EXPERIMENTS IN PHARMACEUTICAL ENGINEERING FOR INTRODUCTORY COURSES

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The year of 2010 marked one of the highest points of the pharmaceutical industry, where it had the second largest earnings of all industries.[1] The pharmaceutical industry also increased its worldwide profit growth of 4.2% to approximately 800 billion USD that year.[2] This is substantial growth, considering that in the year 2007, the pharmaceutical industry amassed revenue of 315 billion USD.[3] These economic factors are coupled with shifting paradigms of the industry, such as a move toward shorter drug development times and an increased openness to change existing processes, which will increase the need for chemical engineers with pharmaceutical training.[4] In 2010, 5% of employed chemical engineers and 14% of all biomedical engineers in the United States worked in pharmaceutical and medicinal manufacturing.[5, 6] From 2004 to 2014, roughly 76 thousand jobs are to be created in the pharmaceutical and medicine manufacturing sector, while basic chemical manufacturing jobs are to decrease by roughly 46 thousand in that same timespan.[7]

As the demand for engineers has increased in the pharmaceutical industry, universities have found a need to provide engineers with education in the field of pharmaceutical engineering. Pharmaceutical engineering is defined as the design of pharmaceutical and diagnostic products and the associated manufacturing processes.[8] Several universities have incorporated pharmaceutical engineering education into advanced degree studies. Some examples of universities that have introduced pharmaceutical engineering programs on the graduate level are Rutgers University, the University of Michigan, and the New Jersey Institute of Technology. All three of these universities offer a master's degree program

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in pharmaceutical engineering, while Rutgers University also offers a pharmaceutical engineering option for Ph.D. students in chemical and biochemical engineering. This pharmaceutical engineering option requires five courses that focus on the different aspects of pharmaceutical engineering.[9]

Stevens Institute of Technology offers a master's degree program in pharmaceutical manufacturing. The goal of this program is to provide students with a strong background in Good Manufacturing Practices, project management, and pharmaceutical facilities. This is considered an interdisciplinary program, administered by the mechanical engineering department.[10] In addition, Purdue University offers graduate scholarships from the Department of Education's Graduate Assistance in Areas of National Need program for students to continue research in the field of pharmaceutical engineering. These graduate students also have the ability to be part of an international exchange program, gain industry experience through internship opportunities, and conduct supervised teaching to prepare them for a career in academia.[11] Due to the expanding interest in pharmaceutical engineering training, the National Science Foundation funded an Engineering Virtual Organization to facilitate the creation and sharing of pharmaceutical engineering educational information.[12] From this funding, the website <www.PharmaHUB.org> was created, and is now used to compile and share pharmaceutical engineering research, technology, and educational resources.

With this increased interest in pharmaceutical engineering at the graduate level, there has been some diffusion into undergraduate curricula. A majority of the universities that have developed undergraduate pharmaceutical engineering programs are found in Europe. In 2003, the University of Basel, in Switzerland, introduced a bachelor's program in pharmaceutical engineering.[13] For the most part, however, colleges and universities tend to offer pharmaceutical specializations within traditional bachelor's degree programs. This is especially true in the engineering colleges of the United Kingdom and Scandinavia. In these countries, the pharmaceutical industry is a major contributor to the country's economy. For example, 40 percent of all exports from the Republic of Ireland are pharmaceuticals.[14] In the United States, the University of Iowa offers a pharmaceutical specialization for undergraduates. This specialization can be obtained through higher-level electives that focus on different aspects of pharmaceutical sciences, such as drug delivery systems and basic pharmacology.[15] Stevens Institute of Technology also offers a pharmaceutical manufacturing concentration for students of mechanical engineering. This specialization is obtained through courses that incorporate pharmaceutical facility design, validation, and hands-on projects in the field of pharmaceutical manufacturing.[16]

Within these specializations, a majority of emphasis is on upper-level undergraduate courses, such as creating special topic courses that focus on pharmaceutical sciences. At the New Jersey Institute of Technology, a class focusing on drug transport and pharmacokinetics was implemented as a specialty topic course for students wishing to obtain a specialization in pharmaceutical engineering.[17] The Georgia Institute of Technology has a course for senior and graduate-level students in the field of pharmaceutical engineering; specifically drug design, development, and delivery.[18] Rutgers University has a Pharmaceutical Engineering Training Program, which allows both graduates and undergraduates to work on projects based on realistic problems found in the pharmaceutical industry. These projects deal mainly with product manufacturing or process research and development.[19]

Although new upper-level elective courses can be developed to include pharmaceutical engineering concepts with relative ease, there is a level of difficulty when trying to incorporate concepts into lower-level undergraduate courses. In particular, the concepts have to be appropriate for students who are just beginning their undergraduate study. In addition, these concepts might have to be presented in ways that can be applicable to different engineering majors. There is also the complexity of adding new courses into an already saturated curriculum. One approach is to modify existing courses so that they have a focus in pharmaceutical engineering and at the same time, meet student learning outcomes. For example, problem sets developed at Rowan University for use in lower-level undergraduate courses contain material and energy balances that incorporate different aspects of pharmaceutical engineering.[20,21] In addition to using problem sets, incorporating pharmaceutical concepts into laboratory experiments can be used to reinforce the course's existing educational objectives. One of the initial efforts in this was the development of a first-year laboratory experiment that focused on an investigation of the controlled release principles of drug delivery methods through the dissolution of a lozenge.[22]

This paper presents synopses of several experiments that have been developed for use in a lower-level, laboratory-based course. These experiments were designed to not only introduce pharmaceutical concepts, but also to reinforce basic engineering educational objectives such as: understand and apply core science and mathematics principles; work individually and in teams to identify and solve engineering problems; and design and conduct experiments as well as analyze and interpret data.[23] The experiments discussed in this paper will be grouped by the pharmaceutical engineering concept that they encompass; either pharmaceutical fundamentals, drug manufacturing, drug formulation/delivery, or pharmacokinetics/pharmacodynamics. These experiments can also be used in tandem with course materials developed by others to further reinforce pharmaceutical concepts. The problem sets that were developed by Rowan University,[20, 21, 24, 25] and other supplemental course materials available from PharmaHUB,[26, 27] may be used to provide more detail about topics—such as the regulatory issues, quality control, experi-

TABLE 1
Raw data of mass measurements for the Tablet Statistical Analysis Lab

Trial Number	Advil® Brand Mass (grams)	Generic Brand Mass (grams)
1	0.4784	0.3354
2	0.4837	0.3300
3	0.4715	0.3296
4	0.5019	0.3280
5	0.4840	0.3383
6	0.4842	0.3284
7	0.5050	0.3307
8	0.4930	0.3365
9	0.4804	0.3272
10	0.4845	0.3362
Average	0.4870	0.3320
Std. Dev.	0.010	0.004
Variance	$9.72 \cdot 10^{-5}$	$1.52 \cdot 10^{-5}$

mental design, and batch processing—that are relevant to the pharmaceutical industry.

