Two Basic Pharmacy Courses with Strong Experimental (Laboratory) Components

Boka W. Hadzija
Robert P. Shrewsbury

ABSTRACT. In the School of Pharmacy at the University of North Carolina at Chapel Hill, two required basic pharmaceutics courses are taught in the first professional year. Each three-credit course has a separate one-credit laboratory component that has experiments to help illustrate the theoretical concepts presented in the lectures. These lab exercises were generally qualitative in nature and contained no quality-control assessment evaluation of extemporaneously compounded prescriptions. The redesign of these courses and their laboratory components was initiated in the 1994-95 academic year. This article describes the current status of one of the courses (Phar 61) and gives an example of one of the redesigned laboratory exercises (capsules). In this example, students formulate capsules and learn the quality assessment aspects of capsules, inspect their visual appearance, test for weight variation, and test for content uniformity. In data collected in the spring 1996 semester, more variability occurred in the content uniformity measurements than in weight variation. Since the prescription required the students to make a trituration, it is suggested that making the trituration a homogeneous mixture is the reason for more variability in the content uniformity. *[Article copies available for a fee from The Haworth Document Delivery Service: 1-800-342-9678. E-mail address: getinfo@haworth.com]*

Boka W. Hadzija, Ph.D., is Professor of Pharmaceutics and Robert P. Shrewsbury, Ph.D., is Associate Professor of Pharmaceutics at the University of North Carolina at Chapel Hill School of Pharmacy, Chapel Hill, NC 27599-7360.

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INTRODUCTION

In the School of Pharmacy of the University of North Carolina at Chapel Hill, two required basic pharmaceutics courses are taught in the first professional year, Phar 51 in the fall and Phar 61 in the spring. Each three-credit-hour course has a separate one-hour laboratory component that has experiments to help illustrate the theoretical concepts presented in the lectures (Phar 51L and Phar 61L). These lab exercises were generally qualitative in nature and contained no quality-control assessment of extemporaneously compounded prescriptions.

It has become evident that pharmacy students need more practical experience in their basic pharmaceutics courses. This can be achieved by providing "hands-on experiences," problem-solving cases, discussions, and laboratory experiments that have well-defined objectives and outcomes. The laboratory components of the two basic pharmaceutics courses give the students their first opportunity to apply the theoretical information from their coursework to pharmacy practice (1). We have attempted to introduce substantial modifications to the courses by redesigning the laboratory components and raising our expectations of student performance.

The redesign of the courses and laboratories was initiated in the 1994-95 academic year. Table 1 lists the individual lectures and laboratory exercises, with the number of 50-minute lectures and three-hour laboratories assigned to each topic, respectively. Students are given reading assignments to prepare for each class and laboratory exercise. Laboratory introductions (50 minutes) are presented before each exercise and are used to describe each experiment and method.

DESCRIPTION OF COURSE MATERIAL

Lecture Content

The plan for developing two lectures on capsules was based on the assumption that the basic science presented was necessary to prepare future pharmacists to be active participants in the development and evaluation of various capsule products for therapeutic use (2). The lectures begin with the general description of capsules and their use in patients of different age groups and continue by covering the classification of capsules (hard and soft gelatin), where an understanding of general features and usefulness of each class is emphasized.

Hard Gelatin Capsules. Students learn the three steps in the preparation of hard gelatin capsules: (a) developing and preparing the formulation

TABLE 1. Lectures and Laboratory Outline

Lectures	Laboratory Experiments
Colloids (3)	Colloids (1)
Suspensions (2)	Suspensions (1)
Emulsions (2)	Emulsions (1)
Semisolids (3)	Semisolids (2)
Suppositories (1)	Suppositories (2)
Sterile Dosage Forms (6)	Parenteral Admixtures (1)
Ophthalmic Solutions (1)	
Powders (3)	Powders (1)
Capsules (2)	Capsules (1)
Tablets (2)	Tablets (1)
Aerosols (3)	
Radiopharmaceuticals (2)	Radiopharmaceuticals (1)
Polymeric Systems (2)	
Novel Drug Delivery Systems (5)	
Pharmaceutical Biotechnology (5)	

with selection of the capsule size, (b) filling the capsules, and (c) outside cleaning and polishing of the final product.

