Development of a New "Advanced Medicinal Chemistry" Laboratory Course for Stage 3 Undergraduate Students

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Introduction

Medicinal Chemistry is the overlap between Chemistry and Biology and is concerned with design of new drugs. This aspect of Chemistry is reflected in the Pharmaceutical industry, where drugs are discovered to aid and prevent health-related problems. During stage 3 of a Medicinal Chemistry degree, it is compulsory to participate in a laboratory course based on the biological aspect of Chemistry. This involves studying the structures, development and metabolism of general and specific drugs. This course also highlights the importance of structure in molecules, and helps students to relate specific aspects of structure to function. Throughout previous years this laboratory course was only focused on exploring synthetic methods and was lacking a biological component of drug chemistry. The spotlight of this project was to bring Biology into the Medicinal Chemistry laboratory course.

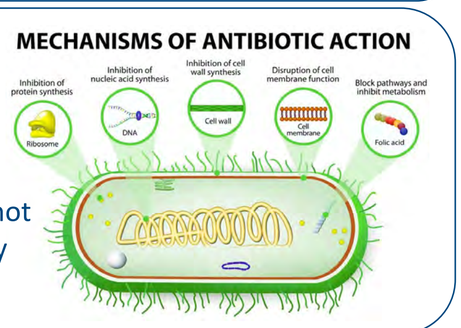
Aims

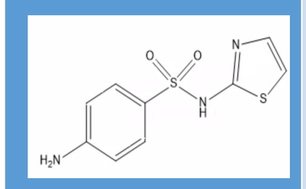
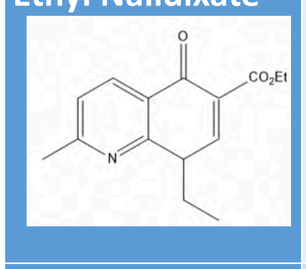
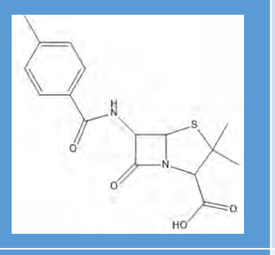
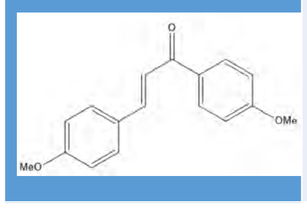
To create a new medicinal chemistry laboratory course which:

- Consists of 3 different and exciting experiments using different techniques
- Includes bioassay to reflect on the biological aspect of Medicinal Chemistry
- Is cost effective, reproducible, and is feasible within the time-scale

Which Drugs to Make?

- Used literature from other research to determine which molecules have antifungal/antibacterial activity
- The product and start materials must not be very toxic and must be cheap to buy



Group of Drugs	Importance
Sulfonamides 	Sulfonamides are widely used as antimicrobial drugs, used to treat bacterial infections such as water infections. There are also used to prevent infection of burns. The experiment itself was extremely volatile and unreliable. After altering and repeating the experiment, the product was only produced on one occasion. Therefore, the preparation of sulfathiazole was removed from the laboratory course.
Ethyl Nalidixate 	Nalidixic Acid provides is often used to treat UTI infection (water infections). Ethyl Nalidixate provides the backbone to many antibiotics currently on the market, making it an interesting and modern molecule to study. The experiment itself is complex, but produced an extremely high yield on repeated attempts, making it reliable.
Penicillin 	Penicillins are one of the most well-known antibiotics and were the first type of antibiotic that doctors used. The experiment itself took a lot of work to perfect as there were many different starting materials to test. Overall, we found one specific derivative that produced a high yield, which was extremely pure. This derivative was found to be antibiotic, making this experiment a success.
Chalcones 	Chalcones, similar to Ethyl Nalidixate, provide the core to many different biological compounds. Therefore, they are deemed as important molecules. The experiment itself was long but simple, consecutively producing a high yield.

