

## RESEARCH

# Impact of Required Versus Optional Remake of a Preparation on Pharmacy Students' Compounding Accuracy

Elizabeth L. Alford, PharmD<sup>a</sup>, and Robert P. Shrewsbury, PhD<sup>b</sup>

<sup>a</sup>Le Bonheur Children's Hospital, University of Tennessee Health Science Center, Memphis

<sup>b</sup>Eshelman School of Pharmacy, University of North Carolina at Chapel Hill

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**Objective.** This retrospective study investigated the impact of a required vs an optional remake requirement 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 over a 3-year period were compared for differences in the analyzed content of the active principal ingredient and the number of students who successfully compounded the preparation on the first attempt.

**Results.** Students' compounding accuracy was significantly better for the ketoprofen (pluronic lecithin organogel [PLO]) emulsion ( $p = 0.003$ ) and mock co-enzyme Q10 troches ( $p < 0.001$ ) when remaking an inaccurate preparation was optional rather than required. There were no significant differences in the parameters for the other compounded preparations.

**Conclusion.** Student performance did not decrease when students were given the option to remake an inaccurate preparation. Factors such as the difficulty of the preparation, time spent compounding, and impact on the student's final course grade also may have influenced student performance.

**Keywords:** compounding, preparation analysis, assessment

## INTRODUCTION

The art and science of compounding is unique to the pharmacy profession, and for this reason, colleges and schools of pharmacy often include practical compounding laboratories in the curriculum to ensure student competency in this area. The American Association of Colleges of Pharmacy Council of Sections convened a task force to assess compounding education within the curriculum of its member institutions partly because there is not a national standardized compounding curriculum.<sup>1</sup> The report showed that the amount of training a student receives in compounding education depends on the individual institution's curriculum.

A fundamental requirement of any compounding education curriculum is the assessment of student abilities. Several assessment methods can be used, such as physically observing the student while performing a compounding operation, reviewing a laboratory report in which the student describes what was done and/or observed during a compounding operation, conducting an analytical

procedure of the finished compounded preparation, measuring a physical attribute of the finished preparation, or a combination of these techniques.<sup>2</sup>

Although some pharmacy educators feel that every college and school of pharmacy should use analytical testing in compounding courses to encourage accuracy,<sup>3</sup> only a few institutions appear to be doing this. In a study by Kadi and colleagues, students completed 2 different preparations, a potassium permanganate aqueous solution and a citrated caffeine syrup, that were each analyzed using a spectrophotometric assay. Approximately 46% and 22% of the preparations were not within  $\pm 10\%$  of the nominal concentration on the students' first attempt at compounding the solution and the syrup, respectively.<sup>4</sup>

The curriculum at the University of North Carolina Eshelman School of Pharmacy includes a compounding component integrated within the 5-semester Pharmaceutical Care Laboratory course sequence. The compounding component leads the students through a series of approximately 26 compounding exercises covering most of the dosage forms used in contemporary pharmacy compounding practice. The assessment tools used include laboratory report documentation, direct observation of the student's compounding techniques, measuring physical attributes of the finished preparation, and analyzing

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**Corresponding Author:** Robert P. Shrewsbury, PhD, Eshelman School of Pharmacy, University of North Carolina at Chapel Hill, 301 Pharmacy Lane, Chapel Hill, NC 27599-7574. Tel: 919-962-0093. E-mail: bob\_shrewsbury@unc.edu

the compounded preparation for the content of the active principal ingredient. The pharmaceutical analysis of the compounded preparations is carried out using spectrophotometric assays or high performance liquid chromatography (HPLC) procedures.

For several years, the preparation analyses were used as the basis for assigning a grade for the compounding exercise. Typically, the preparation analysis accounted for 50% of the student's grade, with the other 50% consisting of the accuracy of the label and laboratory report, as well as the student's counseling abilities. Students received either the full score or a zero grade, dubbed the "analysis requirement," depending on whether their preparation was within an acceptable standard range (typically  $\pm 10\%$  of the label amount or concentration of the active principal ingredient). If the preparation was outside the range, the student was required to remake the preparation to receive the full score. After several years of requiring students to remake an inaccurate preparation, students were given the option to remake the preparation. The objective of this retrospective study was to determine the impact of changing the remake analysis requirement to an optional remake provision.

