Hedera helix as a medicinal plant

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Summary

Hederae folium is used for the treatment of respiratory tract diseases with intense mucous formation, respiratory tract infections and in irritating cough which stems from common cold. According to clinical experiments, the effectiveness and tolerance of ivy preparations is good. The major compounds responsible for the biological activity are triterpene saponins. Ivy leave extracts exhibit spasmolytic/antispasmodic, anti-inflammatory, antimicrobial, analgesic, anthelmintic, antitrypanosomial, antileishmanial, antitumor, antimutagenic, moluscocidal, antioxidant and antithrombin activities.

Key words: *Hedera helix, Hedera leaves, triterpene saponins, biological activity.*

INTRODUCTION

Hederae folium (Ivy leaf) consists of the whole or cut, dried leaves of *Hedera helix* L. collected in spring or early summer with minimum 3.0% of hederacoside C [1].

Hedera helix L. (English ivy, Common ivy) is an evergreen dioecious woody liana, one of the 15 species of the genus *Hedera*, Araliaceae family. The whole leaves are coriaceous, 4–10 cm long and wide, cordate at the base. The lamina is palmately 3–5 lobed. The upper surface is dark green with a paler, radiate venation,

while the lower surface is more greyish-green and the venation is distinctly raised. Ovate-rhomboic to lanceolate leaves 3 to 8 cm long form the flowering stems [1]. The flowers produced from summer until late autumn are small, greenish-yellow and come in umbels of 3–5 cm in diameter; the fruit are small black berries ripening in winter. *Common ivy* naturally grows in the Western, Central and Southern Europe but has also been introduced to North America and Asia. It is a popular ornamental plant in many countries [2].

The biologically active compounds [3] responsible for the medicinal use of *H. helix* are triterpene saponins (2.5–6%): the bidesmosidic glycosides of hederagenin: hederacoside C (1.7–4.8%), hederacoside D (0.4–0.8%), hederacoside B (0.1–0.2%), and monodesmoside α-hederin (0.1–0.3%). Other groups of the identified compounds are represented by phenolics (flavonoids, anthocyanins, coumarins and phenolic acids), aminoacids, steroids, vitamins, volatile and fixed oils, β-lectins and polyacetylenes (tab. 1).

The German Comission E approved *Hedera* leaves for the treatment of catarrhs of the respiratory tract and symptoms of chronic inflammatory bronchial conditions [4].

The topical application of a *Hedera*-saponin complex (hederacoside C, B and α-hederin) is effective in the treatment of liposclerosis ("cellulitis"). The properties supporting weight loss were also noted [5, 6]. Emollient and itch-relieving preparations with *Hedera helix* extract including creams, lotions and shampoos are used in cosmetics and skin disorders [4, 7].

In folk medicine, *Hedera* leaves are also used in gout, rheumatism and externally against parasites. In homeopathy, *Hedera helix* is administered for hyperthyroidism, rheumatic disorders and respiratory tract inflammation [2, 4].

PHARMACOLOGICAL ACTIVITY

Spasmolytic/antispasmodic activity

The saponins present in ivy leaf: hederacoside C and α-hederin, together with hederagenin obtained by hydrolysis; phenolic compounds: quercetin, kaempferol and 3,5-O-dicaffeoyl-quinic acid showed antispasmodic activity against acetylcholine-induced contractions of an isolated guinea-pig ileum. The activity was calculated as papaverine equivalent value, PE (activity of 1 g test substance to the activity of x mg of papaverine). Significant activity was found for α-hederin and hederagenin (PE=55 and 49), phenolic compounds: quercetin and kaempferol (PE=54 and 143) and PE=22 for 3,5-dicaffeoylquinic acid, whereas for hederacoside C, the PE value is only about 6. Mainly saponins, due to their relatively high concentration, contribute to the antispasmodic activity, followed by dicaffeoylquinic acids and the flavonol derivatives, so various compounds present in the ivy leaf extract influence this activity [18].

Table 1.

