Supplement information

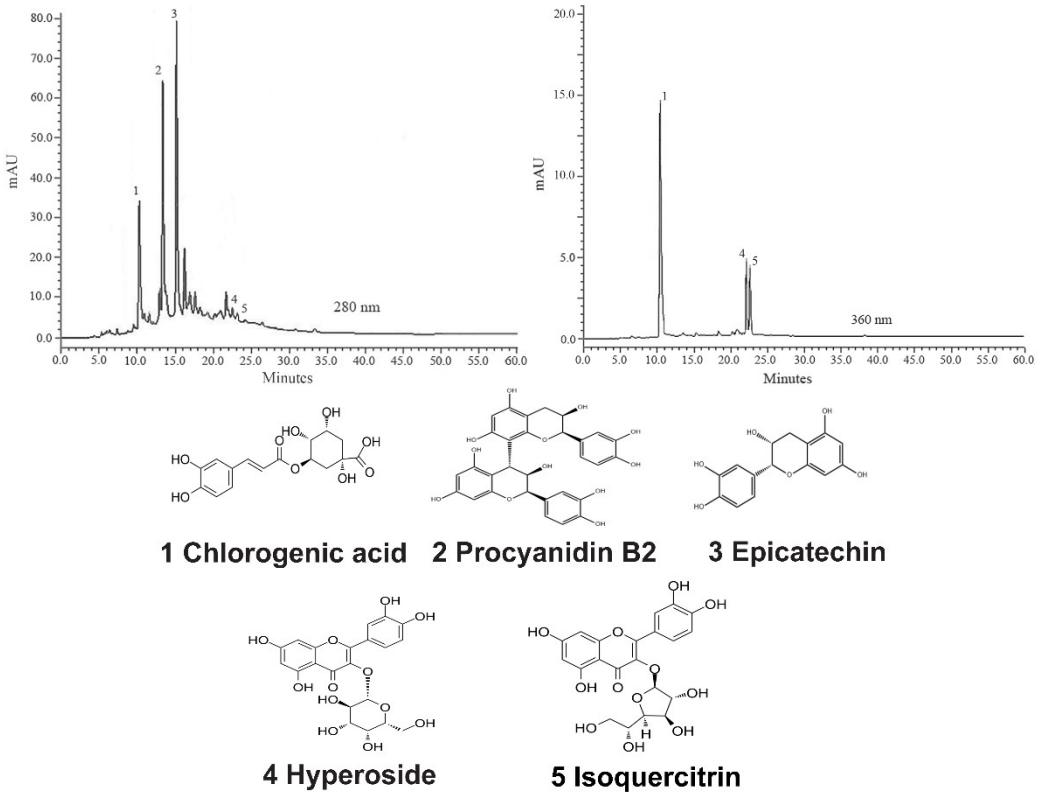

Fig. S1 High performance liquid chromatography profile of phenolic compounds in HFE.

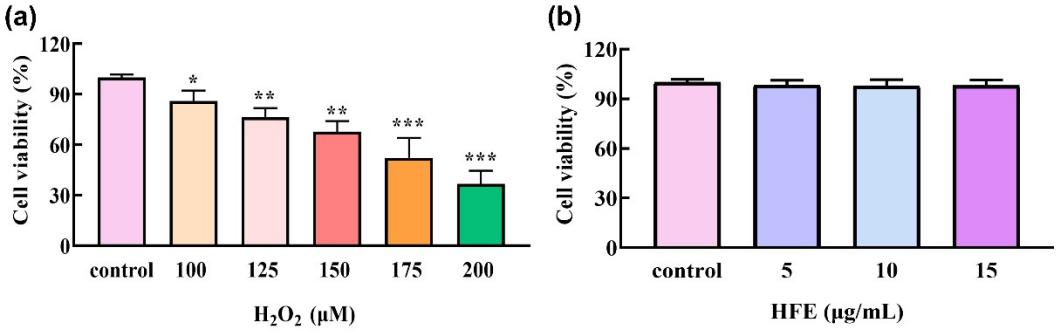

Fig. S2 Effects of H_2O_2 and HFE on PC12 Cell viability. (a) Effect of different concentrations of H_2O_2 on cell viability. (b) HFE had uninjurious effect on nerve cells.

