RESEARCH ARTICLES

Evaluation of Basic Compounding Skills of Pharmacy Students

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Objective. To evaluate the accuracy of pharmacy students compounding skills.
Methods. Potassium permanganate aqueous solution ($KMnO_4$) and citrated caffeine syrup were compounded by 2 first-year pharmacy classes in 2 consecutive years.
Results. Approximately 54% of the students prepared the $KMnO_4$ solution within ±10% of the nominal concentration at the first attempt. The "not pass" formulation errors ranged from -75% to >200%. For the citrated caffeine syrup, 78% of the students prepared the medicine within ±10% of the nominal concentration in the first attempt. The "not pass" formulation errors ranged from -89% to 269%. For the citrated caffeine syrup preparation, there was no significant difference between using an electronic digital balance or a torsion balance ($p>0.05$) with respect to accuracy.
Conclusion. The results from this study were comparable with those reported for pharmacists across the country, both in the number of formulations failing potency analysis and in the range of error observed. Objective assessment of pharmacy student compounding skills should be employed to determine competency.

Keywords: compounding, analysis, balances, solutions

INTRODUCTION

The teaching of compounding in colleges and schools of pharmacy has had a rich and varied history and is recognized as an important part of pharmacy education. In the early and middle 20th century, compounding had a prominent place in the curriculum due to the extensive amount of compounding required in pharmacy practice. At that time and currently the practice of compounding was regulated by state pharmacy practice acts and was supervised by state boards of pharmacy. Up until the 1980s, the compounding of a prescription was an independent component of the examinations administered by most state boards of pharmacy that had to be passed for licensure.[1,2] The prescriptions compounded were evaluated for acceptable quality and usually assayed for accuracy.[1,2] With the increased availability of preformulated drug products, there has been a decreasing need for compounding in pharmacies.[3] Many state boards of pharmacy changed their laws and testing so that currently only 5 state boards of pharmacy (New York, Kentucky, Connecticut, Georgia, and North Carolina) require compounding of a prescription for licensure. However, in the current Model State Pharmacy Act and Model Rules of the National Association of Boards of Pharmacy, compounding expertise is addressed and requires that the applicant "graduated and received the first professional undergraduate degree from a college or school of pharmacy that has been approved by the Board of Pharmacy."[2] Essentially relying on pharmacy schools to verify that a student can safely and accurately compound a prescription.

Concomitant with this decreased emphasis on compounding in pharmacy practice and regulation, there has been a decreased emphasis on prescription compounding within the pharmacy curriculum.[4-6] The didactic material covering the theory, principles, and techniques used in the compounding of various dosage forms still remains as a component in the curriculum of pharmacy schools. The importance of this didactic material is reinforced with the NAPLEX licensure examination in which 19% of the competency statements involve compounding.[7] Anecdotal evidence suggests that the amount of prescription compounding in the pharmacy curriculum has been reduced to provide increased emphasis on the dispensing of preformulated prescriptions, medication therapy management, communication skills, clinical counseling, physical assessment and informatics.[4,6]

Therefore, it may be perceived that compounding is no longer a major component of retail pharmacy; how-

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ever, any registered pharmacist is entitled by law to extemporaneously compound a prescription. Based on limited data, various reports have suggested that 1%-10% of all prescriptions filled in the United States are compounded.[8,9] Given an estimated 3.14 billion prescriptions were dispensed in the United States in 2002, even a small percentage would indicate that millions of compounded prescriptions are dispensed each year.[8,10] Because of this, numerous organizations, including the United States Pharmacopoeia/National Formulary, the Food and Drug Administration (FDA), and several states have been establishing new guidelines or regulations to improve the quality of compounded products.[1,11]

There are a number of examples of the prevalence of compounding errors in the literature. In 1974, of 100 pharmacies that filled a prescription for 5% salicylic acid in 70% isopropyl alcohol, only 58% of the solutions were within ±10% for salicylic acid content with a range of 0 to 208%.[12] In a study to determine the accuracy and variability observed for compounding 2 different concentration of an intravenous theophylline preparation, depending on the method used for compounding, the absolute percent error relative to the labeled concentration ranged from 2.2%-13.7% with a range of 0 to 41.2%.[13] A report of prescription dispensing errors revealed that 7.5% were compounding errors.[14] Recently, the FDA analyzed 29 products made by 12 compounding pharmacies, 36% of the solutions failed the assay or potency testing (product was not within ±10%).[15] Although a number of caveats exist prior to the interpretation of this literature, if these numbers are extrapolated to the number of prescriptions compounded in 2002, millions of compounded prescriptions may have failed potency assays. These results are disturbing and raise the question to what extent the teaching of compounding in colleges and schools of pharmacy may contribute to this problem.

