al. (1972)
	50	isobutyl phthalate	222	aerial parts	Fujita et al. (1972)
	51	*n*-butyl phtalate	222	aerial parts	Fujita et al. (1972)
	52	di-*n*-butyl phatlate	278	aerial parts	Fujita et al. (1972)
Alkaloids					
	53	lythranine	467	aerial parts	Fujita et al. (1967); Fujita et al. (1970); Fujita et al. (1971a)
	54	lythranidine	425	aerial parts	Fujita et al. (1967); Fujita et al. (1970); Fujita et al. (1971a)
	55	lythramine	479	aerial parts	Fujita et al. (1967); Fujita et al. (1970); Fujita et al. (1971a)
	56	lythrancine-I	453	aerial parts	Fujita et al. (1971a); Fujita and Saeki (1972)
	57	lythrancine-II	495	aerial parts	Fujita et al. (1971a); Fujita and Saeki (1972)
	58	lythrancine-III	537	aerial parts	Fujita et al. (1971a); Fujita and Saeki (1972)
	59	lythrancine-IV	579	aerial parts	Fujita et al. (1971a); Fujita and Saeki (1972)
	60	lythrancine-V	579	aerial parts	Fujita and Saeki (1973b)

Phytochemical classification	No.	Constituent name	molecular weight	Part of plant	References
	61	lythrancine-VI	537	aerial parts	Fujita and Saeki (1973b)
	62	lythrancine-VII	537	aerial parts	Fujita and Saeki (1973b)
	63	lythrancepine-I	437	aerial parts	Fujita et al. (1971a); Fujita and Saeki (1971, 1972)
	64	lythrancepine-II	479	aerial parts	Fujita et al. (1971a); Fujita and Saeki (1971, 1972)
	65	lythrancepine-III	521	aerial parts	Fujita et al. (1971a); Fujita and Saeki (1971, 1972)
Other compounds					
	66	phytol	296	aerial parts	Manayi et al. (2013c)
	67	5-hydroxypyrrolidin-2-one	101	aerial parts	Manayi et al. (2013c)
	68	dodecanoic acid	200	aerial parts	Manayi et al. (2013c)
	69	methyl gallate	184	aerial parts	Rauha et al. (2001)
	70	loliolide	196	aerial parts	Fujita et al. (1972)

6. Pharmacological reports

The studies regarding bioactivity of extracts from *Lythrum salicaria* started in 19th century. The results of early experiments due to their incompatibility with current experimental standards were placed in section 4.2. An overview of contemporary pharmacological evaluations carried out for *Lythrum salicaria* is presented below in detail.

6.1. Antidiarrheal activities

The studies referring to main traditional application of *Lythrum salicaria* are generally focused on its influence on intestine contractility. Vincent and Segonzac conducted *ex vivo* examinations on guinea pig isolated ileum revealing, that *Lythrum salicaria* extract expressed tonic effect. Interestingly, when to pre-incubated with extract ileum histamine or acetylcholine was added, a significant reduction of the sensitivity to both stimulants was observed (Vincent and Segonzac, 1954). Further studies revealed no influence on guinea pig ileum contractility of extract applied alone, however at high concentrations, the response to subsequent stimulation with acetylcholine was inhibited or even inverted. In pre-activated with acetylcholine ileum, the extract produced a spasmogenic effect, but there was no definite relationship between dose and response. Such effect was also observed after extract addition

following barium chloride challenging (Torrent Marti, 1975). Antidiarrheal activity of Salicairine was demonstrated by Brun et al. (1998). Salicairine has been a commercially available liquid extract preparation elaborated in France for the treatment of dysentery and diarrhea, containing 16.5% of dry extract from flowering tops of *Lythrum salicaria.* Experiments conducted on mice model have shown inhibitory activity towards castor oil-induced diarrhea. The mechanism of this effect was linked to an increase in fluid and electrolytes absorption together with slowing down abnormally induced intestinal transit. *Ex vivo* experiments performed on isolated rat duodenum confirmed spasmolytic activity by inhibition of barium chloride and acetylcholine induced contractions, while PGE1 triggered decrease of net fluid absorption in tied off colon in rats was significantly reversed by Salicairine. The effects were comparable with known antidiarrheal drug- loperamide, but conversely to it, Salicairine did not impair normal intestinal transit and had less impact on physiological fluid absorption indicating different mechanism of action. However recent studies conducted by Bencsik (2014) in contrary demonstrated spasmogenic activity of *Lythrum salicaria* herb extracts of different polarities.

Above limited and contradictory results regarding *Lythrum salicaria* influence on intestinal functions concentrated on *Lythrum salicaria* effect towards intestine contractility do not exhaust a topic of its anti-dysentery and antidiarrheal activity. They generally refer only to symptomatic amelioration without considering possible impact on etiological factors being responsible for the diseases. Such complex studies would be desirable, especially when heterogeneity of diarrhea and dysentery origin is taken into account. The detailed summary of literature data on antidiarrheal activities of *Lythrum salicaria* is given in Table 7.

Table 7.
Summary of studies regarding *Lythrum salicaria* antidiarrheal activities.

Type of extract/standardization/isolated principle	Test model	Effect	Dose/duration	Ref.
Herb aqueous extract	Isolated ileum of guinea pig	Tonic effect (extract applied alone) Sensitivity to acetylcholine and histamine↓	2-5 mL of 10% extract in 50 mL of buffer	Vincent and Segonzac (1954)
Flowering top 45° ethanolic extract (fresh)	Isolated ileum of guinea pig	No effect (extract applied alone)	0.9774-97.4400 mg/mL	Torrent Marti (1975)
		Basal tone↑ (stimulation with ACh)	1.9488-9.744 mg/mL	
		Basal tone↑↑ (stimulation with $BaCl_2$) (dd)	0.9774-97.4400 mg/mL	
Flowering tops liquid extract- Salicairine (16.5% of dry extract)	Female Swiss mice	Castor oil induced diarrhea (number of total feces↓ 25-40%) Charcoal (normal) gastrointestinal transit (-)	0.5-1.0 mL/kg b.w. (p.o.)	Brun et al. (1998)
	Male Wistar rats	Bisacodyl-induced increase in large intestine transit (transit time↑ 220-380%)	0.4-2.0 mL/kg b.w. (p.o.)	
	Isolated male Wistar rat	Barium chloride induced	0.005-0.02 mL/mL bath	

	duodenum	contractions↓		
		Acetylcholine induced contractions↓		
	Isolated male Wistar rat colon	Normal net fluid absorption↑	0.01 mL/mL bath	
		PGE1 induced net liquid secretion↑		
Flowering top hexane extract (sonication at 40 °C)	Isolated ileum of guinea pig	Contractility↑	0.5 mg of plant material (calculated)/5 mL bath	Bencsik (2014)
Flowering top chloroform extract (sonication at 40 °C)		Contractility↑		
Flowering top ethyl acetate extract (sonication at 40 °C)		Contractility↑		
Flowering top 50% ethanolic extract (sonication at 40 °C)		Contractility↑↑ (dd)		

(dd)- dose dependent effect
(-)- no effect

6.2. Anti-inflammatory and anti-oxidant activities

Diseases traditionally treated with *Lythrum salicaria* are closely associated with excessive inflammatory response; therefore several studies were conducted regarding this mode of action. The influence on pro-inflammatory signaling was observed for extract from whole plant material on rat kidney epithelioid NRK-52E cells challenged with LPS. The significant reduction of cytokine-induced neutrophil chemoattractant 1 (CINC-1) production was determined. Polar fractions were shown to be responsible for the effect (Ha et al., 1997). Tunalier et al. (2007) examined antioxidant properties in cell-free systems using fractions obtained by subsequent extraction of plant material with solvents of increasing polarity. The strongest antioxidant activity was observed in the case of native water extract. *In vivo* animal model revealed anti-inflammatory and anti-nociceptive activities for 50% aqueous methanolic extract. In contrast to acetyl salicylic acid used as a positive control, none of the studied fractions/extracts caused gastric ulceration. The authors suggested that flavonoids, especially *C*-glucosidic isoorientin and isovitexin (which amounts were determined in fractions/extract using HPLC-DAD) are compounds responsible for observed effects. However the dominating compounds-ellagitannins, which are visible in provided chromatograms of polar fractions at low retention times were not subjected to analysis. Considering studies on qualitative and quantitative analysis of aqueous extracts from *Lythrum salicaria* (Granica et al., 2014; Piwowarski and Kiss, 2013) it can be suspected that these not assigned peaks represent polar *C*-glucosidic ellagitannins having very low retention times if analyzed on reverse phases HPLC columns (C18, C8). *Lythrum salicaria* herb aqueous extract was shown to inhibit hyaluronidase activity. The observed effect was stronger than for the known hyaluronidase inhibitor- heparin. It was also strong inhibitor of elastase release from *ex vivo* stimulated neutrophils (Piwowarski et al., 2011). Further studies have shown, that dominating *C*-glucosidic ellagitannins- dimeric salicarinins A, B and C (**3-5**) together with monomeric vescalagin and castalagin (**1-2**) were responsible for these effects. *Lythrum salicaria* herb aqueous extract was also examined on other pro-inflammatory functions of human neutrophils. It was shown to modulate LPS triggered production of IL-8, was active towards cytochalasin A/f-MLP stimulated elastase and myeloperoxidase release (MPO) and strongly

decreased f-MLP and PMA induced reactive oxygen species production. Dimeric salicarinins A, B and C (**3-5**) were indicated as mainly responsible for anti-inflammatory activity of *Lythrum salicaria* L. herb together with slightly weaker, but also active monomeric vescalagin and castalagin (**1-2**). (Piwowarski and Kiss, 2014). *Lythrum salicaria* was also demonstrated to possess anti-oxidant activities in many screening studies. Inhibition of *Lythrum salicaria* extract towards methyl linoleate oxidation (Kahkonen et al., 1999), lipid peroxidation and direct $O_2\bullet^-$ scavenging (Coban et al., 2003), antioxidant activity against the ABTS•+ (Mantle et al., 2000) and DPPH• (The Local Food-Nutraceuticals Consortium, (2005; Lopez et al., 2008; Manayi et al., 2013a) were determined.

Above data can initially support traditional use of *Lythrum salicaria* in gastrointestinal tract, skin and mucosa diseases possessing inflammatory background, however more complex *in vitro* and *in vivo* studies would allow to fully elucidate its anti-inflammatory properties together with their mechanisms. The detailed summary of literature data on anti-inflammatory and anti-oxidant activities of *Lythrum salicaria* is given in Table 8.

Table 8.
Summary of studies regarding *Lythrum salicaria* anti-inflammatory and anti-oxidant activities.

