Systematic Investigation of Mechanism of *Cichorium glandulosum* on Type 2 Diabetes Mellitus Accompanied with Nonalcoholic Fatty Liver Rats

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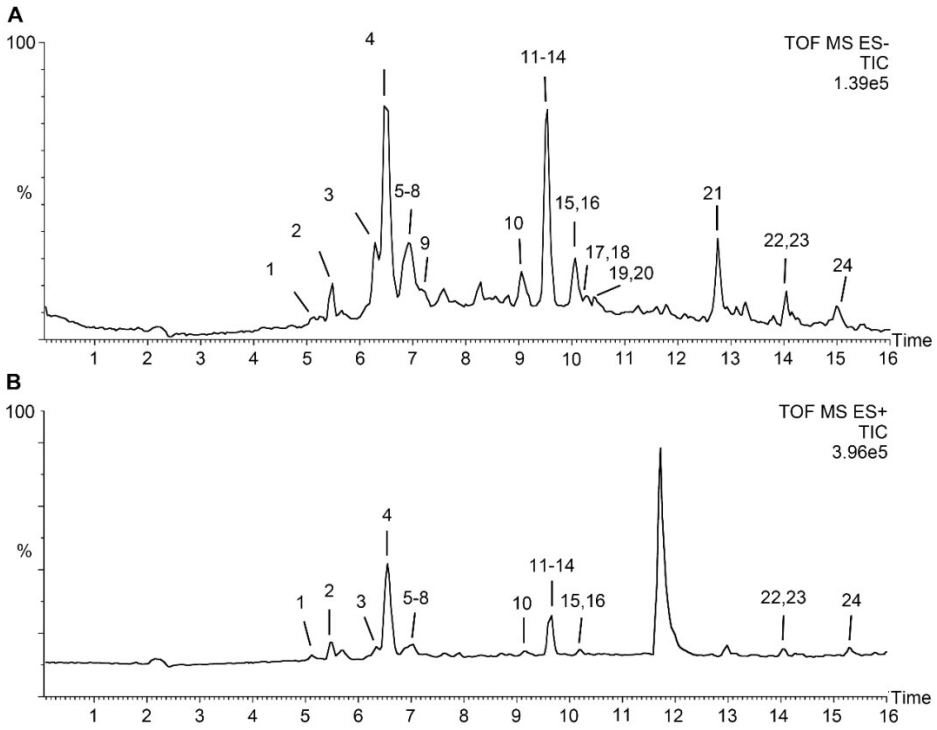
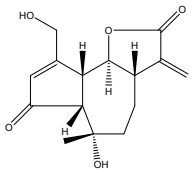
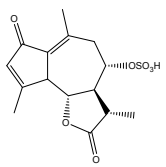
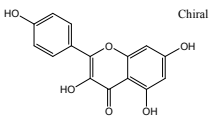
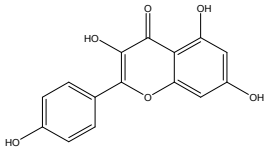
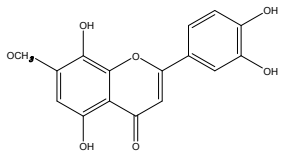
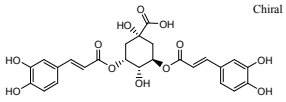
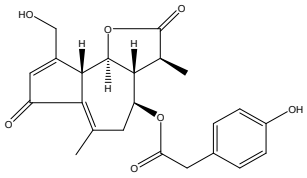
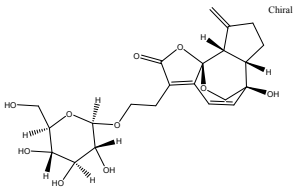
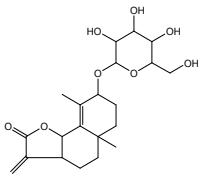
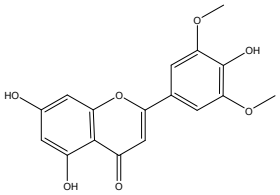
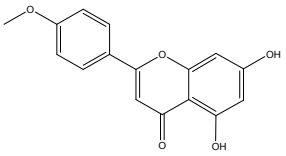
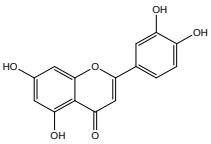
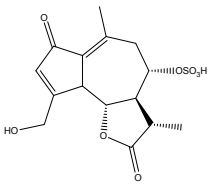


