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Inhibition of the intestinal postprandial glucose transport by gallic acid and gallic acid derivatives

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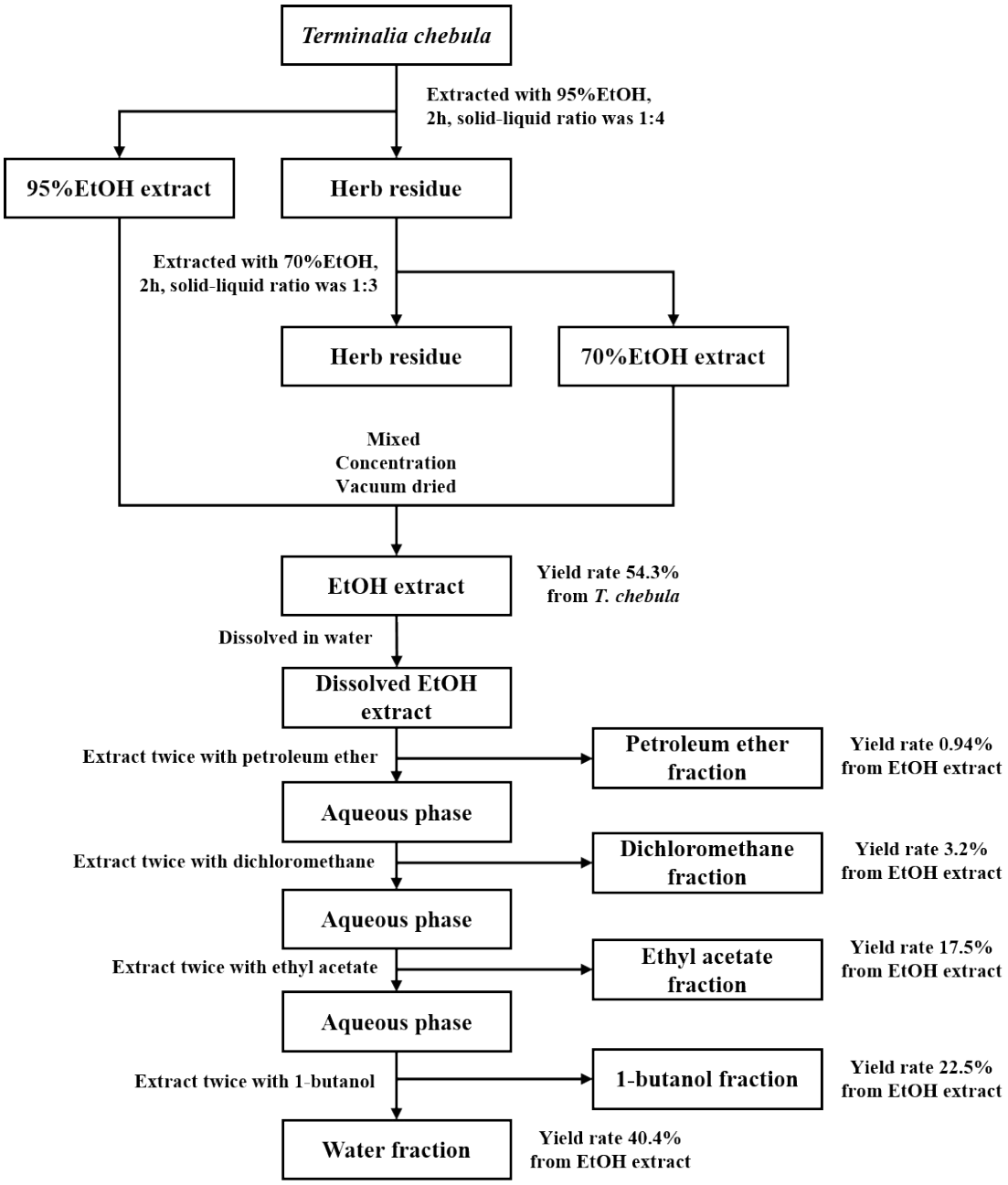


Figure S1. Flow chart of the extraction and fractionation from *Terminalia chebula* Retz., fructus immaturus.

