Dermatological Preparations: Ointments and Pastes

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Dermatological preparations are among the most frequently compounded preparations because of their wide range of uses. The preparations include solutions, suspensions and gels, emulsions, lotions, creams, ointments, and pastes. Dermatological products that are manufactured and not typically compounded include aerosols and devices such as transdermal patches, tapes, and gauzes.

General Uses of Dermatological Formulations

Dermatological formulations generally are used for the following purposes:

- To protect the skin or mucous membranes from chemical or physical irritants in the environment, permitting the skin to rejuvenate and heal.
- To provide an emollient (skin softening) effect by hydrating the skin.
- To provide a topical vehicle for medications for local (anti-infective, antipruritic, astringent, keratolytic) or transdermal/systemic effect (e.g., nitroglycerin).
- To provide lubrication between intertriginous areas, areas where the skin rubs together.

Protective formulations contain materials that will protect the skin from various external factors such as moisture, air, sun, and chemicals. These formulations may be either a base or a base containing active pharmaceutical ingredients. For example, sunscreen agents that prevent the infiltration of ultraviolet rays may be included in various types of dermatological products.

Emollients are preparations that soften the skin surface. They contain fatty components such as mineral oil, petrolatum, or paraffin. Oleaginous compounds also may maintain soft skin by forming an occlusive layer on the skin surface, thereby reducing or retarding the evaporation of water.

A *dermatological* vehicle is a formulation that releases an active drug to the application site. The release (diffusion) of the drug depends on the type of vehicle as well as the solubility (hydrophilicity/lipophilicity) of the drug in that vehicle. The extent to which a drug is absorbed into the skin is influenced by several factors, including the area to which the ointment is applied, the condition of the skin (whether intact, denuded, or diseased), the method of application, and the total amount of drug released from the vehicle.

This chapter deals with two dermatological formulations: *ointments* and *pastes*. Ointments are generally used on dry, scaly lesions because their emollient properties will aid in rehydrating the skin. They also stay on the skin longer. Pastes contain more solid material than ointments do, so they tend to be stiffer in texture, and often do not melt or soften at body temperature. Pastes are topical preparations that are typically applied to an area that requires protection.

Lotions and creams are also common dermatological formulations and have been discussed in the chapters on suspensions and emulsions. *Lotions*, which can be either suspensions or emulsions, are fluid liquids that typically are used for their lubricating effect. *Creams* are emulsions that possess a fluid consistency and typically are opaque, thick liquids or soft solids used for their emollient properties.

Dermatological products/preparations offer many advantages:[1]

1. Avoids gastrointestinal drug absorption, avoiding the degradation of active ingredients by gastrointestinal pH and enzymatic activity, and drug interactions with food, drink, and other orally administered drugs.
2. A route of administration when other routes are not available, as with vomiting or diarrhea.
3. Avoids the first pass effect.
4. Noninvasive route of administration.
5. Provides extended therapy with a single application, improving compliance.
7. Drug therapy can be terminated rapidly by removal of the preparation.

The disadvantages of ointments and pastes include:

1. Ability to deliver limited amounts of active ingredients may restrict the use of these preparations to more potent drugs.

2. Some patients develop contact dermatitis, necessitating discontinuation.

Structure of the Skin

Regardless of the formulation, all dermatological preparations are applied to the skin. The skin is the largest and heaviest organ in the body, accounting for about 17% of a person's weight. Its major function is to protect the underlying organ systems from trauma, temperature, humidity, harmful penetrations, moisture, radiation, and microorganisms. It is composed of three layers of stratified tissue: epidermis, dermis, and subcutaneous (Fig. 15.1). The skin is 3 to 5 millimeters thick, depending on the part of the body. The thickest parts of the skin are the palms of the hands and the soles of the feet, and the thinnest parts are the eyelids and genitals.

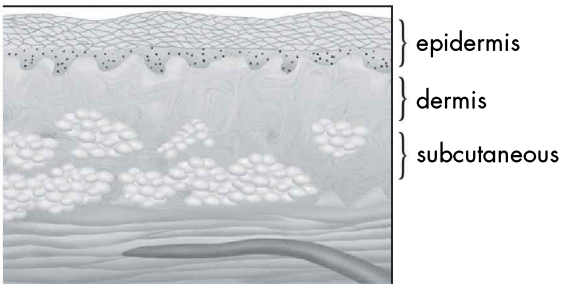


Figure 15.1 The three layers of the skin: epidermis, dermis, and subcutaneous.

The *epidermis* is approximately 75 to 150 microns thick except in the palms and soles of the feet, where it is 400 to 600 microns. The outermost part of the epidermis contains sebum, sweat, and several layers of dead cells called the *stratum corneum*. The innermost part of the epidermis is a layer of living cells called the *stratum germinativum*. In normal skin, the stratum germinativum continually produces viable cells, which progress toward the skin surface. As the cells progress, they die and displace the cells in the stratum corneum, which are sloughed off to the environment. As the cells die, they become flattened and lose their nuclei, and the organized cell contents are replaced with keratin fibrils. The turnover time from germination to sloughing is about 21 days.

The stratum corneum is the barrier to drug penetration through the skin. Approximately 10 microns thick, it can swell to approximately three times its original thickness and absorb about five times its weight in water. When the stratum corneum hydrates, it becomes more permeable. Therefore, occlusive dressings often are used to hydrate the stratum corneum and increase the penetration of certain drugs. Dermatoses such as eczema and psoriasis also can hydrate the stratum corneum and increase the absorption of some drugs.

The *dermis* contains blood capillaries, nerve fibers, hair follicles, and sweat and sebaceous glands. Sweat glands yield their product through ducts ending on the skin surface. Oil glands and hair follicles from the dermis also terminate on the skin surface. The *subcutaneous* layer consists of connective tissue and adipose tissues. Its primary role is to protect the body from mechanical impacts.

