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GALIUM VERUM -A REVIEW

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Abstract:
The phytochemical analysis of Galium verum showed that the plant contained oil, iridoid glycosides, phenolics, flavonoids, carbohydrates and amino acids. The previous pharmacological studies showed that Galium verum possessed antioxidant, cytotoxic, antimicrobial, protective and endocrine effects. This review will highlight the chemical constituents and pharmacological effects of Galium verum.

Keywords: *Galium verum, pharmacology, chemical, constituents*

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INTRODUCTION:

A large and increasing number of patients in the world use medicinal plants and herbs for health purpose. Therefore, scientific scrutiny of their therapeutic potential, biological properties, and safety will be useful in making wise decisions about their use. Many recent reviews showed that plants produce many secondary metabolites which are bio-synthetically derived from primary metabolites and constitute an important source of many drugs[1-20]. The phytochemical analysis of Galium *verum* showed that the plant contained oil, iridoid glycosides, phenolics, flavonoids, carbohydrates and amino acids**.** The previous pharmacological studies showed that *Galium verum* possessed antioxidant, cytotoxic, antimicrobial, protective and endocrine effects. This review was designed to highlight the chemical constituents and pharmacological effects of *Galium verum*.

Plant profile:

Synonyms:

Asterophyllum galium Schimp. & Spenn., *Galium affine* Roth, *Galium alpinum* Schur, *Galium approximatum* Gren. & Godr., *Galium atropatanum* Grossh., *Galium floridum* Salisb., *Galium gironae* Sennen, *Galium glabratum* Klokov, *Galium glabrum* Hoffm., *Galium leonis* Sennen, *Galium luteoverticillatum* St.-Lag., *Galium luteum* Lam., *Galium luteum* St.-Lag., *Galium mauryi* Sennen, *Galium minutum* L., *Galium ochroleucum* Rochel ,*Galium bracteolatum* Sennen, *Galium densiflorum* Ledeb., *Galium caucasicum* Lag., *Galium densiflorum* f. *leiocarpum* Printz, *Galium ochroleucum* var. *approximatum* [Gren. & Godr.] Rouy, *Galium officinale* Gaterau, *Galium pallidiflorum* Schur, *Galium praecox* A.Kern., *Galium pseudoverum* Schur, *Galium rubioides* Suter, *Galium ruthenicum* Willd., *Galium serotinum* Munby, *Galium squarrosum* Sennen, *Galium sylvestre* var. *glabrum* [Hoffm.] Nyman, *Galium tenderiense* Klokov, *Galium vernum* subsp. *alpinum* [Schur] Nyman, *Galium vernum* var. *ruthenicum* [Willd.] Nyman, *Galium trichophyllum* Wulfen, *Galium tuberculatum* C.Presl, *Galium tomentellum* Klokov, *Galium verosimile* Roem. & Schult. *Galium verum* var. *albidum* Hartm., *Galium verum* f. *album* Nakai, *Galium verum* var. *asiaticum* Nakai, *Galium verum* var. *compactum* Touss. & Hosch., *Galium verum* f. *crebrifolium* Rouy, *Galium verum* var. *intermedium* Nakai, *Galium verum* var. *japonalpinum* Nakai, *Galium verum* var. *lasiocarpum* Ledeb., *Galium verum* var. *leiocarpum* Ledeb., *Galium verum* var. *leiophyllum* Wallr., *Galium verum* var. *littorale* Bréb., *Galium verum* f. *luteolum* Makino, *Galium verum* var. *luteum* [Lam.] Nakai, *Galium verum* subsp. *maritimum* [DC.] Adema, *Galium verum* var. *maritimum* DC. , *Galium* verum var. *pallidiflorum* F.Gérard, *Galium verum* var. *pallidum* Celak., *Galium verum* var. *praecox* Láng ex Hagenb., *Galium verum* f. *puberulum* Serg., *Galium verum* var. *ruthenicum* Nakai, *Galium verum* f. *ruthenicum* [Willd.] Rouy, *Galium verum* subsp. *ruthenicum* P. Fourn., *Galium verum* f. *subpubescens* Serg., *Galium verum* var. *Subulatum* Tinant, *Galium verum* var. *supinum* Tinant, *Galium verum* var. *tomentosum* C. A. Mey., *Galium verum* f. *tomentosum* [C. A. Mey.] Nakai, *Galium verum* var. *trachycarpum* DC., *Galium verum* var. *trachyphyllum* Wallr., *Galium verum* f. *trichanthum* Ancev, *Galium verum* subsp. *verum*, *Galium verum* var. *verum*, *Galium verum* f. *verum*, *Galium wettsteinii* Ullep. and *Rubia vera* [L.] Baill[21].

