Table S1. Nuclear magnetic resonance characteristic signals of identified metabolites in red kidney bean.

No.	Metabolites	Assignment	δ ^{1}H multiplicity	Source
1	Valine	γ′-CH_3 γ-CH_3	1.01 (d,6.6 Hz), 1.06 (d,7.2 Hz)	K&C
2	Lactate	β-CH_3	1.34 (d,6.6 Hz)	K&C
3	Threonine	CH_3	1.35(d,4.8 Hz)	K&C
4	Alanine	β-CH_3	1.49 (d,7.2 Hz)	K&C
5	Arginine	β-CH2 γ-CH2	1.70 1.9 (m)	K&C
6	Acetic acid	CH_3	1.93 (s)	K&C
7	Acetamide	CH_3	1.99 (s)	K&C
8	GABA	α-CH_2	2.30 (t, 7.8 Hz)	K&C
9	Pyruvic acid	CH_3	2.36 (s)	K&C
10	Succinic acid	CH_2	2.44 (s)	K&C
11	Citrate	α-CH_2 α′-CH_2	2.55 (d,16.2 Hz), 2.71 (d,16.2 Hz)	K&C
12	Trimethylamine	CH_3	2.88 (s)	K&C
13	Choline	$N(CH_3)^+$	3.19 (s)	K&C
14	Betaine	$N(CH3)^+$	3.27 (s)	C
15	Fucose	1-H	4.55 (d,7.8 Hz) 5.18 (d,3.6 Hz)	C
16	Galactose	1-H	4.61 (d,7.8 Hz) 5.22 (d,3.6 Hz)	C
17	Glucose	1-H	4.64 (d,7.8 Hz) 5.21 (d,3.6 Hz)	C
18	Lactose	1-H	4.72 (d,7.2 Hz)	C
19	Raffinose	1-H	4.97 (d,3.6 Hz)	K&C
20	Stachyose	1-H	4.98 (d,3.0 Hz	K&C
21	Sucrose		5.42 (d,3.6 Hz)	K&C
22	Fumaric acid	CH	6.53 (s)	K&C
23	Unknown		8.04(t, 7.8 Hz) 9.11(s)	C
24	Formic acid	H-C=O	8.47 (s)	K&C
25	Adenosine	2’-H 2-H 8-H	6.03(d, 6.6 Hz) 8.24 (s) 8.36 (s)	K
26	Tyrosine	2-H 3-H	6.86 (d, 8.4 Hz) 7.19 (d, 8.4 Hz)	K
27	Phenylalanine	Ar-CH	7.4 (t, 7.8 Hz)	K
28	Uridine	1′-CH 2=CH	5.91 (d, 4.2 Hz) 7.94 (d,7.8 Hz)	K
29	Trigonelline	8-H 4-H	4.46 (s) 8.11 (dd, 6.6 Hz,7.8Hz)	K

	5-H	8.87 (dd, 7.8 Hz,6.6Hz)
	2-H	9.16 (s)

[a] Peaks observed as singlet (s), doublet (d), triplet (t), quartet (q), and multiplet (m).

[b] "C" stands for coat and "K" represents kernel.

Table S2. Identification of compounds in red kidney bean by UPLC-MS data.