Local and Systemic Effects of Dermatological Preparations

Dermatological preparations can produce a *local drug effect* either on or in the skin (Table 15.1). The preparations serve as protectants, lubricants, emollients, or drying agents in addition to any therapeutic benefit from incorporated active drugs. Examples of topical injuries that are treated via the local activity of dermatological preparations include minor skin infections, itching, burns,

Table 15.1 Tips and Explanations of Proper Ointment Use

Patient Tips for the Proper Use of Ointments	Explanations
Drug absorption varies with the site of application. Use the recommended site and rotate locations within that site.	Rotating locations allows the skin to regain normal permeability after being occluded and prevents skin irritations. Skin sites can be reused after one week.
Applications should be to clean, dry skin.	Do not use oily, irritated, inflamed, broken, or callused skin. These sites will alter absorption.
Do not use skin lotion at the application site.	Lotions hydrate the skin, which will alter the partition coefficient of the drug between the ointment and the skin.
Use application sites that are not rubbed by clothing movement.	Clothing may remove the ointment. If the site is covered by clothing, use a protective pad over the area.
Use application sites that are not subjected to being rubbed off on another person or pet.	The preparation can be transferred to others causing unintentional dosing.
Wash hands thoroughly before and after applying ointment. Do not rub eyes or touch mouth while handling ointment.	Prevents transfer of the ointment, and restricts application to appropriate site.
Do not wash the application site for a few hours after application.	The ointment must remain in place to ensure time for the therapeutic activity to occur.
If sensitivity, intolerance, or skin irritation results, seek re-evaluation.	It is necessary to ensure that the ointment is the appropriate therapy.
Apply a thin film of preparation unless otherwise noted.	Most absorption occurs from the ointment most in contact with the skin.
Continue to use the preparation for a short while after the symptoms or injury resolves unless otherwise noted.	The surface of the skin may heal before the underlying areas. The additional time will ensure these areas also have time to heal.

Adapted from "Transdermals: The Skin as Part of a Drug Delivery System" by L. V. Allen, Jr., International Journal of Pharmaceutical Compounding, 15, no. 4 (2011): 308–315.[1]

diaper rash, insect stings and bites, athlete's foot, corns, calluses, warts, dandruff, acne, psoriasis, and eczema.

Dermatological preparations can also be used to provide *systemic drug delivery* as the result of *percutaneous absorption*. The preparation is placed on the skin, and the active ingredient penetrates the epidermis into the dermis and subcutaneous tissues, where it is absorbed into the systemic circulation. Some dermatological preparations provide continual percutaneous absorption. The transdermal patch is the primary example of this type of preparation (Fig. 15.2). Another example is the solid lipid nanoparticle (SLN).[2] This is a percutaneous carrier system for emulsions, liposomes, and nanoparticles with particles in the range of 50 to 1,000 nanometers.

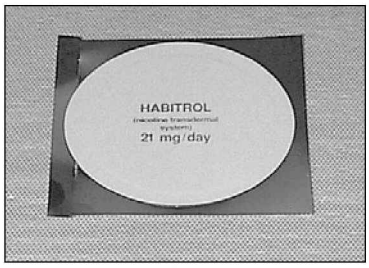


Figure 15.2 A transdermal patch.

Percutaneous absorption of drugs generally results from direct penetration of the drug through the stratum corneum. It is composed of approximately 40% protein (mainly keratin) and 40% water, with the balance being lipid substances such as triglycerides, free fatty acids, cholesterol, and phospholipids. The lipid content is concentrated in the extracellular phase the stratum corneum and forms most of the membrane that surrounds the cells. The lipid content, therefore, becomes an important determinant of absorption since most of a drug's absorption is through the intercellular channels by passive diffusion. The rate of drug absorption generally depends on the drug's concentration and aqueous solubility, and the oil-water partition coefficient between the stratum corneum and the vehicle. Substances with both aqueous and lipid solubility characteristics are good candidates for percutaneous absorption.[1] The extent of percutaneous absorption is the result of three competing processes:

1. The potential of the drug to cross the stratum corneum.
2. The potential of the drug to leave the preparation.
3. The influence of the preparation on the stratum corneum.

Although the percutaneous absorption of drugs is a complex process, several generalizations are possible:

- Absorbed particles are generally less than 1 micron (0.6 kDa) in size.[3] Commonly used ointment mills can reduce the particle size to about 20 microns.
- Active ingredients with molecular weight greater than 400 may have limited absorption into the dermis. But drugs with molecular weights of 100 to 800 can be adequately absorbed if they have a suitable lipid and aqueous solubility.[1]
- The active ingredient should have an octanol: water partition coefficient (log P) value between +1 and +2.[2] High values are characteristic of hydrophobic chemicals; low values are characteristic of hydrophilic chemicals.
- Absorption is different when an active ingredient is applied to different skin areas. This is related to the partition coefficient since some areas have less fat (e.g., behind the ear, forehead, genitalia, scalp), and other areas have more fat (e.g., abdomen, arch of the foot, arms, buttocks, palm of the hand).
- More active ingredient is absorbed when a larger skin surface area is used. As an example, the rate of fentanyl absorption from transdermal patches is related to the patch size, as shown in Table 15.2.

Table 15.2 Fentanyl Absorption Based on Patch Size

Size of Patch (cm^2)	Fentanyl Content in Patch (mg)	Dose Absorbed (mcg/h)
10	2.5	25
20	5	50
30	7.5	75
40	10	100

- Greater "rubbing in" of the ointment results in greater absorption of the active ingredient.
- Greater absorption occurs when the preparation is applied to the skin in a thin layer/application compared to a thicker application.
- Preparations or dressings that increase hydration of the skin enhance absorption.
- The longer the preparation remains in contact with the skin, the greater the absorption.
- The unionized form of a drug will have greater absorption compared to the ionized form.

Penetration Enhancers

The major disadvantage of the dermal route of administration is that the amount of drug that can be absorbed into or through the skin is about 2 mg/hour. This is not an absolute value and would obviously depend on the drug, the formulation, the surface area of application, and the site of administration. However, this rate may become a significant limitation if the route is being used for percutaneous absorption.

To overcome this potential limitation, several ingredients added to products/preparations are used as *penetration enhancers*, which promote the percutaneous absorption of drugs. More than 275 chemical compounds have been cited in the literature as skin penetration enhancers.[1] These enhancers improve the solubility of the active drug in the stratum corneum and facilitate the drug's

diffusion into the systemic circulation. The selection of an enhancer for a formulation is based on its efficacy, its dermal toxicity, and its physicochemical and biological compatibility with the other ingredients in the product/preparation. It is important to realize that no one penetration enhancer possesses all desirable attributes. The sidebar lists some preferred characteristics to look for in penetration enhancers.

