

A photograph of a historic brick building at Georgia Tech, featuring large, three-dimensional, yellow and white letters spelling 'ITC' mounted on its facade. The building has a dark roof with white cupolas and a decorative cornice. The sky is a clear, deep blue.

UNDERGRADUATE RESEARCH AT GEORGIA TECH

Pete Ludovice
CHBE

Transdermal delivery enhanced by magainin pore-forming peptide

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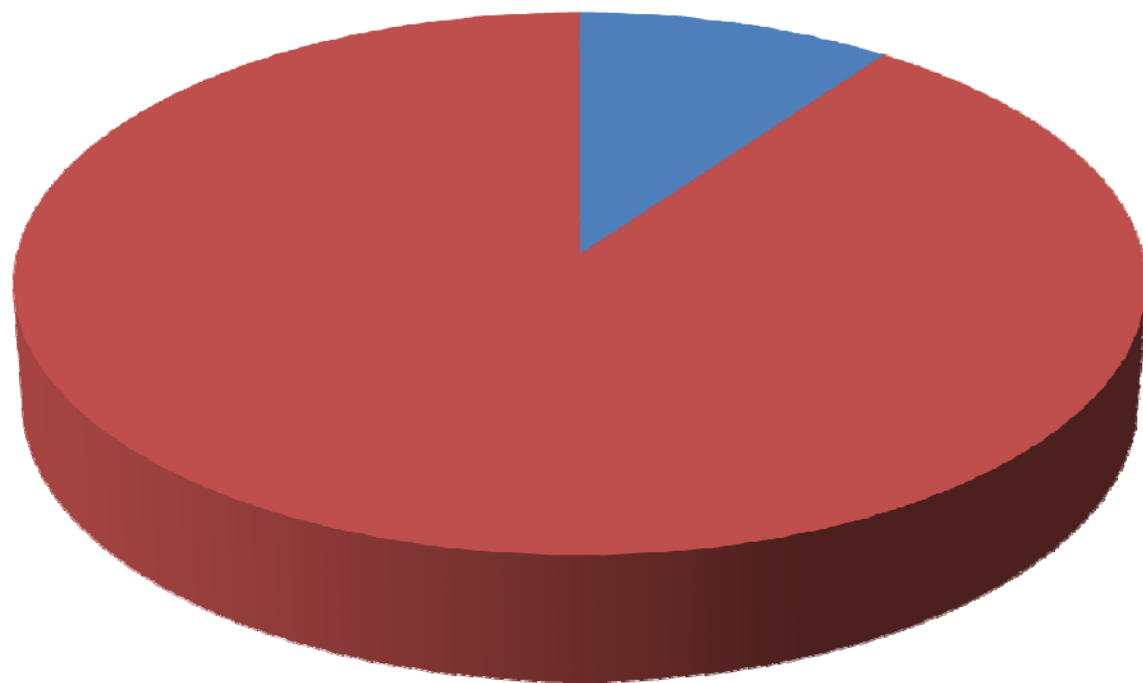
Abstract

In this study we tested the hypothesis that magainin, a peptide known to form pores in bacterial cell membranes, can increase skin permeability by disrupting *stratum corneum* lipid structure. We further hypothesized that magainin's enhancement requires co-administration with a surfactant chemical enhancer to increase magainin penetration into the skin. In support of these hypotheses, exposure to a known surfactant chemical enhancer, *N*-lauroyl sarcosine (NLS), in 50% ethanol solution increased in vitro skin permeability to fluorescein 15 fold and the combination of magainin and NLS-ethanol synergistically increased skin permeability 47 fold. In contrast, skin permeability was unaffected by exposure to magainin without co-enhancement by NLS-ethanol. Furthermore, confocal microscopy showed that magainin in the presence of NLS-ethanol penetrated deeply and extensively into *stratum corneum*, whereas magainin alone penetrated poorly into the skin. Additional analysis by Fourier-transform infrared spectroscopy, X-ray diffraction, and differential scanning calorimetry showed that NLS-ethanol disrupted *stratum corneum* lipid structure and that the combination of magainin and NLS-ethanol disrupted *stratum corneum* lipids even further. Altogether, these data suggest that NLS-ethanol increased magainin penetration into *stratum corneum*, which further increased *stratum corneum* lipid disruption and skin permeability. We believe this is the first study to demonstrate the use of a pore-forming peptide to increase skin permeability. This study also presents the novel concept of using a first chemical enhancer to increase penetration of a second chemical enhancer into the skin to synergistically increase skin permeability to a model drug.

