Supplementary Materials: **Figure S1**. Structure of secondary metabolites isolated from the ethanolic resinous exudate of *A. balsamica*. **Figure S2:** HPLC-DAD chromatogram a) Standards of the major compounds of the *A. balsamica* plant, at a concentration of C1=465 mg/L (time ret.=60.8 min); C2=277 mg/L (time ret.=57.1 min); C3=255 mg/L (time ret.=63.5 min); and C4=255 mg/L (time ret.=9.6 min); b) Ethanolic resinous exudate from wild plant; c) Ethanol:Water=50:50 extract from wild plant, and d) Ethanol:Water=25:75 extract from *in vitro* plant. **Figure S3.** Histopathological analysis of tissues from animals dosed with the product (concentrated plant extract) at 2000 mg/kg after 28 days. a) H&E lung. Mild focal thickening of alveolar walls; b) H&E lung. Focal area of tissue consolidation; c) H&E liver. No histological alterations; d) H&E kidney. No histopathological alterations. The blue arrow indicates the observation. H&E: methodology applied with hematoxylin eosin. Image captured at 100x. Scale 100μm. **Table S1**: Structural elucidation of natural compounds. **Table S2.** Equation of the straight line and correlation factor of calibration curves for total polyphenols and flavonoids, by UV-VIS spectrophotometry, and for the major compounds C1 to C4, by HPLC-PDA. **Table S3.** Mass percentage of the major compounds C1 to C4, by HPLC-PDA, in the different botanical products. **Table S4**: Initial body weight of animals dosed with 2000 mg/kg of active concentrated extract. Group 1 and group 2. **Table S5**: Evaluation of body weight of animals treated with 2000 mg/kg of active extract 7 and 14 days after administration; **Table S6**: Monthly arithmetic mean of minimum temperature, maximum temperature, temperature range, and monthly accumulated precipitation during the trial period; **Table S7**: Record of temperatures and precipitation on the day of application; **Table S8**: Evaluation of macroscopic pathologies (necropsy) in animals treated with 2000 mg/kg of active extract after 28 days. **Table S9**: Summary of clinical signs evaluated in rats.

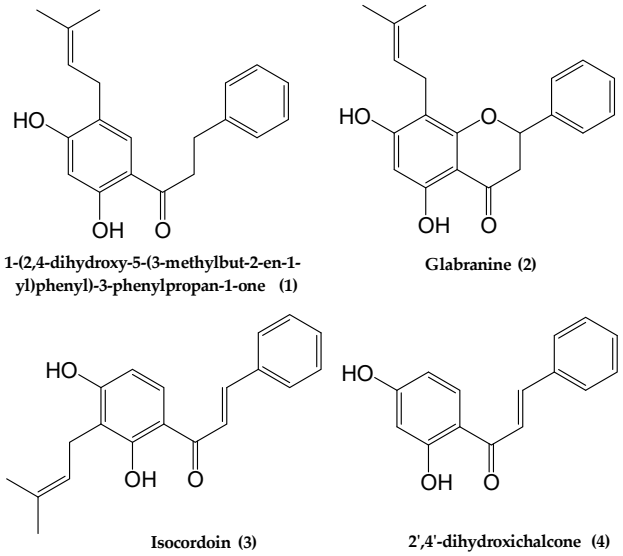


Figure S1. Structure of secondary metabolites isolated from the ethanolic resinous exudate of *A. balsamica*.

