

## Supporting Information

# Disaggregation of Amylin Aggregate by Novel Conformationally Restricted Aminobenzoic Acid containing $\alpha/\beta$ and $\alpha/\gamma$ Hybrid Peptidomimetics

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## Characterization data of peptides 1 to 9:

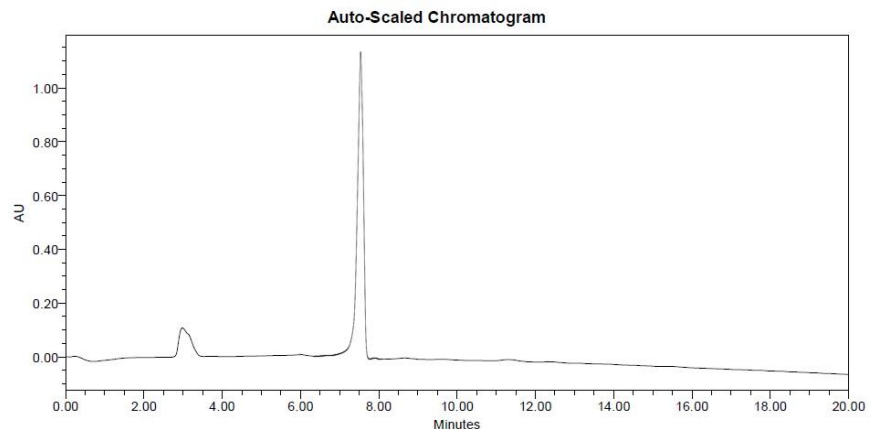


Figure S1 : HPLC profile of the purified peptide 1.

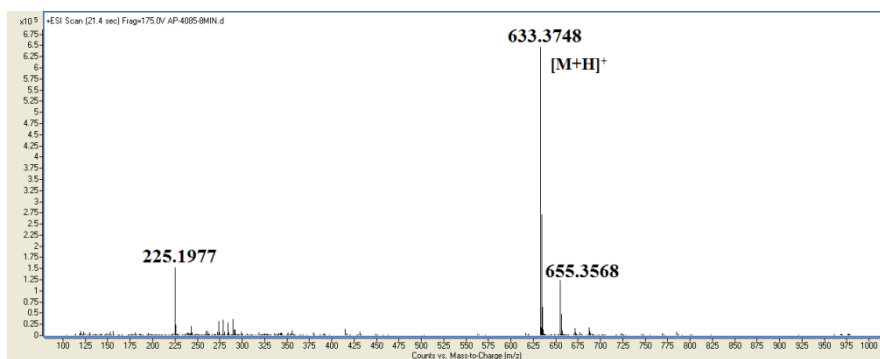


Figure S2. Mass spectrum of peptide 1. Calculated mass for  $C_{30}H_{49}N_8O_7$  is 633.3724  $[M+H]^+$ , observed 633.3748  $[M+H]^+$  and calculated mass for  $C_{30}H_{48}N_8O_7Na$  is 655.3544  $[M+Na]^+$ , observed 655.3568  $[M+Na]^+$ .

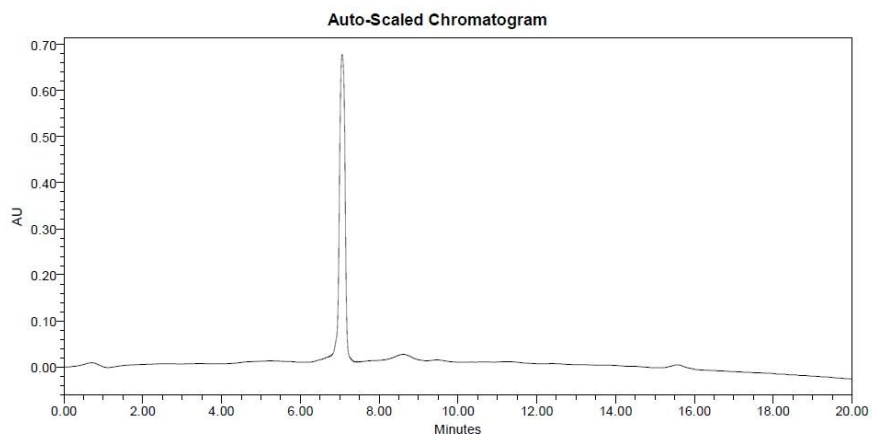
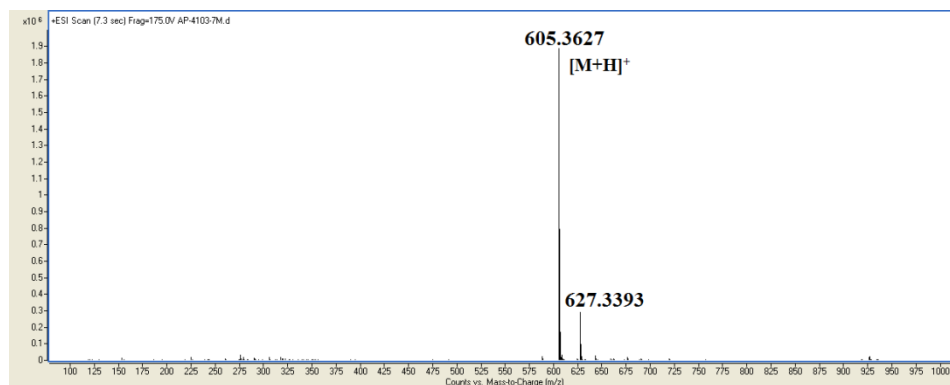
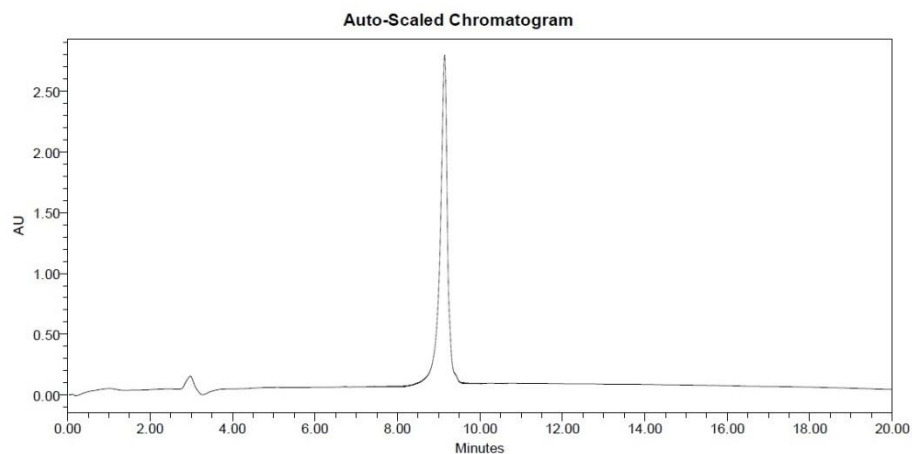


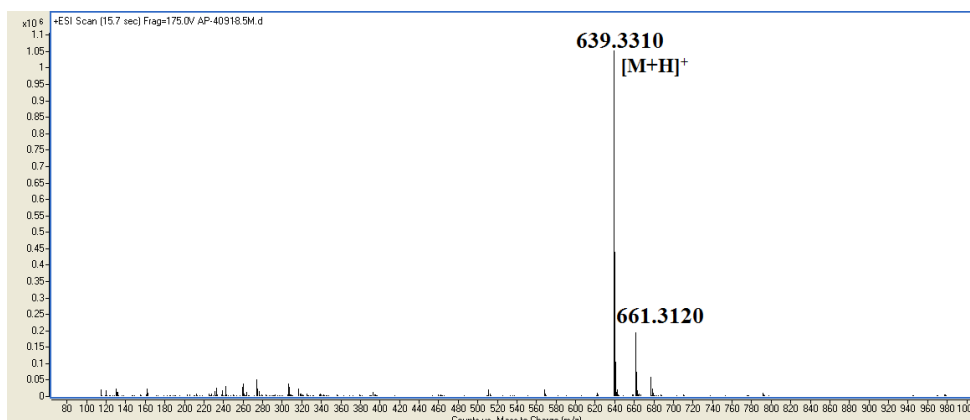
Figure S3. HPLC profile of the purified peptidomimetic 2.



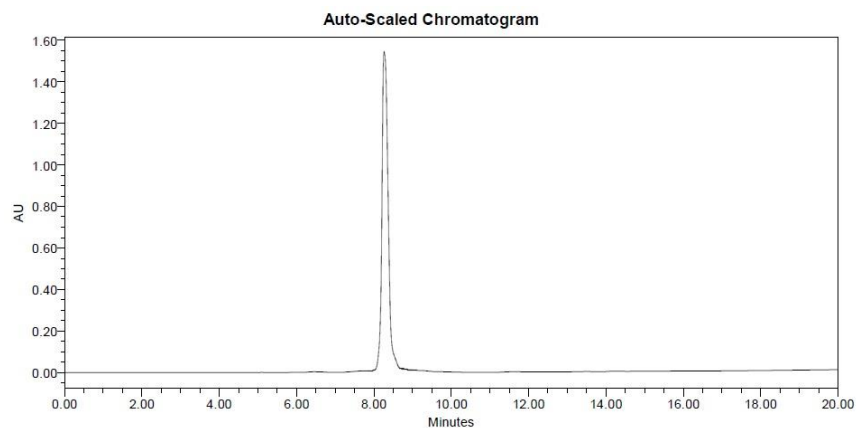
**Figure S4.** Mass spectrum of peptidomimetic **2**. Calculated mass for  $C_{28}H_{45}N_8O_7$  is 605.3411  $[M+H]^+$ , observed 605.3627  $[M+H]^+$  and calculated mass for  $C_{28}H_{44}N_8O_7Na$  is 627.3231  $[M+Na]^+$ , observed 627.3393  $[M+Na]^+$ .



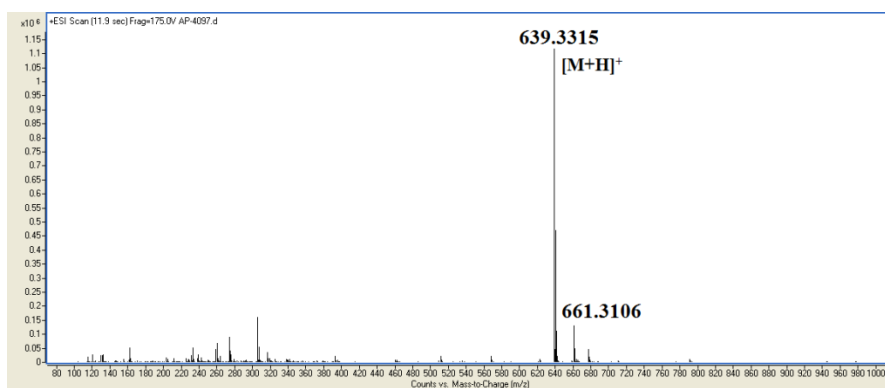
**Figure S5.** HPLC profile of the purified peptidomimetic **3**.