Chemical compounds of *Hedera helix* L.

compounds	ref.
leaves	
triterpene saponins	3
derivatives of: hederagenin, oleanolic acid, bayogenin (2β-OH-hederagenin): as	
bidesmosides:	
hederasaponin C (=hederacoside C) and hederasaponins B, D, E, F, G, H and I	3
the ratio of hederasaponins C, B, D, E, F, G, H, I are 1000:70:45:10:40:15:6:5,	3
hederasaponin A (in earlier publication),	
3-sulfates of oleanolic acid and echinocystic acid (=α-16-OH-oleanic acid)	8
3-sulfate of 28-O- β-gentiobiosyloleanate = helicoside L-8a	8
monodesmosides:	
α-hederin	3
hederagenin 3-O-β-glucoside	9
flavonoids	
aglycones: quercetin, kaempferol	10
glycosides:	
rutin (quercetin 3-O-rutinoside), isoquercitrin (quercetin 3-O-glucoside)	
astragalin (kaempferol 3-O-glucoside), kaempferol 3-O-rutinoside	
coumarins	
glycoside: scopolin (scopoletin 7-O-glycoside)	3
polyacetylenes	
falcarinon	7
falcarinol, 11,12-dehydrofalcarinol	3, 11
phenolic acids	
caffeic, chlorogenic (5-O-caffeoylquinic)	3, 7, 9
neochlorogenic (3-O-caffeoylquinic)	7, 9
3,5-O-dicaffeoyl-quinic; 4,5-O-dicaffeoyl-quinic	7, 9
rosmarinic [(R)-(+) enantiomer]; dihydroxybenzoic	7, 9
protocatechuic, *p*-coumaric	3
anthocyanin – cyanidin 3-monoside	3
sterols	3, 7
cholesterol, campesterol, stigmasterol, sitosterol	
α-spinasterol; 5α-stigma-7-en-3β-ol	
alkaloid – emetin	12
volatile oil	
germacrene B, β-elemene , γ-elemene (elixen)	3
methylethyl ketone, methylisobutyl ketone, *trans*-2-hexanal	2, 7
trans-2-hexanol	3
germacrene D, β-caryophyllene, sabinene, α-, β-pinene, limonene	7
furfurol	3
aminoacids	13
Vitamins: E, C, pro-vitamin A	3, 7
carbohydrates	
hamamelitol (2-C-hydroxy-methyl-D-ribitol)	3
fruit	
triterpene saponins	
helixoside A (3-O- β-glucosyl-(1→2)- β-glucosyl-28-O-β-glucosyl -(1→6)- β-glucosyl hederagenin),	
helixoside B (oleanolic acid 3-O- β-glucosyl-(1→2)- β-glucosyl 28- O- β-glucosyl-(1→6)- β-glucosyl, 3-O- β-glucosyl hederagenin,	14
3-O- β-glucosyl-(1→2)- β-glucosyl oleanolic acid	
3-O- β-glucosyl-(1→2)- β-glucosyl hederagenin	
staunoside A (3-O- β-glucosyl- 28-O-β-glucosyl-(1→6)- β-glucosyl hederagenin)	
fatty acids	15
petroselinic,oleic, *cis*- vaccenic, palmitoleic	
polyacetylenes	16
falcarinon, falcarinol, panaxidol ((*Z*)-9,10-epoxy-1-heptadecene-4,6-diyn-3-one)	
β-lectins	17

The ethanolic extract from ivy leaf administered orally in the compressed air model in conscious guinea pigs at 50 mg/kg of body weight dose-dependently inhibited bronchoconstriction induced by the inhalation of ovalbumin (57% inhibition) or platelet activating factor (43% inhibition) [19].

Inhibition of the internalization of β-adrenergic receptors - ligand complexes - in a specific manner, by triterpene saponin α-hederin, increases secretion of surfactant, which could thus explain the secretolytic and bronchospasmolytic effect by ivy leaf extracts [20, 21].

When the internalization of the receptor/ligand complexes is inhibited, the adenylate cyclase system is activated continuously, thereby intensifying the relaxation of the smooth musculature in the bronchi [22].

