RESEARCH

Long-term Results of an Analytical Assessment of Student Compounded Preparations

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Objective. To investigate the long-term (ie, 6-year) impact of a required remake vs an optional remake on student performance in a compounding laboratory course in which students' compounded preparations were analyzed.

Methods. The analysis data for several preparations made by students were compared for differences in the analyzed content of the active pharmaceutical ingredient (API) and the number of students who successfully compounded the preparation on the first attempt.

Results. There was a consistent statistical difference in the API amount or concentration in 4 of the preparations (diphenhydramine, ketoprofen, metoprolol, and progesterone) in each optional remake year compared to the required remake year. As the analysis requirement was continued, the outcome for each preparation approached and/or attained the expected API result. Two preparations required more than 1 year to demonstrate a statistical difference.

Conclusion. The analytical assessment resulted in a consistent, long-term improvement in student performance during the 5-year period after the optional remake policy was instituted. Our assumption is that investment in such an assessment would result in a similar benefits at other colleges and schools of pharmacy.

Keywords: compounding, preparation analysis, student assessment

INTRODUCTION

Pharmacy compounding may be defined as the art and science of preparing customized medications to meet a patient's specific needs. Pharmacy compounding declined in the 1950s and 1960s with the increase in mass drug manufacturing; however, one limitation of the latter was that not all patients' needs could be met with the standardized dosages and dosage forms produced. Thus, in recent years, compounding has experienced a regrowth in pharmacy practice, and now accounts for approximately 10% of prescriptions dispensed annually in the United States.[1] This resurgence of activity in pharmacy practice, the development of new compounding technology and techniques, and the increase in compounding research information, suggests that pharmacy compounding will continue to be a viable part of pharmacy practice.

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The American Association of Colleges of Pharmacy (AACP) Council of Sections created a task force to assess compounding education in their member institutions.[2] The report found that there was no standardized curriculum for compounding in colleges and schools of pharmacy, and the amount of compounding training varied widely among programs. The report also found there was no standardized method of assessing student work completed in a compounding exercise.

Assessment of student abilities is a fundamental requirement of any compounding curriculum. Several tools can be used to assess compounding abilities including observing the student performing a compounding operation, reviewing a laboratory report in which the student describes what was done and/or observed during a compounding operation, or measuring a physical attribute of the finished preparation.[3,4] As a fourth option, Almoazen et al encouraged that every school of pharmacy use analytical testing in evaluating compounded preparations.[5]

Although analytical testing of student compounded preparations has been encouraged, few published reports are available. The Virginia Commonwealth University School of Pharmacy evaluated students' compounded

potassium permanganate ($KMnO_4$) aqueous solution and citrated caffeine syrup.[6] Students at the Medical University of South Carolina School of Pharmacy analyzed aspirin capsules made in the compounding laboratory.[7] A similar analytical strategy was utilized at the University of Tennessee's College of Pharmacy, where students compounded 25 milligrams of progesterone suppositories using polyethylene glycol (PEG) bases in one laboratory setting, and then analyzed the preparations in another laboratory.[5] Spectrophotometric and High Performance Liquid Chromatography (HPLC) methods were used to analyze the preparations in these 3 studies. Another study conducted by the Southern Illinois University Edwardsville School of Pharmacy used a vapor pressure osmometer to analyze 3 compounded solutions.[8]

Analyzing compounding preparations is not an uncommon assessment technique, but a consistent application of this technique is lacking in colleges and schools of pharmacy. This is further supported in the results of an AACP Council of Sections task force survey, in which only 8% of the participants responded that they employed analytical assessment.[2] At the UNC Eshelman School of Pharmacy, students completed a 5-course Pharmaceutical Care Laboratory (PCL) sequence that included an integrated compounding education component. All students individually compounded approximately 25 preparations during the PCL. Students were directly observed during their compounding exercise by third-year PharmD candidates (PY3), teaching assistants (TAs), resident TAs (PGY-1 and PGY-2), graduate student TAs, and the course instructors. Their compounding records, preparation labels, and counseling proficiency were assessed by the same team of TAs and instructors. The completed preparations were analyzed by procedures developed by the course instructor.

