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(REVIEW ARTICLE)

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Constituents and biological effects of *Reseda lutea* and *Reseda odorata* grown in Iraq

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Abstract

The current review revealed that *Reseda lutea* contained alkaloids, flavonoids, saponins, anthocyanin, glucosides and tannins, and possessed antimicrobial, anti-inflammatory, insecticidal, antiproliferative and antioxidant effects. While, *Reseda odorata* contained essential oil, phenylethyl mustard oil, luteolin glucoside, luteoloside, amino acids, 2(*S*),4(*R*)-4-(β-D-galactopyranosyloxy)-4-isobutylglutamic,*O*-(α-L-rhamnopyranosyloxy) benzylamine, *O*-hydroxybenzylamine, 2(S),2′(S)-N6-(2′-glutaryl)lysine (l-saccharopine) and 2(S)-2-aminoadipic acid. it exerted antiinflammatory, antioxidant, anticancer and neuroprotective effects.

Keywords: *Reseda lutea; Reseda odorata*; Constituents; Pharmacology; Therapy

1. Introduction

In the last few decades there has been an exponential growth in the field of herbal medicine. 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 and biopesticides[1-14]. The phytochemical analysis of *Reseda lutea* showed that the plant contained alkaloids, flavonoids, saponins, anthocyanin, glucosides and tannins, and the pharmacological studies revealed that it possessed antimicrobial, anti-inflammatory, insecticidal, antiproliferative and antioxidant effects. The chemical analysis of *Reseda odorata* showed that the plant contained essential oil, phenylethyl mustardoil, luteolinglucoside, luteoloside, amino acids,2(*S*),4(*R*)-4-(β-D-galactopyranosyloxy)-4-isobutylglutamic, *O*-(α-L-rhamnopyranosyloxy) benzylamine, *O*-hydroxybenzylamine, 2(S),2′(S)-N6-(2′-glutaryl)lysine (l-saccharopine) and 2(S)-2-aminoadipic acid. While, it exerted antiinflammatory, antioxidant, anticancer and neuroprotective effects. The current review was designed to highlight the chemical constituents and pharmacological effects of *Reseda lutea* and *Reseda odorata*.

2. Plants profile

2.1. *Reseda lutea*

2.1.1. Synonyms

Reseda benitoi, Reseda fluminensis, Reseda gracilis, Reseda lutea var. vivantii, Reseda macedonica, Reseda mucronata, Reseda othryana, Reseda petrovichiana, Reseda podolica, Reseda ramosissima, Reseda truncata, Reseda vinyalsii, Reseda vivantii[15].

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2.1.2. Taxonomic classification

Kingdom: Plantae, Subkingdom: Viridiplantae ,Infrakingdom: Streptophyta, Superdivision: Embryophyta, Division: Tracheophyta, Subdivision: Spermatophytina, Class: Magnoliopsida, Superorder: Rosanae, Order: Brassicales, Family: Resedaceae, Genus: *Reseda*, Species: *Reseda lutea*[16].

2.1.3. Common names

Arabic: khuzami, thail Al-thikh; English: cut-leaf mignonette, hasadi, khuzam, wild mignonette, yellow mignonette; French: rédédajaune; Portuguese: reseda-amarela, reseda-silvestre; Swedish: gulreseda[17].

2.1.4. Distribution

It is distributed in Africa (Algeria, Egypt, Libya, Morocco, Tunisia), Asia (Iran, Iraq, Palestine, Jordan, Lebanon, Syria, Turkey, Russian Federation, Armenia, Azerbaijan, Siberia, Turkmenistan), Europe (Czech Republic, Netherlands, Poland, Slovakia, Belarus, Ukraine, Albania, Bulgaria, Bosnia and Herzegovina, Greece, Croatia, Italy, Malta, Montenegro, Romania, Serbia, Slovenia, Spain, France, Portugal), and also widely naturalized[17].

2.1.5. Description

Herbs annual or perennial, caespitose, 30-75 cm tall, glabrous. Stem branched, angular. Leaves 3-5-parted to pinnatifid, papery; lobes linear, margin repand. Flowers in terminal racemes, yellow to yellowish green; pedicel 3-5 mm. Sepals 6, linear, unequal, shorter than pedicel. Petals 6, rounded-clawed at base, lower 2 entire, lateral two 2- or 3-parted, upper 2 largest, 3-parted. Stamens 12-20. Carpels 3, connate. Capsule erect, cylindric or ovoid to subglobose, obtusely 3-angled, ca. 1 cm, apically 3-cleft. Seeds black, shiny, reniform, ca. 2 mm[18].

2.1.6. Traditional uses

The plant with long history of human use, in Pharaonic Egypt, it was used as an odoriferous in elaborate burial ceremonies [19].The plant was used as a medicinal plant, in salads, in the carpet and rug industry as a source of natural dye, in animal husbandry as a grazing plant and stock food source[20].In Zanjan province- Iran, the root was used as diuretic, laxative and tonic. Chewing the leaves was used for cooling effect and to remove the thirst[21].

