

Supplementary materials

Title: Inhibition of α -glucosidase activity and intestinal glucose transport to assess *in vivo* anti-hyperglycemia potential of dodecyl-acylated phlorizin and polydatin derivatives

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Table S1 Sequences of the primers used for RT-qPCR

Gene	Direction	Primer (5'-3')
<i>β-Actin</i>	Forward	TAGTTGCGTTACACCCTTTCTTG
	Reverse	TCACCTTCACCGTTCCAGTTT
<i>SGLT1</i>	Forward	TTCACGAAGTGGGAGGCTAT
	Reverse	GAGTCGGCCCTTGGAGTGTA
<i>GLUT2</i>	Forward	ATGAGTGGGATGTTTGTGTTGTG
	Reverse	AACTCAGCCACCATGAACCA
<i>PKA</i>	Forward	CCATCAAGGCTATATCCAGGTC
	Reverse	TGCCTTATTGTAGCCCTTGC
<i>Na⁺/K⁺ ATPase</i>	Forward	TTGGGGTTGCTATGGGGATT
	Reverse	TTGGGGTTGCTATGGGGATT

Table S2 Effect of dodecyl phlorizin and dodecyl polydatin on the secondary structure of α -glucosidase

Compound	Concentration (μ M)	α -Helix (%)	β -Sheet (%)	β -Turn (%)	Random coil (%)
Dodecyl phlorizin	0	43.8	13.9	16.7	25.4
	50	39.6	17.7	18.6	24.1
	75	32.7	21.7	18.4	27.2
	90	28.0	24.6	18.0	29.4
Dodecyl polydatin	0	43.8	13.9	16.7	25.4
	50	40.2	17.9	18.8	23.2
	70	37.4	19.0	18.6	24.9
	90	30.7	22.7	18.2	28.4

Table S3 Information on catalytic and allosteric sites of α -glucosidase molecule and docking box

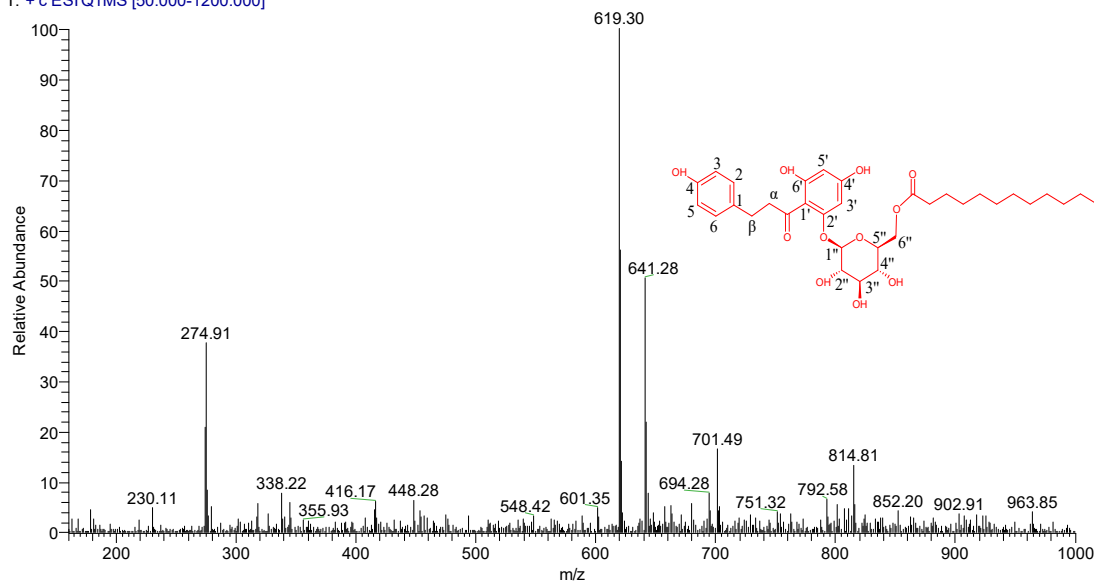
Sites	Box coordinate (X, Y, Z)	Box size (X, Y, Z)	Volum e [\AA^3]	Surface [\AA^2]	Depth [\AA]
Catalytic site 1	20.04, -6.90, 21.77	40, 40, 40	191.49	265.77	10.91
Allosteric site 2	16.11, 11.76, 32.79	60, 40, 56	165.45	371.65	10.31
Allosteric site 3	12.86, -22.07, 14.89	50, 50, 60	156.57	305.71	8.62
Allosteric site 4	13.66, -11.01, 17.57	40, 40, 40	141.82	319.39	7.29
Allosteric site 5	14.09, 1.86, 0.05	50, 46, 48	69.63	120.93	5.43

