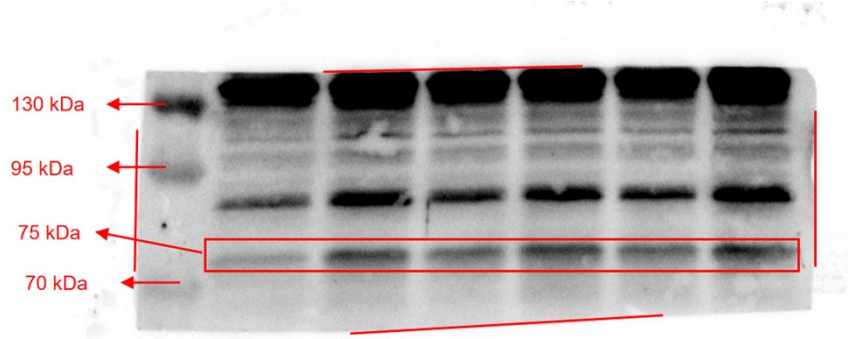
Supplementary Material

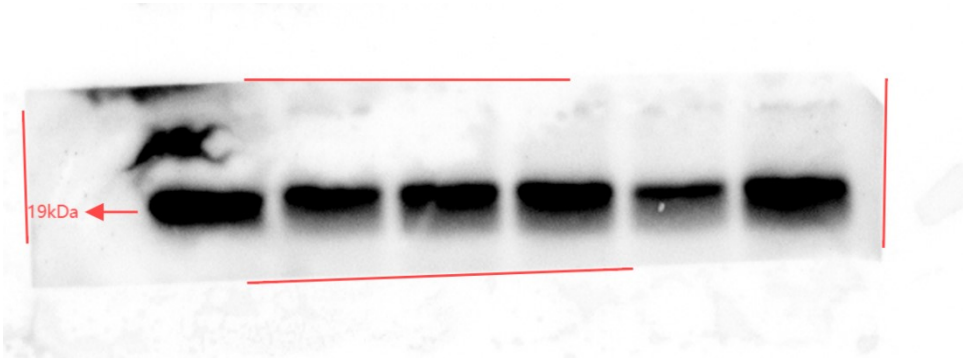
Alliin from garlic as a neuroprotective agent attenuates ferroptosis in vitro and in vivo via inhibiting ALOX15

Western blot data:

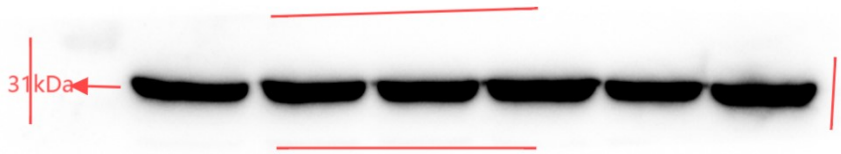
1. The original Western blot data of ALOX15(75kDa) in Fig. 5F. The loading order of the Western Blot lanes from left to right is: Control, Erastin group, Alliin-treated (100 μM, 200 μM, 400 μM) group and positive control drug (Fer-1) group.



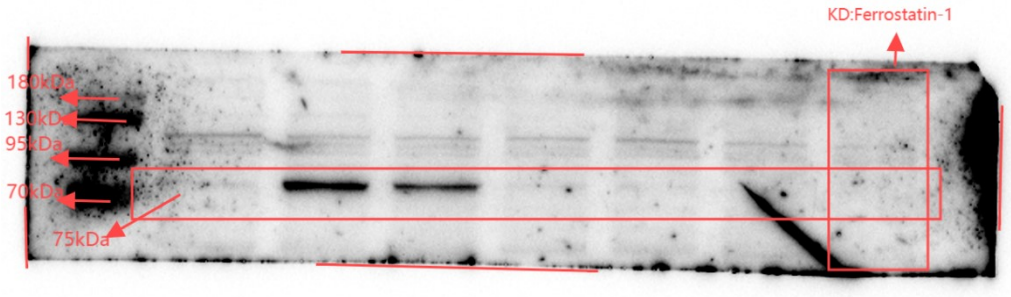
2. The original Western blot data of GPX4(19kDa) in Fig. 5F. The loading order of the Western Blot lanes from left to right is: Control, Erastin group, Alliin-treated (100 μM, 200 μM, 400 μM) group and positive control drug (Fer-1) group.



