

Table S1 Major signaling pathways enriched for six core targets

NO.	Name	Targets
1	Proteoglycans in cancer	ACTB/AKT1/ESR1/SRC
2	Rap1 signaling pathway	ACTB/AKT1/EGFR/SRC
3	Chemical carcinogenesis - receptor activation	AKT1/ESR1/HSP90AA1/SRC
4	Estrogen signaling pathway	AKT1/HSP90AA1/EGFR/SRC/ESR1
5	Lipid and atherosclerosis	AKT1/HSP90AA1/SRC
6	Thyroid hormone signaling pathway	ACTB/AKT1/ESR1/SRC
7	HIF-1 signaling pathway	AKT1/EGFR
8	EGFR tyrosine kinase inhibitor resistance	AKT1/EGFR/SRC
9	AGE-RAGE signaling pathway in diabetic complications	AKT1
10	Breast cancer	AKT1/EGFR/ESR1
11	Nitrogen metabolism	EFGR
12	Prostate cancer	AKT1/HSP90AA1/EGFR
13	VEGF signaling pathway	AKT1/SRC
14	Endocrine resistance	AKT1/ESR1/EGFR/SRC
15	Central carbon metabolism in cancer	AKT1/EGFR/
16	Melanoma	AKT1/EGFR
17	Non-small cell lung cancer	AKT1/EGFR
18	Glioma	AKT1/EGFR
19	Bladder cancer	EGFR/SRC
20	Carbohydrate digestion and absorption	AKT1

TableS2 Add sample recovery results of PRA

Compound	Original quantity (μg)	Adding quantity (μg)	Measured quality (μg)	Sample recovery (%)	Average recovery (%)	RSD (%)
paeoniflorin	144.1608	150.00	286.7466	95.06	98.4398	2.47
	143.9010	150.00	290.1122	97.47		
	144.1750	150.00	294.1634	99.99		
	144.5430	150.00	293.4953	99.30		
	144.0930	150.00	297.7224	102.42		
	145.9820	150.00	290.5731	96.39		
albiflorin	41.730	48.00	88.9320	98.34	100.1089	2.59
	41.712	48.00	89.0485	98.62		
	41.093	48.00	89.6286	101.12		
	40.883	48.00	87.3548	96.82		
	40.532	48.00	88.9809	100.94		
	40.257	48.00	90.5757	104.83		
oxypaeoniflorin	1.2381	1.40	2.6681	102.14	98.6415	2.33
	1.2530	1.40	2.6615	100.61		
	1.2320	1.40	2.6141	98.72		
	1.2620	1.40	2.5961	95.29		
	1.3130	1.40	2.6651	96.58		
	1.3420	1.40	2.7210	98.50		
gallic acid	6.8720	6.40	13.0625	96.73	98.3994	2.78
	6.8745	6.40	13.3197	100.71		
	6.7920	6.40	13.0471	97.74		
	6.8760	6.40	13.4884	103.32		
	6.9010	6.40	13.0552	96.16		
	6.8920	6.40	13.0199	95.75		
catechin	4.9184	5.20	10.0151	98.01	97.4019	1.41
	5.0010	5.20	9.9640	95.44		
	4.8820	5.20	9.8791	96.10		
	4.9910	5.20	10.1216	98.67		
	4.9830	5.20	10.1469	99.31		
	4.9180	5.20	9.9561	96.89		
1,2,3,4,6-O-Pentagalloylglucose	2.5362	2.50	5.1381	104.08	101.7876	2.53
	2.5380	2.50	5.1268	103.55		
	2.5540	2.50	5.0324	99.13		
	2.4590	2.50	5.0343	103.01		
	2.5370	2.50	5.1267	103.59		
	2.6010	2.50	5.0350	97.36		

TableS3 Add sample recovery results of PRR

Compound	Original quantity (μg)	Adding quantity (μg)	Measured quality (μg)	Sample recovery (%)	Average recovery (%)	RSD (%)
paeoniflorin	212.5364	240.00	459.8839	103.06	101.9084	2.41
	211.9834	240.00	443.4297	96.44		
	213.0294	240.00	459.7618	102.81		
	212.9003	240.00	460.6358	103.22		
	212.0943	240.00	459.4886	103.08		
	213.3094	240.00	460.1340	102.84		
albiflorin	179.9166	182.00	369.8512	104.36	102.5090	2.06
	179.2110	182.00	368.2383	103.86		
	180.3820	182.00	359.9978	98.69		
	178.3920	182.00	367.1357	103.71		
	179.3240	182.00	368.3588	103.87		
	180.4540	182.00	363.4962	100.57		
oxypaeoniflorin	6.6781	5.00	11.4500	95.44	101.5518	3.16
	6.6660	5.00	11.6448	99.58		
	6.6820	5.00	11.8142	102.64		
	6.2350	5.00	11.3618	102.54		
	6.6540	5.00	11.8714	104.35		
	6.3630	5.00	11.6014	104.77		
gallic acid	15.9910	16.2	31.9684	98.63	101.5874	2.24
	16.0110	16.2	32.9960	104.85		
	15.9876	16.2	32.5389	102.17		
	16.0926	16.2	32.5589	101.64		
	15.9926	16.2	31.9960	98.79		
	15.9840	16.2	32.7437	103.45		
catechin	16.7894	16.60	34.1473	104.57	100.2828	3.40
	16.7810	16.60	33.8274	102.69		
	16.7910	16.60	33.2053	98.88		
	16.7730	16.60	33.9209	103.30		
	16.7320	16.60	32.7165	96.29		
	16.7850	16.60	32.7157	95.97		
1,2,3,4,6-O-Pentagalloylglucose	19.8915	20.20	39.4641	96.89	96.2004	0.62
	19.8880	20.20	39.2905	96.05		
	19.9010	20.20	39.4290	96.67		
	19.8730	20.20	39.2916	96.13		
	19.9030	20.20	39.1012	95.04		
	19.8910	20.20	39.3661	96.41		

