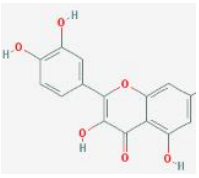
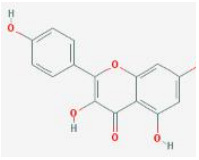
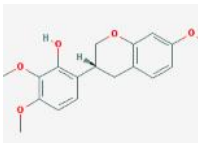
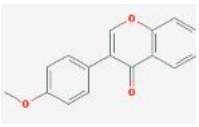
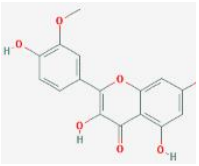
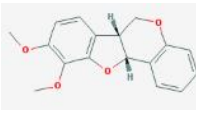
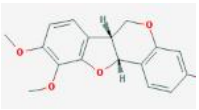
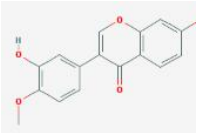
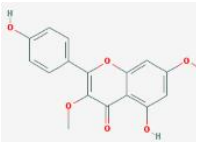
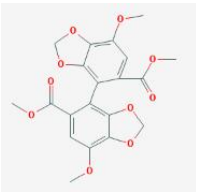
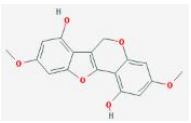
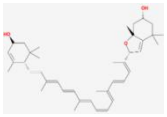
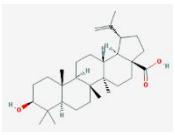
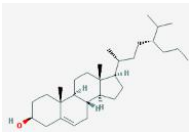
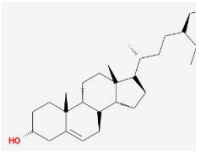
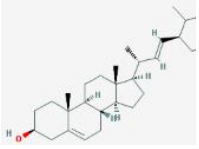
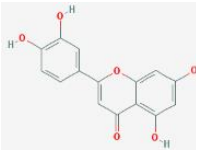
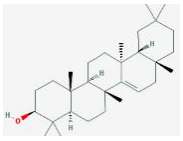
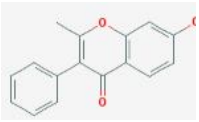
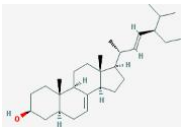
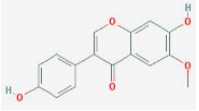
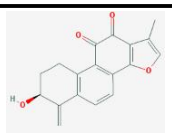
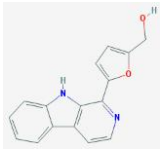
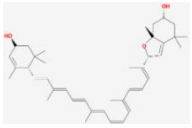
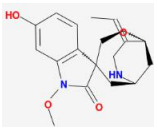
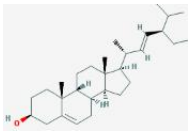
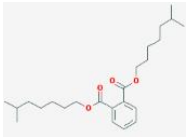
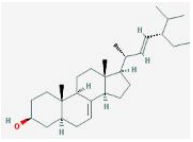
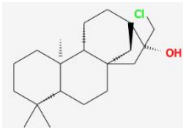
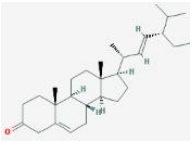
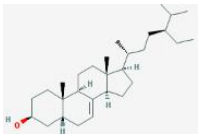
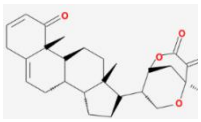
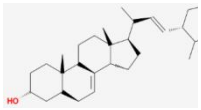
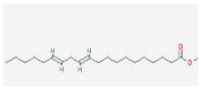
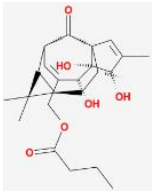
Table 1 *36* candidate compounds in SFI