IDEAL CHARACTERISTICS OF PENETRATION ENHANCERS

- Have no therapeutic activity of their own
- Nontoxic, nonirritating, and nonallergenic
- Rapid onset of action; duration of action should be predictable and appropriate for the active ingredient
- Should not damage the stratum corneum when removed
- Should not promote the diffusion of endogenous compounds in the skin
- Should enhance the penetration in a unidirectional pathway
- Compatible with other ingredients
- Spread evenly on the skin

Adapted from "Penetration Enhancers," by S. J. Newton, *International Journal of Pharmaceutical Compounding*, 17, no. 5 (2013): 370–374.[4]

Table 15.3 Chemical Classification of Penetration Enhancers

Chemical Classification	Examples
Alcohols	Methanol, ethanol, propanol, octanol
Fatty alcohols	Myristyl alcohol, cetyl alcohol, stearyl alcohol
Fatty acids	Myristic acid, stearic acid, oleic acid
Fatty acid esters	Isopropyl myristate, isopropyl palmitate
Polyols	Propylene glycol, polyethylene glycol, glycerol
Anionic surfactants	Sodium lauryl sulfate
Cationic surfactants	Benzalkonium chloride, cetylpyridinium chloride
Amphoteric surfactants	Lecithins
Nonionic surfactants	Spans®, Tweens®, poloxamers, Miglyol®
Lactams	Azone
Sulfoxides	Dimethyl sulfoxide (DMSO), decyl methyl sulfoxide (NDMS)
Terpenes	Limonene; menthol
Ureas	Urea

Adapted from "Penetration Enhancers," by S. J. Newton, *International Journal of Pharmaceutical Compounding*, 17, no. 5 (2013): 370–374,[4] and "Compounding Dermatological Products," by L. V. Allen, Jr., *International Journal of Pharmaceutical Compounding*, 2, no. 4 (1998): 260–264.[5]

Their mechanism of action is related to one or a combination of the following: 1) disruption of the stratum corneum; 2) interaction with intercellular proteins; or 3) improved partitioning of the drug, co-enhancer, or solvent into the stratum corneum. Another possibility is that the penetration enhancers increase drug diffusion into the stratum corneum by dissolving the layer's lipids or denaturing the proteins. Table 15.3 gives examples of penetration enhancers used in dermatological formulations. Other common enhancers include triethanolamine, DMF (dimethyl formamide), N-methyl-2-pyrolidone (NMP), and 2-pyrrolidone (2P).

Another type of penetration enhancer is called a "soft" enhancer. These chemicals have the ability to rapidly decompose into a fatty acid and a glycol, which prevents any damage to the stratum corneum. The most commonly used soft enhancement of percutaneous absorption is 2-n-nonyl-1,3-dioxolane.

There are situations when it is not desirable to enhance the penetration of an active ingredient, but rather, to slow the penetration. How might this be achieved? First and most obvious would be to remove any penetration enhancing ingredients in the formulation. But if the rate of delivery to the subcutaneous tissues is to be less than the absorption rate out of that tissue, then the topical preparation or the device containing the preparation needs to be the rate-limiting step.[1] The composition of the formulation can be designed for the drug to have more affinity to the preparation and escape into the skin at a slower rate. Or the device can have a rate-limiting membrane or absorption barrier to control the amount of medication that can leave the device per unit time.

Iontophoresis and Sonophoresis

Penetration into the skin can be increased using nonchemical or mechanical methods. *Sonophoresis* (also referred to as *phonophoresis*) uses ultrasonic vibrations to increase the penetration of topically applied medications into the skin. A preparation is applied to the skin and allowed to remain for a period of time, after which the ultrasound energy is applied. Therapeutic concentrations within the skin have been achieved for the corticosteroids dexamethasone sodium phosphate and hydrocortisone, and the nonsteroidal anti-inflammatory drugs ketoprofen and naproxen.[6] Many other active pharmaceutical ingredients have been successfully used including lidocaine, tetracycline, and penicillin.

Iontophoresis is another nonchemical method used to enhance the penetration of topically applied drugs. The use of iontophoresis as a drug delivery method dates back to the first part of the 1900s when it was demonstrated that ions could be driven across the skin by means of an electrical current. The enhanced transport of iontophoresis is based on the principle that ions repel like ions. The method has been used to enhance the absorption of local anesthetics (e.g., lidocaine), analgesics, dexamethasone, verapamil, and propranolol. The method has also been used with larger molecules such as amino acids, peptides,

and proteins.[1,6,7,8] The availability of diclofenac sodium, ketoprofen, and piroxicam in powder form, coupled with increased understanding and skill in the use of chemical absorption enhancers, has brought the skills of the compounding pharmacist to the attention of innovative medical prescribers in the field of sports medicine.[6] Successful treatments have been devised for bicipital tendinitis, Achilles tendinitis, hamstring and quadriceps strains, lumbar sacral strains, and bursitis. The advantages of these mechanical methods can be summarized as:

- The active ingredient avoids gastrointestinal and systemic effects.
- Treatments can be used in younger patients where systemic administration is to be avoided.
- Convenient, brief, and easily remembered dosing schedules improve compliance.

Ointment Bases

An ointment base is most often a collection of ingredients to form a preparation/product that has smooth consistency, a viscous texture, and an unctuous feel. Ointment bases alone have therapeutic activities and should not be considered as inert ingredients in an ointment preparation/product. Ointments can also have active pharmaceutical ingredients incorporated into them, in which case the therapeutic activity of the product/preparation would be the result of both the base and the API.

There are many ointment bases available to the compounder. For example, the USP–NF has an official list of bases. There are also many commercially available ointment bases.[9]

The five classes or types of ointment bases that can be differentiated on the basis of the physical composition of ointment bases are:

1. oleaginous bases
2. absorption bases
3. w/o emulsion bases
4. o/w emulsion bases
5. water soluble or water miscible bases.

