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Interactive Pedagogical Tools to Integrate Pharmaceutical Applications in the Chemical Engineering Curriculum: News from the ASEE 2012 Summer School

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abstract

The pharmaceutical industry plays a key role in today's global economy and chemical engineers can make strong contributions to the industry. In addition, pharmaceutical process and product applications provide an excellent vehicle to introduce students to novel technologies and experimental design and data analysis techniques. This work focuses on the development and implementation of interactive modular experiments, demonstrations and calculations to engage students and introduce them to the chemical engineering aspects of the pharmaceutical industry. This work includes particle and powder processing and drug delivery experiments and demonstrations, pharmaceutical engineering problem sets and life cycle analysis applications. Through these experiments, demonstrations and interactive analysis experiences, students are introduced to pharmaceutical applications, experimental design and Quality by Design (QbD) methodologies in ways that engage and enhance learning. This work is the basis for a workshop presented at the 2012 ASEE – Chemical Engineering Division (CHED) Summer School. The interactive and self-contained workshop modules are highlighted. These modules can be easily integrated into the traditional undergraduate chemical engineering curriculum through laboratories/demonstrations. This project is part of the educational/outreach activities of the NSF-ERC on Structured Organic Particulate Systems.

introduction

Over the past several years, X University faculty members have been engaged as Educational Outreach Partners with the NSF-sponsored ERC on Structured Organic Particulate Systems hosted by Rutgers University (with member schools: New Jersey Institute of Technology, Purdue University and University of Puerto Rico-Mayaguez). The goal of this educational partnership has been to develop and disseminate undergraduate materials related to pharmaceutical technology and to seek ways to integrate this into the undergraduate engineering curriculum.[1-3] Pilot testing at X University, including the use of some of the materials in the Freshman Chemical Engineering course at the State University of New York-Stony Brook,[4] has yielded positive assessment results. This work has resulted in the development of classroom problems, laboratory experiments and demonstrations that can be used throughout the undergraduate engineering curriculum and for K-12 outreach. The results have been disseminated through ASEE conference papers, and some of the problem sets described in this paper will be used in the next edition of Felder et al. [5]

Current efforts include expanding the dissemination of this material through the ASEE Chemical Engineering Division (CHED) Summer School. This will help extend the reach of these materials to an audience of educators early in their careers who will be able to directly impact the students they teach. The 2012 ASEE-CHED Summer School was held at the University of Maine in Orono, Maine, July 21- 27. The Summer School included over 20 workshops and many opportunities for faculty to network and share ideas. Participants could attend workshops of their choice fitting their professional and teaching interests. The workshop described in this work was attended by 30 participants and the workshop slides and references were disseminated to all 150 Summer School attendees.

Particulate systems can be found in more than 90% of chemical and pharmaceutical processes.[5] Integration of laboratory experiments and demonstrations that include particulate systems is an excellent way to integrate particle technology into the traditional engineering curriculum and familiarize students with this important technology and the pharmaceutical industry. The pharmaceutical industry employs one in eight chemical engineers, second only to the chemical process industry. The expanding role of chemical engineering in pharmaceutical production demands the inclusion of pharma-related concepts in chemical engineering courses throughout the curriculum. Successful curriculum improvement requires a new approach to integrating concepts of batch processing, solid-liquid separation techniques, solid-solid particulate processing, drug formulation and delivery, and technology at the nano-scale. Students must have a solid grasp of chemical engineering fundamentals and the perspective necessary to work successfully side-by-side with pharmacists, pharmacologists, medicinal chemists, and materials chemists in this highly multidisciplinary field.

The field of pharmaceutical engineering is quite broad and involves the manufacture of the active pharmaceutical ingredients (API) and drugs in the final dosage form as well as their therapeutic delivery. The interface of pharmaceutical science and chemical engineering is crucial for understanding the basis of structured organic particulate systems (SOPS), a term that describes the multi-component organic system that comprises a drug, nutraceutical, and any medicinal formulation.

The workshop modules highlighted here can be used as part of traditional engineering courses, in specialty topics courses and in K-12 outreach efforts. The workshop introduced 2012 ASEE-CHED Summer School participants to the essential concepts of pharmaceutical engineering in a way that they can easily integrate into the undergraduate curricula at their home institutions. Interactive exercises where workshop participants learn new concepts and are engaged to explore ways to improve the courses they teach were an essential component of the workshop. The team-based interactive approach practiced at X University was used to integrate concepts of new technologies into the traditional undergraduate chemical engineering curriculum through laboratories/demonstrations, in-class/homework problems, and case studies. This approach has been shown to significantly enhance student learning and interest in technology. It is also essential for outreach efforts to increase interest in and preparation for engineering studies among K-12 students.[6]

workshop modules

Each module in the workshop is self-contained and can be adapted for use in traditional undergraduate chemical engineering courses and K-12 outreach efforts. The modules include interactive team-based activities that workshop participants can adapt and integrate into courses at their home institutions.