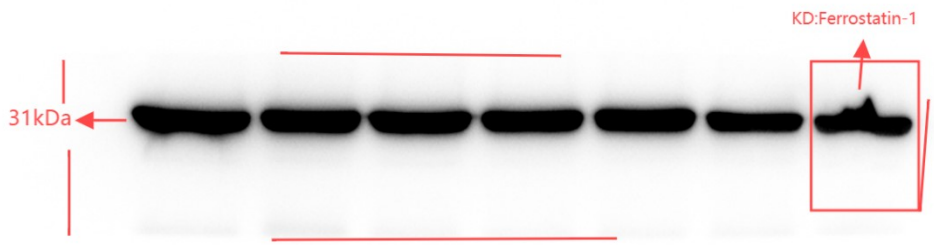
3. The original Western blot data of GAPDH(31kDa) in Fig. 5F.



4. The original Western blot data of ALOX15(75kDa) in Fig. 6A. (The cropped section is the band for the ferroptosis inhibitor Fer-1. This data is not needed in the corresponding part of the manuscript, so the image was cropped.). The loading order of the Western Blot lanes from left to right is: ALOX15-WT (Control) group, ALOX15-WT (Erastin) group, ALOX15-WT (Alliin, 400 μM) group, ALOX15-KD (Control) group, ALOX15-KD (Erastin) group, ALOX15-KD (Alliin, 400 μM) group.

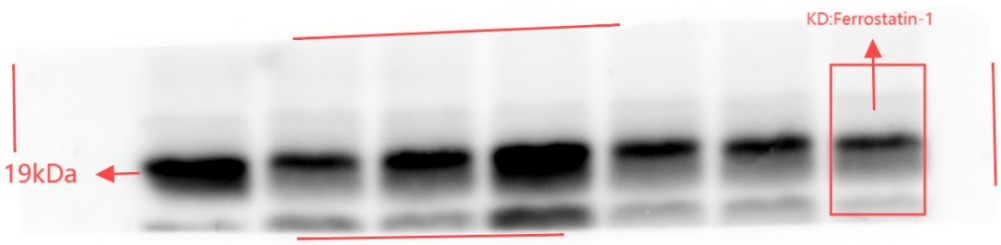


5. The original Western blot data of GAPDH(31kDa) in Fig. 6A. (The cropped section is the band for the ferroptosis inhibitor Fer-1. This data is not needed in the corresponding part of the manuscript, so the image was cropped.)

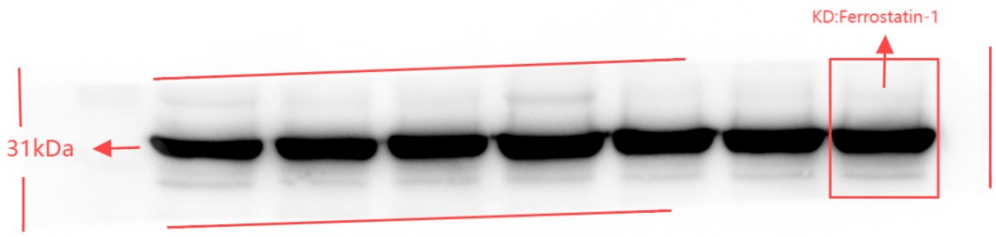


6. The original Western blot data of GPX4(19kDa) in Fig. 6C. (The cropped section is

the band for the ferroptosis inhibitor Fer-1. This data is not needed in the corresponding part of the manuscript, so the image was cropped.). The loading order of the Western Blot lanes from left to right is: ALOX15-WT (Control) group, ALOX15-WT (Erastin) group, ALOX15-WT (Alliin, 400 μM) group, ALOX15-KD (Control) group, ALOX15-KD (Erastin) group, ALOX15-KD (Alliin, 400 μM) group.



