

## Chemical Constituents and Pharmacological Effects of *Lythrum Salicaria*- A Review

Ali Esmail Al-Snafi

Department of Pharmacology, College of Medicine, Thi qar University, Iraq.

**Abstract:** *Lythrum salicaria* contained wide range of chemical constituents included alkaloids, tannins, anthocyanins, glycosides (salicairine), triterpene, sterols, steroids, organic acids, phenolic aids, and flavonoids. Thee pharmacological studies revealed that it exerted many therapeutic effects included antioxidant, antimicrobial, anticancer, intestinal, hypoglycemic, anitnflammatory, analgesic, antitussive, dermatological, haemostatic, anticholinesterase activity and enhancement of osteoblastic proliferation. This review will designed to highlight the chemical constituents and pharmacological effects of *Lythrum salicaria*.

**Keywords:** constituents, pharmacoloy, *Lythrum salicaria*.

Date of Submission: 27-05-2019

Date of acceptance: 13-06-2019

### I. INTRODUCTION

In the last few decades there has been an exponential growth in the field of herbal medicine. It is getting popularized in developing and developed countries owing to its natural origin and lesser side effects. Plants generally produce many secondary metabolites which are bio-synthetically derived from primary metabolites and constitute an important source of chemicals which are used as pharmaceuticals, agrochemicals, flavours, fragrances, colours, biopesticides and food additives<sup>(1-35)</sup>. *Lythrum salicaria* contained wide range of chemical constituents included alkaloids, tannins, anthocyanins, glycosides (salicairine), triterpene, sterols, steroids, organic acids, phenolic aids, and flavonoids. Thee pharmacological studies revealed that it exerted many therapeutic effects included antioxidant, antimicrobial, anticancer, intestinal, hypoglycemic, anitnflammatory, analgesic, antitussive, dermatological,, haemostatic, anticholinesterase activity and enhancement of osteoblastic proliferation. This review will designed to highlight the chemical constituents and pharmacological effects of *Lythrum salicaria*.

#### Plant profile:

#### Synonyms:

*Chabraea vulgaris*, *Lythrum anceps*, *Lythrum argyi*, *Lythrum intermedium*, *Lythrum salicaria* var. *anceps*, *Lythrum salicaria* var. *glabrum*, *Lythrum salicaria* subsp. *intermedium*, *Lythrum salicaria* var. *mairei*, *Lythrum salicaria* var. *salicaria*, *Lythrum tomentosum*<sup>(36)</sup>.

#### Taxonomic classification:

**Kingdom:** Plantae, **Subkingdom:** Viridiplantae, **Infra kingdom:** Streptophyta, **Superdivision:** Embryophyta, **Division:** Tracheophyta, **Subdivision:** Spermatophytina, **Class:** Magnoliopsida, **Superorder:** Rosanae, **Order:** Myrtales, **Family:** Lythraceae, **Genus:** *Lythrum*, **Species:** *Lythrum salicaria*<sup>(37)</sup>.

#### Common names

**Arabic:** Farandal, Furfool, salekariabanafsajia; **Chinese:** qianqucai; **English:** purple loosestrife, purplelythrum, spiked loosestrife; **French:** salicaire, bouquet violet, bouquets rouges, caroncule de dindon; **German:** Blut-Weiderich; **Japanese:** miso-hagi; **Portuguese:** abre-o-sol, quebra-arado, vassourinha; **Spanish:** Arroyuela, Salicaria; **Swedish:** fackelblomster<sup>(38)</sup>.

#### Distribution:

The plant is widely distributed in the northern hemisphere (Europe, Asia, North Africa, and North America), but it can also be found in Australia and New Zealand. It is native to Europe and Asia (Afghanistan, Albania, Armenia, Austria, Azerbaijan, Belarus, Belgium, Bosnia, Herzegovina, Bulgaria, China, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Georgia, Germany, Greece, Hungary, Iran, Iraq, Ireland, Italy, Japan, Jordan, Korea, Latvia, Lebanon, Liechtenstein, Lithuania, Luxembourg, Macedonia, Malta, Moldova, Mongolia, Montenegro, Netherlands, Norway, Pakistan, Palestine, Poland, Portugal, Romania, Russian Federation, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Syrian, Taiwan, Turkey, Ukraine,

United Kingdom). It is also native to Algeria and Tunisia, and introduced to Australia, Canada, Chile, New Zealand, South Africa and United States<sup>(39-40)</sup>.

### **Description:**

It is an erect, perennial herb, 2 to 6 feet in height. Stem: purple loosestrife stems are herbaceous but they arise from a semi-woody base; the four-angled stem can be glabrous to pubescent. Leaves are opposite or in whorls; they are narrow to narrowly oblong, with a heart-shaped base that connects directly to the stem. The roots of purple loosestrife form a dense mass around the semi-woody base. Flowers: Purple loosestrife flowers are magenta, or occasionally white or light pink, with 5–7 petals. The inflorescence is spike-like, 4–20 inches tall. The fruit is a capsule generally containing, 100 or more, tiny, dark colored seeds. Seed capsules remain on the plants through the winter, disseminating seed on a continual basis<sup>(41)</sup>.

### **Traditional uses:**

*Lythrum salicaria* was known as medicinal plant from the ancient Greek and Roman times. The aerial parts of *Lythrum salicaria* were used internally for the treatment of diarrhea, chronic intestinal catarrh, hemorrhoid, eczema, as a decoction or fluid extract. Externally, it was used in the treatment of varicose veins, bleeding of the gums, hemorrhoid, eczema and vaginitis<sup>(42-45)</sup>.