## METHODS

There is no means to directly measure student effort in making a compounded preparation. However, we hypothesized that student effort could be inferred by examining the analytical data when a required remake was enforced versus when an optional remake was in place. Students may be less diligent when a less stringent assessment is used. A larger variation in the preparation active principal ingredient analysis and the number of students who successfully compounded the preparation on the first attempt might reflect a decrease in a student's attention to detail, carefulness in measuring ingredients, etc. Thus, this information was collected for several compounded preparations and reviewed to determine if student diligence decreased. The preparations reviewed in this study cover a span of 3 years, and were selected from all of the preparations analyzed during that period to give a range of simple to complex preparations. In both the cases of required and optional remakes, students were aware of their grade on the first attempt.

The selected preparations were compounded during the regularly scheduled pharmaceutical care laboratory courses. Appendix 1 provides the formulations used and the method used to compound the preparations. The same preparations were made over the study years, and the same analytical techniques and equipment were used to analyze the preparations. A correctly compounded preparation was considered to have an active principle ingredient

strength within  $\pm 10\%$  of the theoretical strength. All analytical procedures were developed in-house by the course instructor. A detailed description of the analysis process used for each preparation is also provided in Appendix 1.

The variation of each compounded preparation in the years when the required or optional remake policy was in force was compared by calculating the mean and standard deviation of the student results. A *z* test was used to test for significant differences in the analysis results because the variance was known. Another measure of the variation was the number of students who compounded the preparation correctly on the first attempt using  $\pm 10\%$  of the theoretical active principal ingredient strength as the criteria for an accurately compounded preparation.

## RESULTS

Table 1 shows the number and percentage of students who accurately compounded the preparation on the first attempt within  $\pm 10\%$  of the labeled active principal ingredient strength. Ninety-eight students (84% of the total number of students compounding the formulation) made diphenhydramine syrup within expected parameters when the remake was required vs 101 students (81%) when the remake was optional. Ibuprofen was compounded within expected parameters by 69 (58%) and 53 (44%) students when the remake was required and optional, respectively. A ketoprofen PLO emulsion was compounded within expected parameters by 20 (17%) and 49 (42%) of students when the remake was required and optional, respectively. Seventy-three (61%) and 38 (32%) students compounded a hydrocortisone stick within expected parameters when the remake was required and optional, respectively.

Table 1. Comparison of Pharmacy Students' Compounding Results When Remake Was Required and Optional in a Course (N = 124)<sup>a</sup>

Preparation	Acceptable <sup>b</sup> Compounding Completed When Remake Was Required, No. (%)	Acceptable Compounding Completed After Remake Became Optional, No. (%)
Diphenhydramine	98 (84)	101 (81)
Ibuprofen	69 (58)	53 (44)
Ketoprofen	20 (17)	49 (42)
Hydrocortisone	73 (61)	38 (32)
Niacin	48 (41)	87 (75)
Mock Co-Enzyme Q10	17 (15)	41 (39)

<sup>a</sup> Number of students enrolled varied between 105 and 124 depending on class and semester.

<sup>b</sup> Within  $\pm 10\%$  of labeled strength.

Forty-eight (41%) and 87 (75%) students compounded a niacin suspension within expected parameters when the remake was required and optional, respectively. Seventeen (15%) and 41 (39%) students compounded a mock co-enzyme Q10 troches within expected parameters when a remake was required or optional, respectively.

