PUBLICATIONS

Wilkinson R., Pincus S., Song K., Shepard J., Weaver A., Labib M., Teintze M. 2013. “Improved guanide compounds which bind the CXCR4 co-receptor and inhibit HIV-1 infection.” Bioorganic & Medicinal Chemistry Letters 23: 2197-2201.

Weaver AJ, Shepard J., Wilkinson R., Watkins R., Walton S., Radke A., Wright T., Awel M., Cooper C., Erikson E., Labib M., Voyich J., Teintze M. Antibacterial activity of THAM Trisphenylguanide Against Methicillin-Resistant *Staphylococcus aureus*. PLoS One. 2014; 9(5):e97742.

Fuchs A.,† Weaver A.,† Tripet B., Teintze M., Ammons M., Copié V. “Allicin Identified as the Principal Antimicrobial Compound in 1,000-Year-Old Bald’s Eyesalve.” International Journal of Antimicrobial Agents, 2016. (*in review)* (†authors contributed equally)

Weaver A., Van Vuren A., Rakesh, Lee R., Copié V., Teintze M. “Exposure of Methicillin-Resistant *Staphylococcus aureus* to Low Levels of the Antibacterial THAM-3ΦG Generates a Small Colony Drug-Resistant Phenotype.” PLoS One. 2016. *(in review)*

Weaver A., Van Vuren A., Teintze M., Copié V., Voyich, J. “Treatment of MRSA with 18-β-Glycyrrhetinic Acid Reduces Cell-to-Cell Interactions and Increases Production of Staphyloxanthin.” *(in preparation)*

PRESENTATIONS

Weaver, A., Tapsak, M. “Experimental Design of Biodiesel Salt Analysis by Flame Photometry.” Department of Chemistry and Biochemistry, Bloomsburg University. 239th American Chemical Society National Meeting: “Chemistry for a Sustainable World.” San Francisco, California (2010). (poster)

Weaver, A., Wilkinson R., Shepard, J., Voyich, J., Teintze, M. “Elucidating the Mechanism of Action of a Novel Antibacterial Agent: THAM-3ΦG.” Department of Chemistry and Biochemistry, Montana State University. Gordon Research Conference: “New Antibacterial Discovery and Development.” Ventura, California (2014). (poster)

Weaver, A., Voyich, J., Copie, C., Teintze, M. “18β-Glycyrrhetinic Acid Results in Increased Pigment Production and Decreased Adherence in Methicillin Resistant *Staphylococcus aureus* Biofilms.” Department of Chemistry and Biochemistry, Montana State University. Montana Academy of Sciences Conference. Butte, Montana (2016). (oral)

MONTANA STATE UNIVERSITY
Mountains & Minds

Department of Chemistry and Biochemistry

Doctor of Philosophy in Biochemistry

D I S S E R T A T I O N D E F E N S E

Mr. Alan J. Weaver, Jr.

B.Sc. Bloomsburg University of Pennsylvania, Bloomsburg, PA (2011)

Monday, October 31, 2016 – 2:10 pm
Byker Auditorium
Department of Chemistry and Biochemistry

“Investigations into the Activity of Synthetic & Natural Products Against Methicillin-Resistant *Staphylococcus aureus*”

Graduate Committee

Dr. Martin Teintze (Research Advisor)
Dr. Valérie Copié (Chemistry)
Dr. Brian Bothner (Chemistry)
Dr. Jovanka Voyich (Microbiology/Immunology)

Future Career

Following successful completion of his dissertation, Mr. Weaver has accepted a Post-Doctorate position at the U.S. Army Institute of Surgical Research (San Antonio, TX) working in the lab of Dr. Kai Leung on the immune response and healing processes associated with burn wounds following bacterial infection.

ABSTRACT

The studies herein investigated and characterized synthetic and natural products having efficacy against methicillin-resistant Staphylococcus aureus, which has become a significant threat to both hospital and community environments due to rapid drug resistance development. THAM-3ΦG is a synthetic compound that showed initial promise as a novel antibacterial against *S. aureus* (MIC 2 mg/L) through membrane disruption. However, following sub-lethal dosing with THAM-3ΦG, *S. aureus* was shown to develop resistance through a small colony variant phenotype, which was defined through 1D 1H NMR metabolomics. Natural products from age-old remedies having efficacy against *S. aureus* were also investigated in this study. Bald's Eyesalve has shown efficacy against *S. aureus*; however, the active antibacterial agent(s) remained unknown. Through molecular size and solvent fractionation, activity was isolated to the small (< 3 kDa), non-polar molecule fraction which lost activity following cysteine treatment. Following NMR spectral analysis, the organosulfur garlic-derived compound, allicin, was identified as the active antimicrobial agent. GRA is a natural product found in licorice root, which was used in ancient Chinese medicine. GRA is known to have efficacy against *S. aureus* and to downregulate key virulence genes. Prolonged exposure of *S. aureus* to GRA revealed significant increases in the pigment staphyloxanthin. Furthermore, NMR metabolomics of short-term treatments revealed a dysregulation of the TCA cycle, which collectively suggests that treatment of *S. aureus* with GRA results in oxidative stress. The efficacy of GRA against *S. aureus* biofilms was also investigated and showed GRA to be ineffective at reducing biofilm CFUs; however, GRA effected biofilm stability. Planktonic studies revealed significant reductions in cell-to-cell interactions beginning at 7.8 mg/L GRA based on optical density measurements and microscopy. Therefore, GRA may serve as part of a novel therapeutic method for treating chronic wound infections. Collectively, these studies utilized NMR to define metabolic phenotypes of bacteria in response to drug treatment and to resolve the active agent in a complex mixture of an age-old remedy. While *S. aureus* was able to overcome the antibacterial activity of THAM-3ΦG, the studies of natural products from age-old remedies may provide future treatment options that require further investigation.

BIOGRAPHICAL NOTES

Undergraduate Studies

2007-2011 Bloomsburg University, Bloomsburg, PA
Bachelor of Science in Chemistry: Biochemistry & Nanotechnology
Minor: Criminal Justice

2009 Bloomsburg University, Bloomsburg, PA
Research: On- & Off-site Quality Control of an Aluminum Water Treatment System
Advisor: Dr. Christopher Hallen

2010 Bloomsburg University, Bloomsburg, PA
Researcher: Development of Quality Control Methods for Campus Made Biodiesel
Advisor: Dr. Mark Tapsak

Awards

2009 Undergraduate Chemical Research Grant, Bloomsburg University
2009 David Murphy Memorial Scholarship, Bloomsburg University
2010 Undergraduate Chemical Research Grant, Bloomsburg University
2014 Chemistry Graduate Association Travel Grant, Montana State University
2014 College of Letters and Science Student Research Travel Grant, Montana State University
2015 Montana Academy of Sciences Student Research Grant
2015 Metabolomics Travel Scholarship, University of Alabama-Birmingham

Conferences & Workshops

2014 Gordon Research Conference: "New Antibacterial Discovery and Development." Ventura, California.
2015 Montana Biofilm Meeting. Montana State University-Center for Biofilm Engineering. Bozeman, Montana.
2015 3rd Annual Workshop on Metabolomics. University of Alabama, Birmingham, Alabama
2016 Annual Montana Academy of Sciences Meeting. Montana Tech, Butte, Montana.
2016 NMR-Based Metabolomics Workshop. University of Wisconsin-Madison.
2016 Montana Biofilm Meeting. Montana State University-Center for Biofilm Engineering. Bozeman, Montana.