

## Supplementary Material

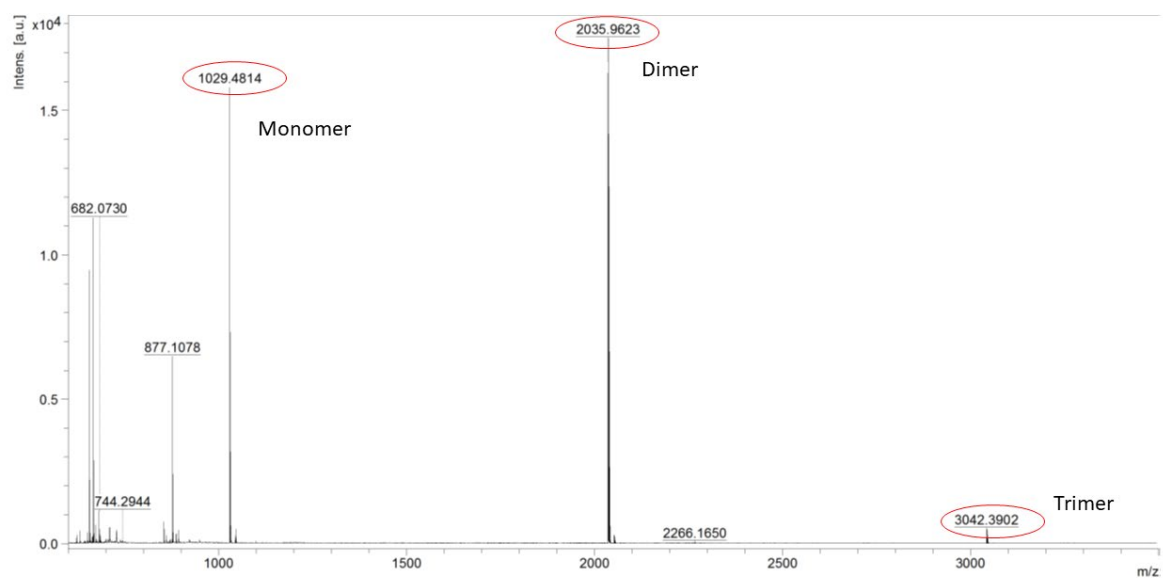
### Encapsulation and Controlled Release of the Therapeutic Neuropeptides Somatostatin and Oxytocin from the Lipidic Bicontinuous Cubic Phase

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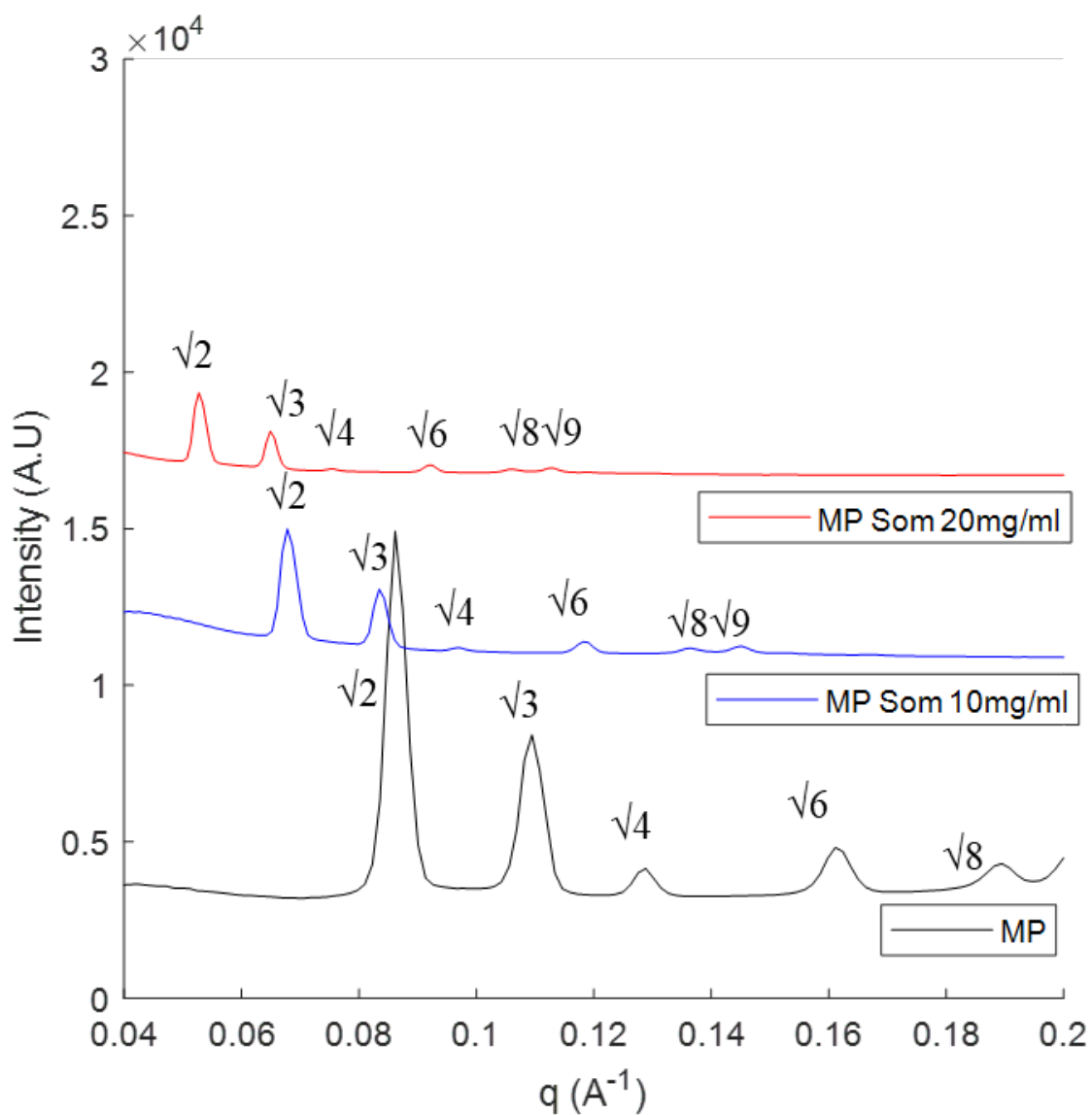