Type of extract/standardization/isolated principle		Test model	Effect	Dose/duration	Ref.
Herb subsequent extraction in Soxlet apparatus, 8h each	Petroleum ether fraction (total phenolics 20.0 mg/g)	Linoleic acid peroxidation	6.0% inhibition	250 µg/mL	Tunalier et al. (2007)
		Malondialdehyde formation (TBA method)	18.4% inhibition		
		Male Swiss albino mice	Carrageenan-induced paw edema (–)	200 mg/kg b.w. (p.o.) 270 min	
			p-benzoquinone-induced writhings (–)	200 mg/kg b.w. (p.o.) 60 min	
	Ethyl acetate fraction (total phenolics 35.7 mg/g) (total flavonoids 49.6 mg/g)	DPPH• scavenging	Antioxidant	IC_{50}=2700 µg/mL	
		Linoleic acid peroxidation	93.8% inhibition	250 µg/mL	
		Malondialdehyde formation (TBA method)	88.5% inhibition		
		Male Swiss albino mice	Carrageenan-induced paw edema (–)	200 mg/kg b.w. (p.o.) 270 min	
			p-benzoquinone-induced writhings (–)	200 mg/kg b.w. (p.o.) 60 min	
	Methanol fraction (total phenolics 191.3 mg/g) (total flavonoids 37.6 mg/g)	DPPH• □scavenging	Antioxidant	SC_{50}=300 µg/mL	
		Linoleic acid peroxidation	49.1% inhibition	250 µg/mL	
		Malondialdehyde formation (TBA method)	64.7% inhibition		
		Male Swiss albino mice	Carrageenan-induced paw edema↓ (28.9%)	200 mg/kg b.w. (p.o.) 270 min	
			p-benzoquinone-induced writhings↓ (30.1%)	200 mg/kg b.w. (p.o.) 60 min	
	50% aqueous methanol fraction (total phenolics 525.8 mg/g) (total flavonoids 37.3 mg/g)	DPPH• scavenging	Antioxidant	SC_{50}=100 µg/mL	
		Linoleic acid peroxidation	85.7% inhibition	250 µg/mL	
		Malondialdehyde formation (TBA method)	86.0% inhibition		
		Male Swiss albino mice	Carrageenan-induced paw edema (–)	200 mg/kg b.w. (p.o.) 270 min	
			p-benzoquinone-induced writhings (–)	200 mg/kg b.w. (p.o.) 60 min	
	Herb aqueous extract (total phenolics 305.22 mg/g) (total flavonoids 27.64 mg/g)	DPPH• scavenging	Antioxidant	SC_{50}=100 µg/mL	
		Linoleic acid peroxidation	84.0% inhibition	250 µg/mL	
		Malondialdehyde formation (TBA method)	92.8% inhibition		
		Male Swiss albino mice	Carrageenan-induced paw edema (–)	200 mg/kg b.w. (p.o.) 270 min	
			p-benzoquinone-induced writhings (–)	200 mg/kg b.w. (p.o.) 60 min	
herb 80% methanolic extract (room temperature, evaporation at 50 ˚C)	Crude extract	Rat kidney epithelioid NRK-52E cells	LPS induced CINC-1 production↓ (71%)	100 µg/mL	Ha et al. (1997)
	Methyl chloride fraction		LPS induced CINC-1 production (–)	50 µg/mL	
	Ethyl acetate fraction		LPS induced CINC-1 production (–)		

	n-butanol			LPS induced CINC-1 production↓ (31%)	
	Polar residue			LPS induced CINC-1 production↓ (45%)	
Herb aqueous extract (40 °C, freeze dried)			Hyaluronidase	Activity↓	IC_{50}=8.1 µg/mL	Piwowarski et al. (2011)
			Human neutrophils (*ex vivo*)	fMLP induced elastase release↓	10 µg/mL	
Herb aqueous extract (40 °C, freeze dried)			Human neutrophils (*ex vivo*)	LPS induced IL-8 production↓ (16.6%)	20 µg/mL	Piwowarski and Kiss (2014)
				fMLP induced elastase release↓ (21.5%)		
				fMLP induced MPO release↓ (49.1%)		
				ROS release↓ fMLP model 67.0% PMA model 66.5%		
			hyaluronidase	Activity↓	IC_{50}=10.1 µg/mL	
		vescalagin	human neutrophils (*ex vivo*)	LPS induced IL-8 production↓ (28.3%)	20 µM	
				fMLP induced elastase release (–)		
				fMLP induced MPO release↓ (58.8%)		
				ROS release↓ fMLP model (69.9%) PMA model (71.1%)		
			hyaluronidase	Activity↓	IC_{50}=3.1 µM	
		castalagin	Human neutrophils (*ex vivo*)	LPS induced IL-8 production↓ (29.8%)	20 µM	
				fMLP induced elastase release (–)		
				fMLP induced MPO release↓ (70.1%)		
				ROS release↓ fMLP model (70.5%) PMA model (63.0%)		
			hyaluronidase	Activity↓	IC_{50}=3.1 µM	
		salicarinin A	Human neutrophils (*ex vivo*)	LPS induced IL-8 production↓ (20.2%)	20 µM	
				fMLP induced elastase release↓ (57.8%)		
				fMLP induced MPO release↓ (98.5%)		
				ROS release↓ fMLP model (80.5%) PMA model (85.4%)		
			hyaluronidase	Activity↓	IC_{50}=1.6 µM	
		salicarinin B	Human neutrophils (*ex vivo*)	LPS induced IL-8 production↓ (40.8%)	20 µM	
				fMLP induced elastase release↓ (61.8%)		
				fMLP induced MPO release↓ (97.1%)		
				ROS release↓ fMLP model (83.6%) PMA model (86.9%)		
			hyaluronidase	Activity↓	IC_{50}=1.6 µM	
		salicarinin C	Human neutrophils (*ex vivo*)	LPS induced IL-8 production↓ (43.3%)	20 µM	
				fMLP induced elastase release↓ (49.4%)		
				fMLP induced MPO release↓ (94.1%)		
				ROS release↓ fMLP model (81.1%) PMA model (92.6%)		
			hyaluronidase	Activity↓	IC_{50}=2.5 µM	
Aerial parts 90% ethanolic extract (under reflux) (total phenolics 628.7 mg/g of extract)			DPPH• □scavenging	Antioxidant	1 mg/mL	The Local Food-Nutraceuticals Consortium (2005)
			Comet assay	DNA damage (-)	0.01 mg/mL	
			Xanthine oxidase	(-)	0.1 mg/mL	
			Acetylcholine esterase	Activity↓		
			Murine brain microvascular endothelial cells	Viability↓↓		
				NO production↓		
			PPARγ binding	Strong inhibition		
			HEK-293 cells	Serotonin re-uptake↓		
			Myeloperoxidase-catalysed guaiacol oxidation	Antioxidant	0.2 mg/mL	
			oxyhaemoglobin bleaching	Antioxidant		
			Malondialdehyde formation	Lipid peroxidation↓↓		
Leaf 80% ethanolic extract			ABTS•+ scavenging	Antioxidant activity	0.31 mM Trolox equivalent/ g plant material	Mantle et al. (2000)
Herb 75% ethanolic extract (Soxlet 24 h)			Xanthine/xanthine oxidase	O_2•$^-$ scavenging	SC_{50}=5.0 mg/mL	Coban et al. (2003)
			Rat liver homogenate induced with $FeCl_2$-ascorbic acid	Lipid peroxidation	SC_{50}=5.3 mg/mL	
Aerial parts subsequent extraction	Dichloromethane	DPPH• scavenging		(-)		Lopez et al. (2008)
	Ethyl acetate			(-)		
	Methanol			Antioxidant activity	SC_{50}=4.8 µg/mL	
	Aqueous			Antioxidant activity	SC_{50}=22.5 µg/mL	
Herb 80% methanolic extract (sonication at room temperature; total phenolics 42.1 mg GAE/g)			Methyl linoleate oxidation	46% inhibition	0.5 µg/mL	Kahkonen et al. (1999)
Aerial parts 80% methanolic extract (percolation) (total flavonoids 5.8 µg/mg (QE); total phenolics 331 µg/mg (GAE); total tannins 340 µg/mg; total polysaccharides 21 µg/mg (GE))			DPPH• scavenging	Antioxidant	SC_{50}=13.5 µg/mL	Manayi et al. (2013a)

(dd)- dose dependent effect
(-)- no effect

6.3. Antimicrobial activities

The effectiveness of external use of *Lythrum salicaria* in the traditional medicine in the treatment of skin and mucosa diseases can be supported by its anti-microbial activity. Ethanolic extracts of *Lythrum salicaria* herb have shown antimicrobial activity against *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Candida albicans*. (Borchardt et al., 2008). These observations are supported by previous reports on the anti-microbial activity of extracts against *S. aureus*, *E. coli* and *C. albicans* conducted by Rauha et al. (2000), Citoglu and Altanlar (2003) together with early studies conducted by Sartory et al. (1949) and Vincent and Segonzac (1954). The latter observed also growth inhibition of responsible for bacterial diarrhea *Shigella* sp. as well as typhoid and paratyphoid bacteria. Inhibition of *Bacillus cereus*, *Mycobacterium smegmatis* and *Micrococcus luteus* growth was determined by Dulger and Gonuz (2004). However growth of *E. coli* and *C. albicans*, which were also included in this study was not inhibited by *Lythrum salicaria* ethanolic extract. Such phenomenon can be explained by the use of 24h extraction in Soxlet apparatus, which could lead to thermal decomposition of active principles, as cited in other studies, which have shown *Lythrum salicaria* to be active, room temperature extraction methods were applied. Dichloromethane extract from herb exhibited antifungal activity against *Cladosporium cucumerinum* and bioautographic TLC analysis has led to isolation of active principles-oleanolic acid (**41**) and ursolic acid (**43**). Methanolic extract inhibited growth of *S. aureus*, *P. mirabilis* and *M. luteus*. Bioguided fractionation led to isolation of vescalagin (**1**) (Becker et al., 2005). Antilisterial activity was determined towards *Listeria monocytogenes* and *Listeria innocua*, without the influence on *Listeria ivanovii* and *Listeria murrayi* growth (Altanlar et al., 2006). Guclu et al. investigated antibacterial efficacy of *Lythrum salicaria* against 30 *Acinetobacter baumannii* and 27 *Pseudomonas aeruginosa* multidrug-resistant (MDR) hospital isolates showing its potent activity towards these pathogens, however not crude extract, but uncharacterized fraction obtained by chromatography on silica gel was used in this study (Guclu et al., 2014). Moderate activity towards *Helicobacter pylori* was determined by Manayi et al. (2013a). Despite the main traditional application of *Lythrum salicaria* in dysentery and diarrhea only preliminary investigations conducted by Vincent and Segonzac (1954) consider the effects on bacterial strains participating in their pathogenesis. Thus further, more advanced studies designed towards this direction are required, especially that historical sources indicate possible influence of *Lythrum salicaria* on enteropathogenic

bacteria strains growth. The detailed summary of literature data on anti-microbial activities of *Lythrum salicaria* is given in Table 9.

Table 9.
Summary of studies regarding *Lythrum salicaria* anti-microbial activities.

