Electronic Supplementary Material (ESI) for Biomaterials Science.

Supporting Information

Virus-like silica nanoparticles enhance macromolecule permeation *in vivo*

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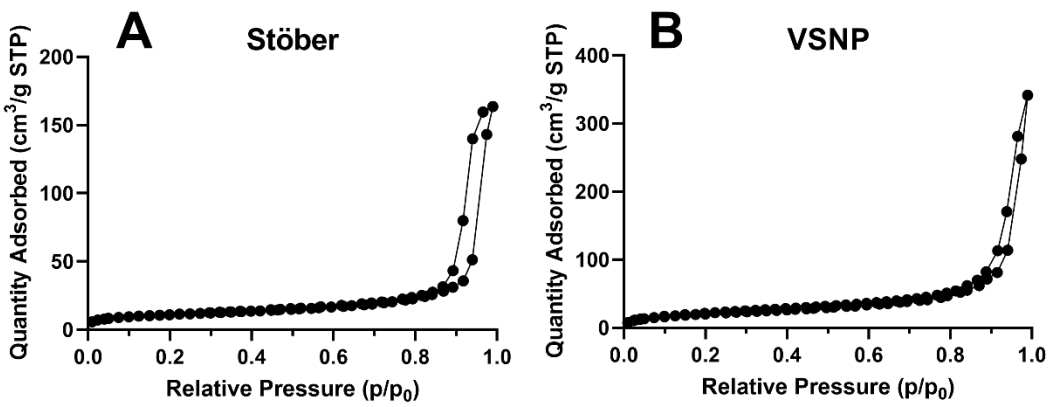

Figure S1. Nitrogen adsorption−desorption isotherms of (A) Stöber and (B) VSNP.

