Supplemental data

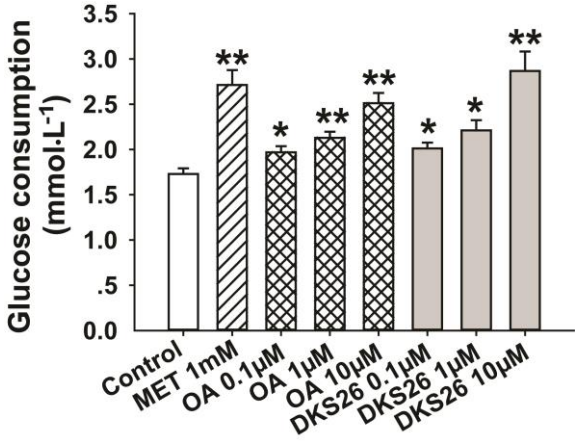

Figure S1 Effects of DKS26 on the glucose consumption in human hepatic HepG2 Cells. OA represented oleanolic acid, MET represented metformin. Values are expressed as mean ± SEM (n= 3). Compared with control group, $^{*}P<0.05$, $^{**}P<0.01$. Glucose consumption = glucose concentrations of blank wells − glucose concentrations of cell plated wells. The glucose consumption values were adjusted by SRB test. This glucose lowering activity *in vitro* showed that DKS26 might have hypoglycemic effects *in vivo*.

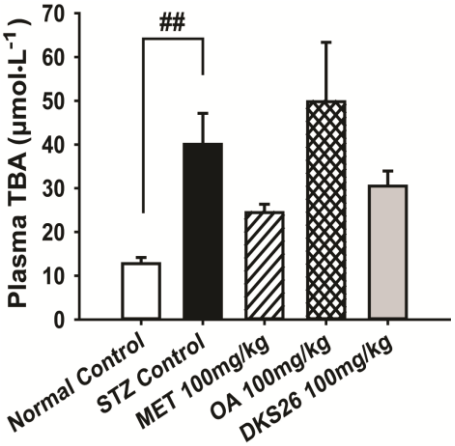

Figure S2 Effects of DKS26 on plasma total bile acids (TBA) levels in STZ-induced diabetic mice for 33 days' administration. OA represented oleanolic acid, MET represented metformin. Values are expressed as mean ± SEM. Normal Control (n = 5), STZ control (n= 7) and other groups (n= 8). Compared with normal control group, $^{\#\#}P<0.01$.

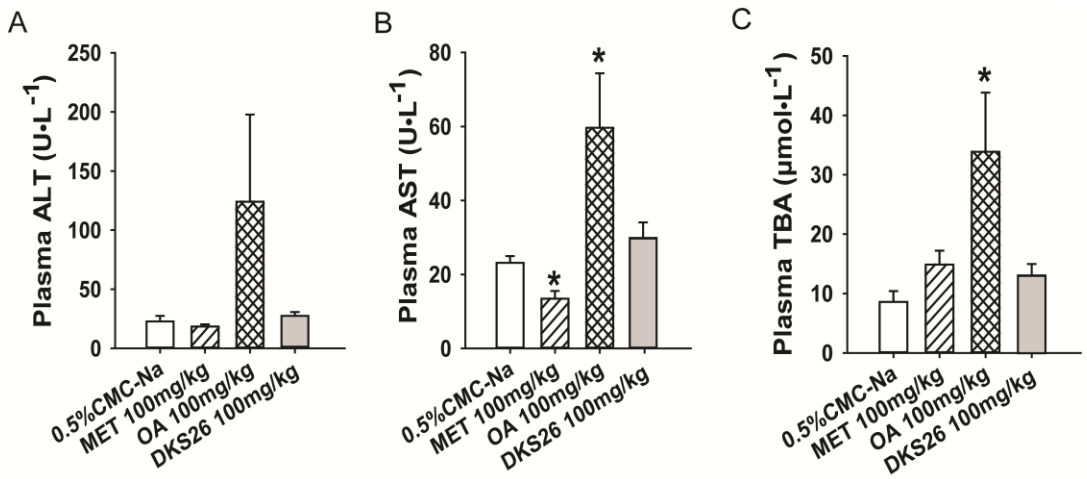

Figure S3 Effects of DKS26 on hepatic function and plasma total bile acids (TBA) levels in normal ICR mice for 8 days. OA represented oleanolic acid, MET represented metformin. Values are expressed as mean ± SEM (OA group n= 5 and other groups n= 6). Compared with control group, $^{*}P<0.05$, $^{**}P<0.01$, $^{***}P<0.001$. These findings indicated that the effect of DKS26 on hepatic injury in normal mice was significantly lower than OA.