Type of extract/standardization/isolated principle	Test model	Effect	Dose	Ref.
Polar extract	*Staphylococcus aureus*	Activity established as 0.25 Oxford units		Sartory et al. (1949)
	Escherichia coli	Growth inhibition		
Herb aqueous extract	*Staphylococcus aureus*	20-30mm inhibition zone		Vincent and Segonzac (1954)
	Shigella sp.	20 mm inhibition zone		
	Escherichia coli	Weak effect		
	typhoid and paratyphoid bacteria	Growth inhibition		
Herb 70% methanolic extract (7 days maceration at 25 ˚C)	*Staphylococcus aureus*	<10 mm inhibition zone	400 µg/paper disc	Moskalenko (1986)
	Bacillus subtilis	(-)		
	Mycobacterium smegmatis	10-15mm inhibition zone		
	Escherichia coli	10-15mm inhibition zone		
	Shigella sonnei	10-15mm inhibition zone		
	Shigella flexneri	<10 mm inhibition zone		
Flower 70% methanolic extract (7 days maceration at 25 ˚C)	*Staphylococcus aureus*	10-15mm inhibition zone		
	Bacillus subtilis	<10 mm inhibition zone		
	Mycobacterium smegmatis	<10 mm inhibition zone		
	Escherichia coli	<10 mm inhibition zone		
	Shigella sonnei	<10 mm inhibition zone		
	Shigella flexneri	(-)		
Herb 80% methanolic extract (sonication at room temperature, concentrated at 35 °C)	*Staphylococcus aureus*	Slight antimicrobial activity	50 µg/cylinder	Rauha et al. (2000)
	Escherichia coli	Antimicrobial activity		
	Candida albicans	Moderate antimicrobial activity		
	Aspergillus niger	(–)		
Herb 80% ethanolic extract	*Staphylococcus aureus*	15 mm inhibition zone	50 µL/paper disc	Borchardt et al. (2008)
	Escherichia coli	10 mm inhibition zone		
	Pseudomonas aeruginosa	7 mm inhibition zone		
	Candida albicans	7 mm inhibition zone		
Herb 80% ethanolic extract (Soxlet-24h, evaporated at 55 ˚C)	*Escherichia coli*	(–)	10 mg/paper disc	Dulger and Gonuz (2004)
	Staphylococcus aureus	12 mm inhibition zone		
	Klebsiella pneumoniae	(–)		
	Pseudomonas aeruginosa	(–)		
	Proteus vulgaris	(–)		
	Bacillus cereus	10 mm inhibition zone		
	Mycobacterium smegmatis	10 mm inhibition zone		
	Listeria monocytogenes	(–)		
	Micrococcus luteus	8 mm inhibition zone		
	Candida albicans	(–)		
	Kluyveromyces fragilis	(–)		
	Rhodotorula rubra	(–)		
Herb dichloromethane extract	*Cladosporium cucumerinum*	Antifungal activity		Becker et al. (2005)
	Staphylococcus aureus	(–)		
	Escherichia coli	(–)		
	Pseudomonas aeruginosa	(–)		
	Citrobacter freundii	(–)		
	Proteus mirabilis	MIC= 1.0 mg/mL		
	Micrococcus luteus	(–)		
	Saccharomyces cerevisiae	MIC= 0.5 mg/mL		
	Candida albicans	MIC= 1.0 mg/mL		
Methanolic extract from herb after dichloromethane extraction	*Staphylococcus aureus*	MIC= 0.5 mg/mL		
	Escherichia coli	(–)		
	Pseudomonas aeruginosa	(–)		
	Citrobacter freundii	(–)		
	Proteus mirabilis	MIC= 1.0 mg/mL		
	Micrococcus luteus	MIC= 1.0 mg/mL		
	Saccharomyces cerevisiae	(–)		
	Candida albicans	(–)		
Ethyl acetate fraction	*Staphylococcus aureus*	MIC= 0.05 mg/mL		
	Escherichia coli	(–)		
	Pseudomonas aeruginosa	(–)		
	Citrobacter freundii	(–)		
	Proteus mirabilis	MIC= 0.5 mg/mL		
	Micrococcus luteus	MIC= 0.5 mg/mL		
	Saccharomyces cerevisiae	(–)		
	Candida albicans	MIC= 0.5 mg/mL		
n-buthanol fraction	*Staphylococcus aureus*	MIC= 0.25 mg/mL		
	Escherichia coli	(–)		
	Pseudomonas aeruginosa	(–)		
	Citrobacter freundii	(–)		
	Proteus mirabilis	MIC= 0.5 mg/mL		
	Micrococcus luteus	MIC= 0.25 mg/mL		
	Saccharomyces cerevisiae	(–)		
	Candida albicans	(–)		
Vescalagin (**1**)	*Staphylococcus aureus*	MIC= 0.062 mg/mL		
	Escherichia coli	(–)		
	Pseudomonas aeruginosa	(–)		
	Citrobacter freundii	(–)		
	Proteus mirabilis	MIC= 0.062 mg/mL		
	Micrococcus luteus	MIC= 0.125 mg/mL		
	Saccharomyces cerevisiae	(–)		
	Candida albicans	(–)		

Herb 75% ethanolic extract (Soxlet)	*Escherichia coli*	11 mm inhibition zone	2 mg/paper disc	Citoglu and Altanlar (2003)
	Pseudomonas aeruginosa	13 mm inhibition zone		
	Bacillus subtilis	9 mm inhibition zone		
	Staphylococcus aureus	9 mm inhibition zone		
	Candida albicans	12 mm inhibition zone		
	Candida galabrata	16 mm inhibition zone		
	Candida krusei	16 mm inhibition zone		
	Listeria monocytogenes	8 mm inhibition zone MIC= 50 µg/mL	2.7 mg/paper disc	Altanlar et al. (2006)
	Listeria ivanovii	(-)		
	Listeria innocua,	11 mm inhibition zone MIC=12.5 µg/mL		
	Listeria murrayi.	(-)		
Herb ethanolic extract, evaporated, dissolved in methanol and chromatographed through silica gel column	*Acinetobacter baumannii* MDR hospital isolates	16 mm mean inhibition zone	850µg/well	Guclu et al. (2014)
	Pseudomonas aeruginosa MDR hospital isolates	18 mm mean inhibition zone		
Aerial parts 80% methanolic extract (percolation)	*Helicobacter pylori*	17 mm inhibition zone	500 mg/mL	Manayi et al. (2013a)
Herb 50% ethanolic extract (sonication at 40 °C)	*Candida albicans*	MIC= 5.0 mg/mL		Bencsik (2014)
	Micrococcus luteus	MIC= 5.0 mg/mL		
	Bacillus subtilis	MIC= 2.5 mg/mL		
	Escherichia coli	MIC= 2.5 mg/mL		
	Pseudomonas aeruginosa	MIC= 2.5 mg/mL		
	MDR *Pseudomonas aeruginosa*	MIC= 2.5 mg/mL		
	Staphylococcus aureus	MIC= 1.25 mg/mL		
	MRSA	MIC= 1.25 mg/mL		
	Staphylococcus epidermidis	MIC= 1.25 mg/mL		

(-)- no effect

6.4. Influence on blood coagulation

First known *ex vivo* studies regarding influence of *Lythrum salicaria* aqueous extract on blood coagulation revealed anticoagulant properties (Vincent and Segonzac, 1954). These observations are supported by recent studies conducted on high molecular weight polysaccharide-polyphenolic conjugate isolated from *Lythrum salicaria* herb regarding its influence on hemostasis, which was shown to also have antagonistic, however controversial properties. The experiments on human plasma and *ex vivo* experiments on plasma obtained from rats intravenously injected with conjugate have shown its anticoagulant activity expressed as significant reduction of activated partial thromboplastin time (aPTT) and in a lesser manner prothrombin time (PT) with little influence on thrombin time (TT) indicating that glycoconjugate is potent to influence factors of intrinsic coagulation pathway stronger that those of extrinsic one. However, the experiments conducted on *in vivo* animal model have shown contradictory results, as the prolongation of clotting time formation for the collected blood samples was observed. The authors concluded that heterogenous character of conjugate (carbohydrate, polyphenolics and protein components) could be the factor responsible for inconsistent results (Pawlaczyk et al., 2010). Further studies on *Lythrum salicaria* conjugate fractionated by ion exchange chromatography pointed three fractions LsF2, LsF7, LsF12 mainly responsible for observed anti-coagulant *in vitro* effects on human plasma. The effects of the crude conjugate and its fractions LsF2, LsF7, LsF12 were compared with unfractionated heparin (144 IU/mg) indicating their activity at the level of 0.7, 2.4, 2.9 and 3.2 IU/mg respectively. On the contrary, fraction LsF3 expressed pro-coagulant activity,

however the effect was very weak and observed at high concentrations (232-465 μg/mL). Unfortunately no *in vivo* experiments on animal model performed analogously to previous study were conducted for fractionated conjugate, what could confirm anti-coagulant or pro-coagulant activity (Pawlaczyk et al., 2011).

6.5. Influence on metabolism

Potential influence on glucose metabolism was indicated by the study conducted on healthy children in 1930's. Salicairine (2 times 20 drops p.o.) was administered before and after subcutaneous injection of phlorizin. Such a treatment was shown to prevent phlorizin induced glycosuria (Spyropoulos, 1930). Above early studies inspired researchers to examine *Lythrum salicaria* influence on glycaemia in animal models, however no such indications were pointed out by known sources regarding traditional use. *Lythrum salicaria* was shown to possess hypoglycemic effects in a few animal studies conducted in 1980's. It was decreasing glucose-induced hyperglycemia in normoglycemic rabbits. The most active extracts were those obtained from flowers and stems. Compounds responsible for above effect were indicated to be present in ethyl ether fractions, for which notable influence on insulin increase was determined (Torres and Suarez, 1980). Further studies conducted on normoglycemic Wistar rats confirmed these observations. The reduced glycaemia after the treatment with ethyl ether extract from stem and ethanolic extract from flowers occurred simultaneously with an enhancement of glucagon content in the liver. The effects were associated with the increase of circulating insulin, however none of the extracts had influence on glucose uptake by the isolated diaphragm. *Ex vivo* experiment indicated the possible mechanism by showing ethyl ether extract at the concentration of 50 mg/mL to be potent in induction of insulin release from isolated islets of Langerhans. Ethyl ether and ethanolic extracts were reducing triglicerides levels while increase in free fatty acids level was observed, without the influence on cholesterol level (Lamela et al., 1985). Similar observations towards reducing glucose level were made when hyperglycemia was induced by epinephrine in healthy rats. Not only in healthy animals, but also in the case of streptozotocin- or alloxan-induced diabetes ethyl ether extract from stems as well as ethanolic one were active towards blood glucose level reduction. Moreover, both stems and flowers extracts reduced the elevated γ-glutamyl transpeptidase activity induced by streptozotocin in rats while the stems extracts reduced the elevated lactic dehydrogenase activity (Lamela et al., 1986). 80% methanolic extract was shown to inhibit pancreatic lipase activity (Sharma et al., 2005) and the extract prepared from leaves was effective in the decrease of enzymatic activity of α-glucosidase (Yoshida et al., 2008). The

detailed summary of literature data regarding the influence of *Lythrum salicaria* on metabolic processes is given in Table 10.

Table 10.
Summary of studies regarding *Lythrum salicaria* impact on metabolism.

Type of extract/standardization/fraction/isolated principle		Test model		Effect	Dose/duration	Ref.
Ethanolic extract (boiling, evaporation at 40°C)	Stem: Crude extract	Australian strain rabbits (normoglycemic)		Glycemia↓ (16.0%)	1g of plant material (calculated)/kg b.w./4h (p.o.)	Torres and Suarez (1980)
	Stem: Petroleum ether fraction			Glycemia↓ (19.2%)	10g of plant material (calculated)/kg b.w./4h (p.o.)	
	Stem: Ethyl ether fraction			Glycemia (–)		
	Stem: Ethyl acetate fraction			Glycemia↓ (21.2%)		
	Stem: Water residue			Glycemia (–)		
	Flower: Crude extract			Glycemia↓ (15.3%)	1g of plant material (calculated)/kg b.w./4h (p.o.)	
	Flower: Petroleum ether fraction			Glycemia↓ (19.2%)	10g of plant material (calculated)/kg b.w./4h (p.o.)	
	Flower: Ethyl ether fraction			Glycemia (–)		
	Flower: Ethyl acetate fraction			Glycemia↓ (21.2%) (dd)		
	Flower: Water residue			Blood insulin level↑		
				Glycemia↓ (16.2%)		
				Glycemia (–)		
	Ethyl ether fraction			Glycemia↓ (21.0%)	5g of plant material (calculated)/kg b.w./45 min (p.o.)	
	Leaf			Glycemia↓ (11.2%)	1g of plant material (calculated)/kg b.w./4h (p.o.)	
	Root			Glycemia (–)	10g of plant material (calculated)/kg b.w./4h (p.o.)	
Flower ethyl ether extract (Soxlet)				Glycemia↓ (21.0%)	10g of plant material (calculated)/kg b.w./4h (p.o.)	
	Ethanolic extract of residue (Soxlet)			Glycemia↓ (10.8%)		
Flower 95% ethanolic extract (boiling)		Male Wistar rats		Glycemia↓ (10.3%)	10g plant material (calculated)/kg b.w./4h (p.o.)	Lamela et al. (1985)
				Muscular glycogen↑ (18%)		
				Muscular glycogen (-)		
				Blood insulin level↑↑		
				Triglycerides level↓		
				Free fatty acids level↑		
				Cholesterol level (-)		
Stem ethyl ether extract				Glycemia↓ (19.1%)		
				Hepatic glycogen↑ (30%)		
				Muscular glycogen (-)		
				Blood insulin level↑		
				Triglycerides level↓		
				Free fatty acids level↑		
				Cholesterol level (-)		
	95% ethanolic extract after ethyl ether extraction			Glycemia (-)		
Flower ethyl ether extract				Glycemia↓ (4.3%)		
	95% ethanolic extract after ethyl ether extraction			Glycemia (-)		
Stem ethyl ether extract		Langerhans islets isolated from adult male Wistar rats		Insulin release↑	50 mg/mL	
				Insulin release (-)	100 and 200 mg/mL	
Flower 95% ethanolic extract (boiling)		male Wistar rats		Glucose induced hyperglycemia↓ (30min)	10g plant material (calculated)/kg b.w (p.o.)	Lamela et al. (1986)
				Epinephrine induced hyperglycemia↓ (90-120min)		
			alloxan diabetic	Hyperglycemia↓		
			streptozotocin-diabetic	Hyperglycemia↓		
				Alkaline phosphatase serum activity (-)		
				γ-glutamyl transpeptidase serum activity↓		
				Aspartate aminotransferase serum activity↑		
				Lactate dehydrogenase serum activity (-)		
				creatine kinase serum activity (-)		
		alloxan diabetic male Charles-River CD-1 mice		Hyperglycemia↓		
Stem ethyl ether extract		Male Wistar rats		Glucose induced hyperglycemia↓ (30min)		
				Epinephrine induced hyperglycemia↓ (60-120min)		
			Alloxan diabetic	Hyperglycemia↓		
			Streptozotoc	Hyperglycemia↓		