Table S4 Binding energy, inhibition constant and hydrogen bonds of substrate and inhibitors with catalytic and allosteric sites

Compound	Site	Binding energy (kcal/mol)	Inhibition constant	Hydrogen bond
pNPG	1	-6.63	13.91 μ M	Asp69, asp215, glu277, arg315, asp352, gln353
Acarbose	1	-4.29	714.62 μ M	Asp69, tyr158, arg213, asp215, glu277, gln279, arg315, asp352, arg442
Phlorizin	1	-7.46	3.4 μ M	Asp69, his112, gln182, glu277, arg315, asp352, glu411, asn415
Polydatin	1	-7.32	4.32 μ M	Arg213, asp215, glu277, asn350, asp352, glu411
Dodecyl phlorizin	1	-1.8	47.78 mM	Tyr158, glu277, gln279, his280, asp352, glu411, arg442
	2	-7.27	4.65 μ M	Asn259, arg270, ser291, his295, glu296
	3	-5.38	113.46 μ M	Asn235, asn317, asn415, glu429
	4	-7.29	4.54 μ M	Asp242, gln279, glu411, asn415
	5	-4.63	2.68 mM	Phe321, thr358, asp362, ser545
Dodecyl polydatin	1	-5.17	162.9 μ M	Asp69, gln279, his280, arg315, glu411

2	-6.74	11.51 μ M	Asn259, arg263, arg270, ile272, his295, asp341
3	-6.07	35.25 μ M	Gly161, asp233, ser311, asn317, glu422
4	-8.60	497.09 nM	Lys156, asp242, asp307, thr310, leu313, arg315, asn415
5	-6.0	40.24 μ M	Leu323, phe360, asp362, lys523

Lauryl Phlorizin ms #19 RT: 0.22 AV: 1 NL: 6.80E6
T: + c ESI Q1MS [50.000-1200.000]



Lauryl Phlorizin ms2 #152 RT: 1.38 AV: 1 NL: 3.27E5
T: + c ESI Full ms2 619.270 [40.000-1200.000]

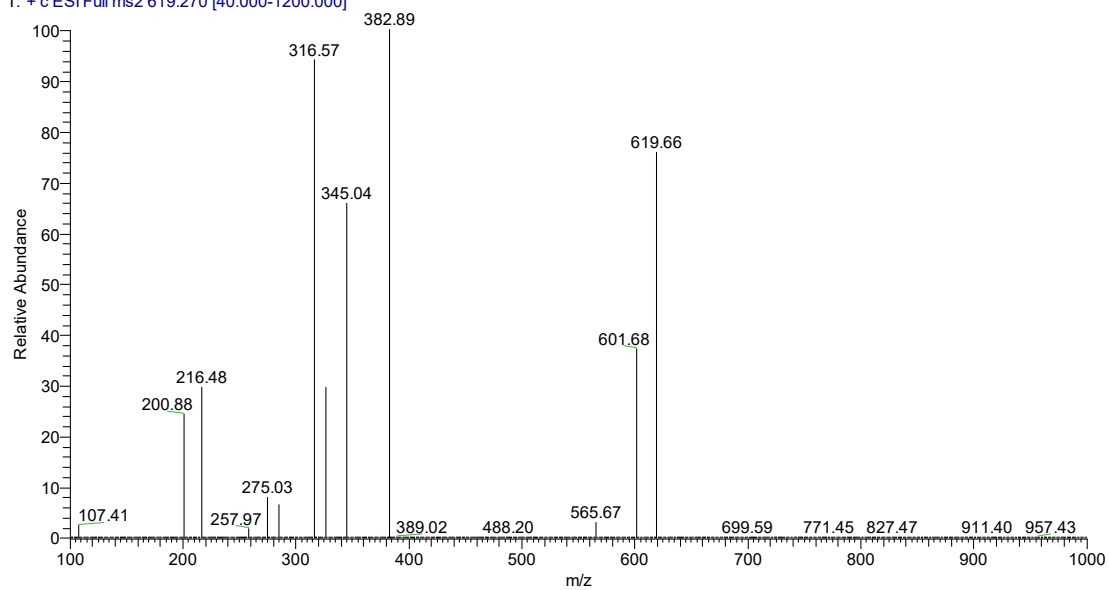
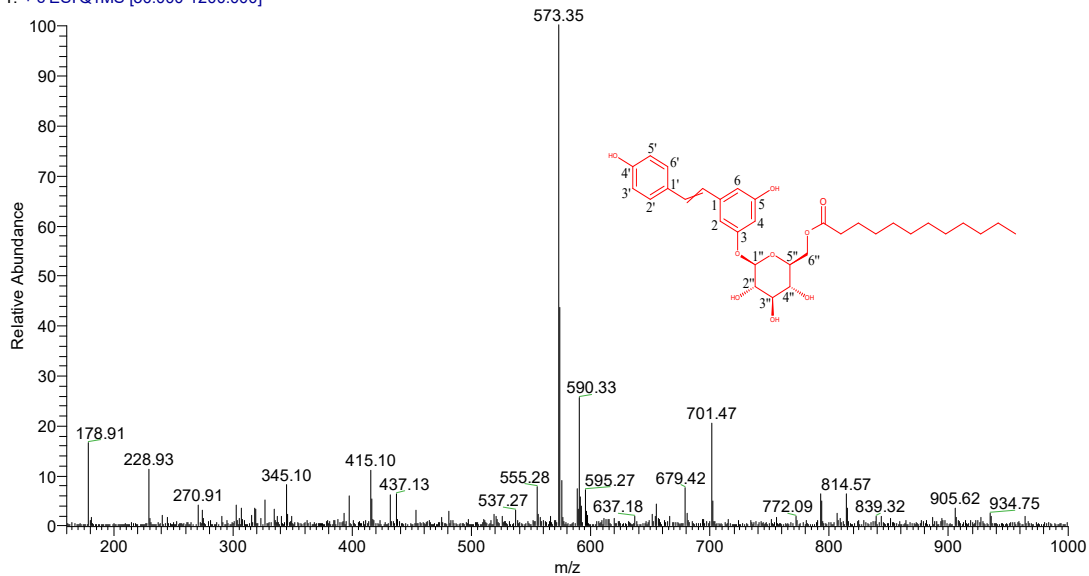


