Supporting Information

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Biological and Chemical Comparison of Natural and Cultivated Samples of *Satureja macrantha* C.A.Mey.

Mehmet Akdeniz[1], Ismail Yener[2], Abdulselam Ertas[3], Mehmet Firat[4], Baris Resitoglu[3], Nesrin Hasimi[5], Sevgi Irtegun Kandemir[6], Mustafa Abdullah Yilmaz[7], Asli Barla Demirkoz[8,9 *], Ufuk Kolak[10] and Sevil Oksuz[10]

[1]The Council of Forensic Medicine, Diyarbakir Group Chairmanship, 21070 Diyarbakir, Türkiye
[2]Dicle University, Faculty of Pharmacy, Department of Analytical Chemistry, 21280 Diyarbakir, Türkiye
[3]Dicle University, Faculty of Pharmacy, Department of Pharmacognosy, 21280 Diyarbakir, Türkiye
[4]Van Yüzüncü Yıl University, Faculty of Education, Department of Biology, 65080 Van, Türkiye
[5]Batman University, Science and Literature Faculty, Department of Biology, 72060 Batman, Türkiye
[6]Dicle University, Faculty of Medicine, Department of Medical Biology, 21280 Diyarbakir, Türkiye
[7]Dicle University Science and Technology Research and Application Center, 21280 Diyarbakir, Türkiye
[8]Haliç University, Faculty of Health Sciences, Department of Nutrition and Dietetics, 34445 Istanbul, Türkiye
[9]AROMSA Research and Development Center, Aromsa Flavours and Food Additives Industry and Trade Inc. Co., 41480 Kocaeli, Türkiye
[10]Istanbul University, Faculty of Pharmacy, Department of General and Analytical Chemistry, 34116 Istanbul, Türkiye

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[*]Corresponding author: E-Mail: aslibarla@gmail.com**:** Phone: +905326209894

1. Biological Activity Methods

1.1. Determination of Total Phenolic and Flavonoid Contents

Phenolic and flavonoid contents expressed as pyrocatechol and quercetin equivalents, respectively, were determined as reported in the literature [1,2]. The following equations were used to calculate total phenolic and flavonoid contents of the extracts:

Absorbance = 0.0309 + 0.0533 pyrocatechol (μg) (r^2 = 0.9963)
Absorbance = 0.0334 + 0.1961 quercetin (μg) (r^2 = 0.9957)

1.2. Antioxidant Activity of the Extracts and Essential Oils

DPPH free radical and ABTS cation radical scavenging activities and cupric reducing antioxidant capacity (CUPRAC) methods were used to determine the antioxidant activity [3-5]. IC_{50} calculations were performed by using the samples with 100, 50, 25, 10 and 1 μg/mL concentrations.

1.2.1. Free Radical Scavenging Activity Method

0.1 mM 160 μL of DPPH solution in methanol was added into 40 μL of sample solutions in methanol at different concentrations. After 30 min. the absorbance values were read at 517 nm. The DPPH free radical scavenging potential was calculated using the following equation:

$$\text{DPPH scavenging effect (Inhibition \%)} = \frac{A_{control} - A_{sample}}{A_{control}} \times 100$$

$A_{Control}$ is the initial concentration of the DPPH$^{\bullet}$
A_{Sample} is the absorbance of the remaining concentration of DPPH$^{\bullet}$ in the presence of the samples or positive controls [3].

1.2.2. ABTS cation radical decolorization assay

Seven milimolar ABTS in H_2O was added into 2.45 mM potassium persulfate to produce $ABTS^{\bullet+}$ and solution was stored in the dark at 25ºC for 12 hours. The prepared solution was diluted with ethanol to get an absorbance of 0.700±0.025 at 734 nm. $ABTS^{\bullet+}$ solution (160 μL) was added to each sample solution at different concentrations. After 30 min, the percentage inhibition at 734 nm was read for each concentration relative to a blank absorbance (methanol) [4]. The following equation was used to calculate the scavenging capability of $ABTS^{\bullet+}$:

$$ABTS^{\bullet+}\text{ scavenging effect (Inhibition \%)} = \frac{A_{control} - A_{sample}}{A_{control}} \times 100$$

1.2.3. Cupric reducing antioxidant capacity (CUPRAC) method

The extracts in distilled water to prepare their stock solution at 1000 μg/mL concentration. Aliquots of 61 mL of 1.0×10^{-2} M copper (II) chloride, 61 μL of NH_4OAc buffer (1 M, pH 7.0), and 61 μL of 7.5×10^{-3} M neocuproine solution were mixed, x μL sample solution (2.5, 6.25, 12.5, and 25 μL) and (67 − x) μL distilled water were added to make the final volume 250 μL. The tubes were stopped, and after 1 h, the absorbance at 450 nm was measured against a reagent blank [5].