No.	t_R	Molecular Formula	Selected ion	Experimental	Theoretical	MS/MS fragmentaion	Identification	Source
30	3.43	$C_7H_6O_4$	$[M-H]^-$	153.0188	153.0182	109.0287	Protocatechuic acid	C
31	3.73	$C_{30}H_{26}O_{12}$	$[M-H]^-$	577.1351	577.1340	407.0768,289.0723, 245.0823,161.0241, 125.0237	B-type procyanidin dimer	C
32	3.93	$C_{45}H_{38}O_{18}$	$[M-H]^-$	865.1988	865.1974	407.0782,289.0725, 245.0829, 125.0238	B-type procyanidin trimer	C
33	4.45	$C_{15}H_{14}O_6$	$[M-H]^-$	289.0720	289.0707	271.0612,245.0819,227.0711,221.0815, 205.0504,179.0345, 125.0236,109.0287	(-)-Epicatechin	C
34	7.24	$C_{30}H_{26}O_{12}$	$[M-H]^-$	577.1351	577.1340	407.0772,289.0724, 245.0815,161.0241, 125.0235	B-type procyanidin dimer	C
35	9.03	$C_{26}H_{28}O_{16}$	$[M+H]^+$	597.1448	597.1450	303.0498	Quercetin-3-O-arabinoglucoside	C
36	12.14	$C_{21}H_{20}O_{12}$	$[M-H]^-$	463.0886	463.0871	300.0279	Quercetin-3-O-hexoside	C
37	14.90	$C_{21}H_{20}O_{11}$	$[M-H]^-$	447.0937	447.0922	284.0330, 255.0299, 227.0349, 151.0034	Kaempferol-3-O-glucoside	C
38	10.97	$C_{27}H_{31}O_{16}$	$[M+H]^+$	611.1606	611.1606	303.0497	Rutinum	C
39	22.82	$C_{15}H_{10}O_7$	$[M-H]^-$	301.0356	301.0342	273.0414,257.0458, 229.0513,178.9982	Quercetin	C
40	25.91	$C_{15}H_{10}O_6$	$[M-H]^-$	285.0407	285.0394	285.0407	Kaempferol	C
41	11.89	$C_{21}H_{21}O_{12}$	$[M]^+$	465.1026	465.1027	303.0499	Delphinidin 3-O-glucoside	C
42	14.89	$C_{21}H_{21}O_{11}$	$[M]^+$	449.1075	449.1078	287.0548	Cyanidin-3-*O*-glucoside	C
43	16.52	$C_{15}H_{11}O_7$	$[M]^+$	303.0497	303.0499	285.0393	Delphinidin	C

44	25.93	$C_{15}H_{11}O_6$	$[M]^+$	287.0548	287.0550	287.0548	Cyanidin	C
45	21.54	C48H78O19	$[M+H]^+$	959.5204	959.5210	441.3718,423.3613, 405.3509	Soyasaponin Ba (V)	K
46	22.09	C48H78O18	$[M+H]^+$	943.5256	943.5261	441.3727,423.3616, 405.3508	Soyasaponin Bb (I)	K
47	24.16	C54H84O22	$[M+H]^+$	1085.5542	1085.5527	423.3617, 405.3511	Soyasaponin αg	K
48	24.37	C54H84O21	$[M+H]^+$	1069.5590	1069.5578	423.3619, 405.3512	Soyasaponin βg	K
49	24.76	C48H74O17	$[M+H]^+$	923.4987	923.4998	423.3617, 405.3507	Soyasaponin γg	K

[b] **"C" stands for coat and "K" represents kernel.**

Table S3. The differential metabolites in B16-F10 cell after treatment of RKBC.

No	t_R	Molecular Formula	Selected ion	Experimental	Theoretical	MS/MS fragmentaion	Identification
1	4.03	$C_{12}H_{25}N_5O_3$	$[M+H]^+$	288.2031	288.2030	271.1755, 270.1911, 253.1662, 175.1191, 86.0970	Leucylarginine
2	4.93	$C_{10}H_{18}N_2O_5$	$[M+H]^+$	247.1292	247.1288	229.1182, 201.1234, 184.0968, 183.1128, 132.1021, 86.0969	L-beta-aspartyl-L-leucine
3	4.97	$C_{12}H_{16}N_2O_4$	$[M+H]^+$	253.1184	253.1183	253.1184, 235.1077, 207.1128, 189.1021, 148.0755, 120.0810, 103.0546	Phenylalanyl-Serine
4	4.92	$C_9H_{17}NO_5$	$[M-H]^-$	218.1025	218.1023	146.0811, 99.0439, 88.0392, 71.0126	Pantothenic acid
5	2.65	$C_9H_{16}N_2O_5$	$[M-H]^-$	231.0977	231.0975	187.1078, 169.0969, 213.0872, 115.0025, 132.0299	Valyl-Aspartate
6	4.99	$C_{13}H_{18}N_2O_4$	$[M-H]^-$	265.1185	265.1182	247.1073, 221.0922, 164.0706, 147.0440, 73.0395	Threoninyl-Phenylalanine
7	4.56	$C_{10}H_{14}N_5O_6P$	$[M+H]^+$	332.0754	332.0754	136.0620, 81.0341	Deoxyadenosine monophosphate
8	4.90	$C_{10}H_{20}N_2O_4$	$[M+H]^+$	233.1498	233.1496	215.1392, 187.1442, 169.1336, 132.1020, 86.0970, 74.0607	Threoninyl-Leucine
9	4.68	$C_8H_{11}NO_3$	$[M-H]^-$	168.0656	168.0655	166.0498, 150.0549, 138.0549, 122.0599, 121.0520,	Pyridoxine
10	4.80	$C_{12}H_{25}N_5O_3$	$[M+H]^+$	288.2031	288.2030	270.1932, 271.1761, 253.1658, 157.1083, 112.0872, 86.0969, 70.0657, 69.0704	Arginyl-Leucine
11	5.02	$C_{14}H_{18}N_2O_5$	$[M-H]^-$	293.1138	293.1131	275.1029, 249.1229, 231.1131, 164.0706, 147.0440, 127.0501	gamma-Glutamylphenylalanine
12	2.21	$C_{10}H_{16}N_2O_7$	$[M-H]^-$	275.088	275.0873	257.0772, 231.0982, 213.0868, 146.0448, 128.0341	gamma-Glutamylglutamic acid
13	3.77	$C_{10}H_{18}N_2O_5$	$[M-H]^-$	245.1134	245.1132	227.1028, 228.1052, 201.1236, 116.0705	Glutamylvaline
14	4.91	$C_9H_{18}N_2O_4$	$[M-H]^-$	217.1184	217.1183	187.1077, 130.0861, 143.1178, 146.0811, 169.0967	Pantothenamide