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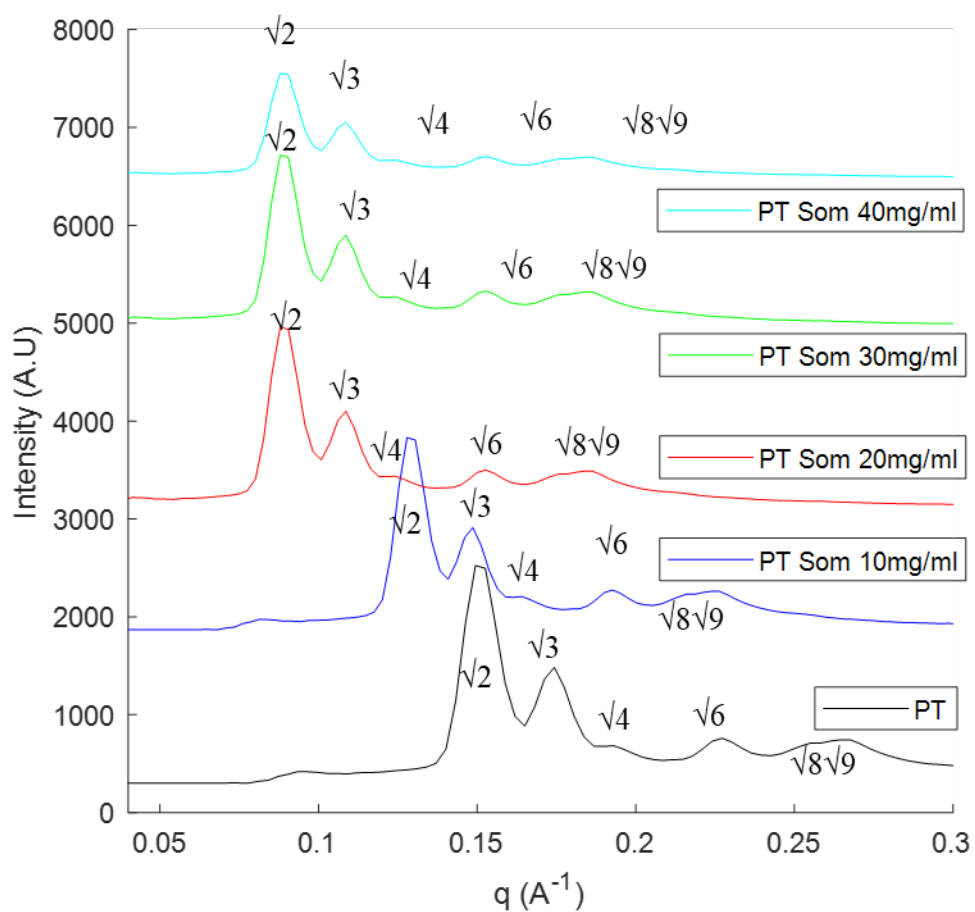
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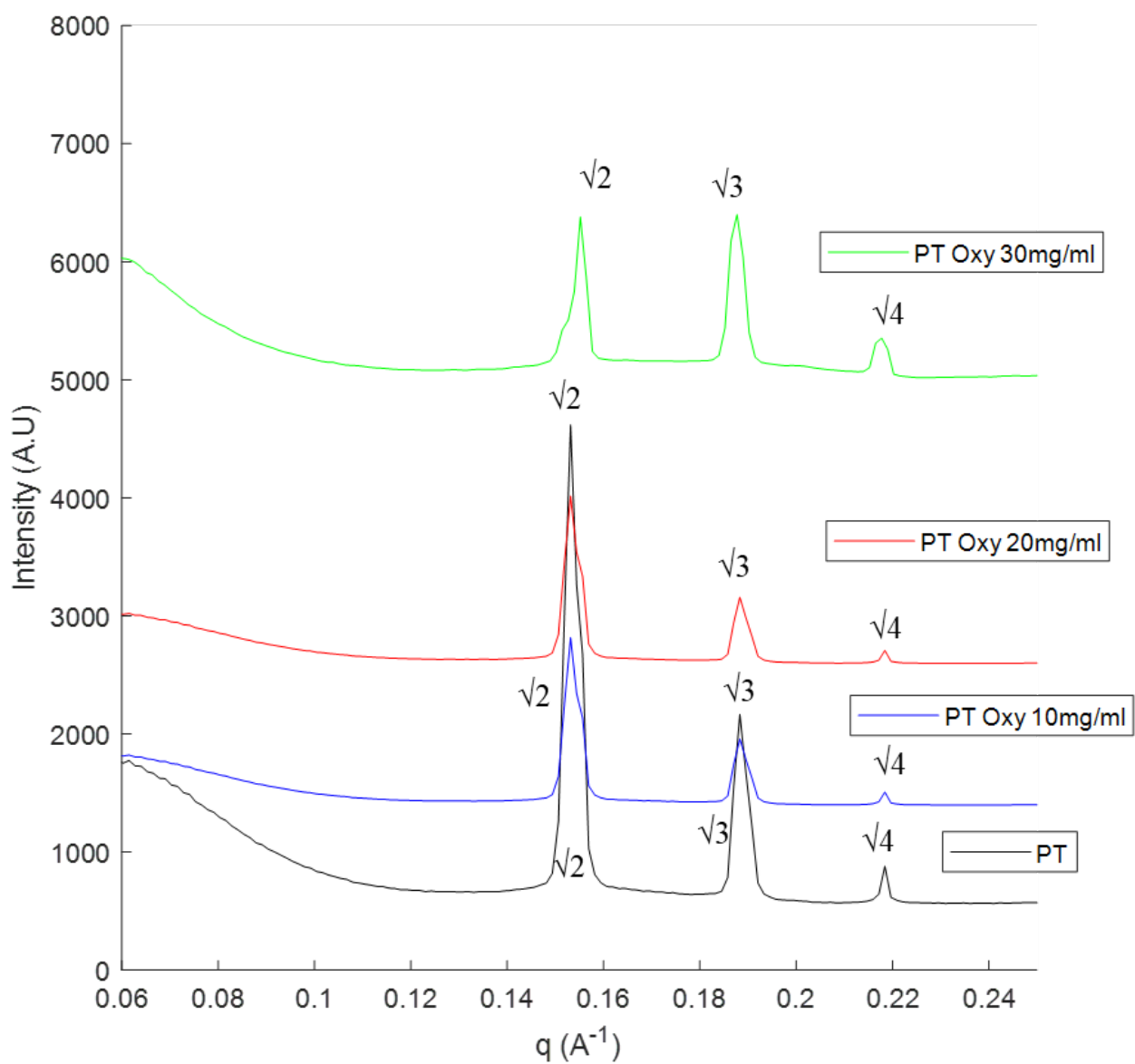
**Figure S1.** Mass spectroscopy analysis of the oxytocin peptide.



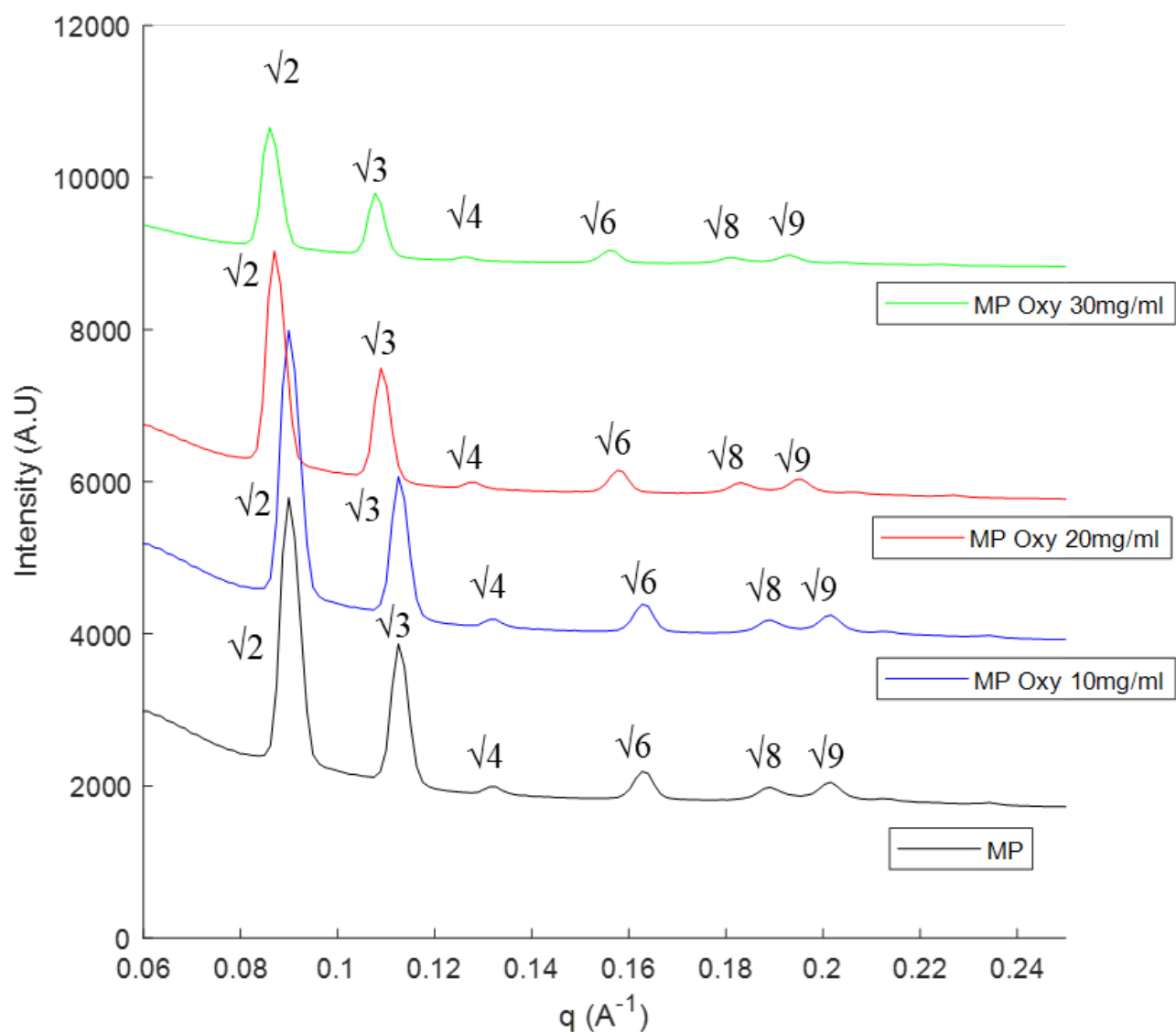