Method Applied to Each Experiment

- The reaction mechanism was constructed for each reaction and ratios of each starting material were formulated. This allowed the development of a clear plan of the reaction steps for each reaction
- Different approaches of generating the molecule was first researched and tested using a small amount of each of the starting materials. This reduced the amount of product wasted, reducing the overall cost
- Each product was analyzed using NMR spectroscopy to establish if the correct molecule had been produced
- The most successful method was altered to increase the yield and purity
- The final method proposal was repeated multiple times on a larger scale, with time records, to ensure feasibility
- The product was purified to allow accurate analysis for student comparison

Acknowledgments

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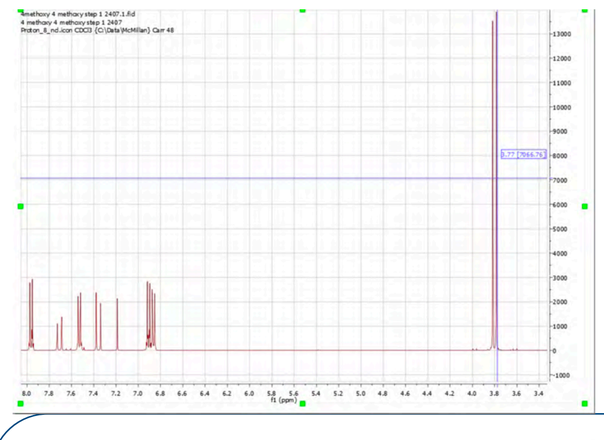
Chemical Analysis

Chemical analysis confirms that the molecule produced is the desired product. It also displays the purity of the product, which is important when deciding how effective the experimental procedure is.

Chemical analysis may include:

- Infra-red (IR) spectrum: This shows which functional groups are in the molecule
- H^1 NMR: Shows the overall structure based on the position of the hydrogen atoms in the molecule
- C^{13} NMR: Shows the overall structure of the molecule based on the position of the carbon atoms in the molecule



This shows the Hydrogen NMR for the Chalcone product. This shows that the product is pure because there are no tiny peaks. Each peak is extremely clear.

Biological Analysis

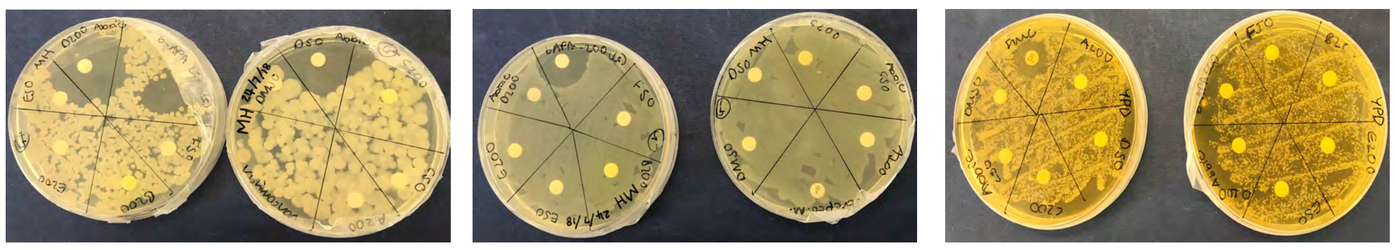
Biological analysis is arguably the most important aspect of the medicinal laboratory course. It allows students to learn a different technique in analysis, which tests for a response against different forms of bacteria and fungi. This mimics the response of the molecule in the human body.

- Each molecule was dissolved and diluted into a solution and placed on discs
- The discs were placed on 3 different Petri-dishes containing: fungus and 2 different types of bacteria
- A known antifungal and antibiotic was placed on the appropriate Petri-dishes as a standard
- The dishes were left overnight, allowing the fungi/bacteria to grow

Results of Biological Analysis

Not all molecules were expected to product a positive result, as it may require harsh and unrealistic conditions for a learning laboratory environment to produce successful drugs. However, this mirrors a research situation, where not all drugs are successful.

- Ethyl Nalidixate – The results displayed a negative response
- Penicillin Product – The results displayed a positive response to one type of bacteria, showing that the product produced is a specific antibiotic
- Chalcone Product – The results displayed a negative response



- Left picture – The Petri-dishes contain a specific bacteria. The bacteria has not grown around the Penicillin discs, showing a positive response. Therefore, the penicillin has a specific antibacterial response. However, the bacteria has grown around all remaining discs shows a negative response
- Middle picture – The Petri-dishes contain a different specific bacteria. The bacteria has not grown around the starting material used for Penicillin but has grown around all products from my experiments showing a negative response
- Right Picture – The Petri-dishes contain a fungus. Only the standard has shown a positive response, showing that none of my products have antifungal properties

Conclusion

- 3 reproducible experiments were constructed, which produced pure products upon analysis
- All experiments stuck to the time-scale of the laboratory course and reflect lecture material
- The biological aspect of the course was predominantly expressed in the analysis of the products, which produced one positive result within the Penicillin product

Overall, this project has been extremely successful and I have thoroughly enjoyed my experience. All aims have been achieved and a new medicinal laboratory course has been outlined.

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