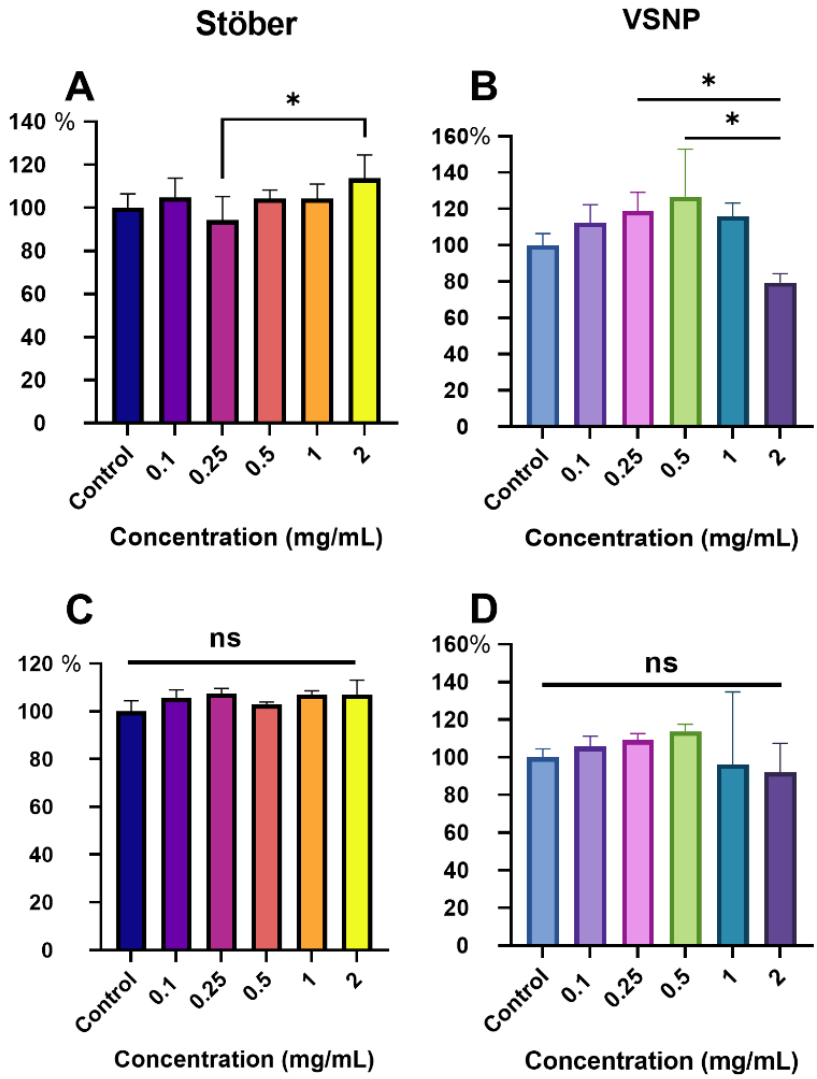

Figure S2. Cell viability test in Caco-2 (A, B) and MTX-HT29 (C, D) cell lines with cationic nanoparticles. Stöber did not show significant toxicity in both cell lines with over 90% cell viability in all groups (A,C). VSNP showed slight (cell viability 79.4%) toxicity in Caco-2 cells (B) but not in MTX-HT29 cells (D). n = 4.

