Supplementary Information (SI) for Analytical Methods.

Table S1 The origins of the SR.

ID	Origin	Batch number
CSR1, WSR1	Heilongjiang, China	200702
CSR2, WSR2	Jilin, China	200712
CSR3, WSR3	Shanxi, China	200520
CSR4, WSR4	Hebei, China	200702
CSR5, WSR5	Neimenggu, China	200420
CSR6, WSR6	Neimenggu, China	200705
CSR7, WSR7	Hebei, China	200801
CSR8, WSR8	Heilongjiang, China	200702
CSR9, WSR9	Jilin, China	191203
CSR10, WSR10	Neimenggu, China	200723
CSR11, WSR11	Hebei, China	200812
CSR12, WSR12	Heilongjiang, China	200712
CSR13, WSR13	Heilongjiang, China	200702
CSR14, WSR14	Hebei, China	200801
CSR15, WSR15	Henan, China	200812
CSR-1^	Neimenggu, China	191220
CSR-2^	Neimenggu, China	191228
CSR-3^	Shanxi, China	200725
CSR-4^	Gansu, China	200801
CSR-5^	Shanxi, China	200705
CSR-6^	Hebei, China	200702

SR: Scutellariae Radix; CSR: Crude Scutellariae Radix; WSR: wine-processed Scutellariae Radix.

Samples with "^" for verification experiments

Table S2 The NO inhibition rate of SR extracts at concentration of 200 μg/mL.

ID	NO Inhibition (%)	ID	NO Inhibition (%)
CSR1	72.47±0.43	WSR1	80.32±2.62
CSR2	46.26±0.76	WSR2	67.70±0.39
CSR3	68.81±0.58	WSR3	63.84±1.05
CSR4	65.74±1.30	WSR4	71.31±2.17
CSR5	53.14±1.73	WSR5	56.83±0.50
CSR6	72.05±3.27	WSR6	74.37±2.23
CSR7	33.92±0.51	WSR7	61.89±2.04
CSR8	72.38±4.36	WSR8	76.99±1.62
CSR9	62.14±1.27	WSR9	85.21±5.46
CSR10	83.90±4.55	WSR10	92.43±0.66
CSR11	67.94±0.72	WSR11	89.01±1.10
CSR12	80.92±0.70	WSR12	67.80±2.05
CSR13	59.62±1.60	WSR13	81.01±0.08
CSR14	36.31±0.57	WSR14	79.38±0.81
CSR15	74.42±0.30	WSR15	56.39±2.49

Table S3 Key components in samples contributing to the anti-inflammatory activities.

No.	Component	Type	VIP[1]	r^2
1	Wogonin	Flavonoid	3.37	0.752**
2	Baicalin	Flavonoid O-glycosides	3.27	0.560*
3	Baicalein	Flavonoid	2.70	0.752**
4	Oroxylin A	Flavonoid	2.66	0.682**
5	Wogonoside	Flavonoid O-glycosides	2.35	0.535*
6	Apigenin-7-O-β-D-glucuronide	Flavonoid O-glycosides	2.10	0.250
7	Oroxylin A-7-O-β-D-glucuronoside	Flavonoid O-glycosides	2.01	0.574*
8	Baicalin methyl ester	Flavonoid O-glycosides	2.01	0.574*
9	Chrysin-6-C-glucoside-8-C-arabinoside	Flavonoid O-glycosides	1.65	0.389
10	Chrysin-6-C-arabinoside-8-C-glucoside	Flavonoid O-glycosides	1.57	0.425

[1]: Variable importance for the projection. [2]: Pearson's correlation coefficients, where * and ** represent statistical significance at $p < 0.05$ and $p < 0.01$, respectively.

Table S4 Calibration curve, linear range, limit of detection (LOD) and limit of quantification (LOQ) of four analytes in SR by UHPLC-QqQ-MS/MS.

