JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
J. Am. Chem. Soc., 1998, 120(30), 7655-7656, DOI:10.1021/ja980566b

Supplementary Material

CD Analyses.

CD spectra were obtained at 0.052, 0.099, 0.205, 0.456, 0.608, 0.958, 1.900, 2.888 mM on a Jasco J-600 spectropolarimeter at room temperature either as a function of concentration or pH. $[\theta]_{217}$ was used as an indication of β structure. A 2.88 mM stock solution of **1** was diluted with 0.2 M phosphate/0.1 M citrate buffer at pH 5.8. The concentration dependency was fit to the following equation,

$$T = \sqrt[n-1]{\frac{K_d\left(1-\frac{(\theta_{ex}-\theta_A)}{(\theta_M-\theta_A)}\right)}{n\left(\frac{(\theta_{ex}-\theta_A)}{(\theta_M-\theta_A)}\right)^n}}$$

where $[\theta]_{ex}$, $[\theta]_A$, and $[\theta]_M$ are mean residue ellipticities of the experimental sample, the monomer and the aggregate respectively at 217 nm, T is the total peptide concentration, K_d is the dissociation constant, and n is the number of peptide molecules per aggregate. A stock solution of **1** was diluted into different phosphate/citrate ratios to achieve a final peptide concentration of 0.76 mM at the indicated pH. The pH dependency of $[\theta]_{217}$ was fit to the following expression,

$$[\theta]_{217} = \frac{\alpha T}{(1 + \frac{H}{K_1} + \frac{K_2}{H})}$$

where K_1 and K_2 are the constants for the two relevant dissociations and T is the total peptide concentration.

Captions.

Figure 1S. Characterization of **1**. **A**. **1** was analyzed by reverse phase HPLC using a Rainin C18 analytical column and a 0 to 80% water-acetonitrile gradient (both containing 0.1% TFA, v/v) over 40 minutes. **B**. MALDI-TOF mass spectral analysis of **1**. **C**. Synthetic peptide was cleaved from PEG at the C-terminus using CNBr[1] in trifluoroethanol/formic acid/water (50/35/15, v/v/v). Products were solubilized in 8 M guanidine HCl and then evaluated by reverse phase HPLC as described above. **D**. The purified peptide from HPLC were analyzed by MALDI-TOF mass spectral analysis.

Figure 2S. Congo Red binding experiments. When performed by the methods described by Klunk et al.,[2] Congo Red showed the characteristic red shift of the absorbance maxium from 493 to 513 nm in the presence of **1** or Aβ(10-35) (data not shown). 10 μl of a solution of **1** at 8 mg/ml and 50 μM Congo Red was dried onto a glass slide and observed microscopically at a mangification of 80,000x. **A**. Fibrils of **1** stained with Congo Red. **B**. Typical apple-green birefringence of the same fibrils was detected with crossed polarizing filters.

Figure 3S. Tissue transglutaminase (tTG) cross-linking of **1**. Using the reaction conditions described by Dudek and Johnson,[3] 2.4 mg of **1** was mixed to the following tTG/peptide ratios (numbers indicate lanes of the gel): 1) no tTG; 2) 0.004/1; 3) 0.02/1; 4) 0.04/1; 5) 0.08/1. The mixtures were maintained for 4 h at 23°C, terminated by the addition of EDTA, and analyzed by 16.5% Tris-Tricine SDS-PAGE.[4]

Figure 4S. Aromatic to α and β hydrogen region of the NOESY data showing the increased cross peak intensity, particularly in the methyl region, with an increase in pH. Lyophilized peptide was dissolved in 0.6 ml of 10% D_2O/H_2O containing 0.5 mM DSS to a final concentration 2.1 mM. The pH was adjusted to 3.0 (**A**) and 5.6 (**B**) with NaOH/HCl and centrifuged for 15 minutes at 14,000 x g. ^{1}H-NMR data were collected on a Varian 500 MHz Unity INOVA NMR spectrometer with a 5 mm probe using a 200 ms flip-back NOESY pulse sequence at 10 °C. 2D Data sets were collected with with 256 FIDs of 2k data points, 64 scans per FID and a spectral width of 5000 Hz. Standard Varian data processing and data acquistion were used.

