**Supplementary Table S1. A list of 82 active compounds in the Cinnamon**

| Compound | Molecular Formula | Molecular Weight (g/mol) |
|---|---|---|
| (3-ethoxy-hexa-1,5-dienyl)-benzene | $C_{14}H_{18}O$ | 202.29 |
| 1-heptadecene | $C_{17}H_{34}$ | 238.45 |
| 1,8-cineole | $C_{10}H_{18}O$ | 154.25 |
| 3-methylbenzothiophene | $C_9H_8S$ | 148.22 |
| 4-(2-propenyl)-phenol | $C_9H_{10}O$ | 134.18 |
| 5-(2-propenyl)-1,3-benzodioxole | $C_{10}H_{10}O_2$ | 162.19 |
| 6-Glucopyranosylprocyanidin B1 | $C_{36}H_{36}O_{17}$ | 740.7 |
| aromadendrene | $C_{15}H_{24}$ | 204.35 |
| benzaldehyde | $C_7H_6O$ | 106.12 |
| benzeneethanol | $C_8H_{10}O$ | 122.16 |
| benzenemethanol | $C_7H_8O$ | 108.14 |
| benzenepropanol | $C_9H_{12}O$ | 136.19 |
| benzyl benzoate | $C_{14}H_{12}O_2$ | 212.24 |
| bicyclogermacrene | $C_{15}H_{24}$ | 204.35 |
| borneol | $C_{10}H_{18}O$ | 154.25 |
| caffeic acid | $C_9H_8O_4$ | 180.16 |
| camphor | $C_{10}H_{16}O$ | 152.23 |
| caryophyllene | $C_{15}H_{24}$ | 204.35 |
| catechin | $C_{15}H_{14}O_6$ | 290.27 |
| chlorogenic acid | $C_{16}H_{18}O_9$ | 354.31 |
| cinnamaldhyde | $C_9H_8O$ | 132.16 |
| cinnamic acid | $C_9H_8O_2$ | 148.16 |
| cinnamtannin-B1 | $C_{45}H_{36}O_{18}$ | 864.76 |
| cinnamyl acetate | $C_{11}H_{12}O_2$ | 176.21 |
| cinnamyl alcohol | $C_9H_{10}O$ | 134.18 |
| cis-isoeugenol | $C_{10}H_{12}O_2$ | 164.2 |
| copaene | $C_{15}H_{24}$ | 204.35 |
| coumarin | $C_9H_6O_2$ | 146.14 |
| cubenol | $C_{15}H_{26}O$ | 222.37 |
| cymene | $C_{10}H_{14}$ | 134.22 |
| docosane | $C_{22}H_{46}$ | 310.6 |
| epicatechin | $C_{15}H_{14}O_6$ | 290.27 |
| eugenol | $C_{10}H_{12}O_2$ | 164.2 |
| eugenol acetate | $C_{12}H_{14}O_3$ | 206.24 |
| ferulic acid | $C_{10}H_{10}O_4$ | 194.18 |
| gallic acid | $C_7H_6O_5$ | 170.12 |
| germacrene-d | $C_{15}H_{24}$ | 204.35 |
| hydrocinnamaldehyde | $C_9H_{10}O$ | 134.18 |
| isospathulenol | $C_{15}H_{24}O$ | 220.35 |
| kaempferol 3-alpha-L-arabinofuranoside-7-rhamnoside | $C_{26}H_{28}O_{14}$ | 564.5 |
| limonene | $C_{10}H_{16}$ | 136.23 |
| linalool | $C_{10}H_{18}O$ | 154.25 |
| methoxy-eugenol | $C_{11}H_{14}O_3$ | 194.23 |
| neohexane | $C_6H_{14}$ | 86.18 |