Primer on Pharmaceutical Engineering

A short introductory primer introduced workshop participants to important concepts of pharmaceutical engineering. The lecture started with some basic "facts and figures" on the industry. Financial data such as worldwide sales, top selling drugs, and leading companies were presented. This was followed by a discussion of the drug development timeline, focusing on the success rate of new drug entities as they progress from discovery, through clinical trials, to final release to the public. An overview of the steps in drug production and use was presented: active pharmaceutical ingredient (API) synthesis, drug formulation, and drug delivery. Manufacturing issues related to batch processing, multiphase drug systems, green engineering, and processing scale were included (Figure 1). This lecture was posted on the ASEE ChE Division web site (www.asse-ched.org/) as well as PharmaHUB (www.PharmaHUB.org).[7]

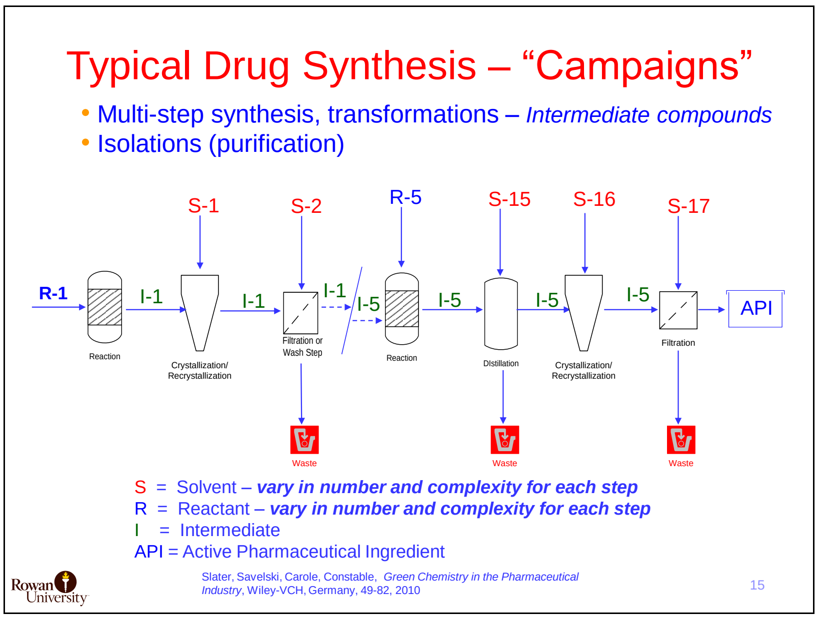


Figure 1. Representative slide illustrating an API synthesis "campaign."

Introducing Pharmaceutical Technology through Educational Materials for Undergraduate Engineering Courses

This workshop module consisted of an interactive presentation integrated with example problems and demonstrations. There were two major parts to this module: illustrative problem sets for lower-division chemical engineering courses focusing on topics from drug formulation to production; and life cycle methodology to evaluate API manufacture. The educational materials convey essential concepts in pharmaceutical terminology, drug delivery, and manufacturing within the context of a material and energy balance calculation. Problems introduce a pharmaceutical "term of art," manufacturing process, or widely used drug or consumer product. For example, one problem explores the role of active pharmaceutical ingredients (API) and excipients (binders, filler, lubricants) in the formulation of drugs through unit conversions and mass/mole/volume composition problems. Other problems are made to convey course objectives in areas such as health, safety, and ethics. The problem (Figure 2) on diethylene glycol poisoning is particularly interesting since it is based on the actual 1930's case of a company distributing a "drug" without proper testing. By using this problem, students learn about drug safety issues within the context of a unit conversion problem. The problem shows how the Food and Drug Administration became the primary regulatory body for the pharmaceutical industry.