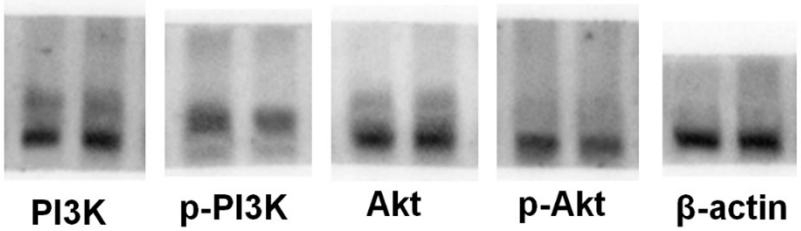

Fig. S3 The western blot images of PI3K, p-PI3K, Akt, p-Akt and β-actin in *C. elegans* with or without 100 μg/mL HFE treatment.

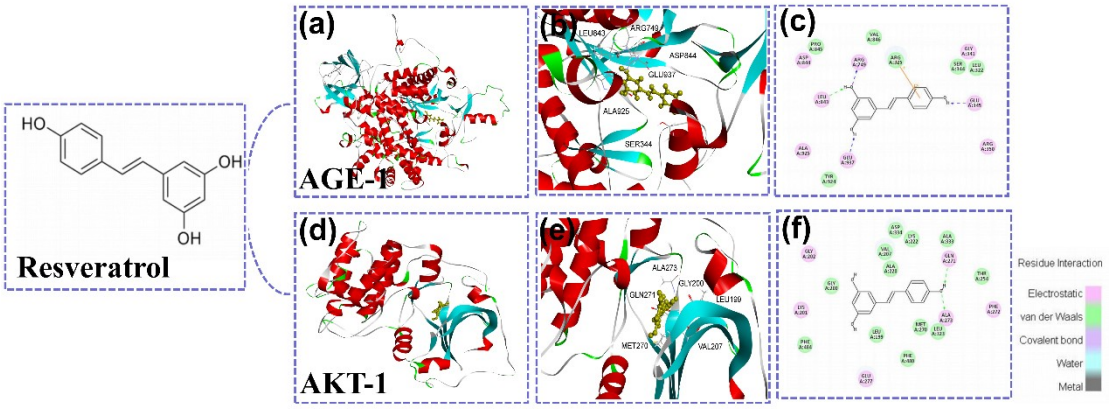

Fig. S4 The molecular docking results of resveratrol and AGE-1, AKT-1, respectively. (a), (b) and (d), (e) showed that resveratrol interacted with AGE-1 and AKT-1, respectively. The maximum interaction between resveratrol and AGE-1, AKT-1 was represented by two-dimensional docking picture (c), (f), respectively.

Table S1 Primers used for Real-time PCR.

Gene	Accession No.	Primer sequences
DAF-2	NM_065249.7	5’-TCGGACGCTATTCATATTACG-3’ 3’-GGCTTATCGGCTACAATCG-5’
AGE-1	NM_064061.6	5’-ATTGTGCTCTCCGAACTC-3’ 3’-GCTGCTCATTCAACTTCTC-5’
AKT-1	NM_001028475.5	5’-AGTCAGCTAAAGCATGGGAGA-3’ 3’-TCTTTGATTTGACGTTCACTGG-5’
DAF-16	NM_001381205.1	5’-TCAAGCCAATGCCACTACC-3’ 3’-TGGAAGAGCCGATGAAGAAG-5’
SOD-3	NM_078363.9	5’-GGCTAAGGATGGTGGAGAAC-3’ 3’-ACAGGTGGCGATCTTCAAG-5’
CTL-1	NM_064578.6	5’-GCGTATCTTCTCCTACAC-3’ 3’-ACTCCTTCACATCATCAC-5’
CTL-2	NM_001027302.8	5’-TACAGTCGGTGGTGAGAG-3’ 3’-GGTGAGTCTGTGGATTACG-5’
MTL-1	NM_072295.6	5’-TGGAGACAAGTGTTGTGAGAAG-3’ 3’-TTAATGAGCCGCAGCAGTTC-5’
CAT-1	NM_001029766.2	5’-CTCCTCGGATTCTCTATCGGTATG-3’ 3’-AAGGCGGCATCGGCAATG-5’
GST-4	NM_069447.8	5’-CTCTTGCTGAGCCAATCCGTATC-3’ 3’-TGACTGACCGAATTGTTCTCCATC-5’
SKN-1	NM_171345.6	5’-CACTGTCTCCTCTCATCATTGG-3’ 3’-GAGTGTCTCTGTGAGTGATATGG-5’
HSF-1	NM_060630.7	5’-CATCATCTTCGGCTCCATCTG-3’ 3’-AATAGTCTTGTTGCGGCTGAG-5’
HSP-16.1	NM_072953.5	5’-CACTTTACCACTATTTCCGTCCAG-3’ 3’-GGCTTGAACTGCGAGACATTG-5’
HSP-16.2	NM_001392482.1	5’-CTCAACGTTCCGTTTTGGT-3’ 3’-CGTTGAGATTGATGGCAAAC-5’
ACT-1	NM_073418.9	5’-GGAATTGCTGATCGTATGC-3’ 3’-CTGTTGGAAGGTGGAGAG-5’

Table S2 Effect of HEF on lifespan of N2 worms.

