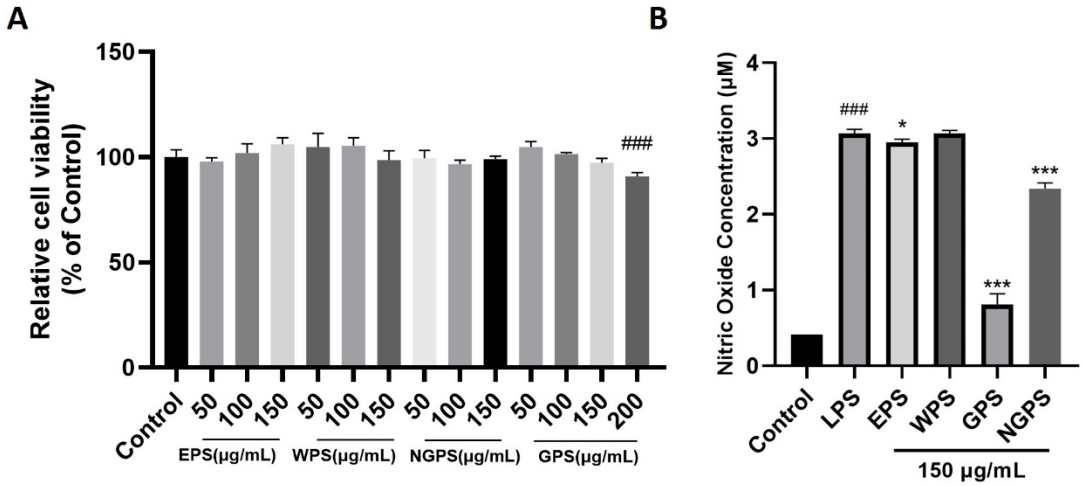

Figure S1 Anti-inflammatory effects of EPS, WPS, NGPS and GPS on LPS-induced RAW246.7 cells in vitro. (**A**) In vitro cytotoxicity of different concentrations of EPS, WPS, NGPS and GPS in RAW264.7 cells following 24 h of incubation, as revealed by CCK-8 assay. (**B**) NO release in LPS-stimulated RAW264.7 cells. (n = 3) Data represent the mean ± SD. ### $p < 0.001$ vs control group; *$p < 0.05$ or ***$P < 0.001$ vs LPS-stimulated group.

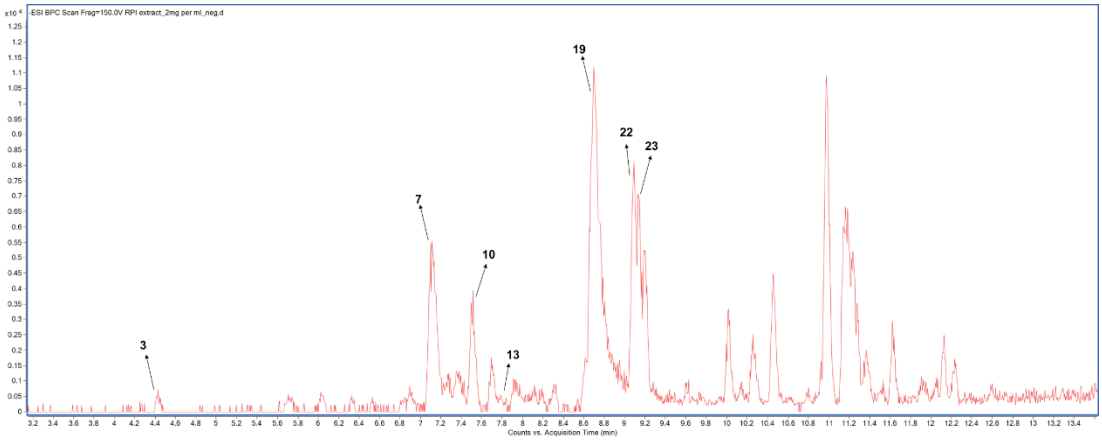

Figure S2 UPLC-Q-TOF-MS total ion current chromatogram of GPS in the negative ion mode.

Table S1. Primer Sequences of Genes

Gene	Sequence（5’-3’）
β-Actin Forward primer	CTGTCCCTGTATGCCTCTG
β-Actin Reversed primer	ATGTCACGCACGATTTCC
IL-6 Forward primer	GTTCTCTGGGAAATCGTGGA
IL-6 Reversed primer	TGTACTCCAGGTAGCTA
IL-1β Forward primer	GAAATGCCACCTTTTGACAGTG
IL-1β Reversed primer	TGGATGCTCTCATCAGGACAG
iNOS Forward primer	CAGGTCTTTGACGCTCGGAA
iNOS Reversed primer	GCCTGAAGTCATGTTTGCCG

Table S2. Information of 30 components of GPS extract determined by UPLC-Q/TOF-MS.