The was used traditionally in Jordan for wound healing, and in the treatment of hypertension[22]. The plant was recommended and extensively utilized for reducing tumors[19].

Parts used medicinally: Roots and leaves[21].

2.1.7. Chemical constituents

The preliminary phytochemical analysis of showed that *Reseda lutea* contained alkaloids, flavonoids, saponins, anthocyanin, glucosides, tannins and luteoline[23-25].

The total phenolic content was 109.01±0.03 in the flowers and 133.52±0.02mg gallic acid equivalent/l in the leaves of *Reseda lutea*, while, the total flavonoid content was 78.72±0.03in the flowers and196.80±0.01 mg quercetin equivalent/l in the leaves[23].

Reseda lutea contained kaempferol, quercetin, flavonol glycosides [kaempferol-3-*O*-[2-*O*-(β-D-xylopyranosyl)-3-*O*-(β-D-glucopyranosyl)]-α-L-rhamnopyranosyl-7-*O*-α-L-rhamnopyranoside, and kaempferol-3-*O*-[2-*O*-((6-*O*-*trans*-*p*-coumaryl) -β-D-glucopyranosyl)-3-*O*-(β-D-xylopyranosyl)]-α-L-rhamnopyranosyl-7-*O*-α-L-rhamnopyranoside], flavonoid sulphates, and flavone *C* and *C*-/*O*-glycosides[25-27].

Tetrasaccharide, glucosinolates(3-hydroxybenzyl glucosinolates and 2-(α-L-rhamnopyranosyloxy)benzyl glucosinolates were also isolated from *Reseda lutea*[25, 28].

Percentage composition of autolysis volatiles of glucosinolatesin the root, flower and fruit of *Reseda lutea* (% respectively) were: benzaldehyde 1.5, –, – ; benzyl alcohol 0.7 ,– , – ; salicylaldehyde 1.2, – , – ; dodecane 0.9, –, –; benzoic acid 7.3, – , – ; benzyl isothiocyanate (BITC) 59.9, – , – ; tricosane – , – , 17.5;pentacosane – , 3.6,22.2; 2-(α-L-rhamnopyranosyloxy)benzyl isothiocyanate – , 74.7,5.2; heptacosane 15.5,10.6,30.1; and nonacosane 9.2,5.2 and 19.6%[23].

Chemical analysis of the aerial parts oil of *Reseda lutea* from Iran, revealed that the oil contained 42 constituents. The main constituents were benzonitrile (17.9%), (*Z*)-phytol (13.0%), *n*-heptacosane (7.5%), β-ionone (6.2%), hexahydrofarnesyl acetone (5.1%), palmitic acid (4.6%), diisobutyl phthalate (3.7%),*n*-nonacosane (2.5%),*n*-tricosane (2.4%) anddibutyl phthalate (2.3%)[20].

Forty ingredients, were identified in the *Reseda lutea* aerial parts essence of plant samples taken from east Azerbaijan province- Iran. The main constituents were decane (9.43%), dodecane (8.41%), undecane (6.34%), hexadecane (6.16%), pentadecane (5.57%), heptadecane (3.89%), tridecane (3.86%), octane (2.7%), rhodinal (2.61%) and decandioic acid, didecyl ester (2.24%)[29].

2.1.8. Pharmacological effects

Antimicrobial effect

The antibacterial activity of *Reseda lutea*was investigated against clinical isolates of *Staphylococcus aureus*, *Staphylococcus epidermidis* and *Escherichia coli*. The extract possessed antimicrobial activities against *Staphylococcus aureus* and *Staphylococcus epidermidis*[29].

Then-hexane, dichloromethane and methanol extracts of the plant were investigated for antibacterial activity against 11 pathogenic bacteria (*Staphylococcus aureus, Staphylococcus aureus* (MRSA)*, Staphylococcus epidermidis, Staphylococcus hominis, L. plantarum, Bacillus cereus, Proteus mirabilis, Escherichia coli, P. aeruginosa* and *Serratia marcescens*).The methanolic extract of *Reseda lutea* possessed antibacterial activity against four bacterial species (*Staphylococcus aureus, Staphylococcus epidermidis, Staphylococcus hominis* and *Serratia marcescens*)[30].

The methanolic leaves and flower extracts of *Reseda lutea* were tested for antimicrobial effect against *Bacillus subtilis, Staphylococcus aureus, Pseudomonas aeruginosa*, *Escherichia coli* and *Candida albicans*. The extracts showed different ranges of antibacterial potential against all the tested bacterial strains. Diameters of zone of growth inhibition of the flower methanolic extract were 10, 20, 10, 13 and 9 mm, and that of the leaves methanolic extracts were 13, 20, 10, 13 and 9 mm against the above microorganisms respectively. The MIC of the flower extract against bacteria was 31.25-62.5 and leaves extract 62.5-125 µg/ml. While against *Candida albicans*, the MIC of both extracts was 125µg/ml[31].

