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# **THE COMPOUNDING PHARMACY**

## **Dosage Forms, Vehicles and Methods**

### **Introduction:**

Prior to the proliferation of chain drug stores, mega drug stores, and pharmacies in supermarkets, big box stores, and insurance company sponsored mail order pharmaceuticals, **all pharmacies were compounding pharmacies**. The privately owned pharmacy featured a pharmacist who was known locally by name. The local doctors knew him. (In those days, it was almost always a him.)

I am the only physician in my family. My father, two uncles, my sister and three cousins were pharmacists. I worked summers in my father's drug store through high school. I remember watching my father and the other pharmacists making up powders, creams, and ointments and filling capsules ordered specially by physicians. There was regular communication between the local doctors and the pharmacists to make sure everything was right. The compounding pharmacies of today bring back that tradition. The chain stores want their pharmacists to fill as many prescriptions a day as possible. That means just counting out pills or putting a label on a commercially prepared box. There is no time to make or "compound" anything.

Virtually all the human steroid hormones are available from pharmaceutical manufacturing companies. They are packaged as powders and stocked at the compounding pharmacy. All three estrogens, Estradiol, Estriol and Estrone, plus Progesterone, Testosterone and DHEA are commonly prescribed. In addition, Pregnenolone, melatonin, androstenedione, both thyroid hormones, T-4 and T-3 as well as freeze-dried pork thyroid are available. Compounding pharmacists also make up many medications for dermatological and veterinary use.

**Some compounded products are easier to make than others.** The time and effort required by the pharmacist will be reflected in the price to the patient. In general, the hormones themselves and the fillers or creams and gels are not that expensive. The pharmacist's time is the main factor in the cost. Some things, like creams, may be just as easy to make in a large batch as a small batch. Buying a larger quantity at one time may save the patient money. These are all good subjects for both patients and physicians to discuss with their compounding pharmacist.

Lets go over some of the medication forms available, some of their uses, advantages and disadvantages.

## **Capsules and Tablets:**

Any hormone that is effective when taken by mouth can be placed in a capsule. Since the quantities of the various hormones are often very small, fillers are used to fill up extra space. Some individuals may be allergic to, or react poorly to, some kinds of filler. Sensitive patients should discuss this with the pharmacist. There are several kinds available including milk sugar and cellulose. **The filler can be varied depending on patient sensitivity. Commercial products also use fillers but doctors and patients have no choice in how they are made!**

Capsules and tablets are easy to take, **convenient, travel well and give consistent, reliable dosage.** Oral dosage generally gives more **reliable absorption** from patient to patient than most other forms. In some cases, if appropriate, several different hormones or **medications can be combined** in a single capsule in dosage proportions chosen by the physician. This is convenient for the patient and usually saves money. One disadvantage, however, is that the component parts cannot later be varied independently. **I usually give separate prescriptions until the dosage is established and stable for that patient.** We can later combine the medications for convenience and cost saving. One other minor disadvantage of capsules is that they are quantized. If I decide to raise or lower her dose, she can't take half or three quarters of a capsule, or a little more than one. **Tablets can be cut and creams or gels can be used in slightly larger or smaller amounts.** Empty capsules come in a variety of colors. This can be used to help patients tell their various medications apart. When prescribing capsules or tablets, the time of administration, whether with food or without, and dosage frequency must be specified.

There are only a few manufacturers of custom-made tablets. One advantage is that **they can be split** for twice a day dosing for the price of one tablet. **Belmar Pharmacy in Colorado** [www.belmarpharmacy.com](http://www.belmarpharmacy.com) has been making tablets for many years. Multiple doses may be advantageous when giving Estradiol or T-3 (triiodothyronine), both of which can be fairly rapidly metabolized.

