INTRODUCTION
As the extent of extemporaneous compounding increases in the practice of pharmacy, numerous methods evolve to aid preparation of the array of dosage forms prepared by pharmacists. The development of novel dosage forms by compounding pharmacists assists in the administration of drug substances to patients who might otherwise be noncompliant, especially among the very young and the elderly. As new methods and techniques are developed, they are shared among pharmacists at local, regional and national meetings. The goal is preparation of safe and effective products using the best available resources and techniques in minimum time. This Secundum Artem issue’s purpose is to share some of these techniques.

We will examine the different types of products being prepared and provide “hints” to save time and prepare better products. In some instances, additional discussion is provided to give the rationale, where needed, for the method or technique.

SOLUTIONS
- Magnetic stirrers, blenders and electric mixers save time and help produce uniform products.
- A stirring rod laid across the top of a beaker or an alcohol spray (ethanol for internal solutions) aids in breaking a foam, or a silicone defoaming agent can be added to the formulation.
- Filtering a liquid can help obtain a clear product.
- An inexpensive pH meter aids prediction and prevention of pH-related incompatibilities.
- Remove stirring rods from the graduate in which a product is prepared before “qs”ing.
- Dissolve salts in a minimum quantity of water before adding a viscous vehicle.
- Stir constantly when combining two liquids to minimize incompatibilities due to concentration effects.
- When incorporating an insoluble material, levigate the powder with a small amount of the vehicle, or a liquid that is miscible with the vehicle.
- Stir smoothly and don’t shake the product to avoid foaming from entrapped air.
- Add high viscosity liquids to low viscosity liquids, with constant stirring.
- To obtain small quantities of items using the dilution or aliquot method, use a solvent, not just a liquid.
- Always be aware of the pH and alcohol concentration of the products prepared.
- When filtering, be aware of what is being retained on the filter.
- When working with hydrocolloids, allow them to hydrate slowly before incorporating.
- When selecting a vehicle, considerations include the drug concentration, solubility, pKa, taste and stability.
- Vehicle considerations also include pH, flavor, sweetener, color, preservative, viscosity, compatibility and, if indicated, suspending and emulsifying agents.
• When preparing elixirs, dissolve the alcohol soluble constituents in the alcohol and the water soluble constituents in the water. Add the aqueous solution to the alcohol solution, with stirring, to maintain as high an alcohol concentration as possible.

• Talc may be used to remove excess flavoring oils. This is accomplished by adding 1-2 g of talc per 100 mL of solution and filtering. During the filtration process, the first portions are returned to the filter until a clear filtrate is obtained.

• Cosolvent systems, mixtures of water, alcohol, glycerin, and propylene glycol, can aid in clarifying solutions that are hazy or cloudy due to insolubility in water.

• Dissolution rate can be increased by immersing the beaker in an ultrasonic bath.

• Small particles dissolve faster than large particles.

• Stirring increases the dissolution rate of a drug.

• Generally, the more soluble the drug, the faster its dissolution rate.

• When working with a viscous liquid, the dissolution rate of a drug is decreased.

• An increase in temperature generally leads to an increase in the solubility and dissolution rate of a drug. Some exceptions are calcium hydroxide and methylcellulose.

• The solubility of a nonelectrolyte drug may be increased or decreased by adding electrolyte.

• An alkaloidal base, or any nitrogenous base of relatively high molecular weight, is generally poorly soluble unless the pH of the medium is decreased (conversion to a salt).

• The solubility of poorly soluble acidic substances is increased as the pH of the medium is increased (conversion to a salt).

• The effectiveness of a preservative may be related to pH. For example, the parabens are generally used within pH range of 4 to 8, chlorobutanol requires pH less than 5 and sodium benzoate is more effective at pH about 4 or lower.

SUSPENSIONS

• Commence powders to a very fine state of subdivision prior to suspending.

• Thoroughly wet powders with a hydrophilic liquid prior to adding the vehicle when preparing an aqueous suspension.

• If the powders are hydrophobic, a surfactant may be used to aid in wetting the powders prior to adding the vehicle.

• Methylcellulose preparations are best prepared by dispersion in about one-third to one-half the total volume of hot water, followed by the addition of the remaining water as ice water or ice.

• Many polymers are easier to disperse by mixing them with a hydrophilic solvent, such as glycerin, prior to

Paddock is your source for compounding actives, compounding vehicles and professional support.