Table 2 compares the resultant analytical concentrations when a remake was required and optional using the analytically determined active principal ingredient amount for the compounded preparations. For the diphenhydramine syrup, the students' performance was not significantly different whether the remake was required ( $2.5 \pm 0.5$  mg/mL) or optional ( $2.5 \pm 0.6$  mg/mL). There were also no significant differences in student accuracy in preparing the ibuprofen effervescent powder when the remake was required ( $4.0 \pm 0.9$  g/50 g) vs optional ( $4.2 \pm 0.6$  g/50 g). Students' accuracy in preparing the ketoprofen PLO emulsion was significantly higher when a remake was optional ( $0.9 \pm 0.2$  g/10 mL) than when it was required ( $0.7 \pm 0.2$  g/10 mL;  $p = 0.003$ ). For the hydrocortisone medication stick, there were no significant differences in student accuracy when a remake was required ( $2.5\% \pm 0.5\%$ ) vs optional ( $2.7\% \pm 0.6\%$ ). No significant differences in preparation were found in the niacin suspension when the required remake data ( $5.4 \pm 0.9$  g/150 mL) and optional remake data ( $5.2 \pm 0.5$  g/150 mL) were compared. There was a significantly better performance on the mock co-enzyme Q10 troches when the remake was optional ( $2.7 \pm 0.5$  g) instead of required ( $1.9 \pm 0.3$  g;  $p < 0.001$ ).

## DISCUSSION

Student performance in compounding did not differ when remaking the preparation was optional or required. This was clearly evident in 4 of the formulations (diphenhydramine syrup, ibuprofen effervescent powder, hydrocortisone stick, and niacin suspension). In compounding the ketoprofen PLO emulsion and mock co-enzyme Q10 troche formulations, the preparations of the groups who

were required to remake them were outside of the expected  $\pm 10\%$  range. However, the preparations of those in the optional remake groups were at the limits of the range. This might suggest that students' compounding was more accurate when an optional remake policy was in force. It might also suggest some variability in year-to-year class data. One possible source of variability in the study could be differences in the ingredients used from year to year. To minimize this variability, in-date preparation ingredients from reputable vendors were used each year. Also, standard curves were used for each group of preparations for all active principal ingredient data included in this study.

The number of students within  $\pm 10\%$  of the labeled active principal ingredient strength was highest for the diphenhydramine syrup, as shown by an 84% and 81% success rate for the required and optional remake groups, respectively (Table 1). In addition, there was a small deviation from the expected active principal ingredient concentration of 2.5 mg/mL for both the required and optional remake groups (Table 2). Because the diphenhydramine syrup was the first preparation that students made during the Pharmaceutical Care Laboratory course sequence, students were more likely to pay close attention to this compound and put forth their best effort. In addition, the overall student workload was lighter at the beginning of the semester; thus, students may have been willing to devote more time toward compounding the preparation.

Interestingly, almost twice as many students correctly compounded the ketoprofen PLO emulsion, niacin suspension, and mock co-enzyme Q10 troches when the remake was optional rather than required (Table 1). In addition, the expected active principal ingredient content for these 3 preparations was significantly closer to the middle of the expected  $\pm 10\%$  range (Table 2). Such a performance when a remake was optional rather than required was not intuitively expected. However, many factors may have contributed to this outcome such as: (1) the time in the semester the compound was done (eg, did

Table 2. Comparison of Analytical Concentrations for Required Versus Optional Remakes in a Laboratory Compounding Course

Preparation	Expected Amount ( $\pm 10\%$ Range)	Required Remake, Mean (SD) <sup>a</sup>	Optional Remake, Mean (SD)	<i>P</i> <sup>b</sup>
Diphenhydramine, mg/mL	2.5 (2.2 - 2.8)	2.5 (0.5)	2.5 (0.6)	0.99
Ibuprofen, g/50 g	3.9 (3.5 - 4.3)	4.0 (0.9)	4.2 (0.6)	0.36
Ketoprofen, g/10 mL	1.0 (0.9 - 1.1)	0.7 (0.2)	0.9 (0.2)	0.003
Hydrocortisone, %	2.5 (2.3 - 2.8)	2.5 (0.5)	2.7 (0.6)	0.64
Niacin, g/150 mL	5.0 (4.5 - 5.5)	5.4 (0.9)	5.2 (0.5)	0.016
Mock Co-Enzyme Q10, g	2.4 (2.2 - 2.6)	1.9 (0.3)	2.7 (0.5)	<0.001

<sup>a</sup> Mean (standard deviation) of student preparation active principal ingredient results.

