Supplementary Information

Nano-antacid enhance pH neutralization beyond their bulk counterpart: synthesis and characterization†

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Materials and Method

Materials

All materials were purchased from Sigma-Aldrich Corporation unless specified and used as received.

Experimental

The experimental plan is summarized in **Table 1**. Details of the experimental plan are described in the following sections.

Table 1: Experimental test plan

Test #	Experiment	Objective	Investigation finding	Notes
1.	Synthesis of vaterite particles	Use of the vaterite particles for antacid performance tests	Spherical vaterite particles having mean size 100 ± 8.5 nm were synthesized	Particles were characterized using TEM, XRD, XPS and DLS
2.	Synthesis of vaterite-magnetite nano-composites	Synthesize stable particles for imaging them in vivo	Composites having magnetite embedded in vaterite and a mean size of 100 nm were synthesized	Particles were characterized using TEM, XRD, and DLS
3.	Nucleation growth of vaterite studied	See the growth of the particles as they are formed	It is observed that vaterite is formed within 5 minutes of start of the synthesis reaction	Characterization done by ex-situ TEM
4 a.	Antacid tests conducted for different concentrations of liquid antacid	Compare antacid property of vaterite with substitute antacids and chemicals	Antacid properties of vaterite particles was better than all compared substitutes	Fordtran's model used for testing
4 b.	Check the dose response profiles of antacids	To mimic the real time churning condition of stomach	Significantly higher antacid activity time of vaterite over TUMS	
4 c.	Variation of stir rate in experiments	Check effect of stir rate at antacid effectiveness	Reduce neutralization time for higher stir rate	
5.	Agglomeration stability test	Check the stability of synthesized particles in various biomedical and industrial solvents	Particles are most stable in Albumin and least stable in water	TR-DLS characterization was done for 30 minutes

X-Ray Diffraction (XRD) Characterization

XRD patterns were obtained by using The Bruker d8 Advance X-ray Diffractometer (Bruker, USA) configured with a Cu X-Ray tube with 1.5418 Å for analysis of powder samples using LYNXEYE_XE detector. For the analysis, fine acetone ground $CaCO_3$ or magnetite $CaCO_3$ nanoparticles were kept on a Zero Diffraction Plate (MTI Corporation, USA). XRD data were scan from 20-60 degrees, with a 0.04 degree step size, a 0.5 second per step count time, with sample rotation turned on (15 rotation per minute), with a coupled two-theta/ theta scan. The Bruker Diffrac.Eva program was used for the evaluation and processing of X-ray diffraction scan data. Search-match operations included search by DI list, by name, using chemistry filters, and creating an International Centre for Diffraction Data (ICCDD PDF) database filter.

XPS Characterization

XPS data analysis was performed using the software Multipak, after performing a Shirley background correction.

Results

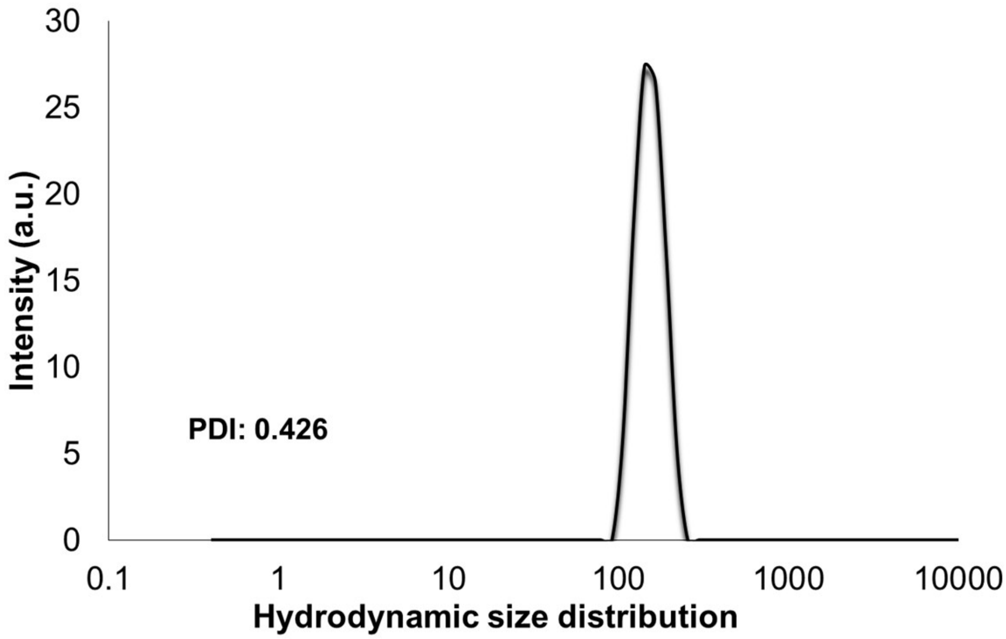
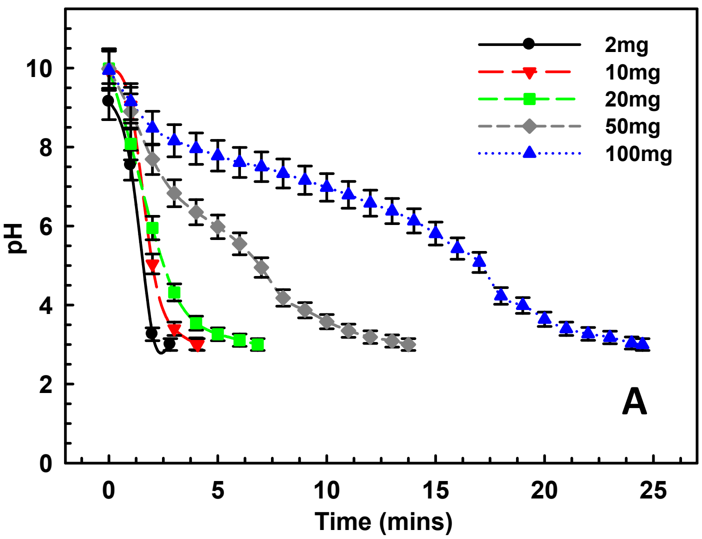