		in diabetic	Alkaline phosphatase serum activity↓		
			γ-glutamyl transpeptidase serum activity↓		
			Aspartate aminotransferase serum activity (-)		
			Lactate dehydrogenase serum activity↓		
			creatine kinase serum activity (-)		
	Alloxan diabetic male Charles-River CD-1 mice		Hyperglycemia↓		
Flower ethyl ether extract	Male Wistar rats		Glucose induced hyperglycemia↓ (30min)		
			Epinephrine induced hyperglycemia↓ (90-120min)		
		alloxan diabetic	Hyperglycemia↓		
Herb 80% methanolic extract (Concentrated at 45 °C)	Porcine pancreatic lipase		Activity↓ (43.9%)	200 µg/mL	Sharma et al. (2005)
Leaf 50% aqueous methanol	Rat intestinal α-glucosidase		Maltase and sucrase activity↓ (ca. 90%)	5.5 mg plant material (calculated)/mL	Yoshida et al. (2008)
Aerial parts 80% methanolic extract (percolation)	Streptozotocin diabetic rats		Glycemia↓ (12.6%)	15 g/kg b.w. (p.o.)	Manayi et al. (2013a)

(dd)- dose dependent effect
(-)- no effect

6.6. Other activities

Aqueous-ethanolic extracts from flowering tops of *Lythrum salicaria* were shown to inhibit dose dependently the stimulatory effect of noradrenaline in the isolated rat vas deferens. Effect on blood pressure was tested on animal model and non-lethal doses (64.96 mg/kg b.w. intravenously) of extracts have resulted in a transient hypotension with a tendency tachyphylaxis. Similar hypotensive effect was observed for tannic acid solution, however it was diminished by neutralization with NaOH, what was not observed in the case of plant extracts (Torrent Marti, 1975). The mechanism of this effect can be attributed to inhibition of calcium flux into cells determined *in vitro* for *Lythrum salicaria* herb 80% methanolic extract (sonication at room temperature, concentrated at 35 °C) on clonal rat pituitary GH4C1 cells model (36.3% inhibition at concentration of 20 µg/mL) (Rauha, 1999).

The high molecular weight polysaccharide-polyphenolic conjugate isolated from *Lythrum salicaria* was shown to possess antitussive activity by its bronchodilatory properties on guinea pig model. Decrease of cough efforts number induced by nebulized citric acid was probably due to the reduction of specific airway resistance. The oral administration of conjugate (dose 75 mg/kg b.w.) caused reduction of specific airway resistance in a more significant manner than salbutamol (10 mg/kg b.w. i.p.) and the effect was still observed 5 hours after administration (Sutovska et al., 2012).

7. Specificity of biological effects.

The case of selectivity of biological effects of *Lythrum salicaria* polar extracts due to high content of ellagitannins should be raised and discussed due to the commonly attributed

unspecific protein binding properties of this group of compounds. Preliminary study of hyaluronidase inhibition of *Lythrum salicaria* extract consisted of additional tests with increased BSA concentration in reaction mixture, which did not affected the inhibitory activity of extract, what could suggest the lack of unspecific binding of active compounds to protein molecules (Piwowarski et al., 2011). Many studies conducted on *C*-glucosidic ellagitannins have shown selectivity towards interaction with enzyme molecules and to our knowledge there are no studies indicating unspecific interactions with proteins (in contrast to other tannis such as condensed tannins or gallotannins). Vescalagin (**1**) was shown to selectively suppress the activity of topoisomerase IIα in comparison with influence on its β isoform at the concentration range of 0.1-100 μM by a redox independent mechanism. Comparison of the effects with castalagin has revealed that β-orientation of the C-1 hydroxyl group of vescalagin (**1**) might play a role in favoring selectivity towards Top2α. The selective inhibitory effect was further confirmed with cellular *in vitro* model (Auzanneau et al., 2012). Selective interaction with topoisomerase II was also shown for vescalin as it was not interacting with other proteins such as BSA or streptavidin (Douat-Casassus et al., 2009). Studies comparing interactions of different polyphenolic molecules with bradykinin molecule have shown, that vescalagin (**1**) despite its polyphenolic structure that has numerous potential hydrophobic contacts with its five aromatic rings and numerous potential hydrogen bonds with its 16 hydroxyl groups due to its HHDP and NHTP units has a more rigid structure and thus low association constant value with bradykinin, what results in a lesser affinity to form unspecific ellagitannin-protein complexes (Richard et al., 2006). The unspecific interactions, especially with proline-rich proteins, such as collagen are commonly attributed to tannins. However study conducted by Tang et al. (2003) has clearly shown, that this phenomenon in the case of vescalagin (**1**), castalagin (**2**), and their dimer (in contrast to condensed tannins and gallotannins), is not strongly marked and even weaker than for di-galloyl-ethylene glycol. In these ellagitannins, the intergalloyl linkages severely restrict the flexibility of galloyl groups, reducing the hydrophobic interactions. Not only enzymatic studies, but also *in vitro* experiments on cell models can indicate specificity of *C*-glucosidic ellagitannins activity. Studies on different tumor cell lines indicated structural dependency of the growth inhibitory effects for vescalagin (**1**) and castalagin (**2**) (Fridrich et al., 2008; Kashiwada et al., 1992).

8. Bioavailability and gut microbiota metabolism

Compounds responsible for biological effects of *Lythrum salicaria* are rather present in polar fractions of extracts. Their dominating constituents are *C*-glucosidic ellagitannins

followed by *C*-glucosidic flavonoids. Due to not fully established bioavailability these compounds should be only referred when external applications are considered. However, in the case of vescalagin (**1**) (*C*-glucosidic ellagitannin dominating in *Lythrum salicaria* extract) the *in vitro* studies have shown promising results, because despite its high hydrophilicity, vescalagin (**1**) was able to rapidly enter the cells and interact with cytoskeleton (Quideau et al., 2011).

Recent *ex vivo* studies have revealed that ellagitannins present in *Lythrum salicaria* can be metabolized by human gut microbiota to low molecular weight dibenzopyran-6-one derivatives called urolithins (Piwowarski et al., 2014b). Urolithins possess good bioavailability and can be present in plasma, urine and feces at micromolar concentrations (Pfundstein et al., 2014). Above observations determine the necessity of taking into consideration the bioactivity not only of native compounds but also microbial metabolites while discussing *Lythrum salicaria* internal use. Especially that urolithins were shown to have impact on signaling processes, which are known to contribute to gastrointestinal tract inflammatory diseases development and progression (Espin et al., 2013; Larrosa et al., 2010; Piwowarski et al., 2014a; Piwowarski et al., 2014b).

9. Toxicity, safety and potential interactions

Lythrum salicaria safety can be concluded basing on its extensive use since ancient times as a medicinal plant also in the therapy of children. Moreover authors usually claim the lack of significant adverse effects following its internal and external use (Caille, 1919; Campardon, 1883; Tunalier et al., 2007). Nevertheless Torrenti Marti (1975) undertook the toxicity issue and evaluated acute toxicity of hydroalcoholic extracts from *Lythrum salicaria* flowering tops on animal model. The LD_{50} of intravenously administered extract varied between 0.1674 and 0.3289 g/kg b.w. When extracts were administered orally in similar doses the symptoms that occurred were mild abdominal contractions, difficulties in respiration, mild hypothermia, which were not resulting in animal death. Cytotoxicity studies on different cell lines have shown weak influence on their viability (Khanavi et al., 2011). *Lythrum salicaria* was shown to interfere with drug transport *in vitro*. The extract decreased the permeability of the verapamil and metoprolol, and increased the ability of paracetamol to permeate across Caco-2 cell monolayers, without showing cytotoxicity at the concentration up to 1mg/mL (Laitinen et al., 2004). To fully evaluate safety of *Lythrum salicaria* preparations more research is needed, especially concerning oral and topical applications. The detailed summary of literature data on toxicity of *Lythrum salicaria* is given in Table 11.

Table 11.
Summary of studies regarding *Lythrum salicaria* toxicity and interactions.

Type of extract/fraction		Test model	Effect	Dose	Ref.
Flowering top 45° ethanolic extract (fresh)		Male and female Sprague-Dowley rats	Acute toxicity (10-15 min)	LD_{50}=0.2826 g/kg b.w. (i.v.)	Torrent Marti (1975)
Flowering top 45° ethanolic extract (fresh) precipitated with albumin				LD_{50}=0.1674 g/kg b.w. (i.v.)	
Flowering top 45° ethanolic extract (preserved for >30 days)				LD_{50}=0.3289 g/kg b.w. (i.v.)	
Flowering top 45° ethanolic extract (fresh) diluted in serum				LD_{50}=0.2230 g/kg b.w. (i.v.)	
Flowering top 45° ethanolic extract (preserved for >30 days) diluted in serum				LD_{50}=0.2270 g/kg b.w. (i.v.)	
Herb 80% methanolic extract (percolation)	Crude extract	Colon carcinoma HT-29 cells	Cytotoxicity	IC_{50}=176 µg/mL	Khanavi et al. (2011)
		Leukemia K562 cells		(-)	
		Breast ductal carcinoma T47D cells		IC_{50}=164 µg/mL	
		Swiss embryo fibroblasts NIH3T3		IC_{50}=144 µg/mL	
	Chloroform fraction	Colon carcinoma HT-29 cells		IC_{50}=246 µg/mL	
		Leukemia K562 cells		IC_{50}=178 µg/mL	
		Breast ductal carcinoma T47D cells		IC_{50}=108 µg/mL	
		Swiss embryo fibroblasts NIH3T3		IC_{50}=71 µg/mL	
	Ethyl acetate fraction	Colon carcinoma HT-29 cells		IC_{50}=217 µg/mL	
		Leukemia K562 cells		IC_{50}=332 µg/mL	
		Breast ductal carcinoma T47D cells		IC_{50}=63 µg/mL	
		Swiss embryo fibroblasts NIH3T3		IC_{50}=81 µg/mL	
	Methanol residue	Colon carcinoma HT-29 cells		IC_{50}=462 µg/mL	
		Leukemia K562 cells		IC_{50}=312 µg/mL	
		Breast ductal carcinoma T47D cells		IC_{50}=405 µg/mL	
		Swiss embryo fibroblasts NIH3T3		IC_{50}=573 µg/mL	
Herb 80% methanolic extract (sonication at room temperature, concentrated at 35 °C) (Total phenolics 42.1 mg GAE/g dry weight)		Drug permeability using Caco-2 monolayers	Permeability of verapamil, metoprolol↓ Permeability of paracetamol↑	0.1-1 mg/mL	Laitinen et al. (2004)

10. Conclusions

The knowledge about the traditional use of *Lythrum salicaria* has been thoroughly elaborated in the presented review. The intrinsic literature overview conclusively indicates that *Lythrum salicaria* used to be a very effective remedy used in European traditional medicine. Despite unquestionable important position its popularity has been weakened during the past few decades. The decrease of *Lythrum salicaria* importance can be linked with the introduction of synthetic drugs: corticosteroids and sulfasalazine in 1950s (Svartz, 1988; Truelove and Witts, 1954) in the therapy of inflammatory bowel diseases. However, nowadays therapies based on these drugs are in a state of decline due to significant adverse effects and recent advances in the understanding of the molecular basis of Crohn's disease and ulcerative colitis. Immunomodulators- particularly anti-TNF-α monoclonal antibodies, and subsequent biologic therapies are being now under intensive development (Zenlea and Peppercorn, 2014).