Compound	Calibration curve	r	Range（ng/mL）	LOD（ng/mL）	LOQ（ng/mL）
baicalin	Y=9626.2X-436010.0	0.9998	0.333-6652.800	0.083	0.333
baicalein	Y=1822.2X-569926.0	0.9992	12.780-3175.000	3.195	12.780
wogonin	Y=8397.1X+13308.0	0.9994	2.016-806.400	0.504	2.016
oroxylin A	Y=3187.4X+12809.4	0.9993	5.970-472.300	2.388	5.970

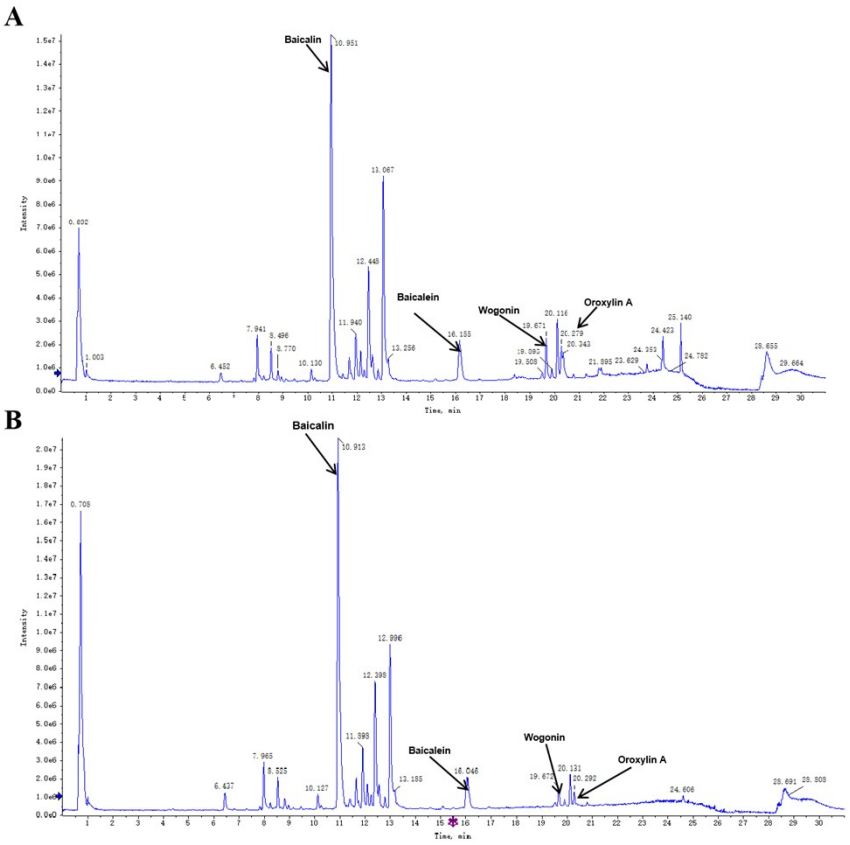

Fig.S1 The typical total ion chromatograms of SR in (A) positive ion and (B) negative ion mode.

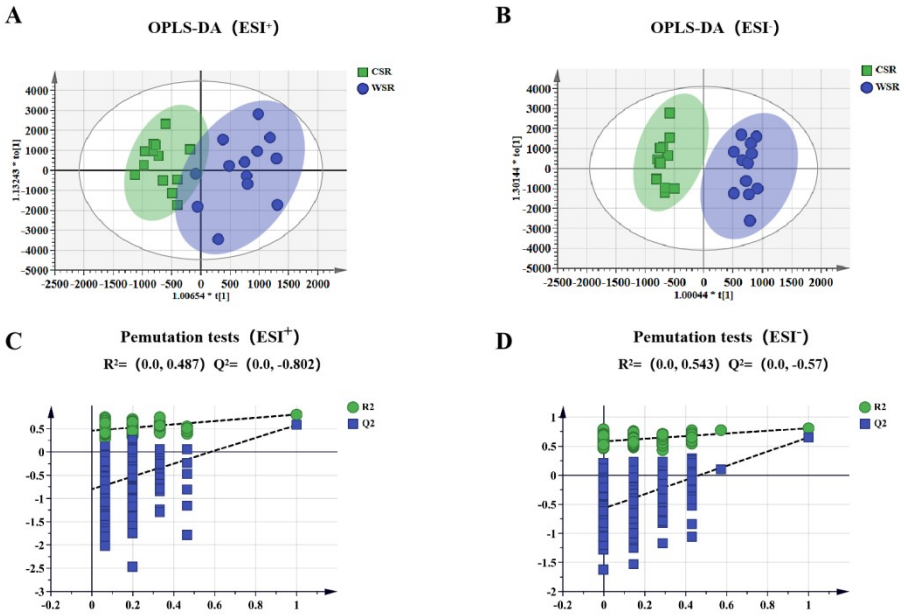

Fig.S2 Relation of the metabolomic profiles and the NO inhibition by a OPLS-DA model for SR. (A) OPLS-DA score scatter plots in positive ion mode, (B) OPLS-DA score scatter plots in negative ion mode, (C) permutation tests (n=200) of OPLS-DA in positive ion mode [R^2 = (0.0, 0.487), Q^2 = (0.0, -0.802)], (D) permutation tests (n=200) of OPLS-DA in negative ion mode [R^2 = (0.0, 0.543), Q^2 = (0.0, -0.57)].