All food and medication taken by mouth, goes through the liver after being absorbed in the intestine. This is called the **liver first pass effect.** Estrogen, for example, has several effects on liver function. On the benefit side, estrogen raises good cholesterol (HDL) and lowers bad cholesterol (LDL) when passed through the liver. On the bad side, that same estrogen raises triglycerides and increases blood-clotting factors. **The relative benefits and deficits must be considered when choosing a route of administration.**

I will discuss specific hormones under their separate sections.

## **Oral Drops:**

In his book on Bioidentical Hormones, **Uzzi Reese, MD** uses oral drops almost exclusively. He has the patient place a few drops of estrogen or Progesterone solution under her tongue for oral absorption. I have had only one patient who was using this method. She constantly was changing her dosage from day to day, and even hour to hour. She was also constantly getting hot flashes. I think the main disadvantage is the difficulty of giving a consistent dose. With practice, I am sure the method could be made to work, but other, more consistent modes of administration are probably superior.

## **Topical Creams:**

Most of the steroid hormones can be administered as topical creams. There are several commercially available formulas. If a given patient has an allergy to one type, another can be substituted.

### **How Dispensed?**

Some pharmacies deliver the creams preloaded into syringes. This makes it easy for the patient to measure out her dose by simply pressing the plunger. Quantities in milliliters are marked on the syringe. Other pharmacies dispense the creams in jars. Cream can be drawn up into a syringe and a measured sample than used by the patient. I have had patients complain about the difficulty of drawing some creams into a syringe from a jar. Other pharmacies provide small measuring spoons. The pre-filled syringe is the least messy, most accurate and easiest for patients to use. The cost may be higher because many syringes must be provided. The pharmacists use a wide bore needle to fill the syringes from the inside.

### **Advantages:**

Since the creams are placed topically and diffuse into the bloodstream, **the first-pass effect is avoided**. Another advantage is **variability of dosing**. If a patient is receiving too much or too little medication, the dose can be adjusted by changing the volume used without having to obtain a whole new prescription. Doses can also be easily divided and used multiple times a day. This **patient controlled freedom** is a useful feature. To use multiple capsules a day, the cost will increase.

### **Disadvantages:**

There is **greater variability of absorption** with creams than almost any of the methods. In general, thin-skinned white women seem to have the greatest absorption and well tanned skin, the least. It is hard to know if patient application technique, skin type or the cream itself is at fault for poor results. **Obtaining blood levels to confirm hormone absorption is a must.**

Creams may be messy and take more time to apply than swallowing a tablet or capsule. Since I believe that absorption through the palm is important, this precludes the patient from immediately washing her hands. Also, immediately touching another person might transfer some of the hormone to another individual.

### **Application:**

There is some disagreement about the best method and site for application. In some courses I have attended, they recommend applying the creams to thin skin areas over a good vascular supply. These areas include the forearm, the back of the knee and inside the elbow. Others recommend application to areas overlying thick layers of fat. These include the thigh and buttocks. In measuring blood levels and asking patients to show me exactly how they apply the creams, I have come to my own conclusions. It is my belief that the palm of the hand actually is the main site of absorption. I instruct patients to measure out the cream into the palm of their hand and rub vigorously onto another surface such as the opposite forearm or the thigh. Some patient would show me placing the cream on one forearm and rubbing with the other forearm. These women invariably have very low levels of the prescribed hormones. I do not recommend the forearm-to-forearm technique.

## **Topical Gels:**

Topical gels differ from creams in that they usually have an **alcohol base**. They tend to dry more quickly and are somewhat less messy than creams.

**Testosterone** is absorbed very efficiently via a topical gel. In fact, I find that excess testosterone levels are very easily achieved. The dosage may need to be one half or even one fourth of the oral dose. Some physicians have recommended using testosterone directly on the clitoris for sexual enhancement. One must use a vaginal type cream. **Alcohol based gels burn if placed on the vulva.**

## **Ointments:**

Ointments are Vaseline (petroleum jelly) based. **They form a barrier against water.** When treating vulvar irritation, frequently, urine leakage is part of the problem. Placing the treatment hormones in an ointment protects the vulvar skin from the urine and also prevents washing the treatment hormones away. I sometimes use Colbetasol (Temovate) ointment 0.05% as the base. Estrogen or testosterone can be added to this ointment by the compounding pharmacist.

