

**Figure S1.** Geographical indication of *Rh. tomentosum* sampling site in Eastern Lithuania (Utena district).

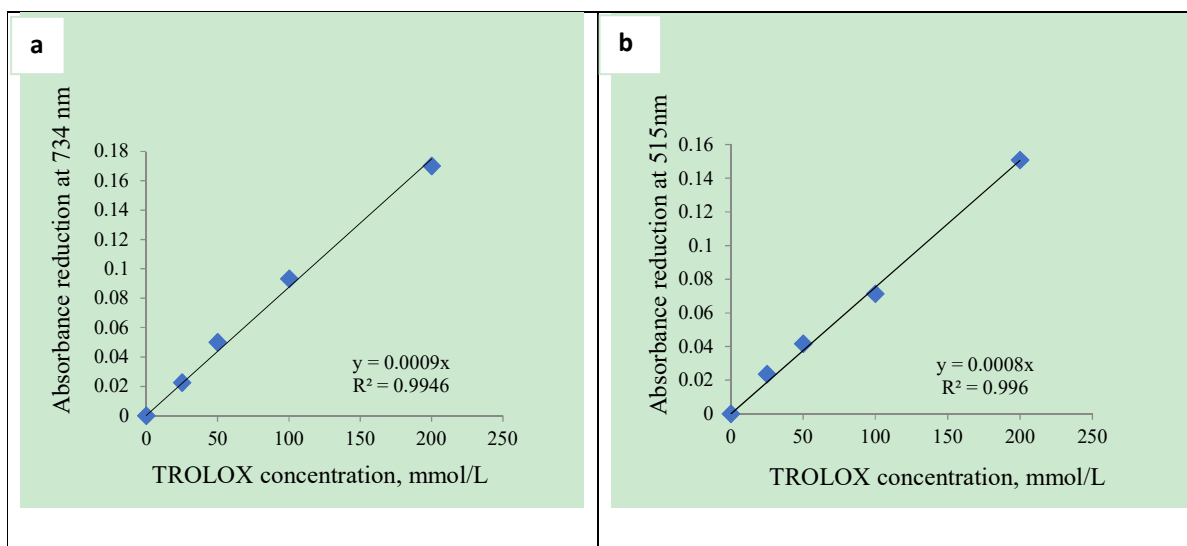
**Table S1.** Summary of studies on bioactivities of *Rh. tomentosum* Harmaja (ex *Ledum palustre* L.) extracts, essential oils or emitted volatiles.

Activity, Evaluation Method	Product, Main Composition	Results
<b>Repellent</b> against host-seeking nymphs of <i>Ixodes ricinus</i> Linnaeus (Acari: Ixodidae) [1]	Extracts in solvents of different polarities and leaf EOs by steam distillation; myrcene, palustrol	EO diluted in acetone (10%) exhibited 95% repellency; extracts in ethyl acetate have shown >70% repellence activity. <i>I. ricinus</i> were deterred from feeding when 10% of EO was introduced.
<b>Repellent</b> against mosquitoes <i>Aedes aegypti</i> (L.) probing on treated cloth [2]	Extracts in solvents of different polarities, by steam distillation and SPME. Extract of leaf EO in ethyl acetate, <i>p</i> -cymene, sabinene, terpinyl acetate	Extracts significantly reduced activity of <i>Aedes aegypti</i> (L.): 83.5% repellency (0.5 ml plant extract).
<b>Insect growth regulating and toxic</b> effects on the metamorphosis stages of <i>Tenebrio molitor</i> (Coleoptera, Tenebrionidae), differential thermocouple calorimetry [3]	Leaves and flowers, extracts in 80% of EtOH (composition not indicated)	Non-lethal mild toxic effects of extracts. The timing of normal and failed ecdysis (after treatment with <i>L. palustre</i> ), the length of intercdysial periods in <i>T. molitor</i> pupae, respiratory and muscular responses of poisoned insects was