Taxonomic classification:

Kingdom: Plantae, **Subkingdom**: Tracheobionta, **Superdivision**: Spermatophyta, **Division**: Magnoliophyta, **Class**: Magnoliopsida, **Subclass**: Asteridae, **Order**: Rubiales, **Family**: Rubiaceae, **Genus**: *Galium*, **Species**: *Galium verum*[22].

Common names:

Arabic: Juisa Khadhra, Kish El-Furash, **English:** lady's bedstraw, yellow bedstraw; **French:** Caille-lait jaune, Gaillet vrai, Gaillet jaune; **Portuguese:** gálio-amarelo, gálio-verdadeiro; **Spanish**: cuajaleche, galio, presera, sanjuanera, agana, cuaja leche, cuajaleches, cuaxaleche, galio de flor amarilla, hierba cuajadera, hierba sanjuanera, quaxa leche, yerba cuajadera, yerba de la grama, yerba de la grana, yerba sanjuanera; **Swedish**: gulmåra, **Turkish**: Sarı yoğurt out[23].

Distribution:

The plant was distributed in **Africa:** Algeria, Morocco, Tunisia; **Asia**: Armenia, Azerbaijan, Georgia, Russian Federation, China, Japan, Korea, Kazakhstan, Kyrgyzstan, Mongolia, Afghanistan, Iran, Iraq, Lebanon, Syria, Turkey, Pakistan; **Europe**: Belarus, Estonia, Latvia, Lithuania, Moldova, Ukraine, Austria, Belgium, Czech Republic, Germany, Hungary, Poland, Slovakia, Switzerland, Denmark, Finland, Ireland, Norway, Sweden, United Kingdom, Albania, Bulgaria, Croatia, Greece, Italy, Romania, Serbia, Slovenia, France, Portugal and Spain[3]

Description:

It is perennial, with rootstock and rhizomes. Stems erect, [5-]15-70[-120] cm tall, 4-angled, densely

puberulent, villosulous, or hirtellous to rarely glabrous and smooth. Leaves in middle stem region in whorls of more than 6 and up to 12, sessile; blade drying papery to subleathery, often blackening, adaxially rather shiny, abaxially paler, linear to linear-oblong, 10-30[-50] × 1-2[-2.5] mm, adaxially glabrous to densely hairy, smooth to sparsely aculeolate, abaxially usually densely puberulent to tomentose, rarely glabrescent or glabrous, base acute to cuneate, margins usually strongly revolute and antrorsely aculeolate, apex acute and shortly mucronate with tip to 1.5 mm; vein 1. Inflorescences thyrsoid or paniculate, terminal and axillary cymes few to many flowered, rather dense and bracteose; axes densely puberulent, hirtellous, rarely glabrous and smooth; bracts ± leaflike, 1.5-3 mm; pedicels 1-3 mm. Flowers fragrant, hermaphroditic. Corolla yellow to white, rotate, ca. 3 mm in diam., glabrous, lobed for 3/4 or more; lobes 4, lanceolate-oblong, subobtuse, acute to apiculate. Mericarps ellipsoid and laterally flattened, 1.5-2 mm, glabrous to densely hispidulous with straight trichomes[24].

Traditional uses:

It was applied externally in poultice, used for indolent tumors, strumous swellings and tumors of the breast. Internally it was used in decoction sweetened with honey, for urinary stone complaints, scurvy, dropsy, hysterics, epilepsy and gout. It was also used in the bleeding of the nose and stomach problems, and it was said that it peculiarly beneficial in scorbutic, scrofulous, and dropsical complaints[25].

The cut and dried aerial parts of *Galium verum* have been used for exogenous treatment of psoriasis or delayed wound healing or as a tea for the cure of pyelitis or cystitis[26]. The plant was also used in traditional medicine as an anticancer medicine applied in most cases as a decoction. It was used in Europe and Northern America for the treatment of cancerous ulcers or breast cancer[27-28].

