

Figure 4. (A) CLSM images of E12 cells after incubation with different particles and specific organelle trackers. Green, F-insulin loaded NCs or NPs; red, specific organelle probes; blue, nuclear; yellow, colocalization green and red signals. Scale bars, 5 μ m. (B) CLSM images of Golgi apparatus and lysosome in E12 cells after the treatment with different specific organelles inhibitors. Golgi apparatus and lysosome were stained with specific probes (red) and the nucleus was stained with Dapi (blue). Scale bars, 5 μ m. (C) Influence of Golgi apparatus and ER inhibitors (brefeldin A and monensin) on the exocytosis of particles. Data was presented as the percentage of the exocytosis amount of the group without inhibitors. Data are means \pm SD ($n = 3$), $*p < 0.05$, versus control group. (D) Influence of lysosome inhibitors (LY294002 and nocodazole) on the exocytosis of particles. Data was presented as the percentage of the exocytosis amount of the group without inhibitors. Data are means \pm SD ($n = 3$), $*p < 0.05$, versus control group.

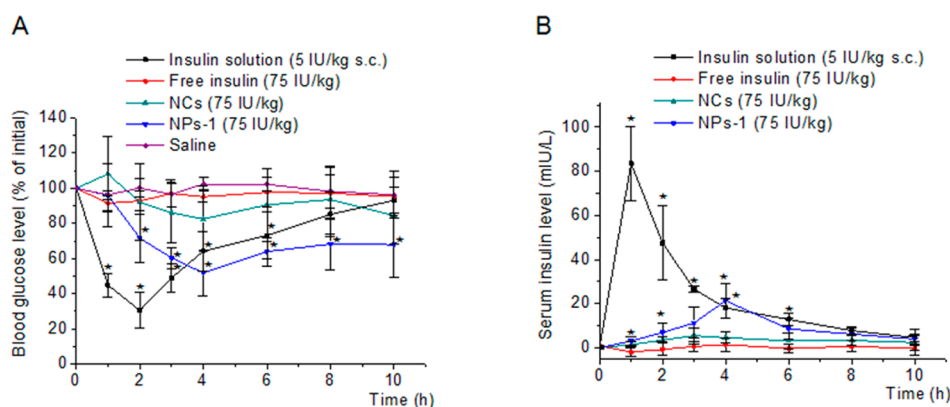


Figure 5. (A) Variation of blood glucose levels of diabetic rats after orally administering insulin loaded particles, insulin solution at dose of 75 IU/kg, subcutaneous injection with insulin solution at 5 IU/kg, or saline via gavage. Data are means \pm SD ($n = 5$), $*p < 0.05$ versus saline group. (B) Variation of serum insulin level of diabetic rats after orally administering insulin loaded particles or insulin solution at dose of 75 IU/kg, or subcutaneous injection with insulin solution at 5 IU/kg. Data are means \pm SD ($n = 5$), $*p < 0.05$ versus oral free insulin group.

threshold for the diagnosis of diabetes (Supporting Information Figure S14). In comparison, NCs only elicited a mild hypoglycemic response. The pharmacological availability (PA %) of different samples related to subcutaneous injection was shown in Table 2. NPs-1

demonstrated a PA % of 6.61%, which was 2.54-fold higher than that of NCs. The pharmacokinetic profiles of insulin were shown in Figure 5B. Subcutaneous injection of free insulin solution at 5 IU/kg resulted in a rapid increase in serum insulin concentration.