Original Papers

Medicinal Plants for the Treatment of Mental Diseases in Pregnancy: An *In Vitro* Safety Assessment

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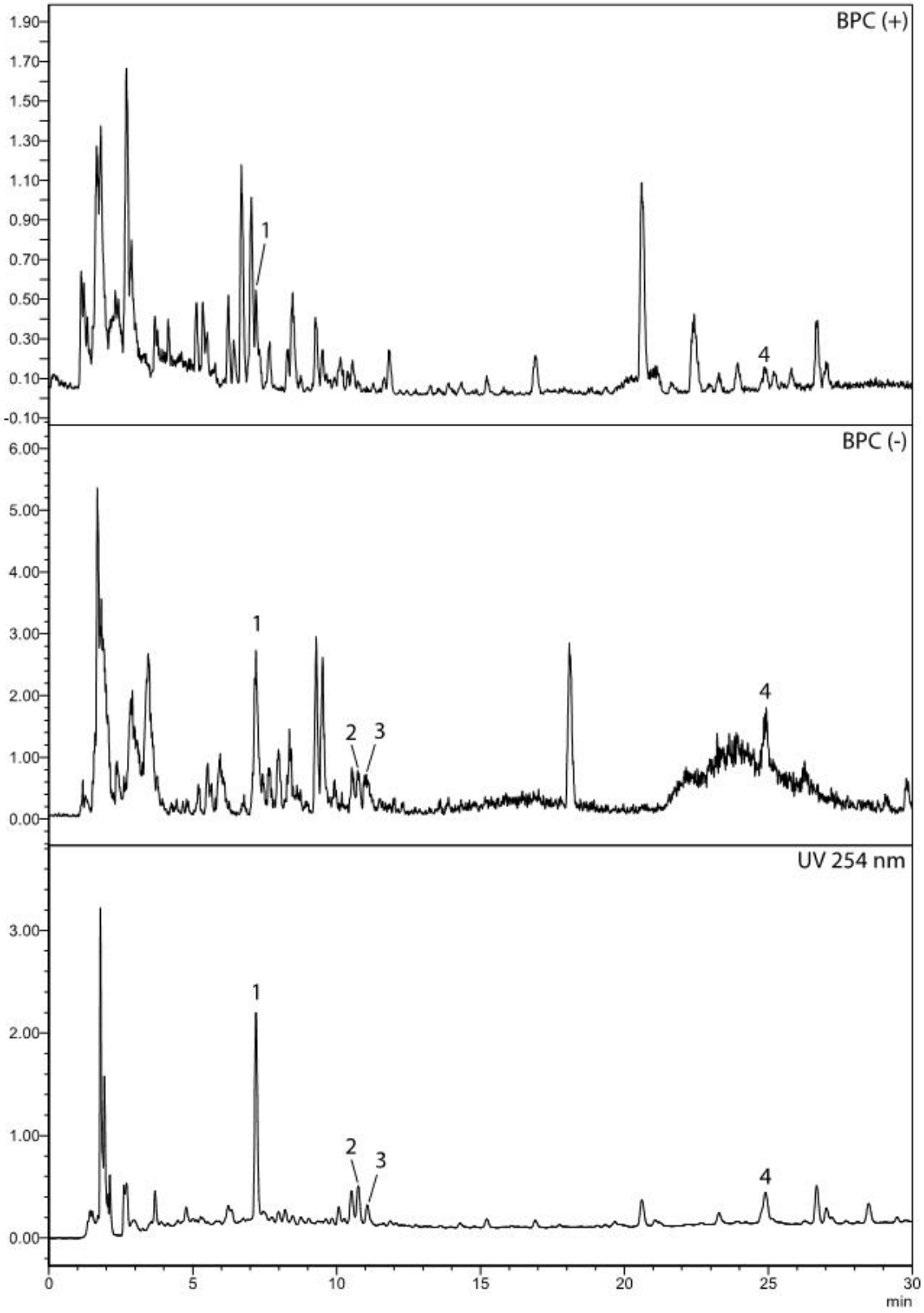

Fig. 1S. HPLC-UV-MS analysis of *Valeriana officinalis* 70% EtOH extract. BPC: base peak chromatogram.
1: chlorogenic acid, **2** and **3:** dicaffeoylquinic acid isomers (tentative assignment), **4:** valerenic acid.

Table 1S. Retention times and spectroscopic data of annotated peaks in *Valeriana officinalis* 70% EtOH extract.