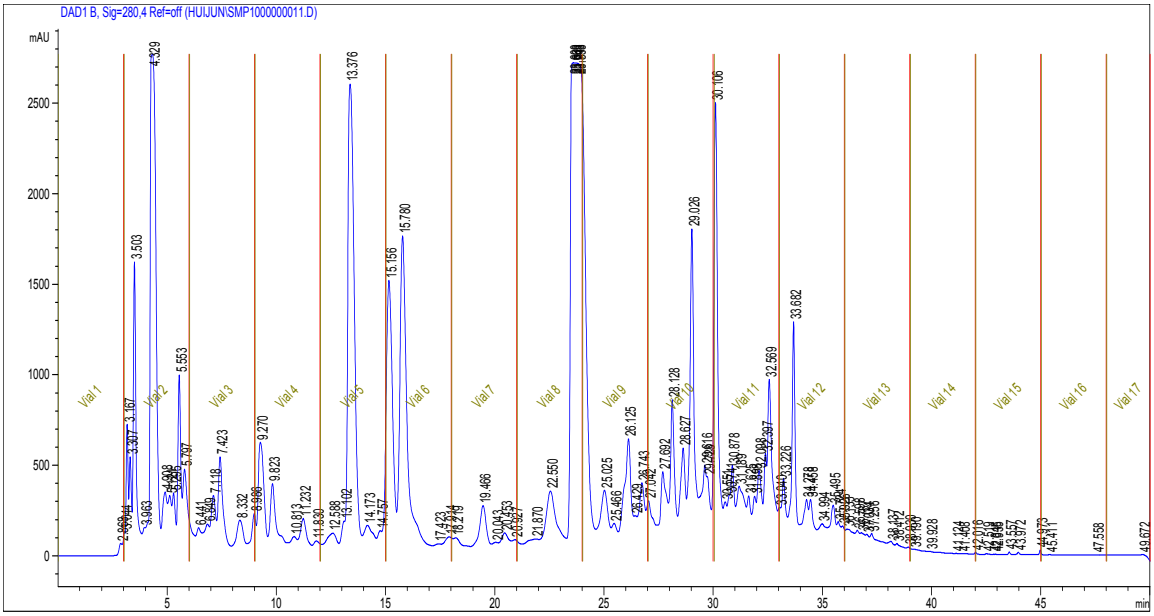
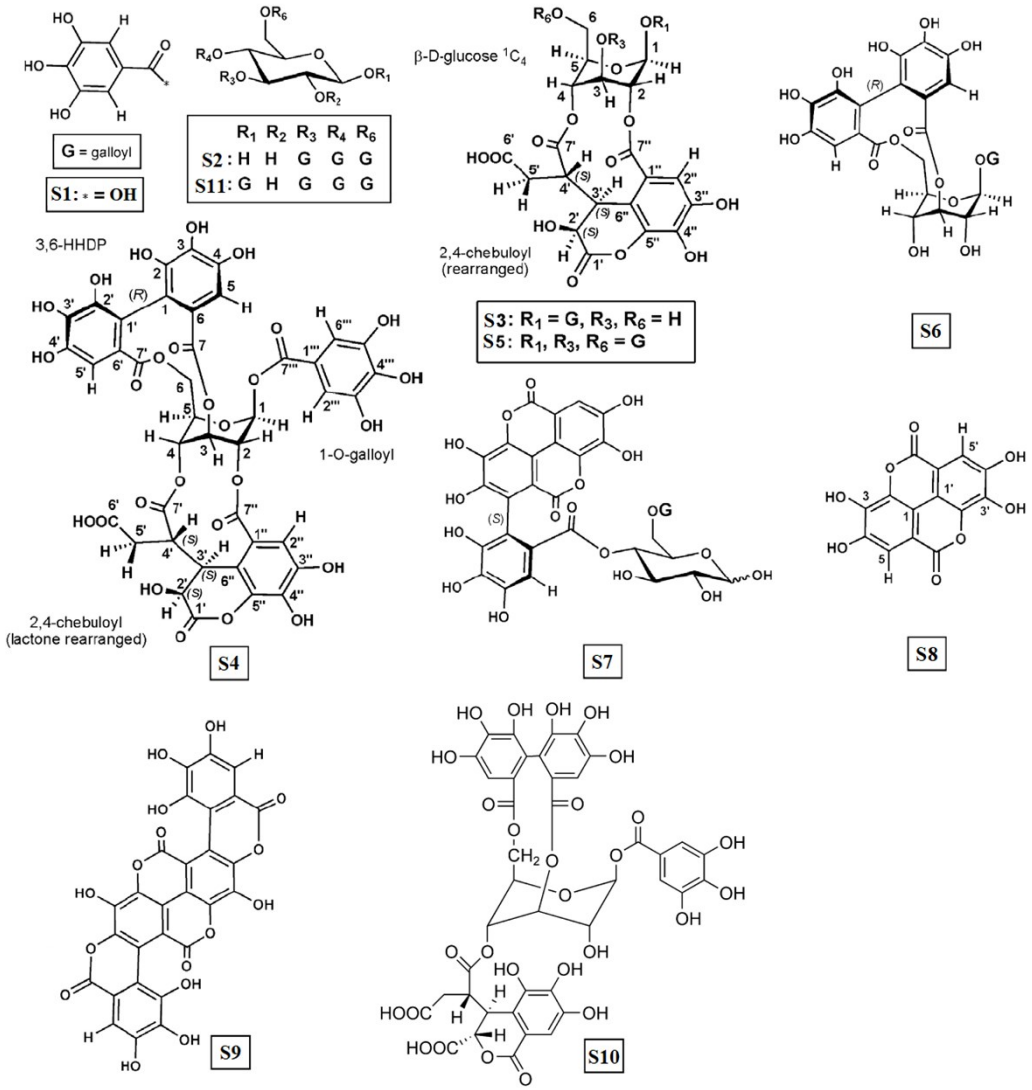


