## Electronic Supplementary Information (ESI)

## for

## Layer-by-Layer Coated Nanoliposome for Oral Delivery of Insulin

Yiming Zhang ${ }^{\text {a }}$, Gordon Minru Xiong ${ }^{\text {a }}$, Yusuf Alib ${ }^{\text {b }}$, Bernhard O. Boehm ${ }^{\text {b }}$, Ying Ying Huang ${ }^{\text {a, },}$, Subbu Venkatramana, ${ }^{\text {a, }}$
a. School of Materials Science and Engineering, Nanyang Technological University, Blk N4.1, Nanyang Avenue, Singapore 639798
b. Lee Kong Chian School of Medicine, Clinical Sciences Building, 11 Mandalay Road, Singapore 308232

* Corresponding authors. Tel.: +656316 8976; fax: +65 6790 9081. E-mail address:
yingyinghuang@ntu.edu.sg (Yingying Huang), assubbu@ntu.edu.sg (S.S. Venkatraman)

Keywords: Layer-by-Layer nanoparticles, nanoliposomes, oral insulin delivery, diabetes mellitus, chitosan
(b)


Number of layers

Figure 1. Extended application of the LbL coating technique on another model protein Bovine Serum Albumin (BSA). Effect of increasing coating layers of chitosan $310-190 / \mathrm{BSA}$ on (a) hydrodynamic size and (b) zeta potential


Figure 2. (a) hydrodynamic size and (b) zeta potential of 11 layers LbL coated liposome in SGF pH 1.2.


Figure 3. Effect of increasing coating layers and polymer length on LbL release and stability in SIF pH 6.8 at $37^{\circ} \mathrm{C}$. (A) comparison of release and stability of 3, 5, and 11 layers of chitosan 310-190/insulin coated LbL liposome in SIF pH 6.8 at
$37^{\circ} \mathrm{C}$. (B) Release and stability of 11 layers of LbL fabricated with different molecular weight of chitosan/insulin in SIF pH 6.8 at $37^{\circ} \mathrm{C}$. DLS was used to measure the particle size. The data is represented by mean $\pm$ standard deviation ( $\mathrm{n}=3, * \mathrm{P}<$ $0.05)$.


Figure 4. Release profile of LbL in PBS pH 7.4 at $37^{\circ} \mathrm{C}$ over 12 weeks. Comparison between release of 3 and 5 layers of chitosan 310-190/insulin coated LbL liposome and insulin loaded HSPC/DPPG liposome core (L0).