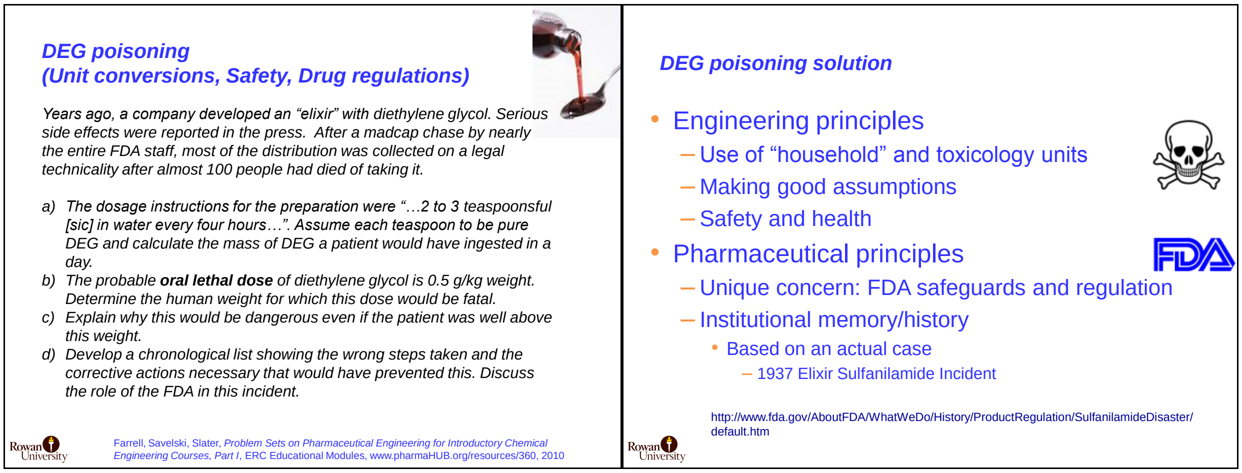


Figure 2. Diethylene glycol poisoning of an "elixir" problem summary

This module of the workshop also included problems in green engineering in pharmaceutical synthesis. A good example of one of these is a problem that requires students to evaluate the "greenness" of two routes to synthesize ibuprofen, the active ingredient in many pain relief medicines. The problem summarized in Figure 3, introduces students to the concept of multi-step syntheses and atom economy. The problem was developed based on an EPA Presidential Green Chemistry Challenge Award. Through solving a problem, students learn how to apply green metrics and why reducing the number of steps in a synthesis route usually results in a greener process.

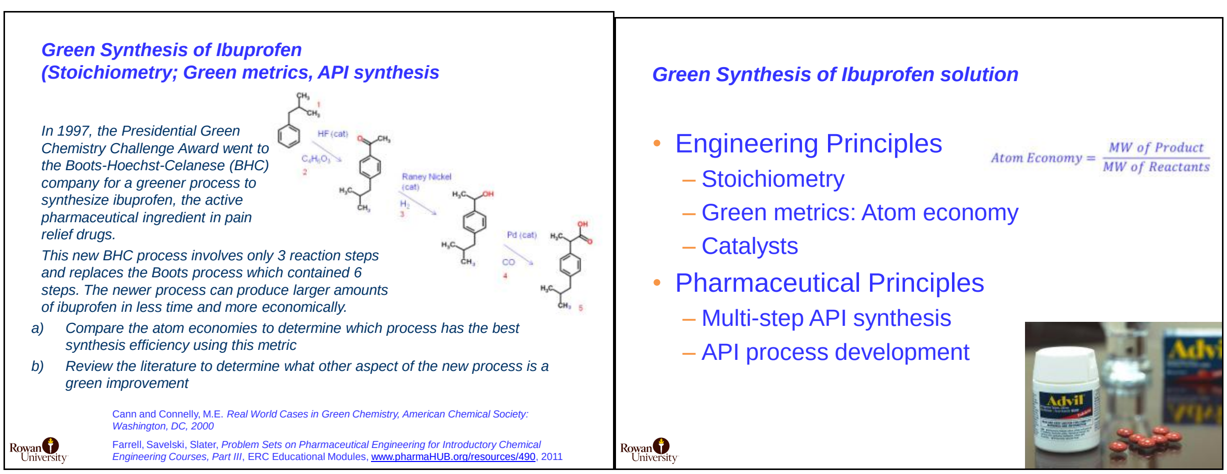


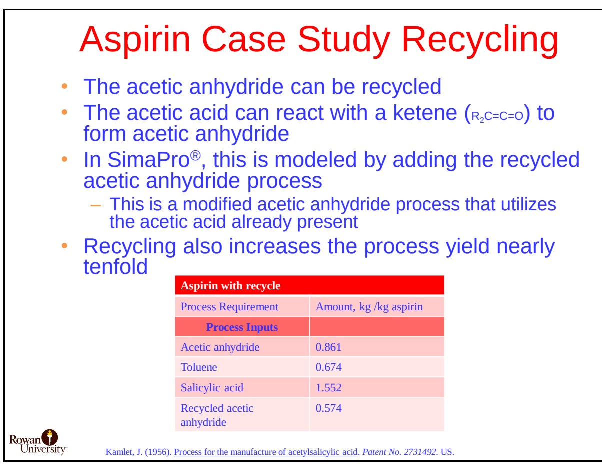
Figure 3. Green engineering problem on the synthesis of ibuprofen

Some of the problems developed as part of this work will be included in the new edition of Felder et al.[5] Supplemental supporting materials widely used for information on manufacturing formulations are referenced in each problem set.[8] A full set of indexed problems was provided to the workshop participants on a CD and the presentation is available on the ASEE ChE Division web site (www.asse-ched.org/) and PharmaHUB (www.PharmaHUB.org).[7]

This module included a presentation on the X University teaching philosophy; which is to integrate new technologies or technical areas into lecture/laboratory activities of existing courses instead of adding additional courses to the curriculum. Through this mechanism, students learn new concepts while achieving the same course learning objectives. For example, in a material and energy course lecture on mass balances on single unit processes, an example of a solids blender can be used where API is blended with excipients to achieve a final formulation for tableting. Students will be introduced to the terminology of drug formulation and unique processing equipment, while achieving the overall educational objective of the lecture.

The second part of the Educational Materials workshop introduced participants to the concept of life cycle assessment and showed how to integrate it into their courses. This module included an overview of life cycle assessment, demonstration on the use of environmental assessment software, SimaPro®, and its process modeling applications. The materials from the module provided workshop participants with the essential elements of life cycle assessment for introductory courses and for processes modeling using software methods for upper-level courses.