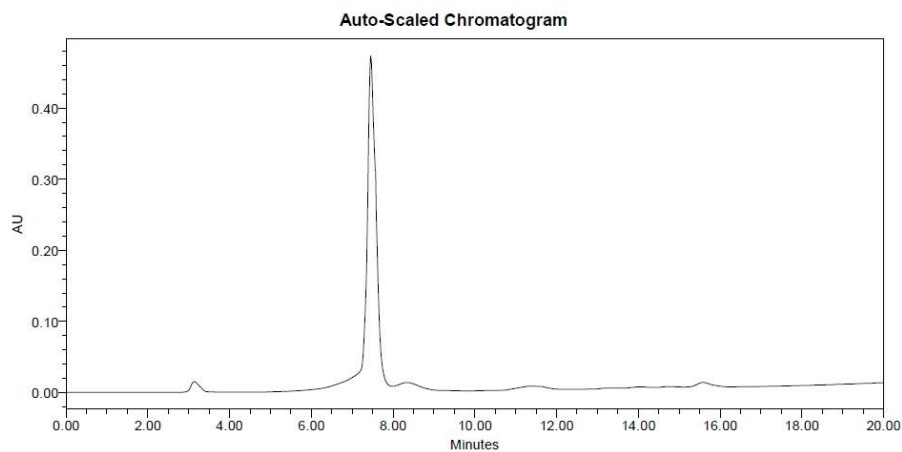
**Figure S6.** Mass spectrum of peptidomimetic **3**. Calculated mass for  $C_{31}H_{43}N_8O_7$  is 639.3255  $[M+H]^+$ , observed 639.3310  $[M+H]^+$  and calculated mass for  $C_{31}H_{42}N_8O_7Na$  is 661.3074  $[M+Na]^+$ , observed 661.3120  $[M+Na]^+$ .



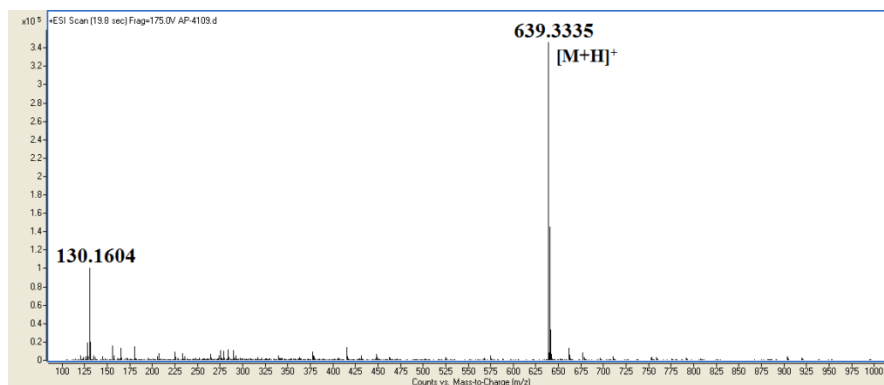
**Figure S7.** HPLC profile of the purified peptidomimetic **4**.



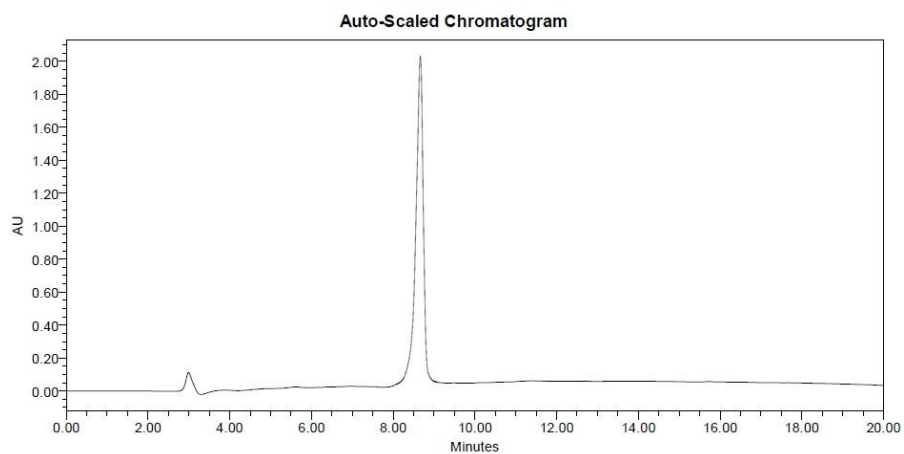
**Figure S8.** Mass spectrum of peptidomimetic **4**. Calculated mass for  $C_{31}H_{43}N_8O_7$  is 639.3255  $[M+H]^+$ , observed 639.3315  $[M+H]^+$  and calculated mass for  $C_{31}H_{42}N_8O_7Na$  is 661.3074  $[M+Na]^+$ , observed 661.3106  $[M+Na]^+$ .



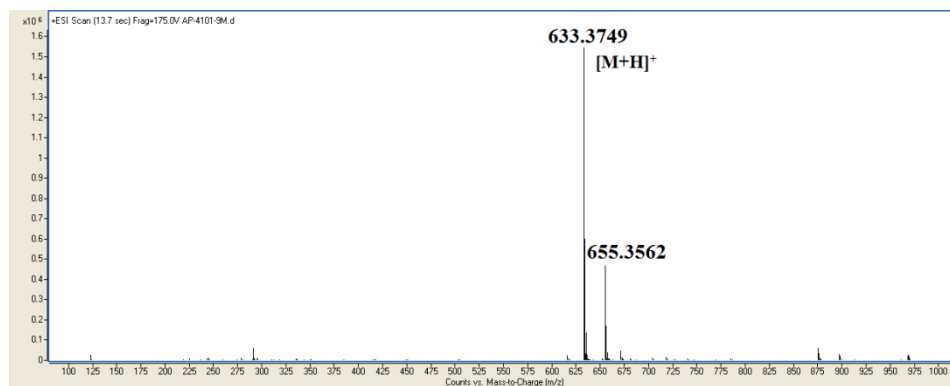
**Figure S9.** HPLC profile of the purified peptidomimetic **5**.



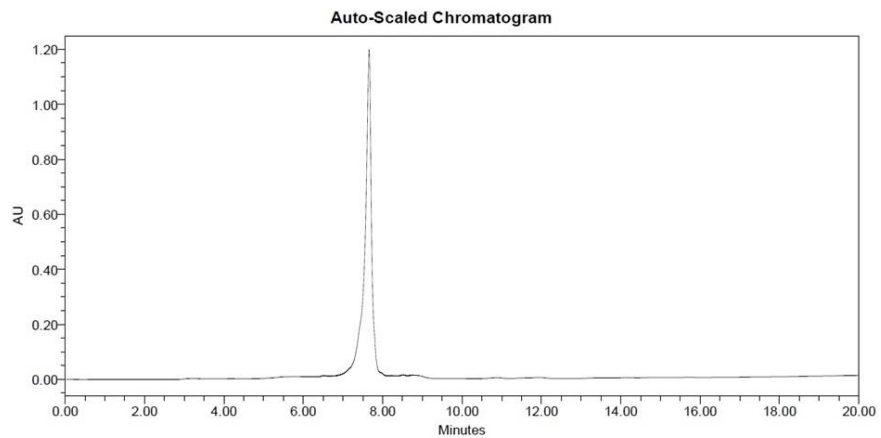
**Figure S10.** Mass spectrum of peptidomimetic **5**. Calculated mass for  $C_{31}H_{43}N_8O_7$  is 639.3255  $[M+H]^+$ , observed 639.3335  $[M+H]^+$ .



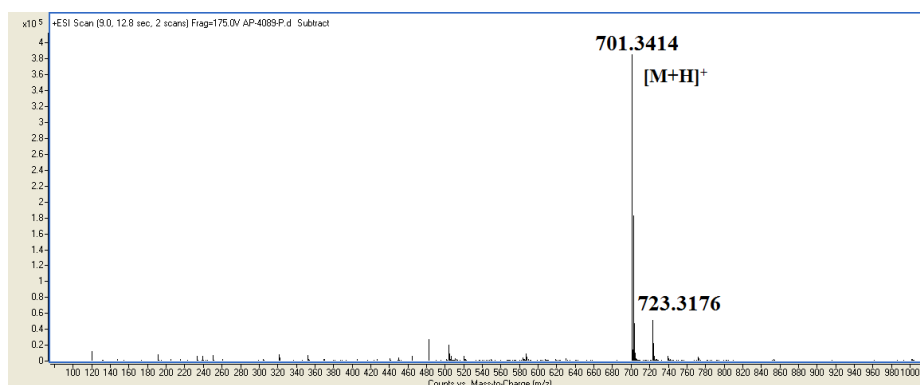
**Figure S11.** HPLC profile of the purified peptidomimetic **6**.



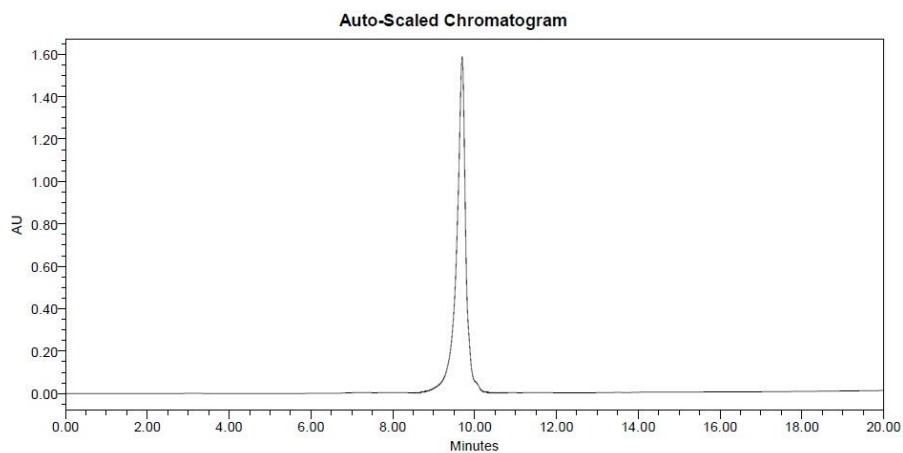
**Figure S12.** Mass spectrum of peptidomimetic **6**, Calculated mass for  $C_{30}H_{49}N_8O_7$  is 633.3724  $[M+H]^+$ , observed 633.3749  $[M+H]^+$  and calculated mass for  $C_{30}H_{48}N_8O_7Na$  is 655.3544  $[M+Na]^+$ , observed 655.3562  $[M+Na]^+$ .



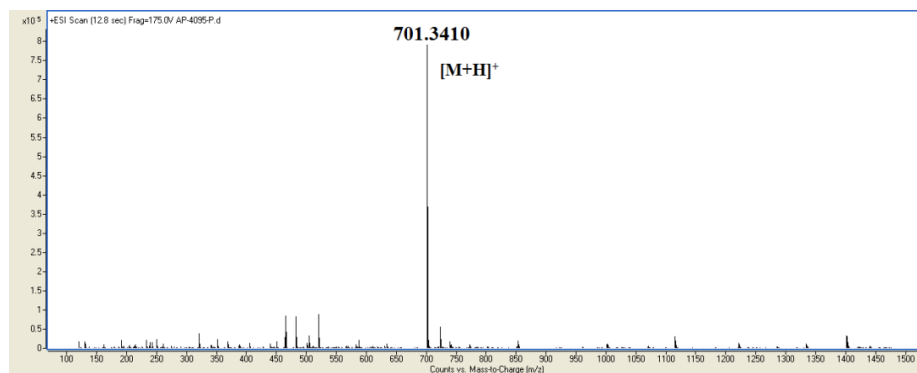
**Figure S13.** HPLC profile of the purified peptidomimetic **7**.