Figure S1 MS and MS/MS spectra of dodecyl phlorizin

Lauryl Polydatin ms #19 RT: 0.23 AV: 1 NL: 1.69E7
T: + c ESI Q1MS [50.000-1200.000]



Lauryl Polydatin ms2 #39 RT: 0.35 AV: 1 NL: 2.32E6
T: + c ESI Full ms2 573.290 [40.000-1200.000]

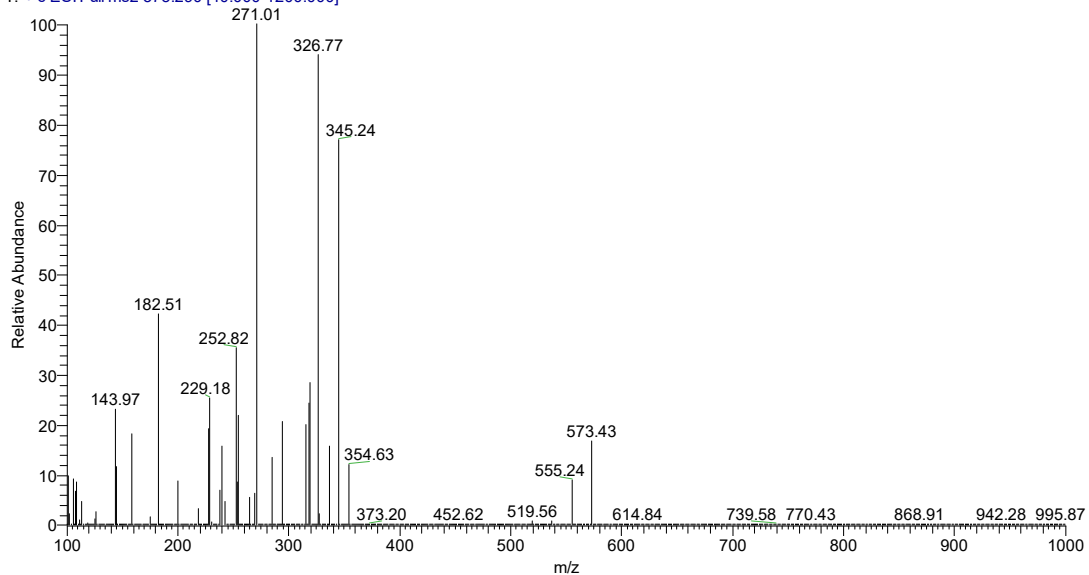


Figure S2 MS and MS/MS spectra of dodecyl polydatin