<sup>b</sup> *p* = difference between required and optional remake groups.

students have more time early in the semester?); (2) the point in the 5-semester laboratory course sequence at which the compounding was done (eg, did students have more compounding experience?); and (3) students' motivation level (eg, were students more self-motivated when the remake was optional rather than required?). More students accurately compounded the hydrocortisone medication stick and ibuprofen effervescent powder when the remake was required, as shown in Table 1 and Table 2. Students often perceive these 2 preparations as the most time-consuming compounds because of the large number of ingredients that must be weighed. Perhaps students were more likely to spend more time accurately compounding these preparations on the first attempt when a remake was required because they did not want to have to spend an immense amount of time remaking the preparation at a later date.

Other colleges and schools of pharmacy have investigated the use of an analysis requirement or assessment tool for pharmaceutical compounding courses.<sup>3</sup> Unfortunately analytical testing is not conducted in most pharmacy schools. As a result, students cannot identify the sources of error affecting the quality of their compounded preparations and may wrongly believe that their compounding techniques are appropriate. Instituting an analysis requirement ensures that students receive feedback regarding their compounding performance, which is beneficial for future pharmacy practice.

Although an analysis requirement is a beneficial assessment tool, it also carries some burdens. The equipment for analysis can be a costly investment. Furthermore,

requiring students to remake compounded preparations incurs an additional cost to operating the compounding laboratory course. The analysis process can also be time consuming, especially with a large class size. Because of this, auxiliary staff members may be necessary to decrease the turnaround time to provide feedback to students, and paying for the extra staff members would increase the overall operating budget of the laboratory course and the workload of the laboratory coordinator.

## CONCLUSIONS

The type of remake requirement for a compounding exercise did not affect student performance in terms of preparation content. However, the perceived difficulty of making the preparation, time spent compounding, and impact on the student's final course grade may influence student performance. Future investigation of factors other than required or optional remake provisions should be conducted to further examine student performance in compounding laboratory courses.

## REFERENCES

1. Shrewsbury R, Augustine S, Birnie C, et al. Assessment and recommendations of compounding education in AACP member institutions. *Am J Pharm Educ.* 2012;76(7):Article S9.
2. Eley JG, Birnie C. Retention of compounding skills among pharmacy students. *Am J Pharm Educ.* 2006;70(6):Article 132.
3. Almoazen H. Why analytical testing is needed in pharmaceutical compounding [letter]. *Am J Pharm Educ.* 2010;74(2):Article 32.
4. Kadi A, Francioni-Proffitt D, Hindle M, Soine W. Evaluation of basic compounding skills of pharmacy students. *Am J Pharm Educ.* 2005;69(4):Article 69.

### Appendix 1. Methods of Preparation and Analysis for the Compounded Preparations

#### DIPHENHYDRAMINE SYRUP

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##### Diphenhydramine Syrup

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Diphenhydramine Hydrochloride	250 mg
Glycerin	5 mL
Simple Syrup NF	30 mL
Vanillin Alcoholic Solution 67mg%	0.2 mL
Distilled Water	q.s. 100 mL
Mix and make Syrup	

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#### Method of Preparation:

1. Weigh the diphenhydramine HCl in a weigh boat.
2. Transfer the powder into a 150 mL beaker.
3. Using a 5 mL syringe, transfer the glycerin into the beaker.
4. Using a 1 mL syringe, transfer the vanillin solution into the beaker.
5. Using a graduated cylinder, measure and transfer the simple syrup.
6. Add a portion of water, put in a stirring bar, and stir the mixture gently until solution occurs.

7. Transfer the mixture into a calibrated prescription bottle.
8. Rinse the beaker with portions of water, adding each portion to the prescription bottle.
9. Bring the solution to final volume.