The experiments were designed to meet the safety standards of a typical undergraduate laboratory and be performed by the students in approximately 2 hours. The cost of these experiments was also considered, so they do not rely on highly specialized equipment and the operating costs are reasonable, allowing the laboratory experiments to be relatively inexpensive in comparison to other chemical and biochemical unit operations. Another point considered when developing these experiments was the ease of the setup.

Two versions of these experiments are available; a student version and an instructor version, both of which can be found on the website <www.PharmaHUB.org>. The PharmaHUB homepage has a Resources section on the left-hand side of the screen, where the tag "Experiments" will automatically direct the user to all the laboratory experiments available. The Teaching Materials quick link can also be used from the PharmaHUB home page. This will bring the user to a screen listing all of the teaching materials available. The user can then find the appropriate lab from the alphabetical listing of educational resources or use the "Experiments" tag to find them.

This paper only includes representative experiments; others are available on the website. The pharmaceutical and engineering concepts that the experiment would incorporate are discussed in a brief introduction, which the students would read before beginning the experiment. The instructor's version includes more detailed procedure, equipment and supplies lists, additional pictures and/or diagrams of correct setups for the laboratory experiments, concepts to reinforce, and a solutions section. To obtain access to the instructor versions, faculty must register to the PharmaHUB website. Currently, the experiments that can be found on PharmaHUB are the following: Tablet Statistical Analysis Lab; Asthma Drug Delivery Lab; Antacid Comparison Lab; Effervescence Reaction Lab; Fluidization of Pharmaceutical Substances Lab; Degradation of Dissolvable Strips Lab; Bandage Comparison Lab; and Creation of Dissolvable Strips Lab.

EXPERIMENTS DEVELOPED

Pharmaceutical fundamentals

One of the introductory laboratory experiments created to acquaint students with the fundamentals of the pharmaceutical industry is the Tablet Statistical Analysis Lab. The objective of this experiment is to conduct a statistical analysis on the mass of analgesics; in this case, ibuprofen tablets. From an educational perspective, the intended outcome of the experiment is that the students will gain experience interpreting data and using some basic statistical analysis methods. Statistics is an important aspect of the pharmaceutical industry, used to determine the reliability and accuracy of data taken from drug samples, monitor and detect the adversities of a process, and assess the capability and reliability of a process.[28]

For this experiment, students take mass measurement of two types of ibuprofen tablets; Advil® brand and a generic store brand. Table 1 shows example raw data of these mass measurements. Students are given 10 samples of each brand, and then take mass measurements using an analytical scale. The first calculations performed are mean ($\bar{x}$), standard deviation (σ), and variance (s) of both brands. Students then determine if the masses of the two brands are significantly different from each other through an F-test. The equation for the F-test, along with the calculations used based on the raw data, is shown as Eq. (1).

$$F_{exp} = \frac{s_1^2}{s_2^2} = \frac{\left(9.726 \cdot 10^{-5}\right)^2}{\left(1.526 \cdot 10^{-5}\right)^2} = 40.63 \qquad (1)$$

For this experiment, the F-critical value was given as 3.18, based on the F-critical value table found in the Montgomery, Runger, and Hubele statistics text.[29] Since the experimental F-value is greater than the critical F-value, the two brands are considered statistically different. A t-test is then used to compare the two sets of data to a known mass of an ibuprofen tablet (μ_0), obtained from the Handbook of Pharmaceutical Manufacturing Formulations.[30] The t-test equation, along with a sample calculation of the t-test for the generic brand, is shown in Eq. 2.

$$t_{exp} = \left| \frac{\bar{x} - \mu_0}{\frac{\sigma}{\sqrt{n}}} \right| = \left| \frac{0.3320 - 0.4800}{\frac{0.00391}{\sqrt{10}}} \right| = 119.8 \qquad (2)$$

The critical t-value, or t-critical, was determined to be 2.262

using a generic t-table in the Montgomery, Runger, and Hubele text.[29] Since the experimental t-value was larger than the t-critical value, it can be concluded that the generic store brand is statistically different than the theoretical value. When the t-test is conducted for the name brand, it was found that experimental t-value was smaller than the critical t-value. This leads to the conclusion that the name brand was not statistically different than the theoretical value. The calculation for this is shown in Eq. (3).

$$t_{exp} = \left| \frac{\bar{x} - \mu_0}{\frac{\sigma}{\sqrt{n}}} \right| = \left| \frac{0.4867 - 0.4800}{\frac{0.00986}{\sqrt{10}}} \right| = 2.136 \qquad (3)$$

From these calculations, students can see that there is a difference between the two brands. In fact, the data shows that the standard deviation for the generic brand was lower than the name brand. The reason is that the generic brand did not have a sugar coating or a polishing coat like the Advil® brand. These coatings are much less regulated than the active pharmaceutical ingredient (API) content of the tablet, and as such, add more variance to the population. The students also see that the generic brand does not correlate well with the literature value, which is also due to the lack of coatings. As such, the values may change depending on the generic brand used for this experiment. Students also perform an outlier test, taking a portion of their data analysis for a box-and-whisker plot to determine any outliers. Students should not find any outliers in their experimental data, since the tablets are subjected to the high standards of pharmaceutical manufacturing.[31] Students also complete an exercise where they are given a table of mass measurements from a hypothetical batch of tablets, and must determine whether or not an outlier exists (Table 2).