It was also used as a demulcent and astringent decoction for the treatment of coloproctitis, summer complaints of children diarrhoea; locally for chronic ophthalmic and as a wash or poultice for leucorrhoea, gleet (gonorrhoeal discharge), and chronic gonorrhoea<sup>(46)</sup>.

**Parts used medicinally:** Aerial parts<sup>(42-45)</sup>.

### **Chemical constituents:**

The preliminary phytochemical analysis of *Lythrum salicaria* revealed that it contained alkaloids, tannins, anthocyanins, glycosides (salicairine), triterpene, sterols, steroids, organic acids, phenolic acids, and flavonoids<sup>(43, 47-48)</sup>.

Different parts of the plant contained: alkaloids (piperidine and quinolizidine derivatives: lythranine, lythranidine, lythramine, lythrancine I–VII, lythrancepine I–III), tannins (1-O-galloylglucose, 6-O-galloylglucose, 1,6-di-O-galloylglucose, galloyl-HHDP-glucose, trigalloylglucose, galloyl-bis-HHDP-glucose, trigalloyl-HHDP-glucose, vescalagin, pedunculagin, castalagin, lythrine A-D), flavonoids (isorientin, orientin, isovitexin, vitexin, rutin, luteolin, apigenin), anthocyanins (cyanidin-3-galactoside, malvidin-3,5-diglucoside), phenolics (gallic acid, methyl-gallate, chlorogenic acid, ellagic acid, vanoleic acid dilactone, isochlorogenic acid, caffeic acid, p-coumaric acid, ellagic acid derivatives: (3,3',4'-tri-O-methylellagic acid-4-O-β-D-(2''-acetyl)-glucopyranoside, 3,3',4'-tri-O-methylellagic acid-4-O-β-D-glucopyranoside, 3,3',4'-tri-O-methylellagic acid), coumarins (umbelliferone-6-carboxylic acid, the furanocoumarin peucedanin, and buntansin), phthalates (dibutyl phthalate, diisobutyl phthalate, diisooctyl phthalate, diisooctyl phthalate, butyl-2-methylpropyl phthalate, phthalic acid), sterols (β-sitosterol), steroids (daucosterol, β-sitosterol), terpenes (loliolide, betulinic acid, ursolic acid, oleanolic acid, erythrodiol, the ursan-type triterpene corosolic acid, 3β-hydroxy-20(29)-lupen-28-oic acid methyl ester) and 5-hydroxypyrrrolidin-2-one, phytol and dodecanoic acid<sup>(47-49, 51-59)</sup>.

The different constituents identified in the hexane, chloroform, ethyl acetate, 50% ethanol of aerial parts of *Lythrum salicaria* (μg/g) respectively: gallic acid 4.78, 3.58, 39.40 and 166.26; catechin 0, 0, 0 and 29.56; caffeic acid 0, 0, 3.86 and 4.60; chlorogenic acid 1.77, 1.96, 1.33 and 171.10; orientin 2.34, 5.22, 7.70 and 471.42; isorientin 8.92, 23.78, 25.38 and 1319.96; vitexin 1.18, 1.74, 3.52 and 88.26; ellagic acid 16.44, 27.70, 49.48 and 1718.56; hyperoside 0, 0, 0 and 25.06; isovitexin 2.84, 4.10, 7.38 and 130.62; rutin 0, 0, 0 and 1.14; luteolin 1.84, 13.30, 44.38 and 98.36; apigenin 2.60, 6.18, 3.40 and 3.06<sup>(40)</sup>.

Total polysaccharides contents of the aqueous – methanol (80%) extract of the aerial parts of *Lythrum salicaria* were 21 ± 0.2 μg glucose equivalent /mg extract<sup>(59)</sup>.

Chemical analysis of the flowering parts of *Lythrum salicaria* revealed the presence of carbohydrates (30%), phenolics (1g contained 1.2 mM of gallic acid equivalent) and proteins (0.8%). The result of compositional analyses of carbohydrate part revealed the predominance of uronic acids (approximately 66%), galactose (approximately 12%), rhamnose (approximately 10%) and arabinose (approximately 9%). Residues indicating the presence of pectic type of polymers, i.e. galacturonan and/or rhamnogalacturonan associated with arabinogalactan in *Lythrum salicaria* glycoconjugate<sup>(60)</sup>.

The total phenol, total flavonoid, and total tannin amounts in hydromethanolic extracts of *Lythrum salicaria* were 331 ± 3.7 μg gallic acid/mg extract, 5.8 ± 0.4 μg quercetin/mg extract, and 430 ± 2.33 μg tannic acid/mg extract, respectively<sup>(61)</sup>.

The total phenolic and total flavonoid contents of *Lythrum salicaria* extracts were investigated using different extracting methods. Total phenolic contents of *Lythrum salicaria* leaf and flower extracts were

between 325.3 - 355.1 mg gallic acid equivalent (GAE) /g of extract, while, the total flavonoid contents of extracts were between 39.59 - 66.34 mg quercetin equivalent (QE) /g of extract<sup>(50)</sup>.

The polyphenol and tannin contents showed difference among the studied plant organs and populations. They were higher in the flowering top than in the other organs. The total polyphenol values ranged from 1.2 to 27.3% (8.3-27.3% in the flowering top, 5.3-23.3% in the leaves, and 1.2-9.9% in the stems). Total tannin values varied between 1.0 and 21.9% (6.6-21.9% in the flowering top, 4.0-20.9% in the leaves, and 1.0-8.4% in the stems)<sup>(50)</sup>.