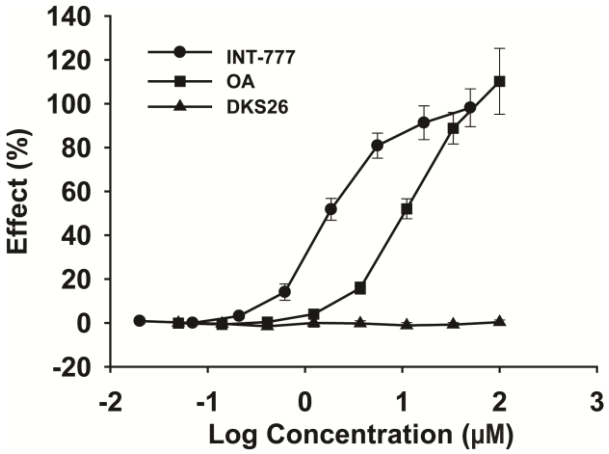

Figure S4 Direct effects of DKS26 on TGR5 in HEK293/pGL4.29/hTGR5 cells. Effect (%) was calculated as relative effect of 20 μM INT-777 regarded as 100%. EC50 was 1.77±0.45μM and 13.66±1.81μM for INT-777 and OA, respectively. OA represented oleanolic acid. Values are expressed as mean ± SD (n= 3).

