TEACHERS' TOPICS

A Laboratory Exercise in Capsule Making

Krista D. Capehart, PharmD

School of Pharmacy, University of Charleston

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Objective. To create and implement a compounding laboratory exercise utilizing a variety of techniques and equipment.

Design. A 3-hour laboratory exercise on preparing compound prescriptions for capsules was developed and taught to first-year doctor of pharmacy (PharmD) students. Students completed appropriate preparations and calculation of ingredients and prepared capsules using a hand-packing technique and a capsule-filling machine. The students then individually weighed the capsules and performed batch testing for uniformity.

Assessment. Ninety-six percent of the students who completed the laboratory performed the necessary calculations for machine-prepared capsules correctly and 100% completed the calculations for the hand-filled capsules correctly. With the hand-filled capsules, 100% of the students processed all 4 units within $\pm 5\%$ of the stated capsule weight and capsules were deemed successful and accurate.

Conclusion. Students acquired a firm grasp of basic compounding techniques and the skills to prepare accurate, safe, and uniform dosage forms for patients.

Keywords: compounding, pharmaceuticals laboratory, dosage form, curriculum, capsules

INTRODUCTION

With the mass-manufacturing of drugs rising over the last century, the art of pharmacy compounding became secondary in the realm of pharmacy practice. However, with the movement toward “pharmaceutical care” or “patient-centered care” and the increase in home health care, compounding remains a relevant technique for pharmacy students to learn. New pharmacy graduates must be prepared to address individualized patient care in a variety of ways, including team-based management of patient health, development of patient-centered care plans, and the preparation and dispensing of medications as a result of the care plan. According to the 2004 Center for the Advancement of Pharmaceutical Education (CAPE) Educational Outcomes and the Supplemental Educational Outcomes based on CAPE for Pharmacy Practice, pharmacists should be able to “accurately compound individual or bulk medications,” including locating formulations, evaluating the stability and suitability of formulations, and using “good compounding practices in the extemporaneous production of a patient-specific delivery system.”^{1,2} Additionally, the North American Pharmacist

Licensure Examination (NAPLEX) continues to place emphasis on compounding in pharmacy practice with the inclusion of 5 of 37 competency statements (or about 11% of all competency statements) on the topic.^{3,4} Even though compounding has seemingly taken a backseat, with as little as a 1 semester course in many doctor of pharmacy curricula devoted to learning the skills required for safe compounding, the necessity of learning and retaining the skills remains.

While pharmacists are no longer expected to prepare or compound every dosage form for every patient, they still utilize their compounding skills in many practice settings. The findings of a survey evaluating the variety of services offered in community pharmacies, including chains, independents, supermarkets, and mass merchandisers, demonstrated that compounding is still offered.⁵ Nearly 88% of pharmacies surveyed provided “general/simple compounding” and 14% provided “specialty/complex compounding.”⁵ Also, a survey of independent community pharmacies in 4 states determined that 94% provided some level of compounding services to their patients. The percentage of compounded prescriptions among all pharmacies was less than 1% of the total prescription volume, while it was 2.3% among the pharmacies that did provide compounding services.⁶ Some estimate the percentage of compounded prescriptions to be as high as 11%.⁷ As new pharmacy graduates take their place in the pharmacy workforce, these pharmacists must

Corresponding Author: Krista Capehart, PharmD, AE-C, Assistant Professor of Pharmacy Practice, School of Pharmacy, University of Charleston, Charleston, WV, 25304. Tel: 304-375-4385. Fax: 304-357-4868. E-mail: kristacapehart@ucwv.edu

be capable and competent to provide the necessary compounding services to the patients who require them, even if only occasionally.

Because compounding retains a presence in some realms of pharmacy practice, patient safety, preparation efficacy, and accuracy of compounded medications must become the primary concern of compounding courses. Retention of compounding skills taught in pharmacy curricula has been examined and is a concern. One study found that 89% of the students achieved a grade of 80% or more on the capsule-making exercise, while only 17% of the students completing the same exercise a year later were able to achieve the same 80% competency score.⁸ Pharmacy college/schools must address compounding techniques and retention of those techniques by students.

As technology advances in all areas, pharmacy compounding is not excluded. Compounding pharmacists have a multitude of equipment available today that was not available 2 to 3 decades ago, and is still not available in many practice settings. Today, pharmacists have ointment mills, electronic balances, and capsule machines to help augment the skill of spatulation, replace the prescription torsion balance, and provide an alternative to the hand packing of capsules. Practice settings that regularly prepare capsules often purchase capsule-filling machines. These machines typically make anywhere from 100 to 300 capsules at a time. While this is an important skill, there are instances, such as those requiring only a small number of capsules, when the machine is impractical and the pharmacist needs to hand pack the capsules. Therefore, it was important that students learn the skills for hand packing capsules, as well as using a capsule machine, and how to ensure content uniformity and weight in both.

