



MELILOTUS OFFICINALIS AND ITS BENEFITS ON PHARMACOLOGY

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Annotation

Melilotus officinalis contained coumarins, melilotin, phenolic acids, flavonoids, steroids, saponins, volatile oils, fats, triterpenes, carbohydrates, sugar, anthraquinone glycosides, mucilage, tannin, bishydroxycoumarin, choline, alcohols, uric acid and many other chemical groups. Antimicrobial, antioxidant, anticancer, anti-inflammatory, neural, protective, sedative, anxiolytic, smooth muscle relaxant, hypotensive and many other pharmacological effects. The current article highlighted the chemical constituents and pharmacological effects of Melilotus officinalis.

Keywords: chemical constituents, pharmacology, Melilotus officinalis.

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. The phytochemical analysis showed that Melilotus officinalis contained coumarins, melilotin, phenolic acids, flavonoids, steroids, saponins, volatile oils, fats, triterpenes, carbohydrates, sugar, anthraquinone glycosides, mucilage, tannin, bis hydroxycoumarin, choline, alcohols, uric acid and many other chemical groups. Antimicrobial, antioxidant, anticancer, antiinflammatory, neural, protective, sedative, anxiolytic, smooth muscle relaxant, hypotensive and many other pharmacological effects. The current article will highlight the chemical constituents and pharmacological effects of Melilotus officinalis.

It is annual to biennial, erect or decumbent plant. Stems erect, 40-100(-250) cm, longitudinally ridged. Stipules linear-falcate, 3-5(-7) mm, entire or with 1 tooth at base; petiole slender; leaflets obovate, broadly ovate, oblanceolate, to linear, 15-25(-30) × 5-15 mm, lateral veins running into teeth, 8-12 pairs, margins shallowly serrate. Racemes 6-15(-20) mm, 30-70-flowered, dense at first, becoming lax in anthesis; bracts equal to pedicels, 1.5-2 mm. Corolla yellow, 4.5-7 mm; standard ± equal to wings and keel. Ovary narrowly ovate; ovules (4-)6(-8). Legume ovoid, 3-5 × ca. 2 mm, veins transversely reticulate, dark brown, apex with persistent style. Seeds 1 or 2, yellowish brown, ovoid, ca. 2.5 mm, smooth



Traditional Uses

The plant was used as aromatic, emollient, demulcent, maturant, tonic, aphrodisiac, carminative to relieve flatulence and externally applied as poultice for pains and aches. The small fruits were used as demulcent, maturant, tonic, aphrodisiac and in leucoderma. Herbal tea was used as a wash and rinse for swelling and swollen glands, abscesses, and swelling of the lymph nodes. Tea herbs, or the flowers themselves, were applied in cases of cold, mucosity, and respiratory and gastrointestinal disorders.

It was also used in idiopathic headaches, long-standing neuralgias, coldness, tenderness, lameness or marked soreness of joints, cold, menstrual colic, ovarian neuralgia, colic with diarrhoea and much.

Parts used medicinally: The whole herb and flowering shoots and fruits were used medicinally.

Physicochemical parameters: Physicochemical parameters of powdered *Melilotus officinalis* (% w/w) were: total ash: 11.25 ± 0.25 , acid insoluble: 2.11 ± 0.12 , water soluble: 6.86 ± 0.19 , methanol extractive value 3.96, aqueous extractive value 13.27, volatile oil 0.59 ± 0.02 and loss on drying 6.69 ± 0.12 .

Chemical constituents: The preliminary phytochemical analysis showed that *Melilotus officinalis* contained coumarins, melilotin, phenolic acids, flavonoids, steroids, saponins, volatile oils, fats, triterpenes, carbohydrates, sugar, anthraquinone glycosides, mucilage, tannin, bis hydroxycoumarin, choline, alcohols and uric acid. The dominant components in total lipophilic compounds of the chloroform extract of *Melilotus officinalis* were 1,3- di-o-methylmyo-inositol (75.503%), acetal (5.874%), palmitic acid (2.252%) and linoleic acid (1.958%). Twenty six constituents were identified in the *Melilotus officinalis* essential oil from Borispol (Ukraine), hexahydrofarnesylacetone (16.64%), β -eudesmol (11.49%) and globulol (8.65%) represented the main constituents. However, the identified compounds and their percentage were: para-hydroxybenzaldehyde 1.96, camphor 3.15, terpinene-4-ol 4.17, 2-methylbenzaldehyde 2.70, aromadendrene 1.38, geranylacetone 1.21, 2,6,10-trimethyldodecane (farnesane) 5.68, β -ionone 0.93, β -ionone-5,6-epoxide 2.08, epi-globulol 3.05, isophytol 1.47, spathulenol 4.27, globulol 8.65, viridiflorol 2.98, epi-eudesmol 2.50, γ -eudesmol 1.98, β -eudesmol 11.49, bisabolon oxide 7.43, hexahydrofarnesylacetone 16.64, methyl palmitate 2.68, methyl linoleate 1.77, methyl linolenate 5.19, phytol 4.52, ethyl linoleate 0.96 and Phytol acetate 1.12%. The main compounds identified in the volatile oils of the methanol extract of the leaves of *Melilotus officinalis* from Syria were: n-docosane (39.82%), hydrocoumarin (15.39%) and methyl 3-(2-hydroxyphenyl) propionate (14.29%), while, the main compounds identified in the volatile oils of the hexane extract of the leaves of *Melilotus officinalis* from Syria were: palatinol (17.77%), 9,12,15-octadecatrienoic acid, methyl ester (12.85%), 1-(dimethylamino)-5-[(4'-ethynylphenyl) ethynyl] naphthalene (12.59%), 2,4-dioctylphenol (9.73%), hexadecanoic acid, methyl ester (8.99%) and eicosane (8.53%)



Hexadecanoic acid, lupanone, lupeol, betulinic acid, oleanolic acid, kaempferol-3-O- β -glucopyranoside were isolated from the methanol extract of whole *Melilotus officinalis*.

