

SUPPLEMENTARY MATERIAL

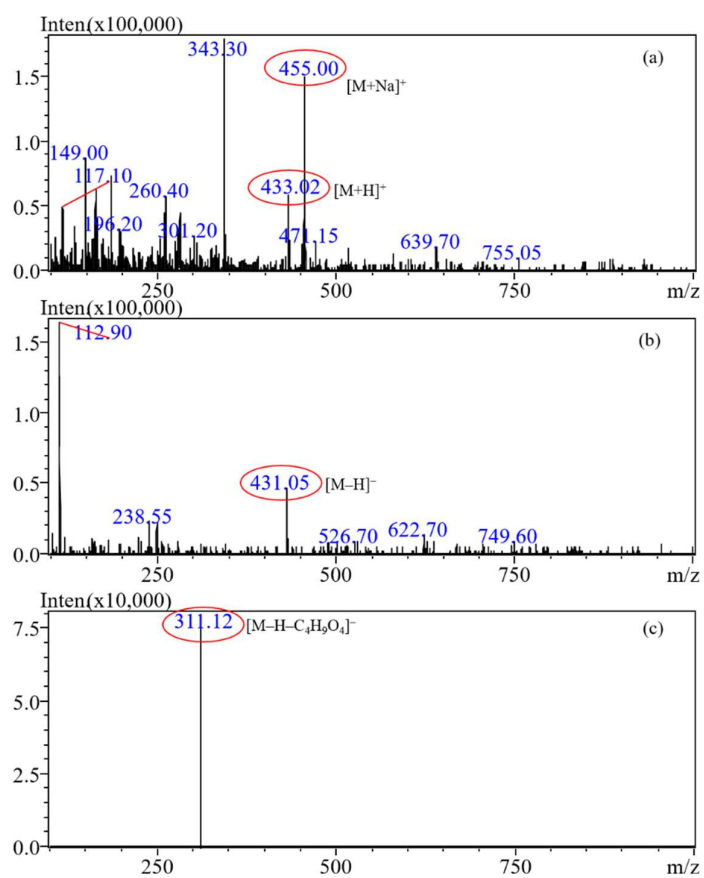


Figure S1. Mass spectrometry (MS) and MS/MS spectrum of isovitexin. (a) MS spectrum in positive mode; (b) MS spectrum in negative mode; (c) MS/MS spectrum in negative mode

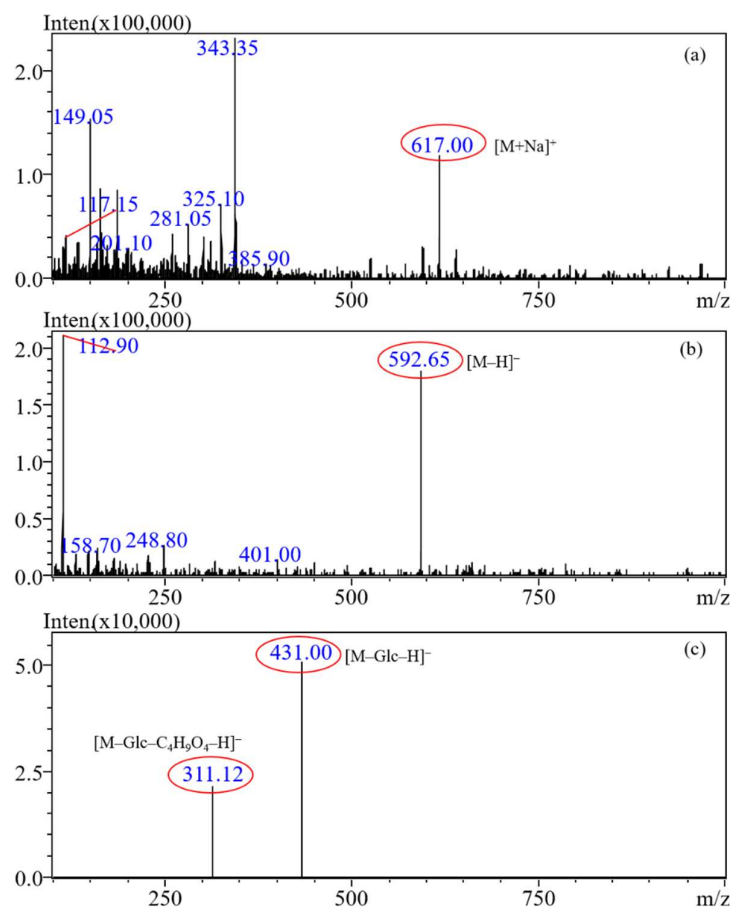


Figure S2. Mass spectrometry (MS) and MS/MS spectrum of isovitexin-3''-O-glucopyranoside. (a) MS spectrum in positive mode; (b) MS spectrum in negative mode; (c) MS/MS spectrum in negative mode.