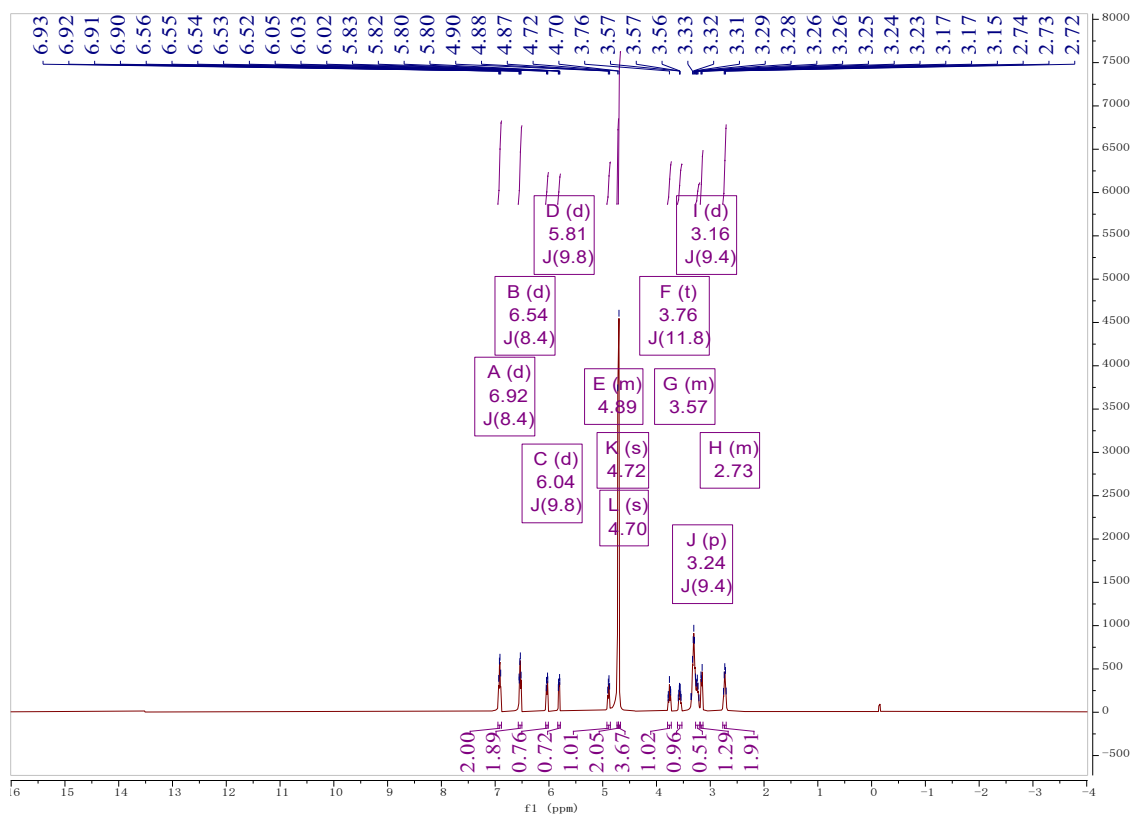


Figure S3a ^1H NMR of phlorizin

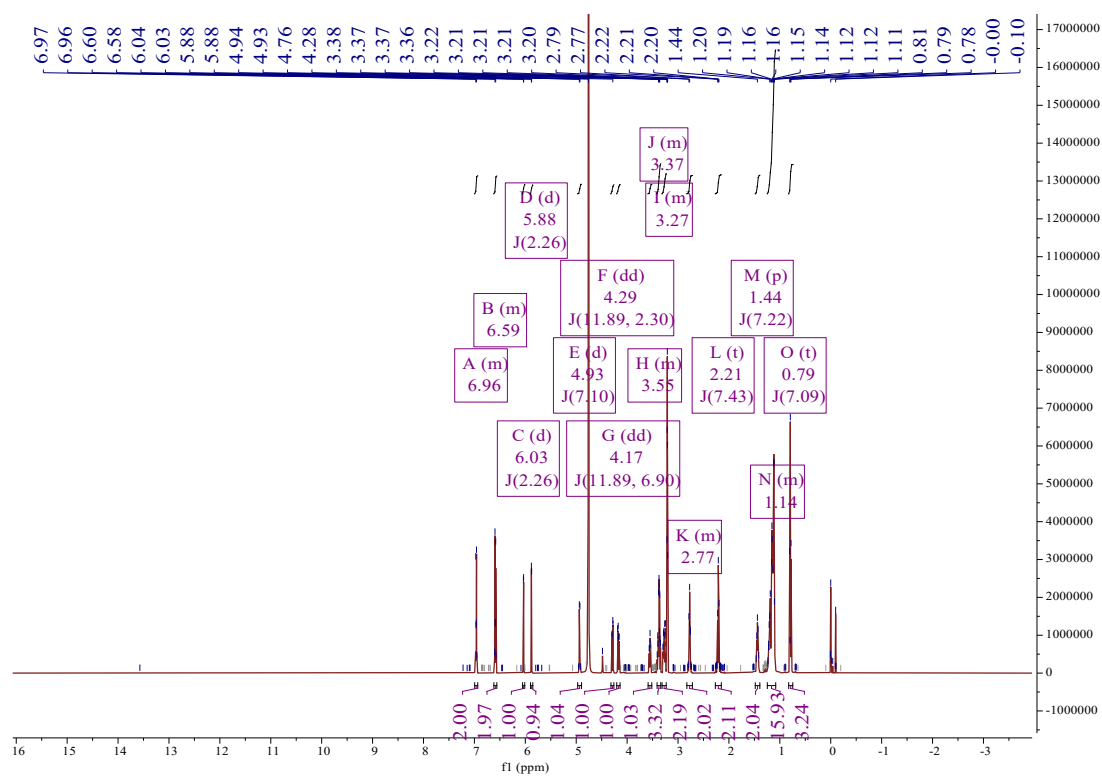


Figure S3b ^1H NMR of dodecyl phlorizin