The Accreditation Council for Pharmaceutical Education's (ACPE) Standard No. 10 of the "Standards of Practice" expect colleges and schools of pharmacy to teach students to "accurately and safely compound drugs."[16] Yet to what extent do schools of pharmacy verify that their students can accurately compound a prescription? Pharmacy students at the Medical University of South Carolina prepared a 50% (w/v) magnesium sulfate solution, and a 8% of the products exceeded the USP specifications. When these students prepared a 0.01% amaranth solution, the relative standard deviation for 3 different laboratory sessions over 3 years ranged from 8.2%-19.0%, indicating a much higher percentage of students were unsuccessful in accurately preparing a more dilute solution.[17] At VCU our compounding laboratory has been a competency-based course that included introduction to medication distribution systems, prescription dispensing, patient counseling and monitoring, compounding solution drug preparations, and drug information retrieval. Prior to this study, the evaluation of the compounding portion of the laboratory was based primarily on the review of written procedure and visual examination of compounded product by a registered pharmacist. This is a time-honored method recognized in the USP/NF.[1] This approach seems to serve our students well based on their success in getting state licensure. We did not perceive there was a problem in our 2 semester compounding laboratory sequence; however, as part of our commitment to quality assessment of our program and to begin documenting our compliance with ACPE's Standard No. 10, an effort was made to provide some quantitative evaluation of our students' compounding skills.

The objectives of this study were to evaluate the accuracy of pharmacy student compounding of 2 solution formulations and to assess the effect of the type of balance employed in compounding on the accuracy of dispensing of the active ingredient in the product.

METHODS

Student and Course Description

The compounding experiments were performed by students during their first year of pharmacy school. In addition to this "Pharmacy Skills Laboratory" (1 semester credit in both the fall and spring semester), the students had previously taken or were concurrently taking the following relevant courses: "Principles of Pharmacy" (3 semester credits that presented the chemical and physico-chemical principles fundamental to the development and use of medication dosage forms including pharmaceutical calculations, prescription orders, weights and measures, and theory of solutions), "Biopharmaceutics and Pharmacokinetics" (4 semester credits that described linear pharmacokinetics and drug and dosage form stability and continued the description of the physico-chemical and biopharmaceutical principles fundamental to the development of pharmaceutical dosage forms). The students were expected to compound 2 prescriptions in a 2.5-hour laboratory session. There were 35-38 students in each of the three laboratory sessions.

Prescriptions

The prescriptions to be compounded were discussed 1 week prior to the laboratory session and 2 registered pharmacists with extensive experience in teaching compounding to pharmacy students were available both prior to and

Table 1. Student Accuracy in the Compounding of a 1:5,000 Potassium Permangenate Prescription (2002)

Measured Concentration (% of nominal value)	Students, No. (%)	Nominal Value Mean % ± SD (range)
First Attempt		
100 % ±10%	64 (59)	98.7 ± 5.8
<90%	26 (24)	73.2 ± 17.9 (24.5 – 89.4)
>110%	14 (13)	0.978 ± 0.066 (111.2 – 169.4)
>200%	5 (5)	NA
Second Attempt		
<90%	15 (14)	74.1 ± 12.0 (48.1 – 89.0)
>110%	10 (9)	131.8 ± 25.15 (111.7 – 187.8)
>200%	4 (4)	NA
Third Attempt		
<90%	10 (9)	80.6 ± 17.2 (30.9 – 87.6)
>110%	6 (6)	125.2 ± 12.3 (110.7 – 138.3)
Fourth Attempt		
<90%	5 (5)	68.1 ± 23.4 (41.6 – 89.3)
>110%	1 (1)	111.1
Fifth Attempt		
<90%	3 (3)	83.4 ± 7.8 (74.3 – 88.5)
Overall Acceptable Products	109 (100)	98.8 ± 6.7