2. Cytotoxic Activity

Human-derived cancer cell series and the Primary Dermal Fibroblasts series were used in this study. For this purpose, the breast cancer cell line (MCF-7), the colon cancer series (HT-29), and the Primary Dermal Fibroblast Series (PDF) were provided. For each cell series, the number of cells to be placed on the platelets was optimized. Twenty-two thousand cells for MCF-7, 20.000 cells for HT-29, and 12.000 cells for PDF were added into the 96-well plates. After incubation for 24 hours, the cells were treated with 10 μL of extracts prepared at different concentrations (10, 25, 50, 100, 200, μg/mL) for 48 hours. After addition of 10 μL of MTT reagent, and then incubation for 4 hours, purple

precipitate occured. A hundred microliters of detergent reagent was added. The plate was incubated in the dark for overnight in humidified atmosphere (37°C, 5% CO_2). The absorbances of the samples were measured using a microplate (ELISA) reader at 570 and 690 nm. Measurements at 690 nm were used as reference absorbances. MTT assay was performed in 3 parallel for each concentration and each MTT assay was repeated 3 times [6,7]. Ethanol used as the extraction solvent were utilized with the same volume as control sample.

3. Anticholinesterase Activity

A spectrophotometric method developed by Ellman et al. [8], was used to indicate the acetyl- and butyryl-cholinesterase inhibitory activities.

Aliquots of 150 µL of 100 mM sodium phosphate buffer (pH 8.0), 10 μL of sample solution and 20 µL BChE (or AChE) solution were stirred and incubated for 15 min at 25ºC, then DTNB (10 µL) is added to mixture. In the next step, by the addition of butyrylthiocholine iodide (or acetylthiocholine iodide) (10 µL) the reaction was started. At the end, final concentration of the tested solutions was 200 µg/mL. BioTek Power Wave XS at 412 nm was used to monitor the hydrolysis of these substrates.

4. Urease Inhibitory Activity

Urease inhibitory activity of the essential oils and extracts was determined according to the reported protocol [9]. Final volume of reaction is 200 µL at pH 8.2. Twenty-five microliters of urease (Jack bean) solution was mixed with 10 µL of each samples (4000 µg/mL) and incubated at 30°C for 15 min. Aliquots were taken and immediately transferred to assay mixtures containing urea (100 mM) in buffer (50 µL) and reincubated for 30 min in 96-well plates. Forty-five microliters from each of phenol reagent (1% w/v phenol and 0.005% w/v sodium nitroprusside) and 70 µL of alkali reagent (0.5% w/v sodium hydroxide and 0.1% sodium hypochloride) were added to wells. Increase in absorbance was measured after 50 min at 630 nm against blank. All reactions were performed in triplicates. Thiourea was used as a positive control. The percentage inhibition was determined by using the following equation:

Urease Inhibition (%) = 100 - (OD test well /OD control) × 100

5. Anti-aging Activity

5.1. Tyrosinase Inhibitory Activity

Tyrosinase inhibition assays were performed according to the method Hearing's protocol [10]. Briefly, the samples were screened for the *o*-diphenolase inhibitory activity of tyrosinase using L-DOPA as substrate. All samples were dissolved in methanol to reach to a concentration of 4000 µg/mL. One hundred fifty microliters of phosphate buffer (pH = 6.8), 10 µL of the samples and 20 µL of the enzyme solution were added to the wells in the microplate, and the initial absorbance at 475 nm was read after stirring for 3 min. This solution was then incubated for 10 min at 37°C, after 10 min 20 µL of L-DOPA was added and incubated again at 37°C, after 10 min the final absorbance at 475 nm was read in the Microplate ELISA reader. Tyrosinase activity (% inhibition) was calculated using the following equation.

Tyrosinase inhibition (%) = 100 - (OD test well /OD control) × 100

All the experiments were carried out at least in triplicate and the results represent means ± SEM (standard error of the mean). Kojic acid was used as a standard inhibitor for tyrosinase inhibition.

5.2. Elastase Inhibitory Activity

Elastase inhibitory activity was determined according to the protocol developed by Kraunsoe et al. [11] with slight modifications. Ten microliters of sample ethanol solution and 20 µL of elastase enzyme solution were added on 40 µL (0.1 M Tris-Cl, pH=8) of buffer solution and incubated for 10

min (37ºC). Afterwards, 30 µL of 1.015 mM substrate (N-succinyl-(Ala)-3-nitroanilide) solution which was prepared with buffer solution (0.1 M Tris-Cl, pH=8) were added and incubated at 37ºC for 20 min. Then, absorbance values were measured at 410 nm.

Elastase inhibition (%) = 100 - (OD test well /OD control) × 100

All the experiments were carried out at least in triplicate and the results represent means ± SEM (standard error of the mean). Oleanolic acid was used as standard reference.