Table S4 Compounds identified from chemical markers of PRA

Samples name	Category	Paeoniflorin (%)	Albiflorin (%)	Oxypaeoniflorin (%)	Gallic acid (%)	catechin (%)	1,2,3,4,6-O-Pentagalloyl glucose (%)
BS-34	I	2.444	0.678	0.034	0.181	0.044	0.115
BS-35	I	2.142	0.753	0.022	0.105	0.070	0.238
BS-36	I	2.946	0.656	0.041	0.207	0.060	0.108
BS-37	I	2.988	0.674	0.044	0.211	0.067	0.264
BS-38	I	2.444	0.654	0.034	0.176	0.046	0.106
Average mass of Class I		2.593	0.683	0.035	0.176	0.057	0.166
BS-3	II	2.455	0.562	0.023	0.101	0.055	0.020
BS-9	II	2.466	0.668	0.022	0.111	0.065	0.028
BS-10	II	2.363	0.689	0.023	0.116	0.066	0.084
BS-14	II	2.315	0.524	0.020	0.093	0.050	0.005
BS-19	II	2.327	0.494	0.019	0.095	0.050	0.015
BS-20	II	2.390	0.488	0.019	0.096	0.047	0.061
Average mass of Class II		2.385	0.587	0.021	0.102	0.055	0.035
BS-1	III	1.950	0.372	0.016	0.104	0.038	0.005
BS-2	III	1.833	0.371	0.015	0.097	0.038	0.005
BS-4	III	1.699	0.572	0.017	0.086	0.056	0.005
BS-5	III	1.903	0.315	0.013	0.073	0.034	0.005
BS-6	III	1.948	0.270	0.012	0.070	0.030	0.005
BS-7	III	2.152	0.483	0.024	0.128	0.072	0.165
BS-8	III	2.218	0.480	0.026	0.126	0.078	0.016
BS-11	III	2.284	0.500	0.026	0.114	0.068	0.007
BS-12	III	2.058	0.411	0.020	0.106	0.047	0.005
BS-13	III	1.495	0.534	0.016	0.077	0.050	0.005
BS-15	III	1.746	0.344	0.015	0.099	0.032	0.005

BS-16	III	1.786	0.384	0.016	0.092	0.036	0.005
BS-17	III	2.261	0.466	0.019	0.094	0.042	0.005
BS-18	III	2.165	0.409	0.015	0.090	0.037	0.005
BS-21	III	2.290	0.435	0.023	0.118	0.072	0.005
BS-22	III	2.194	0.417	0.019	0.120	0.048	0.005
BS-23	III	2.003	0.388	0.013	0.099	0.031	0.005
BS-24	III	2.148	0.425	0.014	0.098	0.035	0.017
BS-25	III	1.773	0.336	0.014	0.080	0.032	0.005
BS-26	III	2.127	0.363	0.016	0.104	0.034	0.005
BS-27	III	2.092	0.470	0.020	0.115	0.053	0.005
BS-28	III	1.876	0.422	0.018	0.103	0.045	0.005
BS-29	III	2.024	0.468	0.020	0.123	0.047	0.015
BS-30	III	2.147	0.392	0.014	0.093	0.037	0.012
BS-31	III	1.802	0.480	0.015	0.107	0.053	0.034
BS-32	III	2.106	0.421	0.018	0.095	0.048	0.032
BS-33	III	2.341	0.441	0.018	0.124	0.048	0.047
Average mass of							
Class III		2.016	0.421	0.017	0.101	0.046	0.016

Table S5 Compounds identified from chemical markers of PRR

Samples name	Category	Paeoniflorin (%)	Albiflorin (%)	Oxypaeoniflorin (%)	Gallic acid (%)	catechin (%)	1,2,3,4,6-O-Pentagalloyl glucose (%)
CS-9	I	2.491	1.119	0.030	0.165	0.003	0.069
CS-10	I	2.577	1.611	0.045	0.220	0.020	0.212
CS-11	I	2.646	1.641	0.044	0.229	0.019	0.250
CS-12	I	2.309	0.225	0.093	0.159	0.004	0.098
CS-15	I	2.078	1.545	0.049	0.100	0.014	0.011
CS-16	I	2.732	0.132	0.112	0.119	0.007	0.112
CS-19	I	1.831	1.475	0.048	0.078	0.002	0.014
CS-20	I	1.873	1.482	0.048	0.078	0.001	0.032
CS-23	I	1.874	1.289	0.040	0.103	0.009	0.012
CS-24	I	1.877	1.000	0.027	0.127	0.004	0.010
CS-27	I	1.801	1.031	0.028	0.129	0.005	0.016
CS-28	I	2.722	1.197	0.032	0.175	0.003	0.447
CS-29	I	2.236	0.214	0.093	0.158	0.004	0.069
CS-31	I	1.961	1.432	0.047	0.089	0.012	0.010
CS-32	I	2.472	0.140	0.105	0.109	0.007	0.193
Average mass of Class I		2.237	1.101	0.056	0.137	0.008	0.132
CS-21	II	3.506	0.146	0.144	0.134	0.019	0.394
CS-22	II	4.014	0.106	0.150	0.083	0.017	0.395
CS-33	II	4.068	0.109	0.149	0.084	0.017	0.392
CS-34	II	3.194	0.131	0.130	0.117	0.022	0.556
Average mass of Class II		3.696	0.123	0.143	0.105	0.019	0.434
CS-1	III	2.581	2.479	0.073	0.210	0.033	0.347
CS-2	III	2.830	2.313	0.063	0.241	0.035	0.396