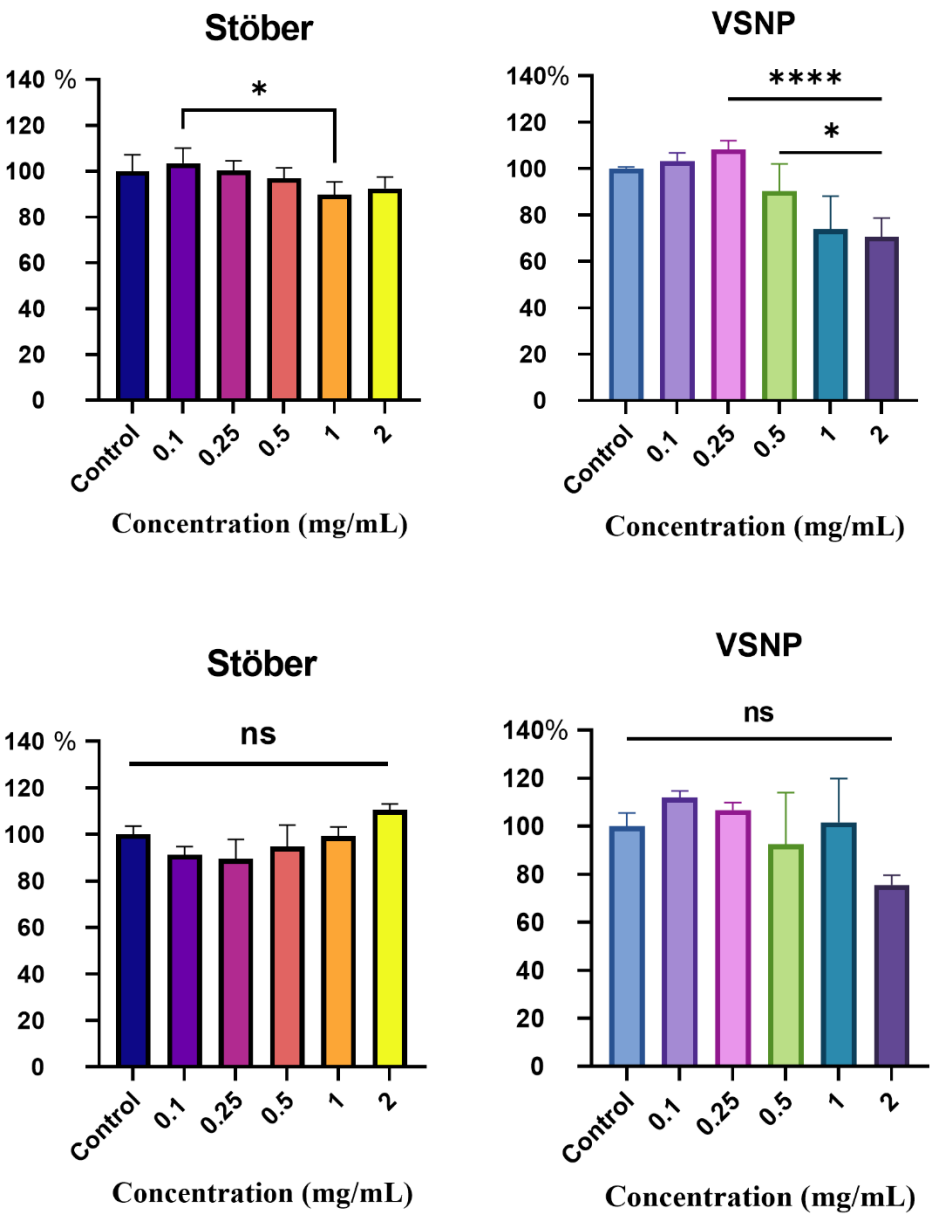

Figure S3 Cell viability test in Caco-2 (A, B) and MTX-HT29 (C, D) cell lines with anionic nanoparticles. Stöber at 1 mg/mL showed toxicity in Caco-2 cell line but had over 90% cell viability (A, C). VSNP showed slightly toxicity in Caco-2 cells at the concentration of 2 mg/mL and 1 mg/mL with around 70-80% viability (B), and 2 mg/mL induced significant cell death in MTX-HT29 cells (D). n = 4.