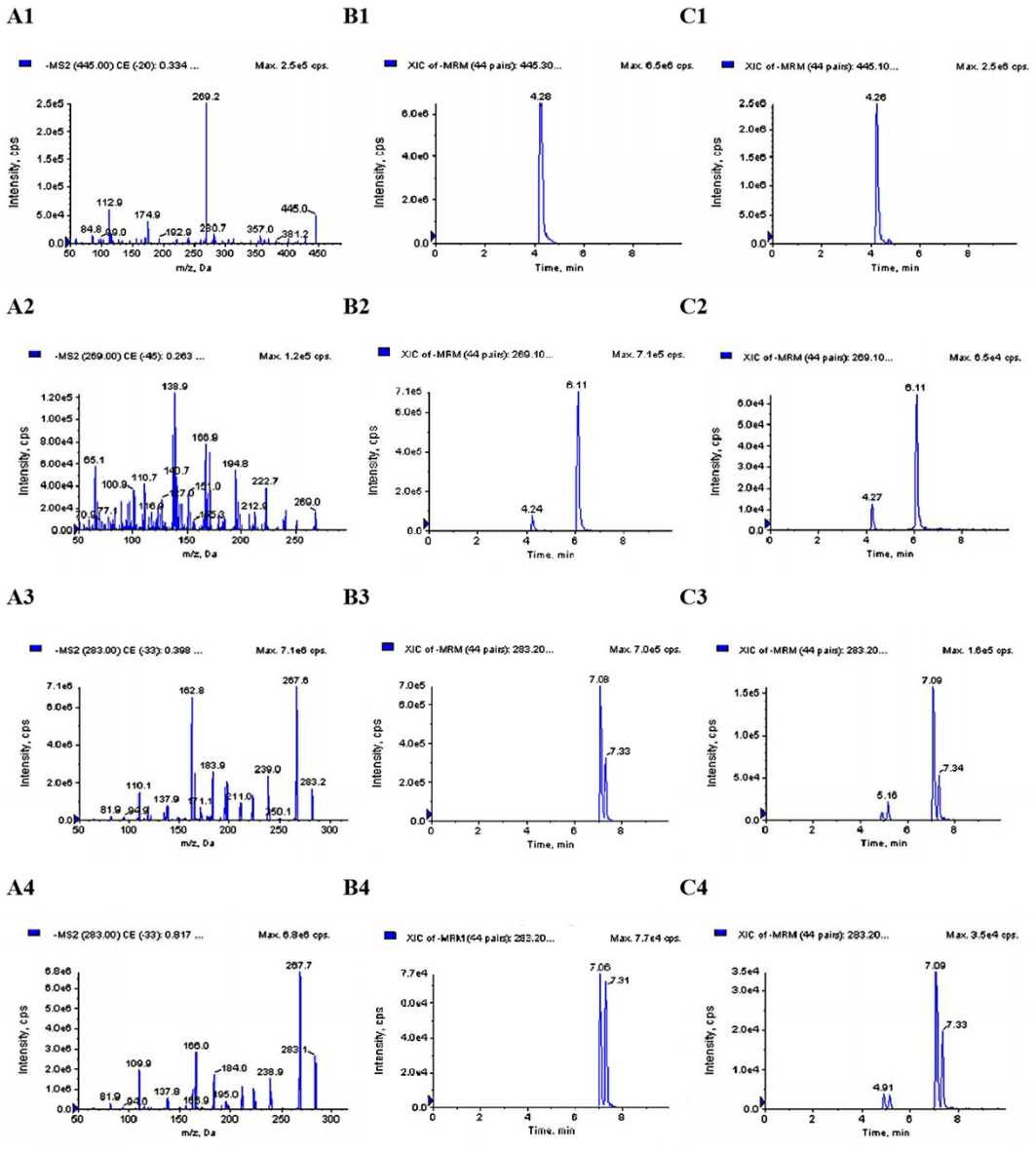

Fig. S3 UHPLC-QqQ-MS/MS chromatograms. The product ion spectrum of (A1) baicalin, (A2) baicalein, (A3) wogonin and (A4) oroxylin A, respectively. MRM of mixed standards of (B1) baicalin, (B2) baicalein, (B3) wogonin and (B4) oroxylin A, respectively. MRM of SR extract sample of (C1) baicalin, (C2) baicalein, (C3) wogonin and (C4) oroxylin A, respectively.