CS-3	III	2.279	2.075	0.061	0.184	0.032	0.206
CS-4	III	2.284	2.023	0.060	0.184	0.030	0.264
CS-5	III	2.346	2.340	0.052	0.222	0.024	0.390
CS-6	III	2.626	2.032	0.076	0.185	0.031	0.313
CS-7	III	2.818	1.786	0.084	0.173	0.021	0.428
CS-8	III	2.386	2.154	0.060	0.159	0.016	0.286
CS-13	III	3.009	2.790	0.099	0.182	0.059	0.562
CS-14	III	2.405	1.696	0.063	0.167	0.023	0.468
CS-17	III	2.394	1.700	0.064	0.167	0.023	0.594
CS-18	III	2.933	2.776	0.082	0.230	0.032	0.643
CS-25	III	2.975	2.359	0.068	0.236	0.034	1.161
CS-26	III	2.548	2.493	0.056	0.232	0.025	1.039
CS-30	III	2.827	2.197	0.085	0.199	0.032	0.954
CS-35	III	2.842	1.781	0.082	0.171	0.016	0.623
CS-36	III	2.581	2.479	0.073	0.210	0.033	0.347
Average mass of							
Class III		2.630	2.187	0.071	0.196	0.029	0.542

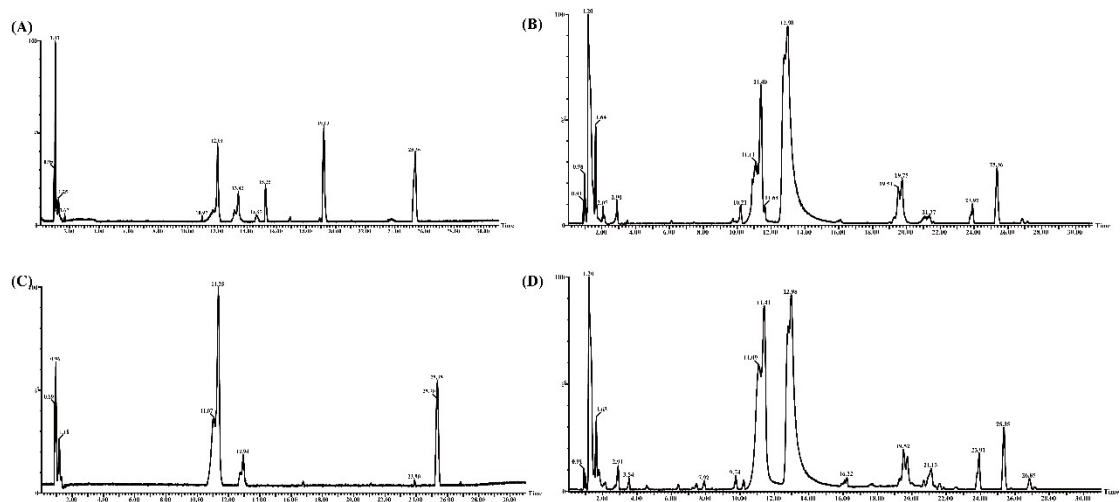


Fig. S1 BPI chromatograms of PRA and PRR in positive and negative ion modes.

(A) Positive ion mode of PRA sample, (B) negative ion mode of PRA sample. (C) positive ion mode of PRR sample, (D) negative ion mode of PRA sample.