| | | |
|---|---|---|
| neophytadiene | $C_{20}H_{38}$ | 278.52 |
| nonadecene | $C_{19}H_{38}$ | 266.51 |
| octacosane | $C_{28}H_{58}$ | 394.76 |
| ortho-methoxy cinnamaldehyde | $C_{10}H_{10}O_2$ | 162.18 |
| *p*-coumaric acid | $C_9H_8O_3$ | 164.16 |
| *p*-cymene | $C_{10}H_{14}$ | 134.22 |
| *p*-hydroxybenzoic acid | $C_7H_6O_3$ | 138.12 |
| *p*-vinylbenzohydrazide | $C_9H_{10}N_2O$ | 162.19 |
| pavetannin-C1 | $C_{60}H_{48}O_{24}$ | 1153 |
| proanthocyanidin-A2 | $C_{30}H_{24}O_{12}$ | 576.5 |
| procyanidin-B7 | $C_{30}H_{26}O_{12}$ | 578.5 |
| protocatechuic acid | $C_7H_6O_4$ | 154.12 |
| quercetin | $C_{15}H_{10}O_7$ | 302.24 |
| rosmarinic acid | $C_{18}H_{16}O_8$ | 360.31 |
| safrole | $C_{10}H_{10}O_2$ | 162.19 |
| salicylic acid | $C_7H_6O_3$ | 138.12 |
| sinapic acid | $C_{11}H_{12}O_5$ | 224.21 |
| spathulenol | $C_{15}H_{24}O$ | 220.35 |
| syringic acid | $C_9H_{10}O_5$ | 198.17 |
| tenuifolin | $C_{36}H_{56}O_{12}$ | 680.8 |
| terpinen-4-ol | $C_{10}H_{18}O$ | 154.25 |
| tetracosane | $C_{24}H_{50}$ | 338.65 |
| trans-cinnamaldehyde | $C_9H_8O$ | 132.16 |
| vanillic acid | $C_8H_8O_4$ | 168.15 |
| vanillin | $C_8H_8O_3$ | 152.15 |
| viridiflorol | $C_{15}H_{26}O$ | 222.37 |
| $\alpha$-amorphene | $C_{15}H_{24}$ | 204.35 |
| $\alpha$-caryophyllene | $C_{15}H_{24}$ | 204.35 |
| $\alpha$-copaene | $C_{15}H_{24}$ | 204.35 |
| $\alpha$-muurolene | $C_{15}H_{24}$ | 204.35 |
| $\alpha$-phellandrene | $C_{10}H_{16}$ | 136.23 |
| $\alpha$-Pinene | $C_{10}H_{16}$ | 136.23 |
| $\alpha$-terpineol | $C_{10}H_{18}O$ | 154.25 |
| $\alpha$-thujene | $C_{10}H_{16}$ | 136.23 |
| β-bisabolene | $C_{15}H_{24}$ | 204.35 |
| β-caryophyllene | $C_{15}H_{24}$ | 204.35 |
| β-terpinene | $C_{10}H_{16}$ | 136.23 |
| δ-elemene | $C_{15}H_{24}$ | 204.35 |

**Supplementary Table S2. Number of violations of cinnamon compounds for "drug likeness" via different pharmacokinetic filters**

| Compound | Filters[a] for drug likeness | | | | | |
|---|---|---|---|---|---|---|
| | Lipinski | Ghose | Veber | Egan | Muegge | Bioavailability Score |
| Cinnamic acid | 0 | 2 | 0 | 0 | 1 | 0.85 |
| Ferulic acid | 0 | 0 | 0 | 0 | 1 | 0.85 |
| *p*-Coumaric acid | 0 | 0 | 0 | 0 | 1 | 0.85 |
| *p*-Hydroxybenzoic acid | 0 | 3 | 0 | 0 | 1 | 0.85 |
| Salicylic acid | 0 | 3 | 0 | 0 | 1 | 0.85 |