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Keywords: Antimicrobial pore-forming peptide; Magainin; *N*-lauroylsarcosine; *Stratum corneum*; Surfactant chemical enhancer; Transdermal drug delivery

Looks more complicated than it is.



 You

 Research Group

Magainin-Mediated Disruption of Stratum Corneum Lipid Vesicles

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and Peter J. Ludovice^{1,2}

Received February 22, 2001; accepted March 12, 2001

KEY WORDS: magainin; stratum corneum; liposome; lipid bilayer; transdermal drug delivery.

INTRODUCTION

Drug delivery across the skin has had great success for drugs such as nicotine, estradiol, and a few others (1,2). However, the vast majority of drugs cannot cross skin at therapeutic rates, due primarily to the formidable barrier presented by skin's outer layer, the stratum corneum. This barrier to transdermal transport is formed primarily by a series of multilamellar lipid bilayers found in stratum corneum's extracellular

contain fewer zwitterionic phospholipids (~5 wt. %) than typical eukaryotic cells, while containing ~16 wt. % negatively-charged fatty acids (8). Given the significant negative charge and limited zwitterion content of stratum corneum, we propose the hypothesis that magainins can disrupt stratum corneum lipid bilayers.

MATERIALS AND METHODS

Materials

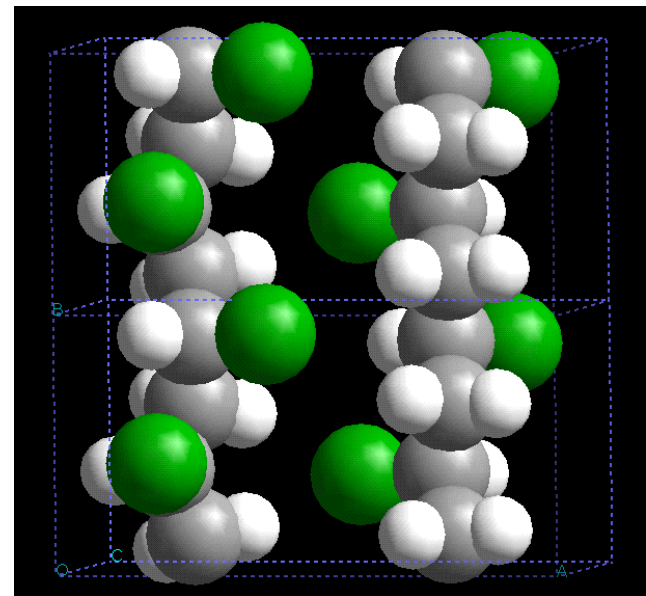
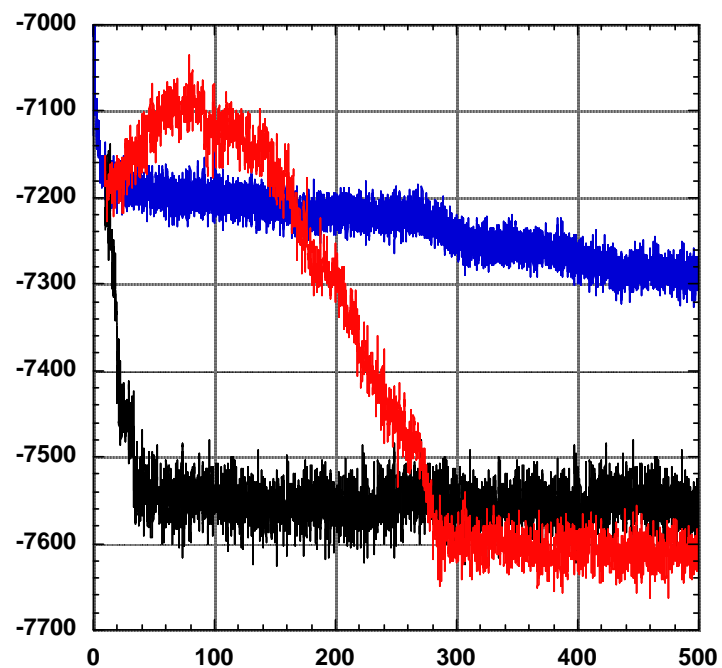
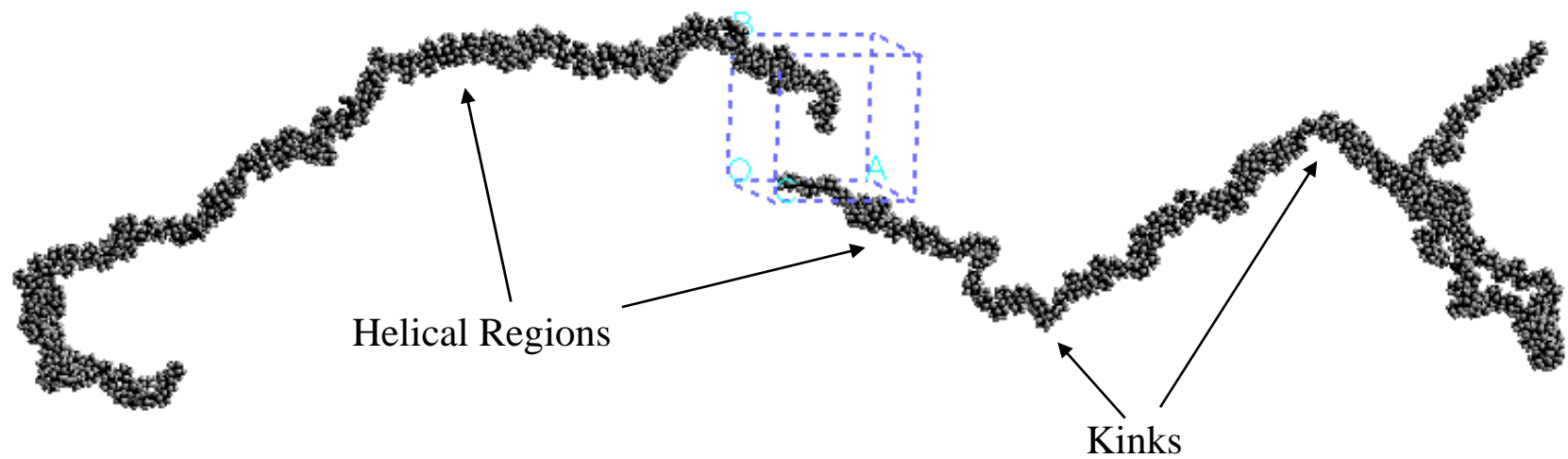
Cholesterol, cholesterol sulfate, palmitic acid, calcein, and ceramides (non-hydroxy fatty acid, prepared by treating bovine brain sphingomyelin with phospholipase C) were purchased from Sigma (St. Louis, MO), methanol from Fisher Scientific (Fair Lawn, NJ) and chloroform from J. T. Baker (Phillipsburg, NJ). The Tris / EDTA / NaCl buffer (pH 7.4) contained 10 mM Tris, 150 mM NaCl, and 0.1 mM EDTA (Sigma). The phosphate-buffered saline (PBS; pH 7.4) contained 10 mM phosphate buffer, 2.7 mM potassium chloride, and 137 mM sodium chloride (Sigma).