7. The original Western blot data of GAPDH(31kDa) in Fig. 6C. (The cropped section is the band for the ferroptosis inhibitor Fer-1. This data is not needed in the corresponding part of the manuscript, so the image was cropped.)



Legends to Figures

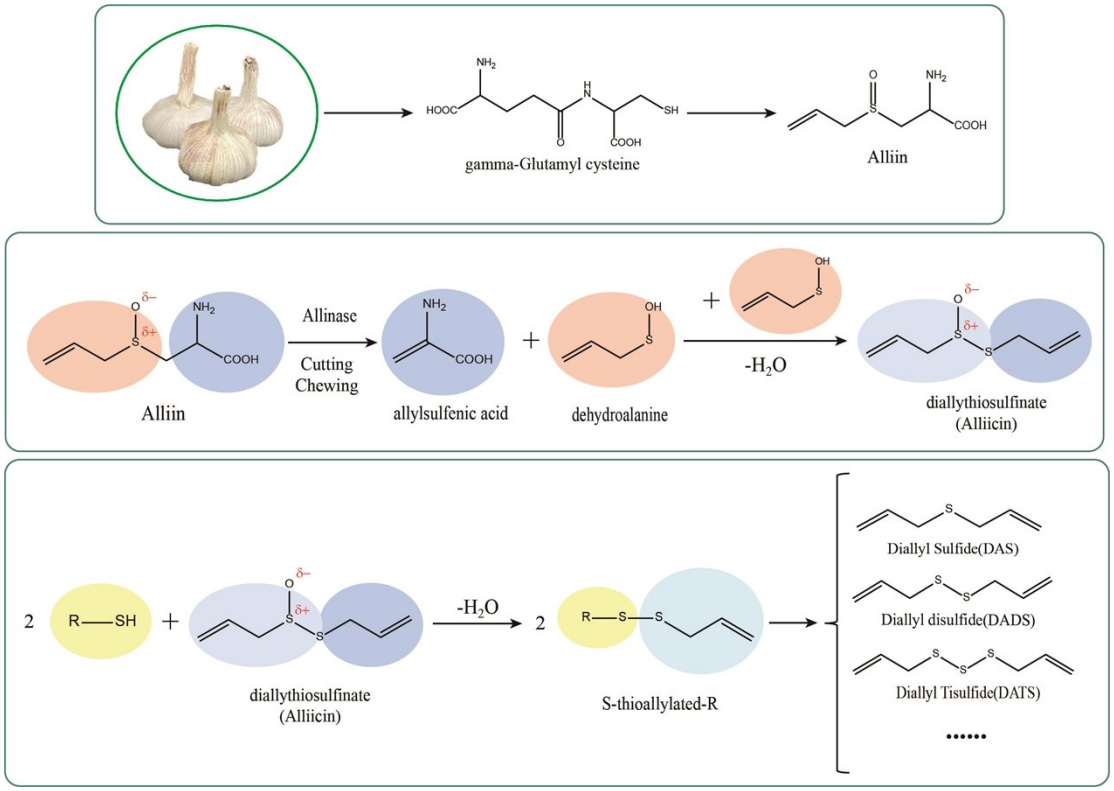
Fig. S1 The process of alliin transforming into allicin.

Fig. S2. PCA plot of the transcriptome among ICH and control group. (A) PCA plot among the two groups. (B) Reactome enrichment of the top 20 pathways. (C) WikiPathways enrichment of the top 20 pathways.

Fig. S3. GO analysis of the differential genes among ICH and alliin group.

Table S1. Garlic Ingredient Information.