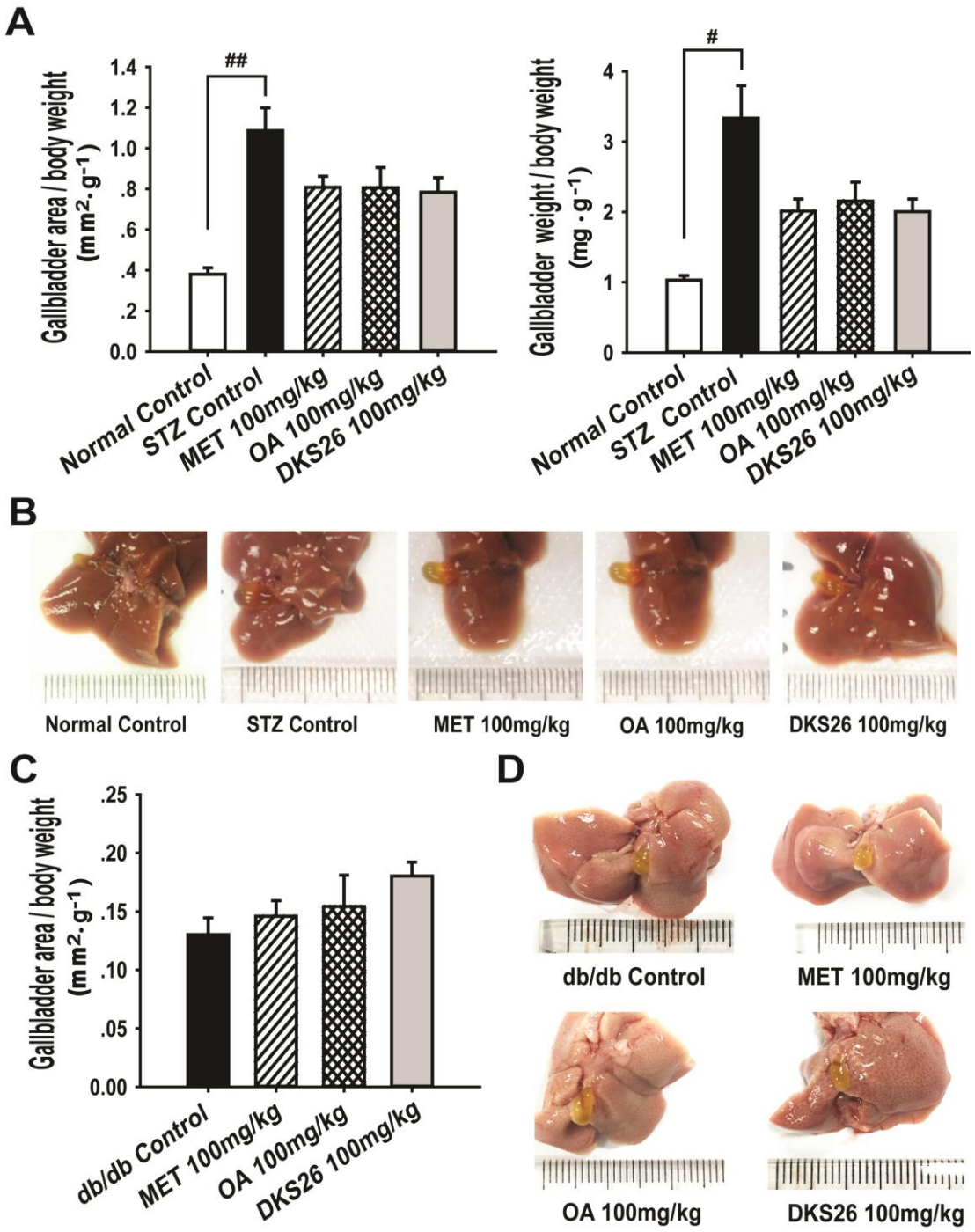

Figure S5 Effects of DKS26 on gallbladder size in STZ-induced and db/db diabetic mice. The gallbladders were removed 2h after the last administration and measured by a vernier caliper or analytical balance. The size of gallbladder was expressed as the cross-sectional area (length x width, mm^2) or weight (mg) and corrected by body weight (g). (A) STZ-induced diabetic mice (normal control n= 5, STZ control n= 7 and other groups n= 8). (B) Db/db diabetic mice (db/db and metformin control n= 7, and other groups n= 8). OA represented oleanolic acid, MET represented metformin. Values are expressed as mean ± SEM. Compared with normal control group, $^{\#}P<0.05$, $^{\#\#}P< 0.01$.

Table S1 Effects of DKS26 on blood glucose with a single administration in STZ-induced diabetic mice.

Groups	Fasting blood glucose (mmol L^{-1})				
	Before	0.5h after	1h after	2h after	3h after
Normal Control	8.6 ±0.3	9.3 ±0.3	8.7 ±0.4	7.1 ±0.8	6.3 ±0.5
STZ Control	25.1 ±1.6$^{###}$	30.0 ±2.1$^{###}$	0.8 ±1.9$^{###}$	30.7 ±1.1$^{###}$	25.2 ±2.0$^{###}$
MET 100mg/kg	24.5 ±2.2	26.3 ±1.7	25.7 ±1.8	19.4 ±3.8*	14.4 ±3.8*
OA 100mg/kg	25.9 ±2.3	25.0 ±3.6	24.5 ±3.6	22.3 ±3.3	19.7 ±1.4
DKS26 100mg/kg	26.1 ±1.9	24.5 ±1.5	22.6 ±3.4	16.9 ±3.2**	16.4 ±4.6

Values are expressed as mean ± SEM. STZ-induced diabetic mice (STZ control n= 6 and other groups n= 5). OA represented oleanolic acid, MET represented metformin. Compared with normal control group, $^{###}P<0.001$; compared with STZ control group, $^{*}P<0.05$, $^{**}P<0.01$.

Table S2 The primer sequences used in this study.

Primers	Sequences (5'→3')
gcg forward	GCACATTCACCAGCGACTACA
gcg reverse	TGACGTTTGGCAATGTTGTTC
PC3 forward	CTTCTTTTCTCTCAGCCCTTCCTAC
PC3 reverse	CATTCATTGACAAACTGCCTCTTC
GAPDH forward	GTCATCCATGACAACTTTGG
GAPDH reverse	GAGCTTGACAAAGTGGTCGT
TNF-α forward	CCAGACCCTCACACTCAGATC
TNF-α reverse	CACTTGGTGGTTTGCTACGAC
IL-6 forward	CCAGAGATACAAAGAAATGATGG
IL-6 reverse	ACTCCAGAAGACCAGAGGAAAT
IL-1β forward	CTTCAGGCAGGCAGTATCACTCAT
IL-1β reverse	TCTAATGGGAACGTCACACACCAG
SREPB-1c forward	CGACATCGAAGACATGCTTCAG
SREPB-1c reverse	GGAAGGCTTCAAGAGAGGAGC
FAS forward	CCCTTGATGAAGAGGGATC
FAS reverse	ACTCCACAGGTGGGAACAAG
PPAR-α forward	TGTCGAATATGTGGGGACAA
PPAR-α reverse	AAACGGATTGCATTGTGTGA
CPT1 forward	GCTCGCACATTACAAGGACAT
CPT1 reverse	TGGACACCACATAGAGGCAG
β-actin forward	GGTCATCACTATTGGCAACG
β-actin reverse	ACGGATGTCAACGTCACACT