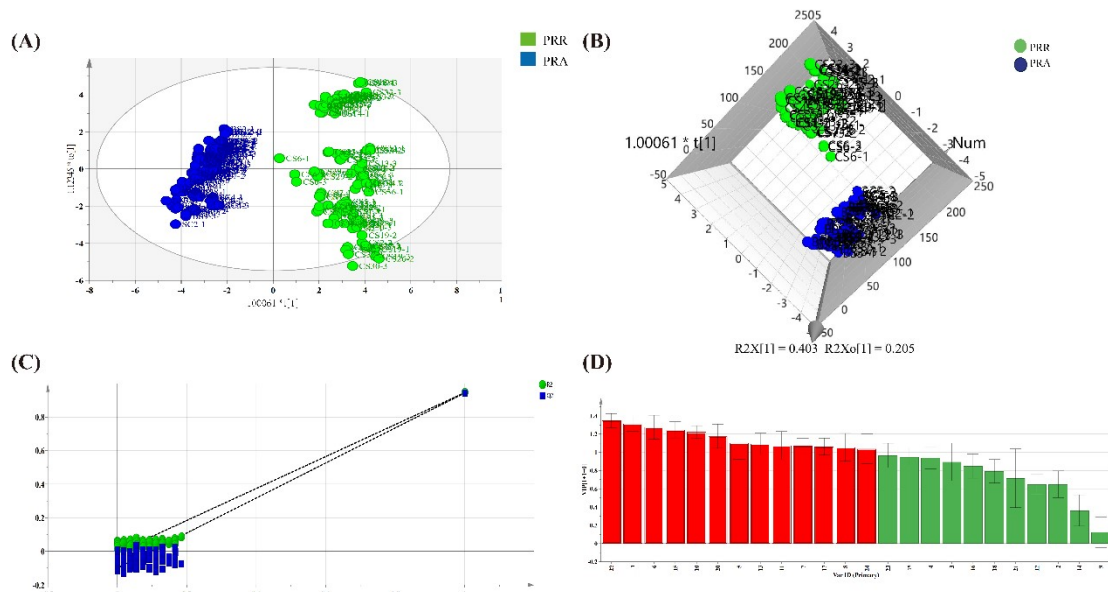


Fig. S2 OPLS-DA results of PRA and PRR.

(A) OPLS-DA scatter score plot, (B) 3D chart, (C) Cross-validation model, (D) VIP plot.

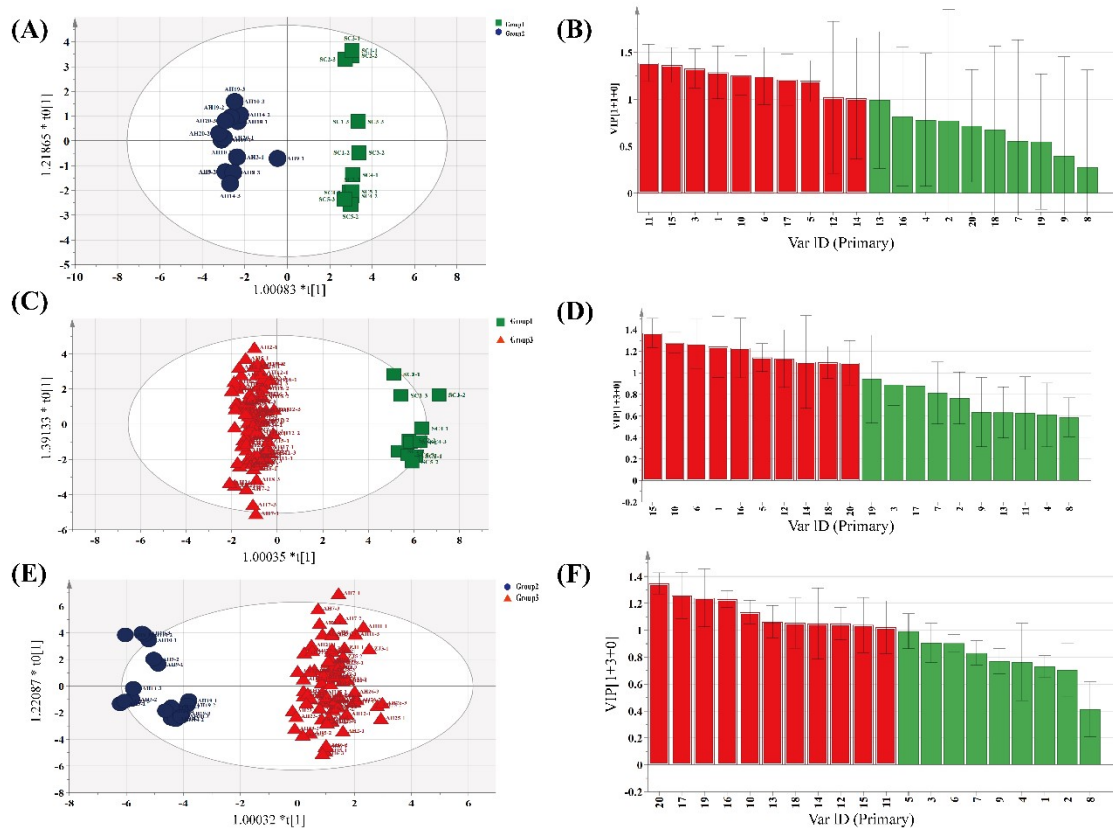


Fig. S3 OPLS-DA score plot and VIP plot for PRA.

(A) OPLS-DA score plot of Group 1 and Group 2, (B) VIP plot of Group 1 and Group 2, (C) OPLS-DA score plot of Group 1 and Group 3, (D) VIP plot of Group 1 and Group 3, (E) OPLS-DA score plot of Group 2 and Group 3, (F) VIP plot of Group 2 and Group 3.