Table S2. Docking score of cmpounds with core target.



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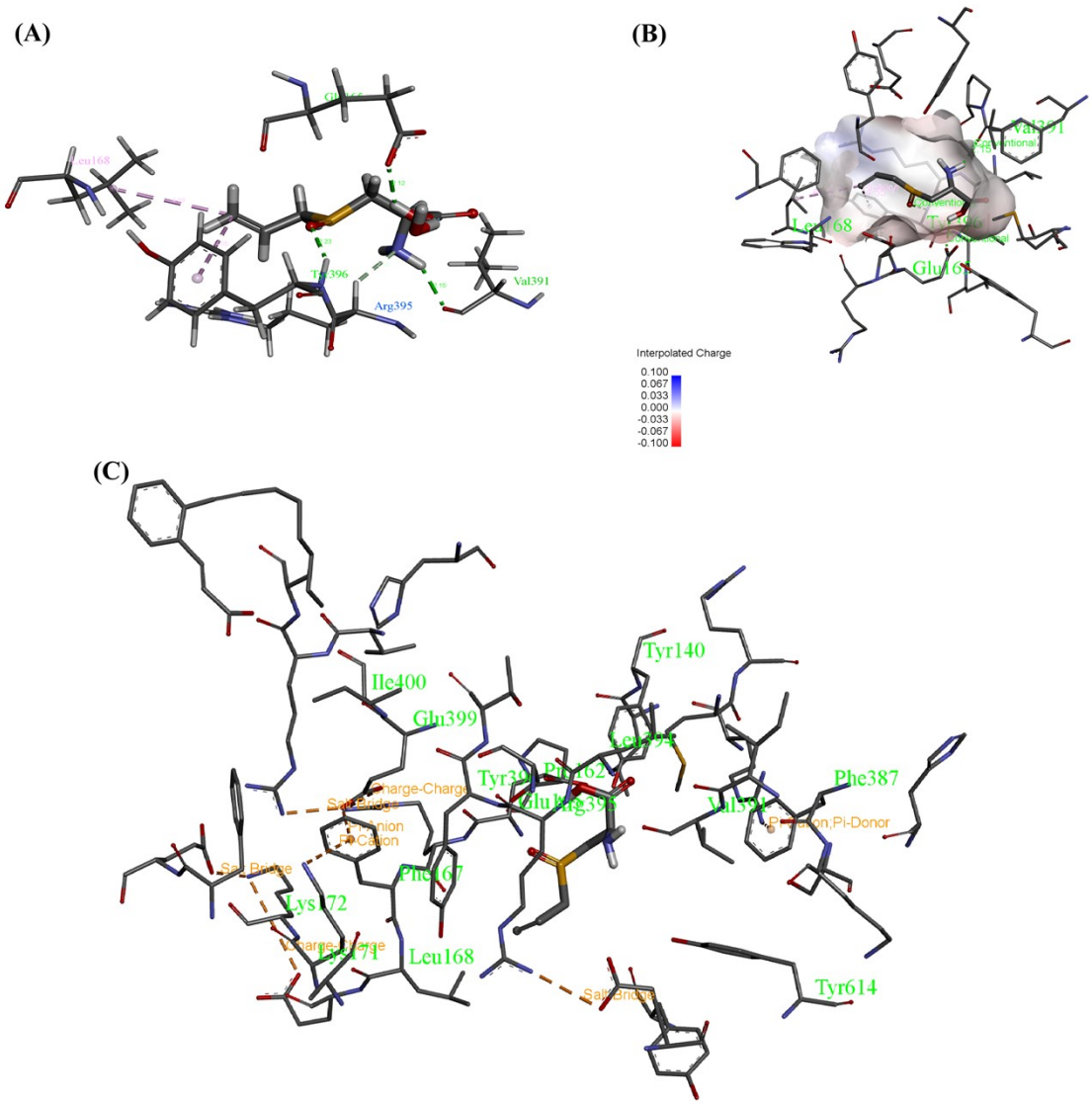

