



Secundum Artem

*Current & Practical Compounding
Information for the Pharmacist.*

*An ongoing CE Program provided by a grant
from Paddock Laboratories, Inc.*

Tips & Hints for Quality Compounding - Part III

GOALS AND OBJECTIVES

Goal: To provide tips and hints in the practice of pharmaceutical compounding that may save time, money and contribute to a more efficient workplace.

Objectives: After reading and studying the article, the reader will be able to:

1. Discuss the methods available to maintain the integrity of empty and filled gelatin capsules.
2. Describe some methods to enhance the effectiveness and compliance using quick dissolving tablets.
3. Discuss the advantages of a gel-cream over simpler gels or creams.
4. List precautions and procedures involved in packaging, labeling and shipping of compounded preparations.
5. Describe quality assurance practices and counseling activities that can aid the pharmacist to become more efficient and effective.

This is the third issue of *Secundum Artem* covering various tips and hints that can be used by compounding pharmacists. The first appeared in Volume 5 Number 1 (covering solutions, suspensions, emulsions, ointments, creams, pastes, gels, lotions-emulsion-type, powders, capsules, ophthalmics, suppositories, troches/lozenges, flavoring/coloring) and the second appeared in Volume 15 Number 4 (covering the facility, equipment, ingredients, procedures, sterile preparations, beyond-use dates, preservation, sterilization and depyrogenation). These are available for download at www.paddocklabs.com.

This issue will cover tips and hints involving tablets, capsules (additional tips), lollipops, gummy bears, patches, sticks, gel-creams, pastes (additional tips), otics, nasals, packaging and labeling, shipping and distribution, patient counseling and administration, sweeteners and quality assurance practices.

Tablets

- See also Vol. 5 Number 1 Tips and Hints on Powders, Capsules as some apply to Tablets.

General

- In working with tablet compositions, passing the blended powder through a sieve will aid in breaking up clumps, etc.
- For faster formulation development, determine the volume per tablet mold multiplied by the number of tablets to be prepared. Weigh the materials that are of fixed weight and place in a graduated cylinder. Add the desired diluent material to the calculated volume in the graduated cylinder; mix, check the volume again and adjust if necessary. Prepare the tablets. Check their final weights.

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This lesson is no longer valid for CE credit after 12/01/13.

Disclaimer

The content and opinions of this article are those of the author and are for educational purposes only. Although the material is based on review of multiple sources of information, it is not all inclusive of information available. Readers should review and consider other publications and materials on this topic and not rely solely upon the information in this article.

Quick Dissolve Tablets

- A small amount of citric acid will increase salivation upon administration and enhance the disintegration rate.
- Xylitol and mannitol can impart a smoother “mouth feel” to these tablets.
- Coating the active drug particle of poorly tasting drugs can make the preparation more acceptable.
- The greater the percentage of highly water soluble ingredients, generally the faster the disintegration and dissolution rate.

Molded Tablets

- To prepare a smaller number of tablets than what the mold is set, simply “mask off” the unused holes using an index card cut to size and residue-free masking tape.
- To aid in the powders holding together after drying, increase the percentage of water if an alcohol/water system is used.

Sintered Tablets

- Heat control is important; it must be sufficiently hot to melt and fuse the mass together but not so hot that it adversely affects the active ingredient.
- Use convection ovens for sintering, not a microwave.
- Be careful if using plastic molds and confirm they can tolerate the heat level and duration used.

Compressed Tablets

- For small numbers of tablets, prepare them individually using a single punch tableting machine and weighing/filling each portion individually.
- Larger numbers of tablets can be prepared using the hopper and placing the powder in the hopper for a complete run.

Capsules (Additional Information)

- The major cause of customer or patient problems with capsules is generally traced to improper conditions during storage and filling, or inadequate final packaging.
- During shipment empty hard gelatin capsules are often protected from moisture or from exposure to large variations in relative humidity by packing in food grade antistatic plastic bags inside heavy-duty corrugated cartons.
- Ziploc®* containers are great for storing empty capsules. They are easy to see-through for identification, keep capsules easily separated, covered and free of dust.
- Tupperware®** also is a good storage container for empty capsules.
- Purchase an accurate humidity measuring device that is accurate to +/-5% relative humidity. These are available from different supply companies and will

generally cost about \$50 each.