Mol ID	Mol Name	OB (%)	DL	Degree	Sourse	2D Structure	Reference
MOL000098	Quercetin	46.43	0.28	167	HQ		(44)(45)
MOL000422	Kaempferol	41.88	0.24	68	HQ		(46)(47)
MOL000378	7-O-methylisomucronulatol	74.69	0.3	48	HQ		(48)
MOL000392	formononetin	69.67	0.21	42	HQ		(49)(50)
MOL000354	isorhamnetin	49.6	0.31	38	HQ		(51)(52)
MOL000380	(6aR,11aR)-9,10-dimethoxy-6a,11a-dihydro-6H-benzofurano[3,2-c]chromen-3-ol	64.26	0.42	25	HQ		(53)
MOL000371	3,9-di-O-methylnissolin	53.74	0.48	25	HQ		(54)
MOL000417	Calycosin	47.75	0.24	25	HQ		(55)(56)
MOL000239	Jaranol	50.83	0.29	16	HQ		(57)
MOL000387	Bifendate	31.1	0.67	8	HQ		(58)(59)

MOL000442	1,7-Dihydroxy-3,9-dimethoxy pterocarpene	39.05	0.48	5	HQ		(60)
MOL004492	Chrysanthemaxanthin	38.72	0.58	5	HQ		(61)(62)
MOL000211	Mairin	55.38	0.78	1	HQ		(48)
MOL000033	(3S,8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-[(2R,5S)-5-propan-2-yloctan-2-yl]-2,3,4,7,8,9,11,12,14,15,16,17-dodecahydro-1H-cyclopenta[a]phenanthren-3-ol	36.23	0.78	1	HQ		(63)
MOL000296	hederagenin	36.91	0.75	1	HQ		(64)(65)
MOL000449	Stigmasterol	43.83	0.76	147	DS		(66)(67)
MOL000006	luteolin	36.16	0.25	58	DS		(68)(69)
MOL006554	Taraxerol	38.4	0.77	53	DS		(70)(71)
MOL003896	7-Methoxy-2-methyl isoflavone	42.56	0.2	46	DS		(72)
MOL004355	Spinasterol	42.98	0.76	39	DS		(73)
MOL008400	glycitein	50.48	0.24	26	DS		(74)(75)

MOL007059	3-beta-Hydroxymethyllenetanshiquinone	32.16	0.41	18	DS		(76)
MOL005321	Frutinone A	65.9	0.34	17	DS		(77)
MOL002140	Perlolyrine	65.95	0.27	6	DS		(78)(79)
MOL004492	Chrysanthemaxanthin	38.72	0.58	5	DS		(61)(62)
MOL008411	11-Hydroxyrankinidine	40	0.66	4	DS		(80)
MOL003036	ZINC03978781	43.83	0.76	3	DS		(81)
MOL002879	Diop	43.59	0.39	3	DS		(82)
MOL001006	poriferasta-7,22E-dien-3beta-ol	42.98	0.76	3	DS		(83)
MOL009274	Fritillaziebinol	55.05	0.34	2	DS		(84)
MOL008407	(8S,9S,10R,13R,14S,17R)-17-[(E,2R,5S)-5-ethyl-6-methylhept-3-en-2-yl]-10,13-dimethyl-1,2,4,7,8,9,11,12,14,15,16,17-dodecahydrocyclopenta[a]phenanthren-3-one	45.4	0.76	2	DS		(85)

MOL006774	stigmast-7-enol	37.42	0.75	2	DS		(86)
MOL008397	Daturilin	50.37	0.77	1	DS		(87)
MOL012377	bessisterol	42.98	0.76	1	DS		(73)
MOL007514	methyl icosa-11,14-dienoate	39.67	0.23	1	DS		(88)
MOL011455	20-Hexadecanoylingenol	32.7	0.65	1	DS		(89)

Supplementary table 1. Network pharmacology analysis of SFI, obtained 36 potential effective substances.