Fig. S2. Molecular docking analysis identifies potential binding regions between alliin and ALOX15. (A) Hydrogen bonding network. (B) Charge distribution map. (C) Electrostatic interaction profile of binding pocket residues

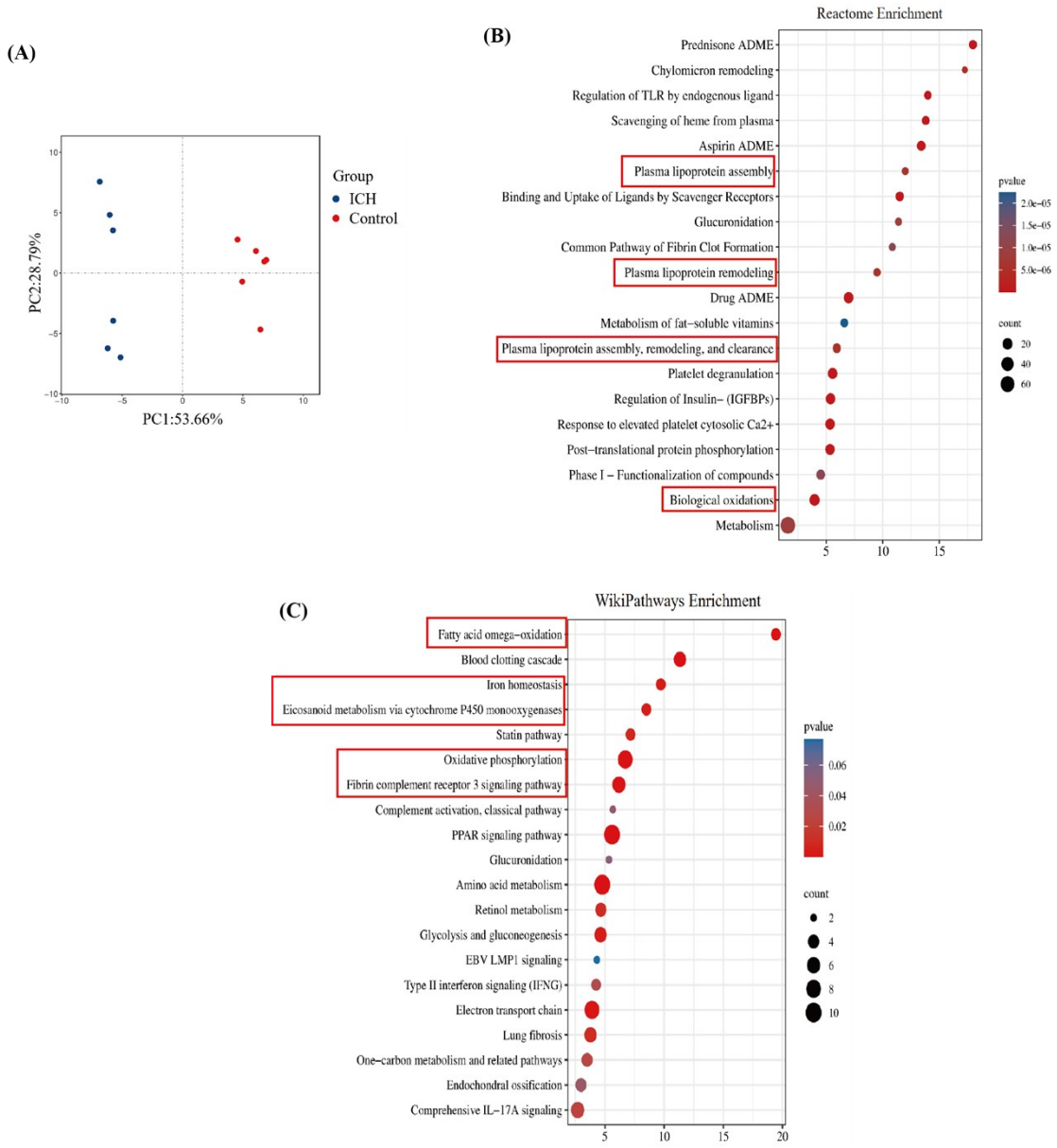

Fig. S3. PCA plot of the transcriptome among ICH and control group. (A) PCA plot among the two groups. (B) Reactome enrichment of the top 20 pathways. (C) WikiPathways enrichment of the top 20 pathways.