		measured. The treated pharate pupae transformed into extra-pupal instars, which is a symptom of juvenilizing effect.
<b>Repellent and antifeedant</b> effects against <i>Hylobius abietis</i> L. and <i>Phylloocta laticollis</i> Suffrian, olfactometry tests [4]	Fresh leaves, extracts in different organic solvents: ethyl acetate, MeOH and hexane; palustrol, ledol, $\beta$ -myrcene	Feeding by the adults and larvae of <i>P. laticollis</i> and <i>H. abietis</i> was significantly reduced by methanol and hexane extracts. Concomitant with less feeding, larval growth was retarded by ethyl acetate extract of the plant
<b>Repellence:</b> system <i>Brassica oleracea</i> var. <i>italica</i> (broccoli)– <i>Plutella xylostella</i> (crucifer specialist herbivore) – <i>Cotesia vestalis</i> (endoparasitoid of <i>P. xylostella</i> ) is influenced by exposure to the natural semi-volatiles emitter plant <i>Rh. tomentosum</i> [5]	Semi-volatiles emitted from branches, main composition of emissions: palustrol (43%), $\beta$ -myrcene (34%), aromadendrene (10%), ledol (9%)	<i>Rh. tomentosum</i> -exposed <i>B. oleracea</i> was less susceptible to <i>P. xylostella</i> oviposition at both night-time (12°C) and day-time (22°C) temperatures and less favoured and damaged by <i>P. xylostella</i> larvae at 12°C. Exposure did not interfere with indirect defence, i.e., attraction of the natural enemy <i>C. vestalis</i> on host-damaged, <i>R. tomentosum</i> -exposed <i>B. oleracea</i> under 22°C, while there was a reduction in attraction (marginal preference towards host-damaged <i>B. oleracea</i> ) under 12°C.
Biological tests on growth of <i>Lemna minor</i> L., and $\alpha$ -amylase activity in wheat seeds and coleoptile sections from 3-day-etiolated wheat sprouts [6]	Leaves and young shoots, EO adsorbed on natural zeolite	Volatile compounds completely inhibited the growth processes of the biotest used.
<b>Analgetic, Anti-inflammatory</b> [7]	EO, aqueous and MeOH extracts (flavonoid components)	Analgesic test: methanol extract (10.0 and 1.0mg/kg) and aqueous extract (10.0mg/kg) decreased the acetic acid-induced writhing response. Anti-inflammatory test: MeOH extract (10.0 and 1.0mg/kg) and aqueous extract (10.0 mg/kg) decreased the paw edema in 2, 3, 4, 5 and 6 hours after lambda-carrageenan administration.
<b>Antibacterial</b> <i>in vitro</i> , broth dilution method, against <i>S. aureus</i> , <i>E. coli</i> , <i>P. aeruginosa</i> , <i>K. pneumoniae</i> [8] <b>Anti-inflammatory</b> <i>in vivo</i> , carrageenan-induced edema in rats [8]	Shoots, aqueous extract and isolated polysaccharide complex Shoots, dry aqueous extract, 40 and 70% in EtOH	Bacteriostatic effect at 1/160 dilution, excluding to <i>P. aeruginosa</i> (1/20 dilution) for polysaccharide complex. 51.5±4.6% Inhibition of edema by 40% EtOH extract, comparable to butadiene.
<b>Anticancer</b> <i>in vitro</i> , mouse leukemia cells L1210 [9]	Aerial part, methylene chloride and MeOH extracts, Soxhlet	99% growth inhibition by methylene chloride extract, 71% growth inhibition by MeOH extract.