*Sample required 1:2 dilution with water prior to reading

during the laboratory session. Following compounding, the product was assayed for drug content using the methods described below. Results were reported as the percentage difference from the nominal concentration. Preparations outside the range of ±10% of the nominal concentration received a grade of "not pass" and the student was required to compound the prescription again. The product was then analyzed and the results reported back. The student repeated the compounding until they had successfully compounded the product within the required limits. Once the prescription assayed within the nominal concentration of ±10%, the student preparation was then further evaluated for correctly interpreting the prescription, detecting errors and omissions, and accurately dispensing the prescription. The following prescriptions were compounded as described below.

Prescription 1. Potassium permanganate 1:5000 solution, 60 mL (1:10,000 solution used in 2003).[18] The recommended procedure for compounding the $KMnO_4$ solution was the following: (1) clean, level, and zero the balance; (2) accurately weigh a calculated amount of $KMnO_4$, reduce crystal size in a glass mortar and pestle, and dissolve in deionized water; (3) quantitatively transfer the solution to a 100 ml graduated cylinder and further dilute to a fixed volume; (4) accurately measure a fixed volume using a 10 ml graduated cylinder and quantitatively transfer it to a clean 100 ml cylinder; (5) fill to volume (60 ml) and transfer to an appropriate bottle, (6) properly label and dispense.

Prescription 1 was prepared during week 9 of the fall semester. The students had previously completed laboratories on the weighing of unknown tablets and fractional weights.[19] In the preparation of prescription 1 they were expected to use the same torsion balance they had previously calibrated.

Prescription 2. Caffeine citrate syrup 1%, 60 ml.[20] The recommended procedure for compounding the 0.6% citrated caffeine solution was as follows: (1) weigh 600 mg caffeine citrate and transfer to a 2 ounce conical graduate, (2) add a sufficient quantity of hot water (2.4 ml) to dissolve the caffeine citrate, (3) fill to volume with syrup (60 ml) and transfer to an appropriate bottle, (4) properly label and dispense.

Prescription 2 was prepared during the third week of the spring semester. The students were randomly assigned to use either a torsion or digital balance.[21,22] Prior to using them, the accuracy of the electronic balances was verified. An unpaired *t* test was used to compare the "not pass" samples prepared using the torsion or electronic balance.

RESULTS

Compounding of Potassium Permangenate Solution

Tables 1 and 2 indicate that 59% and 48% of the pharmacy students had successfully prepared a defined solution of $KMnO_4$ solution on their first attempt in 2002 and 2003, respectively. In prior years usually 2 to 4 students were requested to repeat the exercise based on visual inspection of the formulation. For the students failing to correctly dispense the solutions, the errors were not trivial and ranged from 25% to >200% of the label amount. Even after receiving additional directions and supervision by the laboratory instructors, approximately 15% (in 2002) and 13 % (in 2003) of the students required 3 or more attempts before successfully preparing the solution. The overall variability in measured concentration of successfully compounded products was 6.8 % in 2002 and 5.6 % in 2003 (relative standard deviation).

Compounding of Caffeine Citrate Solution

The caffeine citrate solution was prepared during the second semester of compounding with the results shown in Table 3. This syrup was considered to be simpler to prepare

Table 2. Student Accuracy in the Compounding of a 1:10,000 Potassium Permangenate Prescription (2003)

