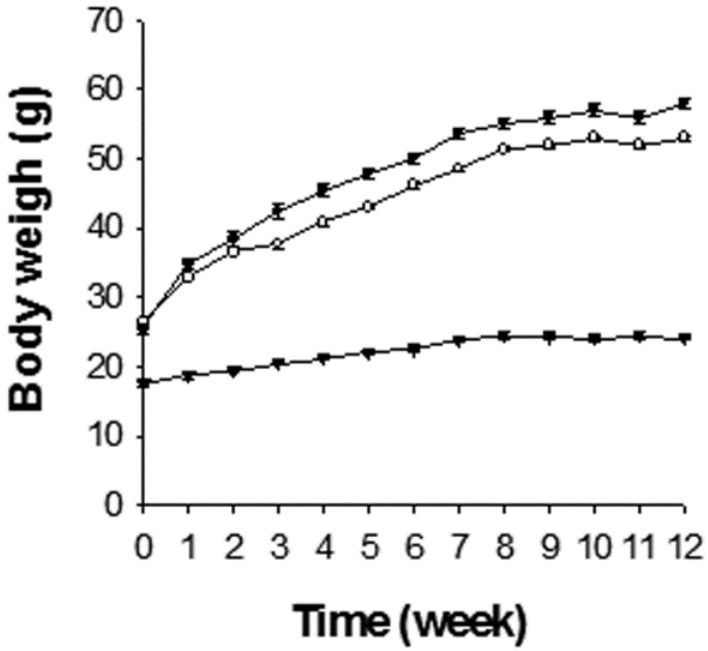
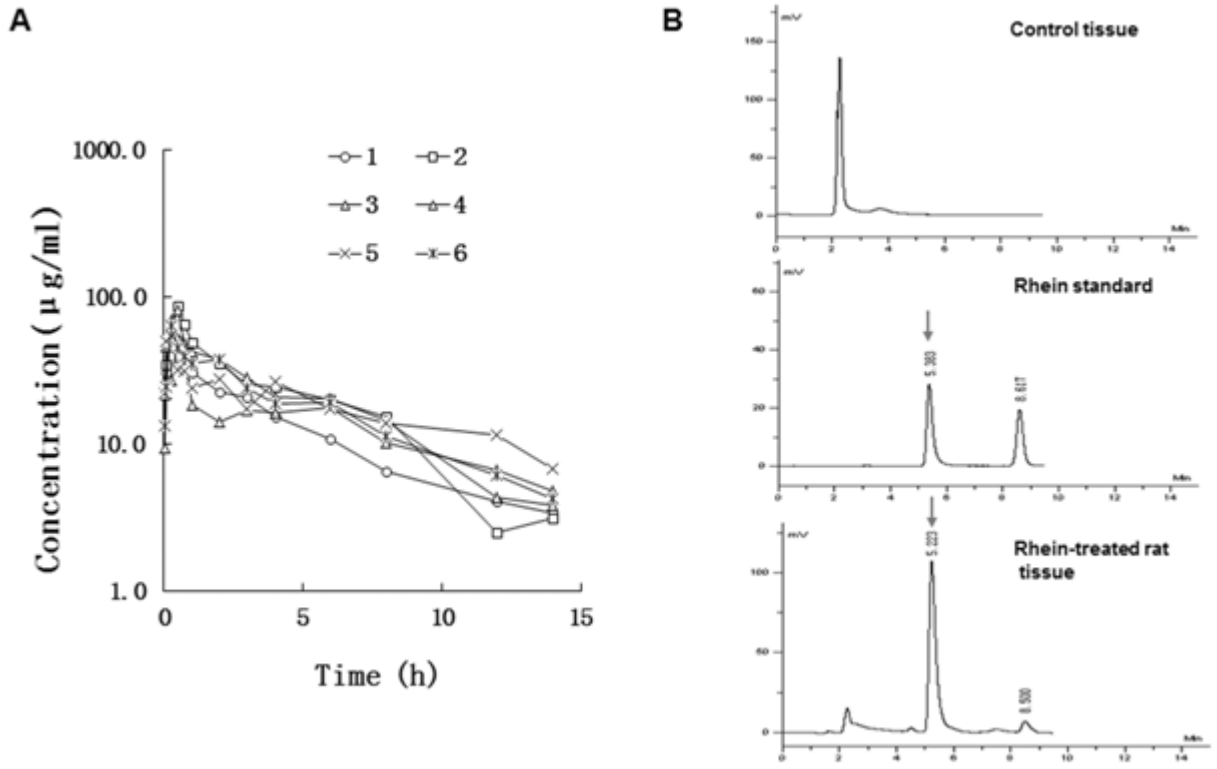
SUPPLEMENTARY DATA