[a] Lipinski's filter: MW ≤ 500 Da, number of H-bond donors ≤ 5, number of H-bond acceptors ≤ 10, logarithm of octanol-water partition coefficient (logP) ≤ 5;
Ghose's filter: 160 ≤ MW ≤ 480, −0.4 ≤ WLOGP (lipophilicity) ≤ 5.6, 40 ≤ the molar refractivity ≤ 130, 20 ≤ number of atoms ≤ 70;
Veber's filter: the number of rotatable bonds ≤ 10, the total polar surface area ≤ 140;
Egan's filter: WLOGP (lipophilicity) ≤ 5.88, the total polar surface area ≤ 131;
Muegge's filter, 200 ≤ MW ≤ 600, −2 ≤ XLOGP3 (lipophilicity) ≤ 5, the total polar surface area ≤ 150, the number of rings ≤ 7, the number of carbons > 4, the number of heteroatoms > 1, the number of rotatable bonds ≤15, number of H-bond acceptors ≤ 10, number of H-bond donors ≤ 5.

**Supplementary Table S3. Physicochemical properties of cinnamon compounds**

| Compound | Physicochemical Properties | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Formula | MW | #Heavy atoms | #Aromatic heavy atoms | Fraction Csp3 | #Rotatable bonds | #H-bond acceptors | #H-bond donors | MR | TPSA |
| Cinnamic acid | $C_9H_8O_2$ | 148.16 | 11 | 6 | 0 | 2 | 2 | 1 | 43.11 | 37.3 |
| ferulic acid | $C_{10}H_{10}O_4$ | 194.18 | 14 | 6 | 0.1 | 3 | 4 | 2 | 51.63 | 66.76 |
| *p*-coumaric acid | $C_9H_8O_3$ | 164.16 | 12 | 6 | 0 | 2 | 3 | 2 | 45.13 | 57.53 |
| *p*-hydroxybenzoic acid | $C_7H_6O_3$ | 138.12 | 10 | 6 | 0 | 1 | 3 | 2 | 35.42 | 57.53 |
| salicylic acid | $C_7H_6O_3$ | 138.12 | 10 | 6 | 0 | 1 | 3 | 2 | 35.42 | 57.53 |

MW, molecular weight; Fraction Csp3, ratio of sp3 hybridized carbons over the total carbon count of the molecule; MR, molecular refractivity; TPSA, topological polar surface area.

**Supplementary Table S4. Lipophilicity of cinnamon compounds**

| Compound | Lipophilicity | | | | | |
|---|---|---|---|---|---|---|
| | iLOGP | XLOGP3 | WLOGP | MLOGP | Silicos-IT Log P | Consensus Log P |
| Cinnamic acid | 1.55 | 2.13 | 1.68 | 1.9 | 1.7 | 1.79 |
| Ferulic acid | 1.62 | 1.51 | 1.39 | 1 | 1.26 | 1.36 |
| *p*-Coumaric acid | 0.95 | 1.46 | 1.38 | 1.28 | 1.22 | 1.26 |
| *p*-Hydroxybenzoic acid | 0.85 | 1.58 | 1.09 | 0.99 | 0.74 | 1.05 |
| Salicylic acid | 1.13 | 2.26 | 1.09 | 0.99 | 0.74 | 1.24 |

iLOGP, implicit log *P* is an in-house physics-based methods relying on Gibbs free energy of solvation calculated by GB/SA in water and *n*-octanol; XLOGP3, the logP value of a query compound by using the known logP value of a reference compound as a starting point; WLOGP, log P method developed by Wildman and Crippen; MLOGP, Moriguchi octanol-water partition coefficient; SILICOS-IT, an hybrid method relying on 27 fragments and 7 topological descriptors; Consensus Log P, arithmetic mean of the values predicted by the five proposed methods.