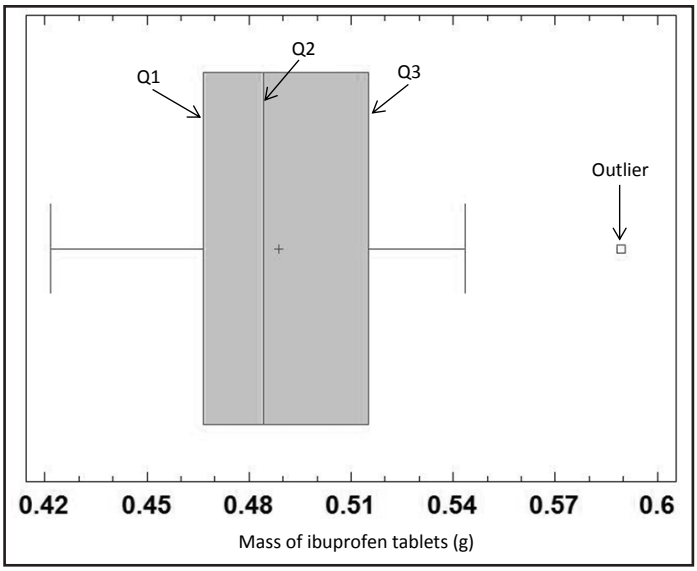


Figure 1. *The box-and-whisker plot for the exercise found in the Tablet Statistical Analysis Lab. The x-axis here is the mass of the ibuprofen tablets in grams. One outlier is clearly visible in this plot.*

Once the data has been sorted from highest to lowest, the students calculate the three quartiles (Q). The first quartile (Q_1) is the median of the lower half of the data, while the third quartile (Q_3) is the median of the higher half of the data. The second quartile (Q_2) is the median of then entire data set. Q_1 and Q_3 are then used to determine the low and high outlier cut-off points (O_L and O_H, respectively). The equations for determining O_L and O_H are shown in Eqs. (4) and (5).

$$O_L = Q_1 - 1.5(Q_3 - Q_1) = 0.4665\,g - 1.5(0.5150\,g - 0.4665\,g) = 0.3938\,g \qquad (4)$$

$$O_H = Q_3 + 1.5(Q_3 - Q_1) = 0.5150\,g + 1.5(0.5150\,g - 0.4665\,g) = 0.5876\,g \qquad (5)$$

A box-and-whisker plot can then be used to show the outliers (Figure 1).

As an introductory experiment, this lab presents important pharmaceutical terminology. Students learn about the different pharmaceutical substances, such as API and the different types of excipients (fillers, binders, glidants, etc.). These technical terms are reinforced through an exercise where students determine the API and look up the first three inactive ingredients or excipients and their functions. In addition, students learn about batch manufacturing processes and receive an introduction to process flow diagrams through a separate exercise. Students are given a manufacturing procedure from the

TABLE 2
Example data from the outlier testing problem in the Tablet Statistical Analysis Lab

Data Provided	Sorted Data (Low → High)	Quartiles
0.4850	0.4217	
0.5198	0.4448	
0.5048	0.4465	Q1 0.4665
0.4857	0.4481	
0.4786	0.4662	
0.5435	0.4668	
0.4448	0.4686	
0.4668	0.4786	Q2 0.4844
0.4465	0.4835	
0.4835	0.4837	
0.4686	0.4850	
0.5211	0.4857	
0.4863	0.4863	Q3 0.5150
0.4217	0.5048	
0.4481	0.5101	
0.4837	0.5198	
0.5895	0.5211	
0.5227	0.5227	
0.4662	0.5435	
0.5101	0.5895	

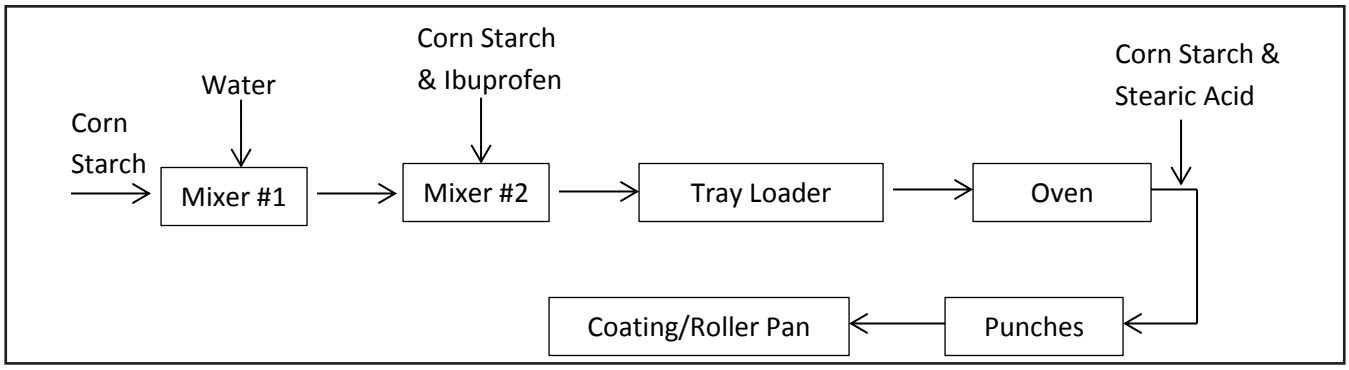


Figure 2. *The solution to the flow diagram exercise found in the Tablet Statistical Analysis Lab.*

Handbook of Pharmaceutical Manufacturing Formulations on how to make coated ibuprofen tablets, read it, and then convert their readings into a flow diagram of this process,[30] shown in Figure 2.

Drug manufacturing

An experiment developed on pharmaceutical processing equipment is the Fluidization of Pharmaceutical Ingredients Lab. This experiment is based on a polymer coating lab for freshmen developed by Rowan engineering faculty.[32] The objective of the lab is to analyze the fluidization of a pharmaceutical ingredient, such as an excipient, and measure basic fluid/particle properties. To do this, students first determine three properties: bulk density, particle density, and bed porosity. This is done through a gravimetric analysis, where the students use a graduated cylinder and water to determine the bulk and particle densities, and then calculate the porosity of the substance using these two parameters. Students then compare the parameter values found experimentally to literature values using particulate databases. The second part of the experiment focuses on fluidization phenomena. The objective of this part is to determine fluidization regimes and the effect of process parameters related to fluidization. The setup of the fluidized bed is shown in Figure 3, in which the excipient is fluidized in air.

Students conduct an experiment to measure the bed height as a function of air flow rate. They notice through this exercise that as bed height starts to increase, fluidization has also started. Pressure drop readings across the column are also taken during this study. Through graphs of these variables, as seen in Figures 4 (page 244), students observe where the slopes of the lines change, denoting transformation from packed bed to fluidized bed behavior. In addition, students receive an exercise in using online reference tools. This exercise asks the students to find an article, through library electronic search tools, that describes the use of fluidized beds in the pharmaceutical manufacture, and discuss it in the next class.