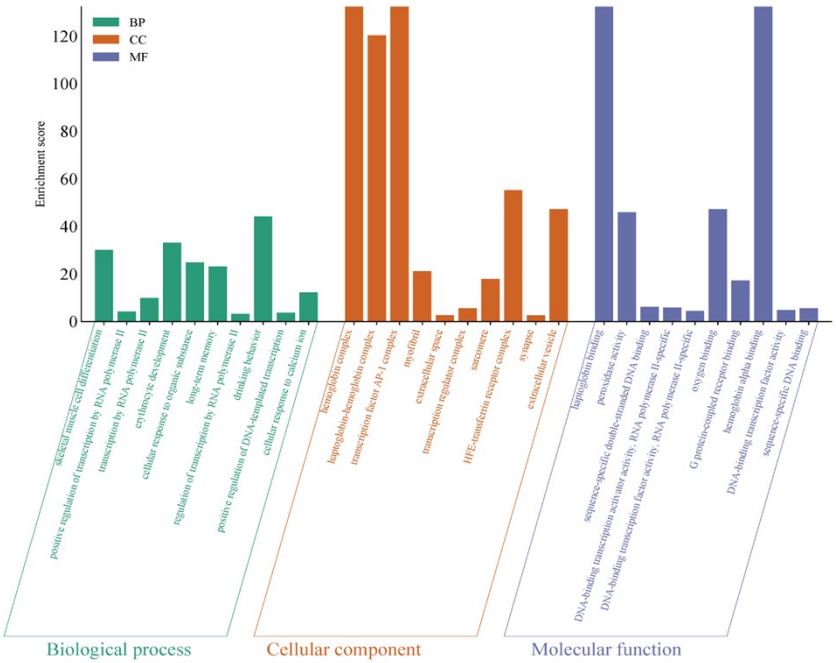

Fig. S4. GO analysis of the differential genes among ICH and alliin group.

Table S1. Garlic Ingredient Information.

