**Supplementary results**

*LC-MS analysis of oregano extracts*

Peak eluting at Rt = 10.1 and 10.4 min (A2, A3 & M3) bothshowed a pseudo molecular ion at [M-H]−  at *m/z* 593. The MS/MS spectra yielded ions at *m/z* 473 (100%) [M-H-120]−, 353 [M-H-240]− (82%), 383 (42%), 503 [M-H-90]− (30%) and the MS3 spectra yielded ions at *m/z* 353 (100%) and 383 (16%). Fragmentation patterns with relatively abundant X ions in the negative ion mode, as observed in the LC-MS spectrum of A2, A3 and M3 (Supplementary Table S1), has previously been described as characteristic of *C*-glucoside flavonoids(1,2). Furthermore, the fragments [M–H–240]– and [M–H–180]– suggest a di-*C*-glucosyl substitution. Because common known glycosylation positions for flavones are on carbons 6 and/or 8 (1, 2), peak eluting at Rt = 10.1 min was identified as apigenin 6,8-di-*C*-glucoside (vicenin-2) and peak eluting at Rt = 10.4 min its isomer, which has recently been isolated from *O. vulgare* ssp. *hirtum*(3,4) and identified in Greek oregano(5).

Peak eluting at Rt = 10.7 min (A4, M4) presented a pseudo molecular ion at [M-H]−  at *m/z* 387 (100%), gave MS/MS ions at *m/z* 207 (100%), 163 (62%), 369 (16%) and MS3 ions at *m/z* 163 (100%). The fragment ion at *m/z* 207 probably derived from neutral loss of one molecule of caffeic acid [M-H-180]− from the molecular ion. The fragment ion [M-H-44]− corresponding to the loss of CO2 molecule is also present in the spectra of most of the phenolics including caffeic acid monomer and its metabolites due to the existence of –COOH group in all of these compounds(6). Thus this peak was tentatively identified as caffeic acid derivative. Peak eluting at Rt = 13.1 min (A5, M7) presented pseudo molecular ion [M-H]− at m/z 537. The MS/MS and MS3 spectra of this peak (with the corresponding fragment ions at m/z 339, 493, 295) allowed the tentative identification of it as salvianolic acid H or I. These compounds could be differentiated from other components possessing the same molecular weight, such as lithospermic acid A and salvianolic acid J. Salvianolic acid H/I fundamentally differed from lithospermic acid A and salvianolic acid J at m/z 339 (base peak) of salvianolic acid H/I and 493 (base peak) of the other two isomers in MS2(7,8).

Three peaks in the HPLC chromatogram of both extracts eluting at Rt = 14.4, 15.1 and 16.0 min gave a quasimolecular ion at *m*/*z* 717 (A7, M10, A8, M11, A10, M13) and a fragmentation pattern in which successive losses of danshensu (198 mu) or caffeic acid (180 mu) units are observed. The loss of danshensu (MW 198) was observed at m/z 519 [M-H-198]−, 321 [M-H-198-198]−, 339 [M-H-198-180]− and 475 [M-H-198-44]−. Similar mass spectra were reported for salvianolic acid B (also known as lithospermic acid B) and other related isomers (salvianolic acids E/L and isosalvianolic acid B) by different authors(7,9). Those compounds derive from the condensation of two rosmarinic acid molecules via an oxidative cyclisation leading to the formation of a 1,2-dihydronaphthalene ring structure. According to the indicated authors all these compounds should elute after the peak of rosmarinic acid, which was not found in the case of peaks eluting at Rt = 14.4 and 15.1 min. Because of this, the above compounds were just tentatively assigned as a salvianolic acid B-lithospermic acid B isomers in accordance with the results of Barros et al., 2013(10). Compounds A10 and M13 were tentatively identified as salvianolic acid B (Lithospermic acid B).

Peak eluting at Rt = 15.7 min (A9, M12) was identified as rosmarinic acid according to its mass spectrum, showing a pseudo molecular ion [M-H]− at m/z 359, and characteristic fragment ions at m/z 161 (100%), 179 (30%) and 197 (30%); its identity was confirmed by comparison with a commercial standard. The [M-H]− ion (*m/z* 491) of peak eluting at Rt = 16.9 min (A11, M14) fragmented into *m/z* 311 (100%) [M-H-180]− and 267 (100%) [M-H-180-CO2]−, thus was tentatively identified as salvianonic acid C according to literature data (12). Peak eluting at Rt = 17.8 min (M15) gave [M−H]− ion at *m*/*z* 551. Compared with [M−H]− ion at *m*/*z* 537, the ≥*m* was 14 Da. Therefore, the above compound was the methylated product of compound with [M−H]− ion at *m*/*z* 537. The MS/MS spectra of this peak yielded ion at *m*/*z* 353 as the base peak, which resulted from the loss of danshensu, while the ion at *m*/*z* 321 resulted from the loss of CH3OH and danshensu. Thus, this peak was tentatively identified as methyl salvianolate H or I in accordance with the results of Liu et al., 2007(11). Peaks eluting at 18.8 (A13, M16) and 21.1 min (A15, M18) were identified as eriodictyol and naringenin, respectively and their identity was confirmed by comparison with commercial standards. Aromadendrin was tentatively identified as it is an isomeric form o- eriodictyol eluting before it. Carvacrol, which was not ionized under the conditions used for analysis, was identified based on the retention time and UV spectrum of standard compound.