The extract of *Reseda lutea* possessed antibacterial effects against *Staphylococcus aureus, Bacillus cereus, Escherichia coli* with the diameters of growth inhibition of 18, 13.8 and 12.7mm at a concentration of 400 mg/ml respectively, while it showed no activity against *Pseudomonas aeruginosa*[32].

Anti-inflammatory effect

Reseda lutea from South-Eastern Spain was tested for anti-inflammatory activity. It possessed anti-inflammatory activity and the primary target was the transcription factor *NF-κB* (with the using of a luciferase-based assay in HeLa cells). In addition the extract was tested *in vitro* for effects on cytokines (IL-6, IL-8, TNF-α) or PGE2 in monocytes and for potential cytotoxic/pro-apoptotic action as well as for their influence on the cell cycle. The extract possessed potent inhibition of *NF-κB* (inhibition level 80–60% at 100 µg/ml), IL-1β andIL-6 (inhibition level of 100–80% at 100 µg/ml.),IL-8 inhibition (inhibition level 80–60% at 100 µg/ml), and caused 80 % cell death at the concentration of 50µ/ml against HeLa cells[33].

5-Phenyl-2-oxazolidinethione isolated from the flowers of *Reseda lutea* was screened for its effect on rat macrophage viability and nitric oxide production. At a concentration of10^{-4}–10^{-6} mol/dm^3, the compounds acted as cytotoxic agents. It exerted prominent nitric oxide production-inhibiting properties, which may suggest an immunomodulatory activity as NO is a well-known inflammation mediator[34].

Antiproliferative effect

Benzyl isothiocyanate and 2-(α-l-rhamnopyranosyloxy) benzylisothiocyanate isolated from the root and flower autolysates, showed significant antiproliferative effects against human A375 (melanoma) and MRC5 (fibroblast) cell lines. Cell cycle analysis revealed apoptosis as a probable mechanism of cell death[23].

Antioxidant effect

The effects of methanol extracts of the flowers and leaves of *Reseda lutea* were investigated on the activity of aldose reductase, catalase, glutathione-S-transferase, and glutathione peroxidase. According to the results, methanol extracts showed no significant activity on aldose reductase. Moreover, none of the studied extracts demonstrated any

reasonable catalase activation potential. But The extract showed good activity onglutathione-S-transferase (IC_{50} 149±0.004 ng/ml for flowers and 403±0.015 ng/ml for leaves) and glutathione peroxidase (IC_{50} 140±0.001 ng/ml for lowers and 490±0.05 ng/ml for leaves)**[35].**

2.1.9. Insecticidal effect

The activity of many Turkish medicinal plants was investigated against mosquitoes *in vitro*. ED_{50} of mosquito larvicidal activity of *Reseda lutea* extracts was 0.15 mg/ml against *Aedes aegypti* and0.07 mg/ml against *Aedes gambiae*[36].

2.2. Reseda odorata

2.2.1. Synonyms

No synonyms are recorded for this species[37].

2.2.2. Taxonomic classification

Kingdom: Plantae, Subkingdom: Viridiplantae, Infrakingdom: Streptophyta, Superdivision: Embryophyta, Division: Tracheophyta, Subdivision: Spermatophytina, Class: Magnoliopsida, Superorder: Rosanae, Order: Brassicales, Family: Resedaceae, Genus: *Reseda*, Species: *Reseda odorata*[38].

2.2.3. Common names

Arabic: khuzami, bulihaetriah; Chinese: mu xi cao, English: bastard rocket, common mignonette, garden mignonette, sweet mignonette, sweet reseda; French: mignonette, résédaodorante; German: gartenresede, Portuguese: minhonete, reseda-de-cheiro; Spanish: miñoneta, reseda de olor; Swedish: luktreseda[39].

2.2.4. Distribution

Reseda odorata is native to Africa, Europe and widely cultivated[39].

2.2.5. Description

Herbs usually annual, to 40 cm tall, glabrous. Stem branched. Leaves subsessile, spatulate or lanceolate to elliptic-oblong, entire or toothed to parted, papery. Flowers in terminal racemes; white or light yellow, or orange-red when cultivated, very fragrant. Sepals 6, narrowly spatulate, 2.5-4 mm, shorter than pedicel. Petals 6, clawed at base, lower 2 entire, lateral 2 digitate, upper 2 digitate with few segments and equaling sepals. Stamens 17-20; filaments subulate. Carpels 3. Capsule pendulous, subglobose or urceolate, 3-angled, ca. 1 cm. Seeds black, shiny, 2-2.5 mm[40].