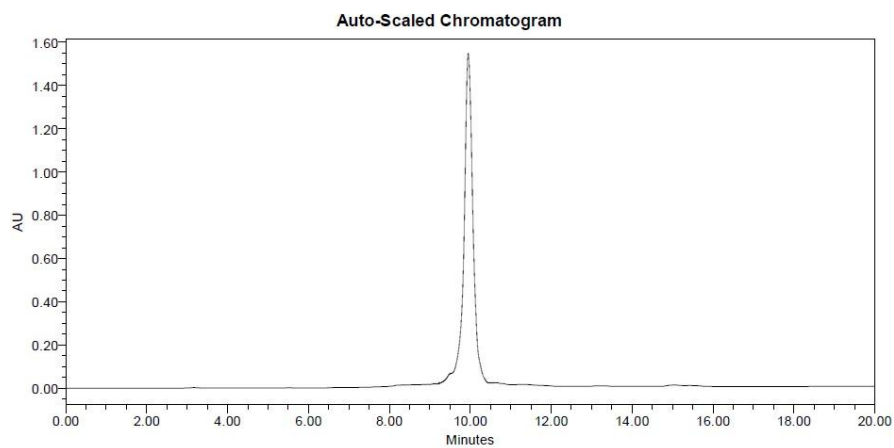
**Figure S14.** Mass spectrum of peptidomimetic **7**. Calculated mass for  $C_{36}H_{45}N_8O_7$  is 701.3411  $[M+H]^+$ , observed 701.3414  $[M+H]^+$  and calculated mass for  $C_{36}H_{44}N_8O_7Na$  is 723.3231  $[M+Na]^+$ , observed 723.3176  $[M+Na]^+$ .



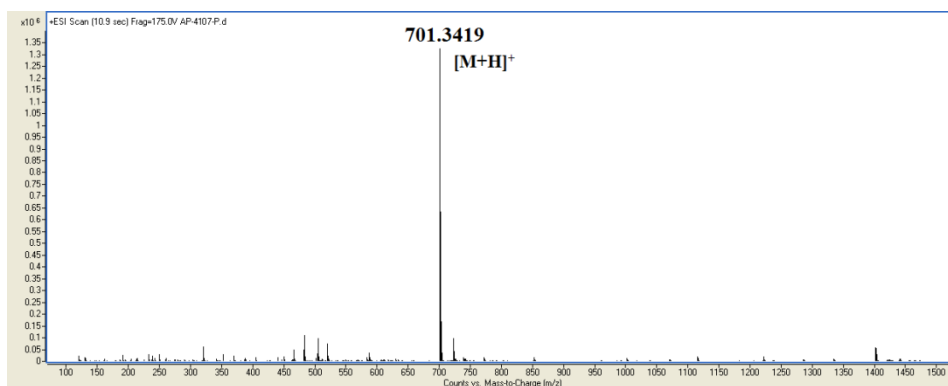
**Figure S15.** HPLC profile of the purified peptidomimetic **8**.



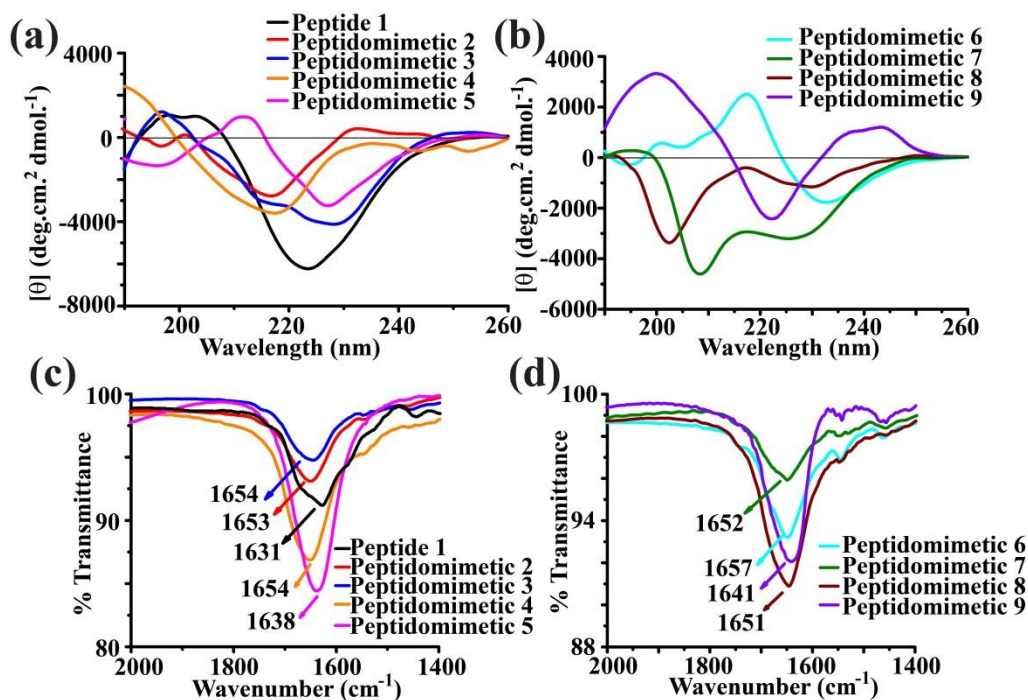
**Figure S16.** Mass spectrum of peptidomimetic **8**. Calculated mass for  $C_{36}H_{45}N_8O_7$  is 701.3411  $[M+H]^+$ , observed 701.3410  $[M+H]^+$ .



**Figure S17.** HPLC profile of the purified peptidomimetic **9**.

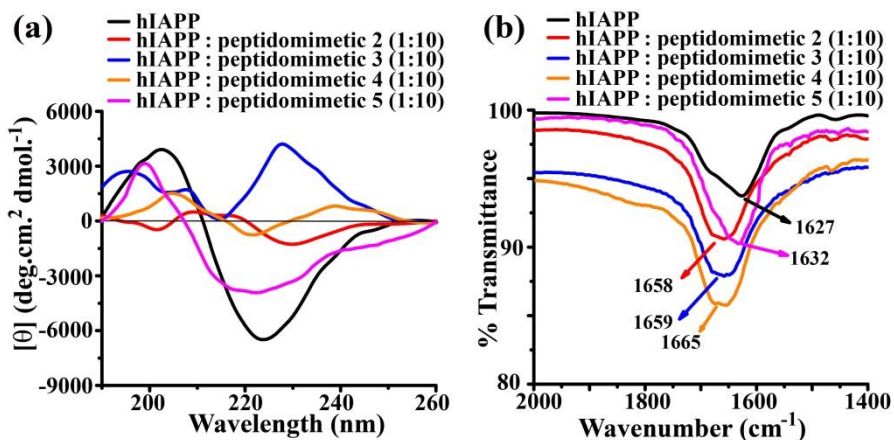


**Figure S18.** Mass spectrum of peptidomimetic **9**. Calculated mass for  $C_{36}H_{45}N_8O_7$  is 701.3411  $[M+H]^+$ , observed 701.3419  $[M+H]^+$ .



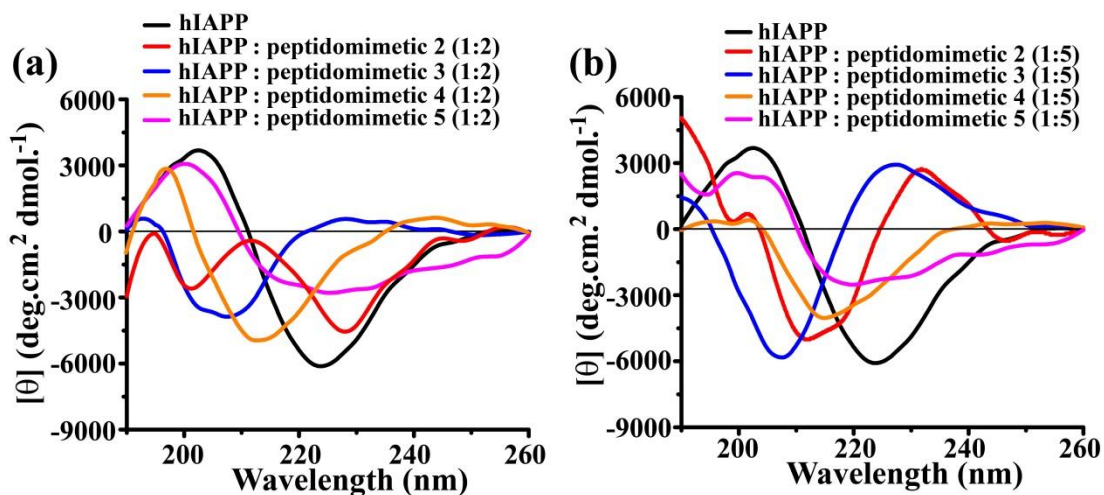
**Figure S19.** (a) & (b) CD spectra of peptide 1-9 and (c) & (d) FTIR spectra of peptide 1-9 respectively. Spectra were taken after 5 days of incubation of the peptides in PBS pH 7.4 at 37 °C.

### Inhibition of fibril formation of hIAPP by BSBHps:

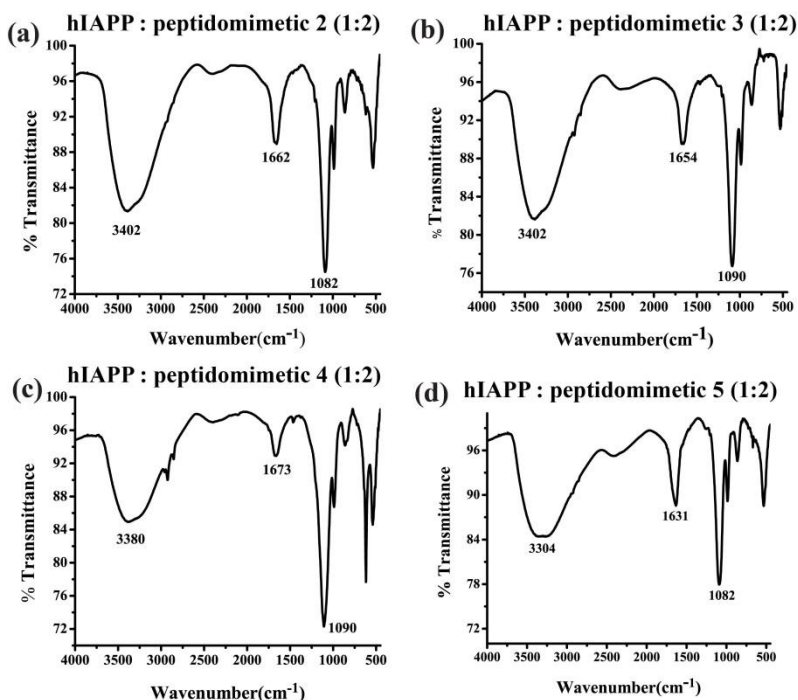


**Figure S20.** (a) CD spectra of hIAPP alone (black), and in presence of 10 fold molar excess of peptidomimetic 2 (red), 3 (blue), 4 (orange) and 5 (magenta). (b) FTIR spectra of hIAPP alone (black), and in presence of 10 fold molar excess of peptidomimetic 2 (red), 3 (blue), 4 (orange) and 5 (magenta). The spectra were recorded after 7 days of incubation at 37 °C. The concentration of hIAPP was 40  $\mu$ M in PBS pH 7.4 (50 mM).