With minimal curricular time devoted to compounding, the time should be utilized to its optimum potential. The *Pharmaceutics II Laboratory* in the first-professional year at the University of Charleston School of Pharmacy covers the legal, practical, and scientific basis of drug preparations and pharmaceutical delivery systems. Within the course, students learn to utilize references in the practice of pharmacy, develop skills and knowledge necessary to interpret compound prescription orders, select appropriate pharmaceutical active and inactive ingredients to prepare an effective dosage form incorporating physicochemical theories of preparation and incompatibilities, and interpret and analyze the legal and ethical implications of compounding specialized dosage forms. This paper addresses the laboratory designed to teach the compounding of capsules, 1 of 11 laboratories developed for the first-year students in the *Pharmaceutics II Laboratory*. At the conclusion of this laboratory exercise, students should be able to: (1) explain the safe and legal use of

color in compounded preparations, especially capsule making; (2) apply techniques for selecting appropriate capsule size for a preparation; (3) demonstrate hand filling of capsules and the use of a capsule-filling machine in making capsules; and (4) demonstrate the ability to check capsule batches for accuracy and uniformity.

DESIGN

The *Pharmaceutics II Laboratory* (PHAR 523L), a 1-credit-hour laboratory required in the first-professional year of the doctor of pharmacy (PharmD) program, met for 3 hours per week during the spring 2007 semester. The capsule laboratory consisted of 2 separate sections: hand packing of capsules and the use of a capsule machine to prepare a batch of capsules to fill a prescription. This laboratory incorporated learning several techniques to enable the student to perform capsule preparation, regardless of the available equipment.

In laboratory sessions prior to the capsule laboratory, students attended lectures where *United States Pharmacopeia (USP)* Chapter 1075, "Good Compounding Practices," and Chapter 795, "Pharmaceutical Compounding – Nonsterile Preparations," were covered.^{9,10} Students discussed the difference between compounding and manufacturing and the importance of standard operating procedures; compounding equipment; selection of dosage form components, including various grades of pharmaceutical components; packaging containers; control procedures; labeling; records; reports; beyond-use dating; and assessing for strength, quality, and purity.^{9,10} Additionally, students were provided with a prelaboratory worksheet that focused on much of the terminology and guidelines utilized in the preparation of compounded capsules. These prelaboratory assignments served to ensure that the students came into the laboratory with a baseline of information regarding the dosage form to be prepared that day.

The students were provided with a prescription to prepare "calcium carbonate 550mg, lactose qs, Mft caps #4, sig: i po bid." The laboratory instructions then took the students through each step of the capsule-making process. The students had to consult a capsule capacity table and select the most appropriate capsule size to use to complete the compounded prescription. The "rule of sixes" and "rule of sevens" capsule selection techniques were explained to the class, but were not applied in this laboratory.¹¹ However, the "best" capsule size was not available to the students. Instead, they were given size 00. This required the students to utilize the capsule capacity table to determine the approximate quantity of lactose, NF needed to utilize the size 00 capsules to prepare the calcium carbonate 550 mg dosage form needed. Students

performed capsule calculations to account for material lost in the blending process and each ingredient was weighed out. Students utilized powdered color to visualize the blending process and the homogeneity of the active ingredient and lactose filler. The standard method of trituration for blending calcium carbonate and lactose with a mortar and pestle was not utilized. Instead, the powders were tumbled in a polyethylene zipper-sealed bag. The powder was then blocked, a process of using a stainless steel spatula to gather the powder together and compress it into a flat surface to make it easier to fill the capsules. The students were taught to individually pack the capsules by punching the capsule end and weighing each capsule to ensure it was appropriately filled. A compounding record of the preparation was completed. For quality control, students calculated the average weight of each capsule, percent error based on the average final capsule weight and the expected capsule weight, and labeled them for dispensing.

Many pharmacies that regularly compound capsules invest in capsule-filling machines. This equipment is expensive and not feasible for a laboratory class of 40 students. Therefore, an alternative had to be devised. A product was located on an herbal supplement web site called The Capsule Machine (Capsule Connection, Prescott, Arizona). It allows the user to make 24 size 00 capsules at a time. The Capsule Machine was reasonably priced at around \$13, so each of the 40 laboratory stations was able to have a machine and each student could independently compound the capsules to fill the prescription that was presented to them. For this section, students were given a prescription for “aspirin 280mg, lactose qs, Mft caps #24, sig: i po q6h prn.” Students were provided with aspirin 325 mg tablets, lactose, NF, powdered color, and clear 00 capsules. Utilizing a capsule capacity table, a weight was determined for the capsules and calculations were performed for each active and inactive ingredient utilized to make the 280 mg aspirin capsules. Unlike the hand-packed capsule section in which bulk powder was used as the active ingredient, this section required the student to use commercially available aspirin tablets and perform calculations to account for excipients added in the manufacturing process. The tablets were triturated using a glass mortar and pestle. The tablet powder and lactose were weighed and geometric dilution and color were used to visualize that the active ingredients were distributed evenly throughout the powder mixture. The Capsule Machine was used to make the 24 capsules to fill the prescription. The capsules were ejected from the machine, cleaned, tumbled, and the compounding record filled out for the 280 mg aspirin capsules. Because quality control is essential to pharmacy compounding, the stu-