References

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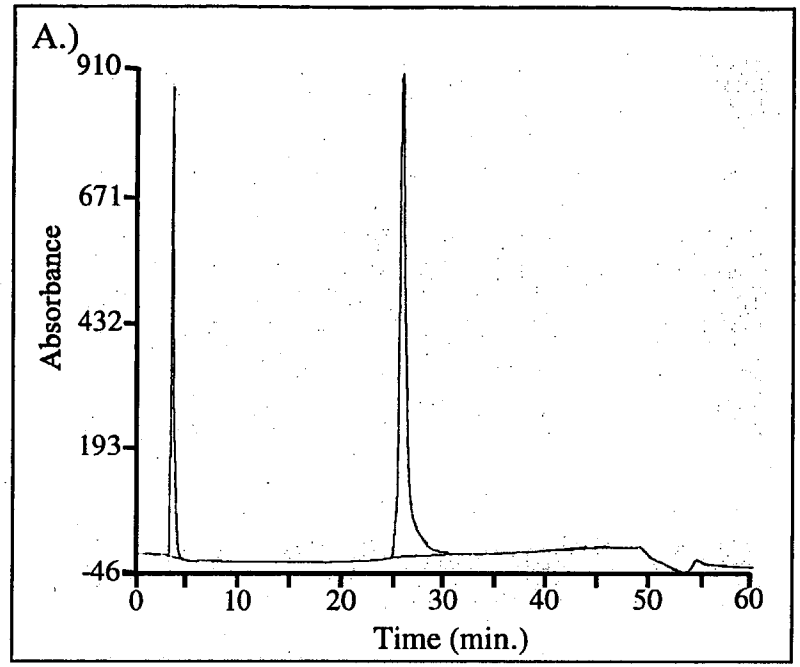