- If filling capsules in a small room 20' x 20', a steam humidifier with a humidistat control, which is available at local hardware stores, can be used with the air jet directed away from the capsules.
- It is important to maintain proper humidity for storage of hard gelatin capsules as they have a moisture content between 13 to 15%.
- Exposure of capsules to high temperatures or cycling between high and low temperatures should be avoided.
- Upon receipt, empty capsules should not be left on the loading dock or in a truck but should be moved inside to proper storage conditions as quickly as received.
- Always inspect your shipment of capsules upon arrival; they should be checked for proper size, whether any capsules are stuck together in clumps that do not come apart or whether they are brittle or shatter very easily during handling or filling. Also, check to see if they are distorted in shape or if the cap is stuck to the body and resist separation. If any of these conditions occur, they should be returned for replacement.
- The proper storage conditions for empty capsules is a relative humidity of about 50% with a range from 40 to 60% and a temperature of 20°C with a range between 15 and 25°C.
- Store capsules away from direct sunlight; away from hot water heating radiators, hot water pipes and steam pipes; on pallets off the ground; away from potential sources of condensation e.g. underwater pipes, but do not store them in freezers.
- If capsules are soft, sticky or don't fit during locking, this can usually be corrected by a dehumidifier and air-conditioning and cooling the air.
- If capsules cling to each other or plastic surfaces due to static electricity, this can generally be corrected by humidifying the air.
- If capsules crack or shatter when pressure is applied, this can generally be corrected by humidifying the air.
- Both empty and filled gelatin capsules should be covered when not being manipulated to minimize moisture loss.
- Bags containing empty capsules should be sealed or tied during shift breaks and shift changes.
- Filled capsules should be stored in plastic containers with lids until they are packed in a final container.
- Capsules should be protected from moisture loss or gain by using at least one layer of plastic packaging such as a bag, bottle, blister pack, etc.
- Do not use a desiccant or other moisture absorbers with capsules as these may absorb moisture from the capsules and cause brittleness.

*Ziploc® is a registered trademark of S.C. Johnson & Sons, Inc.

**Tupperware® is a registered trademark of Tupperware Brands, Inc.

- Eliminate unnecessary headspace in the packaging and avoid the excess use of cotton; do not use cotton that has been treated with furfural as this can interact with the gelatin shell.
- If bottles are packaged for shipment in a cardboard carton, it is often good to add a sheet of corrugated cardboard between the bottle and the bottom of the outer carton to act as a cushion.

Gel-Creams

- See Vol. 5 Number 1 Tips and Hints on Emulsions, Creams, Gels for their application to Gel-Creams.
- Gelling of the aqueous phase of an oil in water emulsion aids in stabilizing the emulsion and minimizes separation; this forms a “gel-cream”.
- Generally, use water-soluble cellulose-type thickening agents for these preparations.
- If a water-soluble drug is to be added, it is generally best to dissolve the drug in a minimum amount of water prior to adding (unless it is not very water soluble).
- Gel-creams can be prepared using electronic mortars/pestles, hand and electric homogenizers and ointment mills.
- When using ointment mills, caution must be observed for the loss of water or alcohol during this process. Water or alcohol may need to be added back into the final preparation to accommodate the loss.
- Like creams, gel-creams can be further diluted to form lotions; the diluent (water or aromatic waters) should be added slowly with sufficient mixing after each addition. Additional preservative may be required to preserve the final preparation or a preserved water can be used.
- Levigating agents, if used, must be compatible with the vehicle used.

Lollipops

- See Vol. 5 Number 1 Tips and Hints on Troches/Lozenges and Flavoring/Coloring for their application to Lollipops.
- Lubricate the molds with a mild, neutral-tasting film of an oil or nonaqueous-miscible liquid.
- Temperature control is critical when preparing the melt to pour into the molds.
- Use commercial candies (flavored) as the base to save time. Be careful heating these, as flavors are volatile and can be lost during preparation of the lollipops.
- Add the active ingredient last to minimize the time at which it is at an elevated temperature.
- If the final lollipops are tacky, dust with confectioners’ sugar.
- If using a microwave, only use the “carousel type” due to hot spots that occur without the carousel.

Gummy Bears

- If tacky, dust with confectioners’ sugar.
- Alternative to molds: Cast onto a glass plate with dam-walls the thickness that is desired; smooth with a glass rod if needed. Once the preparation is cast, then it can be cut into calibrated square pieces or stamped out using a calibrated “cutter” in various shapes.

Patches

- Molds should be selected with the size of the adhesive bandage strip-cover in mind.
- Cast the melt into the selected mold or onto a glass plate with careful attention to the temperature (not too hot-thinning may occur; not to cold-premature thickening may occur).
- Regarding the size of adhesive bandage strips which can be used as the backing, the bandage should expose sufficient adhesive edge to hold the soft patch in place.

Sticks

- See Vol. 5 Number 1 Tips and Hints on Suppositories and Inserts as they apply to medication sticks as well.