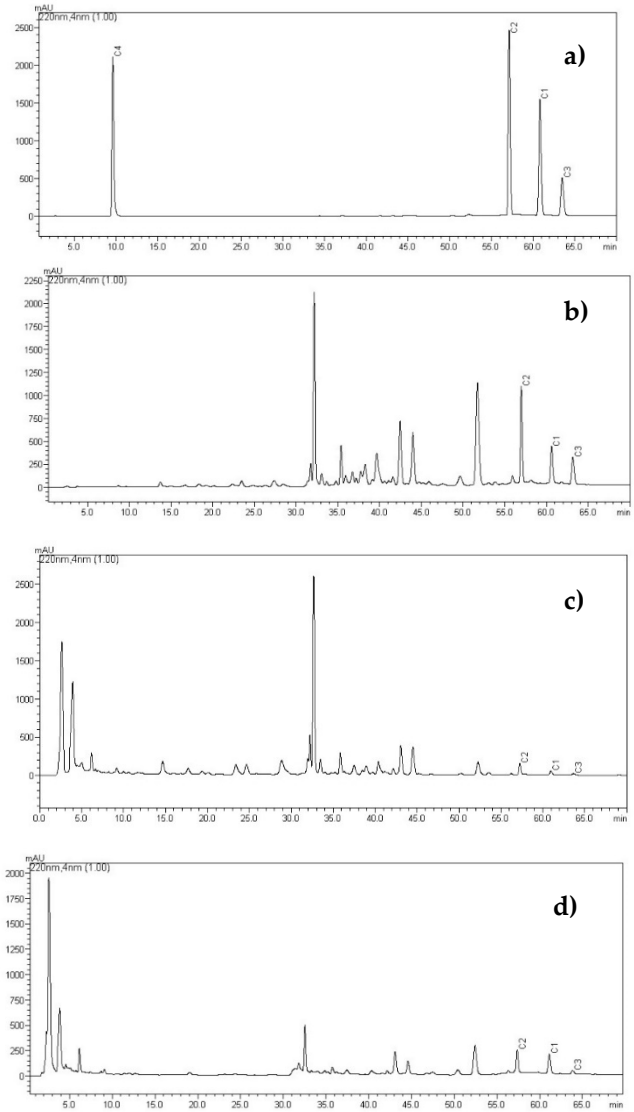


Figure S2: HPLC-DAD chromatogram a) Standards of the major compounds of the *A. balsamica* plant, at a concentration of C1=465 mg/L (time ret.=60.8 min); C2=277 mg/L (time ret.=57.1 min); C3=255 mg/L (time ret.=63.5 min); and C4=255 mg/L (time ret.=9.6 min); b) Ethanolic resinous exudate from wild plant; c) Ethanol:Water=50:50 extract from wild plant, and d) Ethanol:Water=25:75 extract from *in vitro* plant.

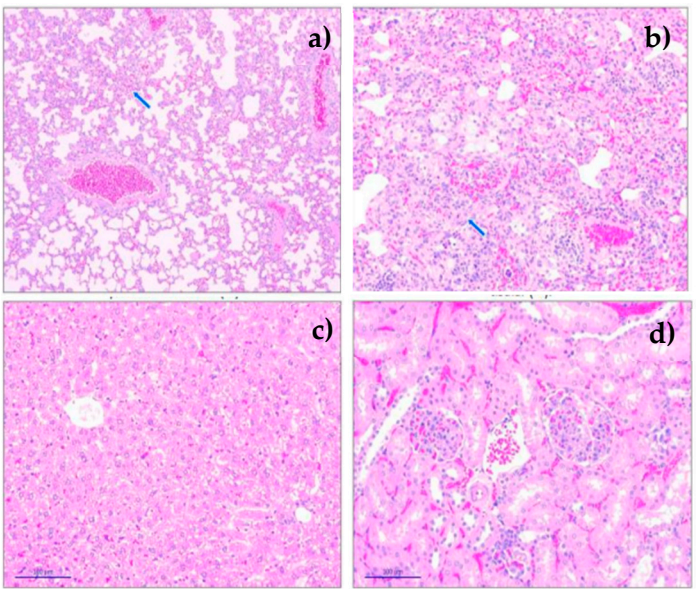


Figure S3. Histopathological analysis of tissues from animals dosed with the product (concentrated plant extract) at 2000 mg/kg after 28 days. **a)** Lung H&E. Mild focal thickening of alveolar walls; **b)** Lung H&E. Focal area of tissue consolidation; **c)** Liver H&E. No histological alterations; **d)** Kidney H&E. No histopathological alterations. The blue arrow indicates the observation. H&E: methodology applied with hematoxylin eosin. Image captured at 100x. Scale 100μm.