Fig. S1. UPLC-MS TIC chromatograms of CG in negative (A) and positive (B) mode. Peak 1: hieracin Ⅱ; Peak 2: lactucin; Peak 3: isoquercetin; Peak 4: 8-deacetvlmatlicarin-8-O-sulfite; Peak 5: astragalin; Peak 6: kaempferol- 7-O-glucoside; Peak 7: kaempferol-7-O-glucuronide; Peak 8: 5,8,3',4'-tetrahydroxy-7-methoxyflavone; Peak 9: isochlorogenic acid A; Peak 10: lactupicrin ethyl ester; Peak 11: lactucopicrin; Peak 12: 11β,13-dihydrolactucopicrin; Peak 13: cichorioside J; Peak 14: cichorioside A; Peak 15: tricin; Peak 16: tilianin; Peak 17: luteolin; Peak 18: isorhamnetin; Peak 19: apigenin-7-O-glucoside; Peak 20: 11β,13-dihydrolactucin-8-O-sulfite; Peak 21: 3β-(2'-methylbutanoyloxy)-8βH-eremophil-7(11)-ene-12,8α(14,6α)-diolide; Peak 22: cichorioside C; Peak 23: sitosterol; Peak 24: 1α,5α-epoxy-4α-hydroxyl-4β, 10β-dimethyl-7αH,10αH guaia-11(13) -en-1-oic acid.

Table S2 Prediction of active ingredients and corresponding ADME parameters of these compounds

MolID	Compound Name	Structure	OB (%)	DL
M01	Hieracin Ⅱ		69.78	0.22
M04	8-deacetvlmatlicarin-8-O- sulfite		37.15	0.31
M05-dg	Astragalin-dg		62.21	0.24
M06-dg	Kaempferol		62.20	0.24

M08	5,8,3’,4’-tetrahydroxy-7-methoxyflavone		49.91	0.30
M09	Isochlorogenic acid A		50.06	0.69
M12	11β, 13-dihydrolactucopicrin		84.49	0.71
M13	Cichorioside J		49.81	0.91
M14	Cichorioside A		35.81	0.68
M15	Tricin		42.32	0.34
M16-dg	Tilianin-dg		37.24	0.24
M17	Luteolin		30.50	0.25
M20	11β,13-dihydrolactucin-8-O-sulfite		50.61	0.35

“-dg” represents the compound that is deglycosylated.

Table S2 Compounds are related to both T2DM and NAFLD

No.	compound
M01	hieracin Ⅱ
M05-dg	astragalin-dg
M06-dg	kaempferol
M08	5,8,3’,4’-tetrahydroxy-7-methoxyflavone
M09	isochlorogenic acid A
M12	11β, 13-dihydrolactucopicrin
M15	tricin
M16-dg	tilianin-dg
M17	luteolin
M20	11β,13-dihydrolactucin-8-O-sulfite

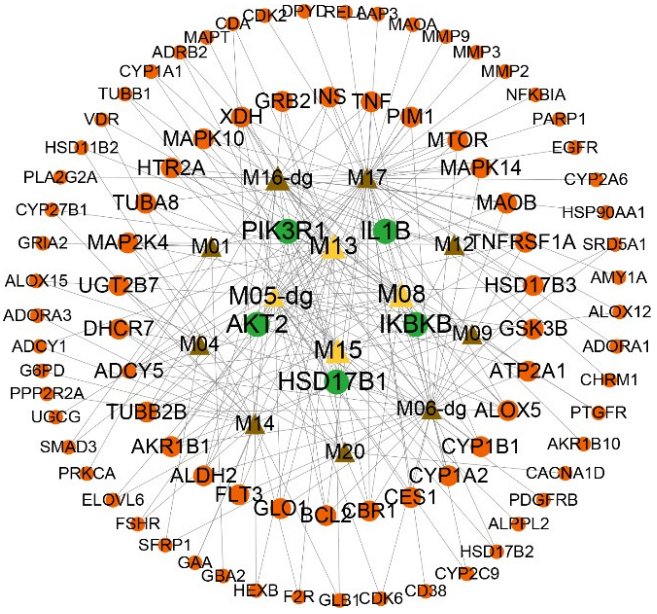


Fig. S2. A global view of C-T network. The triangles are candidate compounds and circles represent potential targets. Besides, yellow triangles and green circles are the most important compounds and targets, respectively.