Genetype	Dose (μg/mL)	Mean lifespan (days)	Maximum lifespan (days)	% Change in mean lifespan	*P*-value
N2	0	14.34±0.05	19.97±0.36	-	-
	25	15.87±0.29	20.02±0.22	11.44	n.s.
	50	16.89±0.29*	21.84±0.26*	19.06	< 0.05
	100	18.14±0.17**	25.17±0.19**	28.43	< 0.01
	200	12.75±0.14	19.39±0.54	-4.49	n.s.
	500	11.38±0.14*	17.69±0.70*	-14.71	< 0.05
N2	0	14.64±0.52	19.83±0.33	-	-
	25	15.95±0.94	20.14±0.19	8.95	n.s.
	50	17.16±0.98*	21.97±0.23*	17.21	< 0.05
	100	18.12±0.76**	25.05±0.18**	23.77	< 0.01

n.s.: no significance.

Table S3 Effect of HEF on longevity of N2 worms exposed to various stresses.

Stress condition	Dose (μg/mL)	Mean lifespan	Maximum lifespan	Unit	% Change in Mean lifespan	*P*-value
H_2O_2	0	1.42±0.08	3.05±0.07	Hour	-	-
	25	1.73±0.05*	3.45±0.18*		21.83	< 0.05
	50	1.81±0.09*	3.61±0.25*		27.46	< 0.05
	100	2.08±0.02**	3.95±0.36**		46.48	< 0.01
Juglone	0	4.04±0.03	8.23±0.08	Hour	-	-
	25	4.76±0.12	9.15±0.16		17.82	n.s.
	50	5.44±0.06*	9.31±0.34*		34.65	< 0.05
	100	6.21±0.13**	10.6±0.53**		53.71	< 0.01
Paraquat	0	3.83±0.02	6.03±0.08	Day	-	-
	25	4.02±0.07	6.16±0.25		4.96	n.s.
	50	4.39±0.11*	7.02±0.36*		14.62	< 0.05
	100	5.14±0.13*	7.28±0.19*		34.20	< 0.05
Heat shock	0	10.03±0.14	12.06±0.06	Hour	-	-
	25	11.08±0.11	13.11±0.19		10.47	n.s.
	50	11.89±0.45*	13.89±0.62*		18.54	< 0.05
	100	12.21±0.76*	15.12±0.37*		21.73	< 0.05
Ultraviolet	0	2.96±0.09	4.51±0.01	Hour	-	-
	25	3.19±0.23	4.73±0.26		7.60	n.s.
	50	3.60±0.31*	5.37±0.15*		21.62	< 0.05
	100	3.97±0.26*	5.58±0.64*		33.95	< 0.05

n.s.: no significance.

Table S4 Effect of HEF on lifespan of N2 worms and mutants.

Genetype	Dose (μg/mL)	Mean lifespan (days)	Maximum lifespan (days)	% Change in Mean lifespan	*P*-value
daf-2(e1370)	0	31.45±0.32	46.30±0.34	-	-
	100	31.15±0.41	45.70±0.13	-0.95	n.s.
age-1(hx546)	0	22.39±0.11	39.37±0.32	-	-
	100	22.54±0.26	39.74±0.65	0.01	n.s.
akt-1(ok525)	0	25.40±0.03	35.93±0.31	-	-
	100	25.30±0.20	36.01±0.55	-0.02	n.s.
daf-16(mu86)	0	15.72±0.51	22.78±0.38	-	-
	100	15.74±0.21	22.68±0.56	0.12	n.s.
skn-1(zu67)	0	17.53±0.19	24.41±0.34	-	-
	100	17.31±0.13	24.48±0.13	1.25	n.s.
hsf-1(sy441)	0	17.47±0.27	24.93±0.35	-	-
	100	17.62±0.34	25.50±0.98	0.86	n.s.
eat-2(ad1116)	0	27.21±0.86	42.44±0.22	-	-
	100	31.00±0.61*	45.78±0.67*	13.93	< 0.05
N2	0	14.64±0.52	19.83±0.33	-	-
	100	18.12±0.76**	25.05±0.18**	23.77	< 0.01

n.s.: no significance.