Measured Concentration (% of nominal value)	Students, No. (%)	Nominal Value, Mean % ± SD (range)
First Attempt		
100±10	52(48)	97.9 ± 5.1
<90	47(44)	76.8 ± 12.5 (28.8 – 89.3)
>110	7(6)	118.8± 4.8 (112.9 – 127.2)
>133	2(2)	NA
Second Attempt		
<90	20(18)	78.3 ± 12.0 (58.6 – 89.4)
>110	3(3)	119.1 ± 6.7 (112.4 – 125.8)
>133	1(1)	NA
Third Attempt		
<90	12(11)	76.2 ± 13.5 (49.3 – 88.3)
>110	2(2)	113.8, 123.1%
Fourth Attempt		
<90	4(4)	84.3 ± 6.5 (75.3 – 89.4)
>110	1(1)	111.8%
Fifth Attempt		
<90	3(3)	± 7.8 (74.3 – 88.5)
Overall	108 (100)	98.1± 5.5

since it required only weighing, dissolution of the active ingredient, and filling the conical graduate to a fixed volume. The students did better in this exercise; however, 22 % of the students in 2003 and 2004 were not able to successfully prepare a 1% caffeine citrate solution. The amount of caffeine citrate present ranged from -89% to 269% of the nominal concentration, with 2 students (in 2003) and 5 students (in 2004) still unsuccessfully preparing the syrup on a second attempt. Table 4 reveals that in 2003, a similar number of students successfully produced their compounded product on both the torsion and electronic balance and that the average percent of deviation from the nominal concentration of the failed products were similar between balances. In 2004, although there were more successful products produced by students using the electronic balance compared to the torsion balance (49 vs 36), again the average percent deviation from the nominal concentration of the failed products were similar between balances.

DISCUSSION

Advocacy for Quality Assurance Testing in Schools of Pharmacy

The medical community and the public expect pharmacists to have the knowledge and skills to accurately compound an extemporaneous prescription.[2,23] This requires that during the training of a pharmacist an assessment of their compounding skills be performed. This was addressed by the pharmacy college at the

Table 3. Student Accuracy in the Compounding of a 1% Caffeine Citrate Prescription

Measured Concentration (% of nominal value)	Students,No. (%)	Mean caffeine citrate, mg/ml ± SD (range)	Nominal Value Mean % ± SD(range)
Spring 2003			
First Attempt			
100±10%	85 (78)	9.8 ± 0.4	-2 ± 4
<90%	11 (10)	7.5 ± 2.0 (2.7 to 8.9)	-25 ± 20 (-73 to –11)
>110%	8 (7)	12.9 ± 1.8 (11.2 to 16.0)	29 ± 18 (12 to 60)
0%	5(5)	NA	NA
Second Attempt			
100±10%	21 (19)	9.7 ± 0.4	-3 ± 4
>110%	2 (2)	11.6, 17.5	16, 75
Spring 2004			
First Attempt			
100±10%	85 (78)	10.0 ± 0.5	0 ± 5
<90%	9 (8)	7.2 ± 2.4 (1.1 to 8.9)	-28 ± 24 -89 to –11)
>110%	13 (12)	14.7 ± 4.4 (11.3 to 26.9)	47 ± 44 (13 to 269)
Second Attempt			
100±10%	17 (16)	9.9 ± 0.5	-1 ± 5
>110%	5 (5)	13.2 ± 2.4 (11.4 to 16.8)	32 ± 24 (14 to 68)

*Does not include 5 preparations that contained no caffeine.

Table 4. Comparison of Student Accuracy in the Compounding of a 1% Caffeine Citrate Prescription Using Either a Torsion Balance or Electronic Digital Balance

Measured Concentration (% of nominal value)	Number of Students*	Mean Caffeine Citrate, mg/ml ± SD, (range)	Nominal Value, Mean % ± SD
Spring 2003			
Torsion Balance			
100±10%	41	9.8 ± 0.4	-2 ± 4
<90%	5	8.4 ± 0.6	-16 ± 6
>110%	4	12.6 ± 1.6	26 ± 16
Electronic Balance			
100±10%	44	9.8 ± 0.4	-2 ± 4
<90%	6	6.7 ± 2.6	-33 ± 26
>110%	4	13.3 ± 2.3	33 ± 23
Spring 2004			
Torsion Balance			
100±10%	36	10.0 ± 0.5	0 ± 5
<90%	4	8.0 ± 1.0	-20 ± 10
>110%	9	14.7 ± 5.1	47 ± 51
Electronic Balance			
100±10%	49	10.0 ± 0.5	0 ± 5
<90%	5	6.5 ± 3.2	-35 ± 32
>110%	4	14.8 ± 3.0	48 ± 30

* Only the results from the initial compounding of the prescription are included.