dents utilized a technique presented in *A Practical Guide to Contemporary Pharmacy Practice*, which is a variation on the *USP* Chapter 905, “Uniformity of Dosage Units.”^{12,13} Ten capsules were selected from the lot of 24 made in the laboratory. Each individual capsule was weighed and the “active ingredient expressed as a percentage of the labeled claim” was calculated. The standard deviation and relative standard deviation for each student’s capsules was determined and then the standards for uniformity of dosage forms criteria were applied to assess whether or not each student’s batch of capsules passed the criteria.¹² Because The Capsule Machine could only make 24 capsules per batch, the students were only able to complete the first 2 tests for uniformity of dosage form units. An alternative to this method of quality control would be to follow the description of quality control measures in the *USP*, Chapter 795, which specifies that when weighing for compounded capsules, powders, lozenges, and tablets, the compounding must “ensure that each unit shall be not less than 90% and not more than 110% of the theoretically calculated weight for each unit.”¹⁰ While this was not done in this laboratory session, this quality control measure is much more precise and would be an appropriate alternative to the method previously described.

Students were assessed on compounding technique, calculation for each of the 2 prescriptions filled, and uniformity and accuracy of the capsules prepared to fill each prescription. Compounding technique was assessed subjectively, based on the instructor’s observations throughout the laboratory and visual inspection of the final dosage forms. Calculations for the preparations were evaluated for accuracy and completeness and final capsule preparations were weighed for quality control (Figure 1). To pass the calculations section of each preparation, the calculations had to be exactly correct.

ASSESSMENT

Ninety-six percent of the students who completed the laboratory performed the calculations for machine-prepared capsules correctly and 100% completed the calculations for the hand-filled capsules correctly. With the hand-filled capsules, 100% of the students had all 4 units within $\pm 5\%$ of the stated capsule weight and capsules were deemed successful and accurate. With The Capsule Machine, approximately 10% of the students’ capsule batches failed to fulfill the criteria for the standards for uniformity of dosage forms from *USP*, Chapter 905. One student layered the lactose, pulverized aspirin, and color in The Capsule Machine. The student had to remove powder from the capsules, blend them, and then refill the capsules using The Capsule Machine. Those whose

Figure 1. Comparison of number of students to successfully complete assigned tasks for capsule-making laboratory.

batches failed to fulfill the criteria had to critique their own technique and determine the changes necessary to improve their skills. Overall, 73 of the 79 students (92%) received a grade higher than 90% for the laboratory exercises.

In their evaluation of the course, including of this laboratory, students responded positively to the course material and techniques presented. Ninety percent of the students agreed or strongly agreed that their understanding of the relationships between concepts was enhanced. Ninety-eight percent agreed or strongly agreed that the materials and activities were relevant to the course objectives.

DISCUSSION

Medication errors are a concern in all healthcare settings and much attention has been focused on the compounding arena as a source of problems. The Food and Drug Administration (FDA) has issued statements regarding the safety of compounding through articles in *Compounding Pharmacy News*, creating regulations, and issuing Significant Compliance Actions.¹⁴ The intention of this laboratory was to provide an opportunity for students to experience several techniques and processes for compounding capsules so that they were better prepared to use whatever equipment they are given in whatever conditions they face in practice. It is also important that students are comfortable with various compounding techniques and realize that the technique that seems easier is not always the best or most efficient method of preparation. With this understanding and the opportunity to prepare capsules in a variety of ways, the author feels the students can better address the concerns and issues that they may confront in practice.

Utilizing the capsule capacity table to determine the most appropriate capsule size proved to be a valuable task. The students were able to apply the information presented to them in the lecture and in readings. Students were confronted with a realistic situation when they were told that the “most appropriate” capsule size was not available and that they would have to improvise with what was on hand. Compounding, like other areas of pharmacy practice, is unique in that more than one technique can be used to create a drug-delivery device that is appropriate for the patient.

Bulk powder and a manufactured product were both used as the source for the active ingredient in this laboratory exercise. Both sources of materials, each used in a different compound, exposed the students to the differences in calculations between bulk powder and manufactured tablets, in which the excipients had to be taken into account. This proved to be a challenging task for several students, but they were able to understand the concept and apply the same principles to other dosage form preparations in other laboratory exercises during the course.