Peak number	Retention time (min)	UV maxima (nm)	ESI MS (+) (m/z)	ESI MS (−) (m/z)	Identification
1	7.2	206, 310, 327	354.9 $[M+H]^+$	353.1 $[M-H]^-$	Chlorogenic acid
2	10.8	209, 310, 327	516.9 $[M+H]^+$ 499.0	515.1 $[M-H]^-$	Dicaffeoylquinic acid
3	11.1	217, 310, 327	516.9 $[M+H]^+$ 499.0	515.1 $[M-H]^-$	Dicaffeoylquinic acid
4	24.9	222	235.1 $[M+H]^+$	233.1 $[M-H]^-$	Valerenic acid

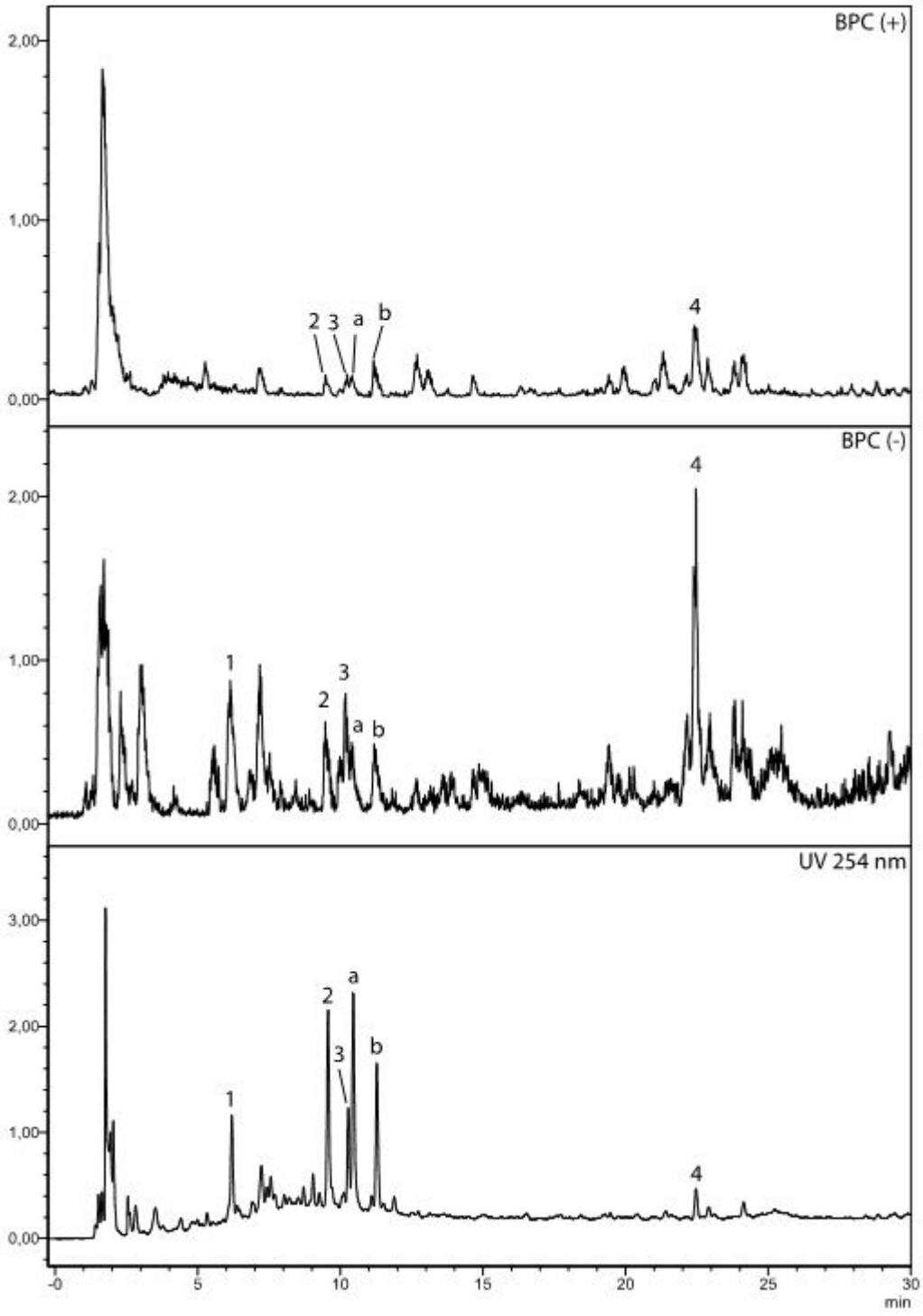

Fig. 2S. HPLC-UV-MS analysis of *Humulus lupulus* 70% EtOH extract. BPC: base peak chromatogram.
1: chlorogenic acid, **2:** isoquercitrin, **3:** kaempferol hexoside (tentative assignment), **4:** xanthohumol, **a:** unidentified flavonoid, MW 550 amu, **b:** unidentified flavonoid, MW 534 amu.