Fig. S1. Particle size distribution of synthesize $CaCO_3$ nanoparticles measured by DLS



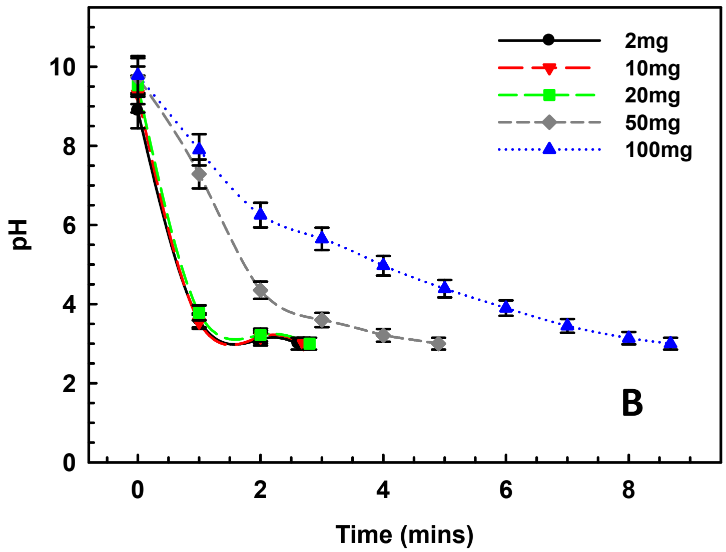


Fig. S2. Antacid profiles for different doses of A - **Synthesized vaterite calcium carbonate**. B – **TUMS regular strength 500 chewing tablet.** The antacid activity of the synthesized vaterite nanoparticles is much more than a commercial substitute antacid such as TUMS for same dosage. The reasons for this would be the higher dissolution of vaterite as compared to the calcite found in TUMS. A difference might also occur due to the lesser mass concentration of $CaCO_3$ in a given tablet of TUMS.