5.3. Collagenase Inhibitory Activity

Collagenase inhibitory activity was determined according to the protocol developed by Thring et al. [12] with slight modifications. Sample solution prepared in 20 µL of DMSO and 10 µL of collagenase enzyme solution (0.8 U/mL) were added into 50 µL of phosphate buffer (pH: 7.5) and incubated at 25ºC for 15 min. Afterwards, 20 µL substrate solution (N-(3-[2-Furyl]acryloyl)-Leu-Gly-Pro-Ala) was added, incubated at 25ºC for 20 min and absorbance values were measured at 340 nm.

Collagenase inhibition (%) = 100 - (OD test well /OD control) × 100

All the experiments were carried out at least in triplicate and the results represent means ± SEM (standard error of the mean). Epicatechin gallate was used as standard reference.

6. Antimicrobial Activity

Antimicrobial activity was determined by disc diffusion method (CLSI, 2007) against Gram-negative (*Escherichia coli* ATCC25922, *Pseudomonas aeroginosa* ATCC27853), Gram-positive (*Staphylococcus aureus* 25923, *Streptococcus pyogenes* ATCC19615) bacteria and yeast (*Candida albicans* ATCC10231). Single colony of microorganisms was inoculated to Muller Hinton buyyon and incubated overnight. Turbidity was adjusted to 0.5 McFarland standard with sterile saline water. 0,1 mL of each culture was spread to Muller Hinton agar petri dishes. Sterile paper discs with 6 mm diameter were impregnated with 0.01 mL of samples and placed in petri dishes. All petri dishes were keep at $+4^0$C for 2 hours. After that petri dishes were incubated at 37^0C 24 hours for the bacteria and 30^0C 48 hours for the yeast. After the incubation period zone diameters of each disc were measured. Ampicillin and fluconazole were used as a positive control for the bacteria and the yeast, respectively. All tests were done in triplicate [13].

Table S1. Terpenoid-steroid-flavonoid contents of *S. macrantha* samples by GC-MS

Compound	RT[a]	Molecular ion-m/z (relative intensity %) (m/z)[b]	Three major fragment ions m/z (relative intensity %)[c]			SM-N[d] (mg analyte/g extract)	SM-C[d] (mg analyte/g extract)
Sclareolide	13.009	250.38 (1.1)	123(100)	235(39.1)	206(21.6)	ND	ND
Sclareol	15.405	308.51 (2.0)	109(100)	191(44.6)	257(18)	ND	ND
Ferruginol	17.091	286.46 (95.7)	271(100)	189(63.5)	201(44.4)	17.5	ND
Cryptanol	17.638	316 (100)	205(24.9)	219(22.7)	301(19.8)	ND	ND
6,7-Dehydroroyleanone	18.821	314.19 (1.1)	298(100)	283(41.8)	265(8.7)	ND	ND
Suginal	19.728	314.43 (2.8)	299(100)	300(20.8)	281(4)	ND	ND
9,10-Dihydro-7,8-dimethyl-2-(1-methylethyl) phenanthrene-3-ol	20.437	266.15 (48)	251(100)	252(19.4)	203(6.8)	ND	ND
Sugiol	21.628	300.44 (69)	285(100)	217(37.5)	243(25.2)	4.2	ND
Inuroyleanone	21.996	346.28 (100)	331(45.9)	261(17.7)	245(2.3)	ND	ND
12-Demethylmulticauline	22.646	264.15 (91.1)	249(100)	234(17.3)	216(16.6)	ND	ND
7α-Hydroxy-β-sitosterol	27.700	430.71 (2.5)	394(100)	135(75.7)	143(69.9)	ND	ND
Salvigenin	28.311	328.09 (100)	313(99.5)	299(27.1)	282(25.3)	7.7	ND
Stigmasterol	30.052	412.36 (100)	255(87.1)	271(66)	300(47.6)	ND	ND
β-Sitosterol	30.795	414.72 (100)	396(58)	303(53.2)	329(51)	18.7	3.1
Sinensetin	31.343	372.37 (19.2)	357(100)	341(20.6)	313(6.4)	ND	ND
Lupenone	31.592	424.37 (36.0)	205(100)	313(27.7)	218(805.2)	ND	ND
α-Amyrin	31.944	426.73 (8.4)	218(100)	189(21.6)	203(21.2)	ND	ND
Lupeol	31.944	426.38 (38.9)	218(463.5)	189(100)	203(98.2)	ND	ND
3-Acetyl lupeol	33.513	468.40 (22.35)	189(100)	121(71.4)	203(35.1)	ND	ND
1α,21α-Dihydroxy-2-3-(1',1'-dimethyl-dioxymethylene)urs-9(11),12-diene	37.636	512.39 (100)	421(19.3)	343(17)	271(17)	ND	ND
Uvaol	37.800	442.73 (1.1)	203(100)	204(16.6)	234(11)	ND	ND
Betulin	38.269	442.73 (11.1)	203(1224.7)	189(100)	411(26.9)	ND	ND
Pyxinol	39.160	476.74 (0.62)	143(100)	400(13.9)	191(9.7)	ND	ND
Lup-(20)29-ene-2α-hydroxy-3β- acetate	39.467	484 (5.5)	416(100)	273(68.6)	189(44.5)	ND	ND
Betulin 3β,28β-diacetate	41.236	526.80 (1.6)	189(100)	466(47.1)	203(39.5)	ND	ND
21α-Hydroxy,2α,3β-diacetoxy urs-9(11),12-diene	43.145	540.38 (100)	405(48.1)	271(43.7)	420(22.1)	ND	ND

