Supplementary information

Identification of mangiferin as a potential Glucokinase activator by structure-based virtual ligand screening

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Contents of Electronic Supporting Information (ESI)

Tables and figures

Table S1. Docking scores / interaction potential of screening hits

Compound	ICM docking score (kcal/mol)	ICM docking mfscore (kcal/mol)
1	-36.65	-90.83
2	-36.06	-95.76
3	-30.0876	-37.75
4	-33.67	-103.7
5	-41.642	-63.2803
6	-33.91	-106.5
7	-18.3546	-130.8188
8	-35.0374	-81.01
9	-27.1581	-127.125
10	-34.9685	-81.71
11	-36.1256	-99.6449
12	-22.9813	-135.3

Table S2. The enzymatic efficacy of screening hits on GK

Compound	SC_{50} (%)[a]	EC_{50} (μM)
none	100	n.p.
1	86.13 ± 5.68	n.a.
2	86.46 ± 5.71	n.a.
3	46.73 ± 1.21	n.a.
4	37.84 ± 12.01	n.a.
5	87.63 ± 5.67	n.a.
6	90.00 ± 3.88	n.a.
7	125.78 ± 2.83	156
8	91.95 ± 0.96	n.a.
9	82.36 ± 6.72	n.a.
10	94.28 ± 1.49	n.a.
11	75.92 ± 6.72	n.a.
12	111.84 ± 2.14	>500

[a]Data reported as mean ± SD (n = 3). SC_{50} was the activate efficacy of the compound stimulatory concentration of 50 μM. The activity percent of the blank control group (untreated GK group) was setted to 100%.

[b]n.p. is not performed in this study.

[c]n.a. is no activation detected in the experiments.

Table S3. Effect of drugs on serum lipids levels in mice. Each value was expressed as mean ± SD (n = 6); *$P < 0.05$, ** $P < 0.01$, compared to the diabetic group. Metformin (200mg/kg) was used as positive control.

Groups	TC (mmol/L)	TG (mmol/L)	LDL (mmol/L)	HDL (mmol/L)
normal	14.42 ± 1.31**	4.63 ± 1.85**	0.38 ± 0.14	3.75 ± 0.48
model	26.0 ± 2.59	12.64 ± 4.67	0.94 ± 0.48	4.16 ± 0.46
MET	27.31 ± 5.64	5.83 ± 1.14	0.39 ± 0.08	3.03 ± 0.20**
7	35.39 ± 8.12	0.99 ± 0.20*	0.33 ± 0.07	2.78 ± 0.62*

Fig. S1. Measurement of binding affinity between conpounds and GK by MST in standard capillaries. The binding curve were shown. **(A)** Kd of 472 ± 20.5 μM for compound **7**, **(B)** 600 ± 36.1 μM for compound LY2608204 were calculated.

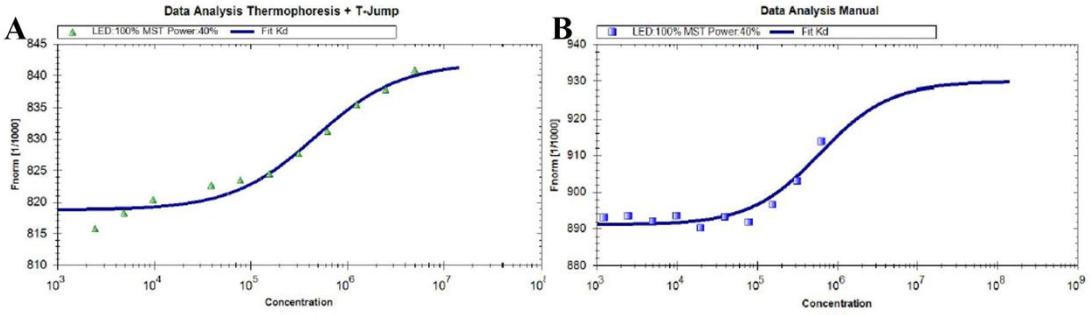

Fig. S2. Hematoxylin and eosin stained of the (A) liver and (B) abdominal white adipose tissue of groups. (A) the normal group; (B) the diabetic group; (C) the metformin-treated group (200 mg/kg); (D) the **7**-treated group. Magnification 200× (liver), 100× (abdominal white adipose tissue) (DXIT 1200, Nikon, Japan).