The pharmaceutical objective of this experiment is to show equipment used in transportation, granulation, coating, and drying of solids.[33] Since the fluidized solid particles act like a fluid, they become much easier to transport through conventional conveying equipment. Students also see how excipient properties affect the fluidization process. The students gain this experience through an exercise that has them compare the Reynolds Number at minimum fluidization, Re_{mf}, of two different excipient substances; Avicel® (microcrystalline cellulose powder) and kaolin (white clay powder). The main difference between these two studies is the average particle size (1.4 μm for kaolin and 180 μm for Avicel®), which is the primary reason the Reynolds Number calculations at minimum fluidization are different. The Reynolds Number (Re) calculation gives students experience in units and conversions, requiring them to convert to one system of units and prove that it is dimensionless. Students are also introduced to fluid flow in calculations and conversion of volumetric flow rates

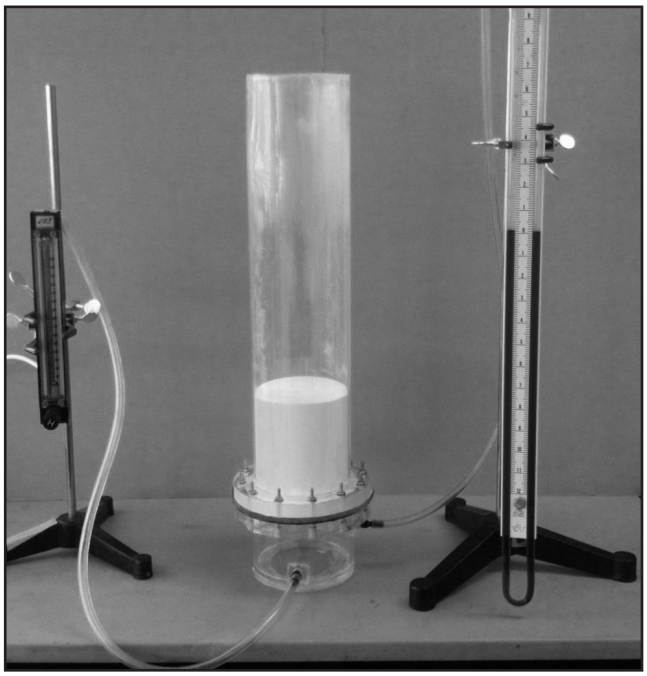


Figure 3. *The fluidized bed apparatus used in the Fluidization of Pharmaceutical Ingredients Lab.*

to a fluid velocity in the bed. Finally, they use a design equation to predict what the Reynolds Number at minimum fluidization (Re_{mf}) should be and compare that to their experimentally determined value. This equation, along with supplemental governing equations, is in Eqs. (6) through (9), and was adapted from Kunil and Levenspiel.[34]

$$Re_{mf} = \sqrt{\left(C_1^2 + C_2 Ar\right)} - C_1 \quad (6)$$

With :
$$Ar = \frac{Dp^3 \rho_g \left(\rho_s - \rho_g\right) g}{\mu^2} \quad (7)$$

$$C_1 = \frac{300\left(1-\varepsilon_{mf}\right)}{7} \quad (8)$$

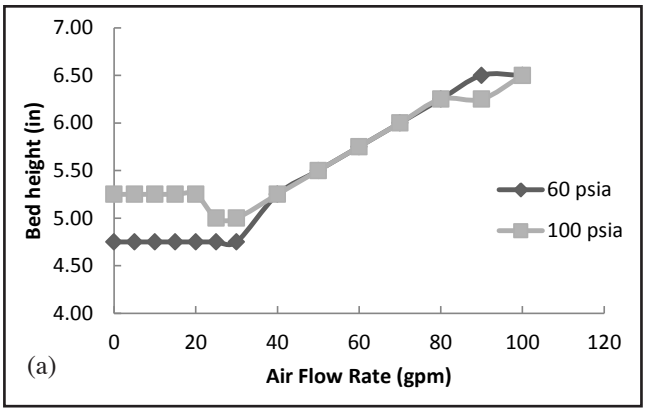
$$C_2 = \frac{\varepsilon_{mf}^3}{1.75} \quad (9)$$

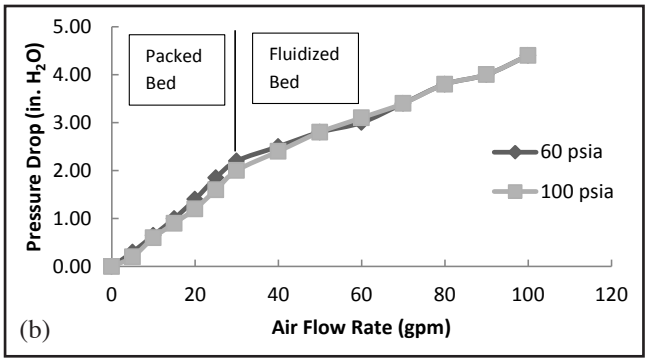
Where ε_{mf} is the void fraction at minimum fluidization; Dp is the diameter of the particle; ρ_g is the density of the fluid; ρ_s is the particle density of the solid; and μ is the viscosity of the fluid. In the Avicel® experiment, the design equation predicted a Reynolds number of 19.36, while experimental data determined a Reynolds number of 19.10, which is within 1.4% difference.

Drug formulation/delivery

One of the drug formulation experiments created focused on the design of a pharmaceutical delivery device. The Asthma Drug Delivery Lab compares three different drug delivery systems for asthma medicines. The first objective of the experiment is to have the students reverse engineer the three systems; a dry powder inhaler, a metered dose "rescue" inhaler, and a nasal spray. Secondly, the students determine the quality control measures of the inhalers and how they deliver a specific dosage each time used.

The dry powder inhaler, an ADVAIR Diskus®, is also known as a diskhaler. The students compare the production design of the Diskus® with a metered dose "rescue" inhaler and a nasal spray through a reverse engineering exercise. Only the ADVAIR Diskus® reverse engineering process is described in this paper, as it was the most technically complex device. First, the students brainstorm the drug delivery mechanism of the diskhaler, using the patient insert as the source of information. Most students will guess that there is some sort of puncture device that allows the medicine to enter the main chamber of the diskhaler, as it is described in the pamphlet as blisters being punctured open. Seeing the inner mechanisms gives the student insight into how the inhaler actually works, using a tearing mechanism to open the blister packets. Since the design utilizes blisters, the device ensures that only a certain amount of the active pharmaceutical substance is released for each use, keeping the rest of the powder fresh inside the individual blisters for subsequent doses. Figure 5 shows a student viewing the inside of the diskhaler, and a schematic is shown as a comparison. This schematic is based on a





Figures 4. *Sample data from the Fluidization of Pharmaceutical Ingredients Lab. a) Air flow rate versus bed height is shown. b) Air flow rate versus pressure drop. Studies used Avicel® PH 200 at 20 °C.*