**Figure S2.** Representative 1-D diffraction plot of intensity vs.  $q$  for MP cubosomes (5wt%) at 37 °C with encapsulated somatostatin. The  $\sqrt{2}$ ,  $\sqrt{3}$ ,  $\sqrt{4}$ ,  $\sqrt{6}$ ,  $\sqrt{8}$  and  $\sqrt{9}$  reflections of a  $Q_{II}^D$  (Diamond) phase may be observed.



**Figure S3.** Representative 1-D diffraction plot of intensity vs.  $q$  for PT cubosomes (5wt%) at 37 °C with encapsulated somatostatin. The  $\sqrt{2}$ ,  $\sqrt{3}$ ,  $\sqrt{4}$ ,  $\sqrt{6}$ ,  $\sqrt{8}$  and  $\sqrt{9}$  reflections of a  $Q_{II}^D$  (Diamond) phase may be observed.



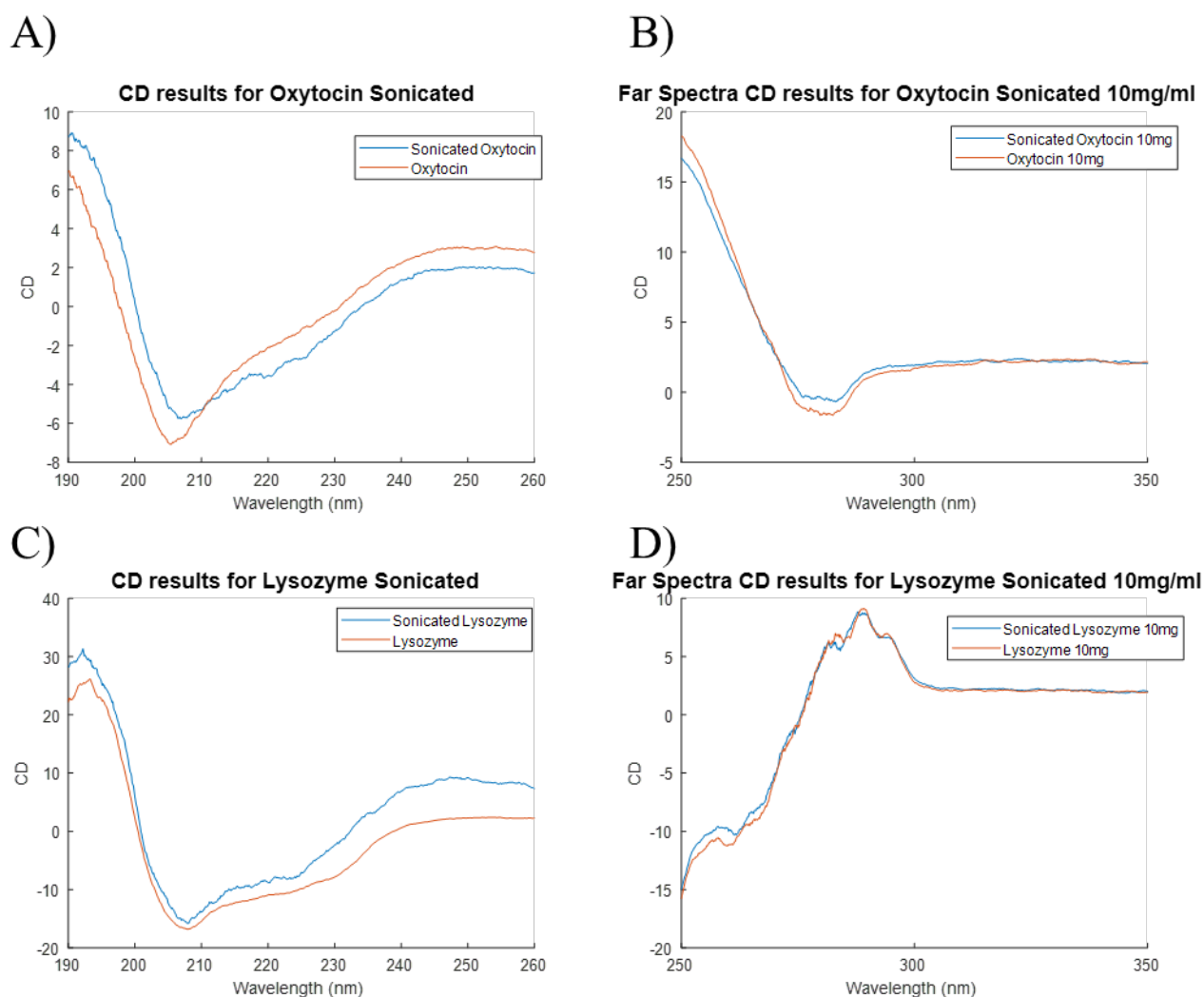