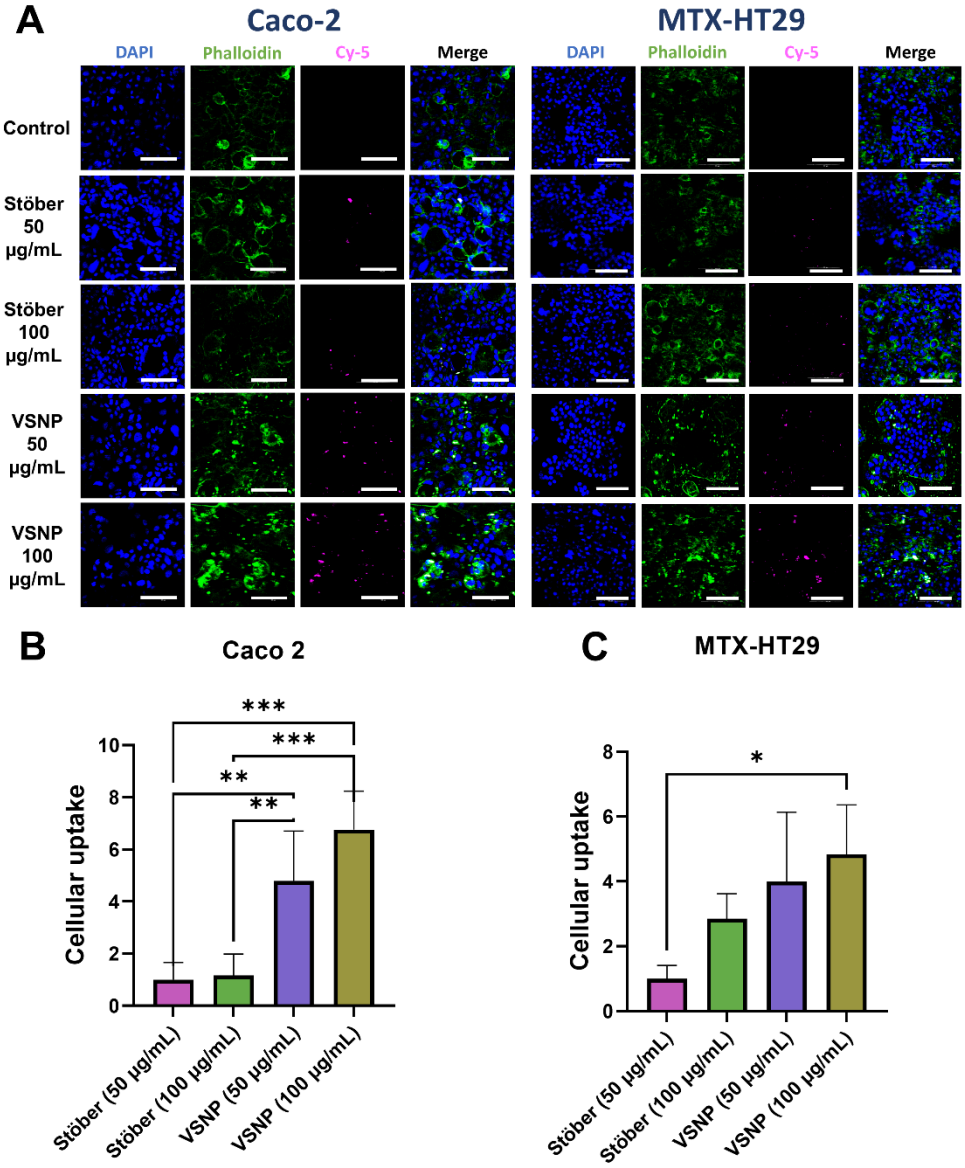

Figure S4. (A) Confocal image of cellular uptake of 60 nm Stöber and VSNP in Caco-2 cell line (left) and MTX-HT29 cell line (right) with concentration of 50 µg/mL and 100 µg/mL. Cell skeleton was stained by phalloidin in green, nuclei stained with DAPI in blue and nanoparticles linked with Cy5 shown in pink. Scale bar: 100 µm. Quantification of cellular uptake from confocal images of 60 nm Stöber and VSNP in (B) Caco-2 and (C) MTX-HT29 cell line treated with 50 and 100 µg/mL dose of nanoparticles for 24h. The fluorescent signal Cy5 and DAPI was analysed by image J with 5 images, and the Cy5 signal was normalized with DAPI. The data showed the fold change of Cy5/DAPI signal compared with Stöber (50 µg/mL). n=5.

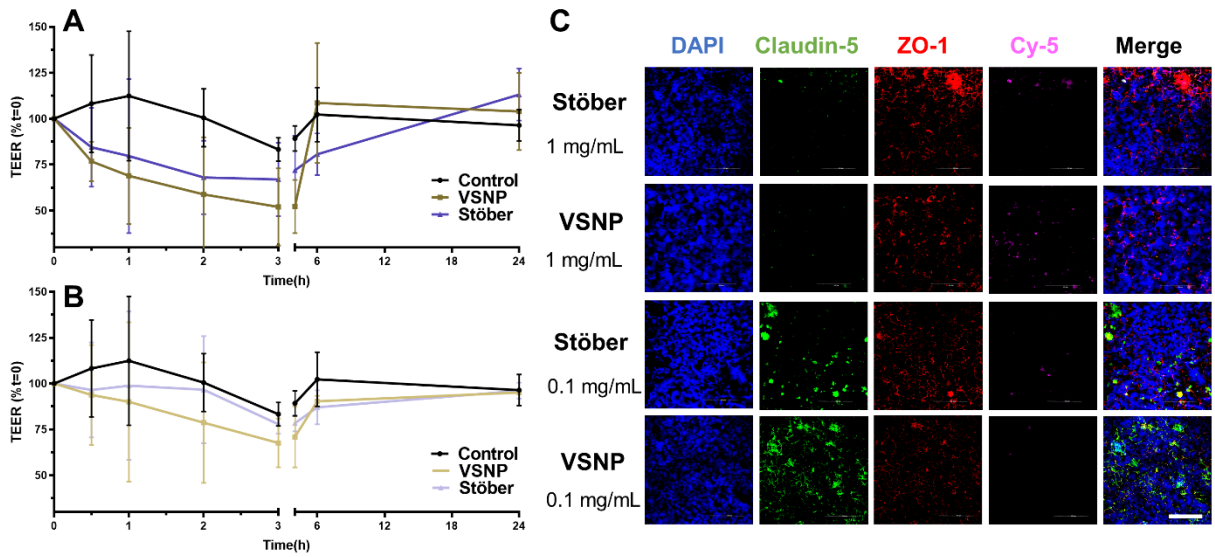

Figure S5. *In vitro* intestinal monolayer permeability in Caco-2 monolayer model. VSNP and Stöber was applied to the apical side of Caco-2 monolayer with (A) 1 mg/mL, and (B) 0.1 mg/mL. The TEER value change was recorded accordingly. (C) Representative confocal images of tight junction after VSNP and Stöber applied to Caco-2 monolayer model. The tight junction protein Claudin-5 was stained in green and Zonula occludens-1 (ZO-1) was stained in red. Silica nanoparticles are loaded with Cy5 (pink), and the nuclei is in blue. Scale Bar: 100 µm. N=3.