a. *Capsule Formulation and Size Selection.* Drugs and inactive components should have similar density and particle size in order to obtain uniform distribution in capsule-filling formulations. Several types of inactive excipients used as additives to the capsule contents are described in class: (a) flow enhancers or glidants, (b) diluents, (c) absorbents, and (d) surface-active agents. This portion of the lectures is followed by information about the amount of formulation to be prepared (drugs and additives) that is necessary to fill a required number of capsules. The students learn about the various sizes of capsules.

b. *Filling the Capsules.* On an industrial scale, large amounts of powder are prepared in a single batch to automatically fill thousands of capsules by machine. In the large-scale processes, the capsule bodies are placed upright, filled, jointed, sealed, and removed. The two most frequently used procedures for filling the capsules are the

bench-top system and the auger-filler method, both of which are continuous-flow systems. In the case of extemporaneous preparation of capsules on a small scale, this can be done either by hand or by using a bench-top capsule filler.

c. *Cleaning and Polishing of Capsules.* Cleaning of capsules and removal of powders from their surface is an important step in the final stages of the preparation of the capsules. The students learn about these procedures, whether done manually on a small scale or in industry, using automatic cleaning and polishing machines.

Soft Gelatin Capsules. Soft gelatin capsules are important because they are used for the encapsulation of liquids: water or water-miscible liquids, oils, polyethylene glycols, or propylene glycols. Addition of sorbitol to gelatin during the manufacturing process makes them soft and pliable.

Conclusion. The lectures conclude with a discussion of the legal requirements for capsules to pass tests of content uniformity and weight variation described by the *United States Pharmacopoeia* (3), whether they are prepared in retail pharmacy or in industry. The requirements of North Carolina law regarding expiration dates on prescription labels is also detailed.

Laboratory Content

In our opinion, it is very important for the students to acquire experience in formulation, analysis, and assessment of pharmaceutical products. A recent experience in which we were asked to analyze suppositories and found that the pharmacist had incorporated 100 times more atropine sulfate than prescribed has confirmed the importance of exposing our students to formulation problems and analytical techniques for the assessment of their products.

The School of Pharmacy has no manufacturing facilities; therefore, the laboratory exercise is limited to the extemporaneous compounding of capsules. The new objective of the laboratory exercise is to give the student "quality assessment" feedback of their compounding techniques. The laboratory is designed to determine the students' abilities to weigh solids, make a trituration, and measure weight variation and content uniformity of their products.

The students were asked to compound the following prescription:

Salicylic acid	4 mg
Lactose qs.	350 mg
M.Ft. D.T.D. caps	#12

The laboratory is equipped with Class A balances, which allow the weighing of 120 mg with less than 5% error. Since the prescription requires only 4 mg, the students must make a trituration where at least 120 mg of salicylic acid is weighed. Lactose is used as a diluent; then the students weigh an aliquot of the trituration (at least 120 mg) and add additional lactose to the aliquot to complete the formulation. The students have made triturations and aliquots in several laboratories before the capsule laboratory, but as a final precaution, their calculations are checked by the teaching assistants before beginning their work.

After making a trituration, the students weigh an aliquot, add the required amount of lactose needed to complete the prescription, and fill the capsules by hand using their Class A balance to determine the final weight of each capsule. This completes the extemporaneous compounding portion of the laboratory.

A quality-control analysis must have an end point or standard by which to compare the students' compounding skills. One suitable standard is the USP Uniformity of Dosage Units (3), specifically, the criteria for Content Uniformity. Another standard might be the "rule" that extemporaneous compounding should be the intended value ± 5%; the origin and validity of this rule is not known.