Classification		Mol ID	Molecule Name	MW	AlogP	OB (%)	BBB	DL	FASA-	HL	Pubmed CID
Organic sulfide	**C1**	MOL007627	diAllS2	146.3	2.62	49.28	1.94	0.01	0.46	4.43	16590
	C2	MOL008359	DATS	210.44	3.8	49.42	2.03	0.01	0.55	8.2	75552
	C3	MOL004046	Dimethyl tetrasulfide	158.36	2.57	51.34	2.14	0	0	12.18	79828
	C4	MOL008365	Propyl n-butyl disulfide	164.37	3.59	62.95	1.91	0.01	0.3	5.48	522458
	C5	MOL008371	2-Ethenyl-1,3-dithia-cyclohex-5-ene	144.28	1.98	9.39	1.7	0.01	0.5		133337
	C6	MOL008349	3-Chlorothiophene	118.59	2.16	12.16	1.9	0.01	0.28		87017
	C7	MOL008355	Allylthiol	74.16	1.23	21.88	1.65	0	0.49		13367
	C8	MOL008363	Methylallyl trisulfide	152.33	2.59	23.2	2.19	0	0.54		61926
	C9	MOL007620	Allitridin	178.37	3.21	28.4	1.98	0.01	0.52		16315
	C10	MOL008361	3-METHYL-2-THIABUTANE	90.21	1.52	31.49	2.18	0	0.36	11.79	15246
	C11	MOL007621	DMDS	94.22	1.39	39.27	2.18	0	0.51	12.5	12232
	C12	MOL007619	Methyl allyl sulfide	88.19	1.41	70.09	1.84	0	0.44	12.01	66282
	C13	MOL007644	Methyldithio-1-propene	120.26	1.87	73.26	2.13	0	0.49	11.84	5366552
	C14	MOL007643	methylallyl disulphide	120.26	2	73.64	2.17	0	0.49	11.94	62434
	C15	MOL008358	Oil garlic	114.23	2.03	74.81	1.91	0.01	0.4	11.61	11617
	C16	MOL008354	allicin	162.3	1.51	78.41	1.22	0.01	0.43	4.83	51380898
	C17	MOL007601	(+)-L-Alliin	177.25	-0.83	86.68	-1.04	0.02	0.38	5.07	51380903
	C18	MOL007630	Propyl Trisulfide	182.41	3.72	40.68	1.91	0.01	0.37	5.54	22383
	C19	MOL007647	Propyl Methyl Trisulfide	154.35	2.85	58.68	2.16	0	0.46	11.26	5319765
	C20	MOL008347	1,2,4,6-Tetrathiepane	170.37	2.38	8.44	1.77	0.01	0.52		520423
	C21	MOL008362	Methyl allyl tetrasulfide	184.4	3.18	9.29	2.14	0.01	0.59		525329
	C22	MOL008357	Thioform	138.3	1.79	9.97	1.44	0.01	0.49		9264
	C23	MOL008348	Dithiolane	106.23	1.27	22.85	2.13	0	0.43		79045

	C24	MOL008351	3-Ethylthiophene	112.21	2.43	40.37	1.81	0.01	0.1	-3.27	74530
	C25	MOL008372	2-ethyl-1,3-dithiane	148.32	2.1	44.35	1.75	0.01	0.36	11.46	521915
	C26	MOL008370	2,5-Dimethylthiophene	112.21	1.78	49.64	1.87	0.01	0	11.93	12514
	C27	MOL008352	3-(isoamylthio)prop-1-ene	144.31	2.99	60.6	2.02	0.01	0.33	1.03	534495
	C28	MOL008374	3,4-Dimethylthiophene	112.21	2.46	84.37	1.91	0.01	0.15	-3.17	79089
	C29	MOL007628	Methyl trisulfide	126.29	1.98	10.72	2.27	0	0.58		19310
Polyphenols	**C30**	MOL001873	Sobrol A	166.19	1.77	64.98	0.68	0.04	0.41	4.5	8434
	C31	MOL006791	Epigallocatechin	306.29	1.65	24.18	-0.82	0.27	0.33		72277
	C32	MOL002850	Butylated Hydroxytoluene	220.39	4.85	40.02	1.8	0.07	0.3	10.36	31404
	C33	MOL002516	Zingerone	194.25	1.63	25.23	0.48	0.05	0.29		31211
	C34	MOL000771	P-Coumaric Acid	164.17	1.64	43.29	0.13	0.04	0.45	4.43	637542
	C35	MOL000492	(+)-Catechin	290.29	1.92	54.83	-0.73	0.24	0	0.61	9064
	C36	MOL012744	Resveratrol	228.26	3.01	19.07	-0.01	0.11	0.49		445154
	C37	MOL011865	Rosmarinic Acid	360.34	2.69	1.38	-1.24	0.35	0.47		5281792
	C38	MOL000492	Catechin	290.29	1.92	54.83	-0.73	0.24	0	0.61	9064
	C39	MOL002695	Lignan	458.55	3.78	43.32	-0.16	0.65	0.19	14.88	261166
	C40	MOL002042	Thymol	150.24	3.24	41.47	1.68	0.03	0.33		6989
	C41	MOL001002	Ellagic Acid	302.2	1.48	43.06	-1.41	0.43	0.43	-1.04	5281855
	C42	MOL000874	Paeonol	166.19	1.29	28.79	0.84	0.04	0.32		11092
	C43	MOL000254	Eugenol	164.22	2.55	56.24	1.32	0.04	0.32	0.92	3314
	C44	MOL000105	Protocatechuic Acid	154.13	0.9	25.37	-0.17	0.04	0.43		72
	C45	MOL000098	Quercetin	302.25	1.5	46.43	-0.77	0.28	0.38	14.4	5280343
	C46	MOL000513	3,4,5-trihydroxybenzoic acid	170.13	0.63	31.69	-0.54	0.04	0.41	11.78	370
	C47	MOL001955	Heriguard	354.34	-0.42	11.93	-1.71	0.33	0.37		1794427
	C48	MOL000360	Ferulic Acid	194.2	1.62	39.56	-0.03	0.06	0.34	2.38	445858