### **Pharmacological effects:**

#### **Antioxidant effect:**

The antioxidant activities of *Lythrum salicaria* extracts (using different extracting methods) were investigated by DPPH, nitric oxide and hydrogen peroxide scavenging activities. Extracts showed a concentration-dependent antiradical activity by inhibiting DPPH radical. IC<sub>50</sub> for DPPH radical scavenging activity was between 45.7 – 792.4 µg/ml. The reducing powers of extracts also increased with the increase of their concentrations. Flower showed significantly more potent reducing power than leaf extracts ( $p < 0.01$ ). The extracts showed weak nitric oxide scavenging activity (between 0.69 and 1.79 mg/ ml). All extracts showed good scavenging activity. IC<sub>50</sub> for H<sub>2</sub>O<sub>2</sub> scavenging was 86.2 -200.6 µg/ ml<sup>(50)</sup>.

The antioxidant activity of *Lythrum salicaria* aerial parts was evaluated by the DPPH method. The methanol extract of *Lythrum salicaria* aerial parts possessed antioxidant activity with IC<sub>50</sub> value of  $4.84 \pm 0.10$ , while aqueous extract of the aerial parts showed IC<sub>50</sub> value of  $22.54 \pm 0.65 \mu\text{g/ml}$ <sup>(62)</sup>.

The antioxidant activity of aqueous – methanol (80%) extract of the aerial parts of *Lythrum salicaria* was also studied using DPPH test. Total flavonoids, and phenols were  $5.8 \pm 0.4 \mu\text{g QE/mg extract}$  and  $331 \pm 3.7 \mu\text{g GAE/mg extract}$ , respectively. IC<sub>50</sub> values for DPPH inhibition of the plant extract was  $13.5 \mu\text{g/ml}$ <sup>(59)</sup>.

The antioxidant effect of ethanolic extract of *Lythrum salicaria* was studied using superoxide anion radical scavenging activity and lipid peroxidation. *Lythrum salicaria* ethanol extract showed concentration-dependent superoxide anion radical scavenging activity and inhibitory effect on lipid peroxidation. At concentration of 0.5, 1, 25, 5 and 10 mg/ml, the ethanolic extract of *Lythrum salicaria* showed inhibitory effects on superoxide anion formation of  $95 \pm 1$ ,  $88 \pm 1$ ,  $78 \pm 3$ ,  $51 \pm 4$  and  $29 \pm 5\%$  of control. While, at concentration of 25, 5 and 10 mg/ml, it showed inhibitory effects on lipid peroxidation of 4388, 68 and 48 % of the control respectively<sup>(63)</sup>.

Different solvents extracts (petroleum ether, ethyl acetate, methanol, 50% aqueous methanol and aqueous extract) of the aerial parts of *Lythrum salicaria* were tested for antioxidant activity using DPPH assay, iron(III) reductive activity and MDA value (TBA method). All the extracts were capable of scavenging DPPH radicals at pH 7.4 in a dose-dependent fashion except for the petroleum ether extract, which was not effective. From the estimated IC<sub>50</sub> values, that aqueous methanolic extract was the most potent scavenger followed by methanolic extract > ethyl acetate extract. In Iron (II) thiocyanate method, the ethyl acetate extract was the more effective extract. The activity was decreased in the following order: ethylacetate > aqueous methanol > water > methanol extract at 0.25% concentration and ethylacetate > water > methanol > aqueous methanol extract at 1% concentration. In MDA value (TBA method), Two concentrations of the water extract and 0.25% concentration of ethyl acetate extract were the most potent extracts. The activity was decreased in the following order: aqueous methanolic extracts > ethyl acetate (1% concentration of the extract) > methanolic extracts<sup>(64)</sup>.

#### **Antimicrobial effects:**

*Lythrum salicaria* hydromethanolic extract moderately suppressed *Staphylococcus aureus* and *Candida albicans* growth<sup>(26)</sup>. The antibacterial effect of liquid extract of *Lythrum salicaria* prepared in methyl alcohol was investigated against 30 *A. baumannii* and 27 *Pseudomonas aeruginosa* strains isolated from hospitalized patients as a nosocomial pathogen. *Lythrum salicaria* extract showed good antibacterial activity against these pathogens. The inhibition zone diameter against *Pseudomonas aeruginosa* was 16.09 mm (minimum 12 mm, maximum 20 mm) and against *A. baumannii* was 18.3 mm (minimum 10 mm, maximum 25 mm)<sup>(65)</sup>.

The antibacterial effects of *Lythrum salicaria* extracts were investigated against *Candida albicans*, *Micrococcus luteus*, *Bacillus subtilis*, *Escherichia coli*, *Pseudomonas aeruginosa*, multi drug resistant (MDR) *Pseudomonas*, *Staphylococcus aureus*, methicillin resistant (MRSA)- *Staphylococcus aureus* and *Staphylococcus epidermidis*. All of the selected strains were sensitive to 50% ethanol in water extract. MICs of 50% ethanol in water extract of *Lythrum salicaria* were 5, 5, 2.5, 2.5, 2.5, 2.5, 1.25, and 1.25 mg/ml against *Candida albicans*, *Micrococcus luteus*, *Bacillus subtilis*, *Escherichia coli*, *Pseudomonas aeruginosa*, MRD *Pseudomonas*, *Staphylococcus aureus*, MR- *Staphylococcus aureus* and *Staphylococcus epidermidis*. *S. aureus*, MRSA, *S. epidermidis*, and *M. luteus* were sensitive to the 50% ethanol in water and distilled water extracts. The greatest inhibition zones were produced by the flowering branches then the leaves and finally the stems.

The hexane and chloroform extracts of *Lythrum salicaria* failed to show any activity against the investigated microbial strains<sup>(40)</sup>.

*Lythrum salicaria* extracts possessed antibacterial activity against *Staphylococcus aureus*, *Proteus mirabilis* and *Micrococcus luteus*, it was also showed activity against the phyto-pathogenic fungus *Cladosporium cucumerinum*. The antifungal activity was attributed to triterpenoids, oleanolic and ursolic acid<sup>(47)</sup>.