<b>Anticancer</b> <i>in vitro</i> , human lympho-blastoid Raji cells [10]	Aerial parts, crude EtOH (40%) extract	99% inhibition at 200µg/mL.
<b>Antidiabetic</b> <i>in vitro</i> , C2C12 murine skeletal myoblasts and the 3T3-L1 murine preadipocyte cell lines [11] <b>Antioxidant activity</b> <i>in vitro</i> , DPPH assay, ascorbic acid was used as the reference antioxidant [12]	Leaves, EtOH (80%) extract with 153.5 µg/mg total phenolic (chlorogenic acid, catechins, taxifolin, quercetin glycoside)	Cytoprotective properties under conditions of glucose toxicity (150mmol/L of glucose) and glucose deprivation (1.1mmol/L glucose) at 6.25µg/mL. Effect on the basal and insulin stimulated 3H-deoxy-glucose uptake in differentiated 3T3-L1 adipocytes at 50µg/mL. Triglyceride level was increased by 3-fold. Strong antioxidant activity, close to that of ascorbic acid.
<b>Antidiabetic</b> <i>in vitro</i> , Caco-2/15 cells; western blot analysis <i>in vivo</i> . Rats, oral glucose tolerance test [12]	Leaves, EtOH (80%) extract with 153.5µg/mg total phenolic	Instantaneous inhibition of differentiated Caco2/15 intestinal cells glucose absorption at 100µg/mL. Reduction of SGLT1 protein expression, AUC of blood glucose levels <i>in vivo</i> .
<b>Antifungal</b> , against <i>A. niger</i> , <i>C. albicans</i> , <i>M. canis</i> , <i>T. rubrum</i> and <i>T. mentagrophytes</i> [13]	EO	EO exhibited antifungal activities from mild to strong.
<b>Antifungal</b> <i>in vitro</i> , micro-broth dilution method, against <i>C. neoformans</i> , <i>S. cerevisiae</i> , <i>A. niger</i> , <i>C. albicans</i> [14]	Leaves, quercetin 3-β-D-(6- <i>p</i> -coumaroyl) galactoside and quercetin 3-β-D-(6- <i>p</i> -hydroxy-benzoyl)	MIC 16-63µg/mL for <i>C. neoformans</i> , <i>S. cerevisiae</i> and <i>A. niger</i> . MIC 250µg/mL for <i>C. albicans</i> . MIC 0.16-10µg/mL for amphotericin B and fluconazole.
<b>Anti-inflammatory</b> , subcutaneous carrageenan injection-induced hind paw oedema in rats [15].	Aerial parts, EO by supercritical fluid extraction (SFE) and hydrodistillation (HD). Palustrol (41.0-43.4%), ledol (23.3-26.7%), ascaridole (4.5-15.1%)	EO enhanced a significant inhibition of oedema (50-73%) for HD oil and (52-80%) for SFE oil. These results were similar to those obtained with piroxicam (70%) and ketoprofen (55%).
<b>Anti-inflammatory</b> <i>in vitro</i> , prostaglandin-synthesizing cyclooxygenase system from sheep seminal vesicles [16]	Aerial part, EO	EO inhibited cyclooxygenase <i>in vitro</i> 46.6% and carvacrol was responsible for 94% inhibition. Ledol did not inhibit the enzyme.
<b>Anti-inflammatory</b> <i>in vitro</i> , prostaglandin biosynthesis assay; PAF-induced exocytosis [17]	Aerial parts, aqueous extract, lyophilized	Moderate inhibition of prostaglandin biosynthesis (50%) and platelet activating factor (PAF)-induced exocytosis (71%).
<b>Antimicrobial</b> <i>in vitro</i> , against <i>S. aureus</i> , <i>S. pneumoniae</i> , <i>C. perfringens</i> , <i>B. cereus</i> , <i>E. aerogenes</i> , <i>K. pneumoniae</i> , <i>C. albicans</i> , <i>M. smegmatis</i> , <i>A. lwoffii</i> and <i>C. krusei</i> [18]	EO and MeOH extracts, EO main composition: sabinene (17.8%), terpinen-4-ol (7.6%) and myrtenal (7.4%)	EO possessed antioxidant and low antimicrobial properties <i>in vitro</i> , while the water-insoluble parts of the methanolic extracts exhibited slight or no antimicrobial activity. EO strongly reduced DPPH* (IC <sub>50</sub> =1.56µg/ml) formation and exhibited a hydroxyl radical scavenging