**Supplementary Table S5. Water solubility of cinnamon compounds**

| Compound | Water Solubility | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | ESOL Solubility | | | Ali Solubility | | | Silicos-IT Solubility | | |
| | Log S | (mg/ml) | (mol/l) | Log S | (mg/ml) | (mol/l) | LogSw | (mg/ml) | (mol/l) |
| Cinnamic acid | -2.37 | -2.37 | 0.629 | -2.54 | 0.423 | 0.002850 | -1.84 | 2.14 | 0.0145 |
| Ferulic acid | -2.16 | -2.11 | 1.490 | -2.52 | 0.586 | 0.003020 | -1.42 | 7.43 | 0.0383 |
| *p*-Coumaric acid | -2.17 | -2.02 | 1.580 | -2.27 | 0.873 | 0.005320 | -1.28 | 8.67 | 0.0528 |
| *p*-Hydroxybenzoic acid | -2.43 | -2.07 | 1.180 | -2.4 | 0.551 | 0.003990 | -1.17 | 9.40 | 0.0681 |
| Salicylic acid | -2.46 | -2.5 | 0.439 | -3.1 | 0.109 | 0.000786 | -1.17 | 9.40 | 0.0681 |

ESOL, Estimating Aqueous Solubility Directly from Molecular Structure; Ali, *in silico* prediction model of aqueous solubility revised by Ali J.; Silicos-IT, predictor for solubility developed by SILICOS-IT; LogSw, decimal logarithm of the molar solubility in water.

**Supplementary Table S6. Pharmacokinetics of cinnamon compounds**

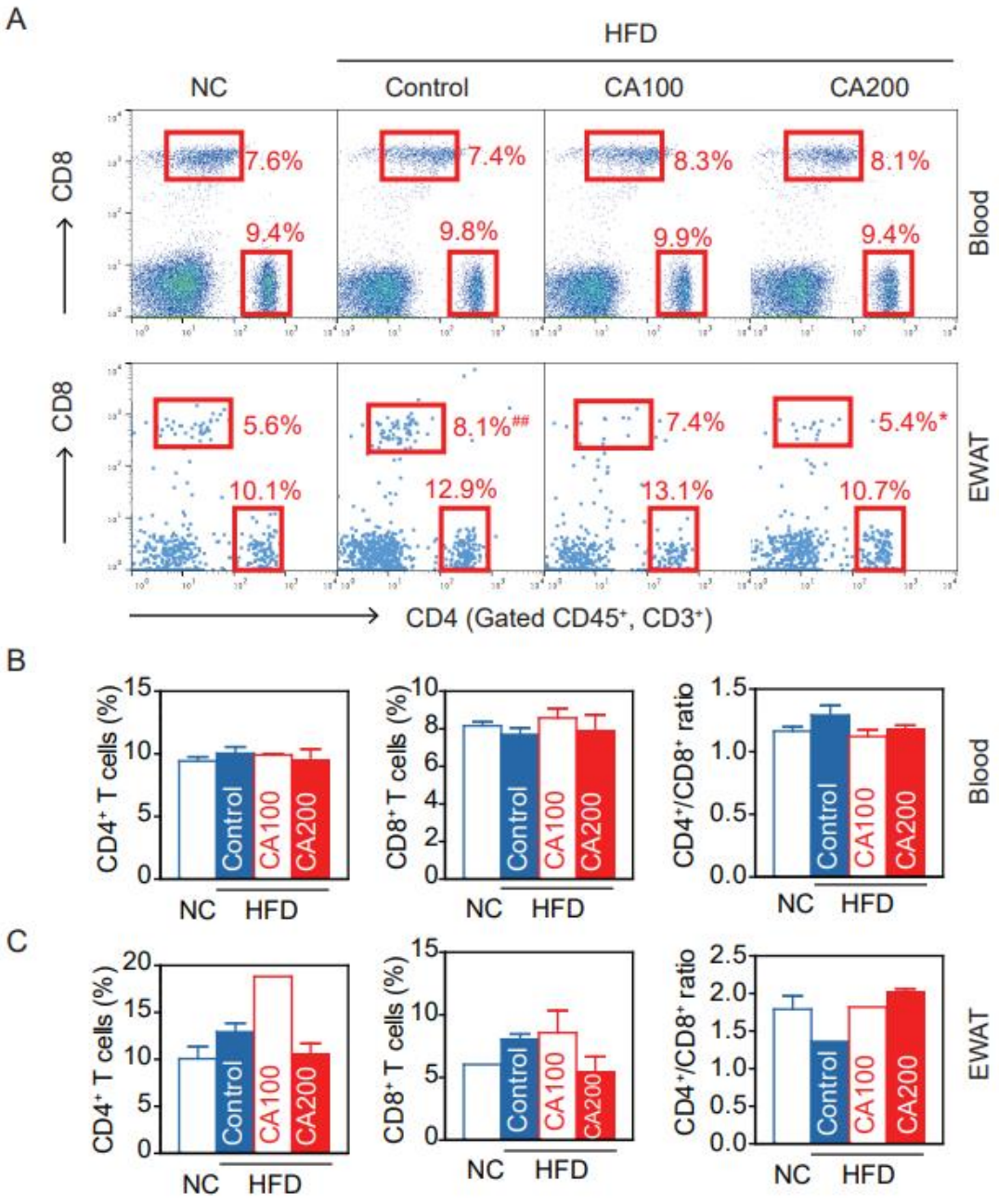
| Compound | Pharmacokinetics | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | GI | BBB | Pgp | CYP inhibition | | | | | log Kp (cm/s) |
| | | | | 1A2 | 2C19 i | 2C9 | 2D6 | 3A4 | |
| Cinnamic acid | -4.388 | 0.961 | 0.059 | 0.082 | 0.036 | 0.021 | 0.117 | 0.001 | -5.69 |
| Ferulic acid | -4.943 | 0.565 | 0.026 | 0.234 | 0.061 | 0.059 | 0.184 | 0.012 | -6.41 |
| *p*-Coumaric acid | -4.884 | 0.451 | 0.036 | 0.054 | 0.035 | 0.087 | 0.218 | 0.011 | -6.26 |
| *p*-Hydroxybenzoic acid | -4.844 | 0.18 | 0.019 | 0.023 | 0.006 | 0.007 | 0.111 | 0.001 | -6.02 |
| salicylic acid | -4.851 | 0.379 | 0.027 | 0.003 | 0.013 | 0.007 | 0.103 | 0.001 | -5.54 |