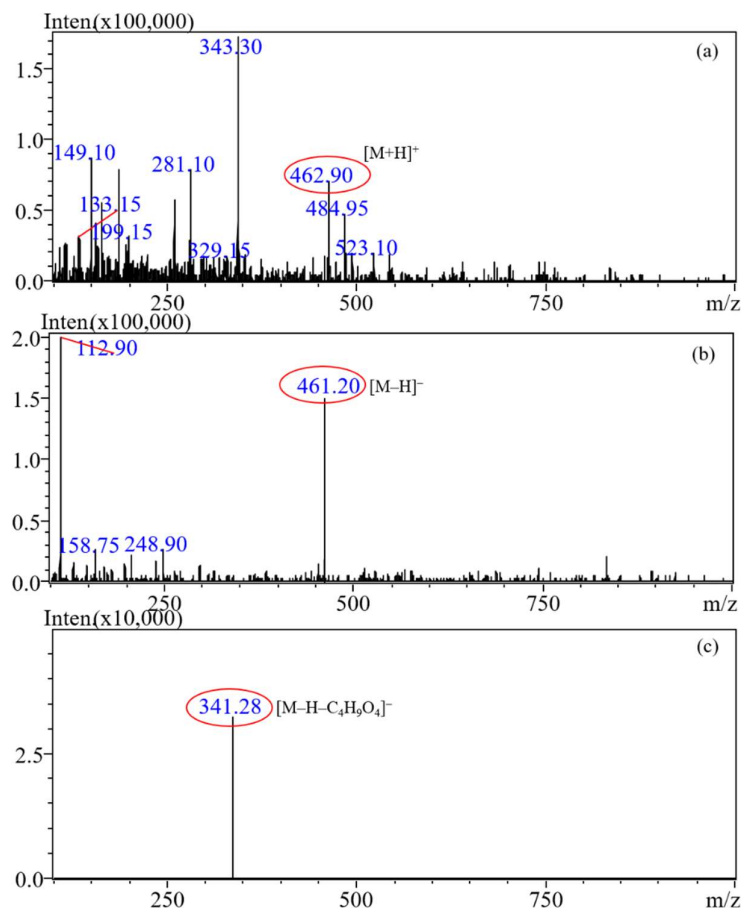


Figure S3. Mass spectrometry (MS) and MS/MS spectrum of isoscoparin. (a) MS spectrum in positive mode; (b) MS spectrum in negative mode; (c) MS/MS spectrum in negative mode.