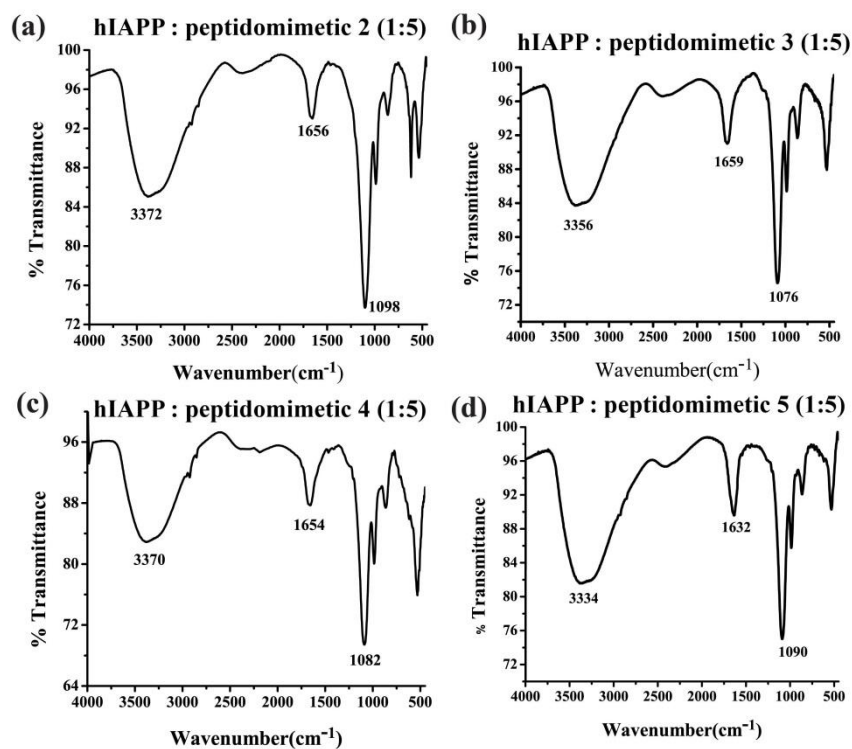




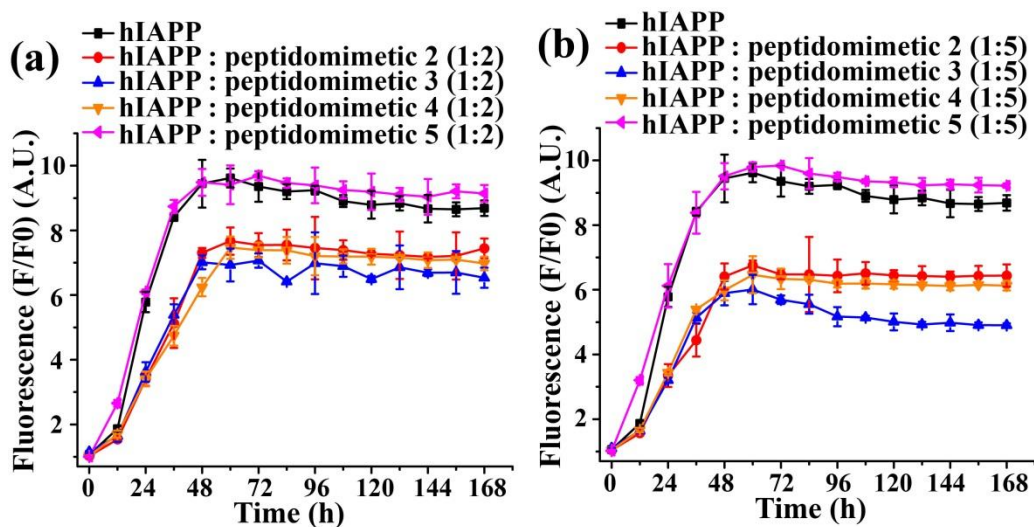
**Figure S21.** (a) CD spectra of hIAPP alone (black), and in presence of 2 fold molar excess of peptidomimetic 2 (red), 3 (blue), 4 (orange) and 5 (magenta). (b) CD spectra of hIAPP alone (black), and in presence of 5 fold molar excess of peptidomimetic 2 (red), 3 (blue), 4 (orange) and 5 (magenta). The spectra were recorded after 7 days of incubation at 37 °C. The concentration of hIAPP was 40  $\mu\text{M}$  in PBS pH 7.4 (50 mM).



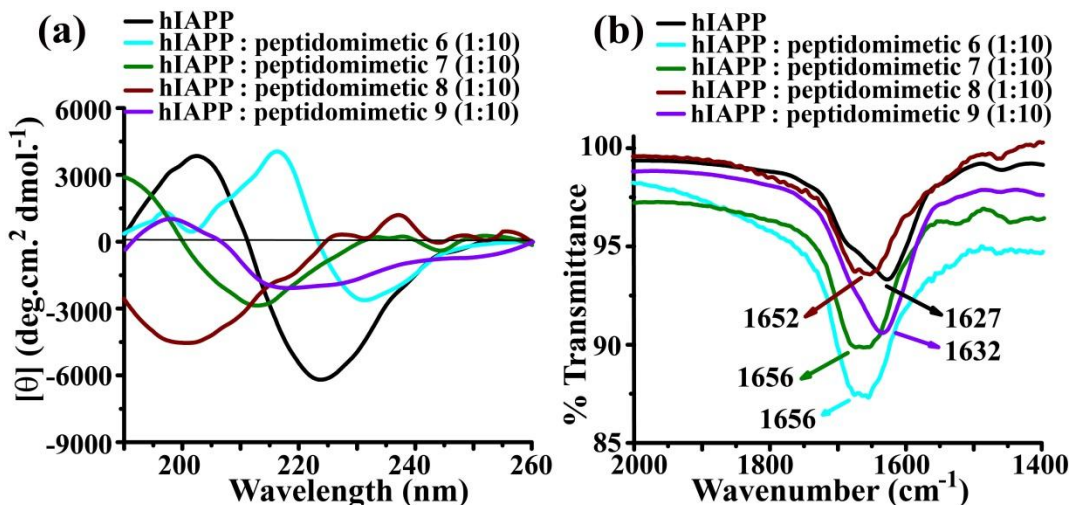
**Figure S22.** FTIR spectra of hIAPP in presence of 2 fold molar excess of peptidomimetic (a) 2, (b) 3, (c) 4 and (d) 5. The spectra were recorded after 7 days of incubation at 37 °C in PBS pH 7.4 (50 mM).



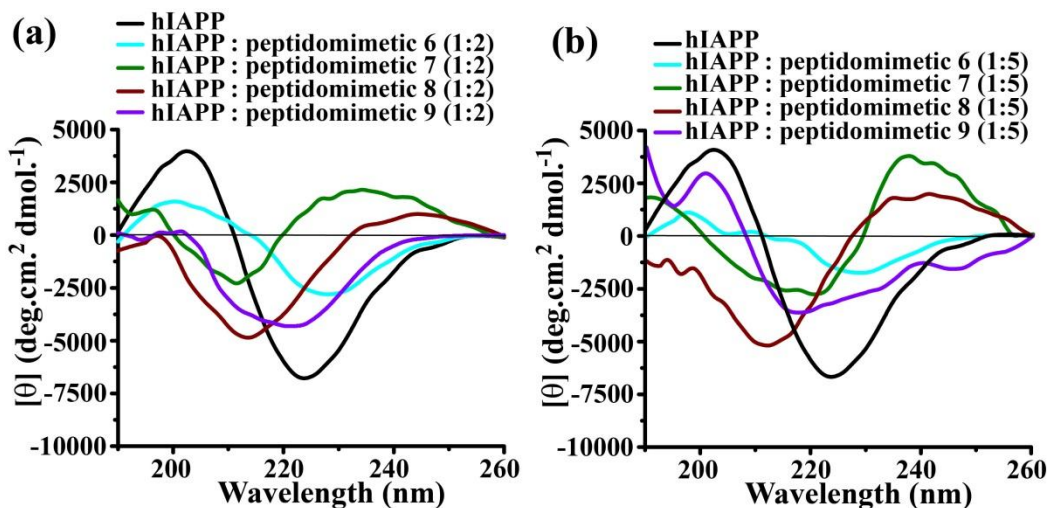
**Figure S23.** FTIR spectra of hIAPP in presence of 5 fold molar excess of peptidomimetic (a) 2, (b) 3, (c) 4 and (d) 5. The spectra were recorded after 7 days of incubation at 37 °C in PBS pH 7.4 (50 mM).



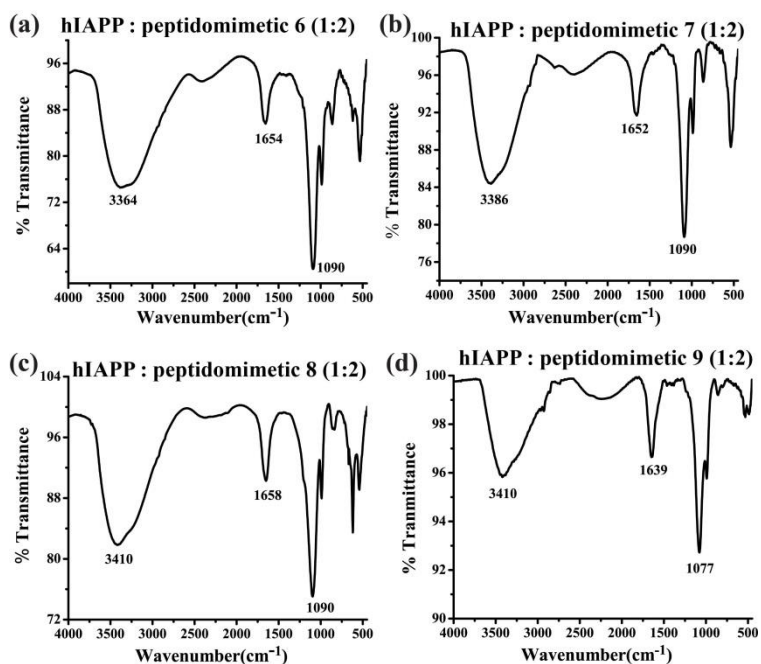
**Figure S24.** Time dependent ThT fluorescence assay of hIAPP (40 μM) in absence (black) and presence of (a) 2 fold molar excess and (b) 5 fold molar excess of peptidomimetic 2 (red), 3 (blue), 4 (orange) and 5 (magenta).