15	5.49	$C_{18}H_{35}N_3O_4$	$[M-H]^-$	356.2546	356.2544	312.2644, 225.1596, 130.0862, 199.1804	Leu-Leu-Leu
16	5.13	$C_{14}H_{20}N_2O_3$	$[M-H]^-$	263.1396	263.1390	219.1493, 164.0706, 115.0865, 91.0541	Valyl-Phenylalanine
17	4.78	$C_{11}H_{20}N_2O_5$	$[M-H]^-$	259.1292	259.1288	241.1183, 215.1392, 171.1492, 130.0862, 102.0549	gamma-Glutamylleucine
18	5.09	$C_{12}H_{24}N_2O_3$	$[M-H]^-$	243.1707	243.1703	199.1807, 197.1646, 130.0862	Leucyl-Isoleucine
19	10.54	$C_{27}H_{51}O_{12}P$	$[M-H]^-$	597.3030	597.3034	281.2479, 78.9578, 241.0110, 259.0211, 315.0480, 152.9947	1-Oleoylglycerophosphoinositol
20	4.09	$C_{10}H_{13}N_4O_8P$	$[M-H]^-$	347.0390	347.0387	211.0004, 150.9784, 135.0302, 96.9684, 78.9578, 92.0240	Inosinic acid
21	12.92	$C_{25}H_{48}NO_7P$	$[M-H]^-$	504.3087	504.3085	307.2635, 140.0110, 214.0479, 196.0372, 152.9947, 78.9580	LysoPE(20:2(11Z,14Z)/0:0)
22	7.79	$C_{18}H_{34}O_5$	$[M-H]^-$	329.2326	329.2323	99.0801, 127.1119, 139.1119, 157.1219, 171.1015, 201.1100, 211.1331, 229.1438,	9,10,13-TriHOME
23	13.88	$C_{25}H_{50}NO_7P$	$[M-H]^-$	506.3234	506.3241	309.2791, 214.0477, 196.0371, 78.9578, 140.0107	LysoPE(20:1(11Z)/0:0)
24	11.16	$C_{23}H_{44}NO_7P$	$[M+H]^+$	478.2931	478.2928	337.2738, 263.2376, 216.0634, 121.1014, 81.0704	LysoPE(0:0/18:2(9Z,12Z))
25	4.70	$C_{10}H_{14}N_5O_8P$	$[M+H]^+$	364.0652	364.0653	152.0569, 135.0304, 110.0352, 97.0288	Guanosine monophosphate
26	3.40	$C_{10}H_{14}N_5O_7P$	$[M+H]^+$	348.0703	348.0704	136.0619, 250.0934	Adenosine monophosphate
27	10.56	$C_{21}H_{42}NO_7P$	$[M+H]^+$	452.2772	452.2772	311.2582, 237.2216, 219.2108, 216.0627, 198.0526	LysoPE(0:0/16:1(9Z))
28	7.74	$C_{13}H_{25}NO_3$	$[M+H]^+$	244.1908	244.1907	226.1803, 198.1856, 83.0861, 85.1016, 97.1016	N-Undecanoylglycine
29	4.28	$C_{10}H_{14}N_5O_8P$	$[M+H]^+$	364.0652	364.0653	152.0569, 135.0306	Cyclic GMP

Table S4. KEGG pathway enrichment for the targets of RKBC.

