Introducing K-12 Students to the Field of Pharmaceutical Engineering

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Abstract

The design, development, and engineering of drugs provide chemical engineers with many opportunities and challenges in the pharmaceutical industry. In an effort to engage the surrounding communities, New York City public and private high school students were introduced to the field of pharmaceutical engineering over the course of six weeks. Through the use of lectures, teamwork activities, and laboratory experiments, students learned about the fundamentals of oral solid dosage forms, drug dissolution, and experimental design. Examples of experiments performed include building their own "in-house" drug dissolution devices, studying the effect of impeller geometry and velocity on dissolution rates, and obtaining drug dissolution profiles for various oral solid dosage forms containing Ibuprofen using UV-Vis spectroscopy. Students were also trained in communication skills, such as writing a technical report and giving an oral presentation.

In this paper, an overview of the program, suggested laboratory exercises, and in-class teamwork activities are provided for those who might consider developing a similar K-12 outreach program focused on pharmaceutical engineering. In addition, examples of perceived enhanced learning by the high school students are provided.

Background

Summer Research Internship Program

The *Summer Research Internship Program* administered at The Cooper Union for the Advancement of Science and Art is a unique research program in that it provides local New York City high school students with a six-week opportunity to perform research in a university setting for free. Funding for this program comes from donors and corporate support from companies such as Con Edison. Admission to the program, which is open to freshman to senior high school students, is competitive and is based on the student's transcript, a written essay, and a letter of recommendation. Once accepted to the program, students are assigned a research mentor and topic to study. Students are required to be present for all six weeks of the program and must contribute to a written final report. In addition, students are required to give an oral technical presentation to all participating students and faculty advisors. Throughout the program, students receive workshops on careers, advice for college admissions, as well as training in developing and improving their technical and communication skills.

Pharmaceutical Engineering

Branching out from chemical engineering, pharmaceutical engineering has recently emerged as a new formal academic discipline [1]. Universities such as Rutgers University and New Jersey Institute of Technology have begun to offer graduate programs to help complement the pharmaceutical industry based in New Jersey [2,3]. In recent years, many graduates of The Cooper Union have gone into careers in the pharmaceutical industry. This has led the lead

author to develop new courses and research thrusts in this area. To complement this initiative, a K-12 outreach program was developed in pharmaceutical engineering. Since the time of this outreach activity, other K-12 and undergraduate activities and modules focused on pharmaceutical engineering have been developed by other institutions [4]. In addition, similar approaches to teaching drug dissolution have been developed for freshman engineering classes [5].

Pharmaceutical engineering is primarily concerned with the design, development, and manufacturing of drugs and drug delivery systems [6, 7, 8]. One of the most common forms of drugs is known as a *solid dosage form*. Examples of solid dosage forms include tablets and capsules, which are commonly taken orally, and are also called *oral solid dosage forms*. These dosage forms primarily consist of two main elements: the active pharmaceutical ingredient (API), which provides the therapeutic effect and the excipients, which are inactive ingredients used to help make the formulation. When combined, these two elements form the drug product. Modifications, such as coatings, are commonly applied to solid dosage forms for numerous purposes, including changing the rate at which the drug is administered.

For a solid dosage form to have a therapeutic effect, the API must dissolve in the human body. Once it does, it becomes *bioavailable* and can have a therapeutic effect. Thus, the dissolution behavior of a drug is extremely important to study the long-term therapeutic effects. Since it is difficult to study the *in-vivo* dissolution behavior of a drug within the human body, *in-vitro* dissolution testers have been developed and approved by the U.S. Food and Drug Administration (FDA) to allow pharmaceutical companies to study the dissolution behavior of solid dosage forms [9]. Drug dissolution testing is an extremely important part of the drug development process because it is used to study the drug release profile and predict the bioavailability of the drug. In addition, the testing can be used to study quality control and drug consistency. There are four main types of drug dissolution testers approved by the FDA. The students who participated in this program developed their own "in-house" version of a type 2 paddle drug dissolution tester, which is one of the most commonly used testers.