Pastes

- See Vol. 5 Number 1 Tips and Hints on Ointments, Pastes for their application to Pastes; new tips and hints are added below.
- When filling multiple containers, soften the paste using low heat to aid in pouring into the final container.
- Measure specific amounts of a paste for application using a small, calibrated melon ball scoop.
- Some pastes can be poured into a cylinder, extruded and sliced into thin wafers for application.

Otic

- See Vol. 5 Number 1 Tips and Hints on Solutions, Suspensions, Ophthalmics for their application to otics.
- Otic dosage forms can include liquids (solutions, suspensions), ointments and powders.
- Inform the patient of whether the otic dosage form is water-miscible or oil miscible as this is important for the patient to understand how to remove the remnants of the dose during later cleaning of the external ear canal.

Nasal

- See Vol. 5 Number 1 Tips and Hints on Solutions, Suspensions, Ophthalmics for their application to nasals.
- Nasal preparations are generally adminis-

tered as “drops” or “sprays”.

- Nasal preparations are generally solutions, suspensions, gels and ointments.
- Sometimes, a spray bottle can be converted to a dropper bottle by removing the dip tube.
- If a longer beyond-use date is needed for aqueous solutions (up to 45 days), package them in smaller quantities and freeze them and instruct the patient to remove one at a time from the freezer for use.
- Systemic effects that may result from nasal absorption of a drug must be considered.

Sweeteners

- Sweetness can be used to transform bad-tasting drugs into acceptable preparations.
- Use sucrose or other sweetener that increases the preparation viscosity if a longer dwell-time or residence time in the mouth is desired.
- Use low concentration sweeteners (artificial, natural) if a more fluid preparation is desired that will exit the mouth more rapidly.
- Stevia can be used to minimize the bitterness taste of many drugs.
- Sorbitol should be used cautiously as it may induce diarrhea in some patients.
- When working with a difficult patient, blank solutions of different sweetening agents can be prepared for the patient to select their preference.

Packaging and Labeling

- Faulty packaging can compromise a quality compounded preparation.
- Potential packaging problems can be encountered with glass (due to its alkalinity; but this depends upon the type of glass) and rubber (as it reacts with many substances).
- Caution should be used in placing any preparation with a pH greater than 7 in glass containers.
- Remember that proper packaging provides protection, presentation, identification, information, containment and convenience.
- Proper packaging can enhance patient compliance.
- The ideal choice, generally, is glass for many solid and liquid preparations for stability purposes.
- The practical choice, generally, is plastic for preparations that are shipped or in households where children may drop and break glass containers.
- For low dose, highly potent and lipophilic drugs, potential sorption to plastic containers that may result in less drug being administered must be considered.
- Light-resistant containers can be opaque or amber for good protection. If a clear, colorless immediate container must be used, then

an outer carton or foil covering may be used to render the container light-resistant.

- For the elderly, use package sizes that are convenient and can be easily manipulated.
- For the elderly, use oversize containers if necessary and labels that are large enough with easy-to-read print.

Shipping and Distribution

- Designate an area in the pharmacy for preparation of prescriptions for shipping.
- Develop detailed SOPs to cover various situations that might arise in shipping of compounded preparations.
- Maintain a “Shipping Log” and follow up telephone calls for confirmation of delivery, as appropriate.
- Notify patients of the expected day of delivery of shipped compounded medications.
- It is generally best to not ship any order out on Friday as the potential for delayed delivery and temperature exposure (both low and high temperatures) is greater.

Patient Counseling and Administration

- Patient counseling is especially important with compounded medications as there are no package inserts or patient information leaflets to provide.
- Counseling should be done at the time of providing the medication to the patient.
- Counseling should involve proper use, storage, handling and disposal of the preparation.
- If any device is used, proper use, care, cleaning and maintenance should also be discussed.
- Counseling should involve instructions to the patient to report any untoward or unexpected effects of the preparation.
- Counseling should include instructions to report any changes in appearance or odor of the compounded preparation.
- Any reported problem from a patient receiving a compounded preparation should be investigated and reported as appropriate.
- Patients should be counseled on the proper administration device and technique, as well as any cleaning procedures for the device.
- If possible, use “models” or actual examples for proper handwashing, aseptic technique, site care and changing of administration sets for sterile preparation administration.
- Implement a program of caregiver training; some commercially available educational materials may be obtained to assist in this task.
- Explain the process of cleaning the in-home preparation area for drug administration.
- Use commercially available models for administration techniques of some more complex dosage forms.