Term	P-value	FDR	Genes
Melanoma	0.0000	0.0000	PIK3CG, HRAS, IGF1, CDK6, HGF, CDK4, AKT1, IGF1R, MAPK1, KRAS, ARAF, MAPK3, FGF2, PIK3R1, AKT2
VEGF signaling pathway	0.0000	0.0000	PRKCA, PIK3CG, HRAS, PTGS2, SRC, AKT1, MAPK1, PTK2, KRAS, VEGFA, MAPK3, RAC1, PIK3R1, AKT2
Rap1 signaling pathway	0.0000	0.0000	PRKCA, PIK3CG, HRAS, DRD2, IGF1, HGF, KIT, EPHA2, SRC, AKT1, IGF1R, MAPK1, KRAS, RAC1, VEGFA, MAPK3, RHOA, FGF2, PIK3R1, AKT2
Ras signaling pathway	0.0000	0.0000	PRKCA, PIK3CG, HRAS, IGF1, HGF, KIT, EPHA2, AKT1, IGF1R, MAPK1, KRAS, VEGFA, MAPK3, RAC1, RHOA, ABL1, FGF2, PIK3R1, AKT2
PI3K-Akt signaling pathway	0.0000	0.0000	PRKCA, PIK3CG, HRAS, CREB1, IGF1, CDK6, KIT, HGF, CDK4, CDK2, EPHA2, AKT1, IGF1R, MAPK1, PTK2, KRAS, RAC1, VEGFA, MAPK3, FGF2, PIK3R1, AKT2
ErbB signaling pathway	0.0000	0.0000	PRKCA, PIK3CG, AKT1, MAPK1, PTK2, HRAS, KRAS, MAPK3, ARAF, ABL1, PIK3R1, SRC, AKT2
HIF-1 signaling pathway	0.0000	0.0000	PRKCA, PIK3CG, AKT1, MAPK1, IGF1R, MAPK3, VEGFA, IFNG, IGF1, NOS2, PIK3R1, AKT2
TNF signaling pathway	0.0000	0.0000	PIK3CG, AKT1, MAPK1, TNF, PTGS2, CREB1, MMP9, MAPK3, IL1B, MMP14, PIK3R1, AKT2
mTOR signaling pathway	0.0000	0.0001	PRKCA, PIK3CG, AKT1, MAPK1, TNF, MAPK3, IGF1, PIK3R1, AKT2
Toll-like receptor signaling pathway	0.0000	0.0113	PIK3CG, AKT1, MAPK1, TNF, MAPK3, RAC1, IL1B, PIK3R1, AKT2
GnRH signaling pathway	0.0000	0.0378	PRKCA, MAPK1, HRAS, KRAS, MAPK3, MMP14, MMP2, SRC
Apoptosis	0.0000	0.0393	PIK3CG, AKT1, TNF, CYCS, APAF1, PIK3R1, AKT2
p53 signaling pathway	0.0000	0.0614	SERPINB5, CYCS, IGF1, CDK6, APAF1, CDK4, CDK2
Melanogenesis	0.0001	0.0696	PRKCA, MAPK1, HRAS, TYR, KRAS, CREB1, MAPK3, KIT
MicroRNAs in cancer	0.0001	0.1304	PRKCA, HRAS, KRAS, PTGS2, SERPINB5, MMP9, VEGFA, RHOA, MMP16, CDK6, ABL1, PLAU
MAPK signaling pathway	0.0002	0.2439	PRKCA, AKT1, MAPK1, HRAS, TNF, KRAS, MAPK3, RAC1, IL1B, FGF2, AKT2
Glutathione metabolism	0.0016	1.9785	GSTM1, GSTT1, IDH1, GGT1, GSTP1
TGF-beta signaling pathway	0.0096	11.4085	MAPK1, TNF, MAPK3, IFNG, RHOA
NF-kappa B signaling pathway	0.0109	12.7813	TNF, PTGS2, LCK, IL1B, PLAU
Cell cycle	0.0349	35.8554	CDK6, ABL1, CDK4, CCNA2, CDK2