One of the case studies provided to workshop participants compares two different processes to manufacture acetylsalicylic acid, the API in aspirin. The case study illustrates how to define the boundaries of the system and calculate the life cycle inventory data for all raw materials, waste, and energy flows in the processes. The life cycle analysis shows how changes made in manufacturing, e.g., recycling byproducts, can lead to environmental impacts well beyond the production plant and define the true carbon footprint of a manufacturing operation (Figure 4). Other examples related to pharmaceutical, food, and consumer products are included in the presentation available on PharmaHUB.[7]



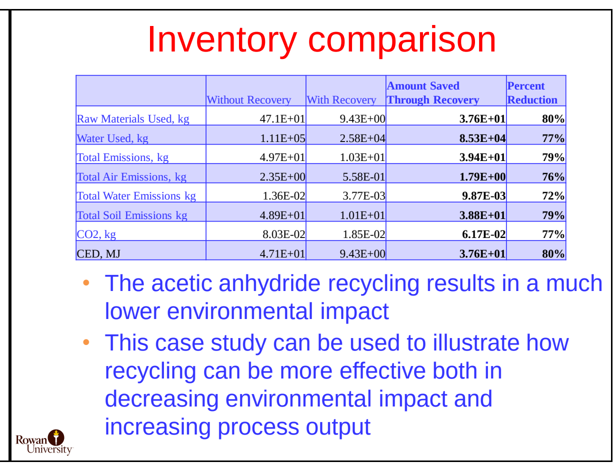


Figure 4. Use of an aspirin case study showing life cycle emissions reductions resulting from byproduct recycling.

PharmaHUB Tutorial

The final part of the workshop was a short presentation on how to use PharmaHUB (www.PharmaHUB.org), which is a resource for supplemental pharmaceutical course material. PharmaHUB is a research, education, and training web site, hosted by Purdue University. The site provides access to materials developed by other universities, especially members of the ERC-SOPS. The workshop lecture showed the attendees the content available on PharmaHUB, through using actual screen images and example materials (Figure 5).

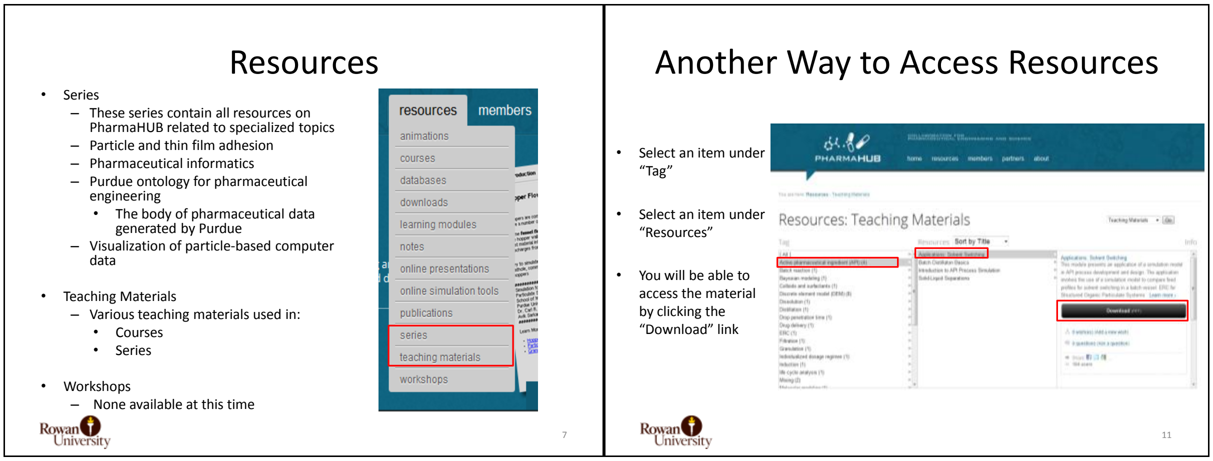


Figure 5 . Illustration of how to access teaching resources on the PharmaHUB web site.

Most of the teaching resource materials provided on PharmaHUB are in a format that can be easily utilized in courses, such as PowerPoint presentations. There are also databases on properties of pharmaceutical raw materials, animations of particle processing, and journal publications. The PharmaHUB Tutorial reviewed examples of materials that could be used for various courses in the chemical engineering curriculum, from introductory courses to senior design. For example, if a faculty member teaching a design course wanted to incorporate a lecture on process development and scale-up, the Pharmaceutical Bulk Drug Production PowerPoint lecture slides (B. Glaser, Rutgers University, 2009) can be used.[9]

particle properties and V-mixing technology

Workshop participants were introduced to several particle technology laboratory experiments and demonstrations. Parts and equipment lists including approximate costs and vendors were made available to workshop participants. Figures 6a and b are workshop presentation slides. Figure 6a shows a two-dimensional hopper demonstration and Figure 6b shows arching in hopper flow.