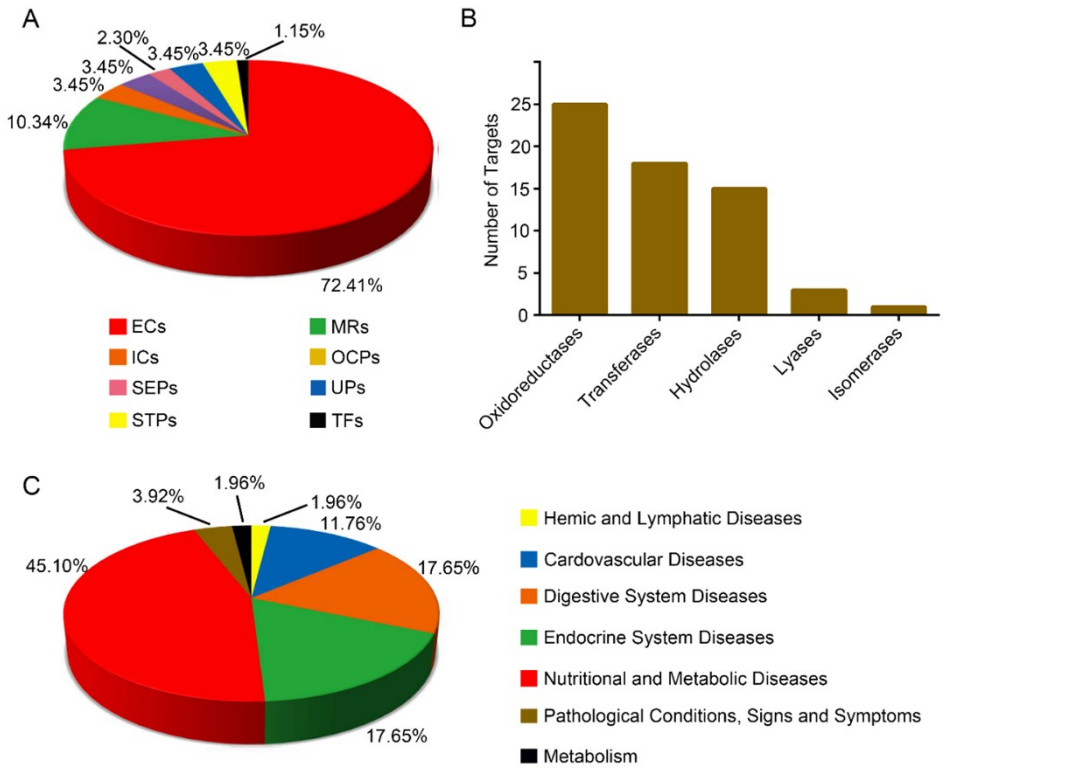


Fig. S3. (A) Distribution of compound targets according to their biochemical classification. (B) Classification of targets in enzyme. (C) Fractions of compound targets according to their therapeutic areas. ECs, enzyme; MRs, membrane receptor; ICs, ion channel; OCPs, other cytosolic protein; SEPs, secreted protein; UPs, unclassified protein; STPs, structural protein; TFs, transcription factor; E17BD, Estradiol 17-beta-dehydrogenase.

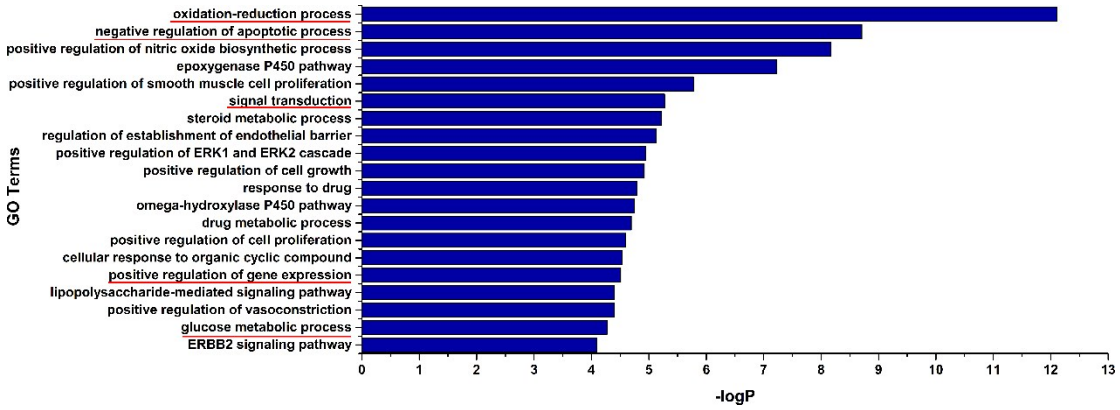


Fig. S4. Biological process in GO analysis. Underlined process represents a process associated with T2DM.