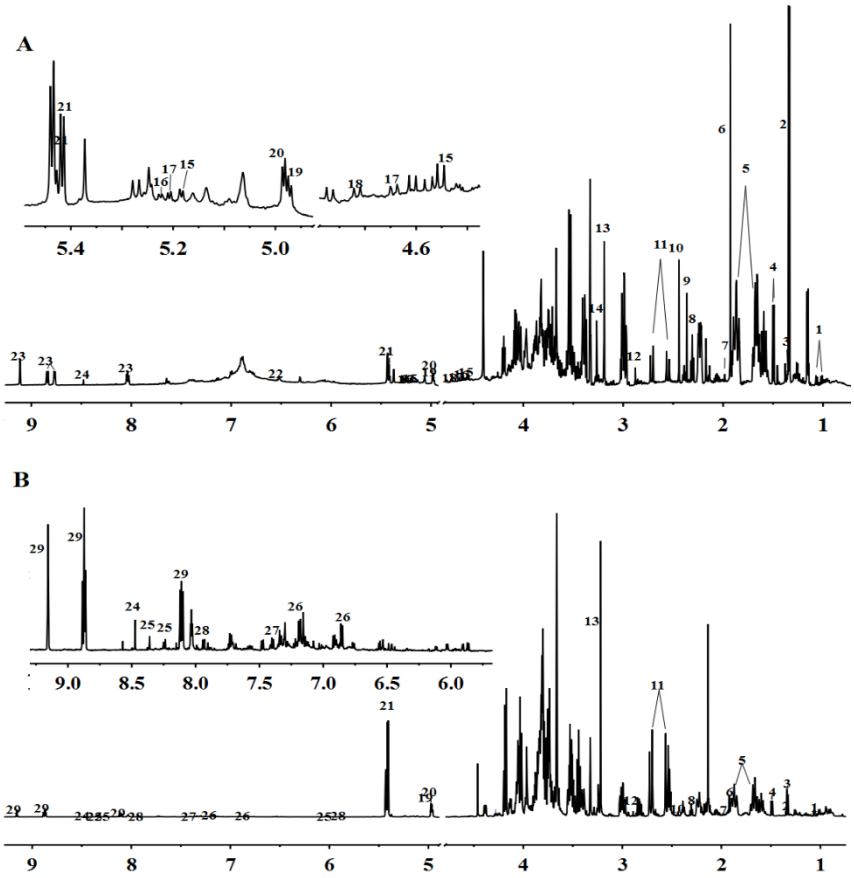

Fig. S1 Typical 600 MHz hydrogen nuclear magnetic resonance spectra of red kidney bean coat and kernel extract. (A) coat, (B) kernel.

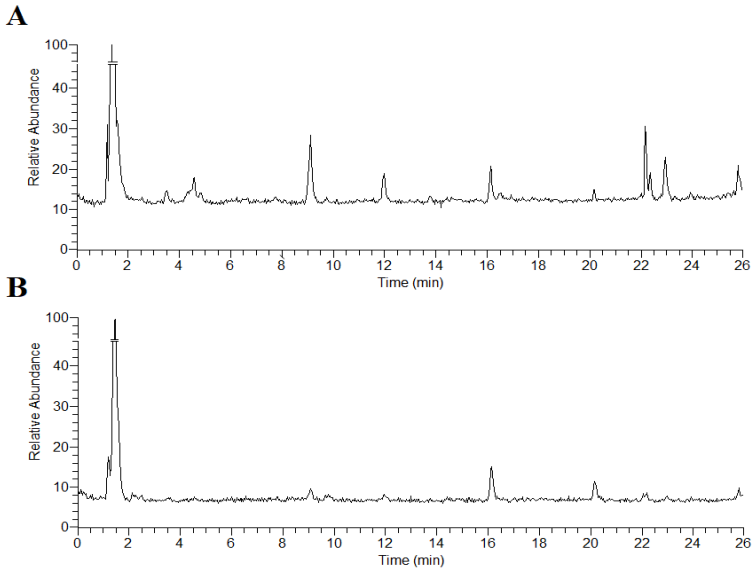

Fig. S2 TICs obtained from the LC-MS from the RKBC extract. (A) TICs in negative ion modes. (B) TICs in positive ion modes.