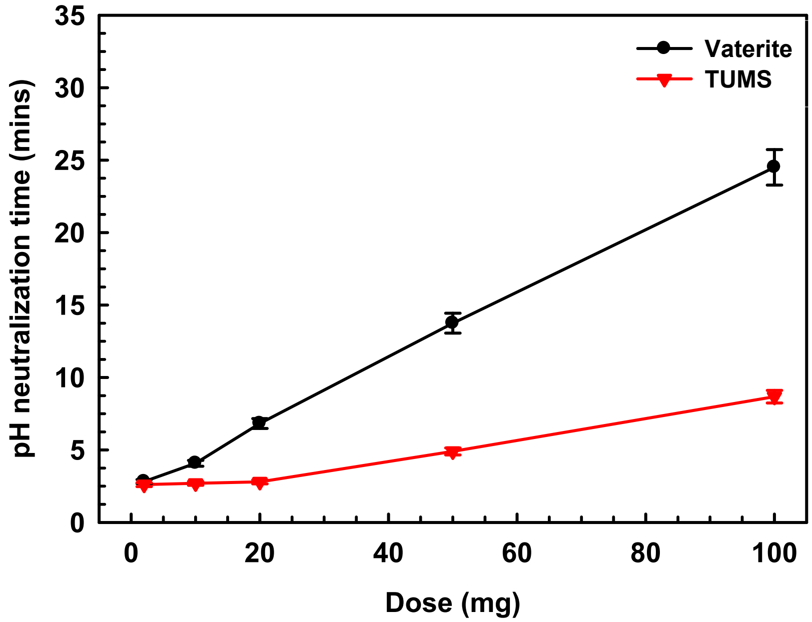


Fig. S3. Dose response curve for the synthesized vaterite nanoparticles and commercially available TUMS chewing tablet. The rate of increase in antacid activity is much larger for the synthesized calcium carbonate when compared to TUMS as is evident from the dose response curves for the two cases.

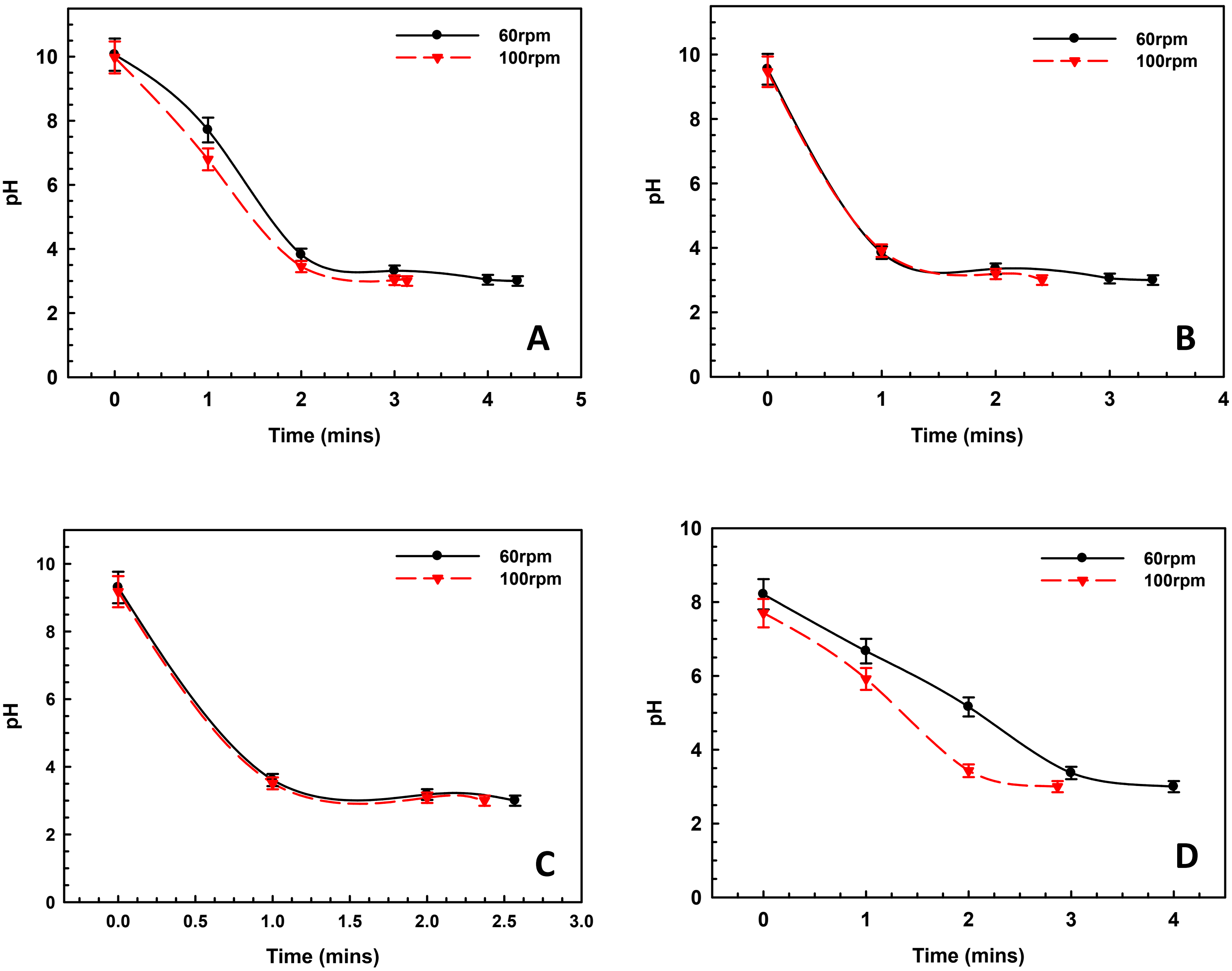


Fig. S4. The antacid profiles for different stirring rates for different substrates having a dose of 10mg. The profiles are of A – Synthesized vaterite particles, B – TUMS, C – Commercial calcium carbonate, D – Sodium bicarbonate. The graphs depict that the antacid activity time decreases with increase in the rate of stirring of the mixture. This could be because at higher rates of stirring, in addition to the antacid, the added hydrochloric acid is easily mixed in the solution as well and hence is more effective in reducing the pH than the antacid is in increasing it.