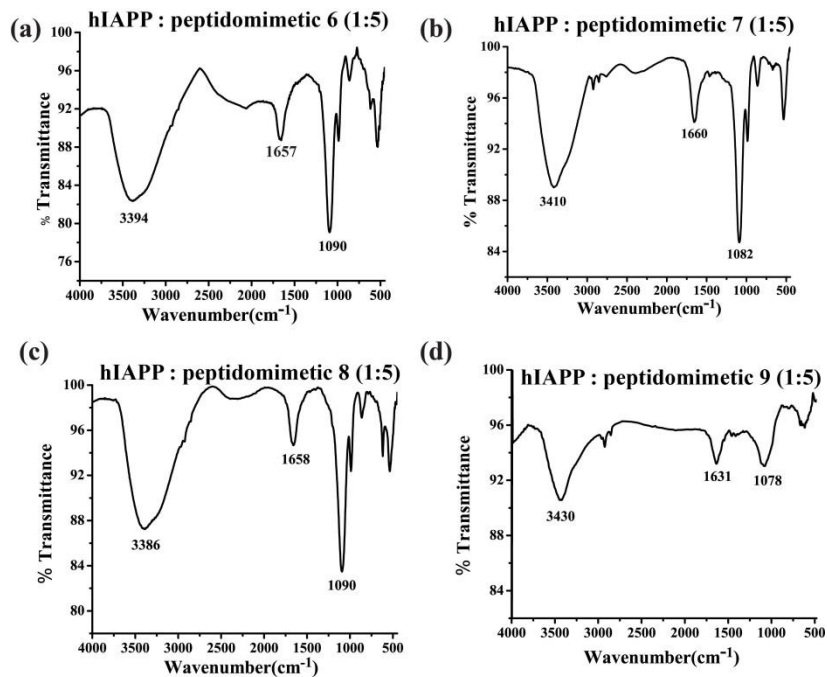
**Figure S25.** (a) CD spectra of hIAPP alone (black), and in presence of 10 fold molar excess of peptidomimetic **6** (cyan), **7** (olive), **8** (wine) and **9** (violet). (b) FTIR spectra of hIAPP alone (black), and in presence of 10 fold molar excess of peptidomimetic **6** (cyan), **7** (olive), **8** (wine) and **9** (violet). The spectra were recorded after 7 days of incubation at 37 °C. The concentration of hIAPP was 40  $\mu$ M in PBS pH 7.4 (50 mM).



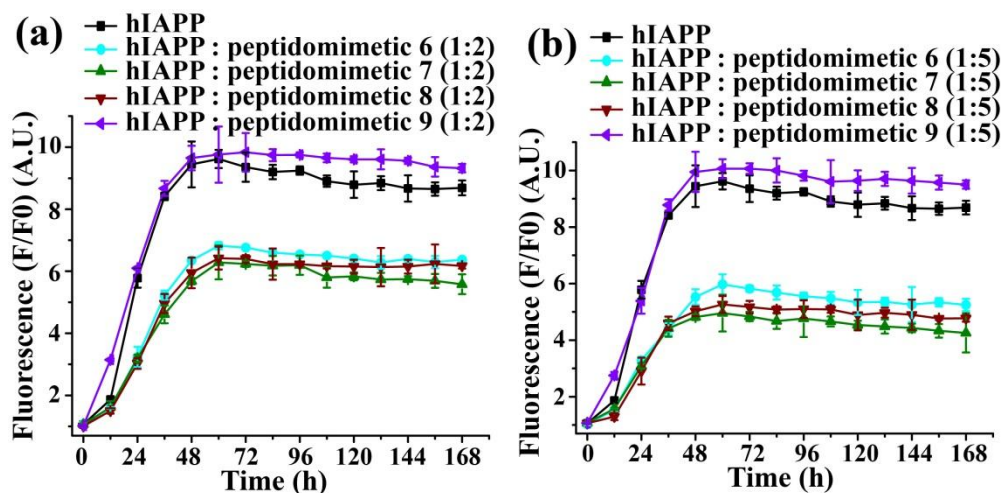
**Figure S26.** (a) CD spectra of hIAPP alone (black), and in presence of 2 fold molar excess of peptidomimetic **6** (cyan), **7** (olive), **8** (wine) and **9** (violet). (b) CD spectra of hIAPP alone (black), and in presence of 5 fold molar excess of peptidomimetic **6** (cyan), **7** (olive), **8** (wine) and **9** (violet). The spectra were recorded after 7 days of incubation at 37 °C. The concentration of hIAPP was 40  $\mu$ M in PBS pH 7.4 (50 mM).



**Figure S27.** FTIR spectra of hIAPP in presence of 2 fold molar excess of peptidomimetic (a) **6**, (b) **7**, (c) **8** and (d) **9**. The spectra were recorded after 7 days of incubation at 37 °C in PBS pH 7.4 (50 mM).

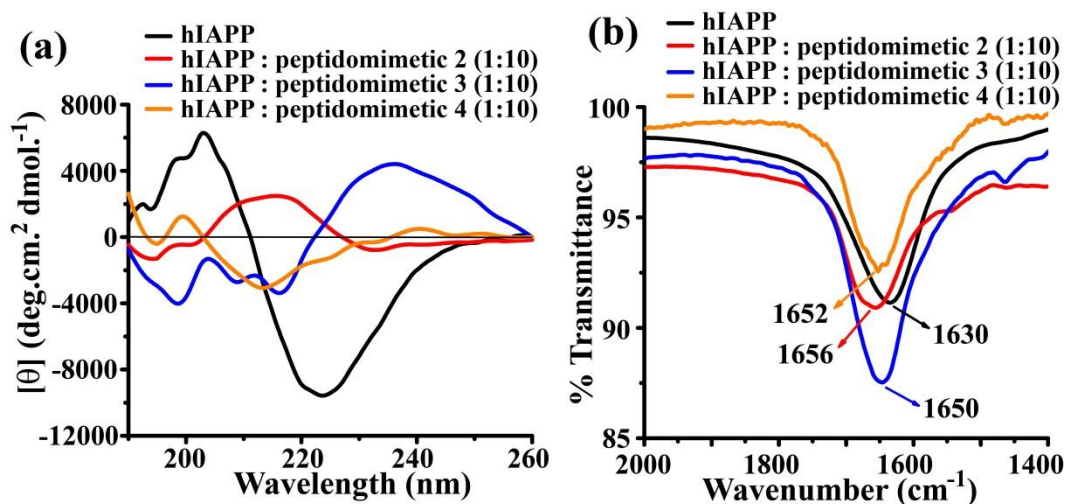


**Figure S28.** FTIR spectra of hIAPP in presence of 5 fold molar excess of peptidomimetic (a) **6**, (b) **7**, (c) **8** and (d) **9**. The spectra were recorded after 7 days of incubation at 37 °C in PBS pH 7.4 (50 mM).

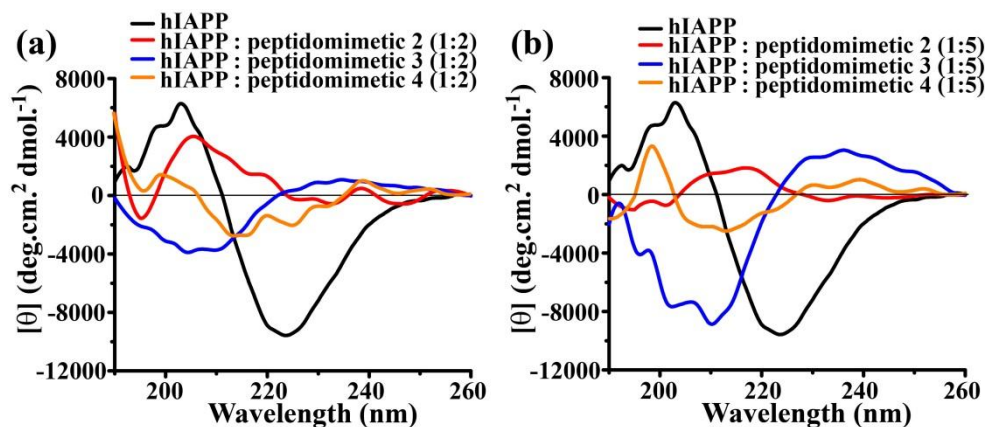


**Figure S29.** Time dependent ThT fluorescence assay of hIAPP (40µM) in absence (black) and presence of (a) 2 fold molar excess and (b) 5 fold molar excess of peptidomimetic 6 (cyan), 7 (olive), 8 (wine) and 9 (violet).

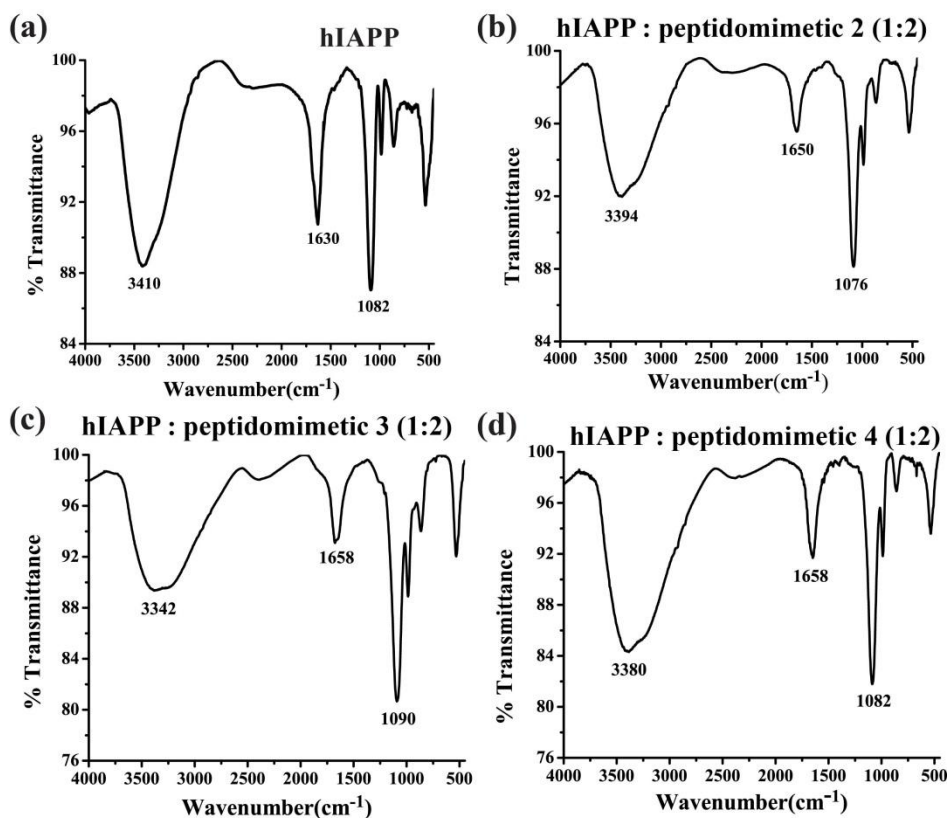
### Disruption of Preformed Amyloid Fibril of hIAPP by BSBHps:



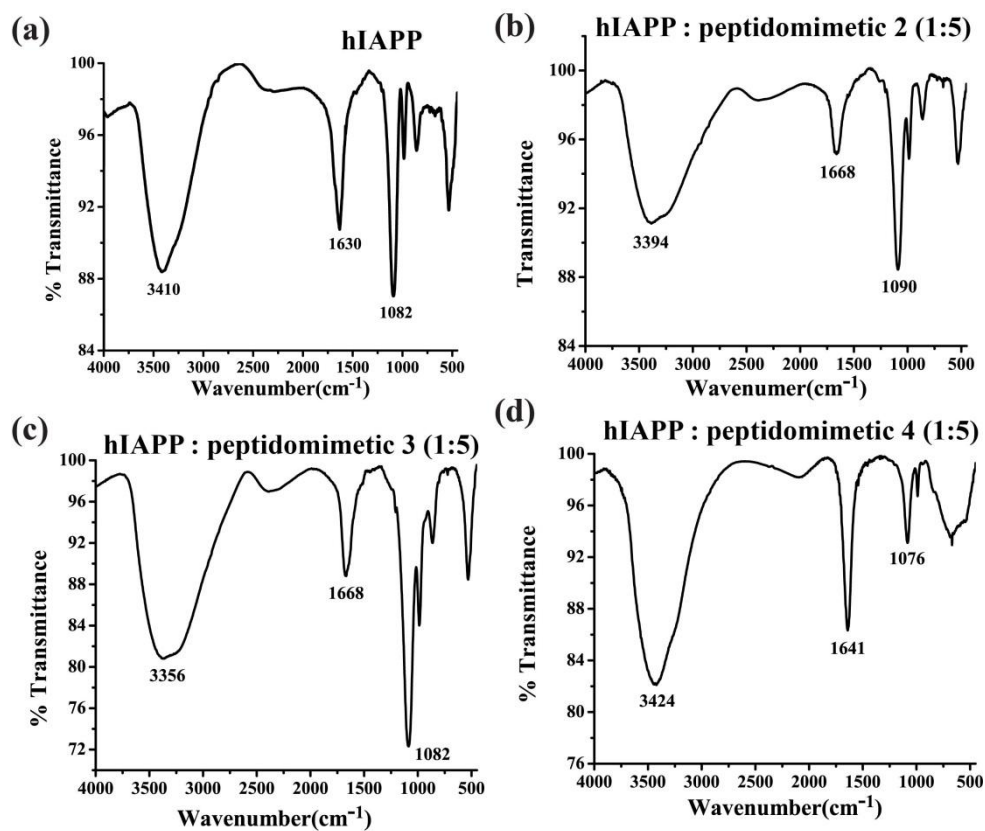
**Figure S30.** (a) CD spectra of hIAPP alone (black), and in presence of 10 fold molar excess of peptidomimetic 2 (red), 3 (blue) and 4 (orange). (b) FTIR spectra of hIAPP alone (black), and in presence of 10 fold molar excess of peptidomimetic 2 (red), 3 (blue) and 4 (orange). The spectra were recorded after 7 (2+5) days of incubation at 37 °C. The concentration of hIAPP was 40 µM in PBS pH 7.4 (50 mM).



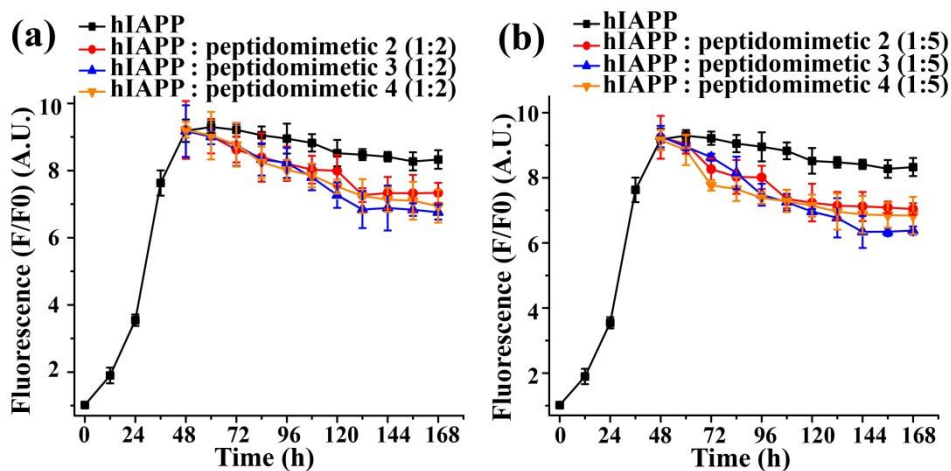
**Figure S31.** (a) CD spectra of hIAPP alone (black), and in presence of 2 fold molar excess of peptidomimetic **2** (red), **3** (blue) and **4** (orange). (b) CD spectra of hIAPP alone (black), and in presence of 5 fold molar excess of peptidomimetic **2** (red), **3** (blue) and **4** (orange). The spectra were recorded after 7 days of incubation at 37 °C. The concentration of hIAPP was 40  $\mu$ M in PBS pH 7.4 (50 mM).



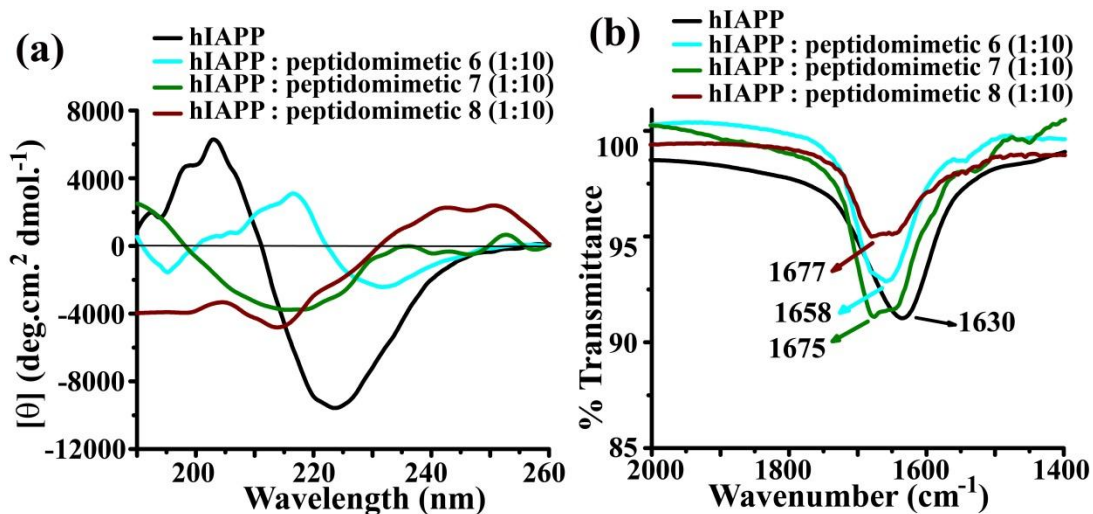
**Figure S32.** FTIR spectra of hIAPP (a) alone and in presence of 2 fold molar excess of peptidomimetic (b) **2**, (c) **3** and (d) **4**. The spectra were recorded after 7 days of incubation at 37 °C in PBS pH 7.4 (50 mM).



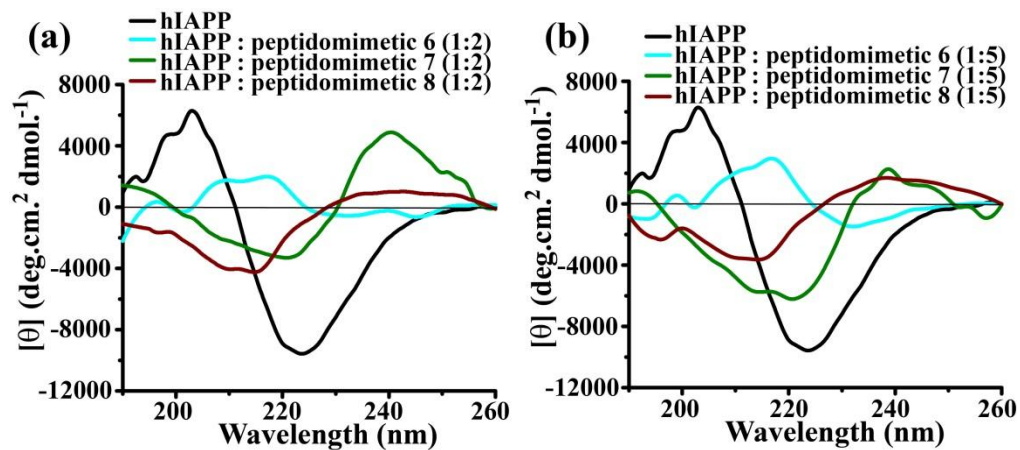
**Figure S33.** FTIR spectra of hIAPP (a) alone and in presence of 5 fold molar excess of peptidomimetic (b) 2, (c) 3 and (d) 4. The spectra were recorded after 7 days of incubation at 37 °C in PBS pH 7.4 (50 mM).



**Figure S34.** Time dependent ThT fluorescence assay of hIAPP (40 $\mu$ M) in absence (black) and presence of (a) 2-fold molar excess and (b) 5 fold molar excess of peptidomimetic 2 (red), 3 (blue) and 4 (orange).

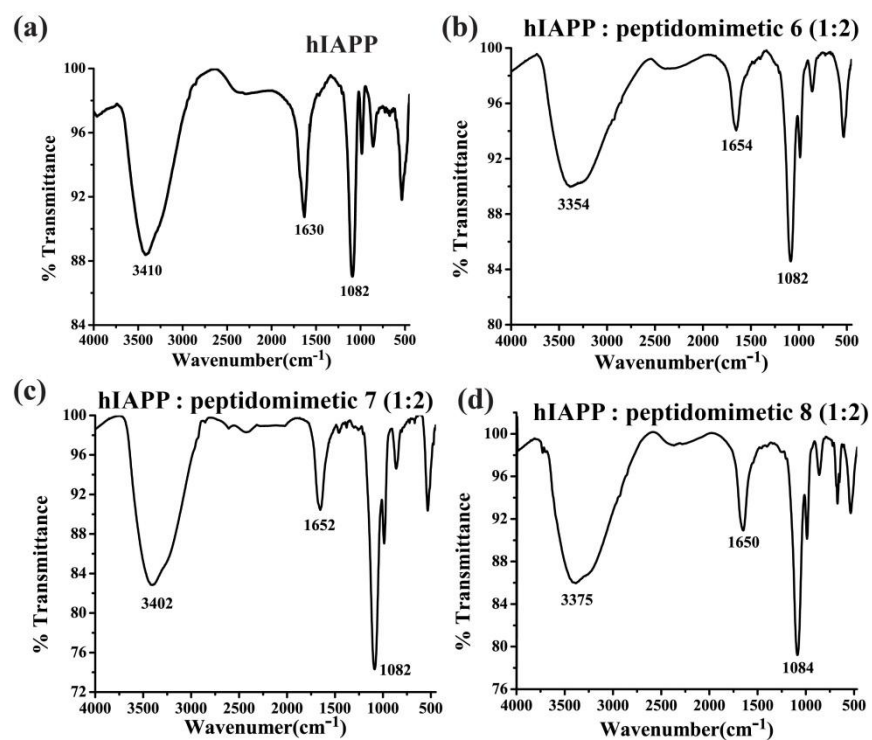


**Figure 35.** (a) CD spectra of hIAPP alone (black), and in presence of 10 fold molar excess of peptidomimetic **6** (cyan), **7** (olive) and **8** (wine). (b) FTIR spectra of hIAPP alone (black), and in presence of 10-fold molar excess of peptidomimetic **6** (cyan), **7** (olive) and **8** (wine). The spectra were recorded.