Vehicles: Aquabase ◆ Dermabase ◆ Fattibase ◆ Hydrocream ◆ Liqua-Gel
Ora-Plus ◆ Ora-Sweet ◆ Ora-Sweet SF ◆ Polybase ◆ Suspendol-S

Actives: Colistin ◆ Dexamethasone ◆ Hydrocortisone ◆ Hydromorphone
Morphine ◆ Progesterone ◆ Testosterone ◆ Triamcinolone... & others

1-800-328-5113
www.paddocklabs.com
adding them to the aqueous vehicle.

- Polymer dispersion is aided by sprinkling onto rapidly agitating water.
- Suspensions should be dispensed in wide mouth prescription ovals so they can be poured easily.

**EMULSIONS**

- Dissolve oil soluble ingredients in the oil phase and water soluble ingredients in the aqueous phase.
- When using a mortar and pestle, light-rapid trituration is more effective than heavy, slow trituration.
- Add water and oil phases slowly under constant agitation.
- Where heat is used, the aqueous phase should be a few degrees warmer than the oil phase.

**OINTMENTS**

- Powders should be reduced to an impalpable form by comminution.
- Mixtures of two or more ointments can be achieved using a plastic bag.
- Ointment can be removed from a plastic bag and placed into tubes by cutting one corner of the plastic bag and squeezing the contents from the bag directly into the ointment tube or jar (simplifies cleanup).
- When preparing large quantities, a kitchen mixer may be advantageous.
- Plastibase™ should not be heated.
- Geometric dilution technique speeds the mixing process for ointments.
- A few drops of mineral oil or other suitable solvent can enhance the workability of drugs that build electrostatic forces.
- Do not use volatile solvents when levigating powders, since the solvent will evaporate and leave crystals of drug behind.
- As when mixing oil and aqueous phases for liquid emulsions, heating the aqueous phase a few degrees higher than the oil prior to mixing generally will help. The aqueous phase tends to cool faster than the oil phase.

**CREAMS**

- Cream bases without active ingredients can be softened in a microwave using a low power setting and short time.
- A humectant such as glycerin, propylene glycol, sorbitol 70% or PEG 300 or 400, added to a cream, will minimize evaporation.
- Use of low heat when preparing creams will minimize evaporation of water.
- Volatile oils should be added only after cooling the preparation. If alcoholic solutions of flavors are to be added, cool the preparation below the boiling point of alcohol first.
- Whether an emulsion is oil-in-water or water-in-oil can be determined by placing a drop of the emulsion/cream onto the surface of water. If the drop spreads out, it is the oil-in-water type. This occurs because the external phase of the emulsion is miscible with water. If it remains in a “ball”, it is probably of the water-in-oil type because the external phase is not miscible with water.
- Generally, the quantity of surfactant required to prepare a good emulsion is about 0.5% to 5% of the total volume.

**PASTES**

- The use of heat in preparing and working with pastes improves workability.
- Levigate insoluble powders with a quantity of melted base.

**GELS**

- Premixing some gelling agents, such as alginic acid, with other powders sometimes aids the dispersion process.
- Bentonite can be dispersed easily by sprinkling on still water, allowing the particles to hydrate and settle to the bottom. Glycerin or a similar liquid also can be used to pre-wet bentonite prior to mixing with water. Complete hydration may take hours.
- The addition of alcohol to some gels decreases their viscosity and clarity.
- When using a propeller device for preparing a gel, keep the propeller at the bottom of the container to minimize incorporation of air into the product.
- Dissolve all agents in the solvent/vehicle prior to adding the gelling agent.
- Carbomer resins are dispersed easily when sprinkled slowly into the vortex of a rapidly-stirred liquid.
- Remove any entrapped air in Carbomer dispersions prior to adding the thickening agent. Air bubbles can be removed by allowing the product to stand for 24 hours or by placing in an ultrasonic bath. A silicone antifoam agent may also be helpful.
- pH is very important in determining the viscosity of Carbomer gels.
- Gelatin gels are prepared by dispersing the gelatin in hot water, then cooling. The procedure can be simplified by mixing gelatin powder with an organic liquid in which it will not swell, such as ethyl alcohol or propylene glycol, adding the hot water, then cooling the gel.
- Tragacanth gels are prepared by adding the powder to vigorously stirred water. Here again, ethanol, glycerin or propylene glycol can be used to pre-wet the powder. Other powders can be mixed with the tragacanth while dry, before adding to the water.
- Generally, natural gums should hydrate about 24 hours to form the best homogenous gel and/or magma.