Consistently reported extensive traditional use of *Lythrum salicaria* in different European regions in dysentery, diarrhea and other gastrointestinal tract-associated ailments indicates its potential effectiveness in at least bringing symptomatic relief. Rapidly emerging knowledge about the etiology of dysentery and diarrhea (Collins, 2014) gives completely new

possibilities of therapeutic strategies development, among which re-examination and re-introduction of neglected traditional medicines- such as *Lythrum salicaria* appears to be a promising approach.

Unfortunately hitherto research concerned on the influence on etiological factors participating in the development of dysentery and diarrhea is insufficient and seems incommensurate with the reports about widely described distinguishing effectiveness of *Lythrum salicaria*. Contemporary research regarding *Lythrum salicaria*, despite very promising outcomes, is too preliminary and sometimes not strictly carried out into the directions, which could explain and support its traditional use based on empirical observations. The results of antidiarrheal activity studies are limited to the determination of influence on intestinal muscle tone. The anti-inflammatory examinations often only report anti-oxidant activities in cell-free systems, while a few animal and cell-based studies lack molecular mechanisms determination. The vast of microbiological studies were routine screenings conducted on standard, not specific to gastrointestinal tract microorganisms, without taking into consideration the influence on enteropathogenic strains growth. Second frequently reported application of *Lythrum salicaria* is external treatment of different skin and mucosa ailments. In this case *in vitro* research regarding anti-microbial and anti-inflammatory activities can also only initially support such traditional use, facing similar limitations as discussed above internal application.

Limited number of animal studies and total lack of clinical trials, despite encouraging information from historical sources, make the therapeutic effectiveness of *Lythrum salicaria* poorly scientifically supported. Further studies should mainly derive from its well-established traditional use in dysentery and diarrhea and comprise of the models, which would more precisely refer to the current knowledge about their pathophysiology.

The compounds, which are potent to contribute to the therapeutic activity are dominating in hydrophilic extracts *C*-glusosidic ellagitannis followed by less abundant *C*-glucosidic flavonoids and thus these secondary metabolites together with still not enough characterized heteropolysaccharides should be mainly referred while external use is investigated. When internal use is addressed additionally to native compounds ellagitannins' bioavailable metabolites- urolithins, should be considered, due to recently determined gut microbiota metabolism of *Lythrum salicaria* extract.

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Table 1.

Historical and current common names of *Lythrum salicaria* and its preparations.

Country/region	Common names
Bosnia and Herzegovina	potočnjak
China	Qian Qu Cai
Czech Republic	kyprij obecný
Denmark	pilebladet kattehale
Finland	rantakukka
France	salicairé à épi, lysimachie rouge, salicaire officinale, salicaire commune
Germany:	Brauner Weiderich, Rother Weiderich, Großes/Gemeines Blutkraut, Blutweiderich, Gemeiner Weiderich, Stolzer Heinrich, Kattsteert
Great Britain	purple loosestrife, blooming sally, purple willow-herbe, rainbow weed, spiked lythrum, salicaire, purple spiked loosestrife, bouquet violet, purple spiked willowstrife
Hungary	füzény
Iran	farandal
Italy	acquarola, riparella, salcerella, salicaria, spergola, verga rossa, canestrell
Japan	ezo-misohagi
Kamchatka	kipri
Lithuania	raudoklé
Netherlands	partijke
Norway	kattehale
Poland	krwawnica pospolita, płaczek, biedrzeniec, sowia strzała, wodohlad, wilczy ogon, lisia ogonia, wierzbienica
Portugal	erva carapau, carapauzeiro
Romania	răchitan
Russia	плакунЬ, плакун- трава, чальчак, или дербенник
Spain	sumidad florida de salicaria, beherantzako bedarra, hierbas de la cagalera, salicaria, makilbelarra, herba de Sant Antoni, té de brazal
Sweden	fackelblomster, fackelros

Turkey	tibbi hevhulma

Table 2. Historical Latin names of *Lythrum salicaria.*

Lysimachia purpurea (Pharm.)
Salicaria vulgaris purpurea (Tournefort)
Lysimachia spicata purpurea, forte Plinii (C.B.)
Lysimachia purpurea spicata (Ger. Park.)
Pseudolysimachium purpureum alterum (Dod.)
Lysimachia purpurea quibusdam spicata (J.B.Raii)
Lythrum foliis oppositis (Roven)
Salicaria spicata (Lamk.)
Salicaria vulgaris (Moench.)

Table 3.

European 16th and 17th century herbals containing monographs referring to Lysimachia.

Title	Author and year
De Historia Stirpium Commentarii Insignes	Leonhart Fuchs (1542)
Petri Andreae Matthioli senensis, serenissimi Principis Ferdinandi Auchiducis Austriae &c. Medici	Pietro Andrea Mattioli (1558)
A New Herball	William Turner (1568)
Stirpium Historiae Pemptades Sex	Rembert Dodoens (1583)
A New Herball or Historie of Plants	Rembert Dodoens (1586)
Kreutterbuch deß hochgelehrten unnd weitberühmten Herrn D. Petri Andreae Matthioli	Pietro Andrea Mattioli (1590)
Herbarz Polski	Marcin z Urzędowa (1595)
The Herbal	John Gerard (1636)
Les Commentaires de M. P. André Matthiolus sur les six livres de Pedacius Dioscoride Anazarbeen, de la Matiere Medecinale	Pietro Andrea Mattioli (1627)
Theatrum Botanicum: The Theater of Plants	John Parkinson (1640)
Crvyd-boeck	Rembert Dodoens (1644)

Table 4.

18th, 19th and early 20th century medicinal dictionaries, manuals and guidebooks containing information about *Lythrum salicaria* use in therapy of gastrointestinal tract ailments.

Title	Ref.
Materia Medica et Chirurgica Juxta Systema Naturae Digesta	Cranz (1762)
Dictionnaire Raisonné Universel des Plantes	Buc'hoz (1770)
Dictionnaire Raisonné Universel d'Histoire Naturelle	Valmont de Bomare (1775)
The Edinburgh New Dispensatory	Duncan (1818)
Dictionnaire des Sciences Médicales	Une Société de Médecins et de Chirurgiens (1820)
Codex Medicamentarius Europaeus	Niemann (1824)
Farmacopea Ferrarese	Campana (1825)
Handbuch für Praktische Aerzte	Richter (1826)
Encyclopédie Méthodique Médecine	Vicq-d'Azyr and Moreau (1827)
Handbuch der Medicinisch-Pharmaceutischen Botanik. Nach den Natürlichen Familien des Gewächsreiches	Nees von Esenbeck and Ebermaier (1830-1832)
Lexicon Medicum	Blancard and Kühn (1832)
Handbuch der Pharmakologie als Erläuterung Aller in der Österr. Pharmakopöe vom Jahre 1834 Enthaltenen Arzneymittel	Meyer (1835)
De Dysenteria	Zadej (1841)
Materiae Medicae Compendium	Folchi (1841)
Medizinisch-Pharmazeutische Botanik	Bischoff (1843)
L'Officine, ou Répertoire Général de Pharmacie Pratique	Dorvault (1844-1910)
Dictionnaire de Médecine de Chirurgie de Pharmacie des Sciences Accessoires et de l'Art Vétérinaire	Littre (1873-1908); Nysten (1833-1865)
American Eclectic Dyspensatory	King (1856)
Formulaire Raisonné des Médicaments Nouveaux	Reveil (1864)
Exposition Universelle de 1867 à Paris. Rapports du Jury International. L'histoire Naturelle Médicale à l'Exposition Universelle	Chatin (1867)
Dictionnaire Encyclopédique des Sciences Médicales	Dechambre (1878)
Deutsche Flora. Pharmaceutisch-medicinische Botanik	Karsten (1880-1883)

Dictionnaire Usuel des Sciences Médicales	Dechambre et al. (1885)
Commentaires Thérapeutiques du Codex Medicamentarius	Gubler (1885)
Formulaire Pratique de Thérapeutique et de Pharmacologie	Dujardin-Beaumetz and Yvon (1887)
Flore Médicale Usuelle et Industrielle du XIXe Siècle	Dupuis and Reveil (1887)
Dictionnaire de Thérapeutique, de Matière Médicale, de Pharmacologie, de Toxicologie et des Eaux Minérales. Tome Quatrième	Dujardin-Beaumetz (1889)
Les Plantes Médicinales Indigènes et Exotiques, Leurs Usages Thérapeutiques, Pharmaceutiques et Industriels	Dujardin-Beaumetz and Egasse (1889)
Plantes Remèdes et Maladies, ou la Médecine Simple et Facile à la Portée de Tous	Lehamau (1894)
Die Heilpflanzen der Verschiedenen Völker und Zeiten	Dragendorff (1898)
Précis de Matière Médicale	Collin (1903)
Les Plantes médicinales de la Picardie	Caussin (1907)
Larousse Médical Illustré	Burnier (1924)
Neues Illustriertes Kräuterbuch	Marzell (1935)
Lehrbuch der Biologischen Heilmittel	Madaus (1938)
Ziołolecznictwo i Leki Roślinne	Muszyński (1949)

Table 5.

Contemporary traditional uses of *Lythrum salicaria*.

Country	Part used	Formulation	Medicinal use/disease treated	Ref.
Iran	Flower	Decoction	Astringent, antihaemorragic, tonic, cleansing. Dysentery, diarrhea, intestinal inflammation, haematuria, leucorrhoea, epistaxis, dysmenorrhea, lupus, eczema, impetigo, female urogenital inflammation	Miraldi et al. (2001)
Jordan	Leaf, seed		Haemorrhoids and internal bleeding	Al-Qura'n (2007)
Portugal	Aerial part	Decoction	Digestive, carminative. Indisposition of intestines, colic, diarrhea	Gaspar et al. (2002)
Spain	Aerial part	Decoction	Antidiarrheal	Gonzalez et al. (2010)
Spain	Inflorescence	Infusion or decoction	Diarrhea, stomach disorders	Menendez-Baceta et al. (2014)
Spain	Herb	Infusion	Lowering blood pressure	Pardo de Santayana

				et al. (2005)
Spain	Aerial part	Infusion	Diarrhea, vomiting, gastroenteritis (in animals)	Akerreta et al. (2010)
Spain	Aerial part	Infusion	Diarrhoea in calves	Bonet and Valles (2007)
Bosnia and Herzegovina	Root		Diarrhea, gastrointestinal tract ailments, blood circulation disorders, skin ailments	Saric-Kundalic et al. (2011)
Romania	Aerial parts	Infusion	Astringent Diarrhoea, dysentery, gastrointestinal disorders, uterine haemorrhages	Tita et al. (2009)
Italy	Fresh aerial parts		Topically as a vulnerary plaster	Di Novella et al. (2013)
Russia (southeast)	Herb	Decoction and infusion	Colitis and stomatitis	Moskalenko (1986)

Table 6. The summary of chemical compounds found in *Lythrum salicaria*, their chemical names and molecular weights.