The anti-*Helicobacter* activity of the *Lythrum salicaria* extract was assessed against clinically isolated strain using disc diffusion method. Clinically isolated *Helicobacter pylori* strain was inhibited at concentration of 500 mg/ml (zone of inhibition:  $17 \pm 0.08$  mm)<sup>(59)</sup>.

The activity of calluses extracts, wild plant, gallic acid, and 3,3',4'-tri-O-methylellagic acid-4-O- $\beta$ -D-glucopyranoside (TMEG) as the main phenolic compounds identified in *Lythrum salicaria* calli were studied against *Candida albicans* using cup plate diffusion method. Anti-candida activity of callus extract was similar to the wild plant extract. Minimum inhibitory concentration values of gallic acid and TMEG were 0.312 and 2.5 mg/ml, respectively<sup>(66)</sup>.

#### **Anticancer effects:**

The cytotoxic activities of fourteen compounds [5-hydroxypyrrolidin-2-one, umbelliferone-6-carboxylic acid, 3,3',4'-tri-O-methylellagic acid-4-O-beta-D-(2"-acetyl)-glucopyranoside, 3,3',4'-tri-O-methylellagic acid-4-O-beta-D-glucopyranoside, daucosterol, phytol, dodecanoic acid, oleanolic acid, 3,3',4'-tri-O-methylellagic acid, corosolic acid, beta-sitosterol, peucedanin, buntansin and erythrodiol] isolated from *Lythrum salicaria* were examined against three cancerous cell lines, colon carcinoma (HT-29), leukemia (K-562), and breast ductal carcinoma (T47D), in addition to Swiss mouse embryo fibroblast (NIH-3T3) cells. Daucosterol, corosolic acid,  $\beta$ -sitosterol and erythrodiol were the most active against the HT-29 cell line with IC<sub>50</sub> values of 192.7, 36.8, 38.2, and 12.8 microg/ml, respectively. Erythrodiol,  $\beta$ -sitosterol, daucosterol, and corosolic acid were 6.4, 2.8, 2.6, and 1.4 times, respectively, more selective than methotrexate. Daucosterol was the most active against the K-562 cell line (IC<sub>50</sub> = 50.2 microg/ml), with a selectivity exceeding that of methotrexate 13.3 times<sup>(49)</sup>.

The extracts and fractions of the aerial parts of *Lythrum salicaria* were investigated for cytotoxic activity against T47D cancer cell lines. Ethyl acetate and chloroform fractions of *Lythrum salicaria* exhibited cytotoxicity against T47D cancer cell line with IC<sub>50</sub> values of 63.1 and 108.2  $\mu$ g/ml, respectively<sup>(66)</sup>.

#### **Intestinal effects:**

The effects of hexane, chloroform, ethyl acetate, and 50% ethanol in water extracts of *Lythrum salicaria* were investigated on isolated Guinea pig ileum. The hexane, chloroform, ethyl acetate and 50% ethanol in water extracts (10  $\mu$ l/5 ml organ bath) produced contractile effects. The largest contractions were elicited by the 50% ethanol in water extract. The effect was concentration-dependent<sup>(40)</sup>.

The n-hexane, chloroform, ethyl acetate and 50% ethanol in water extracts of the air-dried flowering parts of *Lythrum salicaria* were tested for *in vitro* spasmodic properties in Guinea pig ileum. The results showed that *Lythrum salicaria* extracts possessed moderate muscarinic receptor agonistic effect in Guinea pig ileum. The most prominent response was triggered by the 50% ethanol in water extract in a concentration-dependent manner. Atropine, indomethacin and PPADS plus suramin significantly reduced the contractile response caused by this extract. The authors recommended that diluted extracts of *Lythrum salicaria* orally could be used as a mild stimulant of gastrointestinal motility<sup>(67)</sup>.

Salicairine at 0.01 ml/ml, like loperamide at 0.2 mg/ml, significantly increased net fluid absorption in rat colon, either in basal conditions (30 and 64% respectively) or after a prostaglandin E1- induced increase in net fluid secretion (41 and 35%, respectively). Salicairine was able to reduce contractions of isolated rat duodenum induced by barium chloride and acetylcholine, although not completely (about 60%) as seen with loperamide. Salicairine at 0.01 ml/ml, like loperamide at 0.2 mg/ml, significantly increased net fluid absorption in rat colon, either in basal conditions (30 and 64% respectively) or after a prostaglandin E1- induced increase in net fluid secretion (41 and 35%, respectively). The antidiarrheal activity of salicairine could either attributed to an increase in colon net fluid absorption or to a decrease in net fluid secretion<sup>(67)</sup>.

#### **Hypoglycemic effect:**

The hypoglycemic effect of *Lythrum salicaria* extracts was studied in fasting normoglycemic rabbits and glucose- induced hyperglycemic. The greatest hypoglycemic activity was possessed by stem extracts, followed by the flower and leaf, while the root was inactive. Four hours after oral administration, the maximum hypoglycemia was evident in the normoglycemic rabbits. An increased insulin was occurred with the drops in blood glucose, suggesting that the plant may stimulated releasing of insulin<sup>(68)</sup>.

The hypoglycemic effects of several extracts of *Lythrum salicaria* were studied in normoglycemic and hyperglycemic rabbits. The results confirmed the hypoglycemic activity of the plant extracts<sup>(69)</sup>.

The hypoglycemic effect of several extracts from stem and flower of *Lythrum salicaria* were evaluated in rats. Ether extracts from stem or flowers at a dose equivalent to 10 g/kg of crude plant material possessed significant hypoglycemic effects with increasing insulin level, after 4 h of oral administration<sup>(70)</sup>.