Table 2S. Retention time and spectroscopic data of annotated peaks in *Humulus lupulus* 70% EtOH extract.

Peak number	Retention time (min)	UV maxima (nm)	ESI MS (+) (m/z)	ESI MS (−) (m/z)	Identification
1	6.2	203, 300, 325	354.9 $[M+H]^+$	353.1 $[M-H]^-$	Chlorogenic acid
2	9.6	203, 255, 353	465.1 $[M+H]^+$	463.0 $[M-H]^-$	Isoquercitrin
3	10.3	201, 265, 343	448.9 $[M+H]^+$ 286.7	447.0 $[M-H]^-$	Kaempferol hexoside
4	22.5	222, 369	354.9 $[M+H]^+$	353.0 $[M-H]^-$	Xanthohumol
a	10.5	204, 255, 353	550.8 $[M+H]^+$	549.2 $[M-H]^-$	Unidentified flavonoid
b	11.3	205, 265, 346	534.9 $[M+H]^+$	533.0 $[M-H]^-$	Unidentified flavonoid

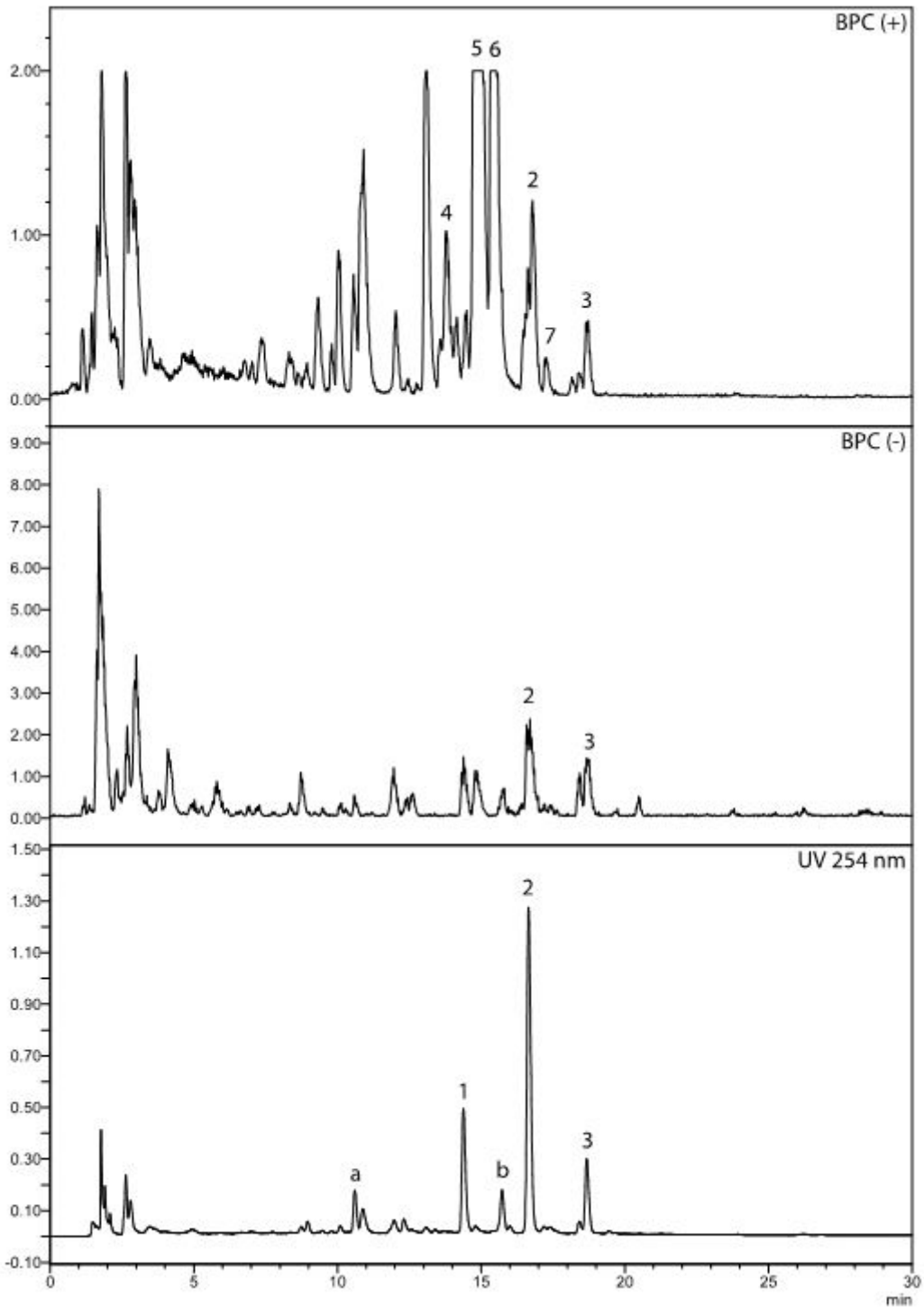

Fig. 3S. HPLC-UV-MS analysis of *Eschscholzia californica* 70% EtOH extract. BPC: base peak chromatogram. **1:** rutin rhamnoside (tentative assignment), **2:** rutin, **3:** rhamnoside of *O*-methyl quercetin (tentative assignment), **4:** protopine, **5:** californidine, **6:** escholzine, **7:** neocaryachine-7-*O*-methyl ether *N*-metho salt (CAS-Nr. 1310405-84-5, tentative assignment), **a:** unidentified flavonoid, MW 772 amu, **b:** unidentified flavonoid, MW 624 amu.

Table 3S. Retention time and spectroscopic data of annotated peaks in *Eschscholzia californica* 70% EtOH extract.

Peak number	Retention time (min)	UV maxima (nm)	ESI MS (+) (m/z)	ESI MS (−) (m/z)	Identification
1	14.4	219, 255, 353	757.1 $[M+H]^+$	755.1 $[M-H]^-$	Rutin rhamnoside
2	16.7	216, 255, 353	611.0 $[M+H]^+$	609.1 $[M-H]^-$	Rutin
3	18.7	204, 254, 353	625.1 $[M+H]^+$	623.1 $[M-H]^-$	Rhamnoside of O-methyl quercetin
4	13.8	* OV	354.0 $[M+H]^+$	-	Protopine
5	14.9	* OV	337.9 $[M+H]^+$	-	Californidine
6	15.5	* OV	324.0 $[M+H]^+$	-	Escholzine
7	17.3	* OV	340.0 $[M+H]^+$	-	Neocaryachine-7-*O*-methyl ether *N*-metho salt
a	10.6	202, 255, 353	773.0 $[M+H]^+$	771.1 $[M-H]^-$	Unidentified flavonoid
b	18.7	204, 254, 353	625.1 $[M+H]^+$	623.1 $[M-H]^-$	Unidentified flavonoid

* UV spectrum overlapped by coeluting flavonoids.