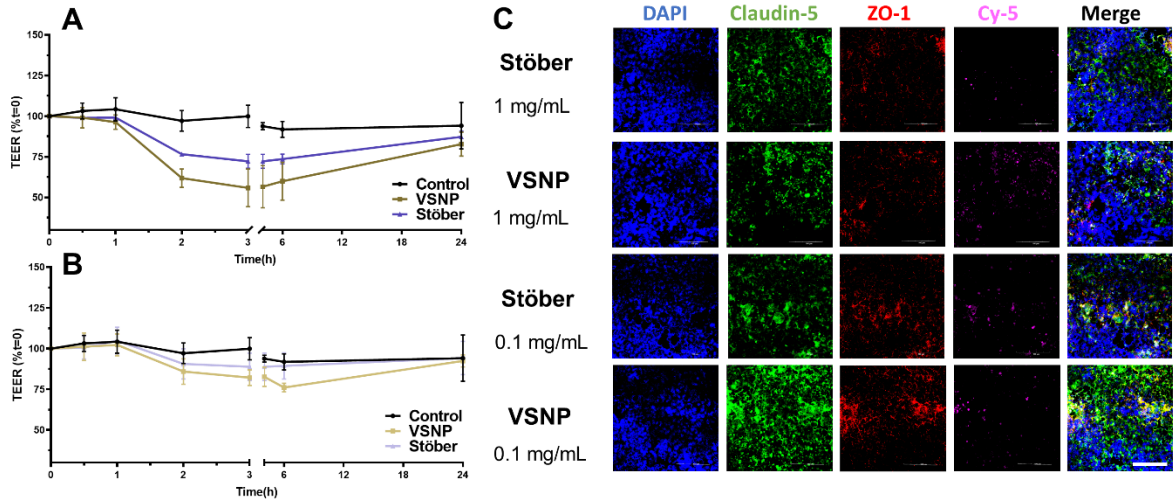

Figure S6. *In vitro* intestinal monolayer permeability in Caco-2/MTX-HT29 co-culture monolayer model. VSNP and Stöber was applied to the apical side of Caco-2/MTX-HT29 co-culture monolayer with (A) 1 mg/mL, and (B) 0.1 mg/mL. The TEER value change was recorded accordingly. (C) Representative confocal images of tight junction after VSNP and Stöber applied to Caco-2/MTX-HT29 co-culture model. The tight junction protein Claudin-5 was stained in green and Zonula occludens-1 (ZO-1) was stained in red. Silica nanoparticles are loaded with Cy5 (pink), and the nuclei is in blue. Scale Bar: 100 µm. n=3.