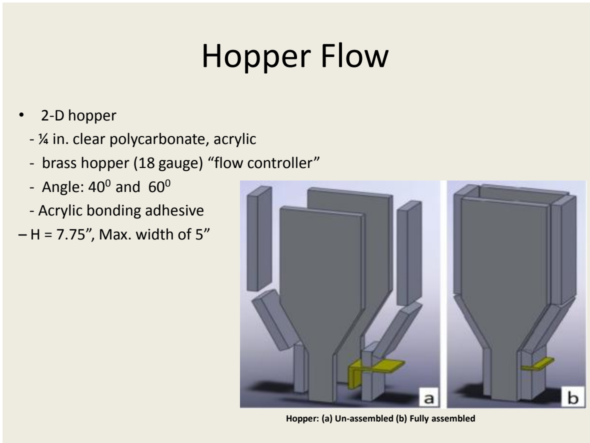


Figure 6a: Hopper flow

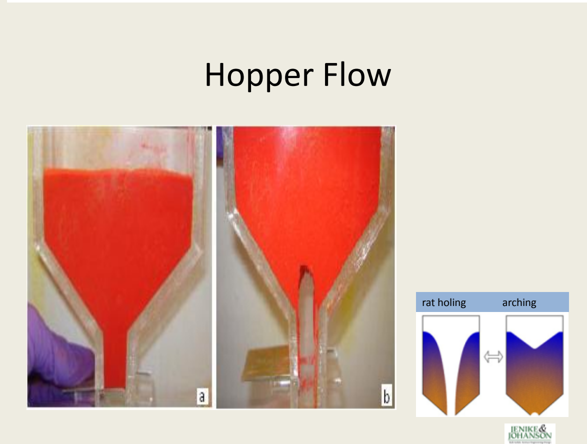


Figure 6b: Arching in hopper flow

Arching is an important problem that limits flow in particulate systems. Workshop participants were introduced to empirical hopper factors and a discussion of how to use this demonstration in first year introductory engineering courses followed. Techniques for introducing estimation in flow problems and arching predictions, and to familiarize students with dimensional analysis and empirical formulations were discussed.

A particle segregation demonstration was also presented at the Workshop. Figure 7 is the slide showing the tumbler particle mixer. Particle mixing characteristics and segregation among particles of different sizes and shapes were discussed. A parts list and construction instruction were made available to workshop participants.

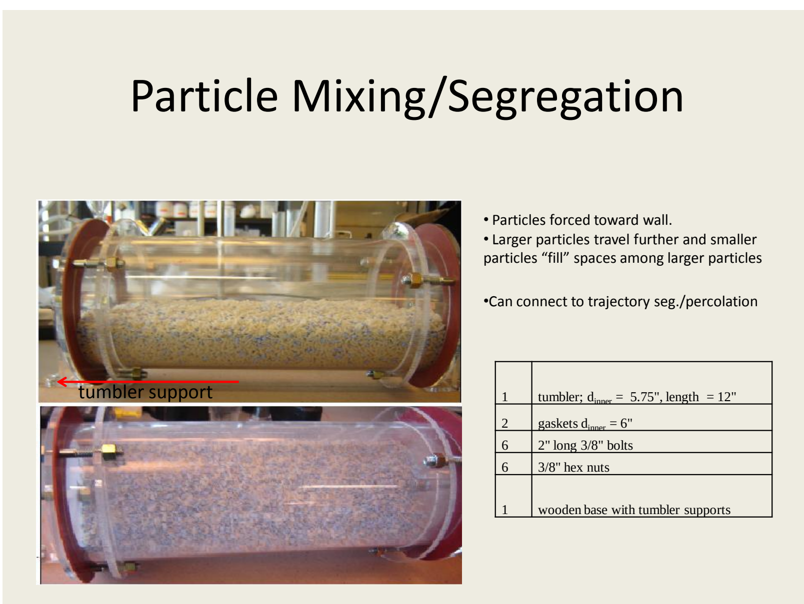


Figure 7: Particle mixing/segregation demonstration

Figures 8 a and b show a bench scale pneumatic transport demonstration and a parts list for the equipment. Workshop participants had an opportunity to discuss the equipment, different adaptations and potential experiments in pneumatic transport. All of these demonstrations are relatively simple to build and are a cost-effective means to integrate interactive learning modules into courses. They are flexible in that they can be used for a range of courses and technical expertise and are adaptable for a variety of experiments.