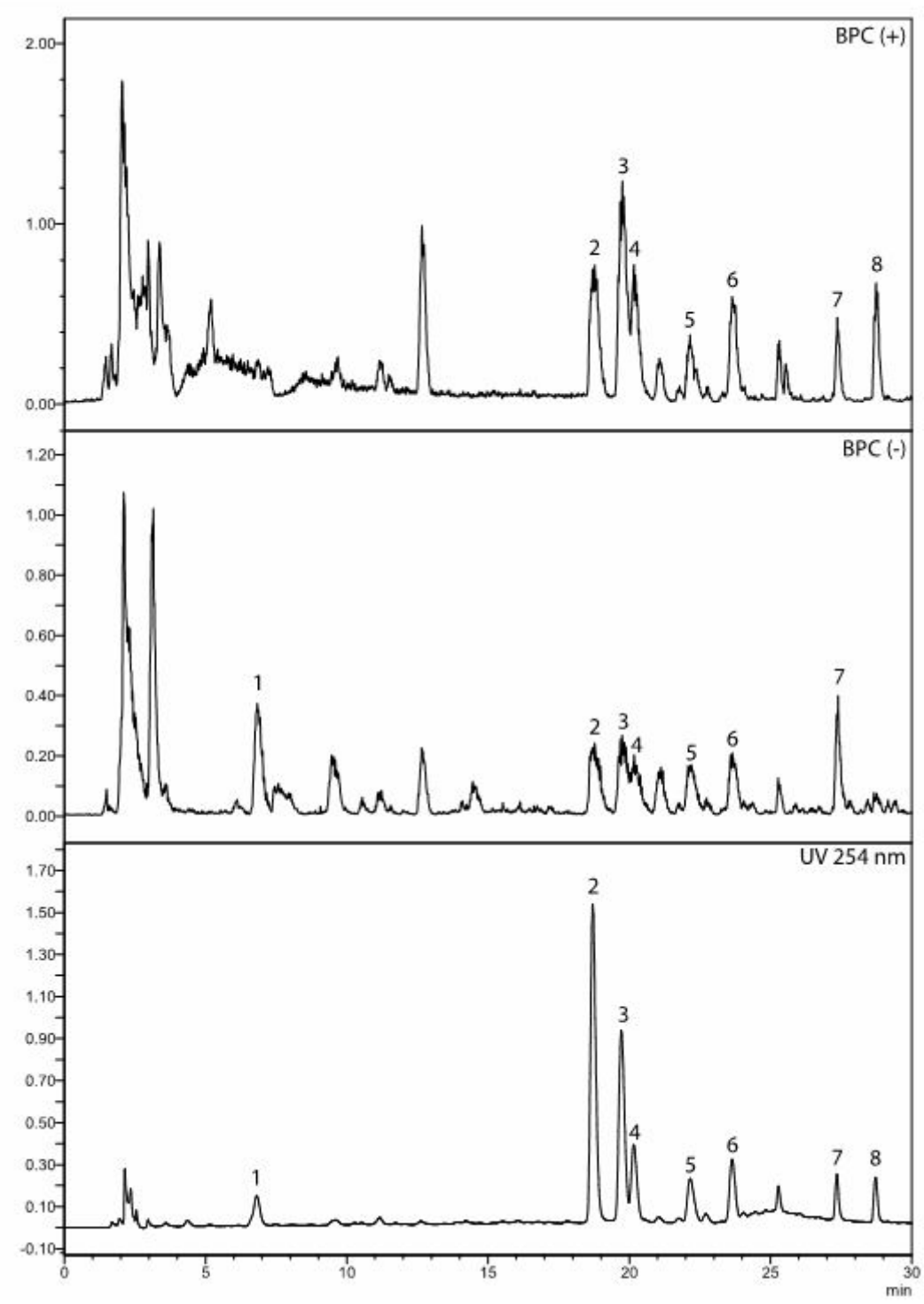

Fig. 4S. HPLC-UV-MS analysis of *Hypericum perforatum* 70% EtOH extract. BPC: base peak chromatogram. **1:** chlorogenic acid isomer (tentative assignment), **2:** rutin, **3:** hyperosid, **4:** isoquercitrin, **5:** miquelianin (quercetin-3-*O*-glucuronide), **6:** quercitrin, **7:** quercetin, **8:** biapigenin.

Table 4S. Retention time and spectroscopic data of annotated peaks in *Hypericum perforatum* 70% EtOH extract.

Peak number	Retention time (min)	UV maxima (nm)	ESI MS (+) (m/z)	ESI MS (−) (m/z)	Identification
1	6.8	210, 300, 325	355.0 $[M+H]^+$	353.1 $[M-H]^-$	Chlorogenic acid isomer
2	18.7	221, 255, 351	609.0 $[M+H]^+$	611.0 $[M-H]^-$	Rutin
3	19.7	215, 255, 353	464.9 $[M+H]^+$	463.1 $[M-H]^-$	Hyperosid
4	20.2	201, 255, 353	465.0 $[M+H]^+$	463.1 $[M-H]^-$	Isoquercitrin
5	22.2	201, 255, 353	478.9 $[M+H]^+$	477.0 $[M-H]^-$	Miquelianin
6	23.6	201, 254, 349	449.0 $[M+H]^+$	447.0 $[M-H]^-$	Quercitrin
7	27.4	204, 254, 370	302.9 $[M+H]^+$	301.0 $[M-H]^-$	Quercetin
8	28.7	208, 268, 330	538.9 $[M+H]^+$	537.0 $[M-H]^-$	Biapigenin