### Process of Analysis

One (1) mL samples of the student preparation were taken without shaking the preparation, and diluted for high-performance liquid chromatographic (HPLC) analysis. For the HPLC analysis, the mobile phase consisted of 750 mL methanol, 50 mL tetrahydrofuran, 5.8 g sodium dioctyl sodium succinate and 1 mL of 85% phosphoric acid adjusted to pH 4.6. A 4.6 x 250 mm C18 10 $\mu$  column was used with a flow rate of 1.4 mL/min. The detector wavelength ( $\lambda$ ) was set at 265, and the injection volume was 25  $\mu$ L. The expected concentration of the student preparation was 2.5 mg/mL.

### IBUPROFEN EFFERVESCENT POWDER

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#### Ibuprofen Effervescent Powder

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Ibuprofen	400 mg/tsp
Sodium Bicarbonate	52.4%
Citric Acid Monohydrate	28.6%
Tartaric Acid	19%
Mix and make Effervescent Powder	

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#### Method of Preparation:

1. Accurately weigh the powders.
2. Combine the powders using geometric dilution.
3. Sieve through a 40 mesh, 5" sieve.
4. Package in airtight container.

### Process of Analysis

Ibuprofen effervescent powder has a bulk density of 1.03 g/mL. From this information, 400 mg/tsp of ibuprofen would be contained in 5.15 g of the preparation, assuming that a teaspoon is equivalent to 5 mL. For each student sample, 0.3 g of the preparation was taken from the top of the container. Ten mL of water was added and when the effervescence stopped, 10 mL of methanol was added. The sample was then hand shaken and injected into the HPLC.

For the HPLC analysis, a mobile phase of 400 mL citric acid and sodium hydroxide buffer and 600 mL acetonitrile was used. A 4.6 x 250 mm C18 10 $\mu$  column was used with a flow rate of 1.1 mL/min. The detector wavelength ( $\lambda$ ) was set at 254 and the injection volume was 30  $\mu$ L. The expected amount of ibuprofen was 3.88 g in 50 g of the effervescent powder preparation.

### KETOPROFEN PLO EMULSION

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#### Ketoprofen PLO Emulsion

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Ketoprofen	10%
Ethoxy Diglycol	2.2 mL
Lecithin Syrup	2 mL
Pluronic F-127 20% Gel	q.s. 10 mL
Mix and make PLO Emulsion	

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#### Method of Preparation:

1. Accurately weigh the ketoprofen in a weigh boat.
2. Add ethoxy diglycol to the weigh boat to solubilize the ketoprofen.
3. Transfer the weigh boat contents to a Luer-Lok syringe. Use portions of lecithin syrup to rinse the weigh boat. Add each rinse to the Luer-Lok syringe. Determine the volume of material in the syringe.
4. Draw up the appropriate volume of Pluronic gel in another Luer-Lok syringe.
5. Carefully remove air from both syringes.
6. Attach a Luer-to-Luer connector to the two syringes, and transfer the emulsion back-and-forth between the syringes until well mixed.
7. Package in an appropriate container.

### Process of Analysis

The students compounded 10 mL of preparation and then dispensed the preparation in individual 1 mL oral syringes. The ketoprofen PLO emulsion was analyzed by dissolving a 0.5 mL sample in 20 mL of tetrahydrofuran and reading in a spectrophotometer at a wavelength ( $\lambda$ ) of 340. The expected number of grams in the 10 mL of preparation was 1.0 g.

### HYDROCORTISONE MEDICATION STICK

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#### Hydrocortisone Medication Stick

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Hydrocortisone	2.5%
Beeswax	30%
Cetyl Esters Wax	30%
Mineral Oil (Heavy)	40%
Mix and make Application Stick	

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#### Method of Preparation:

1. Accurately weigh the powders.
2. Heat to melt the beeswax.
3. When the beeswax is melted, reduce the heat and melt the cetyl esters wax. Use a stirring rod, not a stirring bar.
4. When the cetyl esters wax is melted, remove from heat, add the hydrocortisone and use the mineral oil to rinse the weigh boat.
5. When the hydrocortisone has dispersed in the waxes, cool the mixture until it is “just warm to the back of the hand.”
6. Fill the application stick.