Table 3 the affinity of compunds with proteins

Protein	Compound	Affinity[kcal/mol]
AMPK	Taraxerol	-7.8
	Chrysanthemaxanthin	-7.5
	Mairin	-7.4
	bessisterol	-7.1
	poriferasta-7,22E-dien-3beta-ol	-7.1
	Spinasterol	-7.1
	stigmast-7-enol	-7.1
	(8S,9S,10R,13R,14S,17R)-17-[(E,2R,5S)-5-ethyl-6-methylhept-3-en-2-yl]-10,13-dimethyl-1,2,4,7,8,9,11,12,14,15,16,17-dodecahydrocyclopenta[a]phenanthren-3-one	-7
	hederagenin	-6.8
	Stigmasterol	-6.8
	11-Hydroxyrankinidine	-6.7
	Frutinone A	-6.6
	Perlolyrine	-6.4
	(3S,8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-[(2R,5S)-5-propan-2-yloctan-2-yl]-2,3,4,7,8,9,11,12,14,15,16,17-dodecahydro-1H-cyclopenta[a]phenanthren-3-ol	-6.2
	formononetin	-6.1
	Calycosin	-6
	3,9-di-O-methylnissolin	-6
	glycitein	-6
	Quercetin	-5.9
	7-Methoxy-2-methyl isoflavone	-5.8
	luteolin	-5.8
	7-O-methylisomucronulatol	-5.6
	isorhamnetin	-5.5
	Jaranol	-5.5
	Kaempferol	-5.5
	Bifendate	-5.3
	Diop	-5.2
	methylicosa-11,14-dienoate	-4.3
	20-Hexadecanoylingenol	0
	1,7-Dihydroxy-3,9-dimethoxy pterocarpene	0
	Fritillaziebinol	0

Protein	Compound	Affinity[kcal/mol]
SIRT1	Taraxerol	-7.2
	Chrysanthemaxanthin	-7.1
	Mairin	-6.9
	Stigmasterol	-6.4
	(3S,8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-[(2R,5S)-5-propan-2-yloctan-2-yl]-2,3,4,7,8,9,11,12,14,15,16,17-dodecahydro-1H-cyclopenta[a]phenanthren-3-ol	-6.3
	poriferasta-7,22E-dien-3beta-ol	-6.3
	11-Hydroxyrankinidine	-6.2
	bessisterol	-6.2
	(8S,9S,10R,13R,14S,17R)-17-[(E,2R,5S)-5-ethyl-6-methylhept-3-en-2-yl]-10,13-dimethyl-1,2,4,7,8,9,11,12,14,15,16,17-dodecahydrocyclopenta[a]phenanthren-3-one	-6.2
	hederagenin	-6.1
	Kaempferol	-6.1
	Spinasterol	-6.1
	Frutinone A	-6
	isorhamnetin	-6
	Quercetin	-6
	stigmast-7-enol	-6
	luteolin	-5.8
	3,9-di-O-methylnissolin	-5.7
	glycitein	-5.6
	Jaranol	-5.6
	7-Methoxy-2-methyl isoflavone	-5.4
	Perlolyrine	-5.4
	Calycosin	-5.3
	formononetin	-5.3
	7-O-methylisomucronulatol	-5.1
	Bifendate	-4.8
	Diop	-4.2
	methylicosa-11,14-dienoate	-4.1
	20-Hexadecanoylingenol	0
	1,7-Dihydroxy-3,9-dimethoxy pterocarpene	0
	Fritillaziebinol	0

Protein	Compound	Affinity[kcal/mol]
Akt1	Taraxerol	-8.6
	hederagenin	-8.1
	11-Hydroxyrankinidine	-7.7
	poriferasta-7,22E-dien-3beta-ol	-7.6
	Spinasterol	-7.6
	Mairin	-7.5
	Calycosin	-7.3
	formononetin	-7.3
	stigmast-7-enol	-7.3
	7-Methoxy-2-methyl isoflavone	-7.1
	(8S,9S,10R,13R,14S,17R)-17-[(E,2R,5S)-5-ethyl-6-methylhept-3-en-2-yl]-10,13-dimethyl-1,2,4,7,8,9,11,12,14,15,16,17-dodecahydrocyclopenta[a]phenanthren-3-one	-7
	Stigmasterol	-7
	bessisterol	-6.9
	Frutinone A	-6.9
	luteolin	-6.8
	Perlolyrine	-6.7
	(3S,8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-[(2R,5S)-5-propan-2-yloctan-2-yl]-2,3,4,7,8,9,11,12,14,15,16,17-dodecahydro-1H-cyclopenta[a]phenanthren-3-ol	-6.6
	Quercetin	-6.5
	glycitein	-6.4
	isorhamnetin	-6.4
	Jaranol	-6.4
	Kaempferol	-6.4
	3,9-di-O-methylnissolin	-6.3
	Chrysanthemaxanthin	-6.1
	7-O-methylisomucronulatol	-5.9
	Bifendate	-5.4
	Diop	-4.9
	methylicosa-11,14-dienoate	-4.2
	20-Hexadecanoylingenol	0
	1,7-Dihydroxy-3,9-dimethoxy pterocarpene	0
	Fritillaziebinol	0

