Figure S1. SEM (nanosized and finesized spherical white objects are SiO$_2$ NPs and FPs) and EDXA (arrows indicate silicon) of tissue homogenates. (A) SEM and EDXA of mice orally administrated with different dose of fumed SiO$_2$ NPs. (B) SEM and EDXA of mice orally administrated with fumed SiO$_2$ NPs, stober SiO$_2$ NPs, fumed SiO$_2$ FPs, stober SiO$_2$ FPs.
Figure S2
**Figure S2.** Effects of fumed SiO$_2$ NPs, stober SiO$_2$ NPs, fumed SiO$_2$ FPs and stober SiO$_2$ FPs on apoptosis and protein expression and protein phosphorylation. (A) Apoptosis of mouse pancreas cells (Insulin (red), TUNEL (green), and Nucleus (blue) co-staining). (B) Apoptosis of mouse liver cells (TUNEL (green) and nucleus (blue) co-staining). (C) Protein expression of Cleaved-caspase 3, and protein phosphorylation of IRS1 and Akt. (D) Ratios of Cleaved-caspase 3/β-actin, p-IRS1/IRS1 and p-Akt/Akt. *P < 0.05 vs. the control group. Results are the mean ± SE (n = 10).
Figure S3

(A) Bar chart showing the expression of HO-1 and Nqo1 in control (Cont), week 10, and week 18. The bars are shaded to indicate the levels of expression.

(B) Graph showing the change in T-SOD of liver (IU/mg protein) over time (Week) for different treatment groups: Cont, 100 mg/kg, 100 mg/kg+4-PBA, and 100 mg/kg+NAC. The data points are marked with asterisks to indicate statistical significance.

(C) Graph showing the change in GSH of liver (mg/mg protein) over time (Week) for different treatment groups. The data points are marked with asterisks to indicate statistical significance.

(D) Graph showing the change in T-SOD of liver (IU/mg protein) over time (Week) for different treatment groups. The data points are marked with asterisks to indicate statistical significance.

(E) Graph showing the change in mRNA expression of SOD1, SOD2, GSS, GCLC, and GCLM over time (Week) for different treatment groups. The data points are marked with asterisks to indicate statistical significance.

(F) Bar graph showing the change in T-SOD of serum (IU/mL) for different treatment groups. The data points are marked with asterisks to indicate statistical significance.

(G) Bar graph showing the change in GSH of serum (mg/mL) for different treatment groups. The data points are marked with asterisks to indicate statistical significance.

(H) Bar graph showing the change in MDA of serum (mol/L) for different treatment groups. The data points are marked with asterisks to indicate statistical significance.
**Figure S3.** Oral administration of 100 mg/kg SiO$_2$ NPs increased plasma ROS levels, but oral administration of the same dose of SiO$_2$ FPs did not. (A) Fold changes of genes in the Nrf2 pathway, based on RNA-seq results. (B) Messenger RNA expression of Nrf2. (C) Messenger RNA expression of HO-1. (D) Messenger RNA expression of Nqo-1. (E) RT-qPCR results for ROS-related genes. (F) Levels of T-SOD in sera and livers. (G) Levels of GSH in sera and livers. (H) Levels of MDA in sera and livers. (I) RT-qPCR results for Nrf2 pathway genes. * $P < 0.05$ vs. the control group. Results are the mean ± SE ($n = 10$).
Figure S4. Oral administration of 100 mg/kg SiO₂ NPs induced ER stress, but oral administration of the same dose of SiO₂ FPs did not. (A) RT-qPCR results for ER stress-related genes. (B) Protein expression of ER stress markers. (C) Ratios of ER stress markers. * \( P < 0.05 \) vs. the control group. Results are the mean ± SE (n = 10).
Figure S5. Oral administration of 100 mg/kg SiO₂ NPs activated the NF-κB and MAPK pathways and induced inflammation response in livers of mice, but oral administration of the same dose of SiO₂ FPs did not. (A) RT-qPCR results for inflammation response-related genes. (B) Protein phosphorylation of NF-κB-p65, IκBα, JNK, and p38-MAPK. (C) Ratios of p-P65/P65, p-IκBα/IκBα, p-JNK/JNK, and p-P38/P38. * P < 0.05 vs. the control group. Results are the mean ± SE (n = 10).