Engaging the Students

During the summer of 2011, 16 different students across New York City (from Staten Island to the Bronx) were chosen to be part of the pharmaceutical engineering project. In an effort to engage the students and "break the ice" a series of group activities were developed to introduce the students to chemical engineering, pharmaceutical engineering, and to their fellow teammates.

For the first exercise, students were required to work in groups of two to fill out activity forms that included questions about their teammates (e.g. "what does your teammate plan to learn from participating in this?" Following this, students were given an introduction to the field of chemical engineering. At the end of the lecture, the students were required to work in teams and fill out questions about chemical engineering (e.g. "in what industries do chemical engineers work?"). The third lecture was focused sole on pharmaceutical engineering and introduced the students to the concept of oral solid dosage form and drug dissolution. Following this, students worked in teams and completed the following activity (Figure 1):

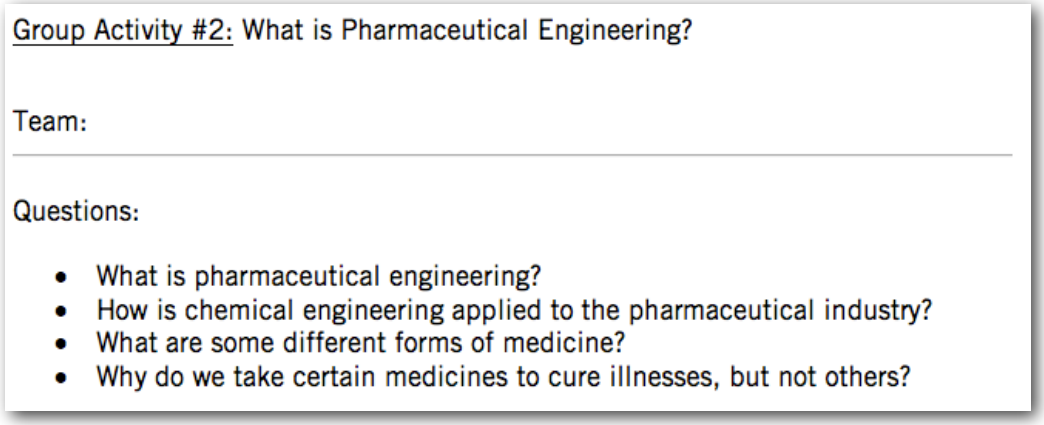

Figure 1 - Pharmaceutical Engineering Group Activity

Another activity that the students worked on was drug research as shown in Figure 2. Since, Ibuprofen was chosen as the drug to be studied during the summer, students were required to look up online information regarding that drug and two others of their choosing. This activity had to be completed in teams and all results were presented in front of the class.

