

## Comparative Effects of *Origanum onites* L. Extract and Carvacrol on the Metabolic Syndrome and Hepatic/Pancreatic Inflammatory Markers in Rats

by

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### Supplementary Materials

**Table S1.** Volatile compound composition of the *Origanum onites* L. extract obtained by supercritical CO<sub>2</sub> extraction. **Table S2.** Histopathological scoring of liver of rats with induced metabolic syndrome (MetS) and treated with carvacrol (MetS+CRV), oregano extract (MetS+OREG) or metformin (MetS+METF), as well as rats without induced MetS (control). **Table S3.** Histopathological scoring of pancreas of rats with induced metabolic syndrome (MetS) and treated with carvacrol (MetS+CRV), oregano extract (MetS+OREG) or metformin (MetS+METF), as well as rats without induced MetS (control).

**Table S1.** Volatile compound composition of the *Origanum onites* L. extract obtained by supercritical CO<sub>2</sub> extraction.

Compound	Relative content (%)	R.T. (min)
Sabinene	0.01	5.29
β-Pinene	0.69	5.37
1-Octen-3-ol	0.06	5.46
β-Myrcene	0.03	5.81
α-Phellandrene	0.01	6.22
α-Terpinene	0.07	6.63
p-Cymene	0.50	6.89
β-Phellandrene	0.03	7.05
1,8-Cineole	0.04	7.12
γ-Terpinene	0.58	8.21
<i>trans</i> -Sabinene hydrate	0.86	8.57
<i>trans</i> -Linalool oxide	0.11	8.78
Linalool	10.22	10.26
<i>cis</i> -Sabinene hydrate	0.02	10.98
α-Campholenal	0.04	11.12
<i>trans</i> -Pinocarveol	0.03	11.72
Camphor	0.04	11.90
<i>endo</i> -Borneol	0.85	13.13
Terpinen-4-ol	0.39	13.77
<i>m</i> -Mentha-1,8-diene	0.15	14.51
2,6-Dimethyl-3,7-octadiene-2,6-diol	0.24	15.93
Carvacrol methyl ether	0.11	17.53
1,4-Dimethoxy-2,3-dimethylbenzene	0.10	17.74
Thymoquinone	0.51	18.24
Hydroxycitronellal	0.07	20.60
Thymol	4.12	20.87
Carvacrol	64.65	22.08
4,5-Epoxy-1-isopropyl-4-methyl-1-cyclohexene	0.67	22.20

Carvacryl acetate	0.51	25.18
$\beta$ -Caryophyllene	1.30	27.54
10 <i>S</i> ,11 <i>S</i> -Himachala-3(12),4-diene	0.29	28.66
1,2-Dihydro-2,2,4-trimethyl-quinoline	0.11	28.94
$\alpha$ -Humulene	0.11	29.49
1-(4-Methoxyphenyl)-1-methoxyethane	0.21	29.85
3-Methoxy-2-(propen-2-yl)cyclohex-2-en-1-one	0.08	30.07
<i>o</i> -(Trimethylsilyl)pheno	0.07	30.23
, (1 <i>R</i> ,4 <i>aS</i> ,8 <i>aR</i> )-1,2,3,4,4 <i>a</i> ,5,6,8 <i>a</i> -Octahydro-7-methyl-4-methylene-1-(1-methylethyl)naphthalene	0.04	31.02
Germacrene D	0.07	31.13
<i>p</i> -Cymen-7-ol	0.03	31.51
Ledene	0.23	32.00
$\beta$ -Bisabolene	1.36	33.10
$\delta$ -Cadinene	0.11	33.73
(3 <i>S</i> ,3 <i>aS</i> ,7 <i>R</i> )-3 <i>a</i> ,4,5,6,7 <i>a</i> -Tetrahydro-3,6-dimethylbenzofuran-2(3 <i>H</i> )-one	0.85	36.54
Caryophyllene oxide	1.00	36.73
Viridiflorol	0.20	37.29
Guaia-3,9-diene	0.11	38.67
6-Methyl-6-[3-methyl-3-(1-methylethenyl)-1-cyclopropen-1-yl]-2-heptanone	0.05	39.96
$\alpha$ -Cadinol	0.60	40.15
[1 <i>S</i> -(1 <i><math>\alpha</math></i> ,7 <i><math>\alpha</math></i> ,8 <i><math>\alpha\alpha</math></i> )]-1,2,3,5,6,7,8,8 <i>a</i> -Octahydro-1,8 <i>a</i> -dimethyl-7-(1-methylethenyl)-naphthalene	0.13	40.32
(4 <i>aRtrans</i> )-Decahydro-4 <i>a</i> -methyl-1-methylene-7-(1-methylethylidene)-naphthalene	0.23	42.60
1,3,5,7-Tetraethyl-1-ethylbutoxysiloxycyclotetrasiloxane	0.09	42.88
6-Methyl-6-[3-methyl-3-(1-methylethenyl)-1-cyclopropen-1-yl]-2-heptanone	0.07	44.05
6-Propyl-bicyclo[3.2.0]hept-6-en-2-one	0.18	46.89
Octadecamethylcyclononasiloxane	0.13	51.15
1-(6,6-Dimethylbicyclo[3.1.0]hex-2-en-2-yl)-ethanone	0.09	51.610
Cuminol	0.29	53.47
2,4,6-Trimethyl-1,3-phenylenediamine	0.12	54.16
3-Methyl-2-(2-methyl-2-butenyl)-furan	0.47	54.84
Methyl palmitate	0.76	55.30
2-Methyl-5-(1-methylethenyl)-2-cyclohexen-1-one	0.07	55.78
Epimanoyl oxide	0.33	57.27
Durenol	0.11	58.98
2,3,5,6-Tetramethyl-phenol	0.06	59.52
4-(2,6-Dimethoxyphenyl)-6,6-dimethylbicyclo[3.3.1]hept-3-en-2-one	0.05	59.83
Manool	0.49	60.39
5,6-Dimethoxy-2-methyl-4 <i>H</i> -naphtho[1,2- <i>b</i> ]pyran-4-one	0.21	61.07
Pyrido[2,3- <i>b</i> ]indole	0.09	62.21
2-(1,1-Dimethylethyl)-4-(1-methyl-1-phenylethyl)-phenol	0.21	63.03