GI, gastrointestinal absorption; BBB, blood-brain barrier permeant; Pgp, permeability glycoprotein substrate; CYP, cytochrome P450; log Kp, decimal logarithm of the skin permeability coefficient

**Supplementary Table S7. Molecular docking binding affinity of cinnamon components to TNF-α, MIF from M1 macrophage, and MMP-12 from M2 macrophage.**

| Compound | Binding Affinity (kcal/mol) | | |
|---|---|---|---|
| | TNF-α | MIF | MMP-12 |
| Cinnamic acid | -5.9 | -7.2 | -6.6 |
| Ferulic acid | -6.6 | -6.6 | -6.2 |
| *p*-Coumaric acid | -6.2 | -7.1 | -7.0 |
| *p*-Hydroxybenzoic acid | -5.3 | -6.4 | -6.2 |
| Salicylic acid | -5.4 | -6.6 | -6.4 |

Tumor necrosis factor-α (TNF-α) (PDBID: 2AZ5) as an inflammatory cytokine, MIF (PDBID: 1GD0) as a pro-inflammatory macrophage, MMP-12 (PDBID: 1JIZ) as an anti-inflammatory macrophage.




**Supplementary Figure S1.** T cell subtype in blood and epididymal white adipose tissue (EWAT) of HFD-induced obesity. (A) Flow cytometry analyses showing the fractions of T cells in blood or EWAT. (B) percentage of blood $CD4^+$ T cells, percentage of blood $CD8^+$ T cells, and ratio of $CD4^+$ and $CD8^+$ T cell in blood, (C) percentage of EWAT $CD4^+$ T cells, percentage of blood $CD8^+$ T cells, and ratio of $CD4^+$ and $CD8^+$ T cell in EWAT. Data are expressed as the mean ± SEM. NC: normal chow, Control: high-fat diet control, CA100: high-fat diet plus cinnamic acid 100 mg/kg, CA200: high-fat diet plus cinnamic acid 200 mg/kg.