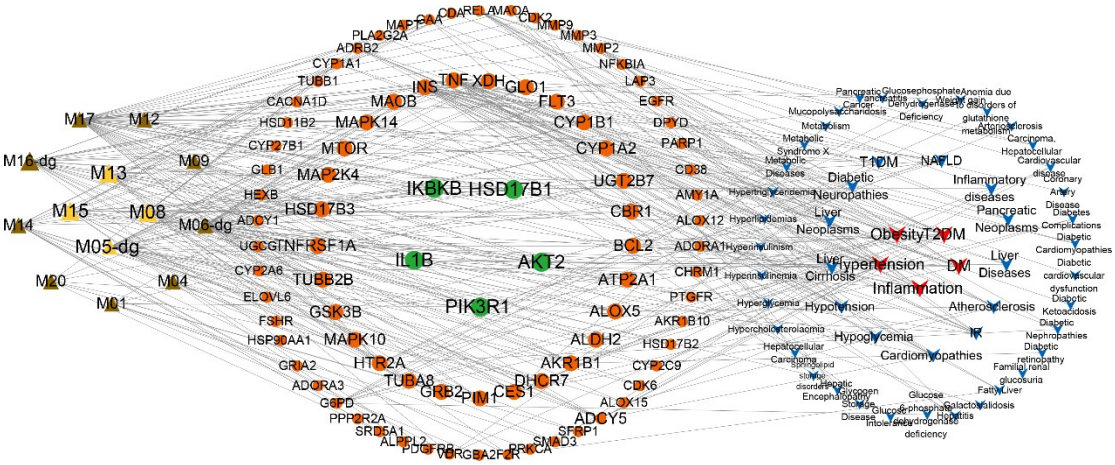


Fig. S5. A global view of C-T-D network. The triangles are candidate compounds, and circles represent potential targets, while V represents pathway. Besides, yellow triangles, green circles and red V are the most important compounds, targets and diseases, respectively.

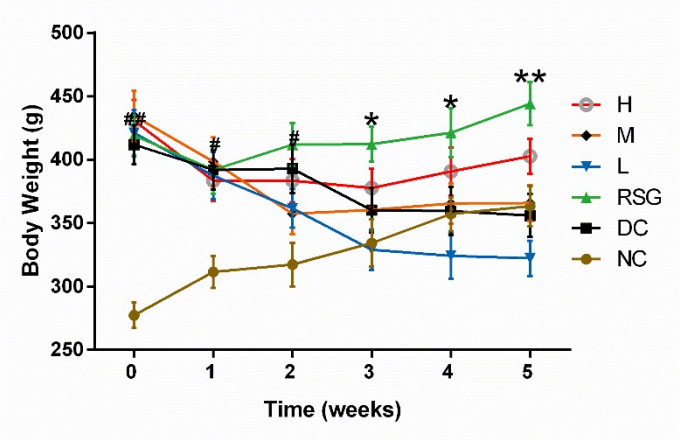


Fig. S6. Effect of CG on body weight in experimental rats. Results are denoted as means ± SD. # $p < 0.05$ and ## $p < 0.01$ compared to the NC group, * $p < 0.05$ and ** $p < 0.01$ compared to DC group.