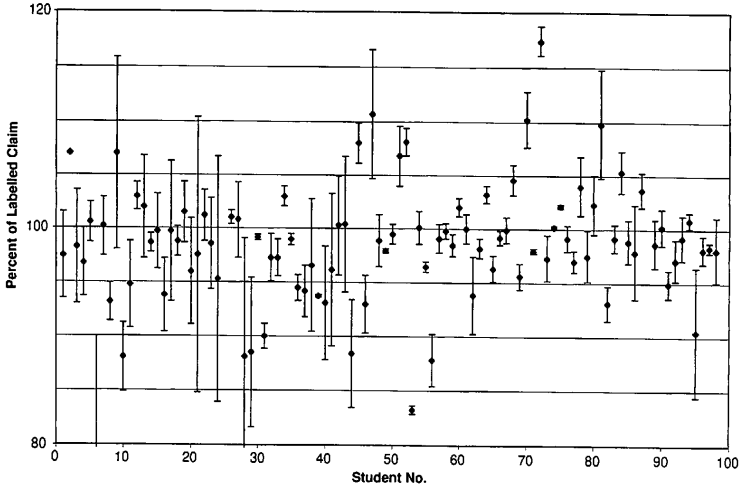
EVALUATIVE DATA

In the capsule laboratory exercise, the weight variation and content uniformity are determined using five capsules. The five capsules are individually weighed on an analytical balance (Fisher X-100), the contents removed, and the empty capsules reweighed. The weight of the capsule content is determined by difference. A weight variation is determined by dividing the measured capsule content by the expected content (350 mg), and expressing the result as the "percent of labelled claim." The students calculate the mean and standard deviation of their data.

These weight variation data from the 1996 spring semester are shown in Figure 1 ($n = 98$). The y-axis shows the variability found in the students' formulations. All but three students had results between 80% and 120%. Of the 95 students, 66 (or 69%) had a mean labelled claim of 100% ± 5%; 85 students (or 89%) had a mean labelled claim of 100% ± 10%. All but two of the 95 students had a mean labelled claim of 100% ± 15%, which is the criteria percentage in the USP Uniformity of Dosage Units.

The individual capsule content is analyzed for the amount of salicylic acid present by dissolving the material in 10 ml of 0.01 N NaOH. A 1:10 dilution of each sample is made using distilled water. The samples are read

FIGURE 1. Weight variation results of an extemporaneously compounded salicylic acid capsule formulation (n = 98). Data represents mean ± standard deviation for five capsules.



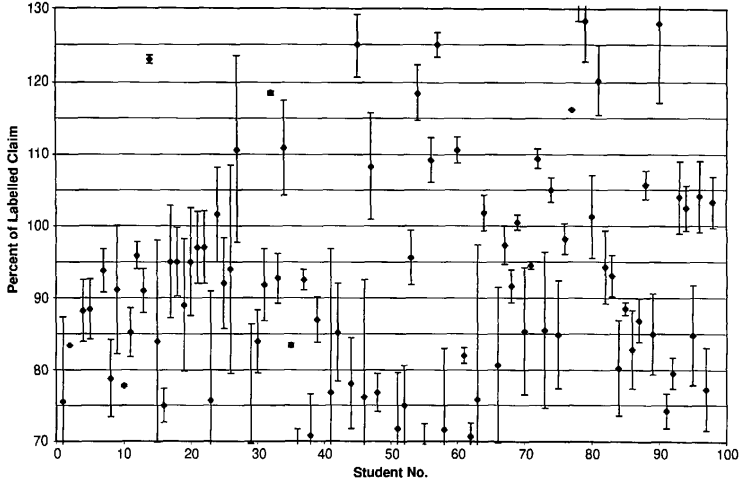
with a UV spectrophotometer (Genesys-5), using disposable methacrylate cuvettes with a suitable blank. Salicylic acid reference standards are made by the teaching staff, and the standards are used to construct a Beer's Law plot, which is used by all the students. Students use Excel 5.0 to fit a trendline to the Beer's Law data and use the generated line equation to calculate the amount of salicylic acid in each capsule. The percent of labelled claim is determined by dividing the measured amount of salicylic acid in each capsule by the intended amount (4 mg) and expressing the result as a percent. The students calculate the mean and standard deviation of their data.