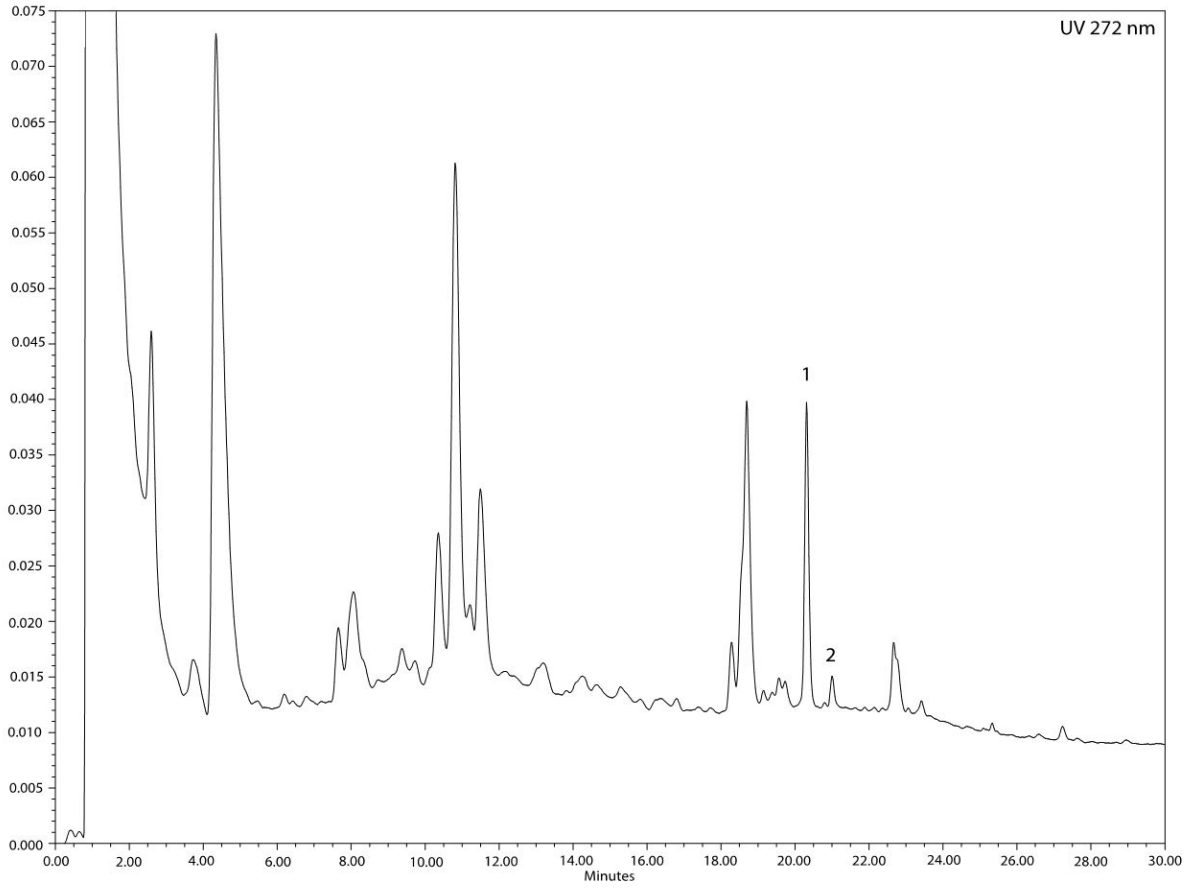

Fig. 5S. HPLC-UV analysis of hyperforin and adhyperforin in *Hypericum perforatum* extract. **1:** hyperforin, **2:** adhyperforin.

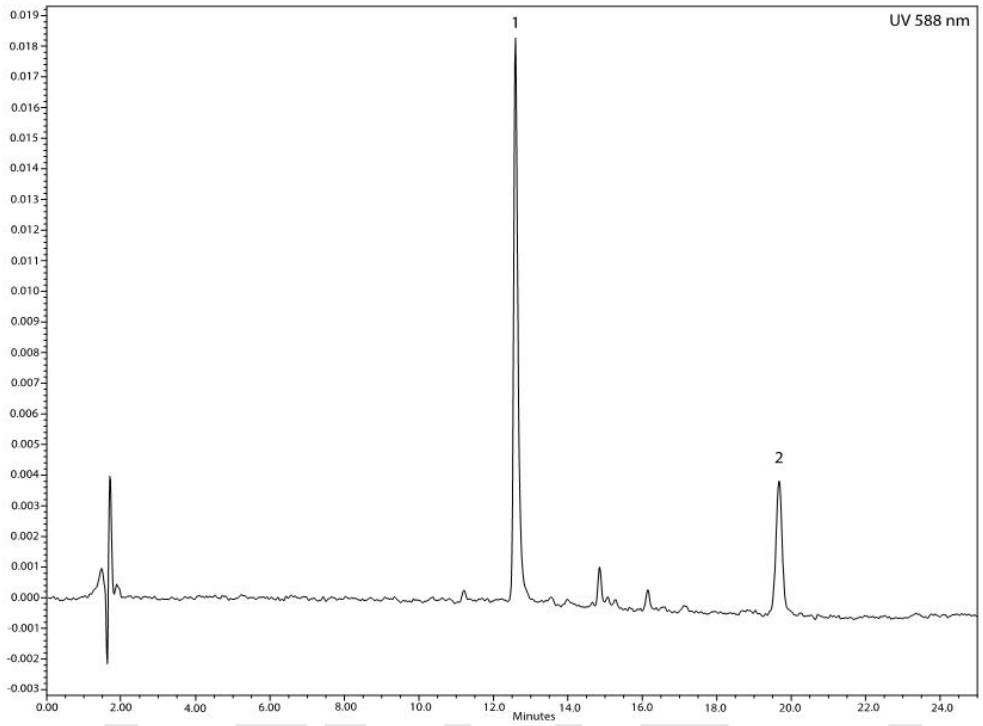

Fig. 6S. HPLC-UV analysis of hypericin and pseudohypericin in *Hypericum perforatum* extract. **1:** pseudohypericin, **2:** hypericin.