Supplementary Figure 1. Effect of Rhein on body weight of *db/db* mice. Note that the body weight of *db/db* mice treated with Rhein was only slightly decreased compared to that without Rhein treatment



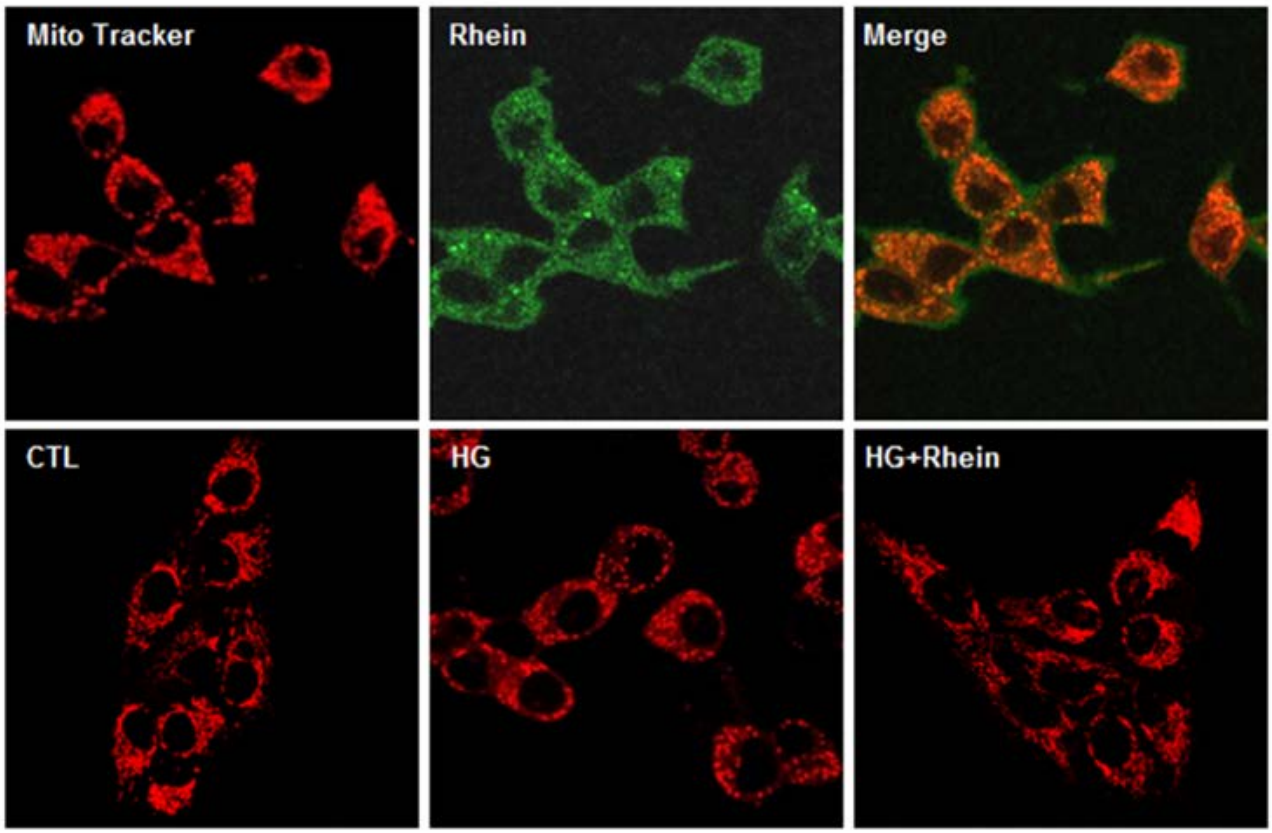
SUPPLEMENTARY DATA

Supplementary Figure 2. The concentration–time curve of Rhein in rat plasma (A) and rat pancreas tissue distribution of Rhein (B).The plasma concentrations of rhein were measured by high performance liquid chromatography with postcolumn fluorescence derivatization (HPLC-FLD). In this experiment, the concentration of Rhein was 70mg/kg bodyweight. For A, total of 6 rats (named as 1, 2, 3, 4, 5 and 6) were used. For B, rat tissues were obtained at 1 h with or without Rhein treatment and then homogenated on ice. Purified Rhein was used as a standard control.