Part used medicinally:

The whole plant[25-28].

Chemical constituents:

The preliminary phytochemical analysis showed that the plant contained oil, iridoid glycosides, phenolics, flavonoids, carbohydrates and amino acids[29-33].

The essential oil of *Galium verum* flowers was composed of [% of the flwers]: 3- methyl - 2 - butanone: 0.02%, amylchloride: 0.02, penten: 3-ol: 0.01, pentanone-2: 0.1, acetoin: 0.2, 2- methyl pentanl-2: 0.04, pyridine: 0.01, 3- methyl pentanl-3: 0.02, 3-methyl-2-buten-1-ol: 0.01, 2,4- pentadione: 0.04, 1- methyl cyclopentanone: 0.04, 3- methyl cyclopentanone: 0.01, Cis-3-hexen-1-ol: 0.82, hexanol: 0.02, diethyleneglycol monomethyl ether: 0.28, benzyl alcohol: 0.22, cis-linalooloxide 0.02, trans- linalooloxide 0.02, linalool: 0.02, benzylnitrile: 0.02, camphor: 0.02, borneol: 0.1, cis-epoxylinalool: 0.01, trans- epoxylinalool: 0.01, α- terpineol: 0.04, 4-vinylphenol: 0.02, O-aminoacetophenone: 0.02, tetradecanoic acid: 0.02, pentadecanoic acid: 0.01, dibutylphthalate: 0.04, hexadecanoic acid: 0.02, eicosan: 0.01, dioctylphthalate: 0.05 and squalene: 0.57[34].

However, Miraz *et al*., found that the oil isolated by hydro-distillation from the aerial parts of *Galium verum* from Iran reached 1.3% [w/w], based on the dry weight. Twenty-three components were identified in the essential oil, the major components were - caryophyllane [26%], caryophyllene oxide [16.2%], and germacrene D [11.2%][29].

Soleimani and Ali Zade identified twenty five components in the essential oil of *Galium verum* representing 97.21% of the oil, the major component were phytol [9.268%], tetradecane [11.764%], hexadecane [12.272%], n-tetradecane [17.932%], 9,12,15-octadecatrienoic acid- methyl ester [8.088%] and hexadecanoic acid- methyl ester [4.318%][35].

The chemical analysis of the constituents of the extract of *Galium verum* from China showed that it contained eleven compounds identified as [+]-pinoresinol 4,4'-O-bis-beta-D-glucopyranoside, epipinoresinol, [+] -medioresinol, isorhamnetin, isorhamnetin 3-O-alpha-L-rhamnopyranosyl-[1-6]-beta-D-glucopyranoside, diosmetin, diosmetin 7-O-beta-D-glucopyranoside, quercetin-3-O-beta-D-glucopyranoside, ursolic acid, ursolic aldehyde and rubifolic acid[36].

Many anthraquinone were isolated from *Galium verum* L. Their structures were identified as 1,3-dihydroxy-2-methylanthraquinone; physcion; 2-hydroxy-1,3-dimethoxyanthraquinone and 2,5-dihydroxy-1,3-dimethoxyanthraquinone, 1,3-dihydroxy-2 methoxymethyl; 1,3-dimethoxy-2-hydroxy, 1,3-dihydroxy-2-acetoxy; 1-hydroxy-2-hydroxymethyl; and 1-methoxy-2-hydroxy anthraquinones. The other two were provisionally identified as 1,3-dihydroxy-2-hydroxymethyl-6-methoxy and 1,6-dihydroxy-2-methyl anthraquinones[37-38].

Asperuloside, an iridoid-type monoterpene glycoside was isolated from *Galium verum.* The highest production of asperuloside can be obtained at full flowering stage of development due to the high iridoid content of the inflorescences[39].

Seven iridoid glycosides, asperuloside, asperulosidic acid, deacetyl-asperulosidic acid, monotropein, 6-*O*-

epi -acetylscandoside, daphylloside and deacetyl-daphylloside; 2 flavonol glycosides, astragalin [= kaempferol 3-O-*β*- glucopyranoside] and rutin [= quercetin 3-O- rutinoside]; and 2 monoterpene glycosides, betulalbuside A and [2E]-2,6-dimethyl-2,7-octadien-1,6-diol-6-*O*- *β*-glucopyranoside, were isolated from the aerial parts of *Galium verum* subsp. *verum*[30].