Supplementary table 3. Molecular docking of SFI to CRF-gene targets. The affinify of compunds with the main proteins of AMPK, SIRT1 and Akt1.

Table 4　40 differential metabolites in all cell samples

	VIP	p.value	FDR
1-Aminocyclopropanecarboxylic acid	1.602262994	0.005074868	0.03754334
2-Hydroxybutyric acid	1.472707402	0.005074868	0.03754334
L-Serine	1.018988377	0.005074868	0.03754334
5,6-Dihydro-5-fluorouracil	1.491822289	0.005074868	0.03754334
L-Asparagine	1.192793899	0.005074868	0.03754334
2-Phenylacetamide	1.143837204	0.005074868	0.03754334
Acetylcholine	1.864338595	0.005074868	0.03754334
L-Methionine	1.494624693	0.005074868	0.03754334
Xanthine	1.920662876	0.005074868	0.03754334
Imidazol-5-yl-pyruvate	1.90084649	0.005074868	0.03754334
L-Histidine	1.485095642	0.005074868	0.03754334
5-Acetamidovalerate	1.394931145	0.005074868	0.03754334
L-Carnitine	1.190601268	0.005074868	0.03754334
1H-Indole-3-acetamide	1.91001781	0.005074868	0.03754334
D-Fructose	2.276940441	0.005074868	0.03754334
L-Tyrosine	1.163651484	0.005074868	0.03754334
Phosphorylcholine	1.463136563	0.005074868	0.03754334
Indolepyruvate	1.037186124	0.005074868	0.03754334
N-Acetyl-D-glucosamine	1.723120107	0.005074868	0.03754334
Nicotinamide riboside	1.299094078	0.005074868	0.03754334
Nicotinamide ribotide	1.022754915	0.005074868	0.03754334
Guanosine 3'-phosphate	1.437947934	0.008239019	0.050351152
gamma-Aminobutyric acid	1.344822251	0.013065227	0.065214782
2-Deoxystreptamine	1.269355911	0.013065227	0.065214782
Alpha-dimorphecolic acid	2.055613825	0.013065227	0.065214782
Ornithine	1.340886211	0.020240571	0.087485074
3'-AMP	1.823033109	0.020240571	0.087485074
Uracil	1.645344232	0.030638988	0.113691028
Phenylacetylglycine	1.788939439	0.030638988	0.113691028
Vanillylmandelic acid	1.317203783	0.030638988	0.113691028
Pyrrole-2-carboxylic acid	1.01533553	0.045327562	0.143367285

2-Dehydropantoate	1.632256994	0.045327562	0.143367285
D-Cathine	1.674119951	0.045327562	0.143367285
3-Indoleacetonitrile	1.343442459	0.045327562	0.143367285
L-Sorbose	1.37354756	0.00277843	0.082746154
D-Glucosamine 6-phosphate	1.884791784	0.005074868	0.082746154
1-Phospho-alpha-D-galacturonate	1.128275443	0.005074868	0.082746154
Pantetheine 4'-phosphate	1.925212522	0.005074868	0.082746154
Citrulline	1.286770048	0.008239019	0.101745008
Ribose 1-phosphate	1.55832126	0.008239019	0.101745008

Supplementary table 4. Metabolomics analysis identified 40 potential biomarkers.