Table S1: Structural elucidation of natural compounds

Compound	^{1}H NMR (400 MHz, $CDCl_3$), δ/ppm:	^{13}C NMR (100 MHz, $CDCl_3$), δ/ppm:
1: 1-(2,4-dihydroxy-5-(3-methylbut-2-en-1-yl)phenyl)-3-phenylpropan-1-one	12.58 (1H, s, OH); 7.43 (1H, s,H-6′); 7.43-7.20 (5H, m, B ring protons); 6.43 (1H, s,H-3′); 5.94 (1H, s,OH); 5.26 (1H, m,H-2′′′); 3.26 (1H, m,H-2); 3.22 (1H, s,H-1′′′); 3.03 (1H, m,H-3); 1.77 (1H, s,H-4′′′); 1.77 (1H, s,H-5′′′).	203.5; 163.7 161.4; 141.0; 135.4; 131.4; 128.6; 128.6; 128.4; 128.4; 126.4; 121.4; 118.8; 113.6; 103.9; 39.8; 30.5; 29.1; 25.8; 17.9
2: Glabranine	11.98 (1H, s, OH); 7.42 (5H, m, B ring protons); 6.18 (1H, s, OH); 6.03 (1H, s,H-6); 5.42 (1H, dd,H-2, J= 3.0 and 12.9 Hz); 5.22 (1H, t, H-2′′, J= 7.2 Hz); 3.33 (2H, d,H-1′′, J= 7.2 Hz); 3.05 (1H, dd, H-3, J= 12.9 and 15.1 Hz); 2.85 (1H, dd, H-3. J= 3.0 and 17.1 Hz); 1.73 (3H, s, H-4′′); 1.63 (3H, s, H-5′′).	196.2; 163.7; 162.2; 159.6; 138.7; 135.1; 128.8; 128.8; 128.7; 128.7; 125.9; 121.5; 106.1; 103.2; 96.9; 78.9; 43.3; 25.8; 21.8; 17.8
3: Isocordoin	13.79 (1H, s, OH); 7.89 (1H, d, J=15.4 Hz, H-2); 7.74 (1H, d, J=8.9 Hz, H-6′); 7.60 (1H, d, J=15.4 Hz, H-3); 7.43 (5H, m, B ring protons); 6.43 (1H, d, J=8.8 Hz, H-5′); 6.15 (1H, s, OH); 5.31 (1H, t, J=7.1 Hz, H-2′′′); 3.48 (2H, d, J=7.1 Hz, H-1′′′); 1.85 (3H, s, H-4′′′); 1.78 (3H, s, H-5′′′)	192.1; 163.9; 161.7; 144.2; 136.0; 134.8; 130.6; 129.3; 129.3; 128.9; 128.9; 121.0; 120.5; 114.5; 114.1; 114.0; 107.9; 25.83; 21.75; 17.95
4: 2′,4′-dihydroxychalcone	13.38 (1H, s, OH); 7.91 (1H, d, J=15.9 Hz, H-2); 7.87 (1H, s, H-3′);7.84 (1H, d, J=8.4 Hz, H-6′); 7.57 (1H, d, J=15.9 Hz, H-3); 7.43 (5H, m, B ring protons); 6.43 (1H, d, J=8.4 Hz, H-5′); 5.92 (1H, s, OH).	191.9; 166.4; 162.7; 144.6; 134.7; 132.0; 130.7; 128.9; 128.5; 120.2; 107.8; 103.8

Table S2. Equation of the straight line and correlation factor of calibration curves for total polyphenols and flavonoids, by UV-VIS spectrophotometry, and for the major compounds C1 to C4, by HPLC-PDA.

Analysis	Standard	Concentration range, in mg/L	Equation of the line, y = mx + b	Correlation factor, r^2
Total Polyphenols	Gallic Acid, Merck, purity ≥ 99 %	60-480	y = 0.0033x + 0.0927	0.9966
Total Flavonoids	Quercetin, Sigma-Aldrich, purity ≥ 99 %	40-400	y = 0.0006x+ 0.0425	0.9999
Compound 1	Purity 98.0%**	58-465	y = 24119x - 158772	0.9998
Compound 2	Purity 98.5%**	34-277	y = 147373x + 693890	0.9985
Compound 3	Purity 98.5%**	32-255	y = 126193x + 384719	0.9982
Compound 4	Purity 98.0%**	32-255	y = 119436x + 451089	0.9990

(**), The compound obtained in the separation was purified, and its purity was determined by HPLC-PDA.

Table S3. Mass percentage of the major compounds C1 to C4, by HPLC-PDA, in the different botanical products.

Botanical products	%C1	%C2	%C3	%C4
Ethanolic Exudate / Wild Plants	3.1	2.9	3.9	< 0.1
Hydroalcoholic Extract Ethanol:water = 25:75 / *In vitro* Plants	0.58	0.21	0.18	< 0.1
Hydroalcoholic Extract Ethanol:water = 50:50 / Wild Plants	0.34	0.1	0.1	< 0.1
Aqueous Exudate / Wild Plants	--	--	--	--

%C: g of compound in 100 g of sample

(--): was not evaluated due to low extraction performance.

Table S4: Initial body weight of animals dosed with 2000 mg/kg of active concentrated extract. Group 1 and group 2.