**Figure S4.** Representative 1-D diffraction plot of intensity vs.  $q$  for PT cubosomes (5wt%) at 37 °C with encapsulated oxytocin. The  $\sqrt{2}$ ,  $\sqrt{3}$ ,  $\sqrt{4}$ ,  $\sqrt{6}$ ,  $\sqrt{8}$  and  $\sqrt{9}$  reflections of a  $Q_{II}^D$  (Diamond) phase may be observed.



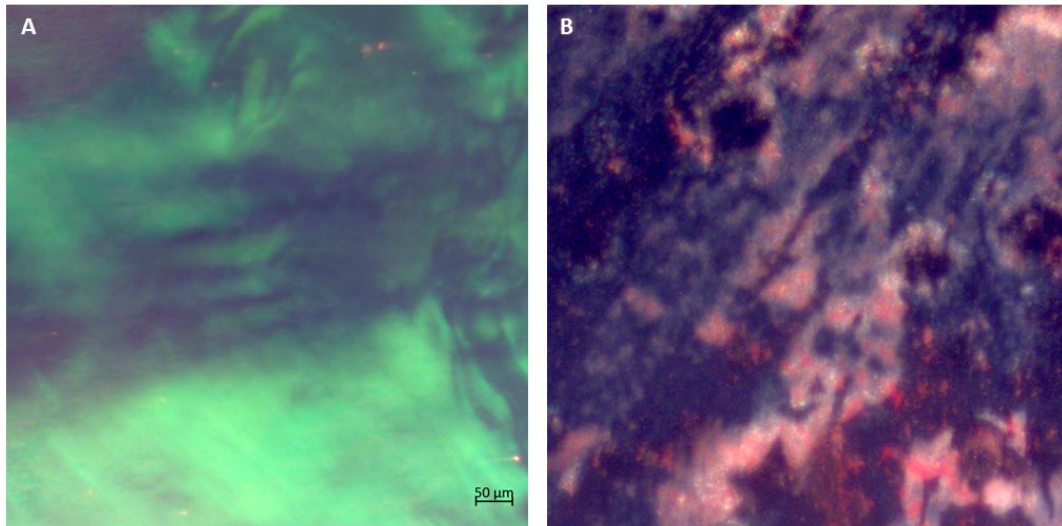
**Figure S5.** Representative 1-D diffraction plot of intensity vs.  $q$  for MP cubosomes (5wt%) at 37 °C with encapsulated oxytocin. The  $\sqrt{2}$ ,  $\sqrt{3}$ ,  $\sqrt{4}$ ,  $\sqrt{6}$ ,  $\sqrt{8}$  and  $\sqrt{9}$  reflections of a  $Q_{II}^D$  (Diamond) phase may be observed.