Medical University of South Carolina by having students analyze a product made in their compounding laboratory in a subsequent pharmaceutical analysis laboratory.[17] This approach appeared to be well received by the students. However, the analysis of the preparation by the student added another variable into obtaining an accurate estimate of the active ingredient in the preparation and caused a modest delay in providing feedback to the student. Therefore, we did not take that approach. Instead we identified 2 prescriptions that were already part of our compounding course and for which a fast and relatively inexpensive analytical procedure could be designed. The assay methods and validation results have been incorporated into this manuscript in Appendix 1 to allow readers to reproduce our studies in their student population.

Generally, the easiest prescription to directly analyze is a solution, thereby minimizing sample preparation time. USP monographs usually require an accuracy of ±10% for the amount of active ingredient in elixirs, solutions, and syrups.[24] In this study the students were expected to prepare a $KMnO_4$ solution and a caffeine citrate solution. The $KMnO_4$ solution was perceived as being the more difficult prescription to prepare since it required weighing, dissolution of active ingredient, measuring an aliquot, and working with a darkly colored solution for which the meniscus is difficult to read.

The expectation that schools of pharmacy would analyze many of the prescriptions compounded by a student would initially appear to be impossible or extremely expensive and is not justified at this time. This would certainly be the case if the analytical procedure used conformed to USP guidelines. However, what is needed at the teaching level are analytical methods that can be quickly and inexpensively done by the student or laboratory supervisor that can provide a reasonable estimate of the quantity of drug in a prescription. These analytical methods may not be as stringent as those used in the pharmaceutical industry, but would be an objective measurement of a student's compounding ability. In this regard the spectrophotometric assay of a colored solution, such as $KMnO_4$, is representative of an assay that could readily be incorporated into a compounding laboratory in most schools of pharmacy. The primary advantage of this assay is that it is inexpensive and quick. A good quality spectrophotometer that is capable of reading wavelengths between 325-1000 nm costs approximately $1500 and is often already available in schools of pharmacy. Other advantages are that minimal skill is required for operation of the instrument and it is portable so it can be brought into the laboratory as needed. A disposable borosilicate glass test tube, which costs approximately $0.04, can be used as the cuvette.

In contrast, the high performance liquid chromatography (HPLC) assay for caffeine required expensive

equipment (>$50,000), although many schools of pharmacy most likely have this type of equipment available. Equally important is the requirement for personnel skilled in use of HPLC instrumentation. After the initial investment the cost for running the assay was minimal ($0.016/vial and $0.068/disposable pipette). Even when using an established protocol and making the students responsible for preparing and labeling their own samples for analysis, the preparation time for the assay was approximately 4 hours and time for HPLC analyses was >16 hours. This meant the students could not receive immediate feedback about their compounding skills.

Regardless of the type of analytical instrumentation used some type of quality assurance for a student's compounded product is needed during their training. Simple, inexpensive, and quick analytical methods are needed for laboratory compounding instructors to assess a student's compounding skills. For example, the simple weighing of an IV solution after addition of a drug was used as quality assurance for cytotoxic drug admixtures in a large university hospital pharmacy.[25] Although this type of analytical measurement does not verify the drug placed in the intravenous solution is correct, it is a quantifiable method that documents that proper technique was used in filling the prescription.

Possible Sources of Student Compounding Errors

While we did not identify the causes of student compounding errors, a number of possibilities are evident. The most probable error is an inaccuracy in the weighing procedure, which may result in products that contain too little or too much active ingredient. Such errors may be expected and with repeated practice the weighing technique of the students improves and acceptable products are compounded.

In the case of the potassium permanganate solution, a potential source of error could be a calculation error. These errors were relatively easy to detect when checking the students calculation following identification of a failed product (which happened only once or twice each year). All calculations for all students were checked after completion of the laboratory and further evaluated for interpreting the prescription, detecting errors and omissions, and dispensing of the prescription.