**LOTIONS (Emulsion-type)**

- Some emulsions can be made in a bottle, which simplifies cleanup.
- A mechanical propeller mixer, such as a Bamix, can be used to prepare elegant lotions. A variety of such mixers is available, some with multiple blades.
- Hand homogenizers can aid in preparing emulsions.
- The smaller the globule size, generally the more stable will be the emulsion.

**POWDERS**
- A coffee grinder will aid particle size reduction for small amounts of powder. Most can be cleaned well with a camel’s hair brush; some can be washed with soap and water.
- Powders with similar particle size and density characteristics can be mixed in a plastic bag using a spatula. This will minimize the quantity of powder floating around in the compounding area.
- Dust masks should be used if a powder is excessively light and escapes into the work area.
- If a powder is too fluffy, it can be compacted slightly by the addition of a few drops of alcohol, water or mineral oil.
- Magnesium stearate, <1% of total weight of mix, can be used to enhance lubrication and flow characteristics of powders.
- Sodium lauryl sulfate, up to 1%, can be added to powders to neutralize electrostatic forces.

**CAPSULES**
- Capsule-filling devices are available for filling 50, 100 or 300 capsules at a time. They are time-savers, if large quantities of capsules are being prepared.
- If a capsule machine is used and fewer than the capacity of capsules is being prepared, the remaining holes can be covered using stiff cardboard, *e.g.* a 3 x 5 or 5 x 7 index card.
- Capsules may be colored by adding a dye to the powder before placing it in a clear capsule. This aids in distinguishing various strengths of powders and capsules.
- Liquids can be incorporated into capsules by mixing with melted polyethylene glycol 6000, 8000 or a related PEG. The mixture can be poured into capsules where it will solidify. The capsule can be closed and dispensed.
- A liquid can be dispensed in capsules by using a syringe to drop the liquid into the capsule bases. The liquid must not be a solvent for the gelatin. This is especially true for oils. Also, the oil can be mixed with a fat or fatty acid, cocoa butter or Fattibase and slightly heated, then mixed and poured into capsules.
- A capsule can be sealed by moistening the open, outer edge of the capsule base or the inner edge of the capsule cap. A slight twist will improve the seal.
- Capsules can be cleaned with a soft cloth or towel, or by placing in a large container about half full of salt, sugar or sodium bicarbonate. The capsules are added to the container and the container rotated. The capsules are separated from the coarse granular material by pouring through a sieve large enough to allow the salt/sugar/sodium bicarbonate to pass through but retain the capsules.
- Sodium lauryl sulfate, up to 1%, can be added to powders to neutralize electrostatic forces.
- Two incompatible ingredients can be kept separate by placing one inside a very small capsule and then placing the very small capsule along with the other powders inside a larger capsule.
- Small tablets of potent drugs can be placed inside capsules along with additional ingredients.
- Locking capsules help to minimize loss of contents, whether powder, liquid or semisolid; they work well with hand-operated capsule filling machines.

**OPHTHALMICS**
- An inventory of sterile dropper bottles will save time by eliminating the need to sterilize containers.
- Small, disposable sterile filters are available for preparing small volumes of ophthalmics.
- Larger, funnel-type sterilization filters are available for preparing larger volumes of ophthalmics, *e.g.* 100-200 mL.