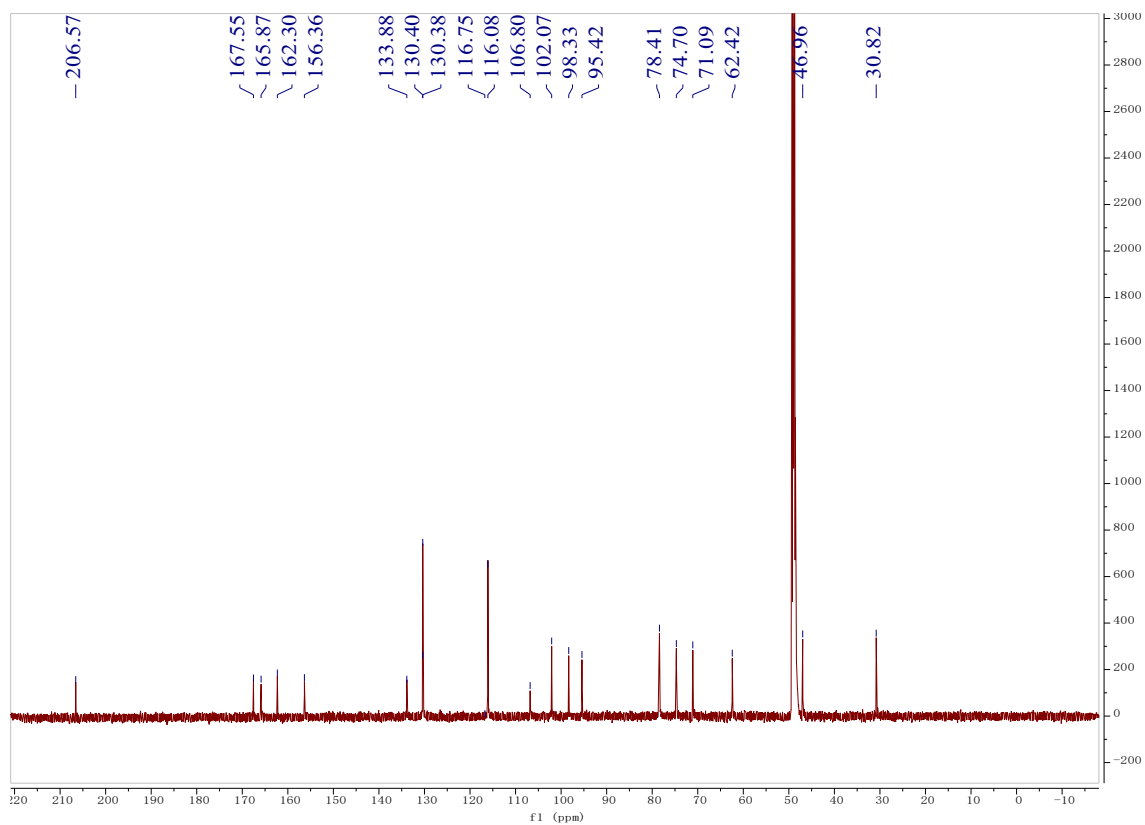


Figure S4a ^{13}C NMR of phlorizin

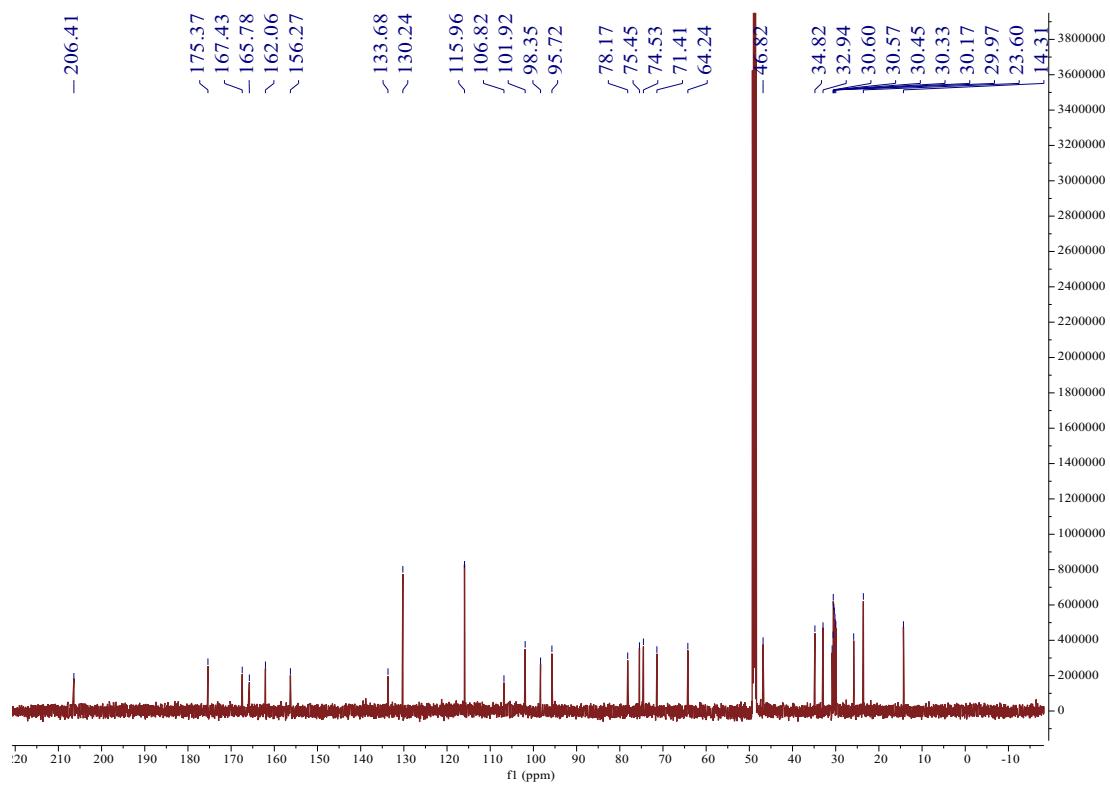


Figure S4b ^{13}C NMR of dodecyl phlorizin