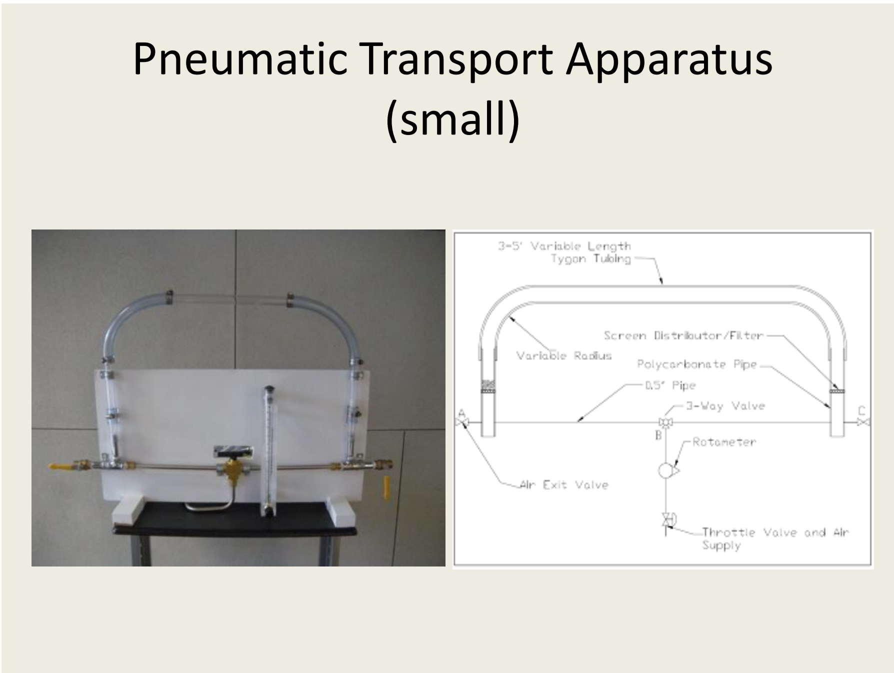


Figure 8a: Bench scale pneumatic transport demonstration

Pneumatic Transport Apparatus Parts List (small)

Part Inventory - Pneumatic Transport Apparatus - SMALL			
ITEM	QTY.	Specification	Purpose/Description
1	6'	1" ID	Tygon Tubing - Thick walled
2	2'	1" OD	Polycarbonate Round tube Clear
3	2	1/2"	Threaded
4	4	1/2" X 3"	Threaded Nipples
5	1	0 - 40 SCFM	Flow meter
6	1	1/2"	Brass Ball Valve
7	6'	1/2" ID	Braided Hose Air Feed
8	1	1/2" Tube	Diverting 3 Port brass ball valve Yor Lock Fittings, Ultra High Pressure
9	5	1/2"	Brass Compression Fitting Adapter for 1/2" Tube
10	1	1/2"	Bronze Globe Valve 1" NPT Female Connections

Figure 8b: Bench scale pneumatic transport demonstration parts list

V-mixing

This module started with a discussion on the background of V-mixers and V-mixing technology. Figure 9a is the slide showing the V-mixer used for the presentation and the laboratory experiment. Figure 9b shows the construction of the V-mixer. Detailed construction instructions and a parts list for the V-mixer were provided to each workshop participant. The V-mixers are operated by a pneumatic motor (Figure 9b) that allows for variable speeds. A compressor providing air at 100 psi was used for the experiment.

