

**Metabolomics Profiling Reveals the Mechanism of Caffeic Acid in Extending Lifespan in
*Drosophila melanogaster***

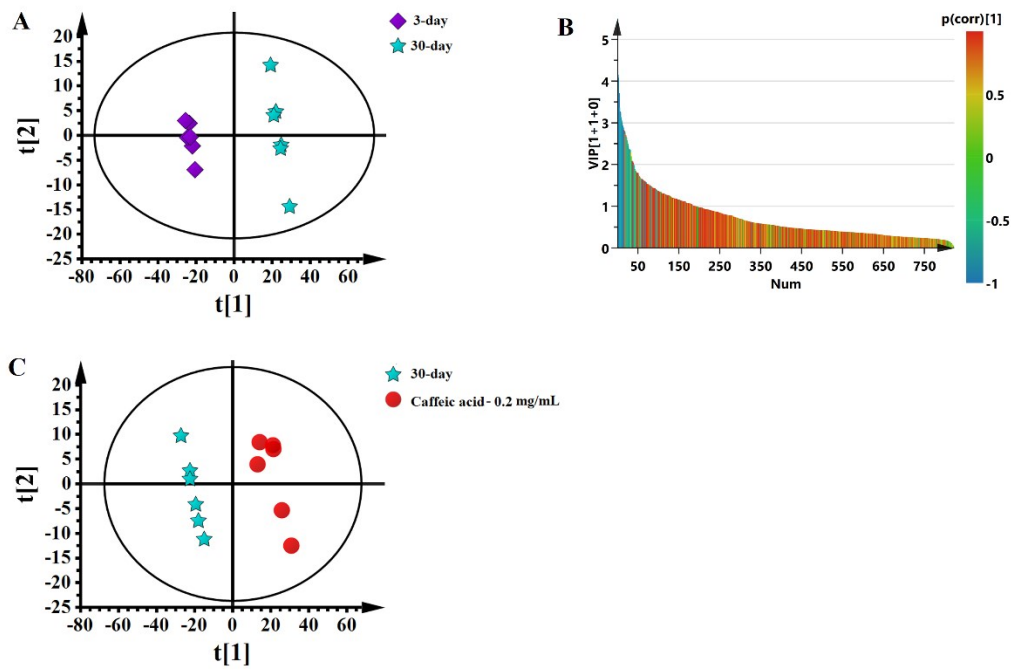
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Supplementary Figure 1. (A) PLS-DA scores plot and (B) VIP-plot of 3-day group and 30-day group, (C) PLS-DA scores plot of 30-day group and 0.2 mg/mL caffeic acid supplementation group.

Supplementary Table 1. Peak attribution in ¹H-NMR spectra for main metabolites in

NO	Metabolites	Moieties	Chemical shifts
1	lipid	terminal-(CH ₂) _n	0.89 (m), 1.25(m)
2	isoleucine	δCH ₃ , δ'CH ₃ , CH ₃ , γCH ₃	0.96 (t), 1.01(d)
3	valine	γCH ₃ , γ'CH ₃	0.99(d), 1.05(d)
4	lactate	αCH, βCH ₃	1.34(d), 4.12 (q)
5	alanine	β CH ₃	1.48 (d)
6	lysine	αCH, β CH ₂ , δCH ₂ , γCH ₂ , ε-CH ₂	1.47(m), 1.72(m), 1.90(m), 3.03(t), 3.79(t)
7	acetate	CH ₃	1.92(s)
8	glutamine	αCH, βCH ₂ , γCH ₂	2.13(m), 2.45(m), 3.80(m)
9	glutamate	γCH ₂	2.35(m)
10	pyruvate	CH ₃	2.36(s)
11	succinate	CH ₂	2.41(s)
12	beta-alanine	αCH ₂ , βCH ₂ ,	2.56(t), 3.19(t)
13	dimethylamine	CH ₃	2.74(s)
14	cysteine	CH ₂	3.03(m)
15	choline	N(CH ₃) ₃	3.21(s)
16	tmao	CH ₃	3.23(s)
17	cystine	CH ₂	3.41(s)
18	tryptophan	CH, CH ₂	3.47(dd), 7.55(d)
19	glycine	CH ₂	3.50(s)
20	glycerol	βCH ₂ , β'CH ₂	3.56(dd), 3.64(dd)
21	beta-d-glucose	βC ₁ H	4.66(d)
22	alpha-d-glucose	CH	5.23(d)
23	uracil	C ₅ H, C ₆ H	5.81 (d), 7.55(d)
24	fumarate	CH=CH	6.53(s)
25	tyrosine	3 or 5-CH, 2 or 6-CH	6.91(d), 7.20(d)
26	histidine	5CH, 3CH	7.09(s), 7.38(s)
27	Phenylalanine	2CH, 4CH, 3CH	7.33 (m), 7.38 (m), 7.43 (m)
28	AMP	C ₄ H-ribose, C ₃ H-ribose, C ₁ H-ribose, CH-ring, CH-ring	4.01 (m), 4.37 (m), 4.51 (m), 6.11(m), 8.24(s)

tissues of flies.

TMAO, trimethylamine-N-oxide; AMP, adenosine monophosphate; s, singlet, d, doublet, dd, doublet of doublet, t, triplet, m, multiplet.

Supplementary Table 2. Differential metabolites in the 30-day group and 0.2 mg/mL caffeic acid supplementation group.

Metabolites	30-d group vs 3-d group	Fold change	Caffeic acid group vs 30-d group	Fold change
lipid	down	0.41	up	0.47
isoleucine	down	0.32	up	0.48
valine	down	0.32	up	0.51
alanine	down	0.32	up	0.50
lysine	down	0.30	up	0.38
acetate	down	0.36	up	0.45
glutamate	down	0.44	up	0.51
pyruvate	down	0.51	up	0.80
succinate	down	0.50	up	0.62
beta-alanine	down	0.32	up	0.34
cysteine	down	0.30	up	0.38
tryptophan	down	0.36	up	0.38
glycine	up	0.75	down	0.31
glycerol	down	0.41	up	0.40
beta-d-glucose	up	0.63	down	0.21
alpha-d-glucose	up	0.54	down	0.24
histidine	down	0.71	up	2.22

