

- 1) Student name: Michael Benvenuti
- 2) Faculty mentor name: Marya Lieberman
- 3) Project title: PADs Project

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

I learned how to work with ImageJ, an image analysis program, and some organic and inorganic chemistry, especially colorimetric reactions. My research was not intensive in the use of equipment because we are trying to create cheap and easy to use paper devices.

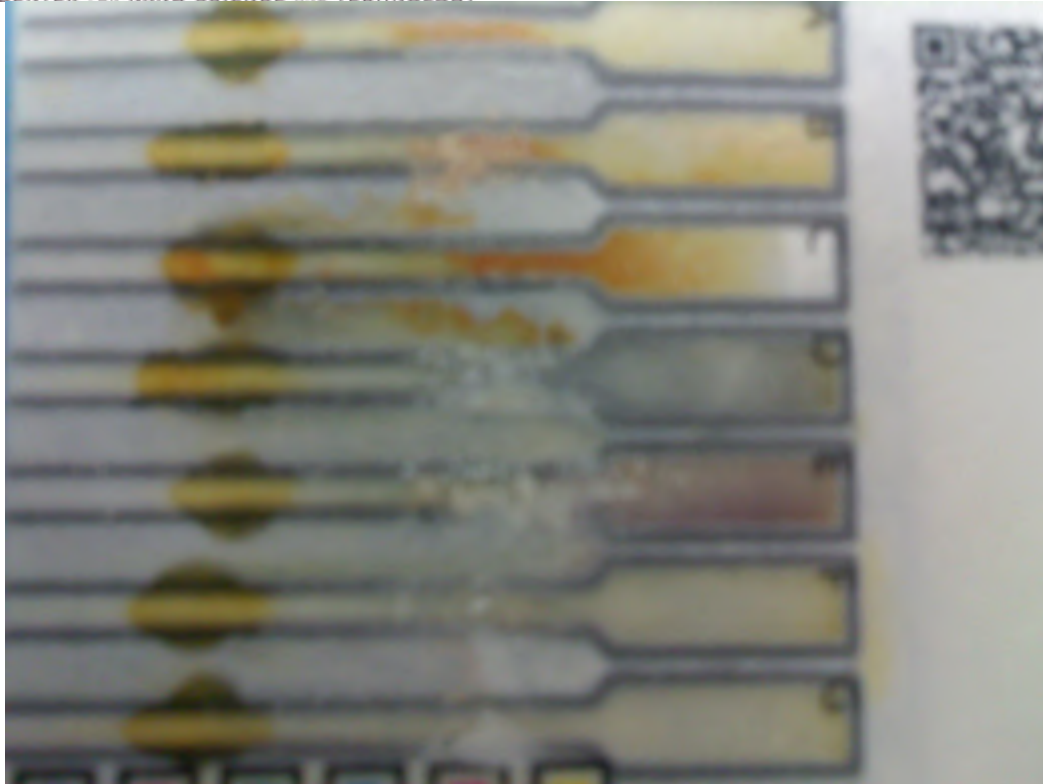
5) Please briefly share a practical application/end use of your research:

My research is into practical applications of colorimetric reactions. The eventual goal is for the paper analytical devices to be used in developing regions to test questionable pharmaceuticals and help eliminate counterfeiting.

Project summary:

Counterfeit and low grade pharmaceuticals are a significant problem, especially in the developing world, and many agencies rely on examining packaging to determine the authenticity of medication. Our goal is to develop a cheap and effective way to determine if medications are authentic. When developing paper analytical devices, the stability of the reagents on the paper is an important consideration in developing effective tests for use in the field. Some of the tests on the devices that are in development to test counterfeit pharmaceuticals lose their efficacy after only several days after being spotted on a piece of paper. Because the PAD must be shipped to remote locations with poor infrastructure and stored until it is needed, the PAD must survive for extended periods of time. Packaging may improve lifetime, but not by the extent necessary to make the tests viable candidates to be used on a PAD. I sought to improve the lifetime and improve the results of these tests by changing the reagents and adding compounds to the solutions before spotting. The tests that posed significant problems were the Ferric chloride test for a variety of excipients, the iodide test for starch, and the 2-nitroaniline test for Tylenol and amoxicillin. Each of these tests suffered from either a lack of strong coloration to indicate positive result or lasted for only several days on the PAD before losing their effectiveness.

I improved the results for each of these tests by changing solvents and adding reagents. After some experimentation, I found that adding some detergent to the ferric chloride test improved its detection of carbonate by helping to wet the sample, giving a more intense dark orange coloration. The addition of polyvinylpyrrolidone to the iodine test for starch significantly increased its lifespan by preventing the evaporation of I_2 , with which the triiodide is in equilibrium. The 2-Nitroaniline test also suffered from a short lifespan in part because not enough reagent was being spotted on the PAD, and the little that was would sublime off of the PAD. The use of organic solvents instead of 1M Tosic acid in water significantly improved results because nitroaniline is more soluble, allowing more reagent to be spotted on the PAD. The presence of more nitroaniline enables the PAD to work for at least two weeks when stored at 35 C, instead of 4 days when Tosic acid is used as a solvent. The color differences between positive and negative results for the tests are detectable by measuring RGB intensities using ImageJ.