## Effect of Sonication on Peptide Secondary Structure

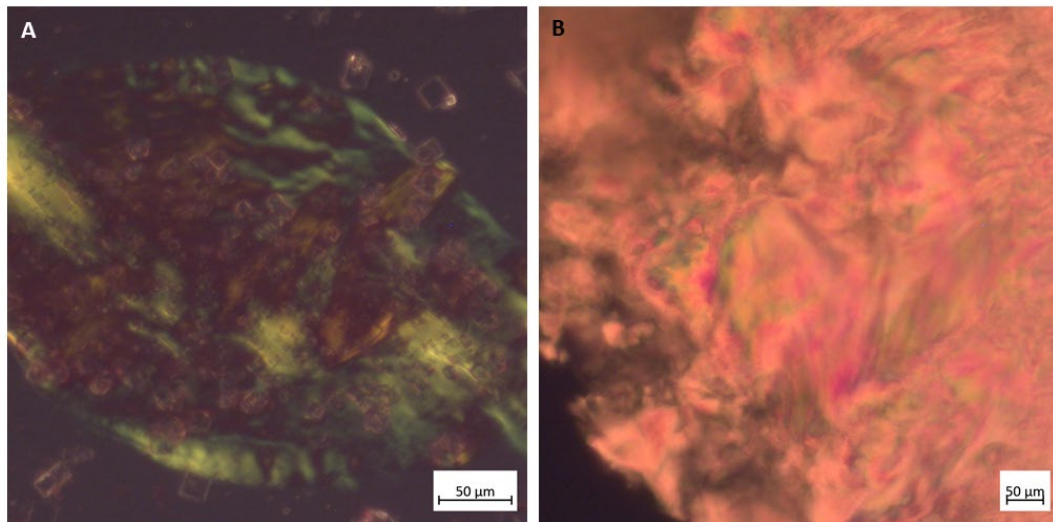
We investigated whether the use of sonication to disperse the bulk cubic phase into cubosomes would induce any change to the structure of incorporated proteins. The effect was investigated for Oxytocin. The effect of sonication on the larger protein lysozyme was also investigated as larger peptides and protein may be more susceptible to denaturation from the mechanical force applied. Figure S6 shows the far-UV spectra for lysozyme and oxytocin before and after 20min of sonication. Note that the time for sonication is considerably longer than that used in the protocol to produce cubosomes. The spectra showed no structural changes in the near or far region of CD spectra confirming that the secondary and tertiary structures of the peptide were unaffected by the sonication process.



**Figure S6.** Benchtop CD spectra results showing A) Near UV spectra for Oxytocin with B) Far UV oxytocin spectra. C) Near UV spectra results for lysozyme with D) Far-UV CD spectra for lysozyme.