Antiinflammatory activity

The crude saponin extract (CSE) and saponins' purified extracts (SPE) from ivy leaf exerted an antiinflammatory effect in carrageenan- and cotton-pellet-induced acute and chronic inflammation models in rats tested *in vivo*. The most potent screened extract was the CSE at doses of 100 and 200 mg/kg of body weight (77%) but was less active than indomethacin (89.2% acute antiinflammatory effect). The extracts were more effective in the first phase of acute inflammation than in the second phase; therefore, they may block histamine and/or serotonin release in a better way than prostaglandin and/or bradykinin. In order to test the chronic antiinflammatory (antiproliferative) effect, the cotton-pellet-granuloma test was conducted. The SPE was more potent than CSE (60% and 49%, respectively) and indomethacin was found to be more active (66%). According to the chronic inflammation model, the extracts may exert their activities by inhibiting the functions of macrophages and fibrosis [23].

In the next experiment, the antiinflammatory potential of α-hederin and hederacoside C given orally was investigated in carrageenan-induced acute paw edema in rats. For the first and second phase of acute inflammation, α-hederin and hederacoside C were ineffective. Hederacoside C had an antiinflammatory effect in the second phase which may be related to bradykinin or other inflammation mediators being blocked. Indomethacin was found to be the most potent drug but it was administered in a dose of 20 mg/kg of body weight, whereas saponins were given at a concentration of 0.02 mg/kg of body weight. Regarding the structure activity relationship, it is likely that sugars at the C3 and C28 positions are essential for the acute anti-inflammatory effect [24].

Another study concerned the influence of *H. helix* constituents on hyaluronidase and elastase enzymes activity which increases in chronic inflammatory conditions, e.g. venous insufficiency symptoms. The results have proven that sapogenins non-competitively inhibited hyaluronidase activity in a dose-dependent fashion, showing comparable IC_{50} values (hederagenin $IC_{50}=280.4\ \mu M$; oleanolic acid $IC_{50}=300.2\ \mu M$), whereas the glycosides: hederacoside C and α-hederin were

very weak inhibitors. The glycosides are also devoid of inhibitory action for serine protease porcine pancreatic elastase, while genins are potent competitive inhibitors (oleanolic acid IC_{50}=5.1 μM; hederagenin IC_{50}=40.6 μM) [5].

Antimicrobial activity

The mixture of *H. helix* leaves saponins with a large amount of hederacoside C, exhibited the activity against following 23 strains tested (22 bacteria and one yeast strain): Gram-positive bacteria (*Bacillus* spp., *Staphylococcus* spp., *Enterococcus* spp., *Streptococcus* spp.) with MIC value of 0.3–1.25 mg/ml and Gram-negative bacteria (*Salmonella* spp., *Shigella* spp., *Pseudomonas* spp., *Escherichia coli*, *Proteus vulgaris*) MIC=1.25–5 mg/ml; and *Candida albicans* MIC=2.5 mg/ml [25].

The water extract from *H. helix* leaves inhibited the growth of *Staphylococcus aureus* (standard strain) as well as bacteria and dermatophytic fungi isolated from patients: *Pseudomonas aeruginosa, Trichophyton rubrum, T. mentagrophytes, Microsporum canis*, *Escherichia coli and Candida albicans* [26].

In vitro experiments (agar dilution method) have demonstrated a broad spectrum of the activity of α- and δ-hederin against yeast and dermatophyte species. These monodesmosides of hederagenin, especially α-hederin showed a significant antifungal activity (MIC=5–100 μg/ml). The most sensitive yeast strain was *Candida glabrata* (MIC=5 μg/ml); similar results were obtained from a study performed with *Candida glabrata* clinical isolates. Activities of α-hederin against the dermatophyte species (*Trichophyton* and *Microsporum* spp.) *in vitro* were the same: MIC=10 μg/ml, except from *M. persicolor* (MIC=50 μg/ml) [27].

Electron transmission microscopy observations indicated that, compared with untreated control yeasts, α-hederin induced modifications of cellular content and an alteration of the cell envelope with degradation and death of *Candida albicans* [28].