TABLE 3
Sample data and results from the Asthma Drug Delivery Lab

Trial Number	Mass of Diskhaler Powder(g)	Mass of Metered Dose Inhaler (g)	Mass of Nasal Spray (g)
1	0.0130	0.0130	0.0867
2	0.0130	0.0128	0.0979
3	0.0127	0.0088	0.0989
4	0.0132	0.0107	0.0854
5	0.0126	0.0130	0.1004
6	0.0123	0.0140	0.0983
7	0.0130	0.0140	0.1022
8	0.0129	0.0148	0.1000
9	0.0124	0.0120	0.0991
10	0.0130	0.0121	0.0986
Average	0.0128	0.0125	0.0968
Std. Dev.	$2.81 \cdot 10^{-4}$	$1.66 \cdot 10^{-3}$	$5.48 \cdot 10^{-0}$

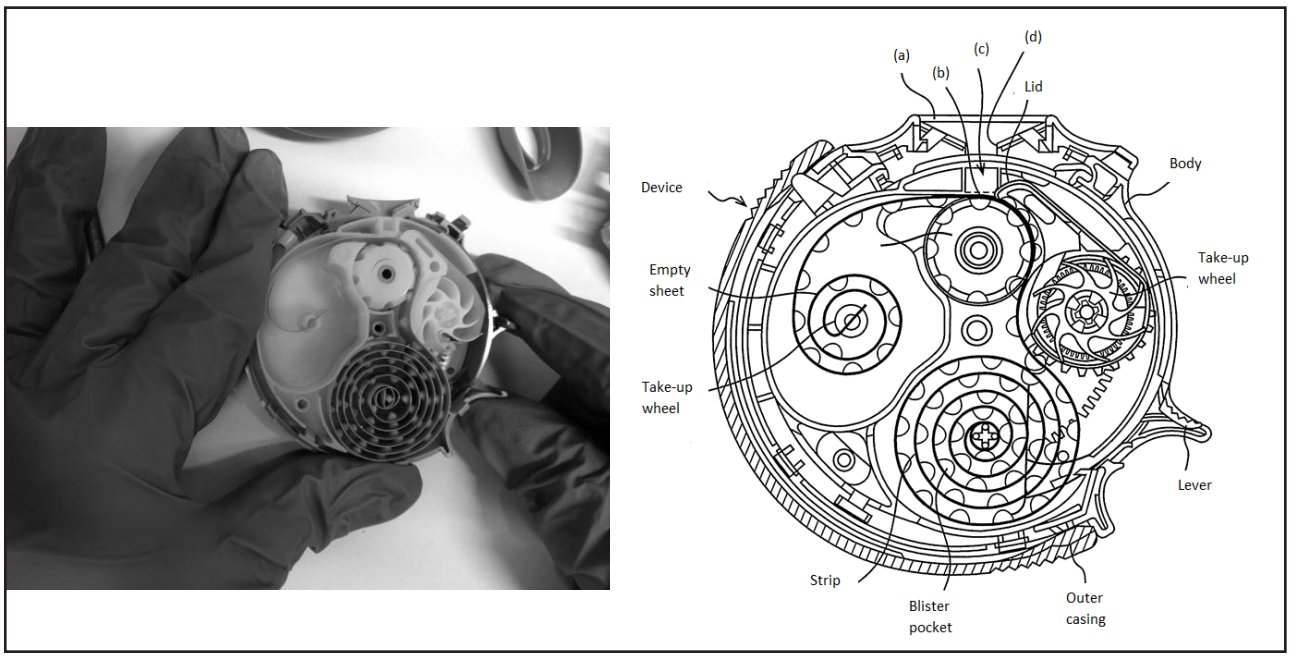


Figure 5. *The inner mechanisms of an ADVAIR Diskus®. On the left is a sample of the student's reverse engineering findings, and on the right is a detailed schematic of a diskhaler from U.S. Patent Application 2009/0314291 A1.[35] Parts a through d are the mouthpiece, opened blister pocket, opening station, and manifold cavity, respectively.*

patent for diskhalers.[35] Students also have to discuss the ergonomics and aesthetics of each of the products, so that they also understand the importance of these two factors on product design in drug delivery.

The second half of this experiment has the students review the quality control aspect of the three devices by taking mass measurements of the doses being delivered and calculating the mean and standard deviation (Table 3). For more information on how these mass measurements were collected, refer to the Asthma Drug Delivery Lab posted on PharmaHUB. From this data, the students compare the standard deviations, and what that implies about the function of the devices. Students observe that the diskhaler has the lowest standard deviation of the three devices, which is due to the design of the device. Similar results are not obtained with the metered dose inhaler and the nasal spray because the metered dose inhaler involves a fluid that easily evaporates and the precision of the nasal spray depends on how well the apparatus is primed. These product designs enter into the discussion of why the standard deviations for those two designs have an order of magnitude difference from that of the diskhaler. Students are also tasked with looking up typical standard deviations for therapeutic dosage delivery.

Another experiment regarding drug formulation and delivery is the Dissolvable Strip Lab. In this experiment, students are tasked with investigating the dissolution rate of ingredients in dissolvable strips. Strip films have become an area of interest in the past few years as an alternative to conventional tablets and capsules, especially for patients suffering from dysphagia.[36] Some examples of consumer products formulated into orally administered strips include breath fresheners, energy supplements, and analgesics for flu and sinus symptoms.[37] In this lab, students work with Sheets™ brand energy strips, containing caffeine and blue food dye. Blue food dye in the product is used to model the release of a pharmaceutical ingredient. The students are to investigate the effect of temperature on the dissolution

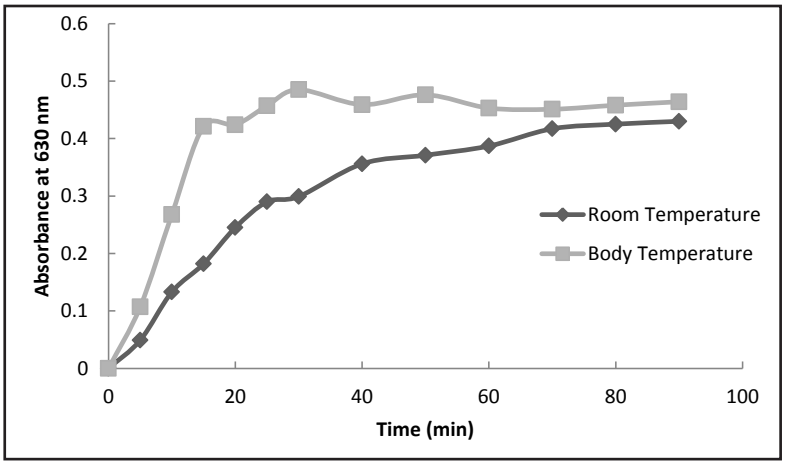


Figure 6. *Sample data from the Dissolvable Strip Lab, using one strip film for each.*

These experiments illustrate basic engineering and science principles, while acquainting students with fundamentals of pharmaceutical engineering.

rate by placing one strip in water kept at room temperature (~ 22 °C), and placing another in water at body temperature (~ 37 °C). To simulate the mouth, a shallow petri dish is filled with 25 mL of water, in which a strip is placed; absorbance measurements are taken at regular intervals, generating graphs as seen in Figure 6. The absorbance values are related to the concentration of the ingredients released by using a standardization curved developed at the beginning of the experiment.