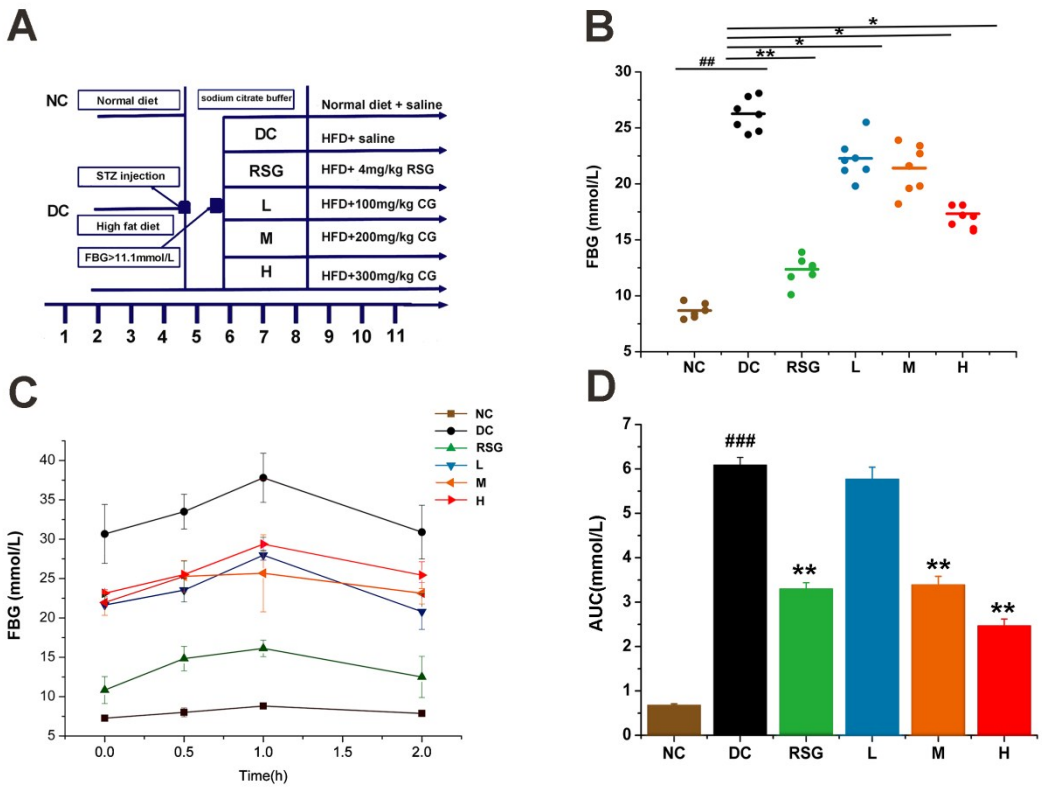


Fig. S7. Experimental design (A), FBG levels (B), OGTT (C) and AUC(D). # P < 0.05 and ## P < 0.01 significantly different compared with the NC group, * p < 0.05 and ** p < 0.01 significantly different compared with DC group.

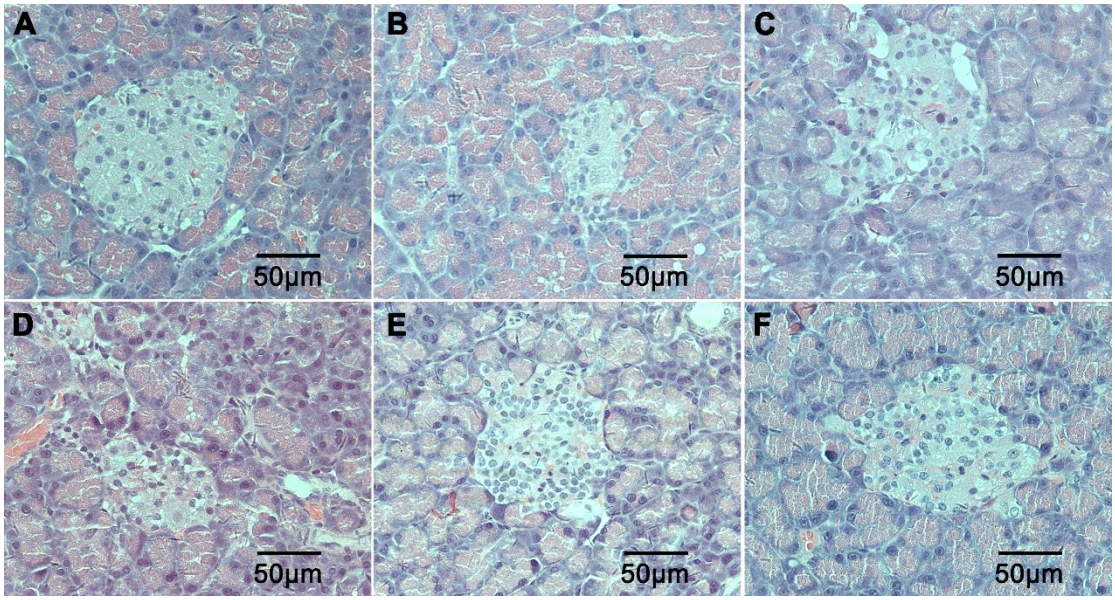


Fig. S8. Effects of CG on pancreatic islet cells in pancreatic issues stained with HE staining in different group rats. Images were obtained from each test group. A: NC group, B: DC group, C: RSG group, D: L group, E: M group, F: H group.