Phytochemical classification	No.	Constituent name	molecular weight	Part of plant	References
Ellagitannins					
	1	vescalagin	934	aerial parts	Becker et al. (2005); Rauha et al. (2001); Piwowarski and Kiss (2013); Granica et al. (2014)
	2	castalagin	934	aerial parts	Ma (1996); Rauha et al. (2001); Piwowarski and Kiss (2013); Granica et al. (2014)
	3	salicarinin A	1883	aerial parts	Piwowarski and Kiss (2013); Granica et al. (2014)
	4	salicarinin B	1883	aerial parts	Piwowarski and Kiss (2013); Granica et al. (2014)
	5	salicarinin C	1883	aerial parts	Piwowarski and Kiss (2013)
	6	pedunculagin	784	aerial parts	Rauha et al. (2001)
	7	lythrine A	1883	aerial parts	Ma (1996)
	8	lythrine B	1883	aerial parts	Ma (1996)
	9	lythrine C	1883	aerial parts	Ma (1996)
	10	lythrine D	1883	aerial parts	Ma (1996)
Tannin related compounds					
	11	1-*O*-galloylglucose	332	aerial parts	Rauha et al. (2001)

Phytochemical classification	No.	Constituent name	molecular weight	Part of plant	References
	12	6-*O*-galloylglucose	332	aerial parts	Rauha et al. (2001)
	13	1,6-di-*O*-galloylglucose	484	aerial parts	Rauha et al. (2001)
Flavonoids					
	14	luteolin	286	aerial parts	Bencsik et al. (2013)
	15	orientin	448	aerial parts	Paris and Moyse (1967); Rauha et al. (2001); Becker et al. (2005); Bencsik et al. (2013); Piwowarski and Kiss (2013)
	16	isoorientin	448	aerial parts	Rauha et al. (2001); Becker et al. (2005); Tunalier et al. (2007); Bencsik et al. (2013); Piwowarski and Kiss (2013)
	17	apigenin	270	aerial parts	Bencsik et al. (2013)
	18	vitexin	432	aerial parts	Paris and Moyse (1967); Rauha et al. (2001); Becker et al. (2005); Bencsik et al. (2013); Piwowarski and Kiss (2013)
	19	isovitexin	432	aerial parts	Rauha et al. (2001); Becker et al. (2005); Tunalier et al. (2007); Bencsik et al. (2013)
	20	hyperoside	464	aerial parts	Bencsik et al. (2013)
	21	rutin	610	aerial parts	Bencsik et al. (2013)
Flavan-3-ols					
	22	catechin	290	aerial parts	Bencsik et al. (2013)
Anthocyanins					
	23	malvidin 3,5-di-*O*-glucoside	655	flowers	Paris and Paris (1964); Paris and Moyse (1967)
	24	cyanidin 3-*O*-glucoside	449	flowers	Paris and Paris (1964); Paris and Moyse (1967)
Phenolic acids					
	25	caffeic acid	180	aerial parts	Torrent Marti (1975); Bencsik et al. (2013)
	26	chlorogenic acid	354	aerial parts	Torrent Marti (1975); Rauha et al. (2001); Tokar (2007); Bencsik et al. (2013)
	27	isochlorogenic acid	516	aerial parts	Tokar (2007); Bencsik et al. (2013)
	28	*p*-coumaric acid	164	aerial parts	Torrent Marti (1975); Tokar (2007)
	29	ferulic acid	194	aerial parts	Tokar (2007)
	30	gallic acid	170	aerial parts	Torrent Marti (1975); Rauha et al. (2001); Tokar (2007); Bencsik et al. (2013); Manayi et al. (2013b)
	31	syringic acid	198	aerial parts	Tokar (2007)

Phytochemical classification	No.	Constituent name	molecular weight	Part of plant	References
	32	vanilic acid	168	aerial parts	Tokar (2007)
Ellagic acid derivatives					
	33	ellagic acid	302	aerial parts	Torrent Marti (1975); Rauha et al. (2001); Tokar (2007); Piwowarski et al. (2011); Bencsik et al. (2013); Piwowarski and Kiss (2013)
	34	3,3',4'-tri-*O*-methylellagic acid	344	aerial parts	Manayi et al. (2013c)
	35	3,3',4'-tri-*O*-methylellagic acid-4-*O*-β-D-(2''-acetyl)-glucopyranoside	506	aerial parts	Manayi et al. (2013c)
	36	3,3',4'-tri-*O*-methylellagic acid-4-*O*-β-D-glucopyranoside	548	aerial parts	Manayi et al. (2013b); Manayi et al. (2013c)
	37	valoneic acid dilactone	470	aerial parts	Rauha et al. (2001)
Coumarins					
	38	umbeliferone-6-carboxylic acid	206	aerial parts	Manayi et al. (2013c)
	39	buntansin	220	aerial parts	Manayi et al. (2013c)
	40	peucedanin	258	aerial parts	Manayi et al. (2013c)
Triterpenes					
	41	oleanolic acid	456	aerial parts	Becker et al. (2005); Manayi et al. (2013c)
	42	corosolic acid	472	aerial parts	Manayi et al. (2013c)
	43	ursolic acid	456	aerial parts	Becker et al. (2005)
	44	betulinic acid	456	aerial parts	Kim et al. (2011)
	45	betulinic acid methyl ester	470	aerial parts	Kim et al. (2011)
	46	erythrodiol	442	aerial parts	Manayi et al. (2013c)
Steroids					
	47	β-sitosterol	414	aerial parts	Fujita et al. (1972); Kim et al. (2011); Manayi et al. (2013c)
	48	daucosterol	576	aerial parts	Manayi et al. (2013c)
Phtalates					
	49	di-isobutyl phthalate	278	aerial parts	Fujita et al. (1972)
	50	isobutyl phthalate	222	aerial parts	Fujita et al. (1972)
	51	*n*-butyl phtalate	222	aerial	Fujita et al. (1972)

Phytochemical classification	No.	Constituent name	molecular weight	Part of plant	References
				parts	
	52	di-*n*-butyl phatlate	278	aerial parts	Fujita et al. (1972)
Alkaloids					
	53	lythranine	467	aerial parts	Fujita et al. (1967); Fujita et al. (1970); Fujita et al. (1971a)
	54	lythranidine	425	aerial parts	Fujita et al. (1967); Fujita et al. (1970); Fujita et al. (1971a)
	55	lythramine	479	aerial parts	Fujita et al. (1967); Fujita et al. (1970); Fujita et al. (1971a)
	56	lythrancine-I	453	aerial parts	Fujita et al. (1971a); Fujita and Saeki (1972)
	57	lythrancine-II	495	aerial parts	Fujita et al. (1971a); Fujita and Saeki (1972)
	58	lythrancine-III	537	aerial parts	Fujita et al. (1971a); Fujita and Saeki (1972)
	59	lythrancine-IV	579	aerial parts	Fujita et al. (1971a); Fujita and Saeki (1972)
	60	lythrancine-V	579	aerial parts	Fujita and Saeki (1973b)
	61	lythrancine-VI	537	aerial parts	Fujita and Saeki (1973b)
	62	lythrancine-VII	537	aerial parts	Fujita and Saeki (1973b)
	63	lythrancepine-I	437	aerial parts	Fujita et al. (1971a); Fujita and Saeki (1971, 1972)
	64	lythrancepine-II	479	aerial parts	Fujita et al. (1971a); Fujita and Saeki (1971, 1972)
	65	lythrancepine-III	521	aerial parts	Fujita et al. (1971a); Fujita and Saeki (1971, 1972)
Other compounds					
	66	phytol	296	aerial parts	Manayi et al. (2013c)
	67	5-hydroxypyrrolidin-2-one	101	aerial parts	Manayi et al. (2013c)
	68	dodecanoic acid	200	aerial parts	Manayi et al. (2013c)
	69	methyl gallate	184	aerial parts	Rauha et al. (2001)
	70	loliolide	196	aerial parts	Fujita et al. (1972)

Table 7.
Summary of studies regarding *Lythrum salicaria* antidiarrheal activities.

Type of extract/standardization/isolated principle	Test model	Effect	Dose/duration	Ref.
Herb aqueous extract	Isolated ileum of guinea pig	Tonic effect (extract applied alone) Sensitivity to acetylcholine and histamine↓	2-5 mL of 10% extract in 50 mL of buffer	Vincent and Segonzac (1954)
Flowering top 45° ethanolic extract (fresh)	Isolated ileum of guinea pig	No effect (extract applied alone) Basal tone↑ (stimulation with ACh) Basal tone↑↑ (stimulation with $BaCl_2$) (dd)	0.9774-97.4400 mg/mL 1.9488-9.744 mg/mL 0.9774-97.4400 mg/mL	Torrent Marti (1975)
Flowering tops liquid extract- Salicairine (16.5% of dry extract)	Female Swiss mice	Castor oil induced diarrhea (number of total feces↓ 25-40%) Charcoal (normal) gastrointestinal transit (-)	0.5-1.0 mL/kg b.w. (p.o.)	Brun et al. (1998)
	Male Wistar rats	Bisacodyl-induced increase in large intestine transit (transit time↑ 220-380%)	0.4-2.0 mL/kg b.w. (p.o.)	
	Isolated male Wistar rat duodenum	Barium chloride induced contractions↓ Acetylcholine induced contractions↓	0.005-0.02 mL/mL bath	
	Isolated male Wistar rat colon	Normal net fluid absorption↑ PGE1 induced net liquid secretion↑	0.01 mL/mL bath	
Flowering top hexane extract (sonication at 40 °C)	Isolated ileum of guinea pig	Contractility↑	0.5 mg of plant material (calculated)/5 mL bath	Bencsik (2014)
Flowering top chloroform extract (sonication at 40 °C)		Contractility↑		
Flowering top ethyl acetate extract (sonication at 40 °C)		Contractility↑		
Flowering top 50% ethanolic extract (sonication at 40 °C)		Contractility↑↑ (dd)		

(dd)- dose dependent effect
(-)- no effect

Table 8.
Summary of studies regarding *Lythrum salicaria* anti-inflammatory and anti-oxidant activities.