Possibly, a number of errors occurred during the compounding procedure itself, including failure to completely dissolve the active ingredient, failure to make accurately to the total final volume of the compounded product, and failure to ensure homogenous mixing of the product prior to dispensing and analysis. A video showing the correct procedure is under development to determine whether this portion of the compounding procedure is responsible for the errors observed.[5]

It was unexpected that 5 students in the 2003 laboratory session would prepare syrups containing no caffeine, especially since they had been notified that the syrups would be analyzed. Why this occurred is unknown; however, once these results were obtained it was observed that present on the dispensing cart were bottles labeled for caffeine citrate and codeine sulfate. The codeine containers contained only lactose and were made available for students completing an exercise for a previous laboratory. Apparently, these students incorrectly used the material in the codeine sulfate container for preparation of their prescription. Since the original purpose of the study was not to assess product selection, an earlier laboratory on accurate product selection was incorporated into the course to attempt to eliminate this problem. This change appeared to be successful since the laboratory in spring 2004 was set up exactly the same as the previous year. Since the late 1980s, mock dispensing stations were removed at VCU due to federal regulations requiring complete labels on all chemicals present at each station. This change was not expected to significantly impact the training of our students. If the reason for the earlier omission error was failure on the student's part to carefully read the label, it may indicate the importance of mock dispensing stations and methods to verify the presence of the correct drug when providing training in accurate dispensing procedures.[26]

Although this report did not identify the cause of these compounding errors, it did evaluate whether the type of balance used contributed to the observed error. Just prior to the preparation of the 1% caffeine citrate syrup in the spring of 2003 the school was in the process of replacing many of the older class A double pan torsion balances with new class A single pan electronic digital balances. The electronic balances are perceived by students to be easier to use, more accurate, and faster than using the torsion balance. The students were given an opportunity to be trained on the use of the electronic balance; however, no students requested this training. When comparing the percent error in the unacceptable formulations prepared using the 2 balances, there was no statistical difference in the magnitude of the error ($p>0.05$; t test). Also, Table 4 shows that there was no difference in accuracy of the final formulation when using an electronic digital or torsion balance for the acceptable formulations. The primary cause for the compounding errors observed for both prescriptions prepared in this study remains to be identified.

CONCLUSIONS

This study documents the need to objectively and quantitatively evaluate the compounding skills of pharmacy students while in training. However, the results of this study leave many important questions unanswered, ie, how do we improve students' compounding skills? The value of these types of assays are that they can be used to determine whether changes and innovations in the teaching of compounding in schools of pharmacy are really successful.[4-6] There remains a need for inexpensive, rugged, and rapid methods to quantitatively evaluate the compounding of ointments, creams, capsules, etc, by students. However, an important caveat is the use of "putative" active ingredients to be used in the compounding exercise. It should either be a chemical occasionally used in compounding or one that has chemical characteristics comparable to those used in the preparation of extemporaneous formulations.

These prescriptions were compounded by pharmacy students during their first year. At this stage of their education students are relatively unfamiliar with the concepts of compounding and often have had no other dispensing experience. Perhaps an additional time for assessment of the compounding skill of a pharmacy student should be made immediately prior to graduation. At this time students will have had additional opportunities to learn compounding skills during their electives or clinical rotations. A long-term goal of students routinely having their compounded products evaluated would be the incorporation of some type of objective and quantitative assessment of the prescriptions compounded in their practice. The role of compounding in pharmacies provides an important service to many patients. Pharmacy graduates must not jeopardize the health of their patients as a result of inadequate training in the art of compounding.

We assume that the pharmacy students at Virginia Commonwealth University are comparable in background to many students in schools of pharmacy in the United States. These students are not unique in their inability to correctly compound prescriptions, since prior reports on the accuracy of compounded prescriptions by pharmacists across the country are comparable, both in number of formulations failing potency analysis and the range of error observed. This report provides documentation that there is a need to objectively and quantitatively evaluate the competency of students' compounding skills in schools of pharmacy.