The experiment introduces the students to spectrophotometry, and the principles related to the methodology used to measure solution concentration. This is done by having the students apply the Beer-Lambert law to determine the molar absorptivity coefficient of the blue food dye at both temperatures, as calculated in Eq. (10). For the Beer-Lambert Law, students use data from their experiment at a time of 80 minutes, which corresponds to when the absorbance readings should reach steady state.

$$\varepsilon_{22} = \frac{A}{\ell c} = \frac{0.425}{(1\text{cm})\left(3.03\cdot10^{-7}\text{M}\right)} = 1.40\cdot10^{-6}\,\text{M}^{-1}\text{cm}^{-1} \quad (10)$$

Where A is the absorbance (dimensionless), ℓ is the measurement cell width, and c is the molar concentration of the sample. The students should notice that the coefficients are identical between the two cases (ε_{22} and ε_{37} are $1.40 \cdot 10^{-6}$ M^{-1} cm^{-1}), which determines that for the ranges used in this experiment, the temperature does not significantly affect the molar absorptivity coefficient. The students are then charged with determining how the Beer-Lambert law and molar absorptivity coefficients can be applied in other engineering applications. Some of the common answers will be wastewater treatment, product synthesis, and algae growth.

The pharmaceutical relevance of this experiment is that students are introduced to a novel drug delivery system. The students also see how the strip film quickly dissolves in water, indicating that the polymer used in the strips breaks down when it comes in contact with water. The concept of higher temperatures affecting the dissolution rate of the strip is also reinforced through an example involving rate laws. In this example, the students use absorbance readings and determine the rate law coefficient, k, for both experimental conditions. Upon calculating, the students see that the rate coefficient is higher for the body temperature experimental run than the room temperature study.

Some additional parts of this experiment have been developed based on advanced instrumentation and the available time. If a broader range spectrophotometer is available, absorbance data can be taken for caffeine at a wavelength of 273 nm. An agitated system can also be used to examine the convective effects on dissolution rate of the strip.

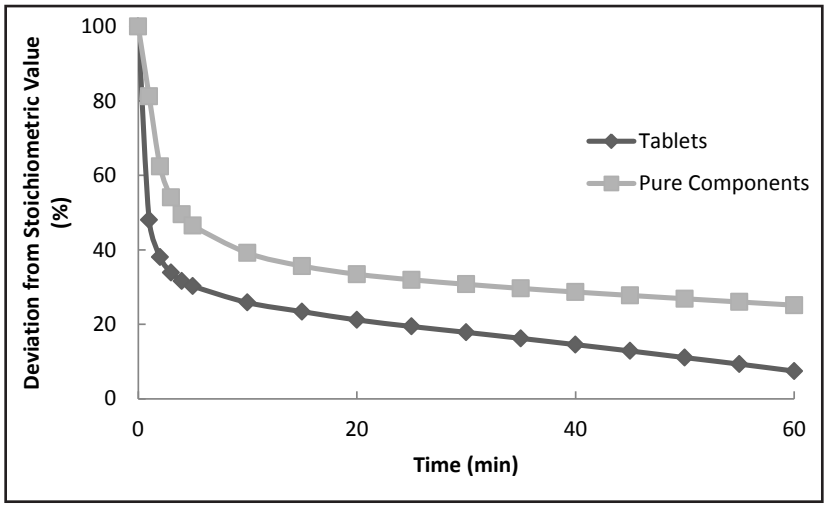


Figure 7. *Alka-Seltzer® Effervescence Reaction laboratory experiment comparing a whole tablet and the individual raw ingredients showing the deviation between actual and stoichiometric values of the effervescence reaction.*

Pharmacokinetics/pharmacodynamics

An experiment developed on pharmacokinetics/pharmacodynamics uses Alka-Seltzer® to investigate the reaction mechanism behind an effervescent reaction. Students evaluate the reaction the tablet has when it comes in contact with water. This experiment, the Effervescence Reaction Lab, evaluates the effect of tablet manufacturing process on the rate of reaction. Students compare the effervescent reaction of a whole tablet of Alka-Seltzer® to the raw ingredients of an Alka-Seltzer® tablet that have been individually obtained. Both the tablet and raw ingredients are allowed to react with water separately, while students take residual mass measurements as time progresses. Students must determine why the whole tablet reacts faster. The students are provided information on

the production process which includes the milling step for the tablet's ingredients, which is the process used to reduce the particle size.[38] Therefore, with greater surface area and a more uniform composition, the reaction proceeds faster than the unmilled raw materials.

By having students measure the amount of mass that left the system, they determine the amount of carbon dioxide (CO_2) gas produced via the effervescence reaction. Using stoichiometry, the students also determine the amount of CO_2 they should have theoretically generated during the reaction. The stoichiometric equation is shown in Eq. (11).

$$C_6H_8O_7(aq) + 3NaHCO_3(aq) \rightarrow 3H_2O(l) + 3CO_2(g) + Na_3C_6H_5O_7(aq) \qquad (11)$$

Using these two values, the students determine the percent difference between their theoretical and experimentally observed values, as shown in Figure 7. They see that the longer the reaction continues the difference between theoretical values and experimental values starts to decrease. By having students determine the percent difference, they learn that theory does not always predict what actually happens in practice.

CONCLUSIONS

Our initial assessment efforts show that the experiments convey both desired pharmaceutical concepts and core engineering objectives. We have done preliminary assessment of the laboratory experiments and have underway assessment of our broader pharmaceutical engineering educational activities. We are presenting some of the results relevant to the experiments developed. Other results from our course development, problem sets, and laboratory activities are planned for a separate paper. Representative results using the Tablet Statistical Analysis Lab are provided, which involved three student groups. The students were individually given a pre-lab test to measure their knowledge of several pharmaceutical and statistical aspects that were covered in the laboratory experiment. Multiple-choice questions included several pharmaceutical concepts such as definition of an API and function of excipients, along with questions about appropriate use of F- and t-tests. A representative question about excipients would be "The substance used in a tablet to take up space in a pharmaceutical product is..." and a representative question about the F-test would be: "The purpose of an F-test is to ...". The correct answer to the excipient question and the F-test question is "filler" and "to compare two sets of data to one another," respectively. After the experiment was completed, a post-lab test was performed and the average of the correct responses of the students is shown in Figure 8. This indicates that the students have a better understanding of pharmaceutical concepts and the purpose of statistical tests after conducting the experiment.