Methyl linolenate	0.21	63.20
Coraxeniolide C'	0.52	63.96
Phenanthrene, 7-ethenyl-1,2,3,4,4 <i>a</i> ,5,6,7,8,9,10,10 <i>a</i> - dodecahydro-1,1,4 <i>a</i> ,7-tetramethyl	0.62	64.19
Methyl stearate	0.17	64.53
Butyric acid 2( <i>Z</i> )-benzylidene-2,5-dihydro-5-oxo-1 <i>H</i> -pyrrol-3- yl ester	0.36	64.85
Ethyl linoleolate	0.81	65.20
Tetracosamethylcyclododecasiloxane	0.39	65.38
(±)-11,12,13,14-Tetrahydro-benzo[ <i>g</i> ]chrysen-11-ol	0.20	65.78

R.T., retention time.

**Table S2.** Histopathological scoring of liver of rats with induced metabolic syndrome (MetS) and treated with carvacrol (MetS+CRV), oregano extract (MetS+OREG) or metformin (MetS+METF), as well as rats without induced MetS (control).

Histopathology parameter	Control	MetS	MetS+CRV	MetS+OREG	MetS+METF
Hydropic degeneration	0.0 (0.0–1.0)	4.0 (2.0–4.0)	0.0 (0.0–1.0)	1.0 (0.0–2.0)	1.0 (1.0–2.0)
Coagulation necrosis	0.0 (0.0–1.0)	4.0 (3.0–4.0)	1.0 (1.0–2.0)	1.0 (0.0–1.0)	0.5 (0.0–1.0)
Sinusoidal dilatation	0.0 (0.0–1.0)	3.0 (3.0–4.0)	1.0 (1.0–2.0)	1.0 (1.0–1.0)	0.0 (0.0–1.0)
Lipid vacuolization	0.0 (0.0–1.0)	4.0 (3.0–4.0)	1.0 (0.0–1.0)	0.0 (0.0–1.0)	0.0 (0.0–1.0)
Hyperemia	0.0 (0.0–1.0)	3.0 (2.0–4.0)	2.0 (1.0–2.0)	1.0 (1.0–2.0)	0.0 (0.0–0.0)

Data are presented as median (min–max). Significant differences ( $p < 0.05$ ) were determined between groups: MetS vs. control for all parameters; MetS vs. MetS+CRV for hydropic degeneration; MetS vs. MetS+OREG for coagulation necrosis and lipid vacuolization; MetS vs. MetS+METF for coagulation necrosis, sinusoidal dilatation, lipid vacuolization, and hyperemia.

**Table S3.** Histopathological scoring of pancreas of rats with induced metabolic syndrome (MetS) and treated with carvacrol (MetS+CRV), oregano extract (MetS+OREG) or metformin (MetS+METF), as well as rats without induced MetS (control).

Histopathology parameter	Control	MetS	MetS+CRV	MetS+OREG	MetS+METF
Disrupted islet architecture	0.0 (0.0–1.0)	4.0 (3.5–4.0)	2.0 (1.0–3.0)	2.0 (1.0–3.0)	3.0 (2.0–3.0)
Islet atrophy	0.0 (0.0–1.0)	4.0 (3.0–4.0)	1.0 (0.0–1.0)	1.0 (0.0–2.0)	0.0 (0.0–1.0)
Hydropic degeneration	0.0 (0.0–1.0)	4.0 (3.0–4.0)	1.0 (0.0–1.0)	1.0 (0.0–2.0)	0.0 (0.0–0.0)
Reduced cellularity	0.0 (0.0–0.0)	4.0 (4.0–4.0)	1.0 (1.0–1.0)	2.0 (1.0–2.0)	0.0 (0.0–1.0)

Data are presented as median (min–max). Significant differences ( $p<0.05$ ) were determined between groups: MetS vs. control for all parameters; MetS vs. MetS+CRV for islet atrophy; MetS+METF for all parameters; MetS+OREG vs. MetS+METF for disrupted islet architecture and reduced cellularity.