These content uniformity data from the 1996 spring semester are shown in Figure 2 (n = 98). The y-axis shows the variability of the students' results. Of the 98 students, 61 had mean labelled claim values between 80% and 120%. Of these 61 students, 15 (or 25%) had mean labelled claim values of 100% ± 5%, 34 (or 56%) had mean labelled claim values of 100% ± 10%, and 47 (or 77%) had mean labelled claim values of 100% ± 15%.

The results from the weight variation test were acceptable, since most students (93 of 98) had a mean labelled claim value of 100% ± 15%, which is recognized by the USP as a criteria for Uniformity of Dosage Forms. However, the content uniformity results were unacceptable, since only 47 of 98 students, or half the class, had a mean labelled claim value of 100% ± 15%. The source of such a poor result could come from the Beer's Law plot, from making and aliquoting the required trituration, or from the analysis. All three procedures had been performed by the students in previous laboratories, where their performance was also evaluated. Little variability was attributed to the analysis or to the Beer's Law plot. The spectrophotometers were checked and calibrated before the lab, and were within manufacturer's specifications. Since only one Beer's Law plot was used by all the students, variation would be minimized. The students' ability to use a Class A balance correctly was demonstrated by the small variability in the weight variation test. Therefore, the majority of the variability most likely came from the students' failure to make a homogeneous trituration.

Currently, students are informed of their ability to formulate the capsule prescription based on a comparison of their data to the acceptable analytical end point. They are encouraged to repeat the laboratory exercise after conferring with the teaching staff. It is our intent in the future to require the students to repeat the exercise if their data is outside of the acceptable variability range. In this manner, we can ensure that the students obtain the necessary competencies.

FIGURE 2. Content uniformity results of an extemporaneously compounded salicylic acid capsule formulation (n = 98). Data represents mean ± standard deviation for five capsules.



PERSONAL REFLECTIONS

Pharmacy and pharmacists are subject to constant and significant changes because of continuous developments, discoveries, and changes in science and technology. To keep abreast of these changes, it is imperative to make periodic modifications and adaptions in the educational programs of pharmacy students in our colleges and universities (4). In pharmacy, we see the basic sciences changing, merging, and even diminishing in importance in our curriculums (5).

However, we feel that the basic sciences should respond to the current changes in practice by raising expectations and quantifying more outcomes of our students. As these data show, preparing a homogeneous powder mixture is not a simple skill for students to master. Our students had to make five triturations before the capsule laboratory, but none of those triturations were analytically assessed. In the capsule laboratory, it was found that the trituration was the major source of variability in content uniformity. This conclusion indicates that all of the triturations made by the students should have been quality assessed.

One goal of redesigning the basic pharmaceutics courses was to acquaint the students with basic methodologies used to assess the quality of their products. The analysis in the exercise described above used UV/VIS spectrophotometers. In the future, high-pressure liquid chromatography will be the primary method of analysis as we quality assess more and more of the multi-component products that our students are required to make.

Another goal of the laboratory exercises is to give the students the opportunity to physically experience those concepts and procedures that are introduced in the lecture sessions. Taken together, these goals give students an understanding of the complexities of formulations and quality assessment. Such understanding will strengthen their proficiency to extemporaneously compound formulations and improve their thoroughness and effectiveness in counseling patients regarding these products.

The analytical assessment has been well accepted by the students because it provides instant feedback. As expected, most students voluntarily repeat the exercise if necessary; however, we believe that the requirement to repeat the exercise should be mandatory.

We have presented our new approach in teaching the basic pharmaceutics courses to strengthen the students' preparedness to practice pharmacy. It should be emphasized that the courses are continually being revised, modified, and improved in order to prepare the students to become not only competent pharmacists and health-care providers, but practitioners

with a strong foundation in the basic sciences and the ability to apply this material to the problems of today and tomorrow. We are starting to place the course materials on the Internet; the URL addresses are www.unc.edu/courses/phar051 and www.unc.edu/courses/phar0511.

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