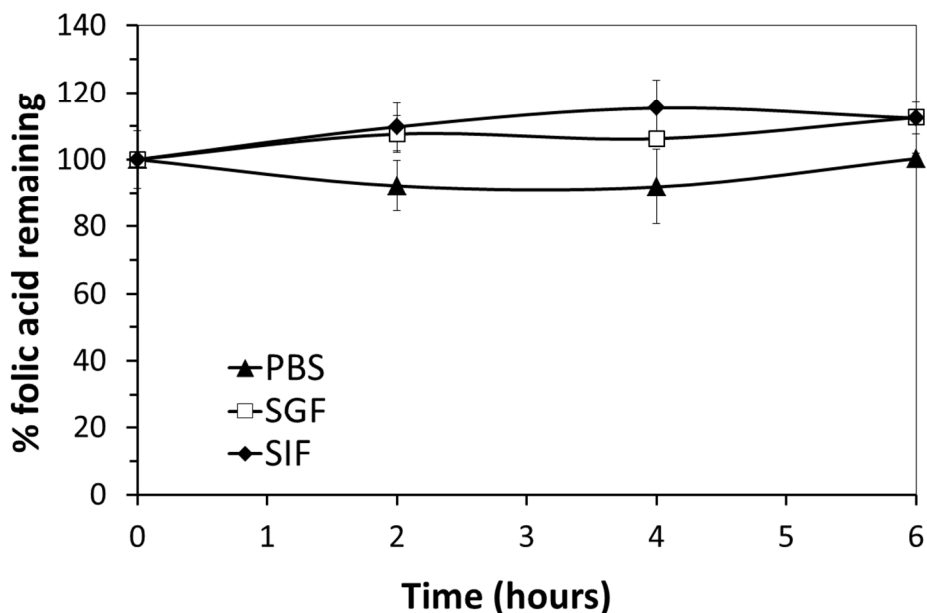


Supplementary Information

Stability of folic acid in simulated gastrointestinal fluids

Simulated gastric fluid and simulated intestinal fluids were prepared according to USP33-NF28. Folic acid (0.1 mg/mL) was added to either PBS or in simulated gastric and intestinal fluids and incubated at 37°C. Aliquots were taken at 0, 2, 4 and 6 hours and diluted with methanol. The diluted samples were analyzed by HPLC using Synergi C-12 column (150 cm x 4.60 mm, 4 µm particle size, Phenomenex, Torrance, CA). The mobile phase consisted of 50:50 v/v mixture of methanol and an aqueous buffer composed of sodium heptane sulfonate (1 g/L) and glacial acetic acid (0.8% v/v) at 0.4 mL/min. Folic acid was measured using a diode array detector at 290 nm. Retention time of folic acid was 4.3 min. These studies indicate that folic acid was stable in the simulated gastric and intestinal fluids for at least 6 h, the duration that folic acid conjugated nanoparticles will likely be in contact with these fluids *in vivo*.



Supplementary Figure 1: Stability of folic acid in phosphate buffered saline (PBS), simulated gastric fluid (SGF) and simulated intestinal fluid (SIF) at 37° C.