OFFICIAL OINTMENT BASES IN THE USP–NF

Caprylocaproyl Polyoxylglycerides
Diethylene Glycol Monoethyl Ether
Lanolin Alcohols
Linoleoyl Polyoxylglycerides
Ointment, White
Oleoyl Polyoxylglycerides
Petrolatum
Petrolatum, White
Polyethylene Glycol
Polyglyceryl 3 Diisostearate
Squalane
Vegetable Oil, Hydrogenated, Type II
Coconut Oil
Lanolin
Lauroyl Polyoxylglycerides
Ointment, Hydrophilic
Ointment, Yellow
Paraffin
Petrolatum, Hydrophilic
Polydecene, Hydrogenated
Polyethylene Glycol Monomethyl Ether
Rose Water Ointment
Stearoyl Polyoxylglycerides
Vitamin E Polyethylene Glycol Succinate

Adapted from "Excipients: USP and NF Excipients, Listed by Functional Category," *USP-NF Online*. (Rockville, MD: United States Pharmacopeial Convention, 2014).[10]

EXAMPLES OF COMMERCIALLY AVAILABLE OINTMENT BASES

Acid Mantle®
Cream Base™
Hydrophilic® ointment
Vanicream™
Velvachol®
Pentravan®
HEB Cream
BHRT Base
Aquaphilic® ointment
Dermabase™
Lanaphilic® ointment
Vanibase® moisturizing cream
Phytobase™
Lipobase®
Emollient Cream Base

Adapted from "Ointments, Creams, and Pastes," by L. V. Allen, Jr, chap. 19 in *The Art, Science, and Technology of Pharmaceutical Compounding*, 4th ed. (Washington, DC: American Pharmacists Association, 2012): 276.[9]

Ointments typically are used on dry, scaly lesions because of their protective and emollient properties, and they stay on the skin for an extended time, which aids in drug absorption. A specific ointment base is chosen for its inherent properties and/or for its potential to serve as a drug delivery vehicle. If an ointment base is chosen as a drug delivery vehicle, it must release the active drug in a reproducible manner. The release (diffusion) rate of a drug from an ointment base is dependent on the properties of the base, as well as the solubility of the drug in the base. Generally, oleaginous (hydrophobic) bases release drugs slowly and more unpredictably because water cannot penetrate the base sufficiently to dissolve the drug. Water miscible or hydrophilic bases tend to release drugs more rapidly and more predictably because water can penetrate into the base. A common laboratory experiment incorporates a drug into different bases and measures the release rate of the drug into a continuously stirred beaker filled with solution. The data from one such experiment are shown in Table 15.4 (http://pharmlabs.unc.edu).

It is easy to see the marked differences in the release rate depending on the type of base. Of course, a different drug with different hydrophilic/lipophilic characteristics would yield different release rates, but the generalizations seem to hold for a wide range of compounds with the wide range of different properties. Once the drug has been

Table 15.4 Release Rate of Salicylic Acid from Various Ointment Bases

Type of Ointment Base	Release Rate of 6% Salicylic Acid
Oleaginous base	31 $\mu g/min^{1/2}$
Absorption base	46 $\mu g/min^{1/2}$
W/O Emulsion base	122 $\mu g/min^{1/2}$
O/W Emulsion base	798 $\mu g/min^{1/2}$
Water miscible base	3,496 $\mu g/min^{1/2}$

released from the base, percutaneous penetration is influenced by several factors, including the area to which the ointment is applied, the condition of the skin (whether intact, denuded, or diseased), and the location and method of application.

Properties of Ointment Bases

Each type of ointment base has different physical characteristics and therapeutic uses based upon the nature of its components. Table 15.5 summarizes the properties of the five types of ointment bases, including the composition, common uses, and examples. Additional ointment bases and their properties have been categorized in this manner.[11]

The ingredients and compounding procedure for several of the ointment bases shown in Table 15.5 are listed below.

White Ointment USP

White Wax	5%
White Petrolatum	95%

Procedure for preparation:

1. Melt the white wax on a hotplate.
2. When the wax has completely melted, add the white petrolatum and allow the entire mixture to remain on the hotplate until liquefied.
3. Following liquefaction, remove from heat and stir the mixture until it begins to congeal.

Hydrophilic Petrolatum USP

Cholesterol	3%
Stearyl Alcohol	3%
White Wax	8%
White Petrolatum	86%

Procedure for preparation:

1. Melt the stearyl alcohol, white wax, and white petrolatum together on a hotplate.
2. Add the cholesterol to the mixture while still on the hotplate, and stir until completely dissolved.
3. Following dissolution, remove from heat and stir the mixture until congealed.

Cold Cream Type

White Wax	12.0%
Cetyl Esters Wax	12.5%
Mineral Oil	56.0%
Sodium Borate	0.5%
Purified Water	19.0%

Procedure for preparation:

1. Melt the white wax and spermaceti together on a hotplate in one container.
2. Add the mineral oil to this mixture and bring the temperature to 70°C.
3. Dissolve the sodium borate in water.
4. Heat the sodium borate solution to 75°C in another container.

Table 15.5 Properties of Ointment Bases

Property	Oleaginous Bases	Absorption Bases	Water/Oil Emulsion Bases	Oil/Water Emulsion Bases	Water Miscible Bases
Composition	oleaginous compounds	oleaginous base + w/o surfactant	oleaginous base + water (<45% w/w) + w/o surfactant (HLB ≤ 8)	oleaginous base + water (>45% w/w) + o/w surfactant (HLB ≥ 9)	polyethylene glycols (PEGs)
Water content	anhydrous	anhydrous	hydrous	hydrous	anhydrous, hydrous
Affinity for water	hydrophobic	hydrophilic	hydrophilic	hydrophilic	hydrophilic
Spreadability	difficult	difficult	moderate to easy	easy	moderate to easy
Washability	nonwashable	nonwashable	non- or poorly washable	washable	washable
Greasiness	greasy	greasy	greasy	nongreasy	nongreasy
Drug incorporation potential	solids or oils (oil solubles only)	solids, oils, aqueous solutions (small amounts)	solids, oils, aqueous solutions (small amounts)	solid and aqueous solutions (small amounts)	solid and aqueous solutions
Drug release potential	poor	poor, but > oleaginous	fair to good	fair to good	good
Occlusiveness	yes	yes	sometimes	no	no
Uses	protectants, emollients (+/–), vehicles for hydrolyzable drugs	protectants, emollients (+/–), vehicles for aqueous solutions, solids, and non-hydrolyzable drugs	emollients, cleansing creams, vehicles for solid, liquid, or non-hydrolyzable drugs	emollients, vehicles for solid, liquid, or non-hydrolyzable drugs	drug vehicles
Examples	White Petrolatum USP, White Ointment USP	Hydrophilic Petrolatum USP, Anhydrous Lanolin, Aquabase™, Aquaphor®, Polysorb®	Cold Cream type, Hydrous Lanolin, Rose Water Ointment USP, Hydrocream™, Eucerin®, Nivea®	Hydrophilic Ointment USP, Dermabase™, Velvachol®, Versabase®, Vanpen™	PEG Ointment USP, Polybase™

5. When both phases have reached the desired temperature, remove both phases from the hotplate and add the aqueous phase slowly and with constant stirring to the oil phase.
6. When the addition is completed, stir the mixture briskly and continuously until congealed.