[a]RT: Retention time; [b]Mother ion(m/z): Molecular ions of the standard compounds (*m/z* ratio); [c]FI (m/z): Fragment ions; [d]The abbreviations for natural *S. macrantha* ethanol extract is SM-N and the abbreviation for ethanol extract of *S. macrantha* cultivated sample is expressed as SM-C, ND: not detected (<LOD).

Table S2. Analytical method validation parameters of LC-MS/MS method

No	Analytes	RT[a]	M.I. (m/z)[b]	F.I. (m/z)[c]	Ion. mode	Equation	r^{2d}	*RSD*%[e]		Linearity Range (mg/L)	*LOD*/*LOQ* (µg/L)[f]	Recovery (%)		*U*[g]	Gr. No[i]
								Interday	Intraday			Interday	Intraday		
1	Quinic acid	3.0	190.8	93.0	Neg	*y*=-0.0129989+2.97989×	0.996	0.69	0.51	0.1-5	25.7/33.3	1.0011	1.0083	0.0372	1
2	Fumaric aid	3.9	115.2	40.9	Neg	*y*=-0.0817862+1.03467×	0.995	1.05	1.02	1-50	135.7/167.9	0.9963	1.0016	0.0091	1
3	Aconitic acid	4.0	172.8	129.0	Neg	*y*=-0.7014530+32.9994×	0.971	2.07	0.93	0.1-5	16.4/31.4	0.9968	1.0068	0.0247	1
4	Gallic acid	4.4	168.8	79.0	Neg	*y*=0.0547697+20.8152×	0.999	1.60	0.81	0.1-5	13.2/17.0	1.0010	0.9947	0.0112	1
5	Epigallocatechin	6.7	304.8	219.0	Neg	*y*=-0.00494986+0.0483704×	0.998	1.22	0.73	1-50	237.5/265.9	0.9969	1.0040	0.0184	3
6	Protocatechuic acid	6.8	152.8	108.0	Neg	*y*=0.211373+12.8622×	0.957	1.43	0.76	0.1-5	21.9/38.6	0.9972	1.0055	0.0350	1
7	Catechin	7.4	288.8	203.1	Neg	*y*=-0.00370053+0.431369×	0.999	2.14	1.08	0.2-10	55.0/78.0	1.0024	1.0045	0.0221	3
8	Gentisic acid	8.3	152.8	109.0	Neg	*y*=-0.0238983+12.1494×	0.997	1.81	1.22	0.1-5	18.5/28.2	0.9963	1.0077	0.0167	1
9	Chlorogenic acid	8.4	353.0	85.0	Neg	*y*=0.289983+36.3926×	0.995	2.15	1.52	0.1-5	13.1/17.6	1.0000	1.0023	0.0213	1
10	Protocatechuic aldehyde	8.5	137.2	92.0	Neg	*y*=0.257085+25.4657×	0.996	2.08	0.57	0.1-5	15.4/22.2	1.0002	0.9988	0.0396	1
11	Tannic acid	9.2	182.8	78.0	Neg	*y*=0.0126307+26.9263×	0.999	2.40	1.16	0.05-2.5	15.3/22.7	0.9970	0.9950	0.0190	1
12	Epigallocatechin gallate	9.4	457.0	305.1	Neg	*y*=-0.0380744+1.61233×	0.999	1.30	0.63	0.2-10	61.0/86.0	0.9981	1.0079	0.0147	3
13	1,5-Dicaffeoylquinic acid	9.8	515.0	191.0	Neg	*y*=-0.0164044+16.6535×	0.999	2.42	1.48	0.1-5	5.8/9.4	0.9983	0.9997	0.0306	1
14	4-OH Benzoic acid	10.5	137,2	65.0	Neg	*y*=-0.0240747+5.06492×	0.999	1.24	0.97	0.2-10	68.4/88.1	1.0032	1.0068	0.0237	1
15	Epicatechin	11.6	289.0	203.0	Neg	*y*=-0.0172078+0.0833424×	0.996	1.47	0.62	1-50	139.6/161.6	1.0013	1.0012	0.0221	3
16	Vanillic acid	11.8	166.8	108.0	Neg	*y*=-0.0480183+0.779564×	0.999	1.92	0.76	1-50	141.9/164.9	1.0022	0.9998	0.0145	1
17	Caffeic acid	12.1	179.0	134.0	Neg	*y*=0.120319+95.4610×	0.999	1.11	1.25	0.05-2.5	7.7/9.5	1.0015	1.0042	0.0152	1
18	Syringic acid	12.6	196.8	166.9	Neg	*y*=-0.0458599+0.663948×	0.998	1.18	1.09	1-50	82.3/104.5	1.0006	1.0072	0.0129	1
19	Vanillin	13.9	153.1	125.0	Poz	*y*=0.00185898+20.7382×	0.996	1.10	0.85	0.1-5	24.5/30.4	1.0009	0.9967	0.0122	1
20	Syringic aldehyde	14.6	181.0	151.1	Neg	*y*=-0.0128684+7.90153×	0.999	2.51	0.77	0.4-20	19.7/28.0	1.0001	0.9964	0.0215	1
21	Daidzin	15.2	417.1	199.0	Poz	*y*=9.45747+152.338×	0.996	2.25	1.32	0.05-2.5	7.0/9.5	0.9955	1.0017	0.0202	2
22	Epicatechin gallate	15.5	441.0	289.0	Neg	*y*=-0.0142216+1.06768×	0.997	1.63	1.28	0.1-5	19.5/28.5	0.9984	0.9946	0.0229	3
23	Piceid	17.2	391.0	135/106.9	Poz	*y*=0.00772525+25.4181×	0.999	1.94	1.16	0.05-2.5	13.8/17.8	1.0042	0.9979	0.0199	1
24	*p*-Coumaric acid	17.8	163.0	93.0	Neg	*y*=0.0249034+18.5180×	0.999	1.92	1.43	0.1-5	25.9/34.9	1.0049	1.0001	0.0194	1
25	Ferulic acid-D3-IS[h]	18.8	196.2	152.1	Neg	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	0.0170	1
26	Ferulic acid	18.8	192.8	149.0	Neg	*y*=-0.0735254+1.34476×	0.999	1.44	0.53	1-50	11.8/15.6	0.9951	0.9976	0.0181	1
27	Sinapic acid	18.9	222.8	193.0	Neg	*y*=-0.0929932+0.836324×	0.999	1.45	0.52	0.2-10	65.2/82.3	1.0031	1.0037	0.0317	1
28	Coumarin	20.9	146.9	103.1	Poz	*y*=0.0633397+136.508×	0.999	2.11	1.54	0.05-2.5	214.2/247.3	0.9950	0.9958	0.0383	1