The use of color as a tracer for the active ingredient in the capsule/drug preparation enabled the students to visualize the blending of the powders and was helpful in illustrating the time and work necessary to adequately mix the powders for uniformity. While there are 4 techniques—spatulation, trituration, sifting, and tumbling—generally accepted for the blending of powders, this laboratory exercise utilized tumbling and trituration.¹⁵ Prior to the exercise, students generally predicted that tumbling the mixture in a zipper-closed polyethylene bag would be much easier than using a mortar and pestle for trituration. However, after dealing with static electricity caused by the bags, different powder characteristics, and powder loss in the corner of the bags, the students generally agreed that using the mortar and pestle was easier. A discussion was held to compare and contrast the 2 methods of blending and how powder characteristics affect the distribution of powders. For the second prescription that utilized the manufactured aspirin tablets, students were required to use the mortar and pestle for trituration and The Capsule Machine to prepare the 24 capsules. Overall, by experiencing 2 blending techniques in the same laboratory the students gained a better understanding of the pros and cons of each method.

Hand packing capsules has been a standard practice of pharmacists for decades. The typical community pharmacist may not make capsules frequently, but a firm grasp of the skill and calculations needed is necessary. Student discussion on the hand packing of capsules focused on the ideas that “nobody does this anymore” and “why learn

this when we have machines to make them?” The students were required to hand fill 4 capsules to fill the prescription, weighing at each step to ensure that the weight was appropriate. While this was a tedious process and the students were easily frustrated at the “hassle” and eager to use the machines, they completed the task and gained a greater appreciation for the technique.

Using The Capsule Machine was something that the students thought was going to be easy and eagerly anticipated while completing the hand-packing exercise. Critically, The Capsule Machine functioned based on the same principles as the larger-volume capsule-filling machines. The students generally felt using the machine was easier than hand filling the capsules, but several students’ capsules did not get locked or were crushed due to too much pressure in the machine.

While it took much less time for most students to compound the 24 machine-filled capsules than the 4 hand-filled capsules, students’ opinion of the process was slightly altered when the *USP* test for uniformity of dosage units was applied. The students calculated the “active ingredient expressed as a percentage of label claim,” evaluated the results, and came to realize that, even if an individual batch of capsules passed the test for uniformity, they may not be comfortable dispensing capsules with individual dosage units that were made using The Capsule Machine. Students whose batches did not meet *USP* specifications proposed reasons for the problems with their batches and shared them with the other students. The most common problem discussed was that students “dumped” the blended powder in the center of The Capsule Machine and failed to adequately distribute the powders to all capsules within the filling machine. Students shared that they were surprised that The Capsule Machine was not more exact. By preparing capsules using both methods, the students were shown that the compounder must know how to utilize the machine properly or the product will be inadequate for patient use. Many of the same students who expressed frustration over hand filling capsules were more than eager to declare later that they would feel more comfortable always hand filling capsules because the product would be more reliable. During the discussion about the laboratory exercise, students realized that either technique could be precise and accurate if the appropriate skills are developed and one knows the limitations and potential downsides of the chosen technique.

The capsule laboratory presented many alternative techniques to preparing capsule dosage forms and working with powders. Because The Capsule Machine only created 24 capsules, the students were limited by not being able to completely assess the capsules for uniformity

of dosage units. Still, the opportunity to learn about and perform the techniques for bulk preparation versus hand filling was beneficial. By having the students first complete all of the techniques in one laboratory session and then use individual techniques in other dosage forms, they were able to learn the intricacies of each step and apply them later to making other dosage forms, including suspensions and suppositories. Applying lessons learned to other situations encouraged retention of concepts and a greater understanding of the importance of compounding in today’s pharmacy practice realm.

SUMMARY

The purpose of the capsule laboratory in the *Pharmaceutics II Laboratory* was to develop skills necessary to compound capsules, as well as confidence in performing the necessary calculations for preparing this dosage form. Given the small amount of time in today’s PharmD curricula devoted to compounding, utilizing all available combinations of techniques and equipment becomes vital. Utilizing hand packing versus a capsule-filling machine, tumbling versus trituration, bulk powder versus manufactured tablets, and individual weighing of capsules versus batch testing for uniformity of dosage form units, students were exposed to a broad range of concepts. Through the combination of this exposure with their successful preparation of capsules and completion of the laboratory, students acquired a firm grasp of basic techniques and will be better able to adapt to requests and their available equipment in order to prepare safe and uniform dosage forms for patients in the future. While technology and time change the requirements of the compounding pharmacist, the basic skills and calculations remain the same. Presenting a wide variety of techniques and equipment to prepare the same dosage form should enable application no matter what is asked of students as pharmacists, or at least provide a reference point going forward into their careers.

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