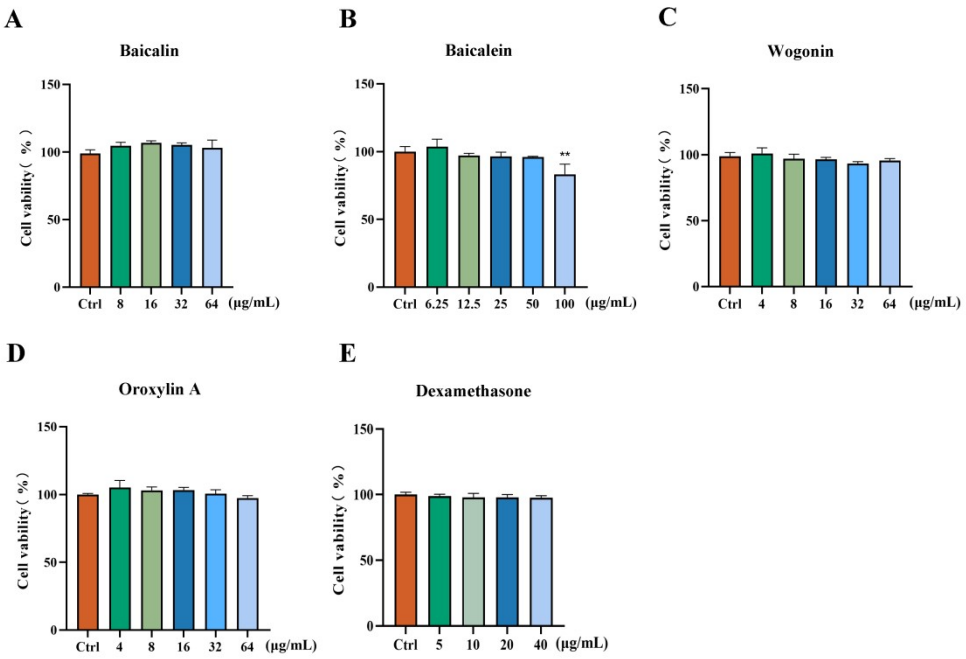

Fig S4 The cell viability of five components were performed on RAW 264.7 cells. (A) The baicalin at concentrations of 8-64 μg/mL, (B) balcalein at concentrations of 6.25-100 μg/mL, (C) wogonin at concentrations of 4-64 μg/mL, (D) oroxylin A at concentrations of 4-64 μg/mL, (E) dexamethasone at concentrations of 5-40 μg/mL. Data shown are the mean ± SD and statistically analyzed using one-way ANOVA test, ** $p < 0.01$ vs. control group.