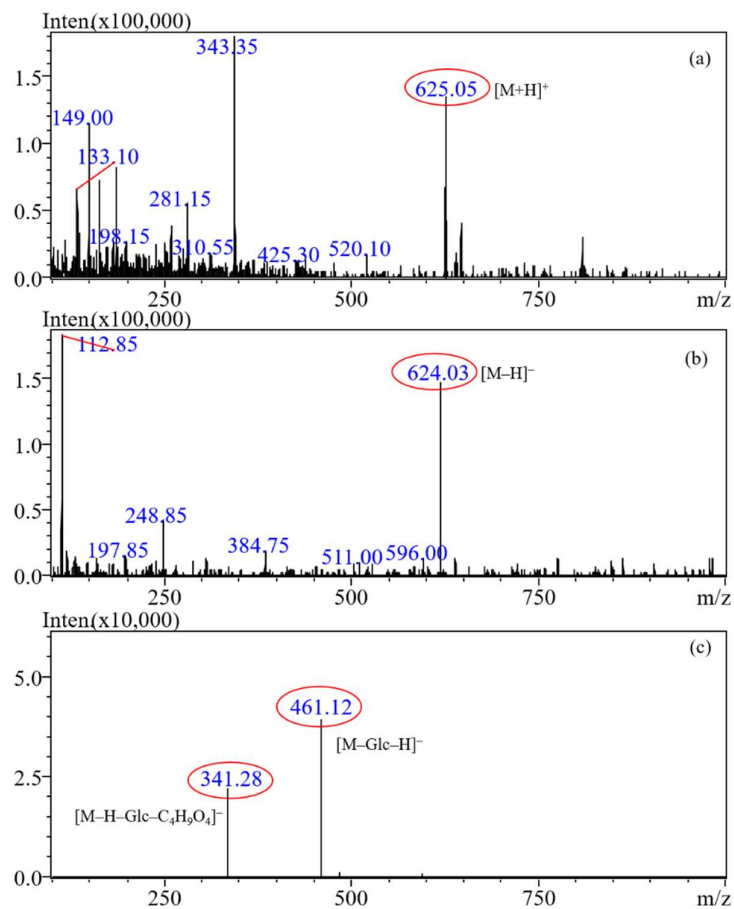


Figure S4. MS and MS/MS spectrum of isoscoparin-3''-O-glucopyranoside. (a) MS spectrum in positive mode; (b) MS spectrum in negative mode; (c) MS/MS spectrum in negative mode.

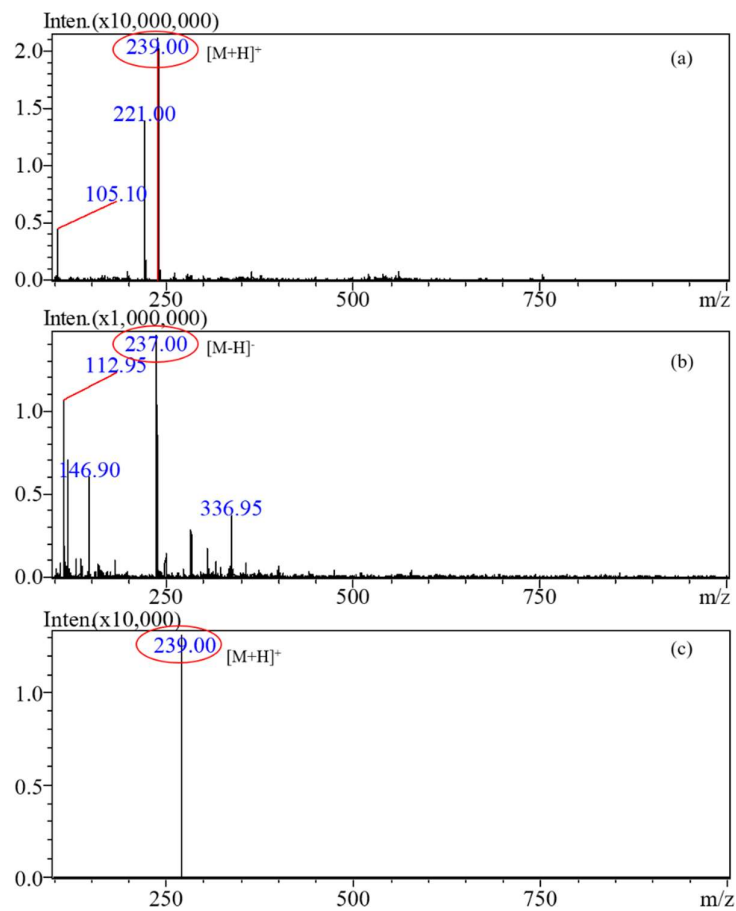


Figure S5. Mass spectrometry (MS) and MS/MS spectrum of TMCA (3,4,5-trimethoxycinnamic acid). (a) MS spectrum in positive mode; (b) MS spectrum in negative mode; (c) MS/MS spectrum in positive mode.