Hydrophilic Ointment USP

Methylparaben	0.025%
Propylparaben	0.015%
Sodium Lauryl Sulfate	1.0%
Propylene Glycol	12.0%`
Stearyl Alcohol	25.0%
White Petrolatum	25.0%
Purified Water	37.0%

Procedure for preparation:

1. Melt the stearyl alcohol and white petrolatum on a hotplate in one container.
2. Heat this mixture to 70°C.
3. Dissolve remaining ingredients in water and heat the solution to 75°C in another container.
4. When both phases have reached the desired temperature, add the aqueous phase slowly and with constant stirring to the oil phase while still applying heat.
5. When the addition is complete, remove from heat and stir the mixture briskly and continuously until it congeals.

Water Miscible Type

Polyethylene Glycol 400	60%
Polyethylene Glycol 3350	40%

Procedure for preparation:

1. Melt the PEGs on a hotplate.
2. Heat the mixture to about 65°C.
3. When the desired temperature is attained, remove the mixture from heat and stir until congealed.

Spreadability

One of the properties of the ointment bases shown in Table 15.5 is termed *spreadability*. Spreadability describes how easily a substance can be applied over the skin and is especially important to consider when working with lipids containing oleaginous, absorption, and water-in-oil emulsion bases. Lipids that spread easily over the skin generally have a greater appeal to patients because they have a rapid absorption, which leads to a less greasy feel. Four general classes of lipids that are included in dermatological bases are shown in Table 15.6 and grouped by their spreadability property.

Dimethicone and cyclomethicone are two of the three USP–NF official water-repelling agents; the third one is simethicone.[10] In addition to their influence on spreadability, the silicones lubricate without feeling oily, reduce the "tacky" feeling associated with many lotions and creams, provide water-repelling characteristics, and enhance and stabilize foams. The physical properties of dimethicone and cyclomethicone are compared with Silicone USP in Table 15.7.

Table 15.6 Spreadability of Common Lipid Components in Ointment Bases.

Lipid Category	Examples	Spreadability
Silicone oils	• Dimethicone • Phenyl methyl polysiloxane • Cyclomethicone	Most spreadable ↕ Least spreadable
Glycerides	• Medium-chain triglycearides • Olive oil	
Moderately polar waxes	• Yellow wax • Isopropyl myristate • Ethyl hexyl palmitate	
Hydrocarbons	• Petrolatum • Soft or liquid paraffin	

Adapted from "Extemporaneous Compounding of Medicated Ointments," by K.Nagel, F. Ali, S. al-Khudari, A. Khan, K. Patel, N. Patel, and A. Desai, *International Journal of Pharmaceutical Compounding*, 14, no. 6 (2010): 472–478.[11]

Table 15.7 Comparison of Physical Properties of Silicones.

Silicone	Viscosity (Centistoke)
Cyclomethicone	4
Dimethicone	20
	100
	200
	350
	500
	1,000
	12,500
	30,000
Silicone USP	575

Adapted from "Ointments, Creams, and Pastes," by L. V. Allen, Jr., chap. 19 in *The Art, Science, and Technology of Pharmaceutical Compounding*, 4th ed. (Washington, DC: American Pharmacists Association, 2012): 276.[9]

Water Content

The inherent water content of the different types of ointment bases is also given in Table 15.8. But an important property to know about an ointment base is whether or not it has the ability to take up water. There are occasions when water will be added to an ointment base as a diluent for other ingredients, or that one of the ingredients is an aqueous or alcoholic liquid. Some ointment bases have a great ability to take up water. However, the amount of water taken up may change the consistency of the base itself. Both of these properties need to be considered when selecting an ointment base for a compounded preparation.

Several ointment bases were evaluated for the amount of water taken up and the change in consistency.[11] The results are summarized:

- PEG bases did take up large amounts of water, but softened as the water began to dissolve the water soluble PEG.

- Oil-in-water (o/w) emulsion bases thinned on incorporation of water; the extent of thinning was dependent on the ingredients present in the individual ointment base.
- Water-in-oil (w/o) emulsion bases did not incorporate as much water as anhydrous bases. It was thought that since water is in the internal phase, there was some amount of water already present in the preparation, limiting the amount of additional water that could be incorporated.
- Anhydrous bases incorporated large amounts of water. The amount of water was specific to the ointment base.

One unexpected result in the study was the ability of White Ointment USP to incorporate large amounts of water. Most references state that oleaginous bases do not accept more than small amounts of water. However, White Ointment USP has white wax as one of its ingredients, and it was found that as the white wax percentage increased, the ability to incorporate water also increased.

Table 15.8 shows the relative amounts of water, alcohol, and lipophilic solvents that can be incorporated into the different types of ointment bases.

Table 15.8 Water, Alcohol, and Oil Solvents That Can Be Incorporated into Ointment Bases

Base Type	Water	Alcohol	Oils
Oleaginous	None	Very limited	Easily, but will decrease viscosity of base
Absorption	Large quantities Aquaphor® absorbs several times its weight	Less volume than water Aquaphor® absorbs equal to its weight	Easily, but will decrease viscosity of base
W/O emulsion	Cold cream, rose water ointment—very little Eucerin®, more than these but less than Aquaphor®	Varied amounts	Easily, but will decrease viscosity of base
O/W emulsion	Absorbs some, but decreases viscosity of base. Hydrophilic ointment and Unibase® take up 30% of their weight	Less volume than water	Some will be taken up and emulsified, but larger amounts may require additional Tween® 80
Water miscible	Very limited without loss of viscosity	Base is soluble in alcohol	Incorporate with levigation with a liquid of intermediate chemical properties (glycerin, propylene glycol)

Stiffening Agents

Preparations may need to be "stiffened" (make more solid, more viscous) to have the characteristics both the compounder and the patient desires. Stiffening agents have higher melting points (50°–100°C), and when blended with ingredients that have lower melting points, will raise the overall melting point of the preparation. Table 15.9 lists the stiffening agents given in the USP–NF.[10]

Table 15.9 Stiffening Agents in the USP-NF

Stiffening Agents	Melting Point (°C)
Castor oil, hydrogenated	85–88
Cetostearyl alcohol	48–55
Cetyl alcohol	46–52
Cetyl palmitate	46–63
Dextrin	
Hard fat	27–44
Alpha-Lactalbumin	50–52, 58–61
Paraffin	46–68
Synthetic paraffin	77–100
Rapeseed oil, fully hydrogenated	
Rapeseed oil, superglycerinated, fully hydrogenated	
Sodium Stearate	245–255
Stearyl alcohol	55–60
Wax, cetyl esters	43–47
Wax, emulsifying	50–54
Wax, microcrystalline	54–102
Wax, White	62–65
Wax, Yellow	62–65