[a]RT: Retention time, [b]MI (*m/z):* Molecular ions of the standard analytes (m/z ratio), [c]FI (*m/z):* Fragment ions [d]r^2: Coefficient of determination, [e]*RSD*: Relative standard deviation, [f]*LOD*/*LOQ* (µg/L): Limit of detection/quantification, [g]*U* (%): percent relative uncertainty at 95% confidence level (*k* = 2), [h]IS: Internal standard, [i]Gr. No: Represents grouping of internal standards, these numbers indicate which IS stands for which phenolic compound.

Table S2. Analytical method validation parameters of LC-MS/MS method (*Continued*)

No	Analytes	RT[a]	M.I. (m/z)[b]	F.I. (m/z)[c]	Ion. mode	Equation	r^{2d}	*RSD%*[e]		Linearity Range (mg/L)	*LOD*/*LOQ* (µg/L)[f]	Recovery (%)		*U*[g]	Gr. No
								Interday	Intraday			Interday	Intraday		
29	Salicylic acid	21.8	137.2	65.0	Neg	*y*=0.239287+153.659×	0.999	1.48	1.18	0.05-2.5	6.0/8.3	0.9950	0.9998	0.0158	1
30	Cynaroside	23.7	447.0	284.0	Neg	*y*=0.280246+6.13360×	0.997	1.56	1.12	0.05-2.5	12.1/16.0	1.0072	1.0002	0.0366	2
31	Miquelianin	24.1	477.0	150.9	Neg	*y*=-0.00991585+5.50334×	0.999	1.31	0.95	0.1-5	10.6/14.7	0.9934	0.9965	0.0220	2
32	Rutin-D3-IS[h]	25.5	612.2	304.1	Neg	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	2
33	Rutin	25.6	608.9	301.0	Neg	*y*=-0.0771907+2.89868×	0.999	1.38	1.09	0.1-5	15.7/22.7	0.9977	1.0033	0.0247	2
34	Isoquercitrin	25.6	463.0	271.0	Neg	*y*=-0.111120+4.10546×	0.998	2.13	0.78	0.1-5	8.7/13.5	1.0057	0.9963	0.0220	2
35	Hesperidin	25.8	611.2	449.0	Poz	*y*=0.139055+13.2785×	0.999	1.84	1.35	0.1-5	19.0/26.0	0.9967	1.0043	0.0335	2
36	*o*-Coumaric acid	26.1	162.8	93.0	Neg	*y*=0.00837193+11.2147×	0.999	2.11	1.46	0.1-5	31.8/40.4	1.0044	0.9986	0.0147	1
37	Genistin	26.3	431.0	239.0	Neg	*y*=1.65808+7.57459×	0.991	2.01	1.28	0.1-5	14.9/21.7	1.0062	1.0047	0.0083	2
38	Rosmarinic acid	26.6	359.0	197.0	Neg	*y*=-0.0117238+8.04377×	0.999	1.24	0.86	0.1-5	16.2/21.2	1.0056	1.0002	0.0130	1
39	Ellagic acid	27.6	301.0	284.0	Neg	*y*=0.00877034+0.663741×	0.999	1.57	1.23	0.4-20	56.9/71.0	1.0005	1.0048	0.0364	1
40	Cosmosiin	28.2	431.0	269.0	Neg	*y*=-0.708662+8.62498×	0.998	1.65	1.30	0.1-5	6.3/9.2	0.9940	0.9973	0.0083	2
41	Quercitrin	29.8	447.0	301.0	Neg	*y*=-0.00153274+3.20368×	0.999	2.24	1.16	0.1-5	4.8/6.4	0.9960	0.9978	0.0268	2