Students were given additional questions on the post-lab test to determine if the experiment helped to advance the broader educational objectives of increasing pharmaceutical interest and experimental methods. The survey asked the students to agree or disagree with a statement about their experience with the laboratory using a Likert scale (1 being a strong disagreement and 5 being a strong agreement with the statement). The statements used in the survey relate to the student's interest in pharmaceutical engineering (I wish to pursue more studies in the field of pharmaceutical engineering), the pharmaceutical aspect of the laboratory (The experiment introduced

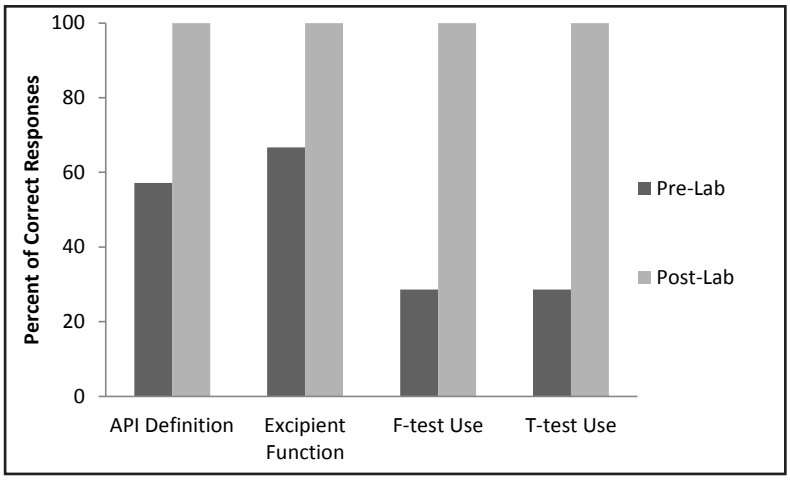


Figure 8. *Pre-lab and post-lab concept test results for the assessment of the Tablet Statistical Analysis Lab.*

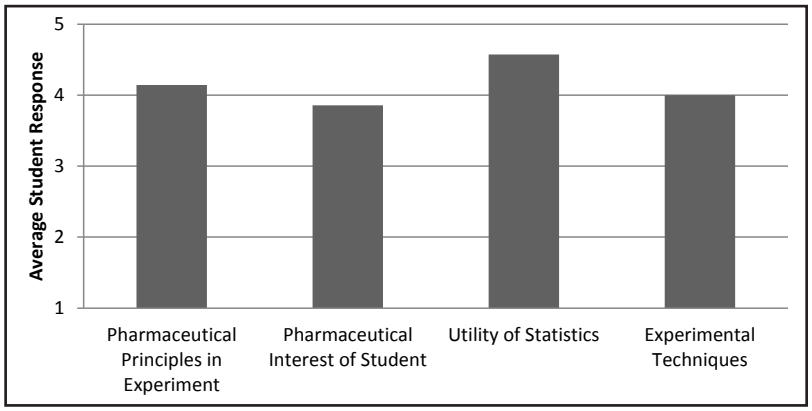


Figure 9. *Post-lab student survey results from the Tablet Statistical Analysis Lab.*

Complete laboratory procedures, both student and instructor versions, are available through the pharmaceutical knowledge and training website, <www.PharmaHUB.org>.

a concept of pharmaceutical engineering), the utility of the statistical tests (I can apply the statistical principles I learned in this lab to other engineering problems), and the educational objectives of the experiment (I had to appropriately use laboratory equipment [scales, etc.] for data collection). The average responses showed that most students gave a response of 4 for all categories of statements (Figure 9). We have also solicited input from current employers about the industrial relevance of the experiments. Representative feedback from one of our pharmaceutical professionals indicates, "These experiments are valuable in exposing engineering students to principles of pharmaceutical engineering."

The experiments developed can be easily integrated into Freshman-level engineering courses. These experiments illustrate basic engineering and science principles, while acquainting students with fundamentals of pharmaceutical engineering. The experiments convey concepts in pharmaceutical fundamentals, drug manufacture, drug formulation/delivery, and pharmacokinetics/pharmacodynamics. Experiments developed to date include: Tablet Statistical Analysis Lab; Asthma Drug Delivery Lab; Antacid Comparison Lab; Effervescence Reaction Lab; Fluidization of Pharmaceutical Substances Lab; Degradation of Dissolvable Strips Lab; Bandage Comparison Lab; and Creation of Dissolvable Strips Lab. The experiments can be used individually to meet specific educational objectives, such as applying statistical methods to manufacturing quality control, or grouped into a theme for more in-depth learning. The experiments have multiple parts that allow faculty to add more complexity or accomplish other learning objectives. These experiments can pique student interest in pharmaceutical engineering and provide background needed for advanced courses or laboratories. Complete laboratory procedures, both student and instructor versions, are available through the pharmaceutical knowledge and training website, <www.PharmaHUB.org>.