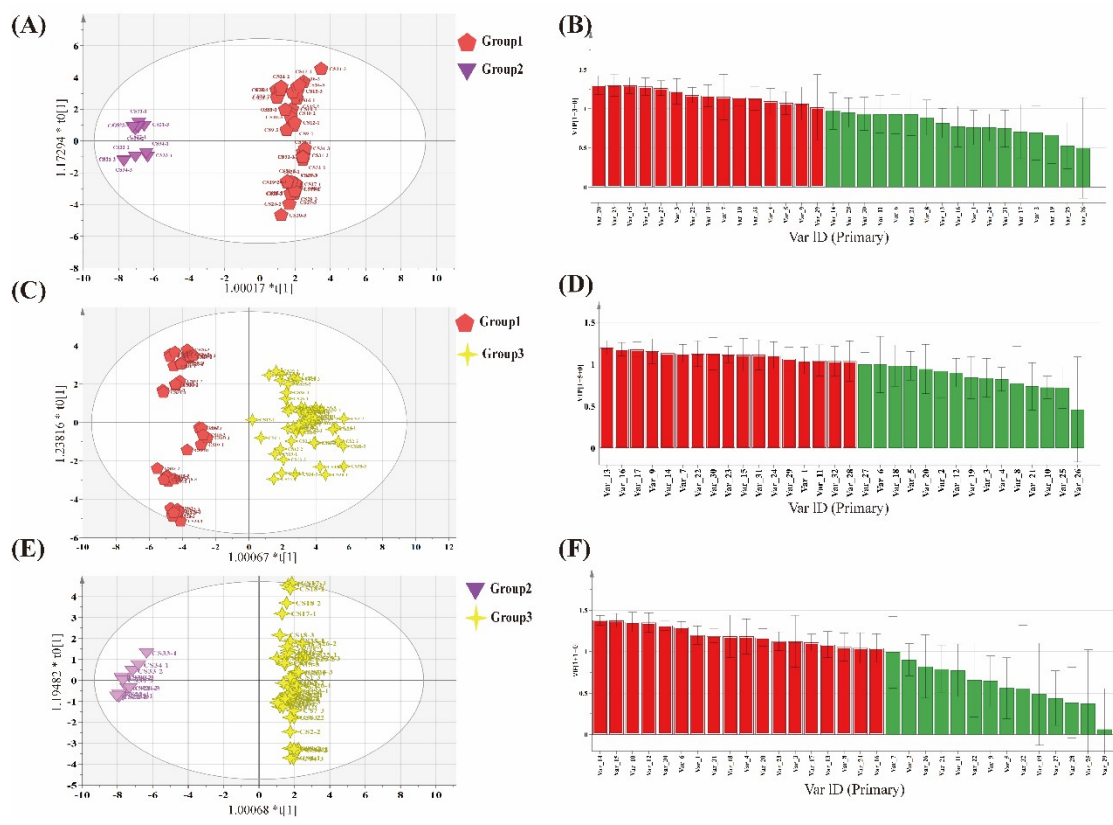


Fig. S4 OPLS-DA score plot and VIP plot for PRR.

(A)OPLS-DA score plot of Group 1 and Group 2, (B)VIP plot of Group 1 and Group 2, (C)OPLS-DA score plot of Group1 and Group 3, (D)VIP plot of Group1 and Group 3, (E)OPLS-DA score plot of Group2 and Group3, (F)VIP plot of Group2 and Group3.

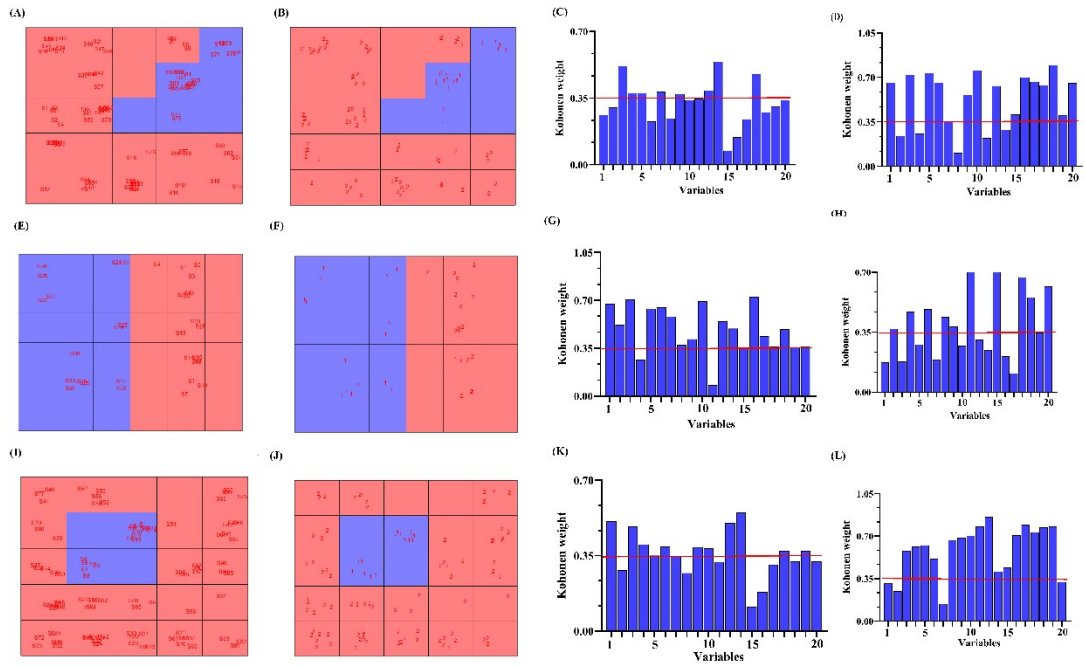


Fig. S5 Kohonen map of PRA samples.