For several years, chemical analysis has been used in the Eshelman School of Pharmacy PCL sequence as the basis for grading compounding preparations. Typically, preparation analysis accounted for 50% of the student's grade (the "analysis requirement"), with the other 50% consisting of the accuracy of the label and compounding record, as well as the student's counseling abilities. Students received either the full score or a zero score for the analysis requirement, depending on whether their preparation was within an acceptable range. The acceptable range was ± 10% of the theoretical amount or concentration of the API in the preparation.

When the analysis requirement was first introduced, students were required to remake their preparation to receive full credit.[9] Improvement in student compounding performance was evident for the 1 compound (diphenhydramine syrup) that was studied. The expectation that students were required to remake their preparation was later modified and students were given the option to remake their preparation for full credit. Changing the requirement to include the "optional" remake assessment strategy did not decrease student performance when comparing the analytical results of 6 compounded preparations that required a variety of compounding skills.[10]

This retrospective study compared the analytical data for 6 compounded preparations made by students at the UNC Eshelman School of Pharmacy over a 6-year period. Four of the preparations were the same as preparations reported in the article that detailed changing from a required to an optional remake assessment strategy. These results showed that the optional analysis requirement brought about a significant and sustained improvement in student compounding performance.

METHODS

Each class of students compounded the same preparations over a 6-year period as part of their regularly scheduled laboratory section in the 5-semester, PCL course sequence. For this study, 6 drug compounds were prepared: diphenhydramine syrup, ibuprofen effervescent powder, ketoprofen PLO emulsion, hydrocortisone medication stick, metoprolol tablet triturates, and progesterone suppositories. These preparations were used to evaluate a broad range of compounding expertise as detailed in Table 1. Preparations were analyzed by either HPLC or spectrophotometric methods to determine the amount or concentration of the API. The same analytical techniques and equipment were used for the analysis of the preparations over the same period. (The formulation ingredients, method of preparation, and analysis scheme for each preparation can be obtained from the corresponding author or from the *pharmlabs.unc.edu* website.)

In the first of the 6 years, students were required to remake the compound if their preparation did not meet the analysis requirement. During the following 5 years, students had the option to remake the compound if their preparation did not meet the analysis requirement. The variation between the year students were required to remake the preparation and each of the years in which students had the option to remake their preparation was compared by calculating the statistical differences between the mean and standard deviation of the student results. A z test (2-tail) was used to test for significant differences since the variances in each group were known. A level of significance of $p < 0.05$ was used. Another measure of the variation was the number of students who compounded the preparation accurately on the first attempt as defined by ± 10% of the theoretical API strength.

Table 1. Preparations Evaluated Using Analysis Requirement and Skills Necessary to Successfully Compound the Preparation

Preparations Compounded by Pharmacy Students	Skills Necessary to Compound the Preparations
Diphenhydramine syrup	1. Weigh single powder 2. Measure liquids
Ibuprofen effervescent powders	1. Weigh multiple solids 2. Uniform powder blending
Ketoprofen PLO emulsion	1. Small batch size 2. Mix in syringes
Hydrocortisone medication stick	1. Weigh multiple solids 2. Prepare semisolids
Metoprolol tablet triturates	1. Weigh multiple solids 2. Uniform powder blending 3. Consistency in tablet weight 4. Content uniformity 5. Calibration of a mold 6. Calculations pertaining to mold calibration
Progesterone suppositories	1. Weigh multiple solids 2. Prepare semisolid 3. Consistency in suppository weight 4. Content uniformity 5. Calibration of a mold 6. Calculations pertaining to mold calibration

RESULTS

There was a consistent statistical difference in the API amount or concentration in 4 of the preparations (diphenhydramine, ketoprofen, metoprolol, and progesterone) in each optional remake year as compared to the required remake year (Table 2). As the analysis continued, the outcome for each preparation approached and/or attained the expected result (stated label amount or concentration). The hydrocortisone stick preparation results indicated 2 years were required before the API outcome was not significantly different from the expected amount. The ibuprofen effervescent powder preparation showed similar, though not identical, results across the 6-year span. Both of these preparations required the students to weigh the preparations multiple times with a Torsion balance, which needed to be re-leveled during the process. Students may not have done this additional releveling in the first years, but through experience may have come to realize it was necessary for satisfactory results in the subsequent years.

Considering a more global view (Table 3), there were 6 preparations compounded over a period of 5 years when the remake was optional, or 30 opportunities to improve the number of students that compounded the preparation correctly on the first attempt. In 80% of those opportunities (24/30), more students did compound the preparation correctly on the first attempt.