Figure S2. 1-butanol extract from *T. chebula* aqueous ethanol extract was divided into 17 fractions after separation by HPLC and collected by Agilent 1260 infinity LC fraction collector (1 tube/3 minutes)



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33 **Figure S3**. Gallic acid and gallic acid derivatives characterization of chemical constituents from
34 active fractions of *T. chebula*. The structures shown are based on UPLC-ESI-Q-TOF/MS data, in
35 some cases ambiguities may remain concerning linkage positions, configuration, etc. Compound
36 numbers, names and molecular formulas are presented in Table 2.

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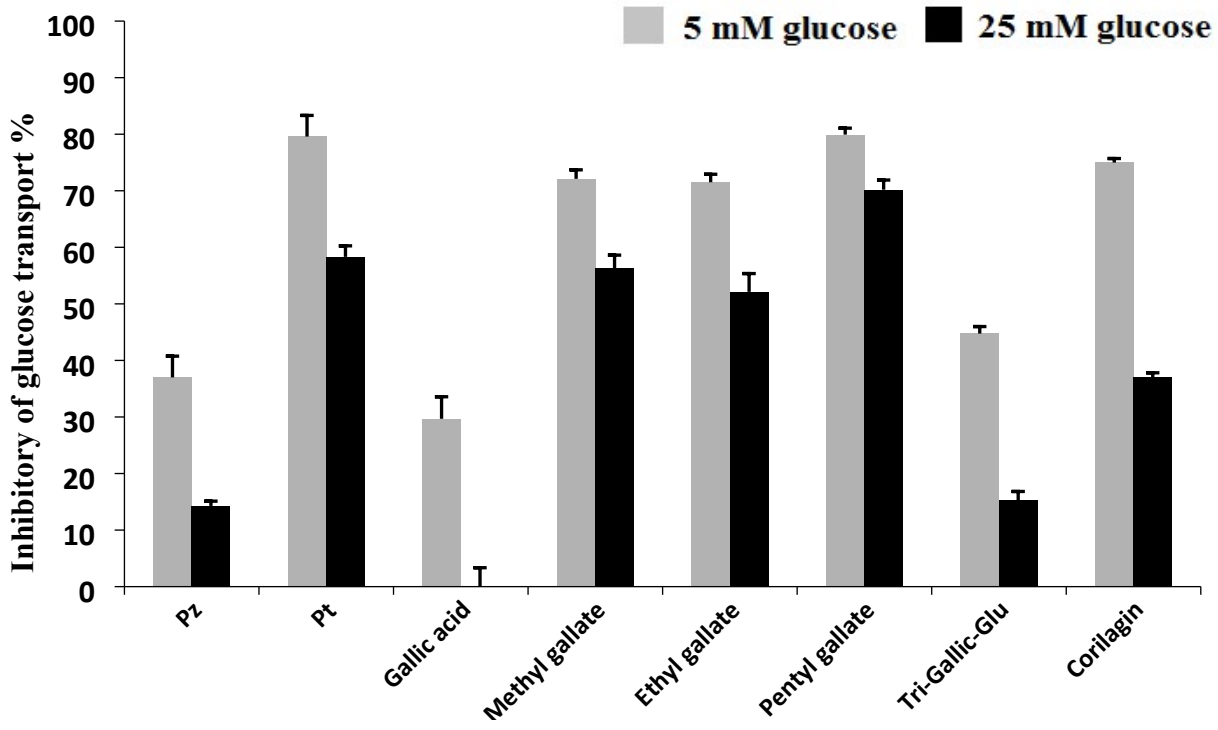

Figure S4. Gallic acid and its derivates inhibition of glucose transport at 5 mM glucose and 25 mM glucose in Caco-2 cells (n=3). Phloridzin (Pz) was tested at 300 μM and Phloretin (Pt) was tested at 150 μM. The other samples were tested at 200 μM.