- Use videotapes or DVDs that are commercially available.
- Develop your own counseling aids, as appropriate.
- Patient Advisory Leaflets must be developed cautiously as these may be used in the event of any litigation that may occur in the future.

Quality Assurance Practices

- One can start slow with a quality testing program and build as experience is gained.
- Start with basic techniques of weighing, volume determinations, pH, observation and supplement with outsourced testing. Incorporate more methods in the pharmacy as experience is gained.
- All personnel engaged in compounding must be adequately and thoroughly trained.
- Keep documentation of all training in personnel files.
- Incorporate and update SOPs for all procedures and equipment in the pharmacy.
- Document all activities as required in the SOPs of the pharmacy.
- Dilutions, concentrates and triturations should be tested for accuracy as they impact many preparations compounded from them.
- The compounder should develop an SOP of what to test, when to test, what methods to use, how to interpret the results, the limits of the tests, and what to do when a preparation is outside accepted limits.
- All equipment must be checked out and verified before use.
- When using an outsourced laboratory, it should be checked out using "split-samples" and other procedures.
- Select an analytical laboratory that is FDA registered and inspected.
- Samples should be obtained and handled properly for testing either in-house or if outsourced.
- All testing results should be filed for future reference. If outside of accepted limits, an explanation of the problem and corrective actions taken should be included.

Miscellaneous

- Take care with packaging organic solvents, strong acids, or caustic agents in dropper bottles with rubber tips...the rubber will deteriorate with potential loss and/or contamination of the contents.
- Geometric addition/dilution is the method of choice for incorporating active ingredients in a vehicle.
- When working with aqueous systems, use the minimum amount of heat for as short a time period as appropriate to minimize water loss

- and potentially, drug loss.
- To use as long a beyond-use date as possible, keep the preparation anhydrous.



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Please circle the most appropriate answer for each of the following questions. There is only ONE correct answer per question.

- Which of the following can aid in the rapid disintegration/dissolution of quick dissolve tablets?
 - Addition of sorbitol to the formula.
 - Addition of a coating for taste-masking.
 - Addition of citric acid to the formula.

A. I only
B. III only
C. I and II only
D. II and III only
E. I, II and III.
- Empty gelatin capsules can be protected by:
 - Storage in sealed plastic bags or containers.
 - Maintaining a relative humidity of about 50%.
 - Storage away from direct sunlight.
 - Dehumidifying the room if the humidity is too high.
 - All the above
- Lollipops can be more easily removed from a mold by:
 - Placing in a freezer
 - Placing in an oven for a short time
 - Coating the mold with an aqueous solution before filling
 - Coating the mold with a thin layer of a neutral oil
 - Dusting the mold with confectioners sugar before filling
- An oil-in-water emulsion cream can be physically stabilized by adding:
 - Methylcellulose
 - Ethanol
 - Glycerin
 - Butylated hydroxyl toluene
 - Methylparaben
- When using an ointment mill, which of the following ingredients may be lost during processing?
 - Water
 - Alcohol
 - Mineral Oil

A. I only
B. III only
C. I and II only
D. II and III only
E. I, II and III.
- Regarding packaging:
 - Glass is best for solutions with a pH greater than 7.
 - Plastic is best for low dose lipophilic drugs.
 - Faulty packaging can compromise quality.

A. I only
B. III only
C. I and II only
D. II and III only
E. I, II and III.
- Patient counseling should include:
 - Proper use, storage, handling and disposal of the preparation.
 - Instructions on the use of any device that may be involved.
 - Instructions on reporting any problem related to the compounded medication.

A. I only
B. III only
C. I and II only
D. II and III only
E. I, II and III.
- Patient counseling can effectively involve:
 - Oral communication
 - Use of models
 - Use of video instruction

A. I only
B. III only
C. I and II only
D. II and III only
E. I, II and III.
- Which of the following sweeteners can be used to mask the bitterness of some drugs?
 - Aspartame
 - Dextrose
 - Sorbitol
 - Stevia
 - Sucrose
- Regarding analytical testing of compounded preparations:
 - Any chemical laboratory can be used.
 - A hospital clinical laboratory is the best choice to use.
 - Both in-house testing and outsourced testing can be used.
 - All analytical laboratories are FDA registered and inspected.
 - All the above are true
- My practice setting is:

A. Community-based	C. Hospital-based
B. Managed care-based	D. Consultant and other
- The quality of the information presented in this article was:

A. Excellent B. Good C. Fair D. Poor
- The test questions correspond well with the information presented.

A. Yes B. No
- Approximately how long did it take you to read the Secundum Artem article AND respond to the test questions?

- What topics would you like to see in future issues of Secundum Artem?

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