Oleanene glucuronide (melilotus-saponin O1), together with soyasaponin, dehydrosoyasaponin, acetylsoyasaponin were isolated from the roots of *Melilotus officinalis* while, soyasapogenols B and E were isolated from the aerial parts.

Pharmacological effects. The antimicrobial effect of the methanolic extract of *Melilotus officinalis* was investigated against Gram positive and Gram negative bacteria. MIC against *Escherichia coli*: 15mg, *Klebsiella pneumoniae*: 18mg, *Proteus mirabilis*: 20mg, *Pseudomonas aeruginosa*: 25mg, *Staphylococcus aureus*: 25mg, *Streptococcus pyogenes*: 30mg, *Bacillus subtilis*: 25mg, *Bacillus cereus*: 25 mg and *Candida albicans* 35mg. The antibacterial activity of the water, acetone, diethyl ether and ethanol extracts of *Melilotus officinalis* was studied against *Klebsiella pneumoniae*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Salmonella typhimurium*, *Salmonella enteric*, *Enterococcus faecalis*, *Staphylococcus aureus*, *Sarcina lutea*, *Bacillus subtilis*, *Bacillus cereus*, *Bifidobacterium animalis subsp. lactis* and *Lactobacillus rhamnosus*. The values of MIC and MMC were in a range of <0.156 mg/ml to >20 mg/ml. The intensity of antibacterial activity depended on the type of extract and the type of bacteria. The extracts were active in the following ascending order: water < ethanol < diethyl ether < acetone. The acetone and the diethyl ether were the most active extracts, while water and ethanol extracts showed significantly lower activity. Gram negative bacteria showed higher sensitivity to the acetone and diethyl ether extracts, but never in concentrations less than 10 mg/ml for MIC and MMC, except for *Escherichia coli* which was sensitive in the concentration of 5 mg/ml of the ether extract for MIC. The antibacterial effect of the aqueous, methanolic and ethanolic extract of *Melilotus officinalis* was investigated against Gram negative bacteria (*Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Serratia marcescens*, *Proteus vulgaris*, *Enterobacter cloacae* and *Klebsiella pneumoniae*) and Gram positive bacteria (*Streptococcus pyogenes*, *Staphylococcus aureus* and *Staphylococcus epidermidis*). The ethanolic extract of *Melilotus officinalis* showed more antibacterial effect than aqueous and methanolic extracts against *S. marcescens* and *S. typhimurium*. *P. vulgaris*, *E. cloacae*, and *E. coli* were susceptible to aqueous extract of *Melilotus officinalis*. However, all the tested bacteria were not susceptible to methanolic extracts. In vitro antifungal activities of *Melilotus officinalis* extracts were evaluated against *C. inconspicua*, *C. guilliermondii*, *C. albicans*, *C. krusei*, *C. lusitaniae*, *C. glabrata*, *C. parapsilosis*, *C. methapsilosis*, and *C. ortopsilosis*. The results showed that *Melilotus officinalis* extracts were active antimycotic agents against wide range of *Candida* species. *C. guilliermondii* and *C. parapsilosis* were the most sensitive.

Dermatological effect: In studying the beneficial effect of the extract of *Melilotus officinalis* in skin care applications, the extract showed an ability of stimulating skin cells and promoting tissue regeneration, preventing skin aging,



and reducing fat deposition. The effects of ethanolic extract at doses ranging from 0.25 to 50 $\mu\text{g/ml}$ (from 1 to 5000 $\mu\text{g/ml}$ in cell viability assays) were evaluated using in vitro tests on HaCaT human keratinocytes, 46BR 1N fibroblasts, and adipocyte cell cultures, and on matrix-degrading enzymes. MTT assay revealed weak effects on cell viability ($\text{IC}_{50} > 1000 \mu\text{g/ml}$) and significant increase of fibroblast growth rate. Cell-free enzymatic assays showed collagenase inhibition, while an ELISA assay revealed efficient stimulation of fibroblast collagen production. Oil-Red-O adipocyte staining showed pronounced lipolytic effect. The effects of *Melilotus officinalis* ointment in the healing of burn wounds were studied in burn ulcers produced on the back of rats. Wound healing contraction and histopathological examination were evaluated at the end of 7, 14, and 21 days. *Melilotus officinalis* preparations significantly improved the quality of wound healing and scar formation and also they were more appropriate treatment choices than silver sulfadiazine.

For the treatment of Alzheimer Disease: The effect of *Melilotus officinalis* extract in Alzheimer disease was studied, regarding its possible role as anti-inflammatory, anti-oxidant agent and its effect on the expression of many genes including DAXX, NFkB and VEGF. The results revealed that the extract caused significant decreased the expression of Daxx, Nfkb and Vegf genes in the sporadic Alzheimer disease rat's model compared to the streptozotocin (STZ)- induced rats. Furthermore, no significant changes were seen in swimming distance and time for finding the hidden platform in the extract- treated compared to the STZ-induced group. No significant changes were observed in the memory level among treated and untreated groups.

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