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REFERENCES

1. United States Census Bureau, 2010 Earnings by Industry, Washington: United States Census Bureau, 2010
2. Cacciotti, J., and P. Clinton, "The Lull Between Two Storms," *Pharmaceutical Executive*, **31**(5), 3 (2011)
3. Report Linker, "US Pharmaceutical Industry Report, 2008-2009," Research in China, April 2009. [Online]. Available: <http://www.reportlinker.com/p0118600-summary/US-Pharmaceutical-Industry-Report.html> [Accessed 28 Aug. 2013]
4. Rosenzweig, M., "Where Are Chemical Engineers Headed," *Chem. Processing Magazine*, **47**(8), 22, 5 Aug. 2004
5. Bureau of Labor Statistics, "Biomedical Engineers," in Occupational Outlook Handbook, 2012- 2013 Edition, Washington, DC, U.S. Department of Labor, 2013
6. Bureau of Labor Statistics, "Chemical Engineers," in Occupational Outlook Handbook, 2012- 2013 Edition, Washington, DC, U.S. Department of Labor, 2013
7. Berman, J.M., "Industry Output and Employment Projections to 2014," *Monthly Labor Review*, pp. 45-69, November 2005
8. Rosas, C., "Process Development," in *Active Pharmaceutical Ingredients: Development, Manufacturing, and Regulation*, New York, Taylor and Francis, 2005, pp. 9-90.
9. Rutgers University, "PhD in Chemical and Biochemical Engineering with an Option in Pharmaceutical Engineering," Rutgers University Department of Pharmaceutical Engineering, [Online]. Available: <http://pharmeng.rutgers.edu/acadPhd.html>. [Accessed 24 July 2013]
10. Stevens Institute of Technology, "Pharmaceutical Manufacturing," Stevens Institute of Technology, 2014. [Online]. Available: <http://www.stevens.edu/ses/me/pharmaceutical-manufacturing> [Accessed April 24, 2014]
11. Purdue University, "GAANN Fellowship in Pharmaceutical Engineering," Purdue University, 2014. [Online]. Available: <https://engineering.purdue.edu/ChE/GAANNpharma/main.html> [Accessed 19 Feb. 2014]
12. Kuriyan, K., A.C. Catlin, and G.V. Reklaitis, "PharmaHUB: Building a Virtual Organization for Pharmaceutical Engineering and Science," *J. Pharmaceutical Innovation*, **4**(2), 81 (2009)
13. Leuenberger, H., N. Menshutina, G. Betz, and M.N. Puchkov, "E-Learning and Development of New Courses and Scientific Work in the Field of Pharmaceutical Technology," *Chimia*, **60**, 80-82 (2006)
14. Byrne, E., "The Role of Specialization in the Chemical Engineering Curriculum," *Education for Chemical Engineers*, **1**, 3-15 (2006)
15. The University of Iowa, "Chemical Engineering - Pharmaceuticals (Major Org)," August 2012. [Online]. Available: <https://www.engineering.uiowa.edu/sites/default/files/cbe/CBE%20Pharmaceuticals%20Maj%20Org%20Seq%202012-08.pdf> [Accessed 19 Feb. 2014]
16. Stevens Institute of Technology, "Areas of Concentration," Department of Mechanical Engineering, 2014. [Online]. Available: <http://www.stevens.edu/ses/me/undergrad/concentrations> [Accessed 24 April 2014]
17. Simon, L., K. Kanneganti, and K.S. Kim, "Drug Transport and Pharmacokinetics for Chemical Engineers," *Chem. Eng. Ed.*, **44**(4), 262 (2010)
18. Prausnitz, M.R., and A.S. Bommarius, "Drug Design, Development, and Delivery: An Interdisciplinary Course on Pharmaceuticals," *Chem. Eng. Ed.*, 45(1), 47 (2011)
19. Glasser, B.J., J. Cole, and F.J. Muzzio, "A Comprehensive Approach to Pharmaceutical Engineering Training," *Pharmaceutical Technology*, **25**(12), 34 (2001)
20. McIver, K., K. Whitaker, V. Dedelva, S. Farrell, M.J. Savelski, and C.S. Slater, "Introductory Level Problems Illustrating Concepts in

Pharmaceutical Engineering," *Advances in Engineering Education*, **3**(1), 1 (2012)
21. Savelski, M.J., C.S. Slater, C.A. Del Vecchio, A.J. Kosteleski, and S.A. Wilson, "Development of Problem Sets for K-12 and Engineering on Pharmaceutical Particulate Systems," *Chem. Eng. Ed.*, **44**(1), 50 (2010)
22. Farrell, S., and R.P. Hesketh, "An Introduction to Drug Delivery for Chemical Engineers," *Chem. Eng. Ed.*, **36**(3), 198 (2002)
23. Accreditation Board for Engineering and Technology, "Criteria for Accrediting Engineering Programs," 27 Oct. 2013. [Online]. Available: <http://www.abet.org/uploadedFiles/Accreditation/Accreditation_Step_by_Step/Accreditation_Documents/Current/2013_-_2014/eac-criteria-2013-2014.pdf> [Accessed 24 Jan. 2014]
24. Farrell, S., M. Savelski, and C. ,S. Slater, "Integrating Pharmaceutical Concepts into Introductory Chemical Engineering Courses - Part I," PhamaHUB.org, 2010. [Online]. Available: <https://pharmahub.org/resources/360> [Accessed 1 May 2014]
25. Farrell, S., M. Savelski, and C.S. Slater, "Integrating Pharmaceutical Concepts into Introductory Chemical Engineering Courses - Part II," PharmaHUB.org, 2010. [Online]. Available: <https://pharmahub.org/resources/389> [Accessed 1 May 2014]
26. Blau, G., "Statistical Model Building and Design of Experiments," PharmaHUB.org, 05 May 2008. [Online]. Available: <https://pharmahub.org/resources/145> [Accessed 24 April 2014]
27. Glaser, B., and H. Pedersen, "Bulk Pharmaceutical Production," PharmaHUB, 2009. [Online]. Available: <https://pharmahub.org/resources/286> [Accessed 1 May 2014]
28. National Science Foundation, "Mathematics & Statistics (QLP Module 6)," The National Science Foundation Database Administration, 2012. [Online]. Available: <http://nsf- dba.com/courses/387/mathematics-statistics-for-the-pharmaceutical-industry> [Accessed 30 Aug. 2013]
29. Montgomery, D.C., G.C. Runger, and N.F. Hubele, *Engineering Statistics*, Hoboken: John Wiley and Sons, Inc. (2011)
30. Niazi, S., "Ibuprofen Tablets," in *Handbook of Pharmaceutical Manufacturing Formulations; Compressed Solid Products*, New York, Informa Healthcare USA, 2009, pp. 317-319
31. The United States Food and Drug Administration, "Code of Federal Regulations: Title 21, Volume 4, Part 211, Subpart F," Office of the Federal Register National Archives and Records Administration, Washington, 2013
32. Hesketh, R.P., C.S. Slater, S. Farrell, and M. Carney, "Fluidized Bed Polymer Coating Experiment," *Chem. Eng. Ed.*, **36**(2), 138 (2002)
33. Davies, W., and W.J. Gloor, "Batch Production of Pharmaceutical Granulatices in a Fluidized Bed I: Effects of Process Variables on Physical Properties of Final Granulation," *J. Pharm. Sciences*, **60**(12), 1869 (1971)
34. Kunil, D., and O. Levenspiel, *Fluidization Engineering*, Boston: Butterworth Heinemann (1993)
35. Anderson, G.J.M., M.B. Davies, M.A. Hailey, M.G. Palmer, and R.I. Walker, "Medicament Dispenser". Unites States of America Patent 2009/0314291 A1, 24 December 2009
36. Mandeep, K., A. Rana, and S. Nimrata, "Fast Dissolving Films: An Innovative Drug Delivery System," *Int. J. Pharm. Research and Allied Sciences*, **2**(1), 14 (2013)
37. Particle Sciences Drug Development Services, *Dissolving Films: A Technical Brief*, vol. 3, Bethlehem: Particle Sciences Drug Development Services (2010)
38. Phykitt, H., "Analgesic Composition and Method of Making the Same," United States of America Patent 8,580,853, 13 June 2011 ❒