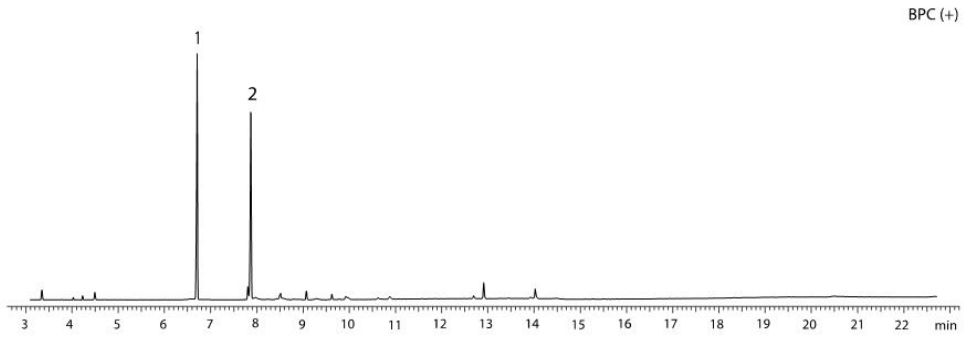

Fig. 7S. GC-MS analysis of *Lavandula angustifolia* essential oil. **1:** linalool, **2:** linalyl acetate.

Table 5S. Retention time, peak area, and identification of constituents of *Lavendula augustifolia* essential oil.

Peak number	Rentention time (min)	Area (%)	Identification	Spectrum identity (%, NIST)
1	6.71	43.4	Linalool	97
2	7.87	38.6	Linalyl acetate	90