(A) distribution maps of G1 and G2 , (B) the assigned groups to samples, (C) weight chart of G1 in two categories (G1 and G2), (D) weight chart of G2 in two categories (G1 and G2), (E) distribution maps of G1 and G3, (F) the assigned groups to samples, (G) weight chart of G1 in two categories (G1 and G3), (H) weight chart of G3 in two categories (G1 and G3), (I) distribution maps of G2 and G3, (J) the assigned groups to samples, (K) weight chart of G2 in two categories (G2 and G3), (L) weight chart of G3 in two categories (G2 and G3).

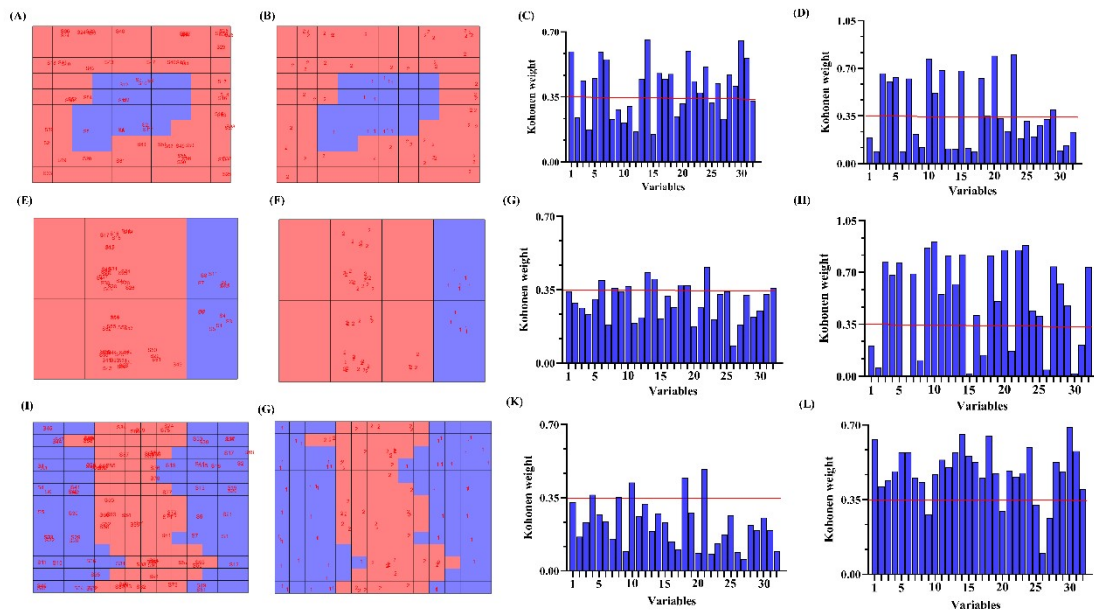


Fig.S6 Kohonen map of PRR samples.

(A) distribution maps of G1 and G2 , (B) the assigned groups to samples, (C) weight chart of G1 in two categories (G1 and G2), (D) weight chart of G2 in two categories (G1 and G2), (E) distribution maps of G1 and G3, (F) the assigned groups to samples, (G) weight chart of G1 in two categories (G1 and G3), (H) weight chart of G3 in two categories (G1 and G3), (I) distribution maps of G2 and G3, (J) the assigned groups to samples, (K) weight chart of G2 in two categories (G2 and G3), (L) weight chart of G3 in two categories (G2 and G3).

