

# The Art of Compounding Revisited

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## INTRODUCTION

Historically, the physician and pharmacist were one and the same. Since there was no pharmaceutical industry until relatively recently, all medications were compounded extemporaneously. In the United States, pharmaceutical manufacturers began to develop prefabricated dosage forms in the latter 1800s. Nevertheless, extemporaneous compounding remained a principal activity of the retail pharmacist. As we progressed into the twentieth century, ready-made medicines proliferated exponentially until, by the end of World War II, they became more the rule than the exception (1).

By the 1960s, the great majority of medicines were available in pre-made form. The need for extemporaneous compounding in both retail and hospital practice declined and became a minimal part of the pharmacist's daily activity. This was followed by a de-emphasis on compounding in many pharmacy curricula.

In the 1970s and 1980s, the profession started to see a resurgence of the art of compounding in a different form. Pharmacists began applying their knowledge and training to compound most of the parenteral dosage forms used in hospitals. Today, intravenous admixture programs are an integral part of pharmacy services in most hospitals. The advent of pharmacokinetic programs and the use of automated drug delivery devices has resulted in an expansion of the pharmacists' role in compounding in the institutional setting (2).

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Today, many retail practitioners have noticed an increase in extemporaneous compounding, either "from scratch" or by alteration of prefabricated dosage forms. The emphasis on home health care has spurred the expansion of sterile products compounding out of the institutional setting and into the retail setting. The progressive shift of the profession to a more clinical orientation has resulted in a focus on optimization of drug therapy. This has led to individualization of drug dosage forms and thus to an increase in extemporaneous compounding. It has been predicted that one of the major characteristics of pharmacy practice in the current decade and beyond will be a return to extemporaneous compounding (3, 4).

### ***AN EXTEMPORANEOUS COMPOUNDING LABORATORY***

Based on this overview of the current status of extemporaneous compounding, as well as comments from practitioners that today's students are deficient in compounding skills, the authors have chosen to reemphasize extemporaneous compounding in the dispensing laboratory taught in the fourth professional year at South Dakota State University's College of Pharmacy. It was decided that the fundamentals of compounding would be reviewed using an active "thinking through" approach rather than by presenting the students with a "cookbook style" set of specific directions. This would allow the students to use a scheme for extemporaneous compounding in which they had to abstract and combine individual compounding techniques and physical pharmacy principles that are often discussed as separate entities in pharmaceuticals courses.

#### ***Lecture***

The format used was introduction of the exercises, with a lecture prior to the first compounding session. The lecture included:

- An overview of extemporaneous compounding (including stability and expiration date considerations)
- The driving forces for increased compounding
- Pharmacist resistance and how to overcome it

- Sources and costs of equipment
- Sources and government restrictions on availability of chemicals
- The compounding vs. manufacturing issue (5-7).

The lecture ended with the presentation of seven questions that should be answered before compounding is begun:

### ***Extemporaneous Compounding: A Systematic Approach***

1. Read the prescription thoroughly!  
(Is it reasonable and appropriate?)
2. What type of product is to be prepared?  
(Solid or liquid, suspension or emulsion, etc.)
3. What are the characteristics of the ingredients?  
(Use references, don't guess!)
4. What, if any, additional materials are needed?  
(Adjuncts for emulsification, flavoring, etc.)
5. What is the order of mixing?  
(Like added to like, heat to liquify, etc.)
6. What, if any, special equipment is needed?  
(Is it available or are there substitutes?)
7. What is the procedure for preparation?  
(List the steps in order.)

### ***Discussion of Sample Prescriptions***

An interactive discussion of the two sample prescriptions followed, using the systematic approach of seven questions. A short summary of these discussions follows the sample prescriptions below. Instructor comments are included in parentheses.

#### ***Sample Rx #1: An Emulsion Base***

Carbowax 4000	6.7
Stearyl alcohol	11.3
Glycerin	10.0
Na lauryl sulf	0.3
Water	5.0

1. The requested product seems reasonable as a base to be used for the incorporation of an active ingredient or simply as an emollient.

2. The product to be prepared is an emulsion, which may be either liquid or semisolid.

3. The Carbowax 4000 and the stearyl alcohol are both relatively high molecular weight, solid, lipid materials. The sodium lauryl sulfate is a solid, anionic detergent used to form an emulsion. Glycerin is a viscous, highly polar liquid that serves as a cosolvent and provides emollient action. (In trying to assess the characteristics of the materials, students tended to classify *stearyl alcohol* as a water soluble liquid. This mistake was useful in emphasizing the importance of using references.)

4. Sodium lauryl sulfate may serve as an emulsifying agent; therefore, additional materials probably will not be needed.

5. The lipid materials should be mixed together using heat to liquify the solids. The highly polar materials should be dissolved in the aqueous cosolvent system. The two phases should then be mixed to form the emulsion.

6. The equipment needed includes: two beakers, stirring rod, and hot plate. A thermometer would be useful. No special equipment is required.