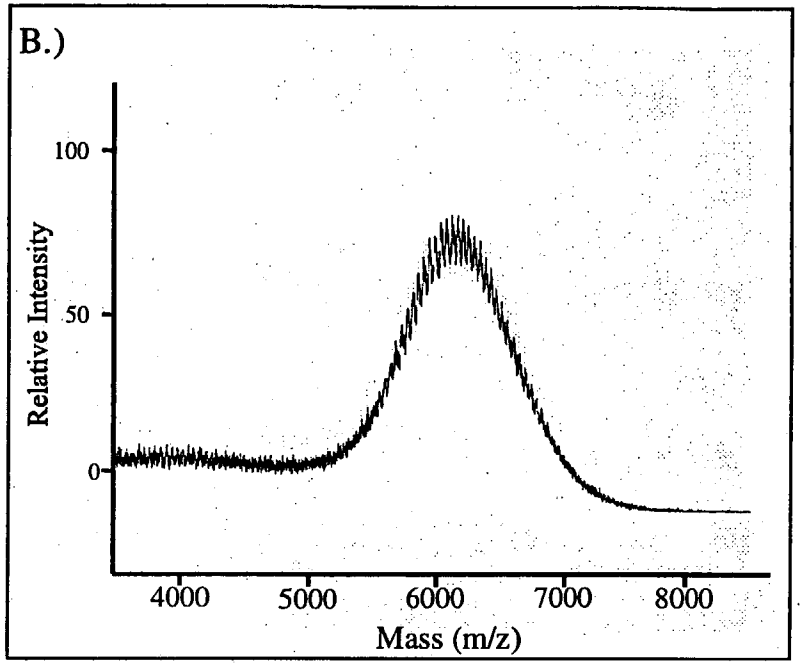
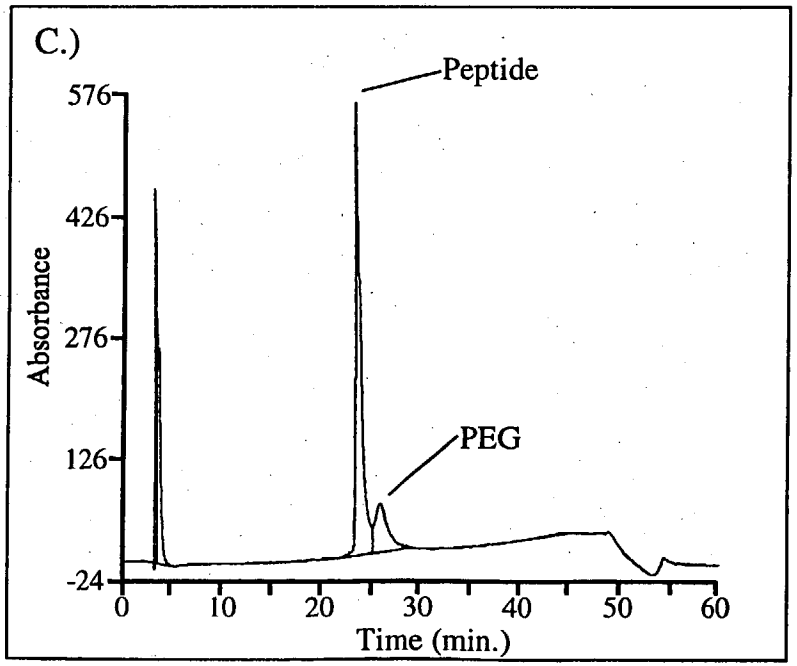
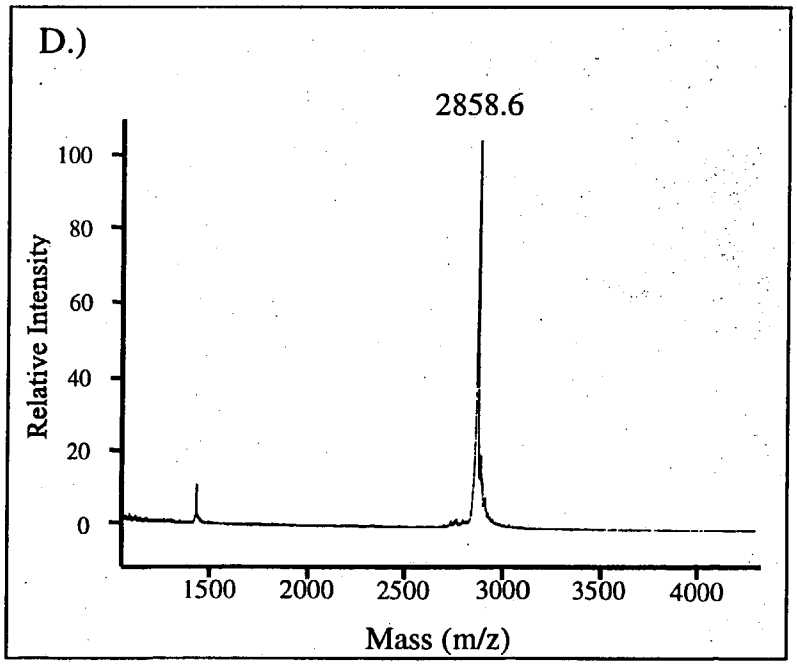