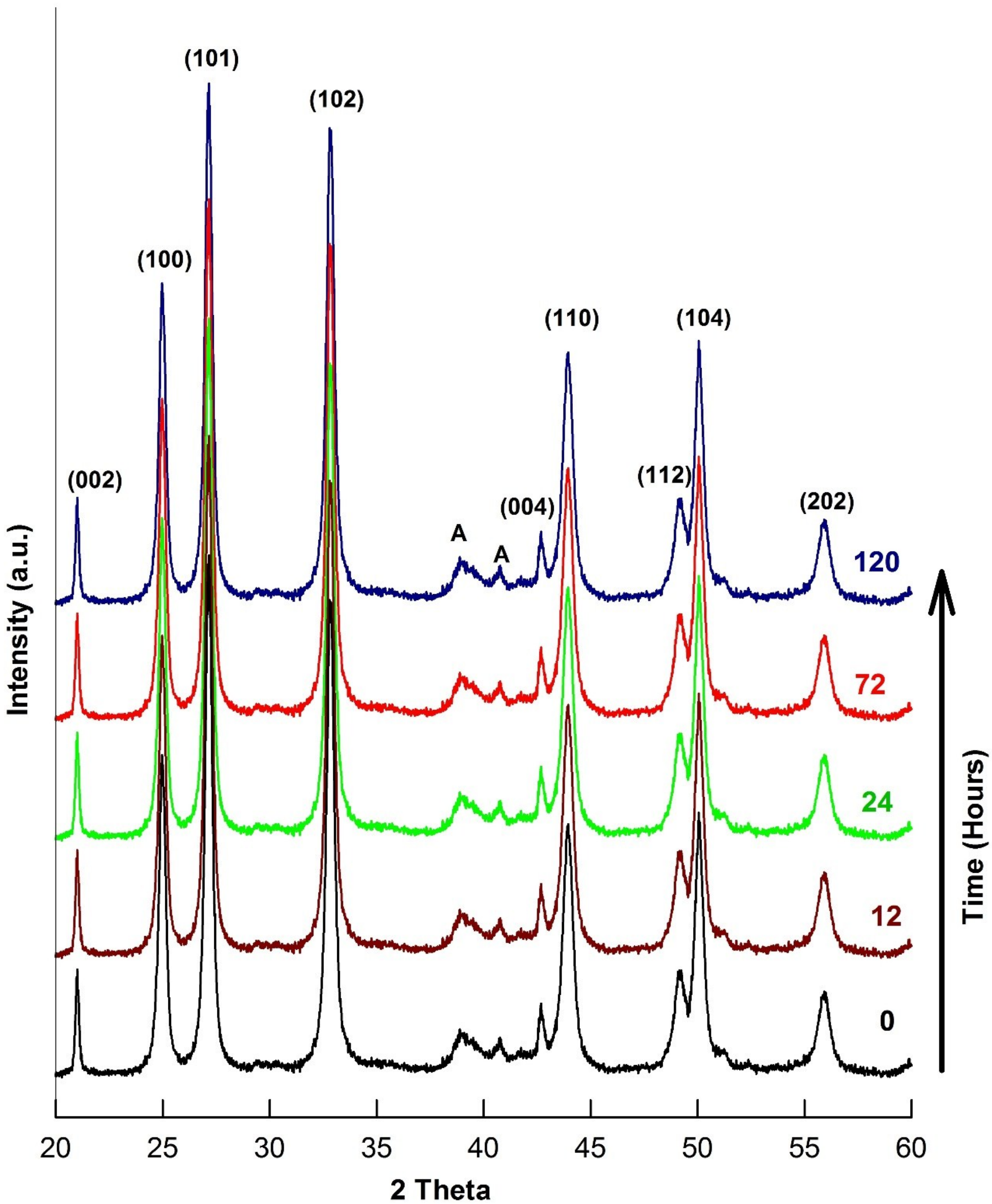


Fig. S5. XRD characterization of synthesized vaterite nanoparticles over the period of time. XRD was recorded for various interval up to 120 hours. It should be noted that there was no change in the crystal structure of the vaterite particles.