Ether extracts of *Lythrum salicaria* stems and flowers exhibited significant hypoglycemic activity in rats with glucose- and epinephrine-induced hyperglycemia. The extracts were also active in alloxan- and streptozotocin- induced diabetic rats and alloxan- induced diabetic mice. Stem and flower extracts reduced the elevated gamma- glutamyl transpeptidase activity. Stem extract reduced the elevated lactic dehydrogenase activity and flower extract accentuated the elevated levels of aspartate aminotransferase induced by streptozotocin<sup>(71)</sup>.

The hypoglycemic effect of aqueous- methanol (80%) extract of the aerial parts of *Lythrum salicaria* was studied in streptozocin- induced diabetes in rats. The extract (at dose of 15 g/kg) reduced the blood glucose level by 12.6% and 7.3% during the second and third hours of administration, respectively<sup>(59)</sup>.

#### **Antinflammatory and analgesic activity:**

Different solvents extracts (petroleum ether, ethyl acetate, methanol, 50% aqueous methanol and aqueous extract) of the aerial parts of *Lythrum salicaria* were tested for anti-inflammatory activity using carrageenan-induced hind paw edema model in mice. Methanol extract showed an inhibitory activity ( $p < 0.05$ ) at 200 mg/kg dose after 270 and 360 min (28.9 and 35.5%, respectively). Other extracts from *Lythrum salicaria* were inactive<sup>(64)</sup>.

Different solvents extracts (petroleum ether, ethyl acetate, methanol, 50% aqueous methanol and aqueous extract) of the aerial parts of *Lythrum salicaria* were tested for anti-nociceptive activity using p-benzoquinone-induced abdominal constriction test in mice. Methanol extract was found to have inhibitory activity ( $p < 0.05$ ) at 100 and 200 mg/kg dose (26.9 and 30.1%, respectively). None of the extracts caused any gastric damage<sup>(64)</sup>.

#### **Antitussive activity:**

A polysaccharide-polyphenolic conjugate isolated from flowering parts of *Lythrum salicaria* was tested for antitussive activity (25, 50 and 75 mg/kg) using citric acid-induced cough reflex in guinea pigs. It reduced the number of cough efforts even 5 h after administration. However, the antitussive effects were lower in comparison with that of codeine. The evaluation of the effect of different doses on airways smooth muscle reactivity revealed more significant effect of *Lythrum* conjugate in comparison with that of salbutamol. Measurements of specific airway resistance revealed the dose-dependent bronchodilatory activity and participation of bronchodilation in antitussive effect of *Lythrum* conjugate<sup>(72)</sup>.

#### **Dermatological effects:**

The wound healing effects of hydromethanolic extracts of *Lythrum salicaria* and *Hypericum scabrum* topical ointments were studied in second-degree burn wounds in rats. Wound contraction percentage with *Lythrum salicaria* and *Hypericum scabrum* was  $89.5 \pm 3.7$  and  $77.6 \pm 4.1$ , respectively. A well-organized epidermal layer and normal appearance in dermis layer were more observable in the *Lythrum salicaria* group. Moreover, *Lythrum salicaria* ointment individually displayed better influence on tissue oxidative stress parameters than *Hypericum scabrum* and the negative control ( $p < 0.05$ )<sup>(61)</sup>.

The effects of extract of aerial parts of *Lythrum salicaria* and its constituents, on keratinocytes, reconstructed epidermis, and skins were evaluated by topical treatment. The extract and one of its major compounds were able to act as pro-differentiating and protecting agents towards skin cells by stimulating the expressions of markers taking part in the structure of epidermis and dermis. The extract also showed beneficial effects on the global morphology of the skin<sup>(73)</sup>.

#### **Haemostatic effect:**

The water-soluble glycoconjugate isolated from the flowering parts extract of *Lythrum salicaria* showed pro-coagulant activity *in vitro*. It completely inhibited plasma clot formation, however, the application of glycoconjugate *in vivo* showed controversial effect on animal blood system in comparison with *in vitro* pro-coagulant activity<sup>(60)</sup>.

#### **Inhibitory effect on Acyl-CoA: cholesterolacyltransferase:**

The triterpenes (betulinic acid and 3 beta-hydroxy-20(29)-lupen-28-oic acid methyl ester) isolated from *Lythrum salicaria* showed inhibitory activities on both acyl-CoA: cholesterol acyltransferase (ACAT1) and Acyl-CoA: cholesterol acyltransferase (hACAT2), (ACAT catalyzes the acylation of cholesterol to cholesteryl

ester and exists in two isoforms, ACAT1 and ACAT2, ACAT1 is in charge of foam cell formation in macrophages, whereas ACAT2 controls the cholesterol absorption in intestinal mucosal cells). These results suggested that *Lythrum salicaria*, which contains triterpenes, might be effective in the prevention and treatment of hypercholesterolemia or atherosclerosis due to its inhibitory effect on Hcat<sup>(55)</sup>.

#### **Enhancement of osteoblastic proliferation:**

The effect of betulinic acid isolated from *Lythrum salicaria*, on the proliferation of osteoblastic MC3T3-E1 cells was examined by checking the cell viability. Betulinic acid showed a tendency of increasing the growth of osteoblastic MC3T3-E1 cells<sup>(58)</sup>.

#### **Toxicity and side effects:**

Many authors mentioned that there were no significant adverse effects following the using of *Lythrum salicaria* internally and externally<sup>(51, 64, 74)</sup>.

The acute toxicity study of hydroalcoholic extracts from *Lythrum salicaria* flowering tops in animal model, showed that the LD<sub>50</sub> of iv administration varied between 0.1674 and 0.3289 g/kg bw. In oral administration of similar doses, mild symptoms were recorded: mild abdominal contractions, difficulties in respiration and mild hypothermia, which were not resulting in animal death<sup>(52)</sup>.