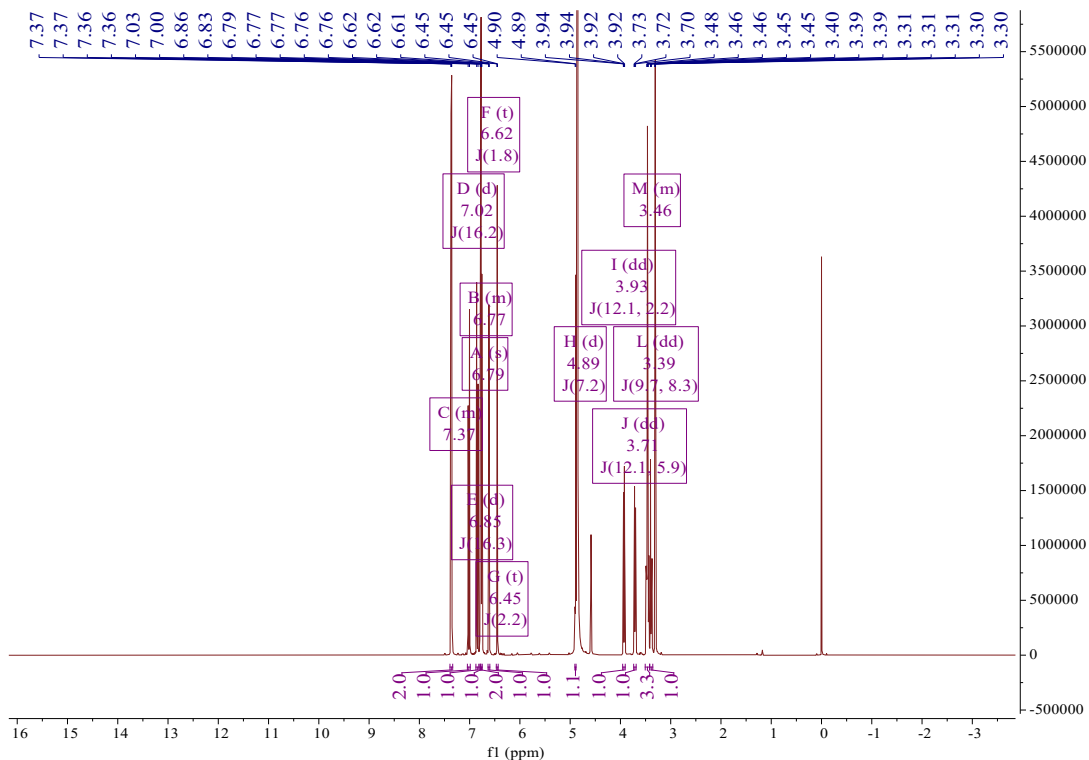


Figure S5a ¹H NMR of polydatin

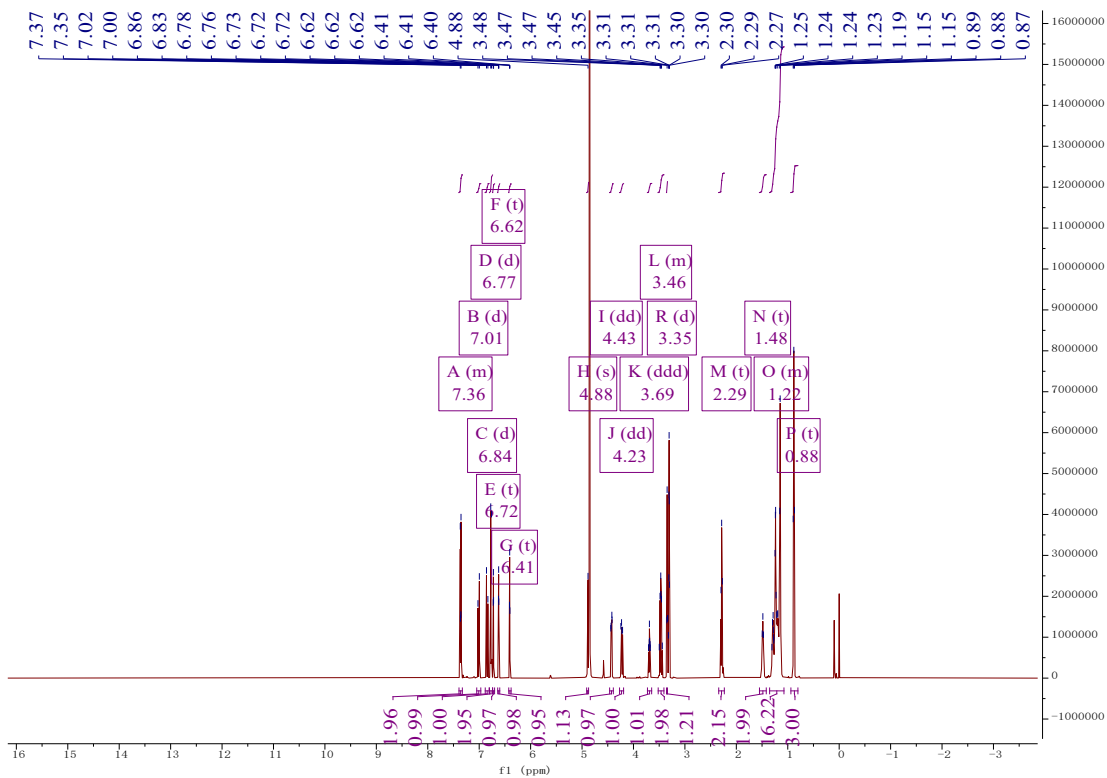


Figure S5b ¹H NMR of dodecyl polydatin