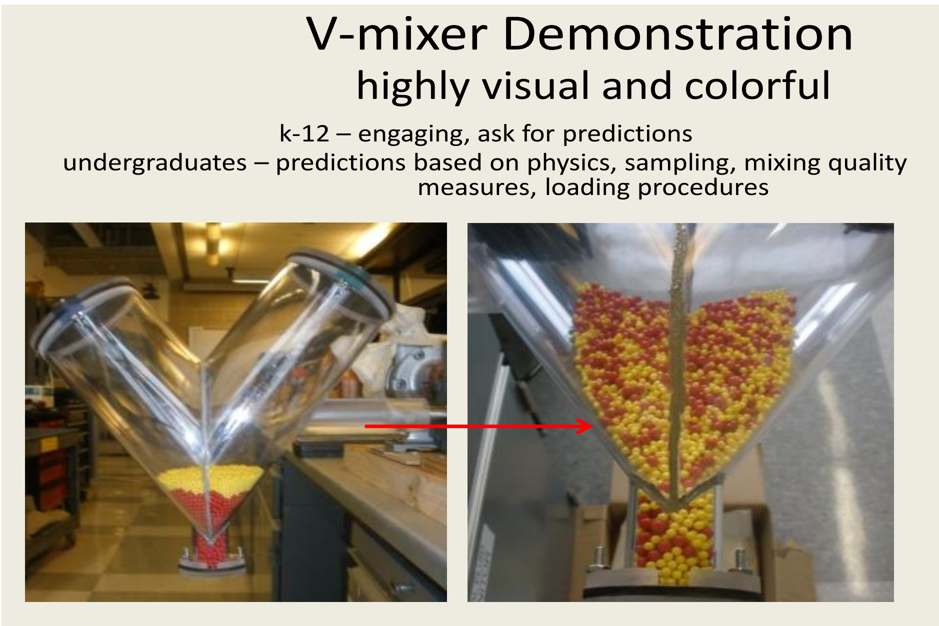


Figure 9a: V-mixer

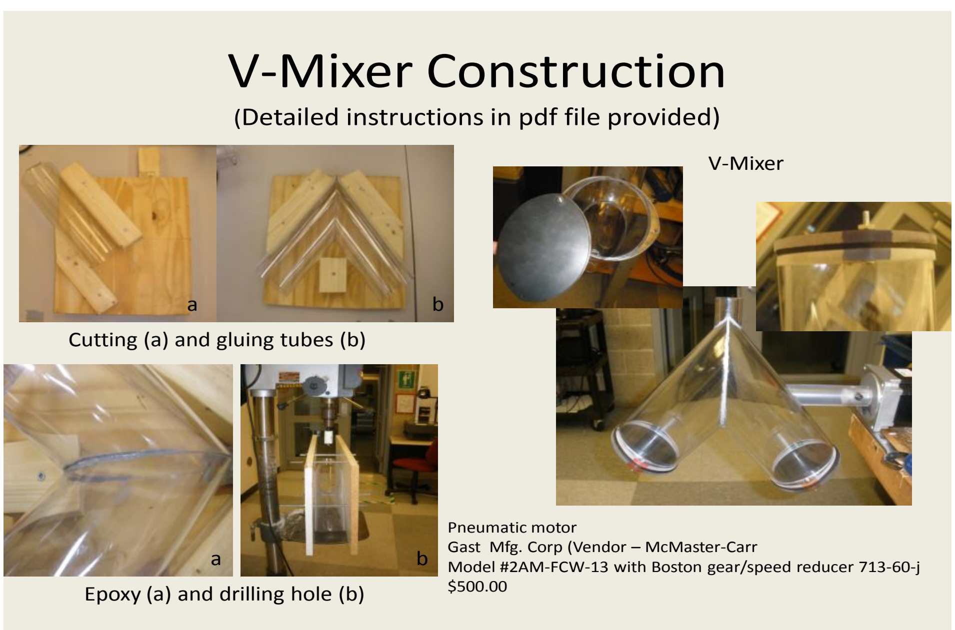


Figure 9b: V-mixer construction

Following the discussion on V-mixer fundamentals and types of mixing in tumbler mixers, experiments involving the use of conductivity and colorimetry to measure mixing quality were described. These experiments were conducted as part of undergraduate research projects at X University. Workshop participants then formed groups by selecting numbers from a container. This provided an opportunity for interaction and a break in the workshop. Each group was assigned a V-mixer and an experimental condition from an experimental design. Figure 10 shows workshop participants during the V-mixer laboratory experiment. Two variables were investigated in the experiment: particle size and initial particle location in mixer (top or bottom). Figure 11 is the slide showing the 2^2 factorial experimental design.

Figure 10: V-mixing experiment - ASEE-CHED division summer school workshop participants

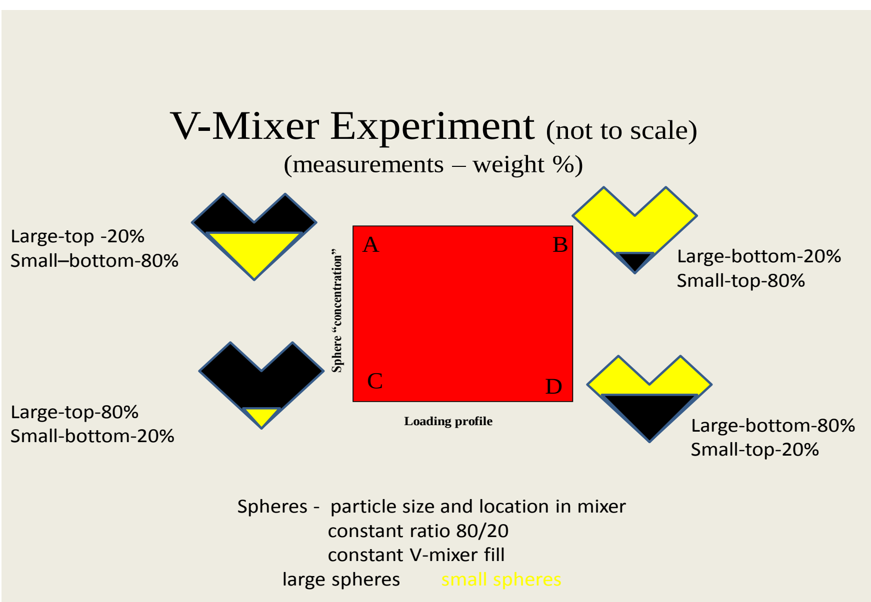


Figure 11: V-mixer experimental design

Each group ran one experimental condition and all workshop participants compared their results. This module included an introduction to experimental designs[10-12] and factorial experimental design tables were provided. Workshop participants could use the factorial designs and design tables provided for any suitable application for any course at their home institutions.