42	Astragalin	30.4	447.0	255.0	Neg	*y*=0.00825333+3.51189×	0.999	2.08	1.72	0.1-5	6.6/8.2	0.9968	0.9957	0.0114	2
43	Nicotiflorin	30.6	592.9	255.0/284.0	Neg	*y*=0.00499333+2.62351×	0.999	1.48	1.23	0.05-2.5	11.9/16.7	0.9954	1.0044	0.0108	2
44	Fisetin	30.6	285.0	163.0	Neg	*y*=0.0365705+8.09472×	0.999	1.75	1.19	0.1-5	10.1/12.7	0.9980	1.0042	0.0231	3
45	Daidzein	34.0	253.0	223.0	Neg	*y*=-0.0329252+6.23004×	0.999	2.18	1.73	0.1-5	9.8/11.6	0.9926	0.9963	0.0370	3
46	Quercetin-D3-IS[h]	35.6	304.0	275.9	Neg	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	3
47	Quercetin	35.7	301.0	272.9	Neg	*y*=+0.00597342+3.39417×	0.999	1.89	1.38	0.1-5	15.5/19.0	0.9967	0.9971	0.0175	3
48	Naringenin	35.9	270.9	119.0	Neg	*y*=-0.00393403+14.6424×	0.999	2.34	1.69	0.1-5	2.6/3.9	1.0062	1.0020	0.0392	3
49	Hesperetin	36.7	301.0	136.0/286.0	Neg	*y*=+0.0442350+6.07160×	0.999	2.47	2.13	0.1-5	7.1/9.1	0.9998	0.9963	0.0321	3
50	Luteolin	36.7	284.8	151.0/175.0	Neg	*y*=-0.0541723+30.7422×	0.999	1.67	1.28	0.05-2.5	2.6/4.1	0.9952	1.0029	0.0313	3
51	Genistein	36.9	269.0	135.0	Neg	*y*=-0.00507501+12.1933×	0.999	1.48	1.19	0.05-2.5	3.7/5.3	1.0069	1.0012	0.0337	3
52	Kaempferol	37.9	285.0	239.0	Neg	*y*=-0.00459557+3.13754×	0.999	1.49	1.26	0.05-2.5	10.2/15.4	0.9992	0.9990	0.0212	3
53	Apigenin	38.2	268.8	151.0/149.0	Neg	*y*=0.119018+34.8730×	0.998	1.17	0.96	0.05-2.5	1.3/2.0	0.9985	1.0003	0.0178	3
54	Amentoflavone	39.7	537.0	417.0	Neg	*y*=0.727280+33.3658×	0.992	1.35	1.12	0.05-2.5	2.8/5.1	0.9991	1.0044	0.0340	3
55	Chrysin	40.5	252.8	145.0/119.0	Neg	*y*=-0.0777300+18.8873×	0.999	1.46	1.21	0.05-2.5	1.5/2.8	0.9922	1.0050	0.0323	3
56	Acacetin	40.7	283.0	239.0	Neg	*y*=-0.559818+163.062×	0.997	1.67	1.28	0.02-1	1.5/2.5	0.9949	1.0011	0.0363	3

[a]RT: Retention time, [b]MI (*m/z):* Molecular ions of the standard analytes (m/z ratio), [c]FI (*m/z):* Fragment ions [d]r^2: Coefficient of determination, [e]*RSD*: Relative standard deviation, [f]*LOD*/*LOQ* (µg/L): Limit of detection/quantification, [g]*U* (%): percent relative uncertainty at 95% confidence level (k = 2), [h]IS: Internal standard, [i]Gr. No: Represents grouping of internal standards, these numbers indicate which IS stands for which phenolic compound.