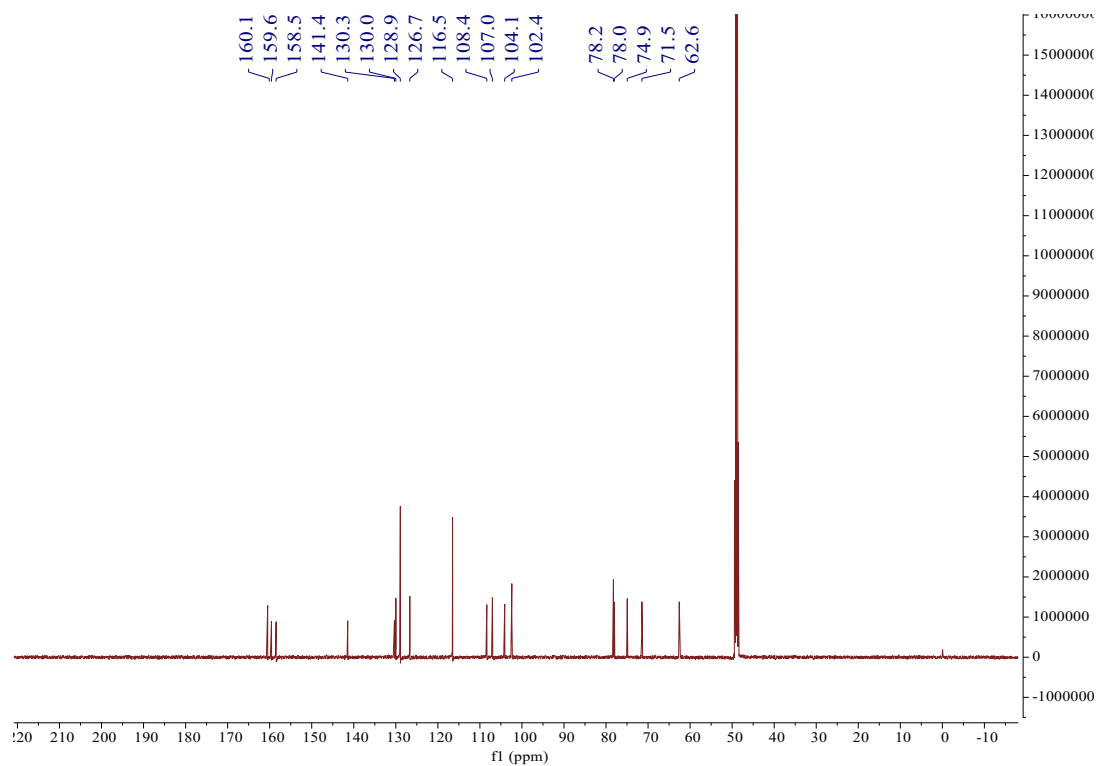


Figure S6a ^{13}C NMR of polydatin

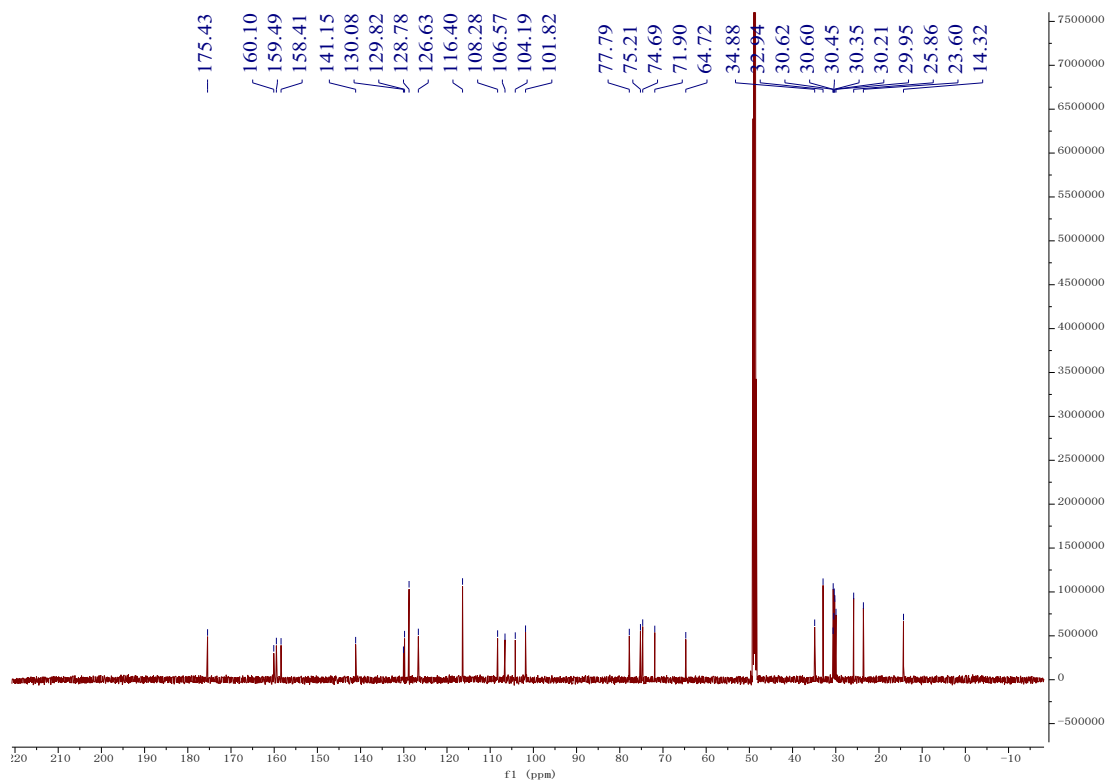


Figure S6b ^{13}C NMR of dodecyl polydatin