Amino acids and their derivatives	**C49**	MOL001477	Tyramine	137.2	0.99	45.11	0.52	0.02	0.32	-2.52	5610
	C50	MOL000067	Valine	117.17	0.24	53.33	-0.14	0.01	0	11.34	6971018
	C51	MOL000068	Isoleucine	131.2	0.7	59.05	-0.11	0.02	0	11.21	7043901
	C52	MOL000429	Asparagine	132.14	-1.85	83.96	-1.15	0.02	0	11.59	6992089
	C53	MOL000065	Aspartic acid	133.12	-1.25	79.74	-1.53	0.02	0	11.38	44367445
	C54	MOL009676	Glutamine	146.17	-1.53	87.9	-1.47	0.02	0.35	11.34	5961
	C55	MOL000055	Lysine	146.22	-0.68	29.33	-1.44	0.02	0		5962
	C56	MOL000052	Glutamic acid	147.15	-0.92	6.66	-1.97	0.02	0		33032
	C57	MOL000041	Phenylalanine	165.21	0.96	41.62	0.22	0.04	0	4.62	6140
	C58	MOL001780	Tryptophan	204.25	1.25	75.93	-0.17	0.08	0.27	-2.49	6305
	C59	MOL000054	Arginine	174.24	-1.11	47.64	-1.04	0.03	0	0.85	6322
	C60	MOL000388	Aminobutyric acid	103.14	-0.62	24.09	-0.57	0.01	0		6657
	C61	MOL003795	Pipecolic acid	129.18	0.4	66.14	0.38	0.02	0.28	11.08	849
	C62	MOL003800	Citrulline	175.22	-1.32	52.96	-1.46	0.03	0.31	0.9	9750
	C63	MOL001477	Tyramine	137.2	0.99	45.11	0.52	0.02	0.32	-2.52	5610
	C64	MOL002321	Oxoproline	129.13	-0.67	96.25	-0.26	0.02	0.34	11.35	7405
Flavonoids	**C65**	MOL010246	Flavonol	238.25	2.57	47.91	0.77	0.16	0.45	19.49	11349
	C66	MOL007930	Hesperidin	610.62	-0.48	13.33	-2.7	0.67	0.31		10621
	C67	MOL000737	Morin	302.25	1.5	46.23	-0.77	0.27	0.41	15.51	5281670
	C68	MOL000481	Genistein	270.25	2.07	17.93	-0.4	0.21	0		5280961
	C69	MOL000422	Kaempferol	286.25	1.77	41.88	-0.55	0.24	0	14.74	5280863
	C70	MOL000008	Apigenin	270.25	2.33	23.06	-0.61	0.21	0.41		5280443
	C71	MOL000006	Luteolin	286.25	2.07	36.16	-0.84	0.25	0.39	15.94	5280445

Table S2. Docking score of cmpounds with core target.

Compound	Docking score (kcal·mol^{-1})
Allicin	-4.0
DAS	-3.6
DADS	-3.6
DATS	-3.6
Alliin	-5.0