N° animal	Sex	Weight Day 0	mg of compound	mL of compound
Group 1				
1	Female	204	408	0.41
2	Female	248	496	0.50
3	Female	200	400	0.41
Group 2				
1	Female	229	458	0.47
2	Female	223	446	0.45
3	Female	251	502	0.51

Group 1 and Group 2 correspond to the administration of step 1 and step 2, respectively.

Table S5: Body weight assessment of animals treated with 2000 mg/kg of active extract 7 and 14 days after administration.

N° animal	Sex	Weight on day 0 (g)	Weight on day 7 (g)	Difference in week 1 (g)	Weight on day 14 (g)	Difference in week 2 (g)
Group 1						
1	Female	204	224	20	233	9
2	Female	248	260	12	272	12
3	Female	200	228	28	239	11
Average (1)		**217.3**	**237.3**	**20.0**	**248.0**	**10.7**
Group 2						
1	Female	229	254	25	261	7
2	Female	223	239	16	243	4
3	Female	251	270	19	273	3
Average (2)		**234.3**	**254.3**	**20.0**	**259.0**	**4.7**

(1) and (2) correspond to the administration of step 1 and step 2, respectively.

Table S6: Monthly arithmetic mean of minimum temperature, maximum temperature, temperature range, and monthly accumulated precipitation during the test period.

Month	Temperature			
	Minimum (°C)	Maximum(°C)	Thermal Oscillation(°C)	Precipitation (mm)
October	7.8	20.0	12.2	37.6
November	9.4	22.0	12.6	36.6
December	10.9	26.8	15.9	0.0
January	13.1	30.5	17.5	0.2

Table S7: Recording of temperatures and precipitation on the day of application.

Date	Temperature			
	Minimum (°C)	Maximum (°C)	Thermal Oscillation (°C)	Precipitation (mm)
02-10-2023	9.6	17.6	8.0	0.0
11-10-2023	7.8	20.1	12.3	0.0
19-10-2023	7.1	24.5	17.4	0.0
31-10-2023	7.4	19.3	11.9	0.0
09-11-2023	9.6	27.7	18.1	0.0
23-11-2023	8.4	27.5	19.1	0.0

Table S8: Evaluation of macroscopic pathologies (necropsy) in animals treated with 2000 mg/kg of active extract after 28 days.

Dose 2000 mg/kg	Females (1)			Females (2)		
	1	**2**	**3**	**1**	**2**	**3**
Nervous	-	-	-	-	-	-
Respiratory	L	-	-	-	-	-
Digestive	-	L	-	L	-	-
Cardiovascular	-	-	-	-	-	-
Hematopoietic	-	-	-	-	-	-
Glandular	-	-	-	-	-	-
Urogenital	-	-	-	-	-	-

(-): No abnormality observed; (P) Presence of abnormality: Degree of severity: (L) Mild. (M) Moderate and (S) Severe. (1) and (2) correspond to the administration of step 1 and step 2, respectively.

Table S9: Summary of clinical signs evaluated in rats.

1. Nervous system and behavior
Excessive grooming
Compulsive behavior: aggression
Seizures
Circular movements
Motor impairment (hyperreflexia or hyporeflexia)
Constant chewing
Paresis (muscle weakness)
2. Respiratory system
Breathing difficulties (dyspnea – hyperventilation)
Epistaxis (nosebleed)
Nasal secretions (mucus)
Pulmonary rales
Coughing/sneezing
3. Digestive system
Constipation
Diarrhea
Rectal prolapse
Excessive salivation
4. Cardiovascular and hematopoietic system
Anemia (paleness in ears and paws)
Cyanosis
Bleeding from natural orifices
5. Skin and Sense Organs
Blepharospasm
Pupillary reflex (mydriasis/miosis)
Profuse lacrimation
Bloody lacrimation (chromodacryorrhea)
Mucous membranes (pallor, cyanosis, or jaundice)
Crepitant skin
Piloerection
Corneal ulceration
6. Urogenital system
Anuria/polyuria
Vaginal prolapse
Preputial/vaginal seromucous discharge

Preputial/vulvar mucosal irritation

7. Musculoskeletal system
Kyphosis
Lordosis
Ataxia
Muscle spasticity
Lameness
Joint inflammation
Immobility

8. Systemic compromise
Cachexia
Coma
Dehydration
Edema
Sunken flanks
Prostration
Anorexia – Adipsia
Abdominal rigidity
Hyperthermia or hypothermia