The largest improvement in the number of students that compounded the preparation successfully on the first attempt was seen with the metoprolol tablets. The most difficult steps in the procedure are adding just enough wetting solution so the powder mixture "sticks" to the pestle (step 3) and completely and tightly packing the cavity plate with the powder mixture (step 4). The reason for the large increase from the required remake year to the optional remake years may have been in the new "end point" of wetting the powder that was described to the students. Metoprolol is alcohol soluble, and the powder volume significantly shrinks when the powder is wetted. The students tried to spread this decreased volume of powder throughout the cavity plate of the tablet mold. By using an "end point" of having the powder stick to the pestle, the metoprolol powder was not wetted to the same degree, therefore the powder volume did not decrease to the same extent, leading to a significantly larger amount of powder to spread throughout the cavity plate.

DISCUSSION

Overall, the data indicated that student performance statistically improved when the analysis requirement was instituted, and the improvement continued in subsequent years. Increased performance when the remake was made optional rather than required was not intuitively expected. However, the following factors may have contributed to this outcome: (1) the compound was completed earlier in the semester when the students were willing to spend more time in compounding the preparation; (2) the compound was completed at a later point in the 5-semester PCL sequence when the students had more compounding experience; and (3) students were more self-motivated when the remake is optional rather than required.

Mechanistic and biological variation should be considered in the interpretation of the data. One source of mechanistic variability would be the differences in the ingredients used from year to year. To minimize this, in-date ingredients from reputable vendors were used each year. Additional sources of mechanistic variance in terms of ingredients could have included balance performance, liquid measurement, and ingredient transfers.

A second mechanistic variability source could have been the analysis procedures themselves. Linearity standard curves were used for each group of preparations in an effort to account for year-to-year and instrument variability. But the number of samples collected from the preparation could have also been an important variable. For

Table 2. Results of Active Pharmaceutical Ingredient (API) Amount or Concentration in Student Preparations Compounded when Analysis Requirement was Required or Optional

API Expected Result	**Required Remake Year**	**Optional Remake Years**			
Diphenhydramine					
2.5 mg/ml	2.3 ± 0.3	2.5 ± 0.3	2.5 ± 0.5	2.5 ± 0.6	2.5 ± 0.30	2.5 ± 0.4
p value		$p<0.01$	$p<0.01$	$p=0.02$	$p<0.01$	$p<0.001$
Ibuprofen						
3.88 g/50g	4.00 ± 0.89	4.16 ± 0.58	3.59 ± 0.37	3.88 ± 0.63	3.88 ± 0.47	3.88 ± 0.64
p value		$p=0.08$	$p<0.001$	$p=0.31$	$p=0.28$	$p=0.87$
Ketoprofen						
1 g/10 ml	0.7 ± 0.2	0.9 ± 0.2	1.2 ± 0.2	1.0 ± 0.4	0.92 ± 0.2	1.0 ± 0.2
p value		$p<0.01$	$p<0.001$	$p<0.001$	$p<0.001$	$p<0.001$
Hydrocortisone						
2.5%	2.5 ± 0.5	2.7 ± 0.6	2.8 ± 0.6	2.5 ± 0.7	2.5 ± 0.9	2.5 ± 0.5
p value		$p=0.03$	$p<0.001$	$p=0.86$	$p=0.82$	$p=0.65$
Metoprolol						
12.5 mg/tab	6.8 ± 1.0	12.5 ± 1.8	11.3 ± 2.0	11.5 ± 1.3	12.7 ± 1.2	12.5 ± 4.1
p value		$p<0.001$	$p<0.001$	$p<0.001$	$p<0.001$	$p<0.001$
Progesterone						
200 mg/supp	168 ± 31	177 ± 25	181 ± 29	200 ± 21	200 ± 34	206 ± 71
p value		$p<0.001$	$p<0.001$	$p<0.001$	$p<0.001$	$p<0.001$

Results are reported as mean and standard deviations of student preparations.
p value calculated with 2-tail *z* test compared to required remake.
$p<0.05$ for significance.

example, the progesterone suppository and hydrocortisone medication stick preparations are semisolids. Semisolid preparations typically require that a base component be melted and insoluble ingredients be dispersed in the melted material. The material is then allowed to cool and is poured into a calibrated mold. The challenge of the preparation is to have the material uniformly distributed when it is poured into the mold. For the analytical