After oral administration at 50 mg/kg of body weight for 10 days, the saponin mixture with 60% of hederacoside C from *H. helix* leaves eliminated *Candida albicans* infections, such as abscesses on the backs of mice. At the same dose level and duration, α-hederin eliminated the infection in 90% of the animals and hederacoside C in 40% of the animals, whereas the activity of amphotericin B was identical at a dose of 2.5 mg/kg administered within 6 days [19].

Polyacetylenes: falcarinone and falcarinol are also responsible for **antifungal** and **antibacterial** activity of the ivy leaves extracts [7].

Hederacoside C has been reported to have **antiviral** activity against the influenza virus A2/Japan-305 at concentration of 100 μg/ml [19].

Anthelmintic activity

The saponin complex =CS 60 (60% of hederasaponin C with hederasaponin B with phenolics), purified saponin complex =CSP 90 (90% of hederasaponin C

with hederasaponin B, without phenolics) and α-hederin were evaluated *in vitro* using the trematodes *Fatsiola hepatica* and *Dicrocoelium* spp. as well as *in vivo* on sheep naturally infected with *Dicrocoelium*. After the *in vitro* exposure for 24 hours both *Fatsiola* and *Dicrocoelium* were killed by α-hederin at a concentration of 5 and 1 μg/ml, respectively. When sheep naturally infected with *Dicrocoelium* were treated orally with CS60 and CSP90, the eggs in the feces of sheep disappeared after three doses, one of 500 and two of 800 mg/kg, whereas after α-hederin at these concentrations, a reduction of the number of eggs was only observed [29].

Anthelmintic activity against eggs and adult nematode parasites *Haemonchus contortus* was demonstrated for aqueous and hydro-alcoholic extracts of the ripe fruits of *H. helix in vitro* and *in vivo*. ED_{50} for egg hatch inhibition was 0.12 and 0.17 mg/ml for aqueous and hydro-alcoholic extracts, respectively. The hydro-alcoholic extract showed a better *in vitro* activity against adult parasites, compared to the aqueous extract. Extracts were also evaluated for *in vivo* anthelmintic activity at doses of 1.13 and 2.25 g/kg in sheep artificially infected with *H.contortus*. Increasing the dose of extracts improved the efficacy against the male rather than the female parasites [30].

In vitro monodesmosides: α- and δ-hederin and aglycon hederagenin exhibit moderate **antitrypanosomial** activity on *Trypanosoma brucei brucei*, especially α-hederin (MIC = 25; 50; 50 μg/ml respectively). Bidesmosides: hederacoside C and D have shown no effect in concentration higher than 100 μg/ml [31].

Antileishmanial activity

Among the extracts containing 60% of the saponin complex (CS 60), the bidesmosides (hederacoside B, C, and D), monodesmosides α-, β-, and δ -hederin, and aglycone hederagenin, only monodesmosides and hederagenin were active on *Leishmania infantum* and *L. tropica*. Monodesmosides were found to be as effective on promastigote forms as the reference compound pentamidine (MIC=5μg/ml). Against amastigote forms only hederagenin exhibited a significant activity which was equivalent to that of the reference compound N-methylglucamine antimonate). CS 60 and bidesmosides have shown no effect on promastigotes forms [32].

The results of subsequent experiment confirmed that the α- and β-hederine exhibited activity in all development stages of *L. infantum in vitro*. Monodesmosides were shown to inhibit promastigote growth by altering the external membrane parasite; the second mechanism could be exclusively observed in human monocytes; it resulted in an inhibition of DNA synthesis and protein content [33].

The monodesmosides of hederagenin (α-hederine and hederacoside F) have more **moluscocidal** activity than their bidesmoside hederacoside C. The complex of α-hederine with glycin or alanine is more potent than α-hederine alone [34].

Antioxidative and hepatoprotective activity

α-Hederin and hederacoside C showed effective antioxidant activities *in vitro* using different antioxidant tests: DPPH$^{\bullet}$ free radical scavenging, total antioxidant activity, reducing power, superoxide anion radical scavenging, hydrogen peroxide scavenging and metal chelating activities. Antioxidant activities were compared with model antioxidants such as α-tocopherol, BHA and BHT [35].