#### **Dose:**

Preparations prescribed in the gastrointestinal tract ailments: powdered herb (3-5 g/day), tincture (20 drops on sugar, 4-5 times a day); syrup for children (1 g of extract/ 30 g of syrup)<sup>(74)</sup>.

## **II. CONCLUSION**

This review discusses the chemical constituent, pharmacological and therapeutic effects of *Lythrum salicaria* as promising herbal drug because of its safety and effectiveness.

## **REFERENCES**

- [1]. Al-Snafi AE. Chemical constituents and medical importance of *Galium aparine* - A review. Indo Am J P Sc 2018; 5(3): 1739-1744.
- [2]. 213- Al-Snafi AE. *Galium verum* -A review. Indo Am J P Sc 2018; 5 (4): 2142-2149.
- [3]. Al-Snafi AE. Pharmacological and toxicological effects of *Heliotropium undulatum* (*H. bacciferum*) and *Heliotropium europaeum*- A review. Indo Am J P Sc 2018; 5 (4): 2150-2158.
- [4]. Al-Snafi AE. Medical importance of *Helianthus tuberosus*- A review. Indo Am J P Sc 2018; 5 (4): 2159-2166.
- [5]. Al-Snafi AE. Pharmacological importance of *Herniaria glabra* and *Herniaria hirsuta* - A review. Indo Am J P Sc 2018; 5 (4): 2167-2175.
- [6]. Al-Snafi AE. Pharmacological effects and therapeutic properties of *Hibiscus cannabinus*- A review. Indo Am J P Sc 2018; 5 (4): 2176-2182.
- [7]. Al-Snafi AE. Chemical constituents and pharmacological effect of *Inula graveolens* (Syn: *Dittrichia graveolens*)- A review. Indo Am J P Sc 2018; 5 (4): 2183-2190.
- [8]. Al-Snafi AE. Pharmacology and medicinal properties of *Jasminum officinale*- A review. Indo Am J P Sc 2018; 5 (4): 2191-2197.
- [9]. Al-Snafi AE. Pharmacological and therapeutic effects of *Juniperus oxycedrus*- A review. Indo Am J P Sc 2018; 5 (4): 2198-2205.
- [10]. Al-Snafi AE. Constituents and pharmacological importance of *Jussiaea repens* - A review. Indo Am J P Sc 2018; 5 (4): 2206-2212.
- [11]. Al-Snafi AE. Therapeutic importance of *Hyoscyamus* species grown in Iraq (*Hyoscyamus albus*, *Hyoscyamus niger* and *Hyoscyamus reticulatus*)- A review. IOSR Journal of Pharmacy 2018; 8(6): 18-32.
- [12]. Al-Snafi AE. Pharmacological and therapeutic activities of *Hedera helix*- A review IOSR Journal of Pharmacy 2018; 8(5): 41-53.
- [13]. Al-Snafi AE. Pharmacological importance of *Haplophyllum* species grown in Iraq- A review. IOSR Journal of Pharmacy 2018;8(5): 54-62.
- [14]. Al-Snafi AE. Chemical constituents and pharmacological activities of *Gossypium herbaceum* and *Gossypium hirsutum* - A review. IOSR Journal of Pharmacy 2018; 8(5): 64-80.
- [15]. Al-Snafi AE. The chemical constituents and pharmacological effects of *Foeniculum vulgare* - A review. IOSR Journal of Pharmacy 2018; 8(5): 81-96.
- [16]. Al-Snafi AE. Pharmacological and therapeutic importance of *Hibiscus sabdariffa*- A review. International Journal of Pharmaceutical Research 2018; 10(3): 451-475.