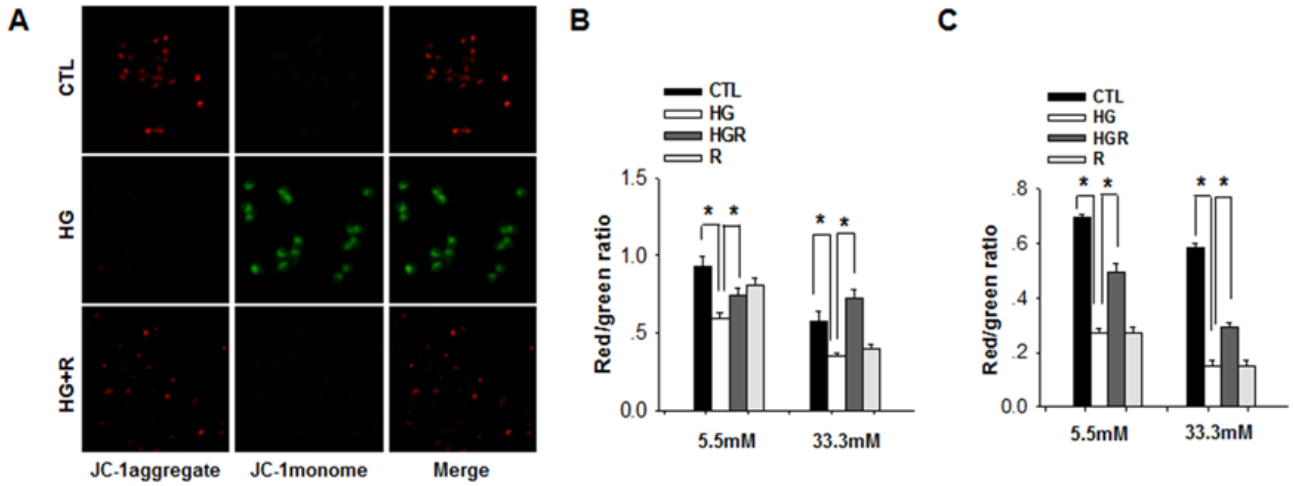
SUPPLEMENTARY DATA

Supplementary Figure 3. The distribution of Rhein in human renal HK2 cells and the changes of mitochondrial morphology induced by HG(33.3 mM). Note that Rhein was largely co-localized with mitochondrial fluorescent probe MitoTracker RED CMXRos at mitochondria, and Rhein treatment protected HK2 cells from HG-induced mitochondrial fragmentation and preserved the filamentous shape of mitochondria (magnification, ×400).