2.2.6. Traditional uses

At the beginning of this century, the natural flower oil of Reseda was used in high class perfumes. The steam distilled Reseda flowers yielded 0.002 percent of a volatile oil. The Reseda-like odor of this oil became apparent only in strong dilution[41].The seeds were applied externally as a resolvent. The root was used in Spain as a laxative, diuretic and diaphoretic[42].

2.2.7. Parts used medicinally

Oil, seeds, roots and flowers[41-42].

2.2.8. Chemical constituents

Essential oils extracted from the roots and from the flowers producing the characteristic scent of*Reseda odorata*. The yellow oil from the flowers is not fluorescent, has a density of 0.961 at 15°C, solidifies when cooled, smells very unpleasantly but becomes attractive if solved in very small concentration. The scent might partly be ascribed to phenylethylmustardoil[43].

A luteolin glucoside, luteolosidehas been isolated from the fresh blossoms and outer parts of the plant[6]. Amino acids[3-(3-carboxy-4-hydroxy-phenyl)-L-alanine (m-carboxy-l-tyrosine)] was isolated from the seeds, and 2(*S*),4(*R*)-4-(β-D-galactopyranosyloxy)-4-isobutylglutamicwas isolated from the flowers of *Reseda odorata*[44-45].

A glucosinolate, *o*-(α-L-rhamnopyranosyloxy) benzylglucosinolate, was isolated from the plant[10].*O*-(α-L-rhamnopyranosyloxy) benzylamine and *O*-hydroxybenzylamine, 2(S),2′(S)-N6-(2′-glutaryl)lysine (l-saccharopine) and 2(S)-2-aminoadipic acid were isolated from *Reseda odorata* [46-48].

2.2.9. Pharmacological effects

Antiinflammatory and antioxidant effects

It was documented that luteolin the main component of *Reseda odorata* was an effective hemeoxygenase-1 (HO-1) inducer, it possessed anti-inflammatory effects in macrophages in a dose-dependent manner, leading to suppression of inducible nitric oxide synthase (iNOS)-derived nitric oxide (NO) production, suggesting the beneficial pharmacological activity of luteolin in inflammatory diseases[49].

Studying of the mechanism of anti-inflammatory effects of luteolin showed that Src in the nuclear factor (NF)-κB pathway, MAPK in the activator protein (AP)− 1 pathway, and SOCS3 in the single transducer and activator of transcription 3 (STAT3) pathway were its major target transcription factors. A clinical trial with a formulation containing luteolin showed excellent therapeutic effect against inflammation-associated diseases[50].

The effects of luteolin was investigated in mice with severe acute pancreatitis (SAP). Cerulein and lipopolysaccharide were used to induce acute pancreatitis in male mice. Amylase, lipase, nuclear factor-κB (NF-κB) and myeloperoxidase activities, in addition to malondialdehyde, tumor necrosis factor α (TNFα), interleukin (IL)-6, IL-10 and HO-1 levels, as well as the expression of HO-1 were determined in serum and/or pancreatic tissue samples. Luteolin protected mice from acute pancreatitis by inducing HO-1-mediated anti-inflammatory and by its antioxidant activities, in association with the suppression of the activation of the NF-κB pathway[51].

In the treatment of age-related neurodegenerative disorders

It also confirmed that luteolin was an efficient therapeutic agent for the treatment and management of age-related neurodegenerative disorders[52].

Anticancer effect

Luteolin (3,4,5,7-tetrahydroxy flavone), a flavonoid isolated from *Reseda odorata* possessed anticancer effects against various types of human malignancies such as breast, colon, pancreatic, prostate, oral, lung, kidney, bladder, ovarian, cervical, placental, skin, liver, gastric, oesophageal cancers and glioblastoma. It prevented the cancer development *in vitro* and *in vivo* by inhibition of proliferation of tumor cells, protection from carcinogenic stimuli, and activation of cell cycle arrest, and by inducing apoptosis through different signaling pathways. It also reversed epithelial mesenchymal transition (EMT) through a mechanism involved cytoskeleton shrinkage, induction of the epithelial biomarker E-cadherin expression, and down-regulation of the mesenchymal biomarkers N-cadherin, snail, and vimentin. Luteolin also increased the levels of intracellular reactive oxygen species by activation of lethal endoplasmic reticulum stress response and mitochondrial dysfunction in glioblastoma cells, and by activation of ER stress-associated proteins expressions, including phosphorylation of eIF2*α*, PERK,CHOP, ATF4, and cleaved-caspase 12[53].

3. Conclusion

This review discusses the chemical constituent, pharmacological and therapeutic effects of *Reseda lutea* and *Reseda odorata* grown in Iraq as promising herbal drugs because of their safety and effectiveness.

Compliance with ethical standards

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