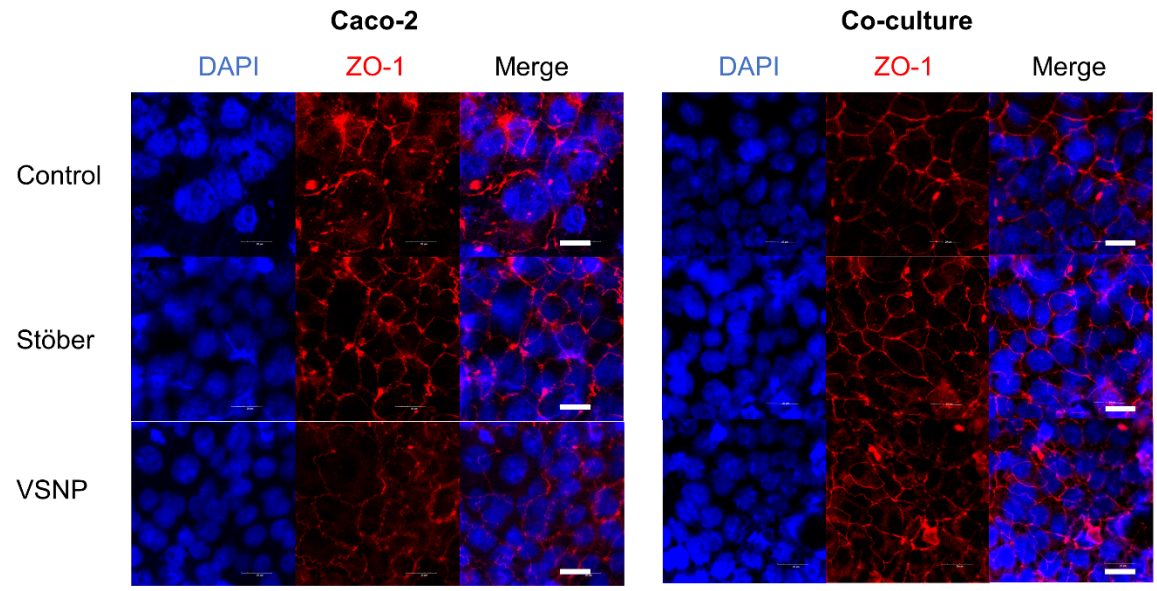

Figure S7. Representative confocal images of tight junction recovery of Caco-2 monolayer model and Caco-2/MTX-HT29 co-culture monolayer model after 24h treated by positively charged Stöber and VSNP. The tight junction protein Zonula occludens-1 (ZO-1) was stained in red, and the nuclei is in blue. Scale Bar: 20 μm.

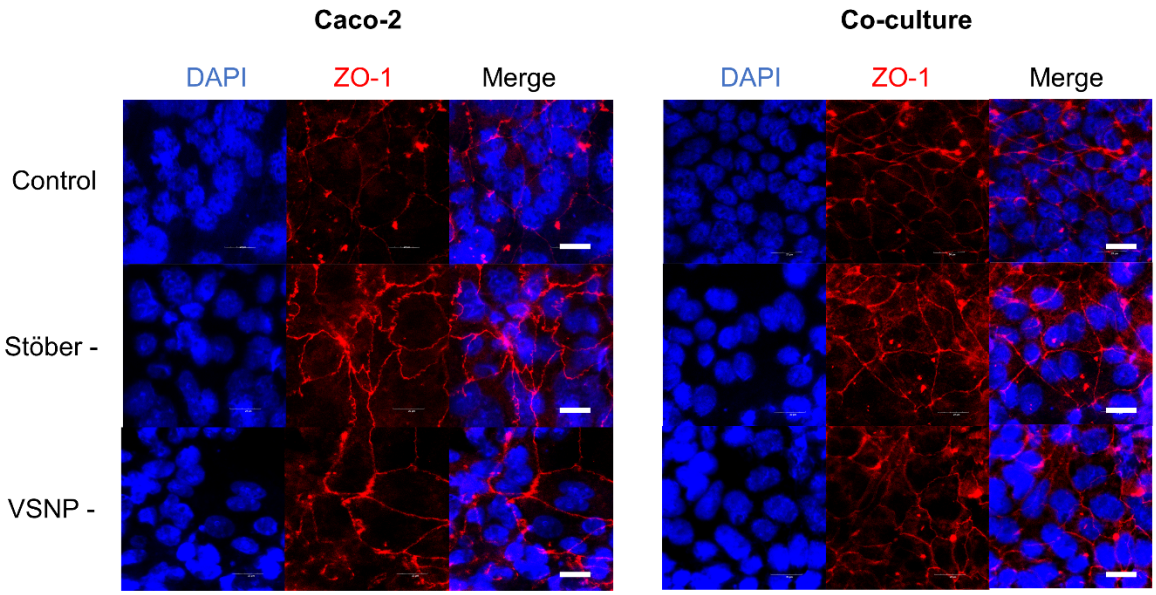

Figure S8. Representative confocal images of tight junction recovery of Caco-2 monolayer model and Caco-2/MTX-HT29 co-culture monolayer model after 24h treated by negatively charged Stöber and VSNP. The tight junction protein Zonula occludens-1 (ZO-1) was stained in red, and the nuclei is in blue. Scale Bar: 20 μm.