Table S5 Molecular docking between resveratrol, procyanidin B2, epicatechin, chlorogenic acid, and hyperoside with receptor proteins.

Ligand name	Receptor name	Interactive residues	Hydrogen bonds involved residues	Binding energy (kJ/mol)	Electrostatic energy (kJ/mol)
Resveratrol	AGE-1	VAL 846, ARG 325, SER 344, GLY 341, LEU 322, GLU 345, ARG 350, GLU 937, TYR 924, ALA 925, LEU 843, ASP 844, PRO 845, ARG 749	LEU 843, ARG 749, ASP 844, GLU 937, ALA 925, SER 344	-65.1628	-6.10753
	AKT-1	ALA 220, VAL 207, ASP 334, LYS 222, ALA 333, GLN 271, THR 254, PHE 272, ALA 372, LEU 323, MET 270, PHE 480, LEU 199, GLU 277, PHE 484, LYS 201, GLY 200, GLY 202	ALA 273, GLY 200, GLN 271, LEU 199, VAL 207, MET 270	-78.297	-9.33945
Procyanidin B2	AGE-1	LEU 717, GLU 906, ASP 909,	VAL 846, ARG 325, ASP 340,	-114.854	-1.49271

		LYS 913, LEU 921, PRO 923, ASN 922, SER 344, LYS 1044, SER 348, GLU 347, ARG 749, ASP 340, VAL 846, ASP 844, ARG 753, LEU 843, ARG753, HIS 716	GLU 347, ASN 922, PRO 923		
	AKT-1	THR 354, VAL 207, GLY 200, LYS 318, GLU 320, ASP 334, LEU 323, LYS 222, ASN 321, PHE 204, GLU 277, THR 203, GLY 202, PHE 279, LYS 201	GLU 320, GLY 202, THR 203, PHE 204, ASP 334, ASN 321	-82.9911	-9.81912
Epicatechin	AGE-1	GLU 906, ALA 925, ARG 749, ASP 844, VAL 846, PRO 845, THR 327, ARG 325, LEU 322, GLY 341, ARG 350,	VAL 846, THR 327, LEU 322, ASP 844, GLY 341, GLU 345	-96.6125	-4.95113

		GLU 345, SER 344, LEU 843			
	AKT-1	ASP 334, LYS 318, ASN 321, GLU 320, PHE 484, LYS 201, GLU 277, GLY 200, LEU 323, ALA 273, ALA 220, PHE 272, GLN 271, LYS 222, MET 270, THR 254, ALA 333, PHE 480, LEU 199, VAL 207	GLN 271, ALA 273, PHE 272, LYS 222, GLN 271, ASN 321	-62.5309	-8.62561
Chlorogenic acid	AGE-1	ASP 844, ARG 749, ALA 925, ARG 753, LEU 843, TYR 924, PRO 923, GLU 906, ARG 350, LEU 322, GLU 345, GLY 341, ARG 325, SER 344	LEU 843, ALA 925, GLU 345, TYR 924, PRO 923, ARG 350	-51.967	-74.663
	AKT-1	VAL 207, LEU 199, ALA 333, LYS 206,	ALA 273, THR 254, GLN 271, GLY 202,	-61.1878	-49.9943

		GLY 202, GLY 200, LEU 224, LYS 222, PHE 204, GLY 205, THR 203, ASP 334, LYS 201, PHE 480, GLU 277, THR 254, PHE 272, ALA 273, ALA 220, GLN 271, MET 270, LEU 323	LYS 222, ASP 334		
Hyperoside	AGE-1	ARG 749, HIS 716, LYS 913, SER 344, SER 348, ARG 1012, LYS 1044, GLU 345, ARG 350, LEU 322, ARG 325, ASP 844	ASP 844, LEU 322, GLU 345, LYS 1044, SER 344, ARG 350	-200.675	-48.1313
	AKT-1	ASP 334, GLU 320, LEU 323, GLY 200, LEU 199, PHE 480, GLU 277, PHE 484, VAL 207, LYS 318, LYS 201, GLY 202,	GLU 277, PHE 480, GLY 202, VAL 207, ASP 334, LYS 318,	-97.2875	-7.71958

GLY 205, PHE 204, LEU 224, LYS 222, GLY 336