2M FeCl_3 and 10% Neutrad PAD with from top chalk, Tums, baking soda, Tylenol, degraded aspirin, talc, gypsum after 2 weeks of storage at 22 C



Nitroaniline test run with Tylenol (top) and talc (bottom) after 7 days of storage at 35 C



Povidone iodine test detects starch in Tylenol after 6 weeks of storage at 22 C

Publications (papers/posters/presentations): I presented the below poster at the summer undergraduate research symposium on August 3. I also have some of my work incorporated in a current patent application.

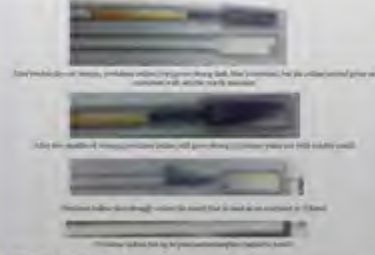
Paper Analytical Device lanes depend on multipart reagents for stability and vivid results

Michael Benvenuti, Marya Lieberman



Paper Analytical Devices (PADs)
 When developing paper analytical devices, the stability of the components on the paper is an important consideration in developing effective tests for use in the field. Some of the tests we've developed that are in development to test analytes in pharmaceuticals have their efficacy after only several days after being opened out of a pack of paper. Because the PADs must be shipped to remote locations each year for maintenance and repair, we've had to re-evaluate the PADs more so for extended periods of time. This has led us to improve the stability and improve the results of these tests by changing the reagents and adding components to the substrate before printing. The tests that we've developed are for the detection of cocaine, heroin, and a variety of compounds that include over the counter and the 2-aminocinnoline for 2-aminocinnoline and amoxicillin. Each of these tests has been subjected to a full year of testing conditions to ensure positive results are achieved for only several days on the PAD before being used in the field.

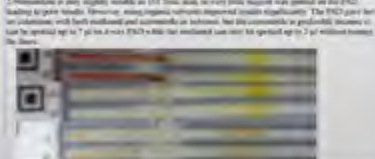
Indole Production Lane
 Indole is used in a variety of ways in the pharmaceutical industry, and as a filter in some pharmaceutical applications. Therefore, it is important to be able to detect it as part of efforts to determine the authenticity of medicines. Indole is used in a variety of ways in the pharmaceutical industry with such as drug synthesis, protein synthesis, and as a marker for drug synthesis. However, the indole is unstable on the PAD because it is a weakly acidic compound and is highly volatile. It is highly volatile and evaporates easily, leaving the PAD useless (usually within a day) after only two days. The indole production can be improved by using a variety of reagents in a variety of ways to stabilize the indole. The addition of various reagents (including sodium hydroxide) to the indole on the PAD has been shown to improve its stability and as a result, it is possible to use the PAD to detect indole in a variety of ways. The use of sodium hydroxide to stabilize the indole on the PAD has been shown to improve its stability and as a result, it is possible to use the PAD to detect indole in a variety of ways. The use of sodium hydroxide to stabilize the indole on the PAD has been shown to improve its stability and as a result, it is possible to use the PAD to detect indole in a variety of ways.



Stability and Reliability
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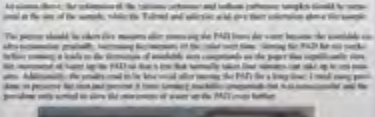
2-Aminocinnoline Test for Amoxicillin and Amoxicillin
 Amoxicillin and amoxicillin are both commonly used antibiotics for which paper tests would be useful in working to determine the authenticity of medicines. A common test for the detection of amoxicillin is the 2-aminocinnoline test. This test is used to detect the presence of amoxicillin in a variety of ways. The use of sodium hydroxide to stabilize the amoxicillin on the PAD has been shown to improve its stability and as a result, it is possible to use the PAD to detect amoxicillin in a variety of ways. The use of sodium hydroxide to stabilize the amoxicillin on the PAD has been shown to improve its stability and as a result, it is possible to use the PAD to detect amoxicillin in a variety of ways.



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Ferric Chloride Test
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References
 1. Michael Benvenuti, Marya Lieberman, "Paper Analytical Devices (PADs) for the Detection of Cocaine, Heroin, and 2-Aminocinnoline for 2-Aminocinnoline and Amoxicillin," *Journal of Pharmaceutical Sciences*, 2018, 107, 1234-1245.
 2. Michael Benvenuti, Marya Lieberman, "Paper Analytical Devices (PADs) for the Detection of Ferric Chloride," *Journal of Pharmaceutical Sciences*, 2018, 107, 1246-1257.

Authors' Agreement
 We would like to thank the University of Notre Dame for its support of this research. We would like to thank the University of Notre Dame for its support of this research.