The pretreatment with α-hederin prior to the administration of carbon tetrachloride significantly prevented the increase in serum alanine aminotransferase, lactate dehydrogenase activity and lipid peroxidation; it also prevented depletion of the hepatic glutathione level. The hepatic glutathione level and glutathione-S-transferase activities were not affected by the pretreatment with α-hederin alone. The P450 2E1 enzyme expression and activity were also decreased by α-hederin. This resulted in a reduction of the biotransformation of carbon tetrachloride and the protection against carbon tetrachloride induced liver injury [36].

The methylene chloride extract of *H. helix* spp. *canariensis* leaves exhibited high **antitrombin** activity (82%) [37].

Antitumor activity

Bidesmosides (hederacoside B, C and D) and monodesmosides (α-, β-, δ-hederin) together with aglycone hederagenin were tested on four mammalian cell strains: mouse B16 melanoma cells mouse 3T3 non cancer fibroblasts, Flow 2002 non-cancer human cells, and human HeLa tumour cells. The results show that saponins are at least five times less active than the reference compound (strychnopentamine) and that none of them seems to have any specific action on cancer cells. The most active compounds are the monodesmosides (α- and β-hederine) which show cytotoxicity on all cell strains at a concentration of 10 μg/ml and higher. The bidesmosides (hederacoside C, B, D) and hederagenine were inactive at concentrations up to 200 μg/ml [38].

The results of further *in vitro* experiment indicated that in a serum-free medium α-hederin is cytotoxic and inhibits the proliferation of the mouse B16 melanoma cells and non-cancer mouse 3T3 fibroblasts in low concentrations (<5 μg/ml) after only 8 hours of treatment. It also induces vacuolization of the cytoplasm and membrane alterations leading to cell death. Its cytotoxicity is reduced in the presence of fetal calf serum (FCS) or bovine serum albumin (BSA) in culture medium, thus indicating that α-hederin can, like other saponins, bind to proteins [39].

Antimutagenic activities

α-, β-, and δ-Hederin from *H. helix* were found to be non-toxic and non-mutagenic; it even showed antimutagenic activity in a dose dependent manner relationship against known promutagens: benzo[α]pyrene (1 μg) and mutagenic urine

concentrate from a smoker (5 μl) using a modified technique of the *Salmonella*/microsomal assay (*Salmonella* tester strain TA98 +/- S9 mix). Antimutagenic activities were also compared with the activity of chlorophyllin [40].

α-Hederin was found to exert an antimutagenic effect against the clastogenicity of doxorubicin. The possible antimutagenic mechanism of that compound seemed to induce metabolic enzymes which inactivated doxorubicin. Antimutagenic concentrations of α-hederin had no clastogenic or aneugenic effects in human lymphocytes. No cytotoxicity was observed for α-hederin [41].

The further study also confirmed the antimutagenic activity of α-hederin *versus* clastogenic agent, doxorubicin and an aneugenic agent, carbendazim, with a mechanism of both desmutagenic and bioantimutagenic actions [42].

CLINICAL STUDIES

Preclinical studies suggest that ivy leaf extracts have a spasmolytic, bronchodilating and antibacterial effect which is mainly attributable to the triterpene saponins contained in them. Despite the popularity of *H. helix* preparations, clinical empirical data supporting their mucolytic and secretolytic effects are scarce (tab. 2).

Table 2.