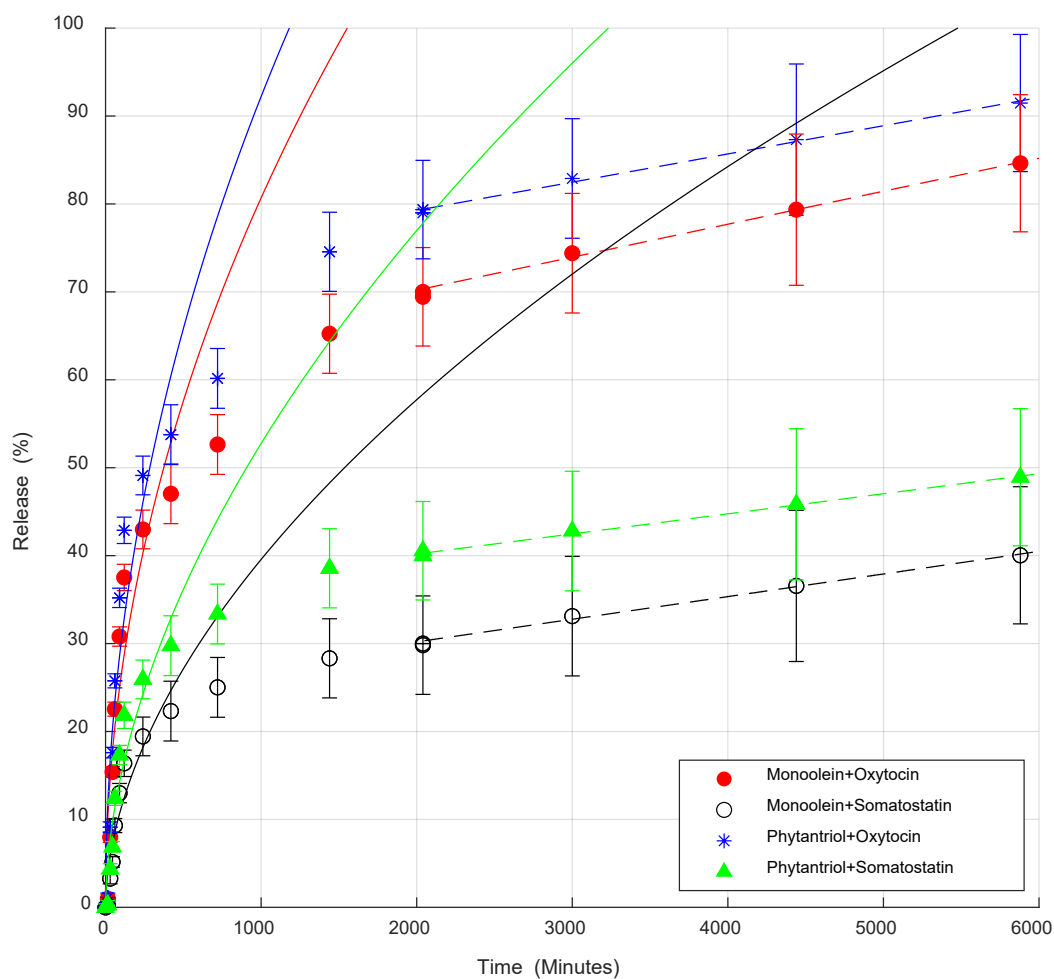


**Figure S7.** Cross-polarized optical microscopic images of Congo Red stained (A) Somatostatin and (B) Oxytocin at a concentration of 10 mg/mL.



**Figure S8.** Cross-polarized optical microscopic images of Congo Red stained (A) Somatostatin alone at 10 mg/mL and (B) Somatostatin with monoolein at a concentration of 10 mg/mL.





**Figure S9** The rate of release of SST-14 and oxytocin from the Monoolein and phytantriol bicontinuous cubic phase over 98 hours (5880 min) . Data have been fitted to the Ritger-Peppas model with  $n$  set to 0.5 i.e. diffusion-controlled release. Dashed lines show a linear fit to the release data from  $\sim 1.5$  days to 4 days.