REFERENCES

1. *Pharmacy Compounding, The United States Pharmacopeia*, 25th edition. Rockville, MD: The United States Pharmacopiel Convention: 2002:2053-7.
2. *Model State Pharmacy Act and Model Rules of the National Association of Boards of Pharmacy*. Park Ridge, Ill: National Association of Boards of Pharmacy; June, 2003.
3. Lowenthal W. Developing competency statement for a baccalaureate program in pharmacy. *Am J Pharm Educ*. 1978;42:28-30.
4. Wurster K. Revision of a Pharmacy practice laboratory: conversion to a competency-based, modified self-paced, block format. *Am J Pharm Educ*. 1980;44:260-2.
5. Sause RB, Goldberg R, Eisen H. The production of video-taped instructional programs in prescription compounding. *Am J Pharm Educ*. 1982;46:258-60.
6. Newton GD, Tracy TS, Popovich NG. The development and implementation of an integrating pharmacy practice laboratory. *Am J Pharm Educ*. 1990;54:138-45.
7. Newton DW. Compounding paradox: taught less and practiced more. *Am J Pharm Educ*. 2003;67:Article 5.
8. Galson SK. Federal and state role in pharmacy compounding and reconsititution: Exploring the right to mix to protect patients. To Senate committee on Health, Education, Labor and Pensions, Oct. 23, 2003. Available at http://www.fda.gov/ola/2003/pharmacycompound1023.htl. Accessed June 23, 2004.
9. Heinrich J. Prescription Drugs - State and Federal Oversight of Drug Compounding by Pharmacies. US General Accounting Office, GAO-04-195T, Oct. 23, 2003. Available at http://www.gao.gov/cgi-bin/getrpt?GAO-04-195T. Accessed June 23, 2004.
10. Pal S. Prescription sales surpass $182 billion in 2002. *US Pharm*. 2003;28:10.
11. Trissel LA. Compounding our problems – again. *Am J Health-Syst Pharm*. 2003;60:432.
12. Rowles B, Keller SM, Gavin PW. The pharmacist as compounder and consultant. *Drug Intell Clin Pharm*. 1974;8:242-4.
13. Dasta JF, Bonfiglio MF, Rague NG, Shields GJ. Accuracy and variability of intravenous theophylline preparations. *Ther Drug Monitoring*. 1990;12:554-7.
14. Seifert SA, Jacobitz K. Pharmacy prescription dispensing errors reported to a regional poison control center. *J Toxicol Clin Toxicol*. 2002;40:919-23.
15. US Food and Drug Administration, Center for Drug Evaluation and Research, Report: Compounded Drug Products. Available at http://www.fda.gov/cder/pharmcomp/survey.htm. Accessed June 23, 2004.
16. Educational Outcomes. 2004 CAPE Advisory Panel, AACP, 2004. Available at http://www.aacp.org. Accessed June 23, 2004.
17. McGill JE, Holly DR. Integration of pharmacy practice and pharmaceutical analysis: quality assessment of laboratory performance. *Am J Pharm Educ*. 1996;60:370-4.
18. Block JH, Roche EB, Soine TO, Wilson CO. *Topical Agents in Inorganic Medicinal and Pharmaceutical Chemistry*. Philadelphia, Pa: Lea and Febiger; 1974: 301-55.
19. *Weighing on an Analytical Balance: The United States Pharmacopeia*, 25th rev. The National Formulary, 20th ed. Rockville, MD: The United States Pharmacopiel Convention: 2002: 2272-4.
20. Crawford SY, Dombrowski SR. Extemporaneous compounding activities and the associated informational needs of pharmacists. *Am J Hosp Pharm*. 1991;48:1205-10.
21. Prescription Balances and Volumetric Apparatus, The United States Pharmacopeia, 25th rev., and The National Formulary, 20th ed. Rockville, MD: The United States Pharmacopiel Convention: 2002:2227-8.
22. American Society of Hospital Pharmacists. ASHP technical assistance bulletin on compounding nonsterile products in pharmacies. *Am J Hosp Pharm*. 1994;51:1441-8.

23. Pancorbo SA, Campagna KD, Devenport JK, et al. Task force report of competency statement for pharmacy practice. *Am J Pharm Educ*. 1987;51:196-206.
24. General Notices and Requirements, The United States Pharmacopeia, 25th rev., and The National Formulary, 20th ed. Rockville, Md: The United States Pharmacopiel Convention: 2002:7.
25. Ritter H, Trissel LA, Anderson RW, Moyer LM, Morales JS,Electronic balance as quality assurance for cytotoxic drug admixtures. *Am J Health-Syst Pharm*. 1996;53:2318 –20.
26. Malzone BL, Raymond GG, AACP Industry Advisory Committee Report, Pharmacy/Dispensing Laboratory Manufacturer Products Resource Survey. *Am J Pharm Educ*. 1993;57:50S-53S.