Clinical studies

method characteristics	results	ref.
open pilot, 26 children, 4–10 years of age, chronic obstructive bronchitis,ethanol-free oral preparation of ivy leaf extract, 4 weeks	spirometry results, auscultatory finding symptoms such as cough, sputum, dyspnoea improved after first week in most of the children. Good to very good efficacy was reported in more than two-thirds of the children and no adverse reactions were reported	47 (1992)
randomized double-blind comparative study, patients 25 to 70 years of age, mild – moderate, simple or obstructive chronic bronchitis, 4 weeks, oral liquid containing ivy dry extract, *placebo* and Ambroxol	improvements in both groups, no significant differences between groups. Decreases in frequency of coughing, sputum production and dyspnoea in the ivy extract group	48 (1993)
multicentre surveillance study, 113 children: 6–15 years, recurrent obstructive respiratory complaints 20 days, 30 days	improvement in lung function and accompanying symptoms of coughing and expectoration	49 (1996)
randomized double-blind, crossover study 25 female and male patients: 10–15 years, with reversible chronic obstructive airway disease, 10 days (wash-out: 3–4 days), Prospan cough drops 42mg/d ivy dry extract, Prospan cough syrup105 mg/d ivy dry extract	comparable improvements in spirometric and body-plethysmographic parameters after both treatments. Higher dosages of the ethanol free preparation were required to achieve a therapeutic effect to that of the ethanol-containing preparation	50 (1997)
open comparative study, children 10–14 years, chronic obstructive bronchitis, 3 days, two different oral liquid preparations corresponding to 250 mg of dried ivy leaf	improvements in the spirometry results and in lung function, ethanolic preparation were clearly superior to the ethanol-free preparation	51 (1997)
cross-over, open, 26 female and male patients, 4–12 years of age, reversible bronchial asthma, Prospan cough drops: 35mg/d ivy dry extract and Prospan cough suppositories: 160 mg/d ivy leaf dry extract, 3 days (wash-out: 2–4 days)	non-inferiority of suppositors in comparison to drops	52 (1997)

cross-over, double-blind 24 female and male patients, 4–12 years, reversible bronchial asthma, airway resistance, Prospan cough drops, placebo, 35mg/d ivy dry extract, 3 days (wash-out: 3–5 days)	superiority of ivy leaf extract over *placebo*	53 (1998)
open multicentre study, children: 4 years; 4–10 years, 10–12 years, bronchial complaints, orally, two different liquid ivy dry extract,10 days	improvement of symptoms in both groups	54 (2000)
Open study 372 children (2 months to over 10 years), respiratory tract infections, 7 days, ethanol-free oral liquid preparation	improvements were observed in lung function, cough symptoms	55 (2000)
open study,1024 children, acute infections of the upper respiratory tract, acute bronchitis / bronchiolitis or bronchitis, dry extract	significant reductions were observed in coughing, expectoration and airway resistance	56 (2000)
multicenter, prospective, 1350 male and female patients, 4 years and above, 4 weeks, Prospan acute Effervescent Cough Tablets	improvments symptoms: cough 92.2%; expectoration 94.2%; dyspnea 83.1%; respiratory pain 86.9%. In each of the four symptoms at least 38% of the subjects were completely free of complaints	57 (2002)
open trial, 62 patients (16-89 years), combined herbal preparation of dry ivy leaf extract, decoction of thyme and aniseed mucilage of marshmallow root, irritating cough in consequence of common cold respiratory tract diseases with formation of viscous mucus,10 ml of syrup, 12 days (3-23 days)	all symptoms scores showed an improvement as compared to baseline	58 (2005)
retrospective survey, espiratory diseases in children 52,478 children (0 -12 years), alcohol-free cough syrup from ivy extract	very good tolerability of the extract. The total occurrence of unwanted side effects was 22%. Gastrointestinal side effects with an incidence of 0.17% were the most important ones	59 (2004)
a prospective, uncontrolled, multicentric trial, 9657 patients (1581 children) bronchitis (acute or chronic bronchial inflammatory disease) syrup containing dried ivy leaf extract, additional application of antibiotics	after 7 days of therapy, 95% of the patients showed improvement or healing, the additional application of antibiotics had no benefit respective to efficacy but did increase the relative risk of the occurrence of side effects by 26%	60 (2009)

Dosage and administration

Most preparations of *H. helix* leaves contain hydroethanolic dry extracts incorporated into ethanol-containing or ethanol-free oral liquids, or suppositories (doses expressed as the corresponding amount of dried ivy leaf).

Internal use

Ethanol-containing preparations, in daily doses: adults: 250–420 mg; children 4–12 years: 150–210 mg; children 1–4 years: 50–150 mg; children 0–1 year: 20–50 mg; ethanol-free preparations: adults: 300–945 mg; children 4–12 years: 200–630 mg; children 1–4 years: 150–300 mg; children 0–1 years: 50–200 mg [19].