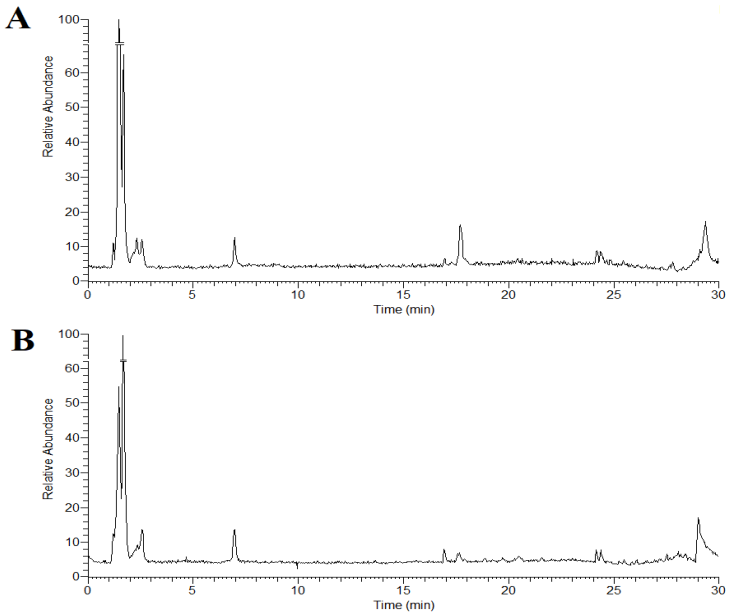

Fig. S3 TICs obtained from the LC-MS from the RKBK extract. (A) TICs in negative ion modes. (B) TICs in positive ion modes.