- [17]. Al-Snafi AE. Chemical constituents, pharmacological effects and therapeutic importance of *Hibiscus rosa-sinensis*- A review. IOSR Journal of Pharmacy 2018; 8 (7): 101-119.
- [18]. Al-Snafi AE. Arabian medicinal plants with antiurolithiatic and diuretic effects - plant based review (Part 1). IOSR Journal of Pharmacy 2018; 8(6): 67-80.
- [19]. Al-Snafi AE. Arabian medicinal plants affected female fertility- plant based review (part 1). IOSR Journal of Pharmacy 2018; 8(7): 46-62.
- [20]. Al-Snafi AE. Arabian medicinal plants for the treatment of intestinal disorders- plant based review (part 1). IOSR Journal of Pharmacy 2018; 8(6): 53-66.
- [21]. Al-Snafi AE. Arabian medicinal plants possessed gastroprotective effects- plant based review (part 1). IOSR Journal of Pharmacy 2018; 8(7): 77-95.
- [22]. Al-Snafi AE. Arabian medicinal plants with analgesic and antipyretic effects- plant based review (Part 1). IOSR Journal of Pharmacy 2018; 8(6): 81-102.
- [23]. Al-Snafi AE. Arabian medicinal plants with antiinflammatory effects- plant based review (part 1). IOSR Journal of Pharmacy 2018; 8 (7): 55-100.
- [24]. Al-Snafi AE and Thwaini MM. Nephro- protective effects of Arabian medicinal plants ( part 1). Research Journal of Pharmaceutical, Biological and Chemical Sciences 2018; 9(5): 1504-1511.
- [25]. Al-Snafi AE and Thwaini MM. Arabian medicinal plants with hepatoprotective activity (part 1). Research Journal of Pharmaceutical, Biological and Chemical Sciences 2018; 9(5): 1469-1497.
- [26]. Al-Snafi AE. Traditional uses of Iraqi medicinal plants. IOSR Journal of Pharmacy 2018; 8 (8): 32-96.
- [27]. Al-Snafi AE. Arabian medicinal plants with dermatological effects- plant based review (part 1) . IOSR Journal of Pharmacy 2018; 8(10): 44-73.
- [28]. Al-Snafi AE. Chemical constituents, nutritional, pharmacological and therapeutic importance of *Juglans regia*- A review. IOSR Journal of Pharmacy 2018; 8(11): 1-21.
- [29]. Al-Snafi AE. Medicinal plants affected contractility of smooth muscles- A review . IOSR Journal of Pharmacy 2018; 8(11): 22-35.
- [30]. Al-Snafi AE, Majid WJ and Talab TA. Medicinal plants with antidiabetic effects - An overview (Part 1). IOSR Journal of pharmacy 2019; 9(3): 9-46.
- [31]. Al-Snafi AE. Fritillaria imperialis- A review. IOSR Journal of pharmacy 2019, 9(3): 47-51.
- [32]. Al-Snafi AE, Talab TA and Majid WJ. Medicinal plants with central nervous activity - An overview (Part 1). IOSR Journal of pharmacy 2019; 9(3): 52-102.
- [33]. Al-Snafi AE. Constituents and pharmacology of *Geum urbanum*- A review. IOSR Journal of pharmacy 2019; 9(5): 28-33.
- [34]. Al-Snafi AE. Medical importance of *Glossostemon bruguieri* – A review. IOSR Journal of pharmacy 2019; 9(5): 34-39.
- [35]. Al-Snafi AE. The medical benefit of *Gnaphalium luteoalbum*-A review. IOSR Journal of pharmacy 2019; 9(5): 40-44.
- [36]. The plant list, *Lythrum salicaria*, <http://www.theplantlist.org/tp11.1/record/kew-2354139>
- [37]. ITIS report, *Lythrum salicaria*, [https://www.itis.gov/servlet/SingleRpt/SingleRpt?search\\_topic=TSN&search\\_value=27079#null](https://www.itis.gov/servlet/SingleRpt/SingleRpt?search_topic=TSN&search_value=27079#null)
- [38]. U.S. National Plant Germplasm System, *Lythrum salicaria*, <https://npgsweb.ars-grin.gov/gringlobal/taxonomydetail.aspx?23022>
- [39]. Kavak S. *Lythrum salicaria*. The IUCN Red List of Threatened Species 2014: e.T164323A42329075. <http://dx.doi.org/10.2305/IUCN.UK.2014-1.RLTS.T164323A42329075.en>.
- [40]. Bencsik T. Comparative Histological, Phytochemical, Microbiological, and Pharmacological Characterization of Some *Lythrum salicaria* L. Populations. Ph.D. dissertation. Department of Pharmacognosy, Medical School University of Pécs, Hungary, 2014.
- [41]. Purple Loosestrife, *Lythrum salicaria* L. (Lythraceae), [https://www.brodheadwatershed.org/pdf/Lythrum\\_salicaria.pdf](https://www.brodheadwatershed.org/pdf/Lythrum_salicaria.pdf)
- [42]. Baytop T. Therapy with Plants in Turkey. Istanbul University Publications, Istanbul, 1999: 374.
- [43]. Rauha J P, Remes S, Heinonen M, Hopia A, Kahkonen M, Kujala T, Pihlaja K, Vuorela H and Vuorela P. Antimicrobial effects of Finnish plant extracts containing flavonoids and other phenolic compounds. Int J Food Microbiol 2000; 56: 3-12.
- [44]. Mantle D, Eddeb F and Pickering AT. Comparison of relative antioxidant activities of British medicinal plant species *in vitro*. J Ethnopharmacol 2000; 72: 47-51.
- [45]. Gonzalez JA, Garcia-Barriuso M and Amich F. Ethnobotanical study of medicinal plants traditionally used in the Arribes del Duero, western Spain. Journal of Ethnopharmacology 2010;131: 343–355.
- [46]. Eisenberg S. Viewpoints on a common weed: *Lythrum salicaria*. Journal of the American Herbalists Guild 2006; 6(2): 39-43.