<b>Antioxidant</b> <i>in vitro</i> , DPPH assay, Fe <sup>3+</sup> -EDTA-H <sub>2</sub> O <sub>2</sub> deoxyribose assay, nonenzymatic lipid peroxidation of rat liver homogenate [18]		effect in the deoxyribose system (IC <sub>50</sub> = 2.7µg/ml), and inhibited the nonenzymatic lipid peroxidation of rat liver homogenate (IC <sub>50</sub> = 13.5µg/ml). The polar phase of the extract showed antioxidant activity.
<b>Antimicrobial</b> <i>in vitro</i> , against <i>Vibrio parahaemolyticus</i> [19]	Aerial parts, EO: α-thujenal (22.5%), β-phellandrene (10.3%), benzene,1-methyl-3-(1-methylethyl) (6.6%)	EO at concentration 5g/L inhibited growth of <i>V. parahaemolyticus</i> obviously.
<b>Anti-proliferative and pro-apoptotic</b> activity <i>in vitro</i> , the influence of EOs on blood lymphocytes' proliferation and apoptosis rates of synovia-derived cells was determined by flow cytometry [20]	Shoot EOs of γ-terpineol and palustrol/ledol chemotypes and microshoots cultivated <i>in vitro</i> of ledene oxide type	EOs had anti-proliferative and pro-apoptotic activity toward CD4 and CD8 T cells, synovia-infiltrating monocyte/macrophages and fibroblast-like synovial cells. At 1:400 dilutions, all tested EOs increased the number of necrotic cells in synovial fibroblasts from RA synovia; and increased proportions of late apoptotic cells in leucocyte populations.
<b>Antithrombin</b> <i>in vitro</i> , thrombin solution from bovine plasma [21]	Aerial parts, MeOH extract, Soxhlet	88% of thrombin inhibition
<b>Hepato-protective</b> <i>in vivo</i> , rats, mice, CCl <sub>4</sub> intoxication [22]	Shoots, dry extract (EtOH 40%)	Extract reduced hexobarbital sleeping time 1.4-and 3.2-fold, respectively, for rats and mice; and improved functional-metabolic and morphological parameters of liver.
<b>Toxicity</b> <i>in vivo</i> , tested on mice [23]	Shoots, 40% EtOH extract, chloroform and hexane fractions of EtOH extract	LD <sub>50</sub> =2.800–3.200mg/kg for 40% EtOH extract after intraperitoneal administration, and no mortality of mice was after intragastric administration of extract at the dose of 10g/kg. LD <sub>50</sub> for the chloroform fraction 350mg/kg (intraperitoneal) and 2.600mg/kg (intragastric), LD <sub>50</sub> =420mg/kg (intraperitoneal) and LD <sub>50</sub> =5.100mg/kg (intragastric) for hexane fraction.
<b>Radioprotective</b> <i>in vivo</i> , mice irradiated with γ-irradiation [24]	Aerial parts, combination with <i>Archangelica officinalis</i> extracts	100% of animals survived after a dose of 6Gy (LD <sub>50</sub> /30); 70% survived after a dose of 7.5Gy (LD <sub>90</sub> /30), and 25% after a dose of 8Gy (LD <sub>100</sub> /12) by 30 day.
<b>Radioprotective</b> <i>in vivo</i> , 30 days albino mongrel male mice irradiated with γ-irradiation (LD <sub>90/30</sub> ) [25]	Aerial parts, combination with <i>Archangelica officinalis</i> extracts	Number of mouse pups was 10.2±0.6 in experimental and 7.4±0.7 in non-irradiated groups. The number of both sexes in the posterity of non-irradiated parents was equal; the number of female pups was 2.3 times larger than that of males.



**Figure S2.** TROLOX standard calibration curves: (a) ABTS<sup>•+</sup> assay; (b) DPPH<sup>•</sup> assay.

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