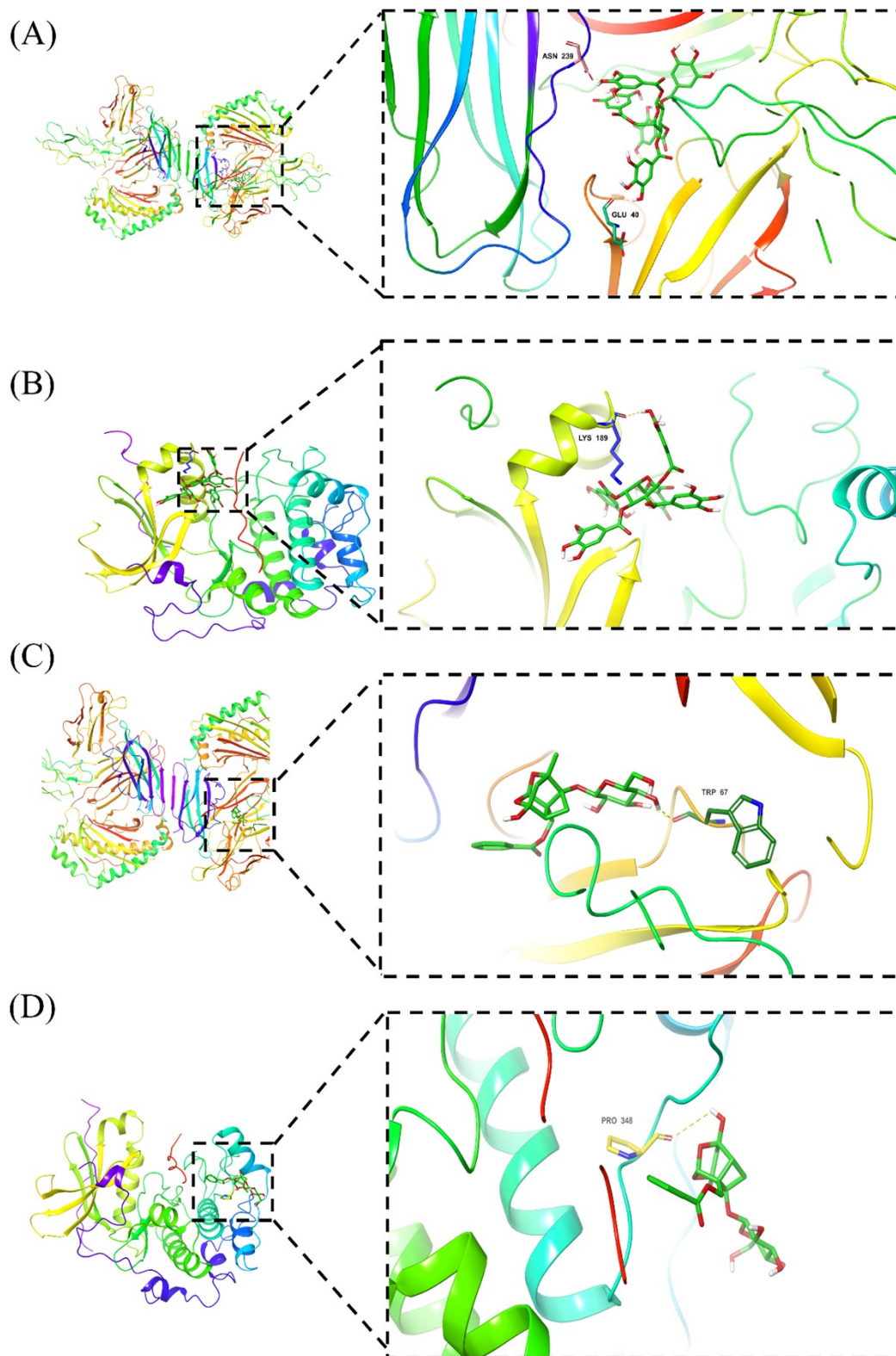


Fig.S7 Molecular docking results.

(A)1,2,3,4,6-O-Pentagalloylglucose-ACTB, (B) 1,2,3,4,6-O-Pentagalloylglucose-AKT1,

(C)paeoniflorin-ACTB, (D) paeoniflorin-AKT1.

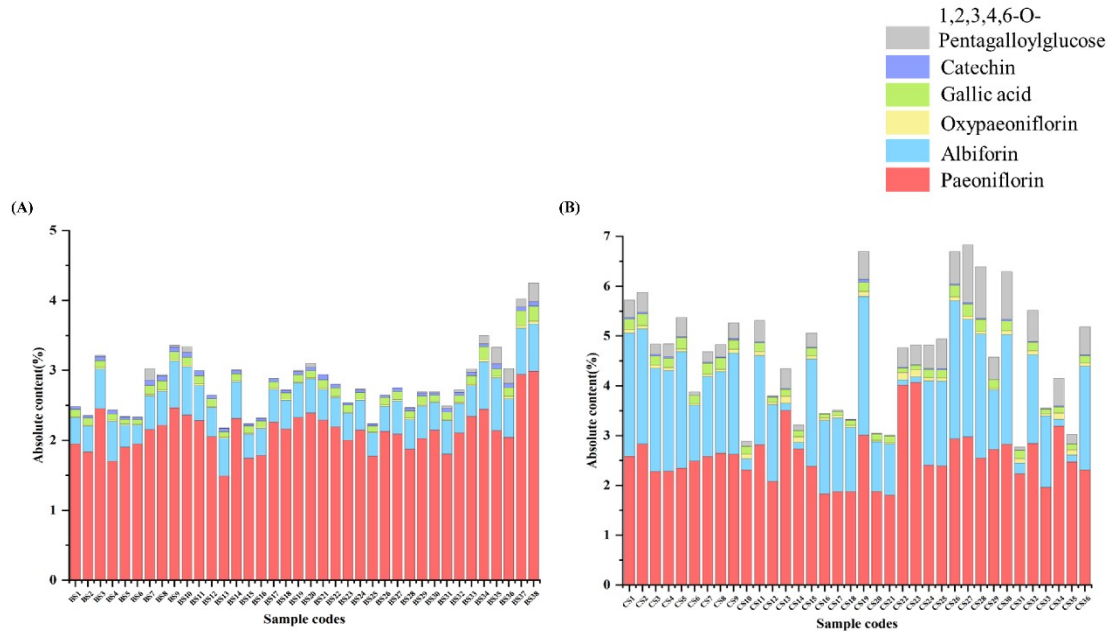


Fig. S8 Histograms of the mean content of paeoniflorin, albiflorin, oxypaeoniflorin, gallic acid, catechin, 1,2,3,4,6-O-Pentagalloylglucose. (A) PRA samples, (B) PRR samples.