Some stiffening agents may produce a dual effect in an ointment base; besides making the ointment more viscous, it may also increase the water-holding capacity of an ointment base. Stearyl alcohol and cetyl alcohol are two examples of stiffening agents that have this dual effect. Adding 5% cetyl alcohol to white petrolatum will create an ointment that will absorb 40% to 50% of its weight in water. If 5% of PEG 3350 is replaced with stearyl alcohol, the new ointment will incorporate 6% to 25% of its weight in water. In hydrocarbon bases, 2% to 5% of Span® 80 will increase the quantity of water taken up in the ointment.[12]

Selecting an Ointment Base

The selection of an ointment base requires many questions be considered:[13]

1. What is the desired release rate of the API from the ointment base?
2. Is the preparation to be used for local or systemic effect?
3. Does the preparation need to be occlusive?

4. Does the preparation need to have good washability?
5. What area(s) is the preparation to be applied?
6. Is the API stable in the ointment base?
7. Will the API alter the consistency of the ointment base?

The *American Journal of Pharmaceutical Education* published a flow chart that takes many of these factors into consideration. It was designed for a student teaching laboratory, but illustrates a simplified method of selecting an appropriate base.[14]

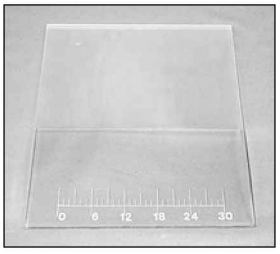
Incorporating a Drug into an Ointment Base

Insoluble powders that are to be incorporated into an ointment base should be in the *finest possible state of subdivision* because these preparations often are applied to sensitive, diseased, or denuded skin areas. Using the finest subdivision will prevent a gritty texture and allow the final preparation to be smooth to the touch. The powder form of the ingredient should be used instead of a crystalline form. The powder may have to be triturated in a mortar and pestle before being incorporated into an ointment base. *Pulverization by intervention* also can be used; the powder is dissolved in a small volume of solvent and the solvent is allowed to evaporate. The powder recrystallizes as very fine particles.

Levigating agents also can be used to reduce the particle size of the powder. When choosing a levigating agent, the one that is selected should be miscible with the ointment base or the part of the ointment base where the drug will reside. Some powders can be incorporated into ointment bases by first dissolving the solid in a solvent or oil that can be taken up by the ointment base. In this technique, use solvents that have low vapor pressures so they will not easily evaporate. Solvents that easily evaporate may crystallize the drug in the base and cause skin irritation upon application. If a powder ingredient has an electrostatic charge, using a few drops of mineral oil or other suitable solvent can enhance the workability of the powder.

For oleaginous, absorption, and w/o emulsion bases, mineral oil is a reasonable levigating agent. Other levigating agents might be castor oil, cottonseed oil, olive oil, or Tween® 80. For o/w emulsion and water soluble bases, glycerin is a good choice. Other possible levigating agents include propylene glycol and polyethylene glycol 400. For some powders, 10 to 15 drops of the agent is a sufficient amount. Other powders require 1 to 2 mL of levigating agent. Sometimes a small portion of melted ointment base can serve as the levigating agent. Use the minimum amount of levigating agent necessary to wet the powders.

Use an ointment slab (or tile) to incorporate a powder into an ointment base using any of the procedures given above. Ointment slabs—either ground glass plates or porcelain—provide a hard, nonabsorbent surface for mixing (Fig. 15.3). *Ointment pads* have the advantage that cleanup is quicker, but the ointment can soak into the parchment paper. Further, the paper can absorb liquids and may tear when using sticky or thick ointments.



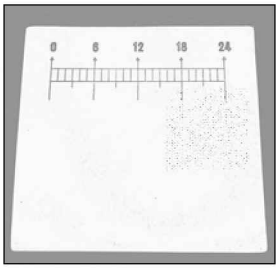


Figure 15.3 Ointment slabs.

Use large metal spatulas instead of smaller metal spatulas because they have the proper combination of flexibility and strength for adequate shearing and mixing. Black rubber or plastic spatulas are not used in ointment compounding.

When preparing a large quantity of ointment, a mixing device of some type might be used instead of an ointment slab and spatulas. Two options are an ointment mill and an electric mortar and pestle. Ointment mills (Fig. 15.4A) produce very smooth and elegant ointments. The electric mortar and pestle (Fig. 15.4B) option allows the mixing to be done and the preparation to be dispensed in the same container.

Comments Specific to Each Ointment Base

Procedures to incorporate drugs into the various types of ointment bases are given below.

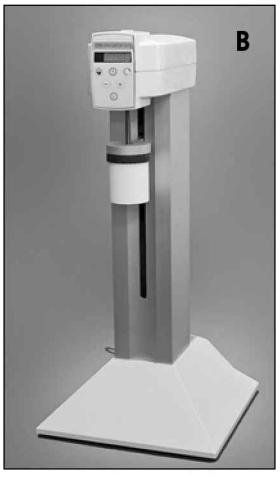


Figure 15.4 An ointment mill (A) and an electric mortar and pestle (B).

Oleaginous Bases

To incorporate an insoluble drug into an oleaginous base, first pulverize the powder on the ointment slab with a spatula or in a mortar and with a pestle. Use a levigating agent to wet the powder, and then incorporate the wetted powder into the ointment base. A good levigating agent is mineral oil, because it is compatible with oleaginous bases. Sometimes, using a small quantity of the base itself as the levigating agent is sufficient.

Generally, the amount of drug to be incorporated into the ointment will be much less than the amount of ointment; i.e., a small amount of drug will be incorporated into a large amount of ointment. The process of *geometric dilution* "dilutes" the drug into the ointment. Geometric dilution involves a series of dilution steps. First the drug is incorporated into an amount of ointment of approximately the same size. Then a

second amount of ointment approximately equal to the first mixture is added and mixed. This stepwise dilution process is continued until all of the ointment has been used. (Fig. 15.5)

Soluble drugs can be incorporated into oleaginous bases by fusion. The base is liquefied over low heat (not to exceed 70°C), then the drug is added to the molten base. The mixture is allowed to cool, with continual stirring.

Absorption Bases

An absorption base is an oleaginous base containing a w/o emulsifying agent. When water is taken up into the base, it will remain a w/o emulsion. Absorption bases typically can incorporate about 50% of their volume in water.