Figure S1: Cultivated and natural samples of *S. macrantha*

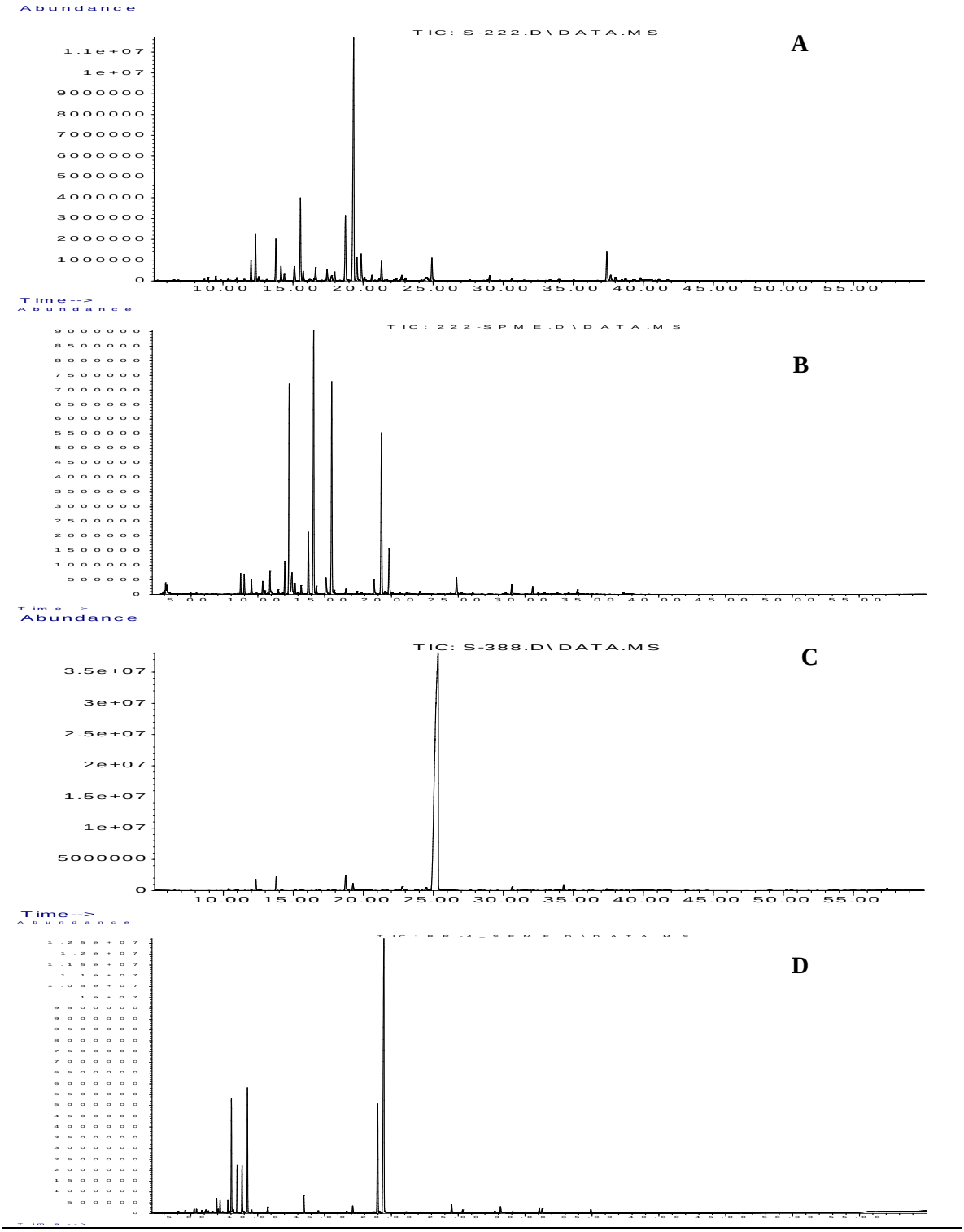

Figure S2: **A:** GC/FID-MS chromatogram of the natural *S. macrantha* essential oil, **B:** GC/FID-MS chromatogram of the natural *S. macrantha* flavour, **C:** GC/FID-MS chromatogram of the cultivated *S. macrantha* essential oil, **D:** GC/FID-MS chromatogram of the cultivated *S. macrantha* flavour