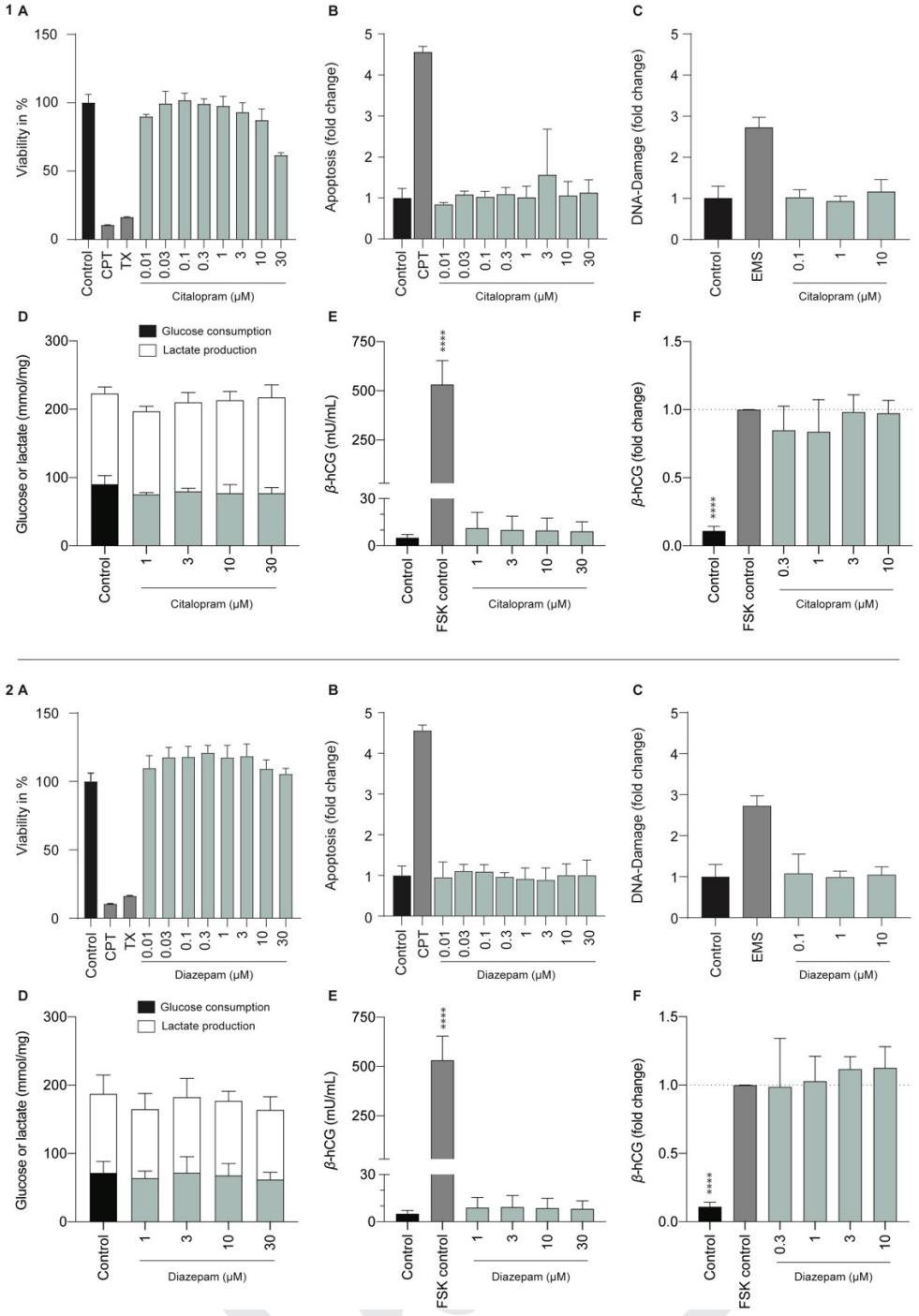

Fig. 8S. Effects of different concentrations of citalopram **(1)** and diazepam **(2)** on *in vitro* safety using undifferentiated BeWo b30 cells. All controls consisted of cell culture media containing 0.2% of DMSO. All data were obtained from at least 3 independent experiments (D–F in triplicate) and are shown as mean ± SD: *$p < 0.05$. **(A)** Effects on cell viability after treatment for 72 h as percent compared to the untreated control; treatments with camptothecin (CPT) and Triton-X-100 (TX) serve as toxicity controls. Results were normalized to untreated control signal = 100%. **(B)** Effects on cell death after treatment for 72 h as fold changes compared to the untreated controls with camptothecin (CPT) for apoptosis. **(C)** Effects on tail DNA after treatment for 3 h as fold changes compared to the untreated control with ethyl methanesulfonate (EMS) as a positive control. **(D)** Effects on glucose consumption and lactate production after