



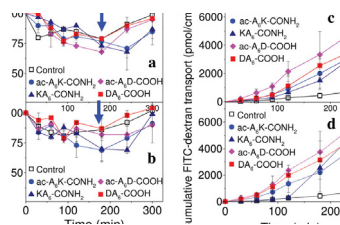
# BIOACTIVE SELF-ASSEMBLING LIPID-LIKE PEPTIDES AS PERMEATION ENHANCERS FOR ORAL DRUG DELIVERY

## Short Description

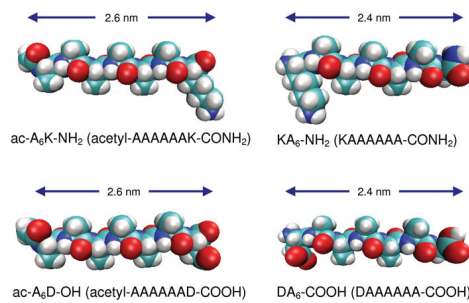
The aim of this work was to examine the potential of ac-A6K-CONH<sub>2</sub>, KA6-CONH<sub>2</sub>, ac-A6D-COOH and DA6-COOH lipid-like peptides as permeability enhancers to facilitate intestinal transport. In vitro transport studies of the macromolecular fluorescein isothiocyanate-dextran through Caco-2 cell monolayers show the permeation enhancing ability of the lipid-like peptides. Ex vivo studies showed increased mucosal to serosal transport of FITC-dextran in rat jejunum and a small increase in the serosal transport of bovine serum albumin in the presence of the ac-A6D-COOH peptide.

## Application Field

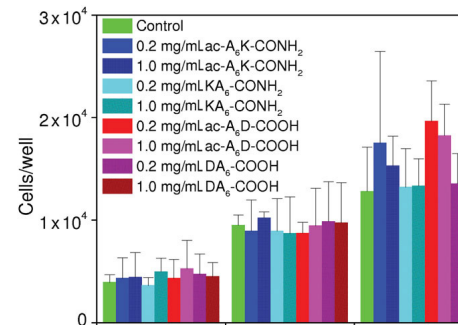
- pharmaceuticals
- self-assembling peptides
- oral drug delivery



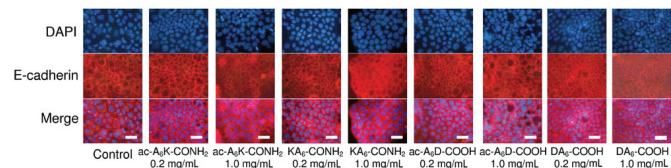
Transepithelial resistance of Caco-2 cell intestinal epithelia in the presence of (a) 0.2 mg/mL and (b) 1.0 mg/mL lipid-like peptides. The arrow indicates the time point at which the peptides were removed from the growth medium and shows the monolayer recovery process. (c and d) Permeation of FITC-dextran from the apical to the basolateral side of Caco-2 cell monolayers at (c) 0.2 mg/mL and (d) 1.0 mg/mL of peptides. Data are shown as mean ± SD (n = 4, p < 0.05 compared with the control).



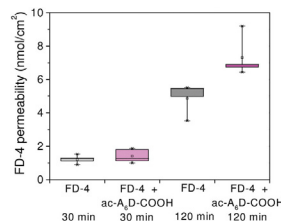
Molecular modeling of amphiphilic, surfactant-like, self-assembling peptides. The peptide length is similar to biological phospholipids. The hydrophobic domain of the peptides consists of six alanines. Color code: cyan, carbon; red, oxygen; blue, nitrogen; white, hydrogen. Graphic illustrations were generated by VMD.



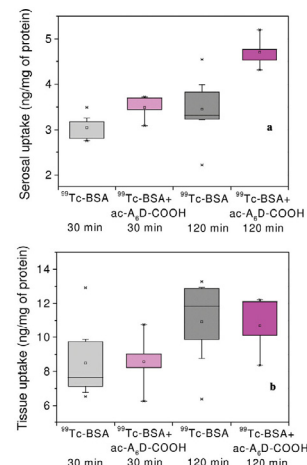
Effect of lipid-like peptides on Caco-2 cell viability after 3, 24, and 48 h in culture. Error bars represent the mean SD (n = 4). The differences in the number of viable cells at each condition compared with the control are not significant (p > 0.05).



Caco-2 cell monolayers treated with 0.2 or 1.0 mg/mL lipid-like peptides for 24 h. E-cadherin stains the adherens junctions of the epithelial cell membrane (red). Cell nuclei were stained with DAPI (blue). Scale bar is 50 μm.



Relative permeability (nmol/cm<sup>2</sup>) of FITC-dextran 4.4 kDa at 30 and 120 min with and without 1.0 mg/mL ac-A<sub>6</sub>D-COOH lipid-like peptide using the everted sacs method. In each box chart, the bottom (X) shows the minimum value and marks the 0th percentile. The bottom of the box marks the 25th percentile and the top of the box marks the 75th percentile. The square symbol (⊠) in the box marks the mean. The top (X) shows the maximum value and 100th percentile. n = 4 sample points.



Effect of the lipid-like peptide ac-A<sub>6</sub>D-COOH on the intestinal absorption of <sup>99</sup>Tc-BSA. (a) Serosal transfer and (b) tissue uptake of <sup>99</sup>Tc-BSA at 30 and 120 min with and without 1.0 mg/mL ac-A<sub>6</sub>D-COOH, using the everted sacs method. In each box chart, the bottom (X) shows the minimum value and marks the 0th percentile. The bottom of the box marks the 25th percentile and the top of the box marks the 75th percentile. The square symbol (⊠) in the box marks the mean. The top (X) shows the maximum value and 100th percentile. n = 4 sample points.

Peptide	Peptide sequence and charge distribution	Net charge at pH 7.4
ac-A <sub>6</sub> K-CONH <sub>2</sub>	acetyl-Ala-Ala-Ala-Ala-Ala-Ala-Lys-CONH <sub>2</sub>	+1
KA <sub>6</sub> -CONH <sub>2</sub>	<sup>+</sup> NH <sub>3</sub> -Lys-Ala-Ala-Ala-Ala-Ala-Ala-CONH <sub>2</sub>	+2
ac-A <sub>6</sub> D-COOH	acetyl-Ala-Ala-Ala-Ala-Ala-Ala-Asp-COO <sup>-</sup>	-2
DA <sub>6</sub> -COOH	<sup>+</sup> NH <sub>3</sub> -Asp-Ala-Ala-Ala-Ala-Ala-Ala-COO <sup>-</sup>	-1

Amino acid sequence and charge distribution of the amphiphilic, self-assembling peptide suspensions. Highlighted domains represent amino acids with positive charge (blue), negative charge (red), and hydrophobic side chains (grey). The charge of the peptides at pH 7.4 was calculated using pKa values from the literature.

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