The total amount of phenolic compounds in the methanolic extract of the aerial parts
was [753 ±21 mg/g of extract] and the total flavonoid content was [151.25 ±8.2 mg/g of extract][40]

However, the total phenolics of two samples from Serbia was [2.44-4.65 mg and 4.57-5.16 mg gallic acid equivalents/g dry extract], and total flavonoids was [6.38-10.70 µg and 15.56-17.96 µg quercetin equivalents/g dry extract][31].

The dried aerial parts of *Galium verum* contained many phenolics and flavonoids included chlorogenic acid: 3.217, [+]-catechin: 1.024, caffeic acid: 2.967, rutin: 1.313, coumaric acid: 1.550, isoquercitrin: 1.339 , quercetin: 0.150, isorhamnetin: 4.286, ferulic acid: 0.836 , [–]-Epicatechin: 0.060, hesperidin: 0.503, fisetin: 0.040 and chrysin: 0.002 mg/ g dry weight[32].

Apigenin 7-*O*-[3,4-di-*O*-acetyl]-*α*-L-rhamno pyranosyl -[1 → 6]-*β*-D- glucopyranoside, diosmetin 7-O-alpha-l-rhamnopyranosyl-[1-2]-[beta-d-xylopyranosyl-[1-6]]-beta-d-glucopyranoside and 3,5,7,3',4',3",5",7",3'",4'"-decahydroxyl-[8-CH[2]-8"]-biflavone were also isolated from the 95% ethanol extract of *Galium verum*[41-42].

Polyphenols identified by HPLC in absolute methanol extracts of the vegetal material of *Galium verum*, were included: chlorogenic acid: 317.85-479.79 mg/100g, rutoside: 178.89- 343.88 mg/100g, luteolin 7-O-glucoside: 22.21-45.71 mg/100g and luteolin: 3.84-5.86 mg/100g[43].

Pharmacological effects:

Antioxidant effect:

The antioxidant properties of methanol extracts of *Galium verum* from two different localities in Serbia were evaluated. Antioxidant activity was assessed in four different model systems. Extracts from both locations expressed very strong scavenger activity, reducing the DPPH• [IC50=3.10 µg/ml and 8.04 µg/ml] and OH radical formation [IC50=0.05 µg/ml and 0.54 µg/ml] and neutralising H2O2 [IC50=4.98 µg/ml and 3.80 µg/ml], in a dose dependant manner. The extracts also showed inhibition of LP [IC50=11.69 µg/ml and 19.47 µg/ml][31].

The antioxidant activities of aerial parts of *Galium verum* were investigated employing various *in vitro* assay systems [DPPH and nitric oxide radical scavenging, reducing power and H2O2 scavenging]. The extract exhibited very potent antioxidant activities in all tested models. IC50 for DPPH radical-scavenging activity was 59.6 ±0.04 µg/ml. The extract exhibited potent reducing power at 50 - 800 µg/ml that were comparable with Vitamin C. The extract also showed very strong nitric oxide-scavenging with IC50 of 1.7 ±0.01 µg/ml. It was capable of scavenging hydrogen peroxide in a concentration dependent manner, the percentage of inhibition was 92.5 %. at 50 µg/ml. The total amount of phenolic compounds in extract was determined as gallic acid equivalents [753 ±21 mg/g of extract] and total flavonoid contents was calculated as quercetin equivalents [151.25 ±8.2 mg/g of extract][40].

The antioxidant properties of methanol extract of *Galium verum*, from localities in Serbia were evaluated, through determination of total phenolics and flavonoids content, as well as DPPH• [1,1-diphenyl-2-picrylhydrazyl] radical scavenging, ABTS•+ [2,2-azinobis-[3-ethylbenzthiazoline-6-sulfonic acid] radical cation decolorization and ferricyanide methods. Methanol extracts of *Galium verum* showed strong free radical scavenging activity [IC50 values of 26.98 µg/ml for DPPH• decolorization assays and 125.14 mg Trolox/ g dry extract for ABTS•+ radical cation decolorization assays] and total reducing power [70.31 µg/ml][44].
Antioxidant and 2,2-diphenyl-1-picrylhydrazyl [DPPH] radical scavenging activities, reducing powers and the amount of total phenolic compounds of aqueous and/or methanolic extracts of *Galium verum* were studied. There was no correlation between DPPH-RSA and total phenolic compounds in methanol extract of *Galium verum*. Methanolic extracts of *Galium verum* showed more effective peroxidation inhibition ability compared with water extract although relatively lower total phenolic compounds than its water extract[45].