### Process of Analysis

Students made 50 g of the hydrocortisone medication stick preparation. A 250 mg sample was removed from the top of the stick, dissolved in 20 mL of tetrahydrofuran, hand-shaken, and left overnight. One (1) mL of this solution was further diluted with 10 mL of tetrahydrofuran and read in a spectrophotometer at a wavelength ( $\lambda$ ) of 242. The expected percentage in the stick preparation was 2.5% hydrocortisone.

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#### Niacin Suspension

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Niacin	5 g
Cetylpyridinium Chloride	0.015 g
Xanthan Gum	0.23 g
Purified Water	45 mL
Suspension Structured Vehicle NF	q.s. 150 ml
Mix and make Suspension	

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#### Method of Preparation:

1. Accurately weigh the niacin and xanthan gum.
2. Add the cetylpyridinium chloride stock solution and the water to a small beaker. Create a small vortex with a stirring bar and slowly sprinkle in the xanthan gum. Allow each addition to dissolve before adding the next addition.
3. Triturate the niacin to create a uniform particle size.
4. Sprinkle niacin into the solution vortex.
5. Add a portion of the Suspension Structured Vehicle into the solution vortex.
6. Transfer the suspension from the beaker to a calibrated plastic prescription bottle.
7. Continuously rinse the beaker with Suspension Structured Vehicle, adding each rinse to the prescription bottle until the required volume is reached.

### Process of Analysis

Niacin suspensions were analyzed by HPLC using an aqueous mobile phase containing 30% acetonitrile, 0.1% phosphoric acid, and 0.1% sodium lauryl sulfate. A 4.6 x 250 mm C18 10 $\mu$  column was used with a flow rate of 1.5 mL/min. The detector wavelength ( $\lambda$ ) was set at 254. The expected concentration of the student preparation was 5.0 g of niacin per 150 mL of suspension.

## **MOCK CO-ENZYME Q10 TROCHES**

### **Mock Co-Enzyme Q10 Troches**

Tartrazine (substituted for co-enzyme Q10)	2.4 g
Aspartame	0.55 g
Silica Gel	0.24 g
Polyethylene Glycol 1450	28 g
Acacia	0.5 g
Citric Acid Monohydrate	0.7 g
Flavoring Oil	2-3 drops
Mix and make Soft Lozenge	

### **Method of Preparation:**

1. Turn on the low temperature hotplate to about 60°C.
2. While hotplate heats, accurately weigh ingredients.
3. Place the PEG 1450 into a small beaker (~ 100 mL) and begin heating. DO NOT ADD A STIR BAR AT THIS POINT.
4. Mix the remaining powders using the geometric dilution technique in the mortar using the pestle.
5. Pass the powder mixture through a 40 mesh sieve onto a glassine sheet.
6. Once the PEG 1450 has melted, add a stir bar, and set at lowest spin rate.
7. Sprinkle the powders into the melted PEG 1450 ensuring each addition is wetted before adding additional powder.
8. While adding the powders, turn the heat off.
9. Once the powders have been added to the PEG 1450, remove the beaker, allow to cool until it is “just warm to the back of the hand.”
10. Add flavoring and stir with glass stirring rod.
11. Pour the mixture into the mold beginning at the B2 position, and pour quickly, overfilling each cavity.
12. Move a spatula over the mold just touching the melted powder mixture. Do not touch the mold. This will spread the mixture evenly over the mold, and still allow each cavity to be overfilled.
13. When the mixture has solidified in the mold, “polish” the surface with a hot air gun.
14. Once the polish has hardened, add a piece of wax paper on top of the troches, and complete the package.

### **Process of Analysis**

One troche that appeared to be complete was selected from the student preparation and dissolved in a pH 10 buffer that was a mixture of 60% of a solution containing 12.37 g boric acid and 100 mL of 1.0 N sodium hydroxide per liter, and 40% 0.1N sodium hydroxide, and left overnight. The supernatant was read in a spectrophotometer at a wavelength ( $\lambda$ ) of 530. The expected number of grams of tartrazine in the troche preparation was 2.4 g.