Type of extract/standardization/isolated principle		Test model	Effect	Dose/duration	Ref.
Herb subsequent extraction in Soxlet apparatus, 8h each	Petroleum ether fraction (total phenolics 20.0 mg/g)	Linoleic acid peroxidation	6.0% inhibition	250 µg/mL	Tunalier et al. (2007)
		Malondialdehyde formation (TBA method)	18.4% inhibition		
		Male Swiss albino mice	Carrageenan-induced paw edema (–)	200 mg/kg b.w. (p.o.) 270 min	
			p-benzoquinone-induced writhings (–)	200 mg/kg b.w. (p.o.) 60 min	
	Ethyl acetate fraction (total phenolics 35.7 mg/g) (total flavonoids 49.6 mg/g)	DPPH• scavenging	Antioxidant	IC_{50}=2700 µg/mL	
		Linoleic acid peroxidation	93.8% inhibition	250 µg/mL	
		Malondialdehyde formation (TBA method)	88.5% inhibition		
		Male Swiss albino mice	Carrageenan-induced paw edema (–)	200 mg/kg b.w. (p.o.) 270 min	
			p-benzoquinone-induced writhings (–)	200 mg/kg b.w. (p.o.) 60 min	
	Methanol fraction (total phenolics 191.3 mg/g) (total flavonoids 37.6 mg/g)	DPPH• □scavenging	Antioxidant	SC_{50}=300 µg/mL	
		Linoleic acid peroxidation	49.1% inhibition	250 µg/mL	
		Malondialdehyde formation (TBA method)	64.7% inhibition		
		Male Swiss albino mice	Carrageenan-induced paw edema↓ (28.9%)	200 mg/kg b.w. (p.o.) 270 min	
			p-benzoquinone-induced writhings↓ (30.1%)	200 mg/kg b.w. (p.o.) 60 min	
	50% aqueous methanol fraction (total phenolics 525.8 mg/g) (total flavonoids 37.3 mg/g)	DPPH• scavenging	Antioxidant	SC_{50}=100 µg/mL	
		Linoleic acid peroxidation	85.7% inhibition	250 µg/mL	
		Malondialdehyde formation (TBA method)	86.0% inhibition		
		Male Swiss albino mice	Carrageenan-induced paw edema (–)	200 mg/kg b.w. (p.o.) 270 min	
			p-benzoquinone-induced writhings (–)	200 mg/kg b.w. (p.o.) 60 min	
Herb aqueous extract (total phenolics 305.22 mg/g) (total flavonoids 27.64 mg/g)		DPPH• scavenging	Antioxidant	SC_{50}=100 µg/mL	
		Linoleic acid peroxidation	84.0% inhibition	250 µg/mL	
		Malondialdehyde formation (TBA method)	92.8% inhibition		
		Male Swiss albino mice	Carrageenan-induced	200 mg/kg b.w. (p.o.)	

			paw edema (−)	270 min	
			p-benzoquinone-induced writhings (−)	200 mg/kg b.w. (p.o.) 60 min	
herb 80% methanolic extract (room temperature, evaporation at 50 ˚C)	Crude extract	Rat kidney epithelioid NRK-52E cells	LPS induced CINC-1 production↓ (71%)	100 μg/mL	Ha et al. (1997)
	Methyl chloride fraction		LPS induced CINC-1 production (−)	50 μg/mL	
	Ethyl acetate fraction		LPS induced CINC-1 production (−)		
	n-butanol		LPS induced CINC-1 production↓ (31%)		
	Polar residue		LPS induced CINC-1 production↓ (45%)		
Herb aqueous extract (40 °C, freeze dried)		Hyaluronidase	Activity↓	IC_{50}=8.1 μg/mL	Piwowarski et al. (2011)
		Human neutrophils (*ex vivo*)	fMLP induced elastase release↓	10 μg/mL	
Herb aqueous extract (40 °C, freeze dried)		Human neutrophils (*ex vivo*)	LPS induced IL-8 production↓ (16.6%)	20 μg/mL	Piwowarski and Kiss (2014)
			fMLP induced elastase release↓ (21.5%)		
			fMLP induced MPO release↓ (49.1%)		
			ROS release↓ fMLP model 67.0% PMA model 66.5%		
		hyaluronidase	Activity↓	IC_{50}=10.1 μg/mL	
	vescalagin	human neutrophils (*ex vivo*)	LPS induced IL-8 production↓ (28.3%)	20 μM	
			fMLP induced elastase release (−)		
			fMLP induced MPO release↓ (58.8%)		
			ROS release↓ fMLP model (69.9%) PMA model (71.1%)		
		hyaluronidase	Activity↓	IC_{50}=3.1 μM	
	castalagin	Human neutrophils (*ex vivo*)	LPS induced IL-8 production↓ (29.8%)	20 μM	
			fMLP induced elastase release (−)		
			fMLP induced MPO release↓ (70.1%)		
			ROS release↓ fMLP model (70.5%) PMA model (63.0%)		
		hyaluronidase	Activity↓	IC_{50}=3.1 μM	
	salicarinin A	Human neutrophils (*ex vivo*)	LPS induced IL-8 production↓ (20.2%)	20 μM	
			fMLP induced elastase release↓ (57.8%)		
			fMLP induced MPO release↓ (98.5%)		
			ROS release↓ fMLP model (80.5%) PMA model (85.4%)		
		hyaluronidase	Activity↓	IC_{50}=1.6 μM	
	salicarinin B	Human neutrophils (*ex vivo*)	LPS induced IL-8 production↓ (40.8%)	20 μM	
			fMLP induced elastase release↓ (61.8%)		
			fMLP induced MPO release↓ (97.1%)		
			ROS release↓ fMLP model (83.6%) PMA model (86.9%)		
		hyaluronidase	Activity↓	IC_{50}=1.6 μM	
	salicarinin C	Human neutrophils (*ex vivo*)	LPS induced IL-8 production↓ (43.3%)	20 μM	
			fMLP induced elastase release↓ (49.4%)		
			fMLP induced MPO release↓ (94.1%)		
			ROS release↓ fMLP model (81.1%) PMA model (92.6%)		
		hyaluronidase	Activity↓	IC_{50}=2.5 μM	
Aerial parts 90% ethanolic extract (under reflux) (total phenolics 628.7 mg/g of extract)		DPPH• □scavenging	Antioxidant	1 mg/mL	The Local Food-Nutraceuticals Consortium (2005)
		Comet assay	DNA damage (-)	0.01 mg/mL	
		Xanthine oxidase	(-)	0.1 mg/mL	
		Acetylcholine esterase	Activity↓		
		Murine brain microvascular endothelial cells	Viability↓↓		
			NO production↓		
		PPARγ binding	Strong inhibition		
		HEK-293 cells	Serotonin re-uptake↓		
		Myeloperoxidase-catalysed guaiacol oxidation	Antioxidant	0.2 mg/mL	
		oxyhaemoglobin bleaching	Antioxidant		
		Malondialdehyde formation	Lipid peroxidation↓↓		
Leaf 80% ethanolic extract		ABTS•+ scavenging	Antioxidant activity	0.31 mM Trolox equivalent/ g plant material	Mantle et al. (2000)
Herb 75% ethanolic extract (Soxlet 24 h)		Xanthine/xanthine oxidase	O_2•⁻ scavenging	SC_{50}=5.0 mg/mL	Coban et al. (2003)
		Rat liver homogenate induced with $FeCl_2$-ascorbic acid	Lipid peroxidation	SC_{50}=5.3 mg/mL	
Aerial parts subsequent extraction	Dichloromethane	DPPH• scavenging	(-)		Lopez et al. (2008)
	Ethyl acetate		(-)		
	Methanol		Antioxidant activity	SC_{50}=4.8 μg/mL	

Aqueous		Antioxidant activity	SC_{50}=22.5 μg/mL	
Herb 80% methanolic extract (sonication at room temperature; total phenolics 42.1 mg GAE/g)	Methyl linoleate oxidation	46% inhibition	0.5 μg/mL	Kahkonen et al. (1999)
Aerial parts 80% methanolic extract (percolation) (total flavonoids 5.8 μg/mg (QE); total phenolics 331 μg/mg (GAE); total tannins 340 μg/mg; total polysaccharides 21 μg/mg (GE))	DPPH• scavenging	Antioxidant	SC_{50}=13.5 μg/mL	Manayi et al. (2013a)

(dd)- dose dependent effect
(-)- no effect

Table 9.
Summary of studies regarding *Lythrum salicaria* anti-microbial activities.

Type of extract/standardization/isolated principle	Test model	Effect	Dose	Ref.
Polar extract	*Staphylococcus aureus*	Activity established as 0.25 Oxford units		Sartory et al. (1949)
	Escherichia coli	Growth inhibition		
Herb aqueous extract	*Staphylococcus aureus*	20-30mm inhibition zone		Vincent and Segonzac (1954)
	Shigella sp.	20 mm inhibition zone		
	Escherichia coli	Weak effect		
	typhoid and paratyphoid bacteria	Growth inhibition		
Herb 70% methanolic extract (7 days maceration at 25 °C)	*Staphylococcus aureus*	<10 mm inhibition zone	400 μg/paper disc	Moskalenko (1986)
	Bacillus subtilis	(-)		
	Mycobacterium smegmatis	10-15mm inhibition zone		
	Escherichia coli	10-15mm inhibition zone		
	Shigella sonnei	10-15mm inhibition zone		
	Shigella flexneri	<10 mm inhibition zone		
Flower 70% methanolic extract (7 days maceration at 25 °C)	*Staphylococcus aureus*	10-15mm inhibition zone		
	Bacillus subtilis	<10 mm inhibition zone		
	Mycobacterium smegmatis	<10 mm inhibition zone		
	Escherichia coli	<10 mm inhibition zone		
	Shigella sonnei	<10 mm inhibition zone		
	Shigella flexneri	(-)		
Herb 80% methanolic extract (sonication at room temperature, concentrated at 35 °C)	*Staphylococcus aureus*	Slight antimicrobial activity	50 μg/cylinder	Rauha et al. (2000)
	Escherichia coli	Antimicrobial activity		
	Candida albicans	Moderate antimicrobial activity		
	Aspergillus niger	(–)		
Herb 80% ethanolic extract	*Staphylococcus aureus*	15 mm inhibition zone	50 μL/paper disc	Borchardt et al. (2008)
	Escherichia coli	10 mm inhibition zone		
	Pseudomonas aeruginosa	7 mm inhibition zone		
	Candida albicans	7 mm inhibition zone		
Herb 80% ethanolic extract (Soxlet-24h, evaporated at 55 °C)	*Escherichia coli*	(–)	10 mg/paper disc	Dulger and Gonuz (2004)
	Staphylococcus aureus	12 mm inhibition zone		
	Klebsiella pneumoniae	(–)		
	Pseudomonas aeruginosa	(–)		
	Proteus vulgaris	(–)		
	Bacillus cereus	10 mm inhibition zone		
	Mycobacterium smegmatis	10 mm inhibition zone		
	Listeria monocytogenes	(–)		
	Micrococcus luteus	8 mm inhibition zone		
	Candida albicans	(–)		
	Kluyveromyces fragilis	(–)		
	Rhodotorula rubra	(–)		
Herb dichloromethane extract	*Cladosporium cucumerinum*	Antifungal activity		Becker et al. (2005)
	Staphylococcus aureus	(–)		
	Escherichia coli	(–)		
	Pseudomonas aeruginosa	(–)		
	Citrobacter freundii	(–)		
	Proteus mirabilis	MIC= 1.0 mg/mL		
	Micrococcus luteus	(–)		
	Saccharomyces cerevisiae	MIC= 0.5 mg/mL		
	Candida albicans	MIC= 1.0 mg/mL		
Methanolic extract from herb after dichloromethane extraction	*Staphylococcus aureus*	MIC= 0.5 mg/mL		
	Escherichia coli	(–)		
	Pseudomonas aeruginosa	(–)		
	Citrobacter freundii	(–)		
	Proteus mirabilis	MIC= 1.0 mg/mL		
	Micrococcus luteus	MIC= 1.0 mg/mL		
	Saccharomyces cerevisiae	(–)		
	Candida albicans	(–)		
Ethyl acetate fraction	*Staphylococcus aureus*	MIC= 0.05 mg/mL		
	Escherichia coli	(–)		
	Pseudomonas aeruginosa	(–)		
	Citrobacter freundii	(–)		
	Proteus mirabilis	MIC= 0.5 mg/mL		
	Micrococcus luteus	MIC= 0.5 mg/mL		
	Saccharomyces cerevisiae	(–)		
	Candida albicans	MIC= 0.5 mg/mL		
n-buthanol fraction	*Staphylococcus aureus*	MIC= 0.25 mg/mL		
	Escherichia coli	(–)		
	Pseudomonas aeruginosa	(–)		
	Citrobacter freundii	(–)		
	Proteus mirabilis	MIC= 0.5 mg/mL		
	Micrococcus luteus	MIC= 0.25 mg/mL		
	Saccharomyces cerevisiae	(–)		
	Candida albicans	(–)		
Vescalagin (**1**)	*Staphylococcus aureus*	MIC= 0.062 mg/mL		
	Escherichia coli	(–)		