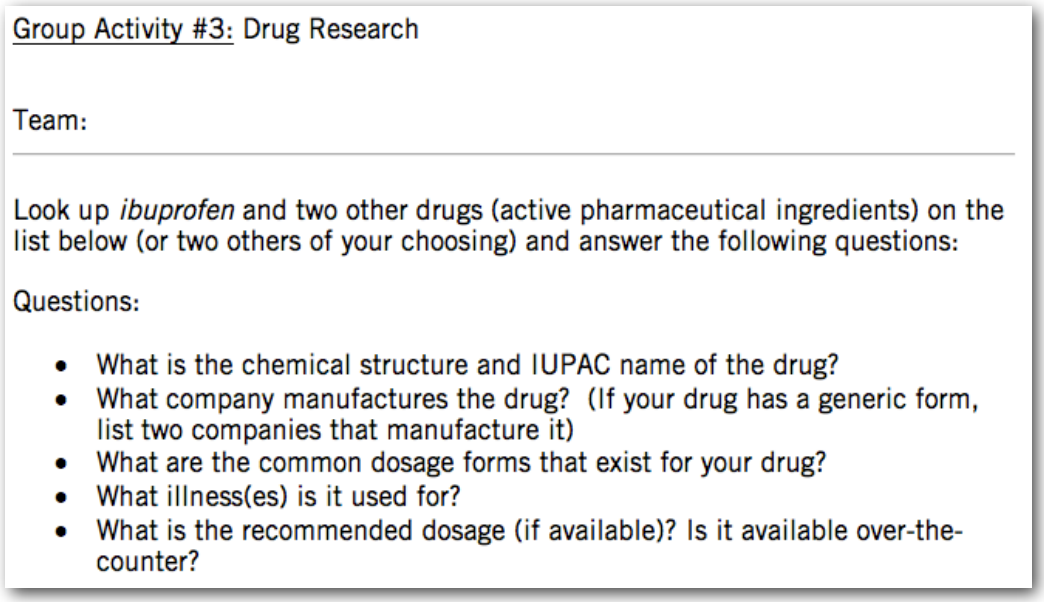

Figure 2 - Drug Research Group Activity

This activity proved to be very successful particularly because it introduced students to drug concepts that they have never thought about (e.g. the company that manufactures the drug). Additionally, the students enjoyed looking up online the different elements of the drug (including structure and equation) and trying to determine if generic forms existed for the drug.
The last group activity was on laboratory safety and experimental design (Figure 3). Once the experimental set-up and overall procedure was discussed, students had to work together on a group activity to review all safety information and laboratory methods. For all group activities, students were able to successfully answer the questions, engage with their teammates, and understand that these activities formed the necessary background prior to beginning experiments.

Group Activity #4: Drug Dissolution – Laboratory Techniques

Team:

Questions:

- What is a "control?"
- What parameters can affect the solubility of a drug?
- Why does using an impeller help promote drug dissolution?
- How will the concentration of the drug be measured after it has dissolved?
- What safety precautions will be taken during the experiments?

Figure 3 - Laboratory Techniques Group Activity

Experimental Set-up

To study the dissolution behavior of ibuprofen, the following apparatus was developed by the students to represent a type 2 paddle drug dissolution tester.