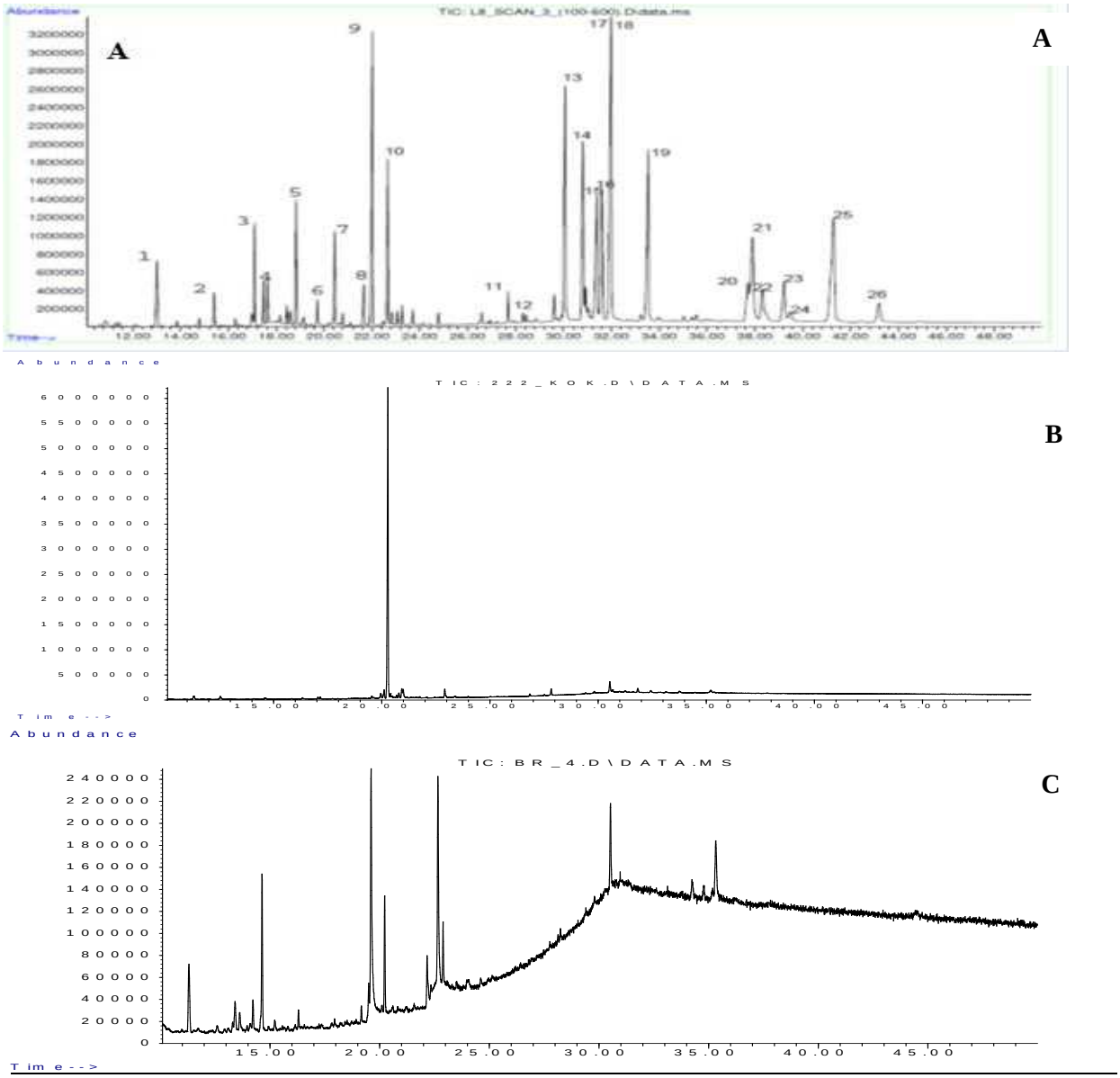

Figure S3: GC-MS chromatograms **A:** TIC chromatogram of standard chemicals analysed by GC-MS method. 1: Sclareolide, 2: Sclareol, 3: Ferruginol, 4: Cryptanol, 5: 6,7-Dehydroroyleanone, 6: Suginal, 7: 12-Hydroxy abieta-1,3,5(10),8,11,13-hexaene, 8: Sugiol, 9: Inuroyleanone, 10: 12-Demetilmulticauline, 11: 7α-Hydroxy-β-sitosterol, 12: Salvigenin, 13: Stigmasterol, 14: β-Sitosterol, 15: Sinensetin, 16: Lupenone, 17: α-Amyrin, 18: Lupeol 19: 3-Acetyl lupeol, 20: 1α,21α-Dihydroxy-2-3-(1',1'-dimethyl-dioxymethylene)urs-9(11),12-diene, 21: Uvaol, 22: Betulin, 23: Pyxinol, 24: Lup-(20)29-ene-2α-hydroxy-3β-acetate, 25: Betulin 3β,28β-diacetate 26: 21α-Hydroxy,2α,3β-diacetoxy urs-9(11),12-diene, **B:** GC-MS chromatogram of the natural *S. macrantha*, **C:** GC-MS chromatogram of the cultivated *S. macrantha*.

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