

## RESEARCH BRIEF

# Analytical Evaluation of the Accuracy and Retention of Compounding Skills Among PharmD Students

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Submitted December 17, 2015; accepted July 6, 2016; published May 2017.

**Objective.** To evaluate the accuracy and retention of compounding skills among students using analytical testing.

**Methods.** Students compounded acetaminophen capsules from the same prescription at three time points (Exercise 1, 2, 3). The compounded products were analyzed (by HPLC) for acetaminophen content and the students' written reports were evaluated for accuracy of calculations and labeling.

**Results.** During Exercise 1, 57.8% of the compounded capsule products were within the acceptable range, 92.2% during Exercise 2 and 75% during Exercise 3. The largest range in acetaminophen content was observed during Exercise 3 (76.08% to 135.2%) mainly due to calculation errors.

**Conclusion.** While most students readily develop compounding skills during regular laboratory coursework, long-term competency depends on constant exposure to compounding activities and the retention of calculation skills.

**Keywords:** compounding, analytical testing, acetaminophen, integration

## INTRODUCTION

Pharmacy compounding provides individualized drug preparations to patients based on their specific medical needs.<sup>1</sup> Compounding of customized medications is required when the desired drug product is commercially unavailable or has to be delivered in some other form or strength or route to the patient.<sup>2</sup> Although mass manufacturing of preformulated drug products by pharmaceutical companies has minimized the need for compounding in pharmacy practice, the profession of pharmacy has been undergoing a paradigm shift toward a more patient-centered care model thus ensuring that compounding still remains a relevant skill for students to learn.<sup>3</sup>

Food and Drug Administration (FDA)-approved drug products undergo intense evaluation and testing and are manufactured and tested according to current Good Manufacturing Practice (cGMP) guidelines. Until recently, pharmacy compounding was subjected to little or variable federal or state regulatory oversight. The current increase in the percentage of compounding-related prescriptions has led to a growing concern about the quality of compounded drugs as compared to manufactured

drugs. There have been several adverse events (some resulting in fatalities) reported recently due to pharmacy compounding errors involving inaccurate dosage, lack of sterility in intravenous (IV) products and improper technique.<sup>2,4</sup> This has caused renewed interest in the teaching and assessment of compounding courses in pharmacy programs. While practical compounding laboratory courses are an integral part of the PharmD curriculum nationwide, there is a wide variation in the amount and assessment of compounding training that students in different institutions receive. The Accreditation Council of Pharmacy Education (ACPE) and the Center for Advancement of Pharmaceutical Education (CAPE) Outcomes both address the compounding instruction requirements for students.<sup>5,6</sup> In a nationwide survey of its member institutions, a task force created by the American Association of Colleges of Pharmacy (AACP) council of sections reported that there was no standardized method of assessing student performance in compounding activities. And while many pharmacy educators understand the importance of analytical testing, the task force reported that only 8% of the respondents representing AACP member institutions actually quantitatively analyze the compounded products of their students during compounding laboratory courses.<sup>1</sup>

In the past few years, there have been some institutions that have included analytical testing of products prepared in compounding courses. In a recent study, Roark and colleagues reported that including analytical

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assessment as part of their compounding course design resulted in a long-term improvement in students' compounding skills.<sup>7</sup> A study at the Virginia Commonwealth University analyzed potassium permanganate aqueous solution and citrated caffeine syrup compounded by students. The authors reported that approximately 46% of the potassium permanganate preparations and 22% of the citrated caffeine syrup were not within  $\pm 10\%$  of the nominal concentrations on the students' first attempt at compounding the two preparations.<sup>8</sup> Another study by Eley and colleagues evaluated the retention of compounding skills among students by having them compound capsules from the same prescription twice (ie, during, and 12 months after completing a compounding course). They found that only 17% of the students achieved the required competency during the second exercise.<sup>4</sup>

Students need to develop and retain compounding skills while simultaneously understanding the importance of quality control procedures and good laboratory practices. Pignato and colleagues reported that integrating analytical testing during a compounding laboratory can lead to better understanding of the importance of product quality among students.<sup>9</sup> There needs to be a greater emphasis not just on the quantity or extent of practical compounding but also on its distribution throughout the PharmD curriculum.<sup>4</sup> While compounding and compounding-related calculations courses are often introduced in the first year (P1) curriculum, better retention of compounding skills could be ensured by integrating and distributing compounding courses and/or related content throughout the curriculum.