Table 3. Percentage of Students Who Compounded the Preparation Correctly on the First Attempt When Analysis Requirement Was Required or Optional % (Total number of students)

Preparation API*	**Required Remake Year**	**Optional Remake Years**				
Diphenhydramine	77.2 (114)	88.1	83.8	79.8	91.0	75.0
		111/126	98/117	99/124	101/111	105/140
Ibuprofen	55.8	38.3	54.5	55.8	66.9	80.5
	67/120	46/120	81/149	82/147	101/151	120/149
Ketoprofen	15.4	39.0	28.0	16.2	41.9	52.3
	18/117	46/118	33/118	24/148	62/148	79/151
Hydrocortisone	59.2	31.9	32.2	38.7	25.2	51.3
	71/120	38/119	39/121	58/150	37/147	78/152
Metoprolol	1.0	62.1	40.5	61.2	76.8	43.1
	1/97	72/116	49/121	74/121	109/142	62/144
Progesterone	37.1	8.8	58.3	74.8	62.3	73.1
	37/97	10/113	70/120	89/119	76/122	106/145

*Active Pharmaceutical Ingredient.

requirement data in this report, only one progesterone suppository or one sample of the hydrocortisone medication stick was analyzed. A better method might have been to analyze 2 samples from each preparation and use the average value for the data analysis.

The major biological variation was the students themselves, as each student would have brought different degrees of experience, foundational knowledge, and comfort level to the compounding laboratory. In addition, students were not compounding in a vacuum. Each academic year brought curricular changes and modifications in teaching, as well as the composition of the class.

Another possible variable among students was that many of them might have been "self-regulating" learners. Schunk and Zimmerman described the self-regulated learning style as "a process by which learners personally activate and sustain cognitions, affects, and behaviors that are systematically oriented toward attaining learning goals."[11] Students who were good self-regulators may have set their goals regarding compounding and sought out instructional assistance when needed. Under the old assessment strategy, in which the remake was required, if students did not meet their learning goal (an accurately prepared compound), they had no choice but to remake it. Under the new assessment strategy, in which the remake was optional, the results showed significant improvements in the accuracy of the compound preparations. This result suggested that if the ultimate decision to remake a below-standard product was an option and not an obligation, motivated self-regulators improved so they would not be forced to make the choice between re-making the product and obtaining a less desirable grade.

Student performance is shaped by myriad variables, so having 100% of the students within the acceptable range on their first attempt when compounding complex preparations is unlikely. In our data, most percentages of students who compounded the preparation correctly on the first attempt were less than 70%, with the exception of the diphenhydramine syrup preparation. However, the analytical results showed that the students who were not successful on the first attempt were not far from the expected range.

Another consideration of using an analysis requirement as an assessment tool would be the additional workload and financial burdens for the course instructor and college. The equipment and supplies for analyzing compounded preparations were a costly investment. Furthermore, the analysis process was time-intensive, especially with a large class size. Because of this, auxiliary staff (ie, graduate students and lab assistants) were required to carry out the analytical procedures for a reasonable turnaround time. These staff costs were an additional expense. Fainlly, allowing students to remake compounded preparations added to the overall cost of the compounding laboratory course.

CONCLUSION

Other colleges and schools of pharmacy have investigated the use of an analysis requirement as an assessment tool for pharmaceutical compounding courses. Unfortunately, analytical testing is not conducted in most pharmacy schools. An AACP Council of Sections task force found that only 8% of survey respondents employed analytical assessment.[2] As a result, students could not identify the sources of error affecting the quality of their compounded preparations and may have falsely believed that their compounding techniques were accurate. Instituting the analysis requirements ensured that students received feedback regarding their compounding performance, which was beneficial for developing their competency.

For colleges and schools of pharmacy contemplating initiating or improving compounding course offerings, serious consideration should be given to analysis assessment as part of the course design. Our use of this assessment method resulted in students developing a consistent, sustainable improvement in their compounding performance, which validated our hypothesis that using an analysis requirement would create a long-term improvement in student performance.

The improvement was demonstrated by 2 measures: (1) greater accuracy in the expected API amount or concentration; and (2) increase in the percentage of students who successfully compounded the preparation on the first attempt. Such improvement may translate into more competent pharmacists who are able to provide better patient care. However, this assessment strategy also required a large time commitment, experienced personnel in the area of pharmaceutical drug product analysis, and monetary expenditure.

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