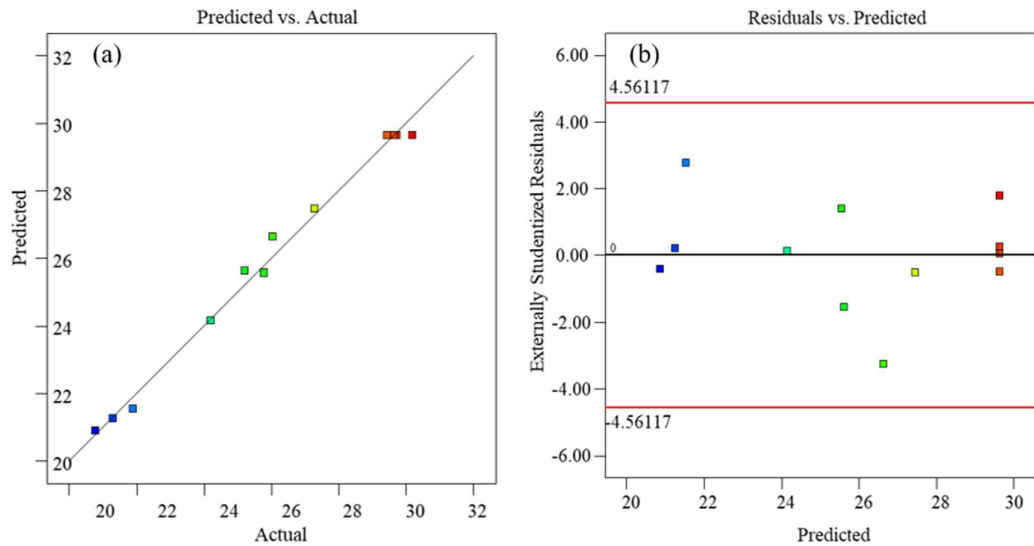


Figure S6. The plot of actual values versus predicted values for extraction 3,4,5-trimethoxycinnamic acid (a) and residual plot (b).

Table S1. Validation data of TMCA (3,4,5-trimethoxycinnamic acid).

Parameters	TMCA
Linearity range (µg/mL)	1–10
Coefficient of determination (R^2)	0.9996
Equation	$y = 360x - 60$
limit of detection (ng/mL)	6.08
limit of quantitation (ng/mL)	18.44
Precision	
Intra-day (%RSD)	0.2–0.6
Inter-day (%RSD)	1.9–3.2
Accuracy	
Intra-day (%RSD)	97.3–101.4
Inter-day (%RSD)	103.1–107.0
Recovery (%)	99.18–107.20
Repeatability	
Retention time (%RSD)	0.23
Content (%RSD)	0.18

^aRSD: relative standard deviation

Table S2. Evaluation of central composite design (CCD) predicted model by ANOVA.

Source	SS ^a	df ^b	Mean Square	F-value ^c	p-Value	
Model	139.99	5	28	175.99	< 0.0001	significant
A-Sonication time	9.23	1	9.23	57.99	0.0001	
B-Methanol-to-material ratio	4.99	1	4.99	31.35	0.0008	
AB	4.84	1	4.84	30.42	0.0009	
A ²	49.51	1	49.51	311.22	< 0.0001	
B ²	26.35	1	26.35	165.65	< 0.0001	
Residual	1.11	7	0.1591			
Lack of Fit	0.8053	3	0.2684	3.48	0.1297	Not significant
Pure Error	0.3083	4	0.0771			
Cor Total ^d	141.10	12				
R ²	0.9921					
C.V. %	1.52		Adjusted R ²	0.9865		
			Predicted R ²		0.9495	

^a SS: Sum of squares. ^b df: Degree of freedom. ^c F value was calculated by mean square of residual divided by mean square of source. ^d Cor total: Sum of squares and df.

Table S3. The response value of prediction and experiment acquired by the optimal conditions ($n = 3$).

	A (min)	B: (mL/g)	Content of TMCA^a Y (μg/g)
Predicted	38.31	6.47	29.81
Experimental	38	6	29.17
Matching (%)			97.85%

^aTMCA: 3,4,5-trimethoxycinnamic acid

Table S4. Primers sequences using for real-time reverse-transcription polymerase chain reaction.

Primer	Sequence
Forward	3'-CTC CAA CGA GAT CGA GTA C-5'
Procollagen	
Reverse	3'-GTT ACA GGA AGC AGA CAG G-5'
Forward	3'-GAT GTG GAG TGC CTG ATG TG-5'
MMP-1	
Reverse	3'-TGC TTG ACC CTC AGA GAC CT-5'
Forward	5'-TAG GAG GTT ATC CTA AAA GCA-3'
MMP-3	
Reverse	5'-CCA GCT ATT GCT CTT CAA GCA-3'
Forward	5'-GAC TCA TGG GAT GAT GAT GAT AAC-3'
IL-1 β	
Reverse	5'-CCA TAC TTT AGG AAG ACA CGG ATT-3'
Forward	5'-TCG GCA TTT TGA ACG AGG TC-3'
IL-4	
Reverse	5'-GAA AAG CCC GAA AGA G TC-3'
Forward	5'-TGG GCT CCA AGC AGA TGC-3'
36B4	
Reverse	5'-GGC TTC GCT GGC TCC CAC -3'