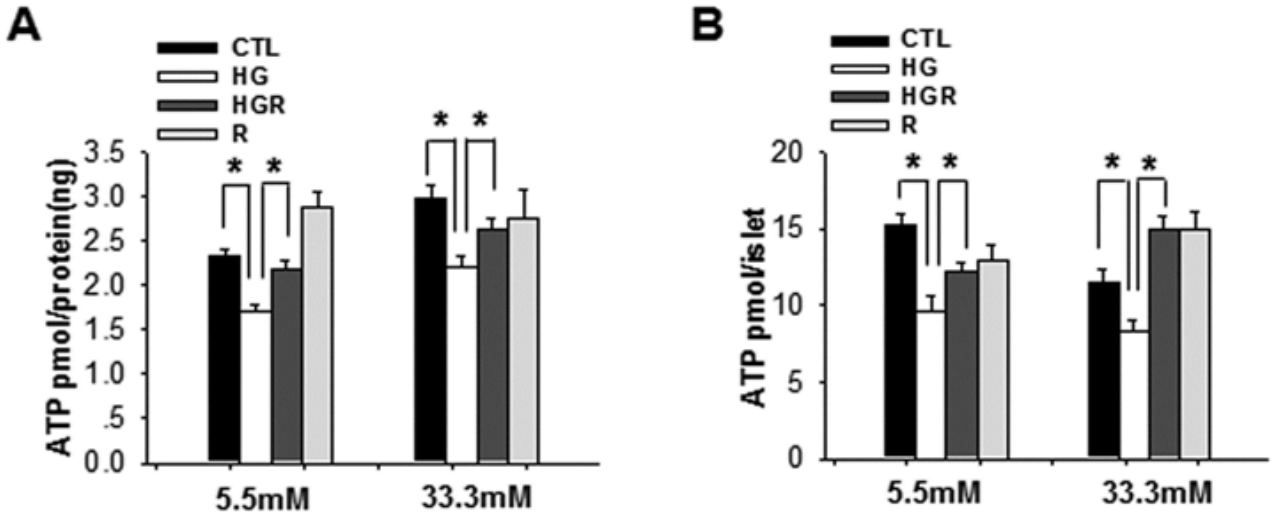


SUPPLEMENTARY DATA

Supplementary Figure 4. The effect of Rhein on mitochondrial membrane potential in NIT-1 cells (A and B) and isolated islets (C). Note that, compared with the control group, high concentration of glucose (HG) decreases the intensity of JC-1 aggregates (red) but increases the intensity of JC-1 monomers (green), whereas Rhein(R) treatment reverses the alteration of JC-1 aggregates and JC-1 monomers induced by HG. *, P <0.05.

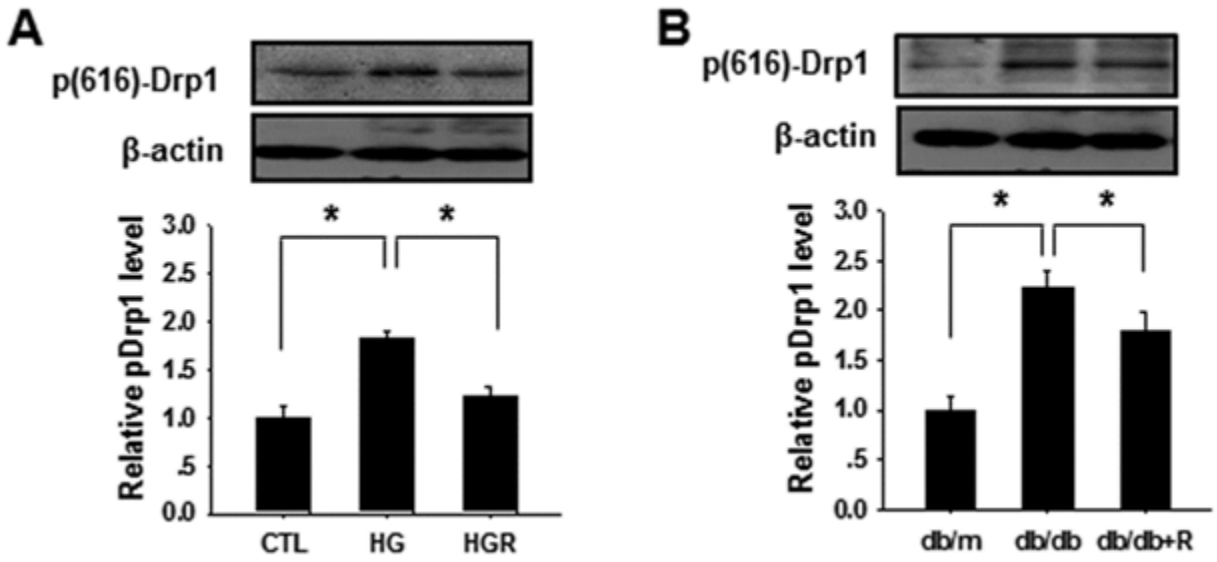


Supplementary Figure 5. The effect of Rhein on ATP production in NIT-1 cells(A) and primary islet β cells (B). Note that high concentration of glucose (HG) inhibits ATP production comparing to control group, whereas Rhein(R) restores the ATP production. *, P <0.05.

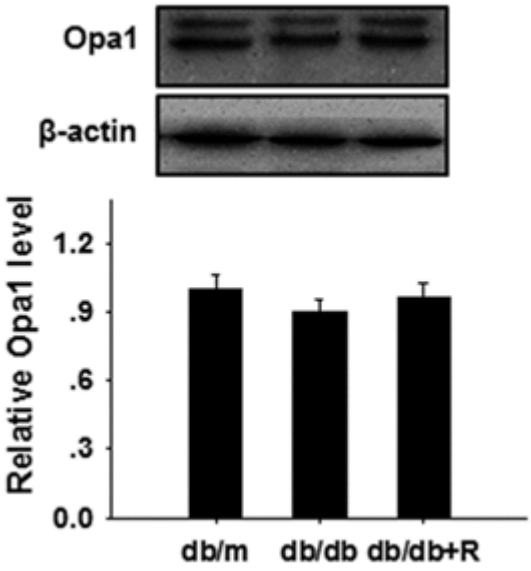


SUPPLEMENTARY DATA

Supplementary Figure 6. Rhein treatment suppresses the active Drp1 (p-Drp1) levels induced by HG in both NIT-1 cells (A) and primary islet β cells (B).*, $P < 0.05$.