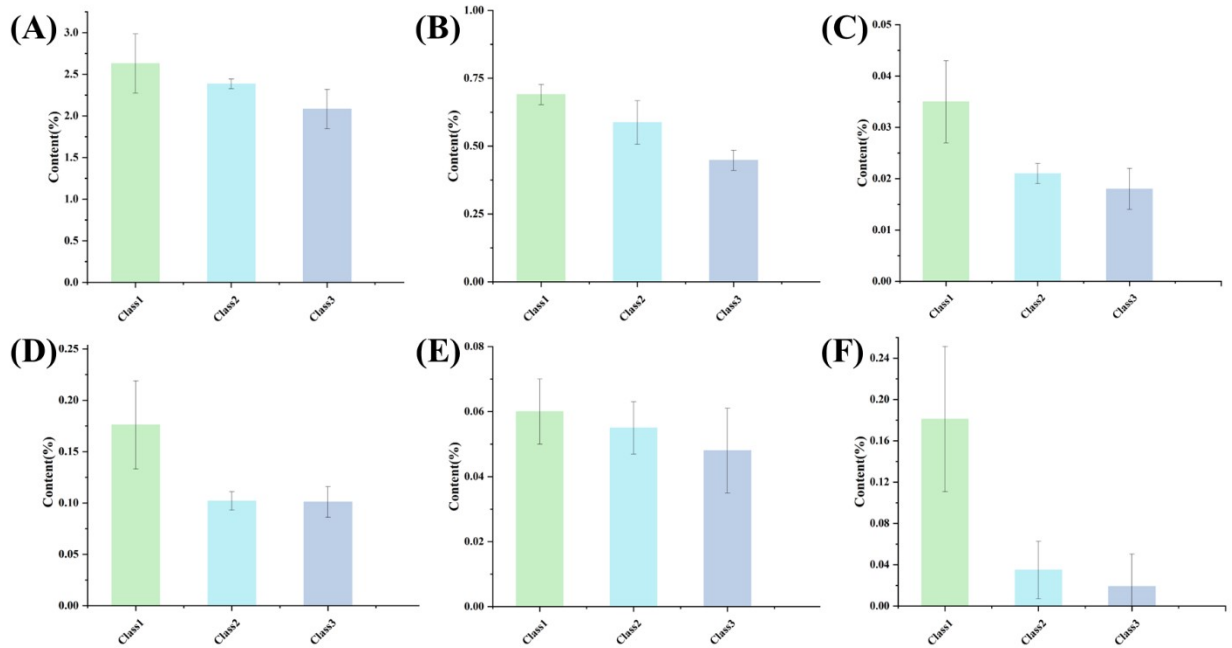


Fig. S9 Distribution of average content of PRA samples.

(A)paeoniflorin, (B) albiflorin, (C) oxypaeoniflorin, (D) gallic acid, (E) catechin, (F) 1,2,3,4,6-O-Pentagalloylglucose.Class1.vs Class2.vs Class3.

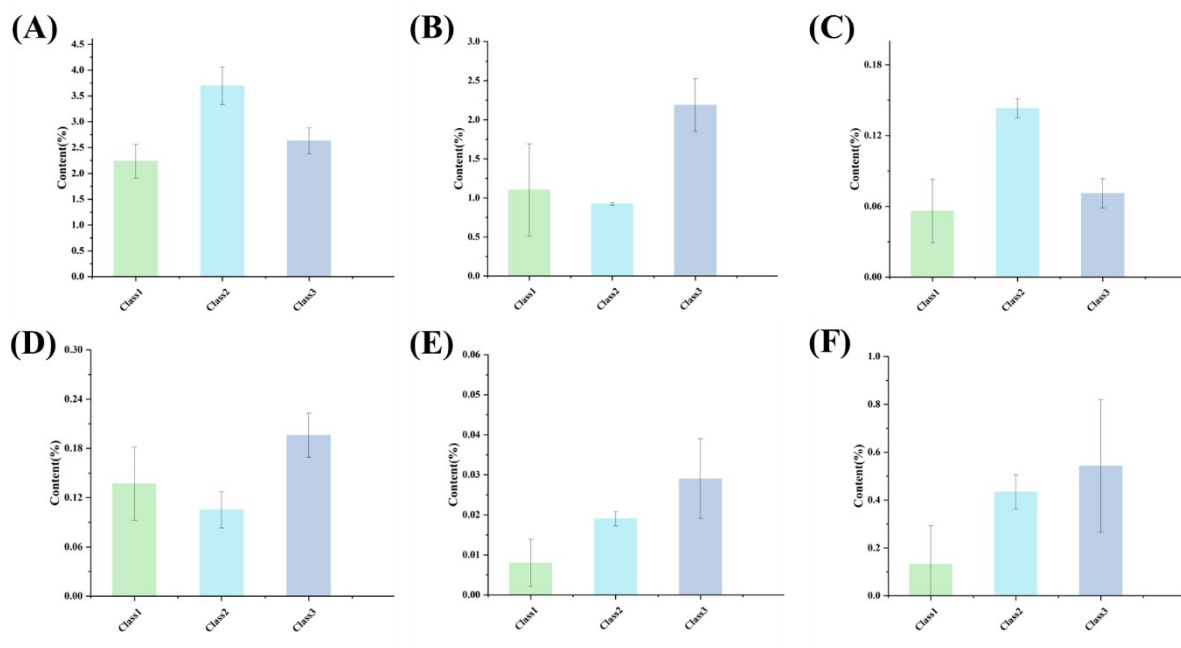


Fig. S10 Distribution of average content of PRR samples.

(A) paeoniflorin, (B) albiflorin, (C) oxypaeoniflorin, (D) gallic acid, (E) catechin, (F) 1,2,3,4,6-O-Pentagalloylglucose.Class1.vs Class2.vs Class3.