7. Procedure:

- a. Weigh or measure all ingredients.
- b. Melt the Carbowax 4000 in a beaker using the lowest temperature possible.
- c. Add the stearyl alcohol to the melted Carbowax and reduce the temperature.
- d. Mix the water and glycerin in the second beaker.
- e. Add the sodium lauryl sulfate and stir to dissolve.
- f. Heat the aqueous mixture to approximately the same temperature as the Carbowax and stearyl alcohol mixture.
- g. Slowly combine the two mixtures, stirring.
- h. Continue stirring until the emulsion forms and the product has cooled.
- i. Package and label the product.

(The instructors noted during the discussion and in subsequent laboratory exercises that the students tended to take the simplistic

approach of desiring to prepare all prescriptions by mechanical mixing. This provided the opportunity to emphasize consideration of the characteristics of the ingredients.)

**Sample Rx #2: Sucralfate Suspension (8, 9)**

Sucralfate	1g (use 1g commercial tab)
Sorbitol 70%	25%
Water	qs 15ml

1. This product is reasonable if a dose other than 1g is to be administered or if a liquid dosage form is appropriate for a specific patient.

2. The product to be prepared is a suspension. (It was necessary to review characteristics of tablets and their ingredients, since the initial response was that the product would be a solution.)

3. Sucralfate, a water insoluble basic aluminum sucrose sulfate, is a disaccharide used as an antiulcer agent. Sorbitol is a water soluble sugar alcohol that functions as a sweetener and slightly increases the viscosity of a solution. Water is the solvent or carrier.

4. It was suggested that a suspending agent might be useful to ensure even distribution and accurate dosing. Consensus was reached that, for small volume extemporaneous preparation, trying to determine a suitable suspending agent would require an inordinate amount of time for experimentation. Therefore, it was decided that a "Shake Well" label would be adequate. (This provided the opportunity to emphasize the use of references, in this case ASHP's *Handbook on Extemporaneous Formulations*. The instructors pointed out that this reference provides compounding instructions, stability information, and the recommendation *not* to use common suspending agents such as acacia or tragacanth.)

5. Since the sucralfate cannot be separated in a practical manner from the excipients in the tablet, the entire content of the commercially available dosage form should be combined with the solvent/carrier. Heat will not be necessary because the desired product is a suspension rather than a solution.

6. No special equipment is required.

7. Procedure:

- a. Triturate the commercially available dosage form in a mortar.
- b. Transfer the resultant powder to an appropriately sized, calibrated dispensing container.
- c. Add the calculated amount (3.75ml/dose) of sorbitol solution.
- d. QS with water to the final volume.
- e. Shake well and label.

### *Compounding Exercises*

During the remaining time in the first compounding laboratory session, each student was assigned one prescription to prepare. For each product, the student was required to hand in a completed report form (see Addendum).

In each of the three subsequent compounding exercises, each student was assigned three prescriptions. The prescriptions included a mixture of traditional, or classical, compounding as well as compounding using commercially available dosage forms. Assignments were made in such a manner that each student received prescriptions of approximately equal difficulty. A report form was required for each prescription.

### *CONCLUSION*

From observation of the students' approach to compounding, the quality of the products, and the results of the student course evaluations at the end of the semester, the instructors were able to draw several conclusions:

- Those students who had had fairly extensive compounding experience/instruction during their summer internships adapted readily to this method and produced excellent products.
- Those students without such experience tended to shortcut the problem-solving approach by plunging right in without using references or thinking through the steps carefully beforehand. The products produced by these students covered a wide spectrum from poor to excellent.
- The student evaluations indicated that some of the students felt the necessity of more instruction with respect to the individual prescriptions prior to the laboratory exercises.

- The prescriptions that posed problems for a significant number of the students were discussed in class following the laboratory exercise. However, based upon the above observations and responses, the instructors think that, in the future, it will be more productive to discuss more of the prescriptions with the students prior to the actual compounding.

In summary, the authors have expanded the laboratory exercises addressing extemporaneous compounding, in both the traditional or classical sense and the alteration of commercially available dosage forms. They have provided a seven-step, systematic problem-solving approach to compounding that is appropriate for and adaptable to any practice setting.

## REFERENCES

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## ADDENDUM

## Prescription Practice Compounding Report

## EXERCISE #

Directions: Prepare the assigned prescription. Package and label it appropriately for dispensing. Fill in the indicated information on this report form and turn in the report form with the product.

Patient: (Yourself) \_\_\_\_\_

Doctor: (Your choice) \_\_\_\_\_

Date: (Today) \_\_\_\_\_

Section: \_\_\_\_\_

Rx

Sig:

Type of product:

**Comments:**

**Method of preparation:** Describe in stepwise fashion in such a manner that a 2nd year intern would be able to produce a product comparable to yours. Numbering steps may be helpful. Complete sentences are not required as long as the directions are fully comprehensible.

**Additional Comments:** include information on stability, bioavailability, etc. indicate appropriate auxiliary labels.