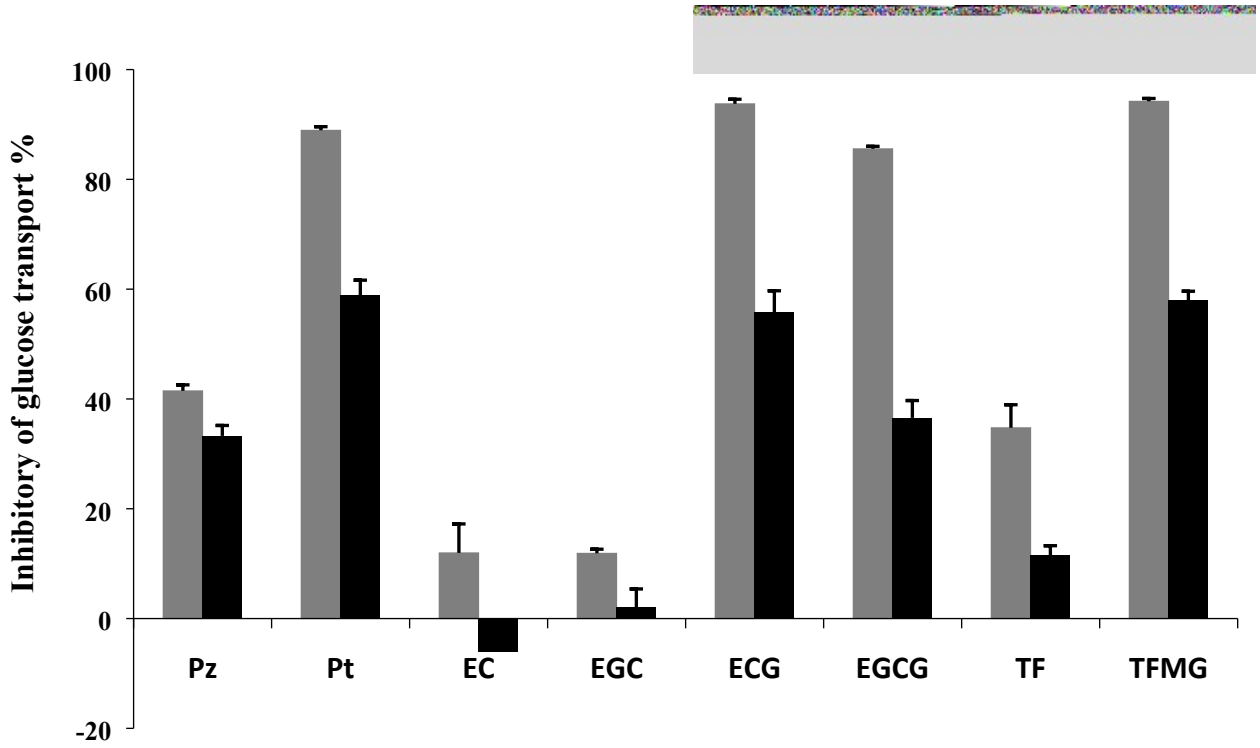

Figure S5. Gallic acid derivates of flavonoids and their original flavonoids inhibition of glucose transport at 5 mM glucose and 25 mM glucose in Caco-2 cells (n=3). Phloridzin (Pz) was tested at 300 μM and Phloretin (Pt) was tested at 150 μM. EC, EGC, EGCG, TF, and TFMG were tested at 200 μM.

Table S1. Glucose transport inhibition of ethanol extract of *Terminalia chebula* Retz., fructus immaturus, dried, and its bioassay directed fractions