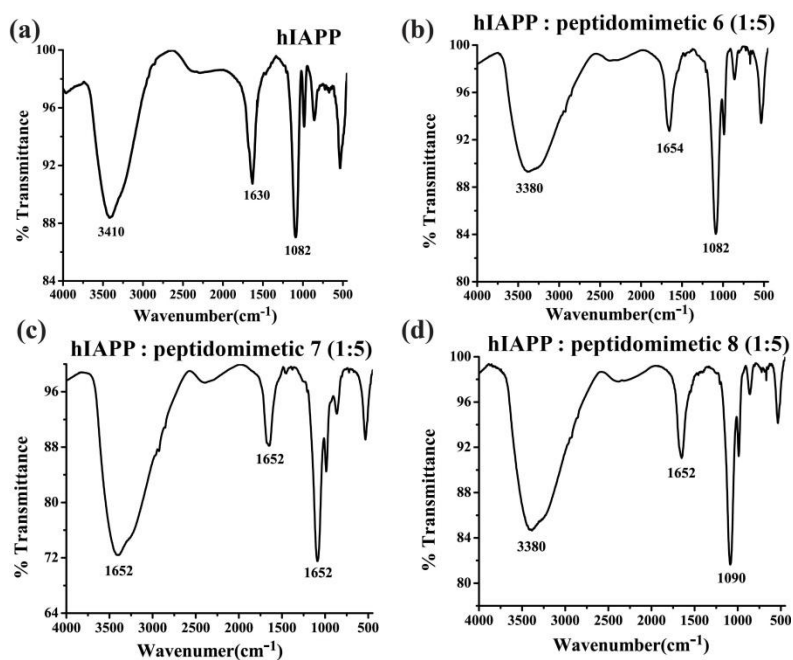


**Figure S36.** (a) CD spectra of hIAPP alone (black), and in presence of 2 fold molar excess of peptidomimetic **6** (cyan), **7** (olive) and **8** (wine). (b) CD spectra of hIAPP alone (black), and in presence of 5 fold molar excess of peptidomimetic **6** (cyan), **7** (olive) and **8** (wine).. The spectra were recorded after 7 days of incubation at 37 °C. The concentration of hIAPP was 40  $\mu$ M in PBS pH 7.4 (50 mM).

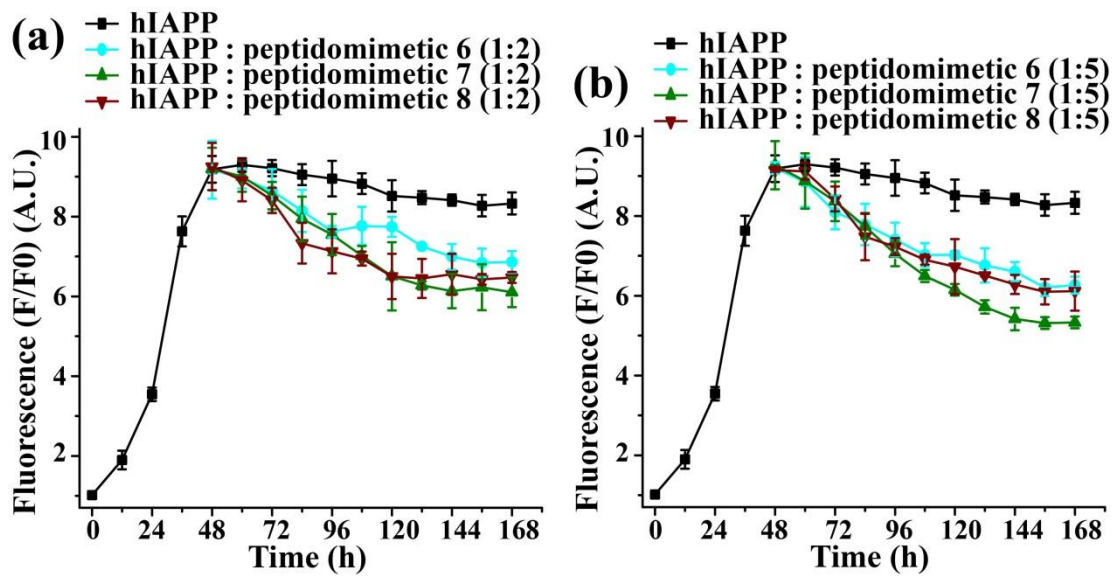




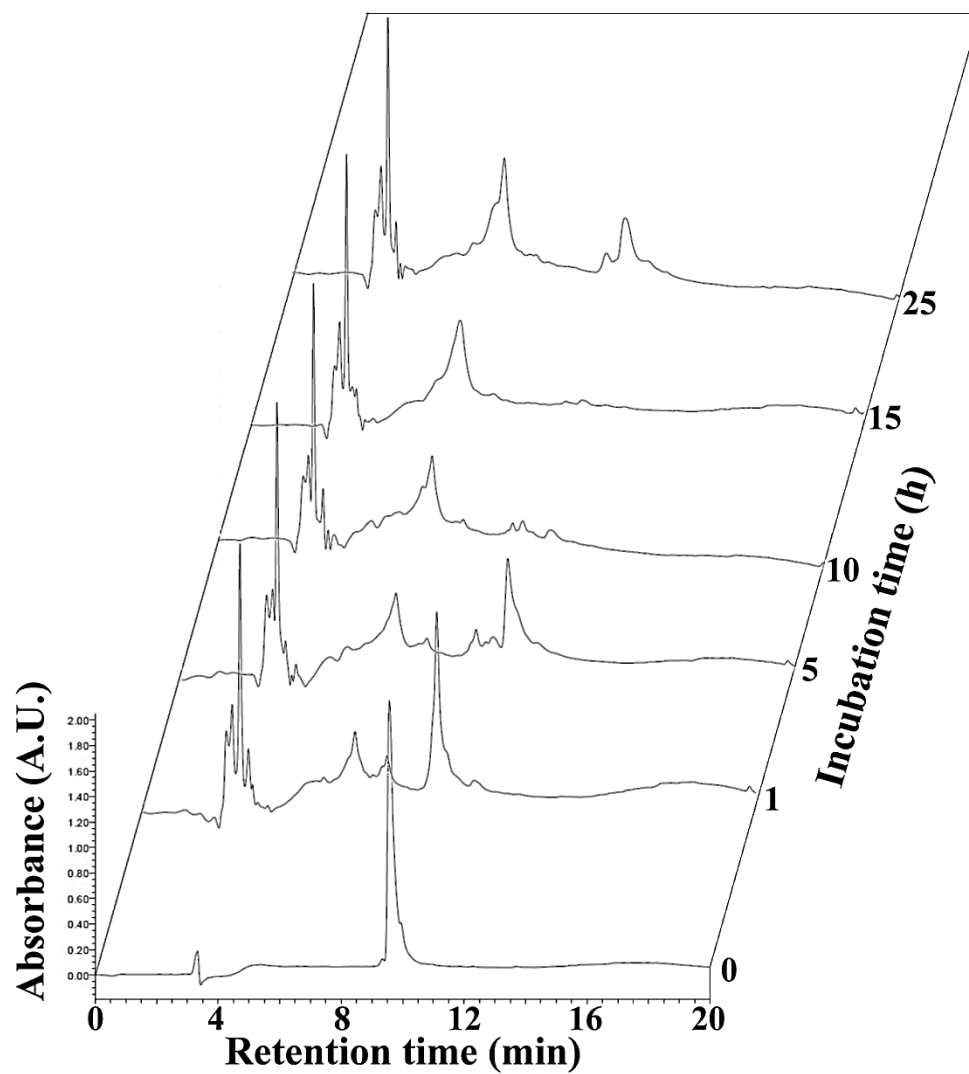
**Figure S37.** FTIR spectra of hIAPP (a) alone and in presence of 2 fold molar excess of peptidomimetic (b) **6**, (c) **7** and (d) **8**. The spectra were recorded after 7 days of incubation at 37 °C in PBS pH 7.4 (50 mM).



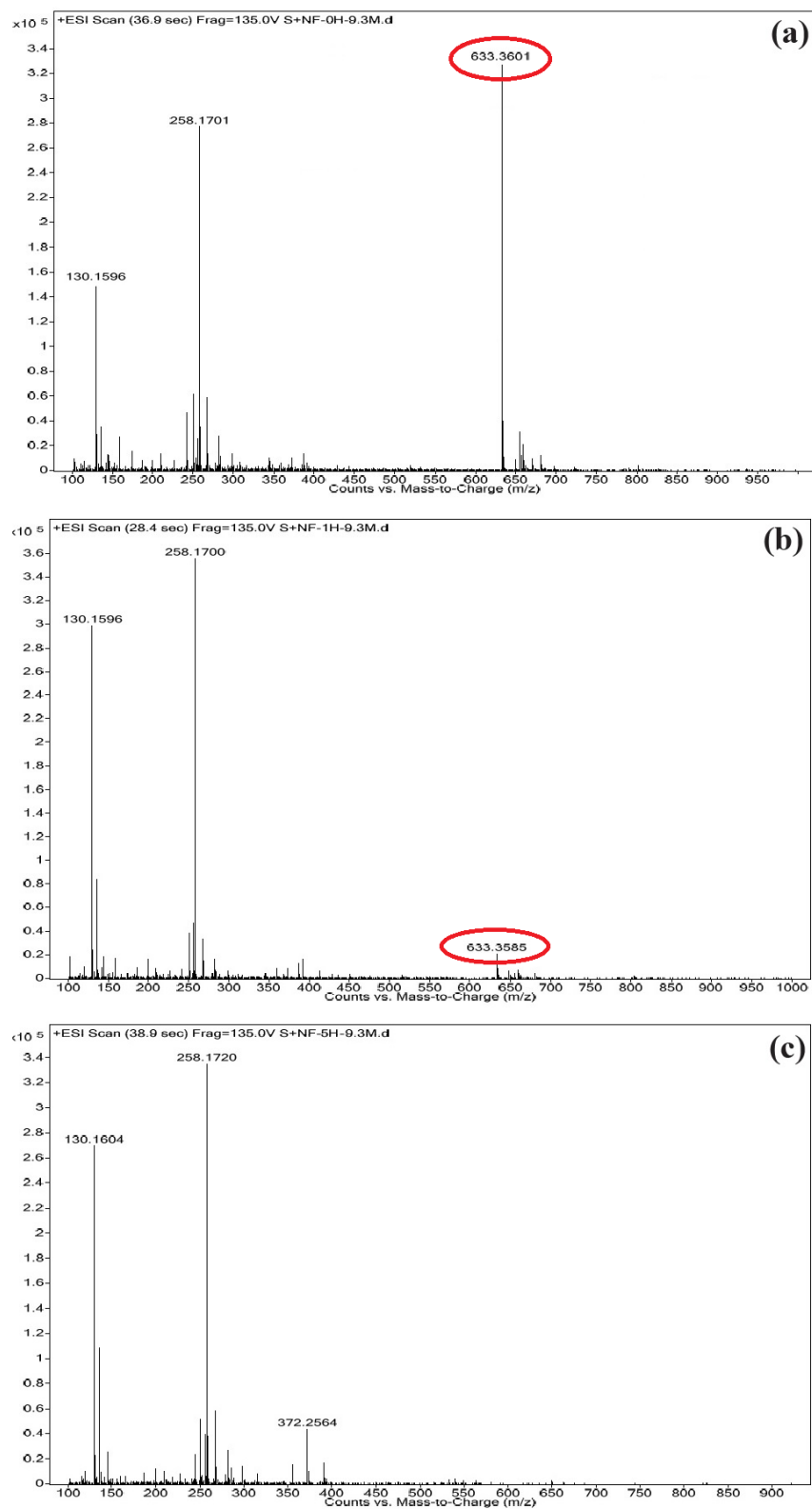
**Figure S38.** FTIR spectra of hIAPP (a) alone and in presence of 5 fold molar excess of peptidomimetic (b) **6**, (c) **7** and (d) **8**. The spectra were recorded after 7 days of incubation at 37 °C in PBS pH 7.4 (50 mM).