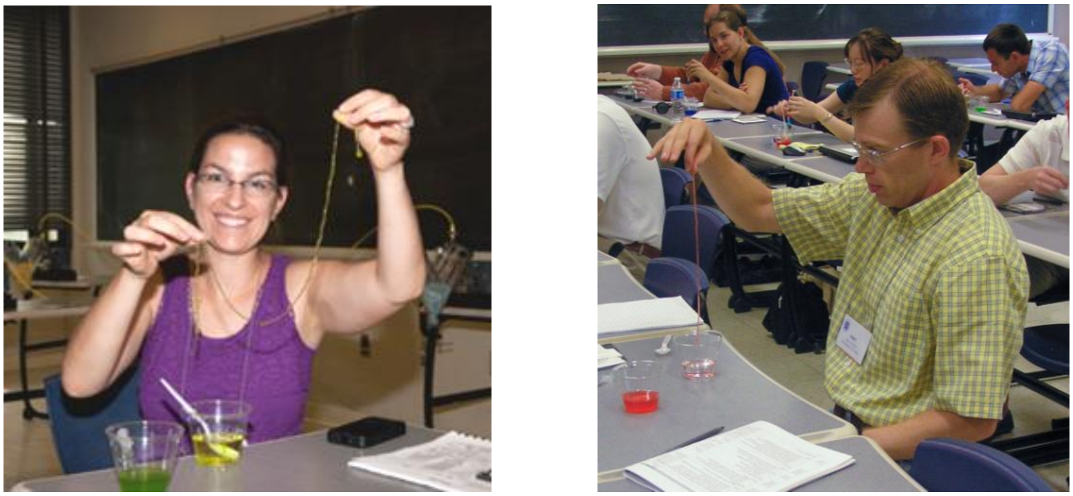
Workshop participants had detailed information on how to design and construct particle property demonstrations and a V-mixer. They were familiar with laboratory experiments and demonstrations illustrating particle properties and V-mixing technology, and had the tools to implement them. Participants could integrate these laboratory experiments and demonstrations in the undergraduate engineering curriculum. In addition, they could apply factorial experimental design principles for V-mixing and other laboratory experiments in any course or application.

drug delivery in the chemical engineering curriculum

This workshop module introduced chemical engineering faculty to drug delivery topics that can be woven into disciplinary core courses. The module included a discussion on the importance of drug delivery technology to the pharmaceutical industry. Drug delivery is a burgeoning field that represents a major growth driver of the pharmaceutical industry today: the global drug delivery technology segment has grown from $15 billion in 2000 to $50 billion in 2008, representing an average compound annual growth rate of 18% in comparison with 10% for the overall pharmaceutical market.[13] Chemical engineers play an important and expanding role in this exciting and inherently multidisciplinary field, which combines knowledge from medicine, pharmaceutical sciences, chemistry and engineering.

Controlled drug delivery systems are engineered to deliver a drug to the body at a predetermined rate for an extended time. Controlled release systems have expanded from traditional drugs to therapeutic peptides, vaccines, hormones, and viral vectors for gene therapy. These systems employ a variety of rate-controlling mechanisms, including matrix diffusion, membrane diffusion, biodegradation and osmosis.[14] Drug delivery system design requires a full understanding of drug and material properties, mass transfer mechanisms, and the processing variables that affect the release of the drug from the system.

Through a hands-on demonstration based on a previously published experiment,[15] workshop participants used a simple and cost-effective experiment to introduce drug delivery system design, formulation and analysis from an engineering viewpoint. This experiment can be adapted for use in freshman or upper level chemical engineering courses. In the experiment, students produce calcium alginate beads loaded with drug and measure the rate of release from the beads for systems having different stir rates, geometries, extents of cross-linking, and drug molecular weight. Transient concentration data are then analyzed to characterize the release profile and rate and to determine the predominant rate controlling mechanism. The purpose of the experiment is to provide engineering students with basic skills relevant to drug delivery while simultaneously introducing or reinforcing concepts related to core science and engineering principles and engineering design. Figures 12a and b show workshop participants during the calcium alginate synthesis experiment.



(a) (b)

Figures 12 a and b: Hands-on drug delivery system experiment

Summary

Self-contained modular educational materials and laboratory demonstrations designed to integrate pharmaceutical engineering in the undergraduate engineering curriculum were developed and presented as a workshop at the 2012 American Society for Engineering Education- Chemical Engineering Division (CHED) Summer School. A tutorial on pharmaceutical engineering with introductory course material supported by example problems and demonstrations was presented. Pharmaceutical engineering problem sets including over 50 examples for a material and energy balance course mapped to individual course topics were made available to workshop participants. Particle properties laboratory experiments and demonstrations were developed and presented. Detailed design and construction instructions along with examples of integration into existing engineering courses were provided to workshop participants. V-mixing fundamentals, including different quality of mixing measures, and a hands-on experiment were presented. Detailed design and construction instructions for a bench scale V-mixer were provided to workshop participants. A hands-on V-mixing laboratory experiment including an introduction and implementation of factorial experimental designs was included in the module. A simple drug delivery demonstration was combined with illustrative example problems to give workshop participants a strong foundation of the engineering aspects of drug delivery. Participants were fully engaged in the workshop through team-based, interactive and hands-on activities, demonstrations and experiments.

The 2012 ASEE-CHED Summer School workshop described here provided educator participants with the tools and conceptual foundation to integrate particle/powder technology with a focus on the pharmaceutical industry into chemical engineering courses and outreach efforts at their home institutions. The integration of technology modules into traditional engineering courses is an excellent way to familiarize students with important industries and technologies without adding courses to the engineering curriculum.

Acknowledgements

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