In the aforementioned AACP task force survey, respondents indicated that majority of the compounding education should be a part of the P1 year (63.5%) and P2 year (53.2%). The survey also indicated that compounding education in member institutions usually involves an average of 2.2 semesters.<sup>1</sup> It appears that most pharmacy schools dedicate one academic year to compounding education while some devote just one semester. Most of the compounding education appears to be taking place in the first and/or second professional years in pharmacy school curricula, with a two to three year hiatus until graduation. Some students may receive additional training from their experiential and post graduate programs or from external programs like those offered by the PCCA (Professional Compounding Centers of America).

A long hiatus in compounding education can adversely impact the retention of compounding skills as demonstrated in the study by Eley and colleagues.<sup>4</sup> While this can lead to students not developing and retaining the

necessary compounding skills as required by the CAPE outcomes and ACPE standards, it can also negatively impact students in states that evaluate compounding skills for pharmacy licensure. New York and Georgia are currently the only two states that assess competency in pharmacy compounding as part of their licensure requirements for pharmacists.

The main objective of this study was to use analytical testing to evaluate the accuracy and retention of compounding skills among students at D'Youville College School of Pharmacy. This project longitudinally tracked student compounding skills before, during and after they formally learned pharmacy compounding in their P2 year laboratory-based course by making them compound the same product during three separate exercises after which their products were analytically tested by High Performance Liquid Chromatography (HPLC).

## METHODS

The curriculum at D'Youville College School of Pharmacy is highly integrated with the pharmaceuticals, pharmacy calculations and compounding content spread over several different courses over the first three semesters. The pharmaceuticals content is taught in an integrated Principles of Drug Action three-course sequence during the first three semesters. Most of the compounding content is offered in the second professional year as a three credit hour Integrated Compounding and Practice course; however, the P1 curriculum includes various dosage forms, related calculations, video and live demonstrations and a hands-on laboratory session. So while students are exposed to some compounding instruction in the first year, they formally learn most of their compounding skills during the Integrated Pharmacy Practice and Compounding course in the second year.

As part of the study design, 64 students in two batches of 32 each had to compound and hand-fill eight acetaminophen capsules based on the same prescription (Figure 1) provided to them during three laboratory sessions (Exercise 1, 2, and 3) in three consecutive semesters. Each student pharmacist was provided with lactose (diluent), capsule sizes from 0 to 5 and commercially available tablets to be used as the acetaminophen source. They were expected to select the right capsule size using the Rule of Seven<sup>10</sup> and calculate the number of tablets and lactose required to fill the prescription. The students also had to submit a written report including these calculations and the complete procedure they employed for the preparation.

Upon submission, the compounded capsules were visually inspected for pharmaceutical elegance (ie, absence of powder, marks, blemishes, cracks, etc.), but


Official New York State Prescription		Name:	Score:
Wilson Franklin, MD 126 Jersey Ave Buffalo, NY 14206		Rx#	LAB USE ONLY
Practitioner DEA Number <input type="text"/>		Source Available:	Quantity: Appearance: Container: Label:
Patient Name: <i>Andy Brown</i> Sex: <input checked="" type="checkbox"/> M <input type="checkbox"/> F Address: <i>4852 Brook Lane</i> City: <i>Buffalo</i> State: <i>NY</i> Zip: <i>14201</i> DOB: <i>X/X/X</i>		Source Information:	
<div style="display: flex; align-items: center;"> <div style="border: 1px solid black; padding: 5px; margin-right: 10px;"> <b>R<sub>x</sub></b> </div> <div> <i>Acetaminophen 80 mg</i>  <i>Filler qs ad 400 mg</i>  <i>Disp #8 capsules</i> </div> </div>			
Prescriber Signature <i>Wilson Franklin, MD</i> <small>THIS PRESCRIPTION WILL BE FILLED GENERALLY UNLESS PRESCRIBER WRITES "daw" IN BOX BELOW</small>		Auxiliary Label (if required):	
Refills: <input type="checkbox"/> <input type="text"/> <input type="text"/> <input type="text"/> PHARMACIST TEST AREA: <input type="text"/> <input type="text"/> <input type="text"/> School of Pharmacy <input type="text"/> Dispense as Written <input type="checkbox"/>			
Maximum Daily Dose (controlled substances only)			

Figure 1. Prescription Given to Students to Compound Acetaminophen Capsules During Exercises 1, 2, and 3.

this was not used as a quality criterion to reject any capsule product. Each capsule also was weighed to test for variation. Three of the capsules from each student were then analyzed using HPLC for acetaminophen content. This study received exemption approval from the D'Youville College Institutional Review Board (IRB).