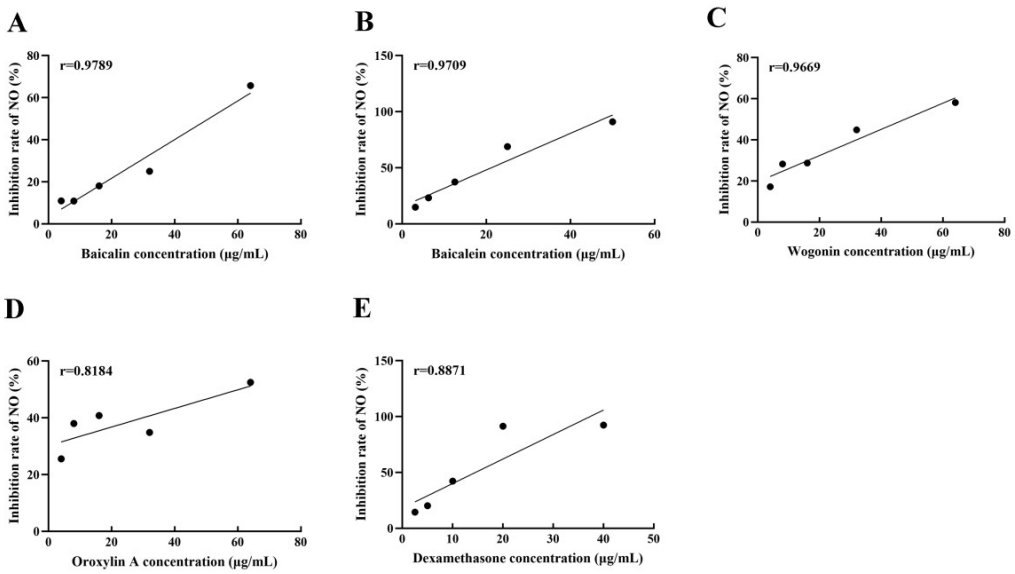

Fig. S5 The dose-dependent graphs of five components based on their NO inhibition rate. (A) The baicalin at concentrations of 4-64 μg/mL, (B) balcalein at concentrations of 3.125-50 μg/mL, (C) wogonin at concentrations of 4-64 μg/mL, (D) oroxylin A at concentrations of 4-64 μg/mL, (E) dexamethasone at concentrations of 2.5-40 μg/mL.

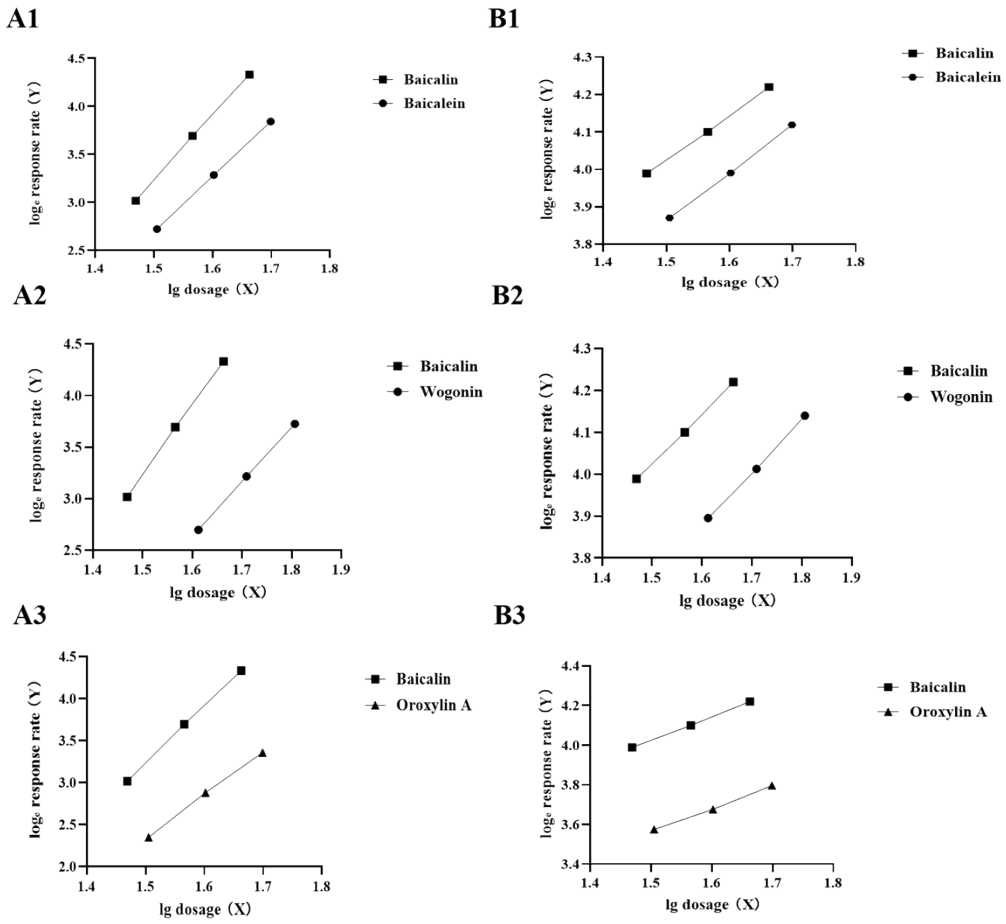

Fig. S6 The inhibition rate on TNF-α production curve of (A1) balcalein, (A2) wogonin, (A3) oroxylin A and reference substance baicalin. The inhibition rate on IL-6 production curve of (B1) balcalein, (B2) wogonin, (B3) oroxylin A and reference substance baicalin.