Cytotoxic effect:

Galium verum decoction was investigated in the and neck cancer cell lines HLaC78 and FADU, its anticancer effects were proved in high doses on both cell lines. Cytotoxicity appeared to be influenced by expression of p-glycoprotein [MDR-1] in the carcinoma cell lines. Mucosal keratinocytes, which void of MDR-1 expression, showed only low

sensitivity to high *Galium verum* concentrations. Sublethal doses of *Galium verum* extract showed strong inhibition of motility, as shown by a spheroid-based invasion analysis on Matrigel-coated surfaces. Inhibition of invasion was significantly more pronounced in the invasive HLaC78 cell line. mRNA expression analysis of matrix metalloproteinases MMP-2 and MMP-9 and their inhibitors TIMP-1/-2 revealed significant TIMP-1 upregulation after an eight hours, *Galium verum* exposition in FADU cells. Gelatinolytic activity was not influenced by *Galium verum* extract in HLaC78, in the FADU cells MMP-2/-9 activity was slightly increased after incubation with Galium extract. In primary mucosal keratinocytes, Galium decoction protected DNA against benz[a]pyrene, one of the most DNA toxic agents in cigarette smoke[27].

The cytotoxicity of *Galium verum* was evaluated *in vitro* against chemosensitive [Hep-2 and HLaC79] and chemoresistant, P-glycoprotein-overexpressing [Hep2-Tax, HLaC79-Tax] laryngeal carcinoma cell lines. Galium aqueous extract was cytotoxic for all cell lines. A detailed spheroid-based 3D invasion analysis of Hep2 and Hep2-Tax in semisolid collagen gels and on different extracellular matrix coatings showed an inhibition of invasion by sublethal concentrations of Galium decoction and proved to be even more pronounced in the more aggressively invading chemoresistant Hep2-Tax cell line. Gelatinolytic activity of MMP-2 was downregulated in three of the four cell lines. Angiogenesis [endothelial tube formation], was not affected by Galium aqueous extract. Gene expression array on HLaC79 and Hep2 cell lines treated with Galium decoction [vs. untreated controls] revealed no unique pathway activation patterns in these cells[46].

Antimicrobial effect:

The antimicrobial activity of water, alcohol [70%] and chloroform extracts was investigated against *Staphylococcus aureus* 15923, *Escherichia coli* 25922, *Pseudomonas aeruginosa* 2789, *Bacillus subtilis* 6633, *Proteus vulgaris* 4636 and *Candida albicans* 885-563. Chloroform extract 20 and 50 g/l showed strong antibacterial activity against all the tested bacteria, diameter of growth inhihition zones at concentration of 20 and 50 g/l were 30.3±0.4 and 32.4±0.3mm against *Staphylococcus aureus*, 12.0±0.1 and 13.2±0.2mm against *Escherichia coli*, 21.2±0.2 and 20.2±0.3mm against *Pseudomonas aeruginosa*, 20.2±0.3 and 30.3±0.4 against *Bacillus subtilis* and 16.1±0.3 and 15.1±0.2 against *Proteus vulgaris* respectively. Alcoholic extract showed activity against *Candida albicans*, while, aqueous extracts possessed no antibacterial and antifungal activities. lipophilic complexes of *Galium verum* showed antibacterial activity against *Staphylococcus aureus* 15923, *Escherichia coli* 25922, *Pseudomonas aeruginosa* 2789, *Bacillus subtilis* 6633 with adiameter zone of growth inhibition of 32.4±0.3, 13.2±0.2, 20.2±0.3, 30.3±0.4 and 15.1±0.2mm respectively[47].

Extracts of *Galium verum* also showed antibacterial activity against pathogenic plants bacteria[48].