treatment for 48 h expressed in mmol and normalized per amount of protein (mg). **(E)** Effects on β-hCG secretion (mU/mL) by BeWo b30 cells upon 48 h treatment with increasing concentrations of citalopram **(1)** or diazepam **(2)** and 50 µM FSK as a positive control. (**F**) Effects on FSK-induced differentiation of BeWo b30 cells as fold changes compared to the FSK control. Cells were pre-treated with test compound or cell culture medium for 24 h, before adding 5 µM FSK for a further 24 h.

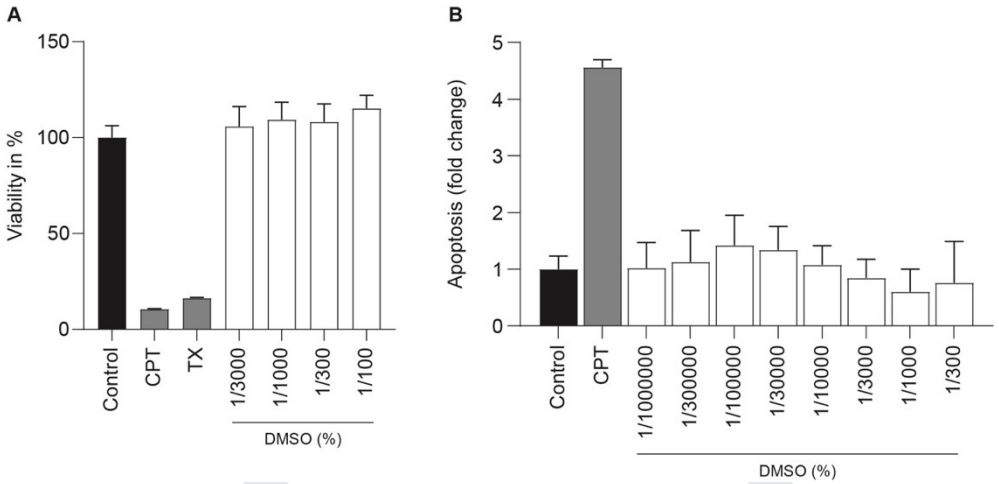

Fig. 9S. (A) Cytotoxic effects of DMSO (0.03–1%) on BeWo b30 cells. Viability assays were performed after a 72 h incubation period. Camptothecin (CPT) and Triton-X-100 (TX) were used as toxicity controls. **(B)** Effects of DMSO (0.0001–0.3%) on cell death after treatment for 72 h as fold changes compared to the untreated controls with camptothecin (CPT) for apoptosis. All data are represented as mean ± SD of three independent experiments ($n = 3$; $p^* < 0.05$).