Incorporating insoluble drugs into these bases can be done mechanically or by fusion. The final destination (internal or external phase of the emulsion) of the drug must be considered when selecting a water soluble levigating agent. The levigating agent should be water soluble or water miscible if the drug will reside in the internal phase (water phase). Water, glycerin, alcohol, and propylene glycol are suitable levigating agents. If the drug will reside in the external phase, mineral oil should be used.

Water soluble ingredients can be added to the water phase of the w/o emulsion. If the drug will dissolve in a small amount of water, the aqueous solution can be added directly to the base using an ointment slab and spatulas. If a larger quantity of water is needed to solubilize the drug or if an aqueous solution is being added to the base, heat may be needed to compound the preparation. It may be necessary to add emulsifier to the emulsion to accommodate the added water. Some commercial emulsions do have the necessary excess emulsifier.

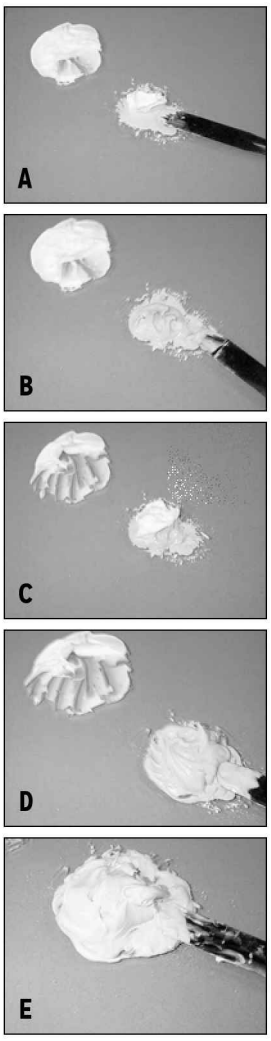


Figure 15.5
Incorporating an insoluble drug into an ointment base using geometric dilution (A) levigate the powder to reduce the particle size and wet the powder; bring a portion of ointment about equal in size to the powder, (B) incorporate the ointment and levigated powder together, (C) bring another portion of ointment about equal in size to the first mixture, (D) again incorporate the ointment and the mixture from the first addition, (E) continue the additional in like manner until all of the powder has been incorporated into the ointment.

W/O Emulsion Bases

Oils and insoluble powders can be incorporated into the external phase directly, using an ointment slab and spatulas. If a levigating agent is to be used with the insoluble powders, it should be miscible with the oil phase; mineral oil is a suitable agent. If the insoluble powder has a different salt form that is oil soluble, consideration should be given to using that salt form. The same comments that apply to incorporating water soluble ingredients into absorption bases apply to w/o emulsion bases.

O/W Emulsion Bases

Water soluble powders can be incorporated directly into the external phase using an ointment slab and spatulas. If the powder is insoluble, the levigating agent should be water miscible, so glycerin, propylene glycol, polyethylene glycol (PEG) 300 or 400, or alcohol is acceptable. If the insoluble substance has a different salt form that is aqueous soluble, consideration should be given to using that salt form.

Incorporating oil soluble ingredients into the o/w preparation may be more difficult. A small amount of oil can be incorporated into the base if there is excess emulsifier. Some commercial products do have the necessary excess emulsifier. If a larger portion of oil is to be added, more emulsifier may have to be added. If heat is used to incorporate the oil, it is important to work quickly so water does not evaporate from the product and cause it to become stiff and waxy.

Water Miscible Bases

Water soluble drugs can be dissolved in a small quantity of water and incorporated using an ointment slab and spatulas. Insoluble powders require a water miscible levigating agent such as glycerin, propylene glycol, or polyethylene glycol 400. Oils can be added to these bases by first mixing the oil with glycerin or propylene glycol, then incorporating the mixture into the base. If the quantity of liquid to add to the base is large, heat may be necessary.

Pastes

Pastes contain more solid material than ointments—at least 20% solids—so pastes are stiffer than ointments. This increased stiffness reduces the percutaneous absorption potential of any drug incorporated in the paste. However, they are not generally used for their absorption potential but rather for their protective action and for their ability to absorb serous discharges from skin lesions. They also remain in place longer than ointments.

Pastes generally are prepared using oleaginous bases and heat. Heat improves the workability of pastes and also allows a high percentage of solids to be incorporated into the base. With such a high content of solids, it is imperative that the preparation be stirred thoroughly and

LIST OF OFFICIAL PASTES FROM USP-NF

- Zinc Oxide Paste
- Nontoxic, nonirritating, and nonallergenic
- Zinc Oxide and Salicylic Acid Paste
- Carboxymethylcellulose Sodium Paste
- Magnesium Hydroxide Paste
- Triamcinolone Acetonide Dental Paste

Adapted from "Monographs," *USP-NF Online.* (Rockville, MD: United States Pharmacopeial Convention, 2014).[15]

continuously during the cooling process to prevent the solids from settling. Preparations should be cooled to the point at which they are viscous fluids before being placed in tubes or jars. If poured into a container while hot, they tend to separate on cooling.

Levigating agents are not used in preparing pastes because the large volume needed may wet the high percentage of solids, causing the paste to liquefy and become less stiff.

Packaging

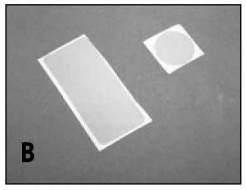


Figure 15.6 Packaging for ointments: (A) jars, and (B) patches.

All of these preparations can be packaged in a variety of devices such as tubes, jars, applicators, syringes, patches, and pump dispensers (Fig. 15.6). The packaging should keep the preparation clean during repeated use, and as free from air exposure and microbial contamination as feasible. All of the packaging devices except the ointment jar meet these criteria. With an ointment jar, a tongue depressor can be used to remove the required quantity of preparation and thereby keep the preparation free from hand contamination. Because of their stiff consistency, pastes usually are packaged in ointment jars.

Packing an Ointment Jar

When hand packing an ointment jar (Figure 15.7), care should be taken to remove air pockets that form as the ointment is packed. Also, the top of the ointment should be smoothed to give the ointment a "finished" look and to keep the ointment from sticking to the jar lid.

Filling and Sealing an Ointment Tube

An ointment tube can be filled using a urethra tip and a plastic bag (Fig. 15.8). A corner of the bag is cut and the tip is secured into position. The bag then is filled with the ointment and squeezed into the open end of an ointment tube. Once the tube is filled, the open end has to be sealed.