Protective effect:

The hepatoprotective activity of *Galium verum* [I and II dry extracts, 25 mg/kg], was studied against carbon tetrachloride-induced acute hepatitis in rats. The hepatoprotective effect of I and II extracts at the dose of 25 mg/kg was characterized by decreased activities of serum alanine aminotransferase [ALT] 2.7-3.5 fold, serum aspartate aminotransferase [AST] 2.4-3.4 fold and ALP 1.2-1.3 fold; whereas the activity of cholinesterase was increased 1.3-1.4 folds. The administration of the I extract decreased thiobarbituric acid reactive substances [TBARS] levels 1.4 fold in the serum and 1.8 fold in the liver homogenate. The administration of the II extract decreased TBARS levels 1.6 fold in the serum and 2.0 fold in the liver homogenate . The histopathological analysis of the liver material of the experimental group showed neither degenerative-dystrophic changes nor significant hemodynamic changes in comparison with the control group. The hepatoprotective effect of the II extract was more pronounced than that of the I extract and was comparable to the hepatoprotective activity of the reference drug, Silibor[49].

The protective effects of diosmetin extracted from *Galium verum* on the thymus of U14-bearing mice were investigated using flow cytometry, peripheral blood lymphocytes were characterized based on the expression of surface markers for T helper cells [CD4+] and T suppressor cells [CD8+]. Serum levels of tumor necrosis factor α [TNF-α], interleukin-2 [IL-2], IL-10, and transforming growth factor β1 [TGF-β1] and a cell proliferation assay were determined with an enzyme-linked immunosorbent assay. The expression of Fas and Fas ligand [FasL] on the thymus was determined by Western blotting. The results showed that diosmetin inhibited tumor growth and significantly increased the thymus weight compared with the control. Diosmetin also elevated serum levels of IL-2 and significantly reduced levels of TNF-α, TGF-β1, and IL-10 in a dose-dependent manner. Histological study and terminal dUTP nick end labeling staining results showed that diosmetin protected thymus tissue against the onslaught of tumor growth by inhibiting thymus lymphocyte

apoptosis. The cell proliferation assay revealed that diosmetin promoted more thymus lymphocytes towards proliferation. The ratio of CD4+/CD8+ T lymphocytes was significantly increased from 0.69 to 2.29 by treatment with diosmetin. Immunoblotting analyses revealed that the expression of Fas and FasL on the thymus was lower in mice in the diosmetin treatment group than in the control mice[50].

Endocrine effect:

The effect of *Galium verum* extract [25 mg extract/100 g bw] on the hypothalamic- pituitary-adrenal axis was evaluated under anakinetic stress conditions, in rats. It appeared that administration of extract, in conditions of exposure to stress, resulted in an enhancement of neurosecretory activity of the hypothalamic paraventricular nucleus - associated with a possible stimulation of CRH release, a possible activation of adenohipophyseal hormones, as well as stimulation of adrenal steroid hormones. Histological results of the study proved that the administration of *Galium verum* vegetal extract in condition of anakinetic stress exposure induced important morphological changes at all constitutive assembly of hypothalamo-hypophyseal-adrenal axis. These results justify the stimulation of secretory activity of the axis[51].

The protective potential of the *Galium verum* hydro-alcoholic extract, on the thyroid and ovarian morphological parameters was studied in rats under anakinetic conditions. The 15 days subchronic anakinetic stress induced by immobilization and darkness caused an inhibition of the thyroid and ovarian functions observed in the histological aspects, while, the administration of the *Galium verum* vegetal extract in a dose of 25 mg/100 g bw caused a stimulation of the thyroid and ovarian activity in rats subjected to a anakinetic stress of 3 hours/day and darkness for 15 days[52].

Antihaemolytic activity:

The efficient antagonizing of ROS-caused haemolysis [antihaemolytic activity] was studied for thirty extracts prepared from ten plants known for their antioxidant activity. Nine of the extracts were more potent than vitamin C, of which *Galium verum* [aerial parts / percolation] and *Scutellaria tournefortii* [aerial parts / polyphenol] extracts were the most potent, with an IC50 of 1.32 and 2.08 µg/ml, respectively[53].

The methanol extracts of *Galium verum* was tested *in vitro* using standard Drabkin's method to evaluate whether these extracts have hemolytic activity. *Galium verum* extracts showed hemolytic activity [44].

Cholinesterase activation:

With the applying of modified Ellman's method, *Galium verum* methanol extracts showed slight activation of human serum cholinesterase [16.28 ± 0.09 %][44].

CONCLUSION:

This review discussed the chemical constituent, pharmacological and therapeutic effects of *Galium verum* as promising herbal drug because of its safety and effectiveness.

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