Appendix 1. Assay Methodology

Instruments and Materials

The UV/Visible spectrum was obtained on a UV-1601 PC UV-Vis Spectrophotometer (Shimadzu, Kyoto, Japan). All other spectrophotometric assays were run on a Spectronic 21D Single Beam Spectrophotometer (Milton Roy, Ivyland, PA). The potassium permangenate ($KMnO_4$) was obtained from Fisher Scientific (Fairlawn, NJ). The cuvettes used for the analysis were borosilicate 12 × 75 mm disposable glass test tubes (Fisher Scientific, Fairlawn, NJ). The pneumatic pipette used was a P5000 Pipetman (Gilson Inc., Middletown, WI) and the vortex device was a Type 37600 Mixer (Thermolyne Corp. Dubuque, IA). The torsion balances used were Model Torbal DRX-3 (Ohaus, Pine Brook, NJ) and the electronic digital balances were Model PB-S, PB153-S (Mettler Toledo, Inc., Columbus, OH). The HPLC used in the study was a Waters® Alliance™ 2690 separation module connected to a Waters® 996 photodiode array detector (Waters Inc., Millford, MA). The column was a Hypersil® Elite ODS, 150mm × 4.6mm I.D., 5µm particle size (Alltech Associates, Inc., Deerfield IL) using a mobile phase of 26% Acetonitrile (v/v) in 0.01M H_3PO_4 at a flow rate of 0.6ml/min. The injection volume was 1µL with UV detection at 290nm.

Assay for Potassium Permangenate

The absorbance of $KMnO_4$ solutions at 0.31 (1:20,000), 0.42 (1:15,000), 0.51 (1:12,500), 0.63 (1:10,000), 0.84 (1:7,500), and 0.90 (1:7,000) mM were measured at 525 nm ($\varepsilon = 2330 \pm 80$) after 0.75, 2.5, 23, 50, and 192 hours. At concentrations of $KMnO_4$ of 0.90 mM (1:7000) the absorbance at 525 nm were obtained after diluting 1.0 ml of $KMnO_4$ solution with 2.0 ml of deionized water, mixing, then reading at 525 nm. Using the absorbance at 525 nm the concentrations from 0.31 – 0.84 mM a plot of absorbance versus concentration was linear (slope = 2.330 ± 0.113, $y_{int} = 0.011 \pm 0.056$, $r^2 = 0.998$). At concentrations of 0.90 mM or greater the reading were >1.999 absorbance units and required dilution prior to reading. The precision for a 0.51 mM solution at 525 nm was 0.52% (%CV, n=8). A calibration standard of $KMnO_4$ was prepared at the start of the week before the laboratory started. The absorbance of the standard solution was stable for 8 days when stored in the dark. The instrument was checked for a zero reading using a cuvette of purified water after each measurement.

Assay for Citrated Caffeine in Syrup

The HPLC procedure was able to directly measure a high concentration of caffeine dissolved in a viscous syrup. Standard solutions containing 5mg/ml, 10mg/ml, 15mg/ml, and 20 mg/mL were prepared by accurately weighing caffeine citrate into a volumetric flask, dissolving in a small amount of water and then making to volume with simple syrup. A standard curve was generated. Three additional 10 mg/mL citrated caffeine solutions were prepared in simple syrup and assayed as quality control standards. Typical calibration data from the first year revealed that caffeine eluted at 3.42±0.0 min. The method was linear from 5.0-20.0 mg/ml caffeine citrate. The slope was 11839 and a y-intercept of 8110 with a correlation coefficient (r^2) of 0.9978. The intra- and inter-day precision of ± 1.01% (n=13) and ± 1.8% (n=20), respectively. The mean accuracy (expressed as a percent difference from nominal) was 1.2%. To evaluate reproducibility of the assay, the 10mg/ml sample was repeatedly assayed after every ten student samples.