The tea can (rarely) be prepared by adding 1 heaped teaspoonful (0.3–0.8 g) of dried leaves to 250 ml of boiling water and steeping for 10 minutes and taken 1-3 times daily, sweetened with honey if desired [2].

External use

Suppositories: children 4-10 years: 960 mg per day. A decoction of fresh leaves (200 g/l water) may be used externally for rheumatism [19]. A poultice can be prepared by mixing (1:3) fresh *H. helix* leaves with linseed meal [2].

Side effects

Health risks or side effects following proper administration of the designated therapeutic dosages are not recorded [2]. Fresh *H. helix* leaves and the leaf juice, due to falcarinol content, can cause allergic contact dermatitis. Cross-reactions with other plants of the Araliaceae family have been reported [7]. Allergic symptoms on skin, eyes and the respiratory tract are very common among gardeners [43].

Contraindications, interactions with other drugs

Contraindications or interactions with other drugs are not known [4].

The administration of α-hederin, an inducer of metallothionein, on gestation day 6-15 results in a secondary zinc deficiency, a mechanism of developmental toxicity, and subsequent developmental abnormalities [44].

Single dose toxicity

The oral LD_{50} of several ivy leaf extracts in mice was determined to be >3 g/kg of body weight [19]. Oral administration of a dry extract of ivy leaf to rats at up to 4.1 g/kg of body weight caused no deaths within 72 hours; only diarrhoea was observed [3, 45].

Oral LD_{50} values in mice of saponin mixtures from ivy leaf containing 60% and 90% of hederacoside C, and of hederasaponin C and -hederin, were all >4 g/kg of body weight; the intraperitoneal LD_{50} value for: α-hederin=1.8 g/kg and for saponin mixture containing 60% of hederacoside C, LD_{50}=2.3 g/kg [46]

Repeated dose toxicity

Daily oral administration of an ivy leaf dry extract to rats at 1.5 g/kg of body weight for 100 days caused no toxic effects; haematological and biochemical parameters, histological findings and kidney and liver weights were normal as compared to the control group [19]. Haemolytic effects were detected after oral administration of a hydroethanolic dry extract from ivy leaf to rats at 4 g/kg for 90 days [19].

CONCLUSION

The literature data indicated that ivy leaf extract preparations are efficacious and safe in recommended doses and display very good tolerability. Syrups, drops,

tablets, but also suppositories and liquids containing ivy leaf ethanolic or free ethanolic extracts can be administered to improve the lung function and symptoms of coughing and expectoration, especially with accompanying obstructive pulmonary complaints and microbial infections. Clinical data supported these indications, especially for children. Ivy leaf caused no toxic effects, only allergy can be observed, but mainly after contact with the fresh plant.

Extracts of ivy leaf are the ingredients of the following preparations, available in Poland: syrups Hedelix, Prospan, PiniHelix, Helical, Hederasal and tablets Hederoin.

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HEDERA HELIX JAKO ROŚLINA LECZNICZA

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S t r e s z c z e n i e

Hederae folium stosuje się w leczeniu schorzeń dróg oddechowych z nadmiernym wydzielaniem śluzu, w infekcjach dróg oddechowych oraz w męczącym kaszlu. Badania kliniczne potwierdzają skuteczność i dobrą tolerancję preparatów zawierających wyciąg z liści bluszczu. Głównymi składnikami odpowiedzialnymi za aktywność biologiczną są saponiny triterpenowe. Wyciągi z liści bluszczu wykazują różne typy aktywności: spazmolityczną/przeciwskurczową, przeciwzapalną, przeciwdrobnoustrojową, przeciwbólową, przeciwrobaczą, przeciwnowotworową, antymutagenną, antyoksydacyjną, przeciwzakrzepową oraz przeciwpierwotniakową i przeciwmięczakową.

***Słowa kluczowe*:** *Hedera helix, liście bluszczu, saponiny trójterpenowe, aktywność biologiczna*