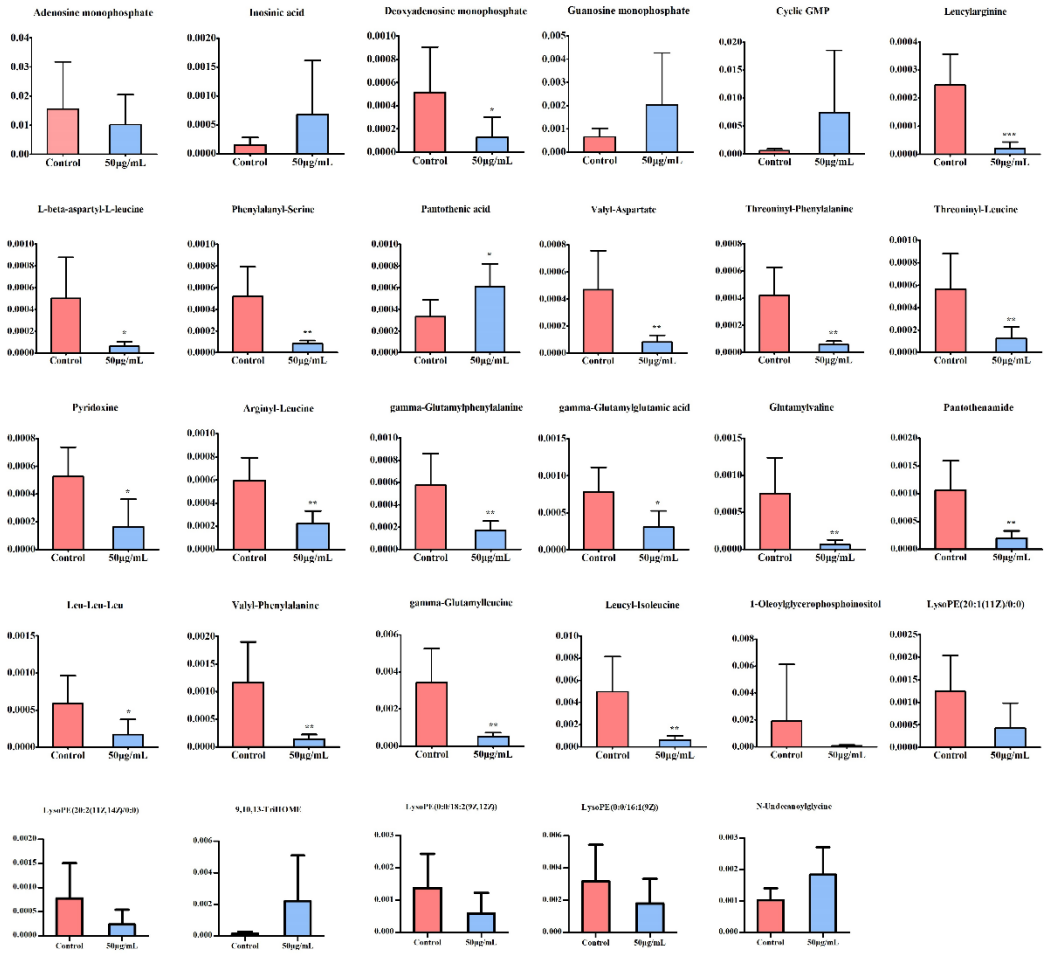

Fig. S4 The histogram showing the levels of differential metabolites between control and the group treated with 50 μg/mL RKBC extract.

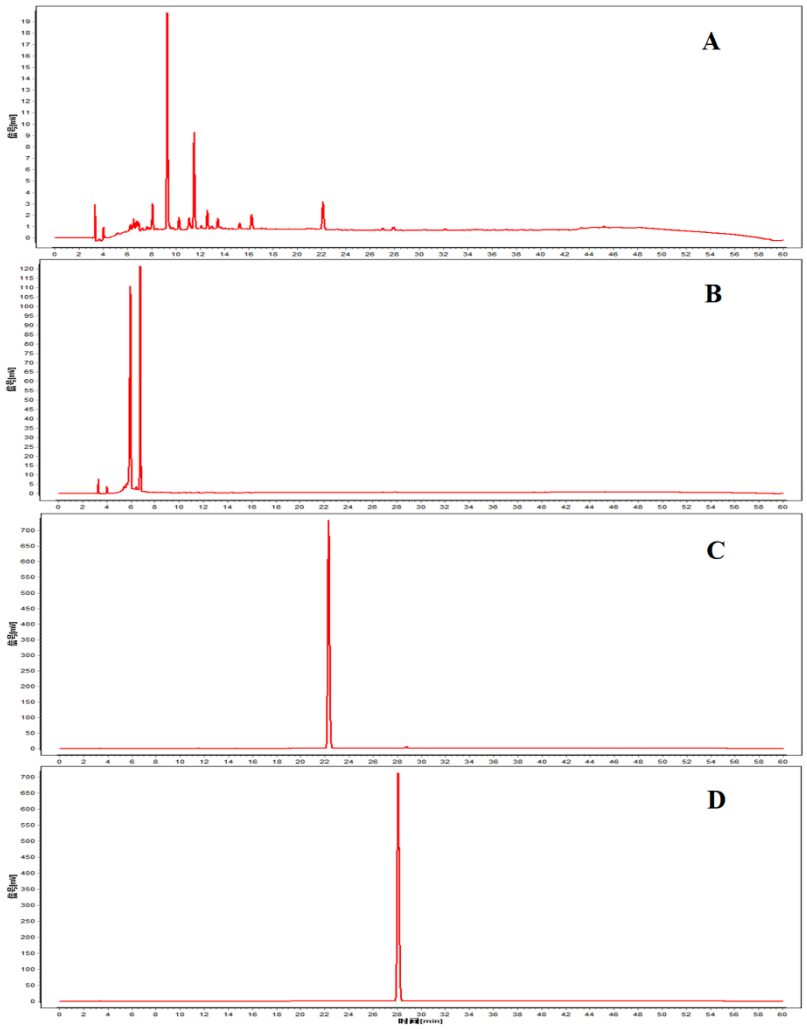

Fig.S5 HPLC spectra obtained of RKBC extract (A), cyanidin-3-O-glucoside (B) quercetin (C), and kaempferol (D). Agela-venusil MP C18 column（4.6 mm×250 mm, 5 μm, Waters）, with mobile phase consisting of 0.1% formic acid in water (phase A) and acetonitrile (phase B) at a flow rate of 1.0 mL/min. The gradient elution program was set as follows: 0-2 min, 90%-80% A; 2-40 min, 80%-45% A; 40-41 min, 45%-20% A; 41-45 min, 20%-20% A; 45-55 min, 20%-90% A; 55-60 min, 90%-90% A. The total chromatographic run time was 60 min. The injection volume was 5μL and the column temperature was at 30°C.