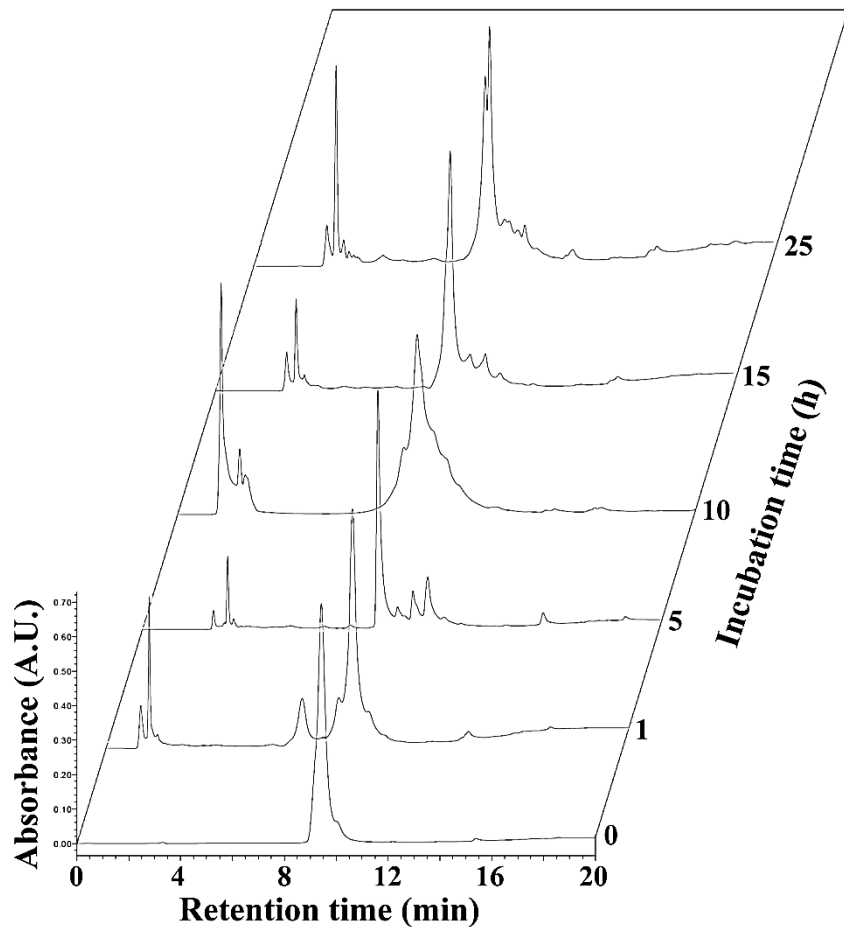
**Figure S39.** Time dependent ThT fluorescence assay of hIAPP (40μM) in absence (black) and presence of (a) 2 fold molar excess and (b) 5 fold molar excess of peptidomimetic **6** (cyan), peptidomimetic **7** (olive) and peptidomimetic **8** (wine).



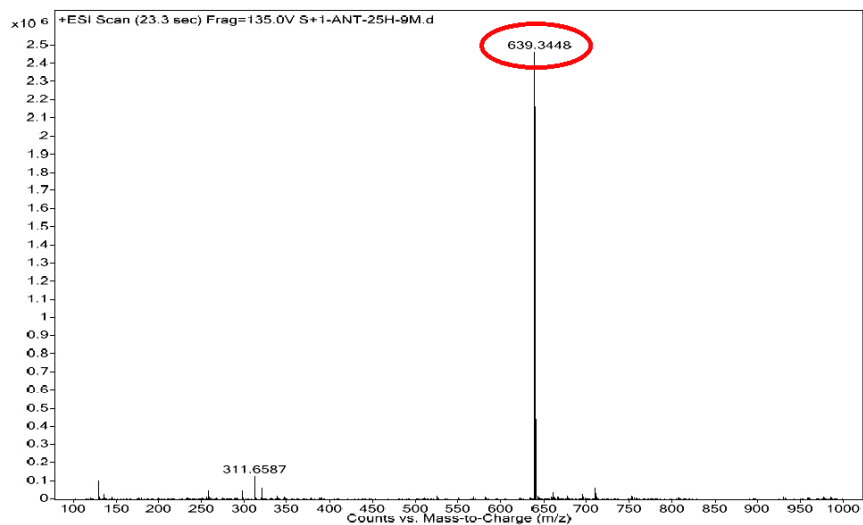
**Figure S40:** Stability kinetics of the peptide **1** in presence of proteolytic enzyme (human serum) monitored by HPLC.



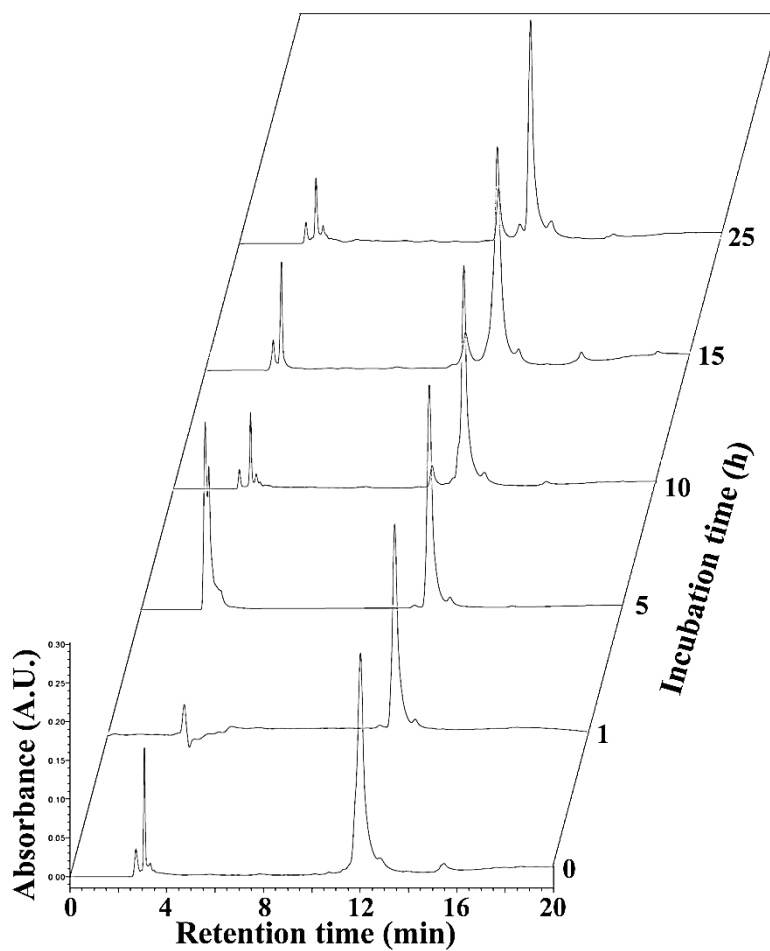
**Figure S41:** Mass spectra of peptide **1** after addition of human serum at (a) 0h, (b) 1h and (c) 5h. Calculated mass for  $C_{30}H_{49}N_8O_7$  is 633.3724  $[M+H]^+$ .



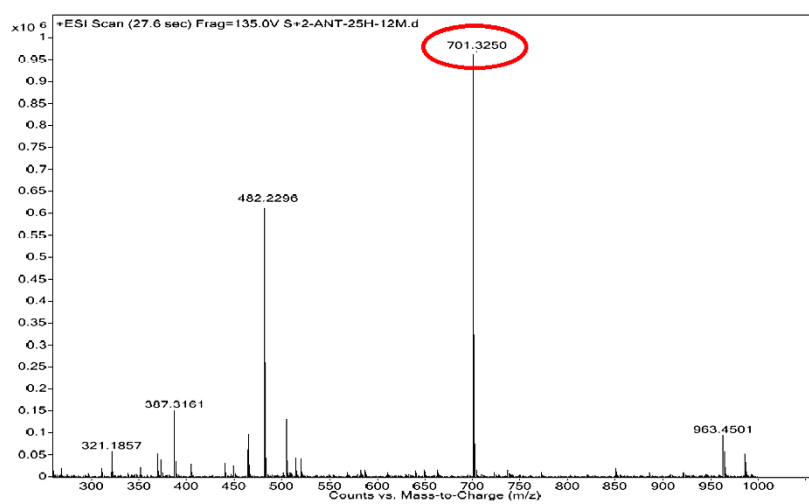
**Figure S42:** Stability kinetics of the peptidomimetic **3** in presence of proteolytic enzyme (human serum) monitored by HPLC.



**Figure S43:** Mass spectra of peptidomimetic **3** after addition of human serum at 25h. Calculated mass  $C_{31}H_{43}N_8O_7$  is 639.3255  $[M+H]^+$  and observed 639.3448  $[M+H]^+$ .



**Figure S44:** Stability kinetics of the peptidomimetic **7** in presence of proteolytic enzyme (human serum) monitored by HPLC.



**Figure S45:** Mass spectra of peptidomimetic **7** after addition of human serum at 25h. Calculated mass  $C_{36}H_{45}N_8O_7$  is 701.3411  $[M+H]^+$ , observed 701.3250  $[M+H]^+$ .