- [47]. Becker H, Scher JM, Speakman JB and Zapp J. Bioactivity guided isolation of antimicrobial compounds from *Lythrum salicaria*. *Fitoterapia* 2005; 76(6): 580-584.
- [48]. Rauha JP, Wolfender JL, Salminen JP, Pihlaja K, Hostettmann K and Vuorela H. Characterization of the polyphenolic composition of Purple loosestrife (*Lythrum salicaria*). *Zeitschrift für Naturforschung C* 2001; 56: 13-20.
- [49]. Manayi A, Saeidnia S, Ostad SN, Hadjiakhoondi A, Ardekani MRS, Vaziriana M, Akhtar Y and Khanavi M. Chemical constituents and cytotoxic effect of the main compounds of *Lythrum salicaria* L. *Z Naturforsch C* 2013;68(9-10): 367-75.
- [50]. Jamshidi M, Shabani E, Hashemi Z and Ebrahimzadeh M A. Evaluation of three methods for the extraction of antioxidants from leaf and aerial parts of *Lythrum salicaria* L (Lythraceae). *International Food Research Journal* 2014; 21(2): 783-788.
- [51]. Piwowarski JP, Granica S and Kiss AK. *Lythrum salicaria* L - underestimated medicinal plant from European traditional medicine- A review. *Journal of Ethnopharmacology* 2015; 170: 226-250.
- [52]. Torrent Marti MT. Estudio farmacognóstico y farmacodinámico de *Lythrum salicaria*, L. *Circular Farmaceutica* 1975; 33: 265-307.
- [53]. Paris M. Contribution à l'étude biochimique de la Salicaire (*Lythrum salicaria* L., Lythracées) et en particulier de ses polyphénols. Pharm Thesis. Travaux des Laboratoires de matière médicale et de pharmacogalénique de la Faculté de pharmacie de Paris 1967.
- [54]. Paris RR and Paris M. 1964. Sur les pigments anthocyaniques de la Salicaire (*Lythrum salicaria* L). *Comptes Rendus* 1964; 258: 361-364.
- [55]. Kim GS, Lee SE, Jeong TS, Park CG, Sung JS, Kim JB, Hong YP, Kim YC and Song KS. Human Acyl-CoA: cholesterol acyltransferase (hACAT)-inhibiting triterpens from *Lythrum salicaria* L. *Journal of The Korean Society for Applied Biological Chemistry* 2011; 54(4): 628-632.
- [56]. Ma X, Ji, C, Wang Y, Zhang G and Liu Y. New tannins from *Lythrum salicaria* L. *Journal of Chinese Pharmaceutical Sciences* 1996; 5: 225.
- [57]. Fujita E, Saeki Y, Ochiai M and Inoue T. Investigation of the neutral constituents of *Lythrum salicaria* L. *Bulletin of the Institute for Chemical Research (Kyoto University)* 1972; 50: 327-331.
- [58]. Kim G, Lee S, Cha S, Song K and Kim Y. Isolation of two triterpenes from *Lythrum salicaria* L and the effect of betulinic acid on the proliferation of osteoblastic MC3T3-E1 cells. *Planta Med* 2010; 76(12): 208.
- [59]. Manayi A, Khanavi M, Saeidnia S, Azizi E, Mahmoodpour MR, Vafi F, Malmir M, Siavashi F and Hadjiakhoondi A. Biological activity and microscopic characterization of *Lythrum salicaria* L. *Daru* 2013; 21(1): 61-67.
- [60]. Pawlaczyk I, Czerchawski L, Kańska J, Bijak J, Capek P, Pliszczak-Król A and Gancarz R. An acidic glycoconjugate from *Lythrum salicaria* L with controversial effects on haemostasis. *J Ethnopharmacol* 2010; 131(1):63-69.
- [61]. Vafi F, Bahramsoltani R, Abdollahi M, Manayi A, Hossein Abdolghaffari A, Samadi N, Amin G, Hassanzadeh G, Jamalifar H, Baeeri M, Heidari M and Khanavi M. Burn wound healing activity of *Lythrum salicaria* L and *Hypericum scabrum* L. *Wounds* 2016; 28(12): 448 - 458.
- [62]. López V, Akerreta S, Casanova E, García-Mina J, Cavero R and Calvo M. Screening of spanish medicinal plants for antioxidant and antifungal activities. *Pharmaceutical Biology* 2008; 46(9): 602-609.
- [63]. Çoban T, Çitoglu CG, Sever B and Iscan M. Antioxidant activities of plants used in traditional medicine in Turkey. *Pharmaceutical Biology* 2003; 41(8): 608-613.
- [64]. Tunalier Z, Koşar M, Küpeli E, Caliş I and Başer KH. Antioxidant, anti-inflammatory, antinociceptive activities and composition of *Lythrum salicaria* L extracts. *J Ethnopharmacol* 2007;110(3):539-547.
- [65]. Guclu E, Genc H, Zengin M and Karabay O. Antibacterial activity of *Lythrum salicaria* against multidrug-resistant *Acinetobacter baumannii* and *Pseudomonas aeruginosa*. *Annual Research & Review in Biology* 2014; 4(7): 1099-1105.
- [66]. Khanavi M, Moshteh M, Manayi A, Shams Ardekani MR, Vazirian M, Ajani Y and Ostad SN. Cytotoxic activity of *Lythrum salicaria* L. *Res J Biol Sci* 2011; 6: 55 - 57.
- [67]. Brun Y, Wang XP, Willemot J, Sevenet T and Demenge P. Experimental study of antidiarrheal activity of Salicairine. *Fundam Clin Pharmacol* 1998; 12(1):30-36.
- [68]. Cadavid I and Calleja J, A preliminary study of hypoglycemic activity of *Lythrum salicaria*. *Journal of Natural Products* 1980; 43(5): 559-563
- [69]. Torres IC and Suarez JC. A preliminary study of hypoglycemic activity of *Lythrum salicaria*. *J Nat Prod* 1980; 43(5):559-563.
- [70]. Lamela M, Cadavid I, Gato A and Calleja JM. Effects of *Lythrum salicaria* in normoglycemic rats. *J Ethnopharmacol* 1985; 14(1):83-91.



- [71]. Lamela M, Cadavid I and Calleja JM. Effects of *Lythrum salicaria* extracts on hyperglycemic rats and mice. *J Ethnopharmacol* 1986; 15(2):153-160.
- [72]. Sutovska M, Capek P, Franova S, Pawlaczyk I and Gancarz R. Antitussive and bronchodilatory effects of *Lythrum salicaria* polysaccharide- polyphenolic conjugate. *Inter J Biol Macromol* 2012; 51:794–799.
- [73]. Jouravel G, Guénin S, Bernard FX, Elfakir C, Bernard P and Himbert F. New biological activities of *Lythrum salicaria* L: Effects on keratinocytes, reconstructed epidermis and reconstructed skins, applications in dermo-cosmetic sciences. *Cosmetics* 2017; 4: 52; doi:10.3390/cosmetics4040052
- [74]. Campardon C. Sur l'emploithérapeutique du *Lythrum salicaria*. *Bull Gen Ther Med Chir* 1883; 105:337–349.

Ali Esmail Al-Snafi. “ Chemical Constituents and Pharmacological Effects of Lythrum Salicaria- A Review.”IOSR Journal of Pharmacy (IOSRPHR), vol. 9, no. 6, 2019, pp. 51-59.