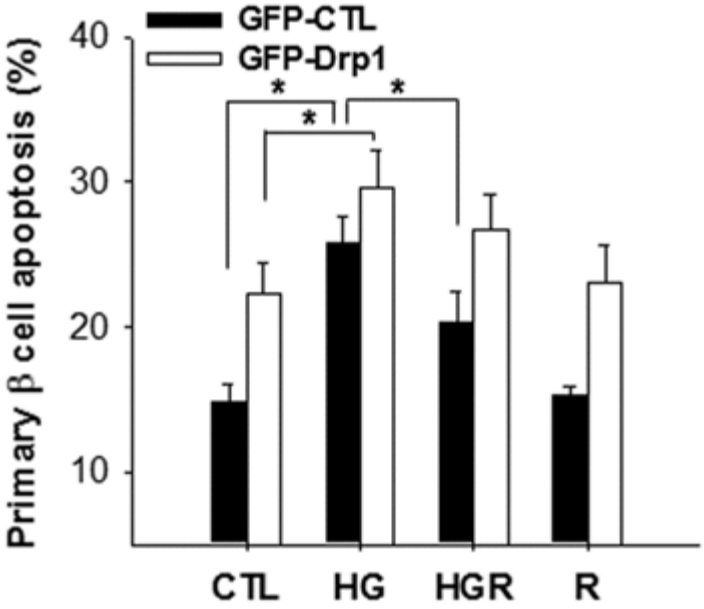


Supplementary Figure 7. The level of Opa1 in isolated mouse islets detected by western blot. Note that Opa1 level in mouse pancreatic β cells is not affected by HG or HG plus Rhein.

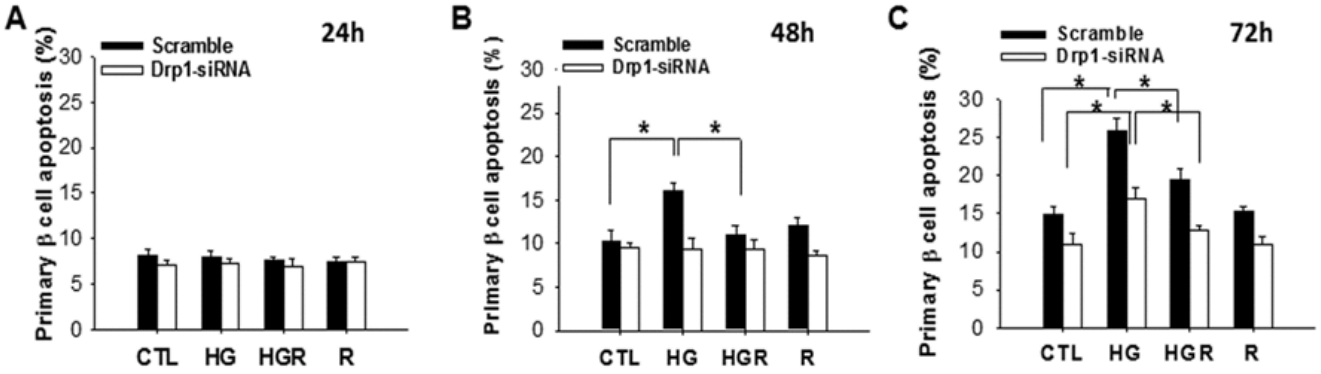


SUPPLEMENTARY DATA

Supplementary Figure 8. Forced expression of Drp1 in primary β cells results in cell apoptosis, which is not reversed by Rhein.*, *P* <0.05.



Supplementary Figure 9. Knockdown of Drp1 level via Drp1 siRNA transfection delays HG-induced primary β cell apoptosis. Note that HG-induced apoptosis of primary β cells transfected with Drp1 siRNA, which occurs at 72 h incubation, is further inhibited by Rhein. *, *P* <0.05.



SUPPLEMENTARY DATA

Supplementary Figure 10. Rhein prevents mouse primary β cells apoptosis though its antioxidant activity. Note that primary β cells treated with HG+Drp1-siRNA+Rhein have a reduced apoptosis compared to cells treated with HG+Drp1-siRNA (A), and that ROS level in primary β cells is affected by HG but not Drp1-siRNA (B).*, P <0.05.