Exercise 1 was conducted as part of the Principles of Drug Action II course during the second semester of pharmacy school. This course covers a lot of the Pharmaceutics content and is mainly didactic but its active learning component includes one introductory compounding laboratory session. Exercise 1 was scheduled during this laboratory session, with students who were already familiar with the fundamentals of drug formulation and dosage forms. The students were provided with a live laboratory demonstration and the calculations/procedure for the capsule products to be compounded based on the prescription provided. Exercise 1 was conducted to obtain a baseline of

student compounding skills during their first introduction to the compounding laboratory.

Exercise 2 was conducted during a laboratory session in the Principles of Drug Action III course during the third semester. This course also covers the pharmaceutics content in the PharmD program and runs in parallel with the Integrated Compounding and Practice course. Exercise 2 was scheduled in the middle of the third semester after the students had compounded several different products in the Integrated Compounding and Practice course and had progressed beyond novice compounders. The students were given the same prescription to compound acetaminophen capsules and were asked to submit their calculations and procedure. The students had no prior knowledge of this exercise and no demonstration or procedure was provided.

Exercise 3 was conducted in the fourth professional semester as part of the Collaborative Learning Practicum IV course. The Collaborative Learning Practicum is a six

semester course sequence that runs through the first three professional years and integrates the content learned by students in all their current courses into a more application-based format such as a clinical case or a laboratory exercise. The students had no prior knowledge of this exercise and no demonstration or procedure was provided. The same acetaminophen capsule prescription was provided to the students. The students received an assignment grade for all three exercises that contributed to their overall course credit.

A standard stock solution (1 mg/ml) was prepared by dissolving 25 mg of acetaminophen in 25 ml mobile phase which was further diluted to prepare individual standards from 20 to 90 mcg/ml. The contents of the three capsules from each student were emptied and combined. An accurately weighed portion equivalent to about 100 mg of acetaminophen was transferred to a 200 ml volumetric flask, diluted with the mobile phase and mixed. This was later filtered through a membrane filter and further dilutions made. The samples were analyzed in triplicate by HPLC.

Our analytical method was adapted and validated based on the article by Shervington and Sakhnini.<sup>11</sup> Chromatographic analysis was achieved isocratically on a C18

column using a degassed mobile phase of acetonitrile/water (60:40, pH 7.0) at a flow rate of 0.4 ml/min with UV detection at 260 nm.

## RESULTS

Exercise 1 was the first time that the students were exposed to the compounding laboratory during their time in the pharmacy program. Of the compounded capsule products, 57.8% were within the acceptable range ( $\pm 10\%$  of the labeled amount of acetaminophen) (Figure 2). Exercise 1 had the most number of compounded products (27 out of 64) outside the acceptable range.

By the time the students got to Exercise 2, they were already several weeks into their compounding course and had considerable experience in compounding several different products including oral, topical and sterile dosage forms. The students appeared better prepared, and most of their capsule products, 92.2% (ie, 59 out of 64), were within the acceptable range (Figure 2).

The results for Exercise 3 indicate that 75% (48 out of 64) of the students' compounded products were within the acceptable range as opposed to 92.2% during Exercise 2 ( $p < .05$ ). The widest range in acetaminophen content (76.08% to 135.2%) was observed during Exercise 3 as