Samples (200 μg/mL)	% Glucose transport inhibition 5 mM D-Glucose	% Glucose transport inhibition 25 mM D-Glucose
Ethanol extract (EE)	57.1±6.1	34.2±2.5
Petroleum ether fraction (PE)	29.7±1.5	7.9±3.4
Dichloromethane fraction (DCM)	48.4±1.0	15.9±2.3
Ethyl acetate fraction (EA)	82.0±0.7	43.4±2.8
1-Butanol fraction (1-But)	88.0±0.5	57.6±2.1
Water fraction (Water)	61.0±1.1	45.0±0.5
1-Bu-1	0.1	-3.2
1-Bu-2	70.4	79.4
1-Bu-3	26.8	-5.0
1-Bu-4	24.5	6.3
1-Bu-5	87.4	102.2
1-Bu-6	84.9	71.0
1-Bu-7	24.3	3.1
1-Bu-8	68.2	55.3
1-Bu-9	49.4	53.2
1-Bu-10	50.7	7.0
1-Bu-11	68.4	14.8
1-Bu-12	38.6	12.3
1-Bu-13	26.8	6.4
1-Bu-14	29.5	9.7
1-Bu-15	25.8	3.5
1-Bu-16	4.9	7.0
1-Bu-17	-21.9	-8.6
Phloridzin	52.8 ± 0.3	17.8 ± 0.2
Phloretin	84.8 ± 4.1	42.2 ± 3.0
Control	0 ±2.0	0 ±1.1

Phloridzin was tested at 300 μM and Phloretin was tested at 150 μM. The other samples were tested at 200 μg/mL.

Table S2 Characterization of chemical constituents from active fractions of *Terminalia chebula* Retz., fructus immaturus, dried in negative mode by UPLC-ESI-Q-TOF/MS

No	Retention time (min)	Compound name	Mol. Formula	Exact mass (calc.)	Theoretical m/z (M-H)	Observed m/z ($M-H^-$)	Mass error (ppm)	Major fragment ions: m/z	Fraction
S1	0.51	Gallic acid	$C_7H_6O_5$	170.022	169.0137	169.0145	4.7	125.0250	1-Bu-2
S2	2.92	Tri-gallic-glu	$C_{27}H_{24}O_{18}$	636.096	635.0884	635.0906	3.5	465.0678, 313.0569, 221.0455, 169 .0150, 125.0246	1-Bu-5
S3	2.74	Chebulanin	$C_{27}H_{24}O_{19}$	652.091	651.0834	651.0863	4.5	634.0777, 482.0676, 169.0143	1-Bu-5
S4	2.88	Chebulagic acid	$C_{41}H_{30}O_{27}$	954.097	953.0896	953.0926	3.1	463.0514, 337.0200, 300.9990, 275.0197, 205.0508	1-Bu-8
S5	4.43	Chebulinic acid	$C_{41}H_{32}O27$	956.113	955.1053	955.1061	0.8	786.0858, 686.0689, 618.0804, 466.0702, 337.0183, 275.0199, 169.0131	1-Bu-11
S6	2.88	Corilagin	$C_{27}H_{22}O_{18}$	634.081	633.0728	633.0734	0.9	300.9991, 275.0204, 249.0405, 169.0149	1-Bu-6
S7	0.78	Terflavin B	$C_{34}H_{24}O_{22}$	784.076	783.0681	783.0702	2.7	784.0689, 451.9984, 300.9988, 275.0193, 250.0425, 187.0397	1-Bu-2
S8	4.61	Ellagic acid	$C_{14}H_6O_8$	302.006	301.1287	301.1277	-3.3	299.9901, 283.9955, 254.9918,245.0081, 228.0048, 201.0184, 173.0237, 145.0292	1-Bu-11
S9	3.67	Gallagic acid	$C_{28}H_{10}O_{16}$	601.997	600.9891	600.9901	1.7	583.9801, 298.9823, 273.0030, 247.0243	1-Bu-8
S10	2.80	Neochebulagic acid	$C_{41}H_{32}O_{28}$	972.670	971.1002	971.0996	-0.6	954.0937, 802.0819, 634.0767, 337.0205, 300.9993, 249.0405	1-Bu-9
S11	3.76	Tetra-gallic-glu	$C_{34}H_{28}O_{22}$	788.107	787.0994	787.1010	2.0	636.0900, 618.0793, 484.0804, 466.0696, 295.0437, 169.0134, 125.0254	1-Bu-8

Tri-gallic-glu: 3,4,6-Tri-O-galloyl-β-D-Glucose

Chebulanin: 1-O-galloyl-2,4-O-chebuloyl-β-D-Glucose

Chebulagic acid: 1-O-galloyl-2,4-O-chebuloyl-3,6-O-HHDP-β-D-Glucose

Chebulinic acid: 1,3,6-tri-O-galloyl-2,4-O-chebuloyl-β-D-Glucose

Corilagin: 1-O-galloyl-3,6-(R)-HHDP-β-D-Glucose

Terflavin B: 4-O-(S)-flavogallonyl-6-O-galloyl-β-D-Glucose

Tetra-gallic-glu: 1,3,4,6-Tetra-O-galloyl-β-D-Glucose