Magainin peptides were synthesized using a PE-Biosystems (Foster City, CA) model 433A peptide synthe-

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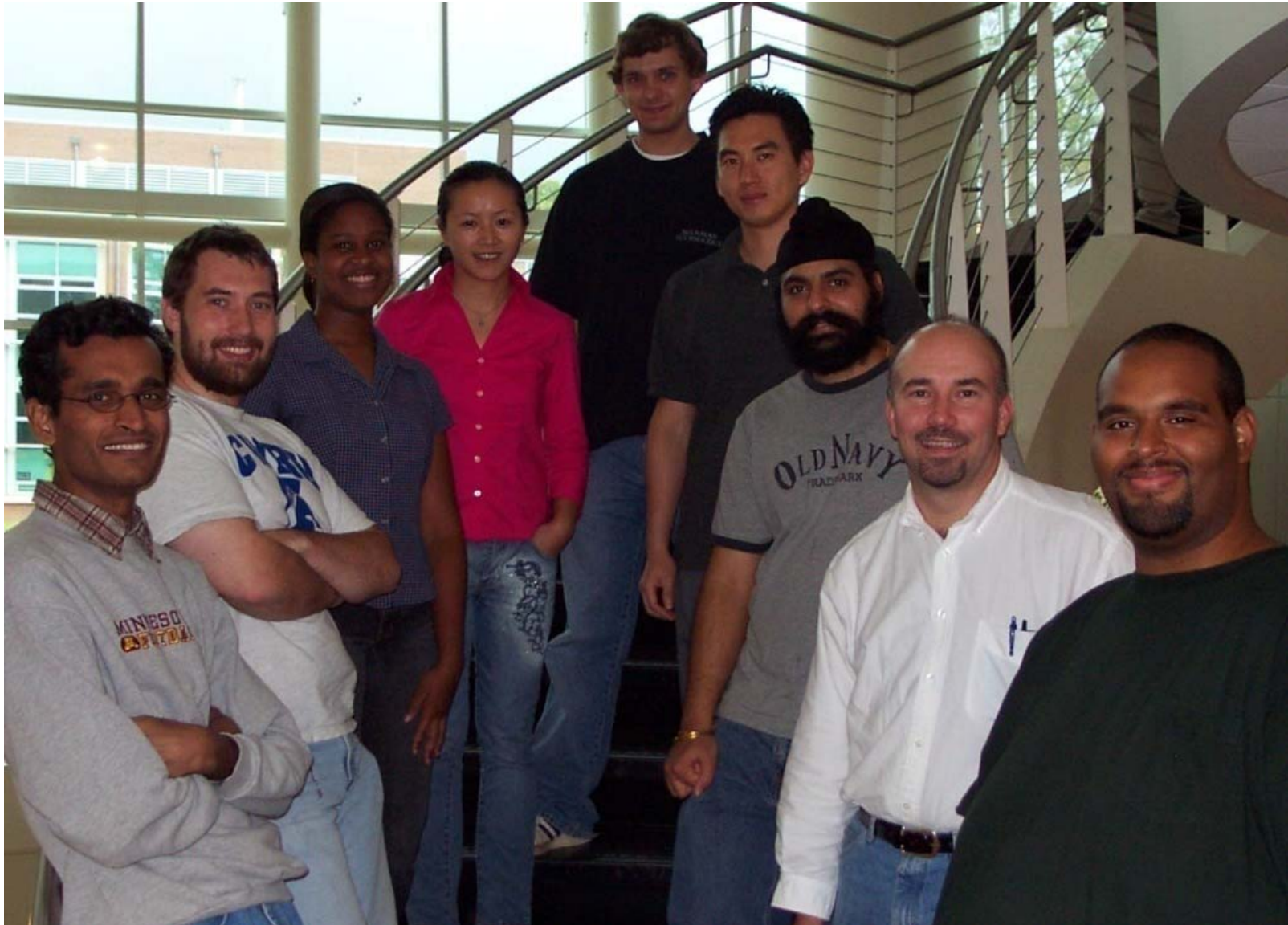
How It Works

- Project usually motivated by faculty
- Can be done for credit (9 hours of work and 3 credit hours)
- Can be done for pay
- You may report to faculty, post-docs or graduate students
- Do at least 2 semesters
- Typically done after sophomore year

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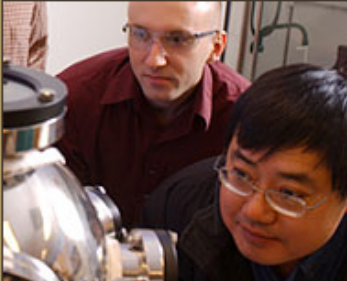

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NanoTECH Research Area Affiliations

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Research Summary

Dr. Ludovice's research interests include molecular-level simulation and trying to prevent the world from using the word nanotechnology to describe everything under the sun.

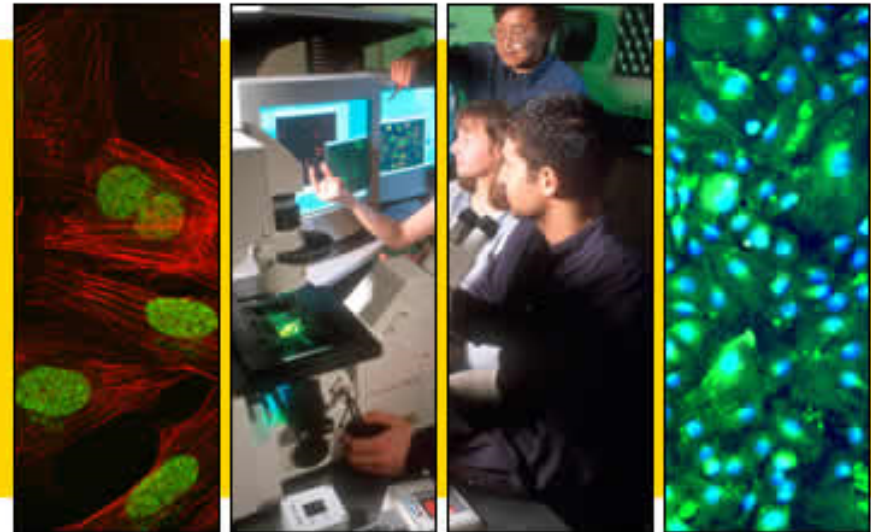
Interdisciplinary Centers: Nanotech



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