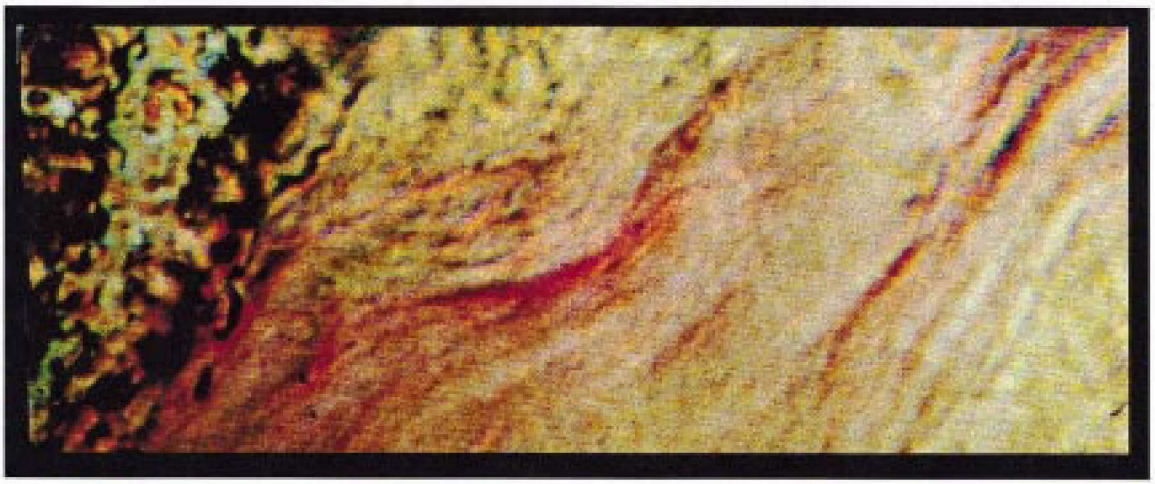


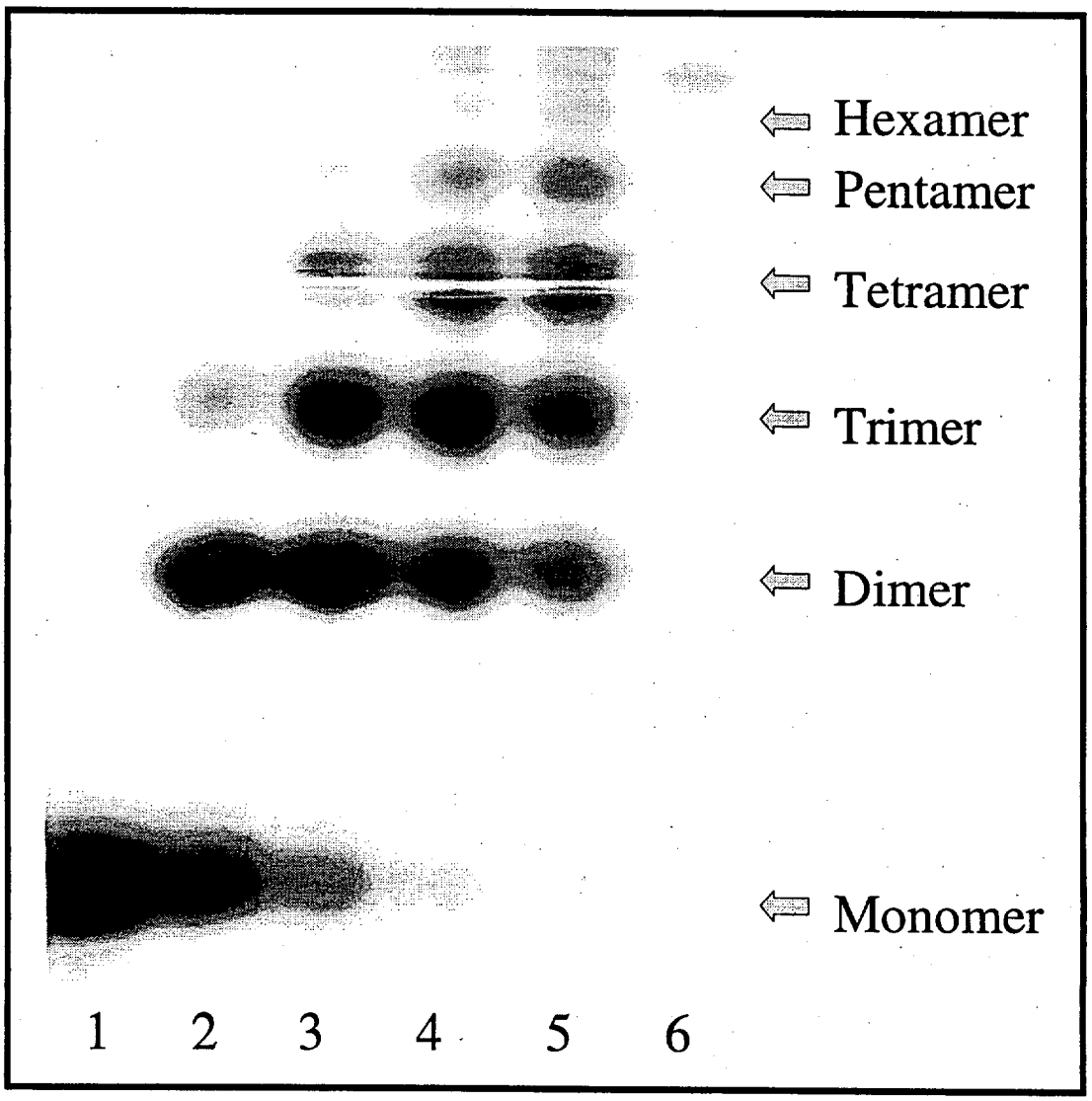


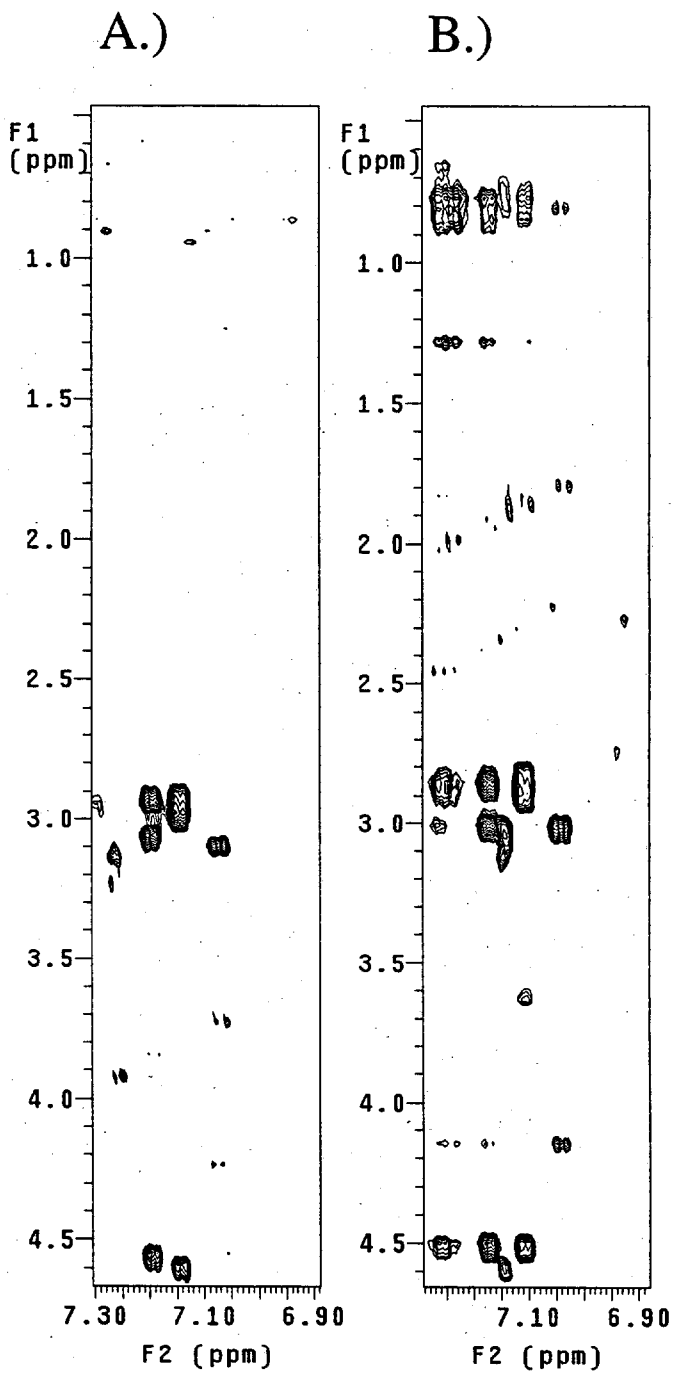


B.)

A.)






A.)
B.)
F1 (ppm)
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
7.30
7.10
6.90
F2 (ppm)