		Pseudomonas aeruginosa	(–)		
		Citrobacter freundii	(–)		
		Proteus mirabilis	MIC= 0.062 mg/mL		
		Micrococcus luteus	MIC= 0.125 mg/mL		
		Saccharomyces cerevisiae	(–)		
		Candida albicans	(–)		
Herb 75% ethanolic extract (Soxlet)		*Escherichia coli*	11 mm inhibition zone	2 mg/paper disc	Citoglu and Altanlar (2003)
		Pseudomonas aeruginosa	13 mm inhibition zone		
		Bacillus subtilis	9 mm inhibition zone		
		Staphylococcus aureus	9 mm inhibition zone		
		Candida albicans	12 mm inhibition zone		
		Candida galabrata	16 mm inhibition zone		
		Candida krusei	16 mm inhibition zone		
		Listeria monocytogenes	8 mm inhibition zone MIC= 50 µg/mL	2.7 mg/paper disc	Altanlar et al. (2006)
		Listeria ivanovii	(-)		
		Listeria innocua,	11 mm inhibition zone MIC=12.5 µg/mL		
		Listeria murrayi.	(-)		
Herb ethanolic extract, evaporated, dissolved in methanol and chromatographed through silica gel column		*Acinetobacter baumannii* MDR hospital isolates	16 mm mean inhibition zone	850µg/well	Guclu et al. (2014)
		Pseudomonas aeruginosa MDR hospital isolates	18 mm mean inhibition zone		
Aerial parts 80% methanolic extract (percolation)		*Helicobacter pylori*	17 mm inhibition zone	500 mg/mL	Manayi et al. (2013a)
Herb 50% ethanolic extract (sonication at 40 °C)		*Candida albicans*	MIC= 5.0 mg/mL		Bencsik (2014)
		Micrococcus luteus	MIC= 5.0 mg/mL		
		Bacillus subtilis	MIC= 2.5 mg/mL		
		Escherichia coli	MIC= 2.5 mg/mL		
		Pseudomonas aeruginosa	MIC= 2.5 mg/mL		
		MDR *Pseudomonas aeruginosa*	MIC= 2.5 mg/mL		
		Staphylococcus aureus	MIC= 1.25 mg/mL		
		MRSA	MIC= 1.25 mg/mL		
		Staphylococcus epidermidis	MIC= 1.25 mg/mL		

(-)- no effect

Table 10.
Summary of studies regarding *Lythrum salicaria* impact on metabolism.

Type of extract/standardization/fraction/isolated principle			Test model	Effect	Dose/duration	Ref.
Ethanolic extract (boiling, evaporation at 40°C)	Stem	Crude extract	Australian strain rabbits (normoglycemic)	Glycemia↓ (16.0%)	1g of plant material (calculated)/kg b.w./4h (p.o.)	Torres and Suarez (1980)
		Petroleum ether fraction		Glycemia↓ (19.2%)	10g of plant material (calculated)/kg b.w./4h (p.o.)	
		Ethyl ether fraction		Glycemia (–)		
		Ethyl acetate fraction		Glycemia↓ (21.2%)		
		Water residue		Glycemia (–)		
	Flower	Crude extract		Glycemia (–)		
		Petroleum ether fraction		Glycemia↓ (15.3%)	1g of plant material (calculated)/kg b.w./4h (p.o.)	
		Ethyl ether fraction		Glycemia↓ (19.2%)	10g of plant material (calculated)/kg b.w./4h (p.o.)	
		Ethyl acetate fraction		Glycemia (–)		
		Water residue		Glycemia↓ (21.2%) (dd)		
		Ethyl ether fraction		Blood insulin level↑		
		Leaf		Glycemia↓ (16.2%)		
		Root		Glycemia (–)		
	Ethyl ether fraction			Glycemia↓ (21.0%)	5g of plant material (calculated)/kg b.w./45 min (p.o.)	
	Leaf			Glycemia↓ (11.2%)	1g of plant material (calculated)/kg b.w./4h (p.o.)	
	Root			Glycemia (–)	10g of plant material (calculated)/kg b.w./4h (p.o.)	
Flower ethyl ether extract (Soxlet)				Glycemia↓ (21.0%)	10g of plant material (calculated)/kg b.w./4h (p.o.)	
Ethanolic extract of residue (Soxlet)				Glycemia↓ (10.8%)		
Flower 95% ethanolic extract (boiling)			Male Wistar rats	Glycemia↓ (10.3%)	10g plant material (calculated)/kg b.w./4h (p.o.)	Lamela et al. (1985)
				Muscular glycogen↑ (18%)		
				Muscular glycogen (-)		
				Blood insulin level↑↑		
				Triglycerides level↓		
				Free fatty acids level↑		
				Cholesterol level (-)		
Stem ethyl ether extract				Glycemia↓ (19.1%)		
				Hepatic glycogen↑ (30%)		
				Muscular glycogen (-)		
				Blood insulin level↑		
				Triglycerides level↓		
				Free fatty acids level↑		
				Cholesterol level (-)		
95% ethanolic extract after ethyl ether extraction				Glycemia (-)		
Flower ethyl ether extract				Glycemia↓ (4.3%)		

	95% ethanolic extract after ethyl ether extraction			Glycemia (-)		
Stem ethyl ether extract		Langerhans islets isolated from adult male Wistar rats		Insulin release↑	50 mg/mL	
				Insulin release (-)	100 and 200 mg/mL	
Flower 95% ethanolic extract (boiling)		male Wistar rats		Glucose induced hyperglycemia↓ (30min)	10g plant material (calculated)/kg b.w (p.o.)	Lamela et al. (1986)
				Epinephrine induced hyperglycemia↓ (90-120min)		
			alloxan diabetic	Hyperglycemia↓		
			streptozotocin-diabetic	Hyperglycemia↓		
				Alkaline phosphatase serum activity (-)		
				γ-glutamyl transpeptidase serum activity↓		
				Aspartate aminotransferase serum activity↑		
				Lactate dehydrogenase serum activity (-)		
				creatine kinase serum activity (-)		
		alloxan diabetic male Charles-River CD-1 mice		Hyperglycemia↓		
Stem ethyl ether extract		Male Wistar rats		Glucose induced hyperglycemia↓ (30min)		
				Epinephrine induced hyperglycemia↓ (60-120min)		
			Alloxan diabetic	Hyperglycemia↓		
			Streptozotocin diabetic	Hyperglycemia↓		
				Alkaline phosphatase serum activity↓		
				γ-glutamyl transpeptidase serum activity↓		
				Aspartate aminotransferase serum activity (-)		
				Lactate dehydrogenase serum activity↓		
				creatine kinase serum activity (-)		
		Alloxan diabetic male Charles-River CD-1 mice		Hyperglycemia↓		
Flower ethyl ether extract		Male Wistar rats		Glucose induced hyperglycemia↓ (30min)		
				Epinephrine induced hyperglycemia↓ (90-120min)		
			alloxan diabetic	Hyperglycemia↓		
Herb 80% methanolic extract (Concentrated at 45 °C)		Porcine pancreatic lipase		Activity↓ (43.9%)	200 µg/mL	Sharma et al. (2005)
Leaf 50% aqueous methanol		Rat intestinal α-glucosidase		Maltase and sucrase activity↓ (ca. 90%)	5.5 mg plant material (calculated)/mL	Yoshida et al. (2008)
Aerial parts 80% methanolic extract (percolation)		Streptozotocin diabetic rats		Glycemia↓ (12.6%)	15 g/kg b.w. (p.o.)	Manayi et al. (2013a)

(dd)- dose dependent effect
(-)- no effect

Table 11.
Summary of studies regarding *Lythrum salicaria* toxicity and interactions.

Type of extract/fraction		Test model	Effect	Dose	Ref.
Flowering top 45° ethanolic extract (fresh)		Male and female Sprague-Dowley rats	Acute toxicity (10-15 min)	LD_{50}=0.2826 g/kg b.w. (i.v.)	Torrent Marti (1975)
Flowering top 45° ethanolic extract (fresh) precipitated with albumin				LD_{50}=0.1674 g/kg b.w. (i.v.)	
Flowering top 45° ethanolic extract (preserved for >30 days)				LD_{50}=0.3289 g/kg b.w. (i.v.)	
Flowering top 45° ethanolic extract (fresh) diluted in serum				LD_{50}=0.2230 g/kg b.w. (i.v.)	
Flowering top 45° ethanolic extract (preserved for >30 days) diluted in serum				LD_{50}=0.2270 g/kg b.w. (i.v.)	
Herb 80% methanolic extract (percolation)	Crude extract	Colon carcinoma HT-29 cells	Cytotoxicity	IC_{50}=176 µg/mL	Khanavi et al. (2011)
		Leukemia K562 cells		(-)	
		Breast ductal carcinoma T47D cells		IC_{50}=164 µg/mL	
		Swiss embryo fibroblasts NIH3T3		IC_{50}=144 µg/mL	
	Chloroform fraction	Colon carcinoma HT-29 cells		IC_{50}=246 µg/mL	
		Leukemia K562 cells		IC_{50}=178 µg/mL	
		Breast ductal carcinoma T47D cells		IC_{50}=108 µg/mL	

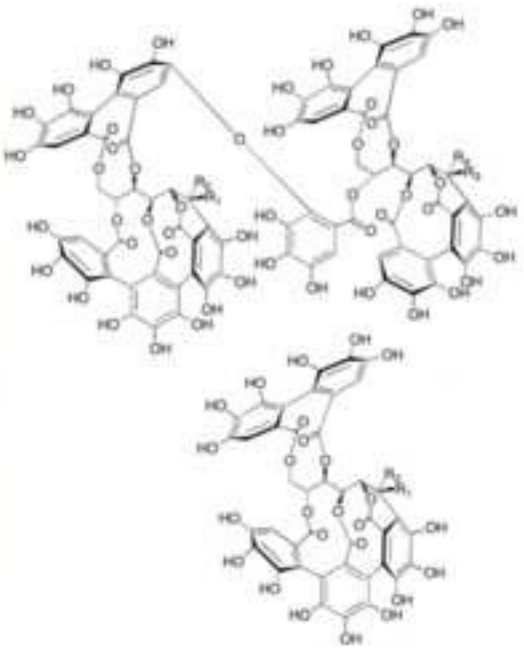
		Swiss embryo fibroblasts NIH3T3		IC_{50}=71 µg/mL	
	Ethyl acetate fraction	Colon carcinoma HT-29 cells		IC_{50}=217 µg/mL	
		Leukemia K562 cells		IC_{50}=332 µg/mL	
		Breast ductal carcinoma T47D cells		IC_{50}=63 µg/mL	
		Swiss embryo fibroblasts NIH3T3		IC_{50}=81 µg/mL	
	Methanol residue	Colon carcinoma HT-29 cells		IC_{50}=462 µg/mL	
		Leukemia K562 cells		IC_{50}=312 µg/mL	
		Breast ductal carcinoma T47D cells		IC_{50}=405 µg/mL	
		Swiss embryo fibroblasts NIH3T3		IC_{50}=573 µg/mL	
Herb 80% methanolic extract (sonication at room temperature, concentrated at 35 °C) (Total phenolics 42.1 mg GAE/g dry weight)		Drug permeability using Caco-2 monolayers	Permeability of verapamil, metoprolol↓ Permeability of paracetamol↑	0.1-1 mg/mL	Laitinen et al. (2004)

Graphical Abstract (for review)

Dysentery

Diarrhea

Skin and mucosa affections



Antidiarrheal

Anti-inflammatory

Anti-oxidant

Anti-microbial