Peak	tR（min）	Assigned Identity	Molecular formula	Identify
1	3.009	Coniferin	$C_{16}H_{22}O_8$	Pos, Neg
2	4.272	Cinnamic acid	$C_9H_8O_2$	Pos
3	4.420	Sweroside	$C_{16}H_{22}O_9$	Pos, Neg
4	5.490	Apocynin	$C_9H_{10}O_3$	Pos
5	5.725	Scrocaffeside B	$C_{30}H_{34}O_{17}$	Pos
6	6.905	Luteoloside	$C_{21}H_{20}O_{11}$	Pos
7	7.152	1,6-dicaffeoyl-β-D-glucopyranoside	$C_{24}H_{24}O_{12}$	Pos, Neg
8	7.523	Verminoside	$C_{24}H_{28}O_{13}$	Pos
9	7.523	Picrosecosides	$C_{32}H_{40}O_{17}$	Pos
10	7.523	Scroneoside B	$C_{25}H_{28}O_{11}$	Pos, Neg
11	7.715	Picrosecosides Ⅰ	$C_{32}H_{40}O_{17}$	Pos
12	7.715	Picrogentiosides C	$C_{32}H_{42}O_{18}$	Pos
13	7.833	Scroneoside A	$C_{23}H_{26}O_{11}$	Pos, Neg
14	8.122	6-Feruloylcatalpol	$C_{25}H_{30}O_{13}$	Pos
15	8.122	Aucubin	$C_{15}H_{22}O_9$	Pos
16	8.180	2-(3,4-dihydroxyphenyl)-ethyl-O-β-D-glucopyranoside	$C_{14}H_{20}O_8$	Pos
17	8.570	Picroside Ⅱ	$C_{23}H_{28}O_{13}$	Pos
18	8.591	Piceoside	$C_{14}H_{18}O_7$	Pos
19	8.708	Luteolin	$C_{15}H_{10}O_6$	Pos, Neg
20	8.799	Picroside Ⅳ	$C_{24}H_{28}O_{12}$	Pos
21	8.799	Piscrosides A	$C_{23}H_{30}O_{13}$	Pos
22	9.024	Piscrosides B	$C_{24}H_{30}O_{12}$	Pos, Neg
23	9.092	Picroside Ⅰ	$C_{24}H_{28}O_{11}$	Neg
24	9.141	Caffeic acid	$C_9H_8O_4$	Pos
25	9.342	Scroside D	$C_{20}H_{30}O_{13}$	Pos
26	9.513	Picrorosides B	$C_{32}H_{36}O_{15}$	Pos
27	10.998	Caffeic acid methyl ester	$C_{10}H_{10}O_4$	Pos
28	11.211	Vanillic acid	$C_8H_8O_4$	Pos
29	11.970	Scroside B	$C_{31}H_{40}O_{16}$	Pos
30	13.819	Palmitic acid	$C_{16}H_{32}O_2$	Pos

Table S3. Residues of ERK, JNK, p38 and Akt interacting with luteolin, luteoloside and Picroside II in the optimal conformation

Protein	Residues	Luteolin	Luteoloside	Picroside II
ERK	Tyr36	hydrophobic, pi-pi stacking	hydrophobic, pi-pi stacking	hydrophobic
	Val39	hydrophobic	hydrophobic	hydrophobic
	Lys54	hydrogen bond	hydrogen bond, pi-cation	hydrogen bond
	Arg67	hydrophobic	—	—
	Asp106	hydrogen bond	—	hydrogen bond
	Lys151	—	—	hydrogen bond
	Ser153	—	—	hydrophobic
	Leu156	—	—	hydrophobic
	Asp167	hydrophobic	hydrophobic	hydrogen bond, hydrophobic
JNK	Ile32	hydrophobic	hydrophobic	hydrophobic
	Gly35	—	—	hydrophobic
	Gln37	—	—	hydrophobic
	Val40	hydrophobic	hydrophobic	hydrophobic
	Lys55	—	hydrogen bond	—
	Gln57	—	hydrogen bond	—
	Glu109	—		hydrogen bond
	Met111	hydrogen bond	hydrogen bond	hydrogen bond
	Ala113	—	hydrophobic	—
	Asp151	—	—	hydrogen bond
	Lys153	—	—	hydrogen bond
	Ser155	—	—	hydrogen bond, hydrophobic
	Leu168	hydrophobic, pi-cation	hydrophobic	hydrophobic
p38	Ile31	hydrophobic	hydrophobic	hydrogen bond, hydrophobic
	Try36	—	hydrophobic	
	Val39	hydrophobic	hydrophobic	hydrophobic
	Ala52	—	—	hydrogen bond, hydrophobic
	Lys54	hydrophobic	hydrogen bond	hydrophobic
	Leu103	hydrogen bond	—	—
	Thr105	—	hydrogen bond	—
	Met108	—	hydrogen bond	hydrogen bond
	Lys114	hydrogen bond	—	hydrogen bond
	Ser153	—	—	hydrophobic
	Leu156	hydrophobic	hydrophobic	hydrophobic
	Cys166		hydrophobic, pi-	hydrophobic

			cation	
	Asp167	—	hydrogen bond	—
Akt	Gly157	hydrogen bond	—	—
	Phe161	—	hydrophobic	hydrophobic
	Val164	hydrophobic	hydrophobic	hydrophobic
	Ala230	hydrogen bond	—	—
	Glu234	hydrophobic	—	hydrogen bond
	Asn279	—	hydrogen bond	—
	Met281	hydrophobic	hydrophobic	hydrophobic
	Thr291	hydrophobic	hydrophobic	hydrogen bond
	Asp292	hydrogen bond	hydrogen bond, hydrophobic	hydrophobic