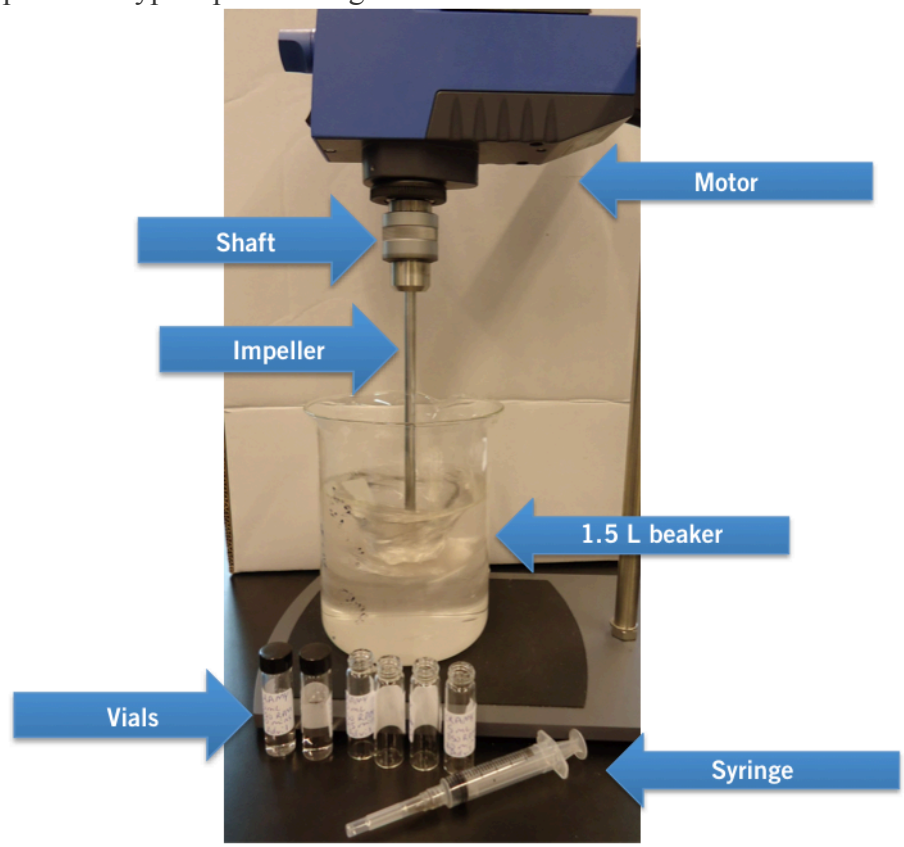

Figure 4 - Experimental Set-up

The experimental set-up (Figure 4) primarily consisted of a motor with shaft (Cole Palmer), an impeller (IKA), and a 1.5 L beaker. Vials and syringes were used to collect samples to study the drug concentration using UV-Vis spectroscopy. Different types of impellers were purchased

from IKA and used for experiments. These included a 3-bladed, 4-bladed, anchor/paddle, and a dissolver impeller. The different geometries of these impellers are shown in Figure 5:

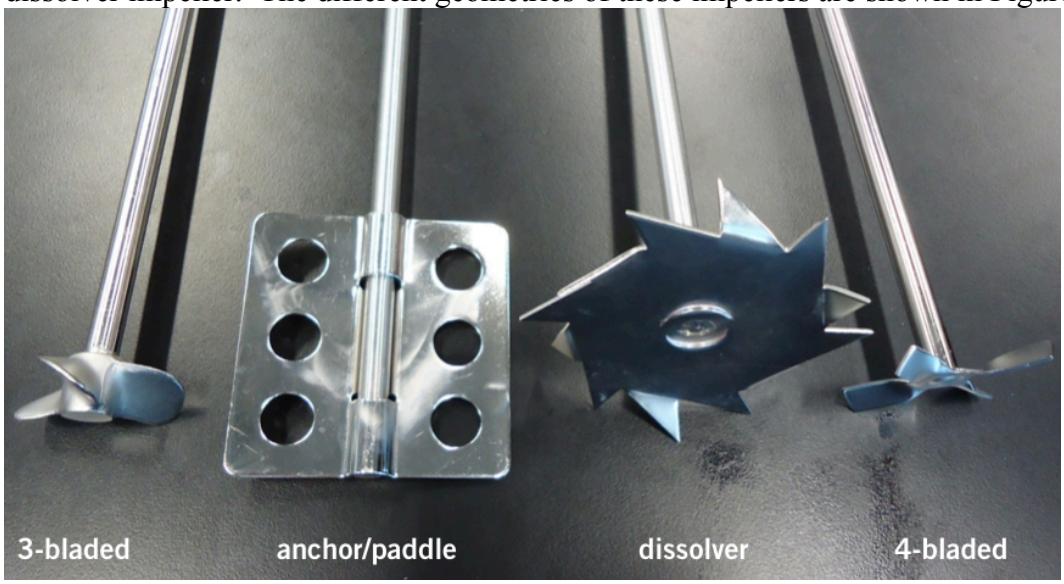

Figure 5 - Impeller Geometries

The solvents that were used to study the Ibuprofen drug dissolution profile were water and phosphate buffer (pH = 6.8). The students learned that the choice of solvent can have a major affect on the dissolution behavior. Phosphate buffer was the only solvent used when measuring the Ibuprofen concentration using UV-Vis spectroscopy [10].

To further illustrate the concepts of oral solid dosage forms, different types of over-the-counter (OTC) Ibuprofen were used in the experiments and can be seen in Figure 6:

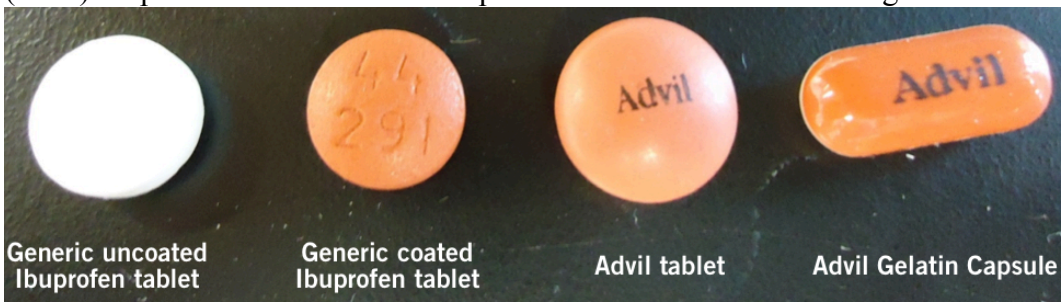

Figure 6 - Types of Ibuprofen solid dosage forms

Experimental Method and Results

One of the first experiments that the students performed was the effect of impeller tip (rotational) velocity on the dissolution behavior of the drugs. The students varied the tip velocity by using the motor. Each team was assigned a different impeller to study and the data was combined together to highlight what differences can occur by using different impellers. In addition, the students learned how the flow behavior can change dramatically based on impeller geometry. The following plot is an example of dissolution time results obtained for uncoated generic

Ibuprofen tablets using different impellers (Figure 7):

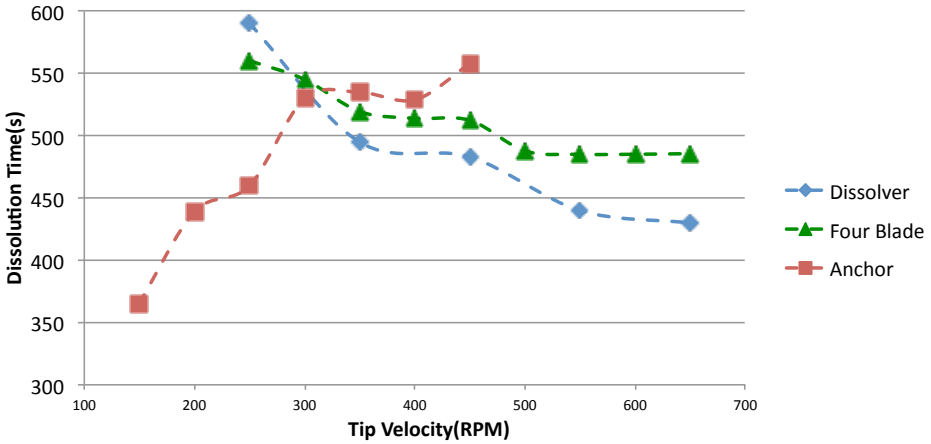

Figure 7 - Dissolution time as a function of tip velocity

From the above plot, students learned that except for the anchor impeller, which exhibited a complex flow field due to its unit geometry, the dissolution time decreased with increasing velocity. This is an expected result based upon the Noyes-Whitney equation and the concepts of convective mass transfer [8].

The next set of experiments was focused on measuring the concentration of Ibuprofen in the apparatus as a function of time. Using the different impellers at various velocities, the students performed the drug dissolution experiments again, but this time, also took samples of the solvent using the syringe and stored them in the vials. A calibration curve of known concentrations of Ibuprofen was developed to assist in determine the concentrations obtained. The following plot shows the concentration (drug release) profile of Advil obtained using the 4-blade impeller at three different tip velocities:

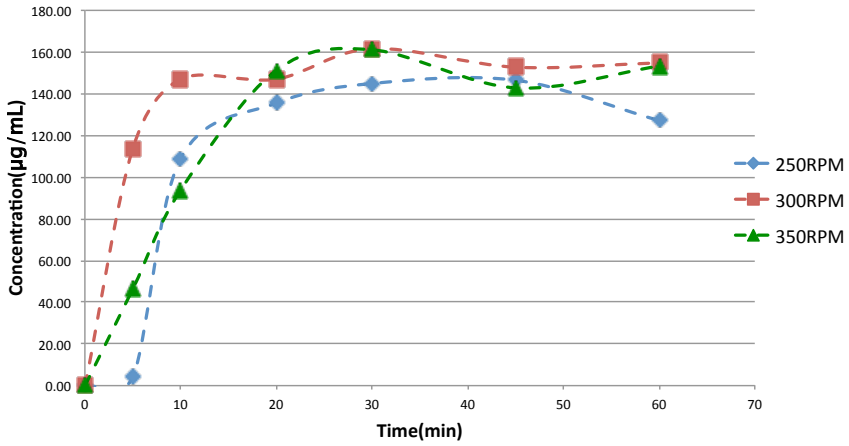

Figure 8 - Ibuprofen Drug Release Profile

From Figure 8, it can be seen that the range of tip velocities used did not have a major impact on the drug release profile. However, from these results, the students learned that the maximum concentration was reached after approximately 10-20 minutes and that the maximum concentration reached a plateau around 20-30 minutes. These results nicely approximate and