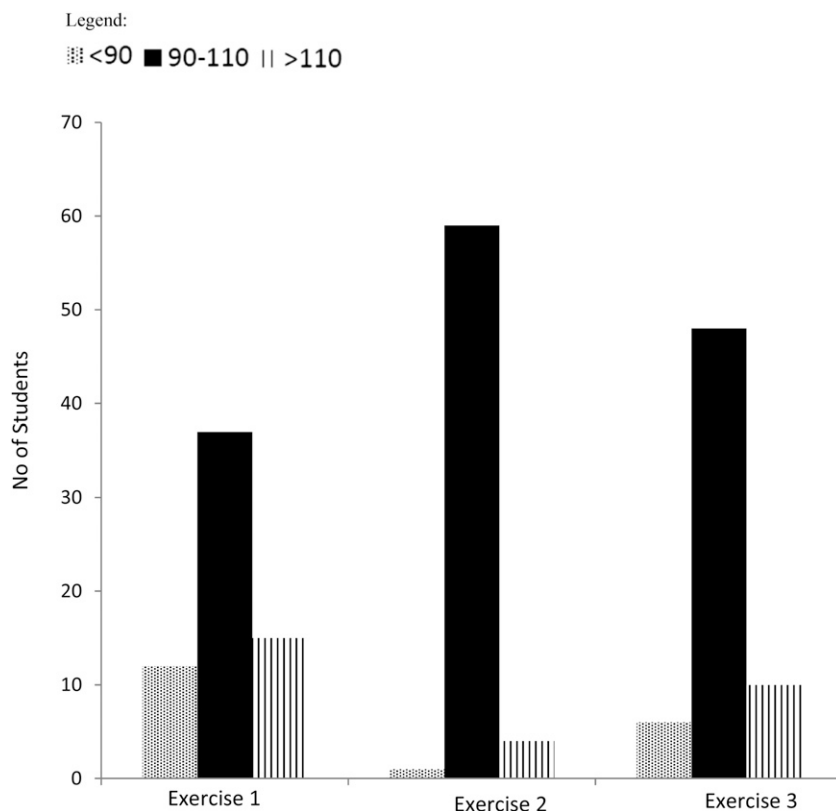


Figure 2. Comparison of the Number of Student Pharmacists Whose Compounded Capsules Were Within and Outside the Acceptable Range for Acetaminophen Content (90% to 110%) Across all Three Exercises.

opposed to a range of 78.4% to 125.5% in Exercise 1, and 87.6% to 118.3% in Exercise 2. Every compounded capsule was weighed as part of variation testing, and the weight of all capsules was found to be within  $\pm 3\%$  of the required weight.

## DISCUSSION

This study followed the same cohort of students over three semesters tracking the development and retention of their compounding skills using analytical testing to measure quality and competency. Each exercise was conducted in two batches of 32 students and care was taken to ensure that students from the second batch would not have an unfair advantage over their peers in the first batch for every exercise. Exercise 1 was a baseline exercise conducted as part of the Principles of Drug Action 1 course. Almost all the students were beginning compounders at this point. During Exercise 2, the students were not aware that the exercise was part of a longitudinal study that involved the same products being compounded by both batches. The exercise was conducted as part of the active learning sessions of the Principles of Drug Action III course while the compounding course was ongoing. Exercise 3 was conducted in two consecutive back to back laboratory sessions on the same day.

There have been few studies in the literature that assess the retention of compounding skills among students using analytical testing in addition to direct observation, visual inspection of the product, and accuracy of calculations. The 2006 study by Eley and colleagues involved P2 students compounding capsules from the same prescription they had been given the previous year. While this study made a significant contribution to compounding education, the authors did not conduct any analytical testing of the students' compounded products in their measurement of competency.<sup>4</sup> Our study used analytical testing (using HPLC) of acetaminophen content as a measure of competency in addition to evaluating the students' reports for accuracy of calculations and labeling at three different time points. The three exercises were conducted during three consecutive semesters with students' skills peaking during Exercise 2, which was conducted concurrently with their main compounding course. This study is unique because it longitudinally followed the students' progress in an integrated pharmacy curriculum using analytical testing of their compounded products as a measure of quality.

Constant exposure to compounding during the curriculum is the key to ensuring better skill retention among students. These skills include technical and procedural knowledge as well as accuracy of labeling and calculations. Our results demonstrate that a quarter (25%) of the students had problems with skill retention as early as one

semester after dedicated and structured compounding instruction (ie, from Exercise 2 to Exercise 3). While this may not be as high as other researchers have reported, it is still significant.

Direct observation by laboratory proctors during regular laboratory sessions revealed that students easily remember the general compounding procedure for most dosage forms, but tend to forget details like calibrating dispensing bottles for liquids or geometric dilution while blending powders. Compounding calculations is another area where students may experience some difficulty. Capsule calculations tend to be more involved as they include calculating the capsule size in addition to the quantities of the active and inactive ingredients. Understandably the students struggled more with recalling and performing the capsules calculations during Exercise 3 than during Exercise 2. This appears to have contributed to the largest range observed in acetaminophen content (76.08% to 135.2%) in the capsules during Exercise 3.

This study was conducted with students at our institution and it remains to be seen if these results are reproducible across other schools of pharmacy. Our observation that some students find it difficult to accurately compound the same prescription even a few months after completing their core compounding course demonstrates the importance of having compounding activities distributed throughout the length of the PharmD curriculum. Integration and active learning have become buzzwords in pharmacy education in the past few years. Integration of compounding instruction need not include just laboratory-based activities but can also independently include other elements of compounding like calculations and labeling requirements. Compounding instruction can always be incorporated into other formats like team-based learning and practicum-based courses. Compounding is a relevant and essential component of pharmacy education and its instruction needs to evolve with the times.

## CONCLUSION

Our results suggest that while students readily develop compounding skills during regular compounding instruction in the pharmacy program, retention of these skills can be a challenge for some students depending on the time interval of compounding inactivity. Robust integration of compounding activities and related calculations throughout the curriculum is of great importance in addressing this issue.

## ACKNOWLEDGMENTS

We wish to thank D'Youville College School of Pharmacy for their support of this project. We also thank Justin Taylor, PharmD, for his assistance with the laboratory analysis.

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