**SUPPOSITORIES**
- A constant-temperature dry bath filled with sand at 37° C will provide the proper temperature for softening and melting fatty acid and cocoa butter bases in a minimum of time.
- Powders should be in an impalpable form prior to incorporation into a suppository base.
- Suppository molds should be kept clean and dry to ease the release of suppositories. If the suppositories stick, a lubricant can be used.
- The removal of suppositories from reusable molds is easier if a lubricant is used. The lubricant must not be a solvent for the suppository base. Use glycerin if vegetable oil or cocoa butter is the base or mineral oil or PAM vegetable spray if polyethylene glycol is the base.
- When molding suppositories by hand, dust a small quantity of talcum powder onto the hands or pill tile to enhance the workability of the suppository material.
- Melts should be poured into suppository molds after the molds have equilibrated to room temperature. Pouring melts into cold molds may result in incompletely-filled cavities and suppositories that tend to fracture easily.
- When pouring suppositories, start at one end and pour continuously without stopping. Do not go to the next mold until the first is filled. A small excess should be “piled up” so that the cavity will be completely full when cooled and contracted.
The maximum quantity of drug and excipients to be incorporated into a suppository generally is about 30% of the total suppository weight. When using plastic disposable molds, be sure the temperature of the melt is lower than that which will melt the mold. Excess material can be removed from suppository molds by dipping a stainless steel spatula in warm water and cutting or trimming the excess material from the mold. The heated spatula blade also will serve to smooth the back of the suppository. To prepare urethral suppositories, a straw or thin glass tube can be used as the mold. A 1 mL tuberculin syringe can be used as a mold, if the lower portion of the barrel is cut off. The urethral suppository can be removed from the syringe barrel by inserting the plunger and forcing the suppository out after slight warming. A large diameter needle, attached to a large syringe filled with the suppository melt, will aid in transferring the product into the 1 mL tuberculin syringe. Suppositories are most elegantly packaged in disposable molds. Vegetable extracts, when moistened by levigation with a small quantity of melted base, will more readily distribute throughout the base. To incorporate hard, crystalline materials, pulverize finely or dissolve in a small quantity of solvent and combine the solution with the base. Liquid ingredients mixed with a powder such as starch will be less fluid and easier to incorporate into a base. A large quantity of powder dampened with a few drops of a bland oil such as mineral oil, or a water miscible liquid such as glycerin, will be easier to incorporate into some bases.

TROCHES/LOZENGES
- Addition of a flavoring oil immiscible in the base is improved by adding a few drops of glycerin or some “intermediate solvent” to the flavoring oil prior to mixing it with the base.
- Soft lozenges can be made from PEG bases, chewable lozenges from glycerin gelatin bases and hard lozenges/troches can be made from sucrose syrup bases.
- If troche molds are unavailable, the plastic snap cap from a plastic vial can be used as a mold. A vegetable spray can be applied to the cap and the preparation poured into the cap. After solidification, the cap can be peeled away from the troche. Alternatively, the melt can be dropped onto a heavy sheet of aluminum foil placed on a bed of ice cubes. The drops will immediately solidify upon contacting the cold foil. They will usually be in a circular form; check weights carefully.

FLAVORING/COLORING
- Drugs with objectionable taste can be prepared as suspensions or incorporated into the internal phases of emulsions with flavoring in the vehicle to enhance their palatability.
- Coloring and flavoring agents should agree, e.g. red for cherry, brown for chocolate.
- Effervescence may mask the taste of salty drugs.

MISCELLANEOUS
- If the same quantity of a liquid is to be measured frequently, a repeating pipettor should be used.
- Micropipets should be used to measure very small volumes of liquid.
- Computerized data bases for formulas and compounding recordscan enhance the compounding process. Master formulas with compounding instructions for frequently compounded products will promote consistency.
- When compounding large quantities of selected products, it may be advisable to refer samples to an analytical laboratory.
- Use of electronic balances instead of torsion balances will speed weighing and allow the pharmacist to check weights of capsules, troches, suppositories, etc., very rapidly. Some balances also have a printer attached to produce a hard copy for record keeping purposes.
- Beakers with handles make manipulations much easier when heat is used in preparation steps.
- Hot plates with magnetic stirrers are versatile and save time.
- Magnetic mixers are available that will allow the mixing of 4 or more beakers of solution simultaneously.
- A “light box” serves several purposes in a compounding pharmacy. It can be used for observing clarity of solutions, turbidity and uniformity of suspensions, and fill levels of suppositories in plastic molds.

SUMMARY
As new methods and techniques are developed by compounding pharmacists, we should all share these with each other to make everyone’s job easier and more efficient, and improve patient care. The Phi Delta Chi motto, “Each Needs the Help of the Other”, is especially applicable to compounding activities. Procedures developed by one pharmacist and shared should lead to others sharing with the originator. With the increased availability of various types of equipment to compounding pharmacists, enhanced efficiency reduces the time required to compound prescriptions. Laboratory equipment catalogs and gourmet cooking suppliers offer many opportunities to upgrade the equipment used in compounding. The use of commercial vehicles for all types of dosage forms also makes compounding more convenient and efficient. Please let us know of your “shortcuts” and “techniques” so they can be shared with others in a new column entitled “Helpful Hints” in future issues of Secundum Artem.