## **Topical Liquids:**

Some pharmacies make a topical liquid on a base of propylene glycol. The fat-soluble steroid hormones dissolve readily into this liquid and are efficiently carried through the skin. Hormones can be dissolved into this base in high concentration, so a full day's dose can be carried in only a few drops that rapidly sink into the skin. The patient can carry a large supply of hormone in a small bottle. There is only one pharmacy in my area that makes this type of preparation and I only have a few patients who have used them. At least one patient was quite happy with the method and her hormone blood levels were right in the desired range. I have some concern with the constant use of the propylene glycol, but it actually is an extremely common ingredient in many, if not most, commercial creams and lotions of all kinds used in the US.

## **Oral Troches:**

Oral troches are small tablets made to dissolve under the tongue or in the cheek. In patients not successful with creams, using the buccal mucosa is a good alternative to topical skin. Some troches are waxy and dissolve slowly. Others dissolve more quickly. Some pharmacies make small troches and some are larger, about one centimeter square. To vary the dose, troches are usually soft and can be cut into smaller doses with a knife.

Theoretically troches are absorbed through the skin of the mouth. I am sure, however, that much of the dose ends up in the stomach and thereby, the liver. They stimulate the production of much saliva. I am also told that Progesterone does not taste very good. Many different flavors can be added as desired. Since Progesterone is a sedative, I usually prescribe it before bed. Some patients complain that the waxy troches take up to twenty minutes to dissolve and they end up waiting for their mouth to be empty so they can lie down.

## **Sublingual Tablets:**

Sublingual tablets are similar to troches but they dissolve much more rapidly than the waxy troches and are smaller. Not all compounding pharmacies make them.

## **Vaginal Creams:**

The base creams used in the vagina are different from the topical vanishing creams. The vagina has an excellent blood supply and **all the hormones pass through the vaginal mucosa quiet efficiently**. As with the commercial yeast products, there are various plungers and other applicators for measuring and inserting the vaginal creams.

### **Advantages:**

Again, we are avoiding first pass through the liver. In treating vaginal dryness, this places estrogens directly on the tissue in the most need of therapy. There is no wet outer skin to delay getting dressed in the morning.

### **Disadvantages:**

Some women do not like to do vaginal insertion. If the cream is used at night and followed by intercourse, I do not know how much would be absorbed by her partner via the penile skin. I don't think any studies have been done. Also, some women have increased Candida infections if they are using the vaginal preparations.

## **Rectal and Vaginal Suppositories:**

In the early 1970s, progesterone vaginal suppositories became popular on PMS treatment. They were made from a cocoa butter base, were messy, and had to be refrigerated. Other bases now exist. Since I use oral progesterone for PMS, I have not ordered vaginal suppositories in years but they should still be efficacious.

All these medications could be used in a rectal suppository, should there be some special reason that other routes of administration could not be utilized.

## **One Caveat:**

**Pharmacists and doctors are human beings. Sometimes human beings make mistakes.** Occasionally I receive phone calls from patients that a medication they have been using is now causing side effects or is not working. **I repeat the laboratory work.** I have, on a few occasions, found that patients had estradiol levels over 2,000 pg/ml or Testosterone over 500 ng/dl. I assume that the pharmacist made a measurement error. On those few occasions, I have had the patient return to the pharmacy and have a new batch made. The patient's symptoms returned to normal and the lab work also returned to normal. **The pharmaceutical manufacturers use human error as a reason to avoid compounded medications. I have written thousands of compounded prescriptions. The errors are very rare. The advantages of compounded medications are great. Safety comes in listening to patient complaints and repeating the blood levels.**