represent the typical drug release profile of Ibuprofen in the human body (therapeutic effect becomes noticeable after 20-30 minutes).

Another set of experiments was performed at a single velocity, which highlighted the effect of the generic form (and coating) on the drug release profile. For these experiments, the students were introduced to the concept of using a "control" when performing experiments. The uncoated generic dosage form was designated as the control. Students found that the coating can have a slight affect on the drug release profile and that the uncoated dosage form had the highest obtainable concentration. This can be seen in Figure 9:

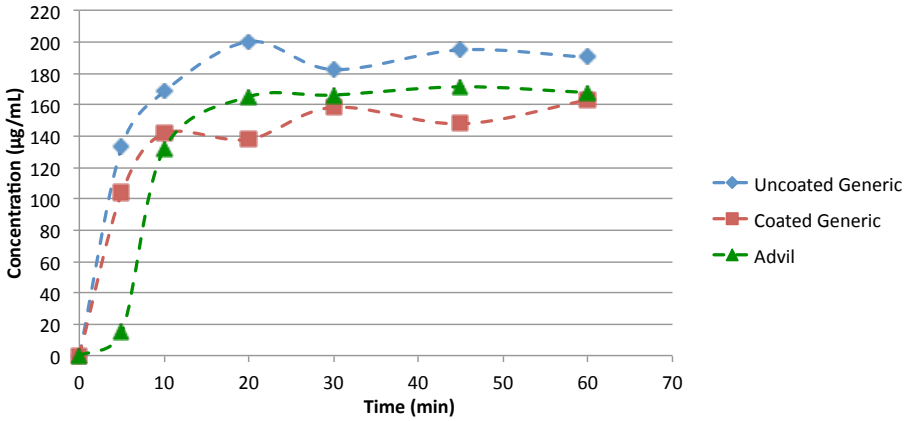

Figure 9 - Drug release profile for different Ibuprofen dosage forms

Conclusions and Lessons Learned

By participating in this program, students learned about aspects of pharmaceutical engineering, particularly drug dissolution testing and oral solid dosage form design. The experiments performed by the students provided an active-learning environment, which focused on aspects of experimental design, such as controls (known concentrations, impellers) and variables (tip velocity).

The advantages of this outreach activity include: (1) students *learned* about the science and engineering behind drug, as well as laboratory and experimental techniques, (2) students *developed* teamwork skills by performing the introductory activities and experiments in teams, and (3) students *improved* their technical communication (oral and writing) skills through the assignment and critiquing of a required final technical report and presentation.

The disadvantages of this outreach activity include: (1) impellers and motors can be costly, (2) concentration analysis requires UV-Vis Spectroscopy and buffer preparation, and (3) dissolution experiments take time (at least 30 minutes).

Overall, this outreach activity was successful in achieving its goal of introducing K-12 students to the field of pharmaceutical engineering. Assessment instruments (i.e. surveys) were given to the students following the program to help determine the success of the program. From the surveys, it was found that most students felt that this activity gave them a better grasp of what engineering is and how chemical engineers can impact the pharmaceutical industry. In addition,

the students felt that they gained much better laboratory techniques, improved scientific writing skills, familiarity with data analysis software (e.g. Microsoft Excel), and helped them to better solve problems and think "outside of the box." Aside from the few disadvantages previously listed, based on the success of the program, the authors strongly recommend this outreach activity to other educators who are interested in introducing K-12 students to the fields of chemical and pharmaceutical engineering.

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