*Macrophage polarization is not affected by MOE*

Since the macrophages are the first cells to infiltrate the pancreas during diabetes induction, we have investigated the effect of MOE on macrophage polarization. Results indicate that the proportion of both pro-inflammatory M1 macrophages and M2 macrophages with anti-inflammatory phenotype in peritoneal cavity, spleen or pancreatic infiltrates is not affected by MOE treatment. Furthermore, MOE treatment did not influence macrophage-derived NO production. Finally, the secretion of both pro-inflammatory (IL-1, TNF) or anti-inflammatory cytokine IL-10 remained unchanged after MOE treatment.

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**Fig. S1.** AOE and MOE chromatograms. (A) Total ion chromatogram (TIC) and UV chromatogram at 280 nm of AOE. (B) Total ion chromatogram (TIC) and UV chromatogram at 280 nm of MOE.

**Fig. S2.** MOE does not affect macrophage function. Percentage of pro-inflammatory M1 (F4/80+CD40+) and anti-inflammatory M2 (F4/80+CD206+) macrophages within peritoneum (A), spleen (B) and pancreatic infiltrates (C) measured by flow cytometry. (D) *Ex vivo* nitrite accumulation as a measure of NO production of PC isolated from diabetic and MOE-treated mice. Cytokine secretion from PC (E) or SC (F) isolated from diabetic or MOE-treated mice. All analyses were performed 10 days post diabetes induction. Groups consisted of 10 mice.

**Supplementary Table S1:** Peak assignments of AOE and MOE.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Rt (min)** | **[M-H]-  (*m/z*) (%)** | **-MS2 [M-H]-  (*m/z*) (%)** | **-MS3 [base peak]- (*m/z*) (%)** | **Compounds** | **Detected in\*** |
| 3.6 | 377 (100), 349 (21), 215 (21) | 341 (100), 179 (27) | 178 (100) | Unknown | M1 |
| 4.4 | 772 (100), 489 (53) | 728 (100), 684 (86) | 684 (100) | Unknown | M2 |
| 4.6 | 629 (100), 447 (61) | 514 (100), 611 (13), 393 (16) | 393 (100), 231 (84) | Unknown | A1 |
| 10.1 | 593 (100) | 473 (100), 353 (82), 383 (42), 503 (30) | 353 (100), 383 (16) | Apigenin-6,8-di-C-glucose (vicenin-2) | A2 |
| 10.4 | 593 (100), 387 (16) | 473 (100), 353 (77), 383 (42), 503 (25) | 353 (100), 383 (17) | Apigenin-6,8-di-C-glucose (vicenin-2) is. | A3, M3 |
| 10.7 | 387 (100) | 207 (100), 163 (62), 369 (16) | 163 (100) | Caffeic acid derivative | A4, M4 |
| 11.4 | 373 (100), 489 (30), 771 (40) | 327 (100), 165 (22) | 161 (100), 249 (22) | Unknown | M5 |
| 12.2 | 373 (100), 489 (27) | 327 (100), 161 (15) | 161 (100), 165 (96) | Unknown | M6 |
| 13.1 | 537 (100) | 339 (100), 493 (34) | 229 (100), 295 (64) | Salvianolic acid H/I | A5, M7 |
| 13.5 | 535 (100) | - | - | Unknown | M8 |
| 13.7 | 369 (100), 539 (39) | 165 (100) | 163 (100) | Unknown | A6 |
| 14.0 | 377(100) | 331 (100), 179 (10) | 179 (100) 119 (36) | Unknown | M9 |
| 14.4 | 717 (100), 369 (15), | 519 (100), 475 (36) 339 (25), 365 (20) | 339 (100) | Salvianolic acid B (Lithospermic acid B) is. | A7, M10 |
| 15.1 | 717 (100), 549 (20), 303 (13) | 475 (100), 519 (81), 555 (23) | 365 (100), 353 (37), 243 (39) | Salvianolic acid B (Lithospermic acid B) is. | A8, M11 |
| 15.7 | 359 (100), 719 (99.9), | 161 (100), 179 (30), 197 (30) | - | Rosmarinic acid | A9, M12 |
| 16.0 | 717 (100), 359 (36), 493, 593 (30) | 519 (100), 321 (19) | 321 (100), 339 (27) | Salvianolic acid B (Lithospermic acid B) | A10, M13 |
| 16.9 | 491 (100) | 311 (100), 267 (6) | 267 (100) | Salvianolic acid C | A11, M14 |
| 17.1 | 287 (100), 491 (17) | 259 (100), 243 (10) | - | Aromadendrin | A12 |
| 17.8 | 551 (100), 535 (42) | 353 (100), 321 (91), 519 (68) | 321 (100) | Methyl salvianolate H/I | M15 |
| 18.8 | 287 (100), 575 (29) | 151 (100), 285 (27) | - | Eriodictyol | A13, M16 |
| 19.6 | 327 (100) | 229 (100), 211 (52), 291 (40) | - | Unknown | A14, M17 |
| 21.1 | 271 (100) | 151 (100), 177 (25), 269 (15) | - | Naringenin | A15, M18 |
| 28.5 | - | - | - | Carvacrol | \* |

Rt, retention time

\*A: Aqueous oregano extract - AOE, M: Methanolic oregano extract - MOE, number indicates the peak in Total ion chromatogram.