1) Student name: Sara Dale
2) Faculty mentor name: Prof. David Go
3) Project title: Surface Acoustic Wave Devices for Chemical Analysis of Counterfeit Pharmaceuticals

4) Briefly describe any new skills you acquired during your summer research:

- Learned how to operate three different models of mass spectrometers, how to prepare and run samples using electrospray ionization and surface acoustic wave ionization, and how to understand the output spectra
- Learned how to run, assess, and repair surface acoustic wave devices
- Learned how to find relevant scientific articles and use them in research
- Learned how to prepare scientific posters and presentations

5) Please briefly share a practical application/end use of your research:
Surface acoustic wave (SAW) devices can be used to analyze drug samples dried on paper. At this point, samples could be dried in the field, brought back to a laboratory, and analyzed via SAW mass spectrometry. Eventually, SAW devices might be used with portable mass spectrometers to detect counterfeit pharmaceuticals in the field.

6) Project Summary:
I. Background

The prevalence of counterfeit pharmaceuticals is a growing problem, especially in many developing countries. While there are a number of ways to test the contents of drugs, one useful method is mass spectrometry (MS), an analytical technique that can directly identify multiple compounds in complex mixtures. However, mass spectrometry requires an ionization source, and given certain conditions, some ionization sources are better than others. One new ambient ionization technique being developed is surface acoustic wave nebulization, which uses surface acoustic wave (SAW) devices to aerosolize and ionize liquid samples. SAW devices are miniature microelectricalmechanical systems that are portable and require only a small amount of power to run. They can be used in conjunction with paper as a source of wicking fluid and can extract compounds dried on paper. Because of these attractive qualities, SAW devices have the potential to be powerful MS ionization sources for analyzing counterfeit pharmaceuticals.

II. Activities and Results

This project tested the applicability of SAW MS to a range of pharmaceuticals and examined SAW extraction of compounds dried on paper. As a preliminary part of this investigation, flow visualization was used to understand how SAW interacts with paper wicks, as it both pumps and aerosolizes the liquid. Using colored dye, the path of the fluid flow was traced and the flow rate was measured. As these tests demonstrated, SAW devices pump liquid in such a way that the analyte is concentrated at a focal point, a property that could possibly be exploited when dealing with low concentrations of MS samples. In addition, the velocity of SAW pumping was seen to be faster than the velocity of capillary flow, which confirms prior findings on the pumping power of SAWs.

The next part of the project examined the range of SAW MS by assessing twelve different drugs, mostly antimalarials and antibiotics that are commonly used in Africa: acetaminophen, amodiaquine, amoxicillin, ampicillin, artemether, artesunate, chloroquine,

clavulanic acid, lumefantrine, pyramethamine, quinine, and sulfadoxine. Each drug was tested multiple times using SAW MS, and the spectra were compared to parallel electrospray ionization (ESI) MS spectra and to literature spectra. As a further check, MS/MS on the parent peak verified that SAW MS was detecting the correct compound. SAW MS was able to detect every drug that ESI MS could detect, although the absolute intensities of the peaks were smaller for SAW MS. Future work will attempt to increase peak intensities by using voltage applied to the paper wick.

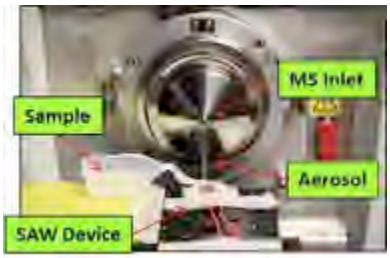

Fig. 1. SAW MS Apparatus.

The last part of the project tested SAW extraction and consequent MS for different solvents and drying times using the antimalarial drug quinine as the model system. Samples were prepared by wetting strips of paper in 10 uM quinine solutions composed of different solvents (acetonitrile/deionized water, methanol/deionized water, or tap water), and then drying the strips for different lengths of time (a few hours, a day, or a week). Each sample was then rewet in solvent and ionized by the SAW device into the mass spectrometer. MS detection was successful for all combinations of drying times and solutions, but the greatest signal intensity corresponded to a drying time of a week and to the acetonitrile/deionized water solution. The fact that signals appeared for all solvents and drying times, however, is very encouraging, as it demonstrates that samples of drugs can be dried on paper in the field and then sent back to a laboratory for later analysis. Future research will focus on evaluating the performance and detection limits of SAW MS extraction on a range of pharmaceuticals.


Fig. 2. Process of preparing samples for extractive SAW analysis. a) Saturation of a paper strip. b) Paper strips drying. c) Rewetting in solvent. d) Placement on SAW device.

This project was conducted in collaboration with the Notre Dame and St. Mary's group that works on paper analytical devices (PADs) for the detection of counterfeit pharmaceuticals. There were many joint group discussions, which detailed the current situation in Africa and explained more fully the ultimate goal of both groups. These meetings were especially helpful in highlighting which pharmaceuticals are commonly used and counterfeited in Africa and which are the most important to test with SAW MS. Further, because both projects are concerned with detecting the same drugs, there were many opportunities for sharing information on how to

prepare drugs for visualization, on analysis of spectra, and on different methods of detection. In addition, working with the Notre Dame and St. Mary's group meant involvement in discussions about new PAD designs that will be able to detect target compounds and store them for later SAW analysis.

Publications:

1) Sara K. Dale, Daniel Taller, Li-Jing (Larry) Cheng, Hsueh-Chia Chang, and David B. Go, “Surface Acoustic Waves: Fundamentals and Applications,”Advanced Diagnostics and Therapeutics Symposium, Notre Dame, IN, 2012.

2) Sara K. Dale, Daniel Taller, Marya Lieberman, and David B. Go, “Paper-SAWN: Paper Storage and Delivery Coupled to Surface Acoustic Wave Nebulization for Mass Spectrometry Analysis of Pharmaceuticals,” in preparation.