Other methods may be used to fill ointment tubes, but regardless of the filling method, the tube must be sealed before dispensing. Figures 15.9 and 15.10 show two methods for sealing ointment tubes.

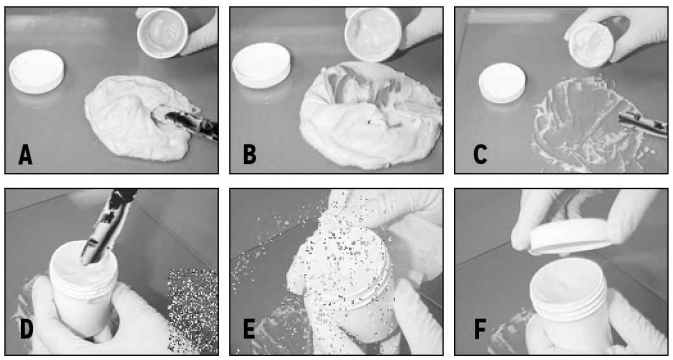


Figure 15.7 Hand packing an ointment jar: (A) Take some of the ointment and fill the bottom crevices, (B) work additional ointment along the sides of the jar, rotating the jar while filling it, (C) continue adding ointment, (D) make a professional looking finish and keep the ointment from sticking to the lid of the jar by slightly depressing the spatula toward the center while rotating the jar, (E) clean the jar threads with a tissue, and (F) put on the lid.

Devices That Dispense Measured Amounts of Ointment

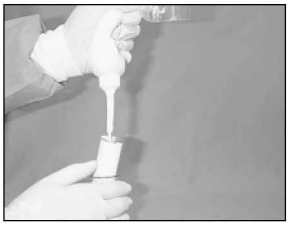


Figure 15.8 Filling an ointment tube.

Several products are available that allow patients to easily dispense metered dosages with a degree of accuracy. Among these are the AccuPen™, Topi-Click®, and Exact Dose dispensers for Unguator® jars.

Figure 15.9 An electric vacuum pump tube sealer.

The AccuPen™ device (Fig. 15.11) can be used as a replacement for single-dose syringes because it delivers a small amount of preparation, about 0.25 mL with 2 actuations. As its name implies, the AccuPen™ is designed to be used like a pen, with a button on the nondispensing end. The pen can be locked by turning the button on the end clockwise and unlocked by turning it counterclockwise. The dispenser has a window on its side to indicate the amount of preparation remaining inside the device.

The Topi-Click® dispenser (Fig. 15.12) functions like a syringe in that it involves moving a plunger to force a preparation through a barrel-like jar. The base of the dispenser rotates and "clicks" with each quarter of a turn to indicate that a volume of 0.25 mL has been displaced from inside the jar. A patient can be told the number of clicks to use to dispense the appropriate dose of the preparation. The ointment can be easily spread onto the application site directly from the Topi-Click® because of the dome-shaped applicator, which prevents the patient from contacting the ointment with their hands. In addition, there is a marking on the container indicating when there are

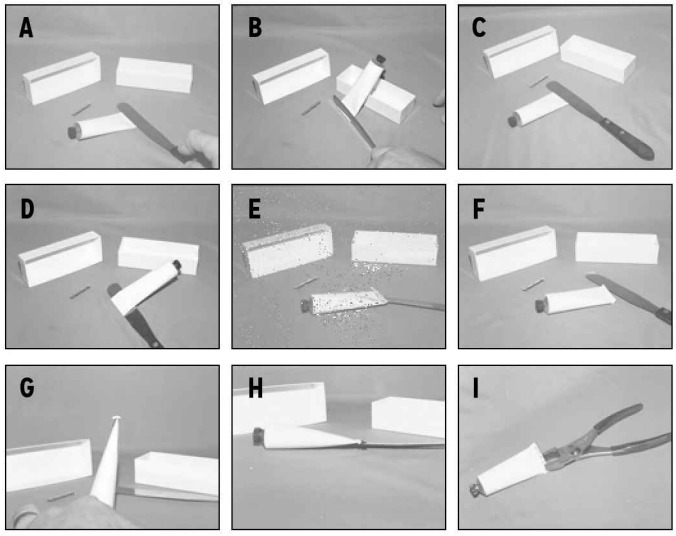


Figure 15.10 Sealing an ointment tube by hand: (A) using a stainless steel spatula, flatten the last 1/2 inch of the ointment tube; (B) with the edge of the spatula, make one fold 1/8 inch from the end of the tube; bending the tube all the way over the spatula; (C) using the spatula, make a second fold 1/4 inch from the end of the tube; (D) again bend the tube all the way over the spatula; (E) turn the ointment tube over and make a third fold 1/8 inch from the end of the tube; (F) this will create a "T" at the end of the tube; (G) side view of the "T" at the end of the tube; (H) turn the edges of the "T" down onto the tube and place the clip on the tube; (I) use pliers or a suitable crimping tool to collapse the clip onto the tube; (J) dispense the tube in a telescoping box.

32 or 12 clicks remaining, to help remind the patient when it is time to order a refill.

Figure 15.11 AccuPen™.

An experiment in the student compounding laboratory compared a mock progesterone emollient cream dispensed from the AccuPen™ and the Topi-Click®. Students made the cream preparation that was calamine, PEG 1450, diphenhydramine, and Emollient Cream™ and packaged the two devices according to the manufacturers' instructions. The cream was dispensed into weigh boats multiple times (n=5) and weighed with an electronic balance by each student (n=139). The tapped density of the cream (approx.. 0.97 g/mL) was used to convert the weight of cream to the volume of cream dispensed by the device. The AccuPen™ is to dispense 0.25 mL with 2 actuations, and the Topi-Click® is to dispense 0.25 mL with 1 click.

Figure 15.12 Topi-Click® dispenser.

Data collected from the students shows that the AccuPen™ dispensed the stated volume only a few times, whereas the Topi-Click® did not meet its volume at all. From the AccuPen™, more than half of the students actuated an average volume between 0.08 to 0.1 mL (Fig. 15.13A), most of which were approximately 0.085 mL (Fig. 15.13B). The Topi-Click® showed more variation in dispensed volumes. The outcomes of this experiment cannot be directly compared to the manufacturers' claims, however, because the viscosities and densities of the preparations used to calibrate the devices are not known. It is to be expected that differences in physical properties would yield different results. As with any metered dosing device, both dispensers should be calibrated before dispensing to patients.

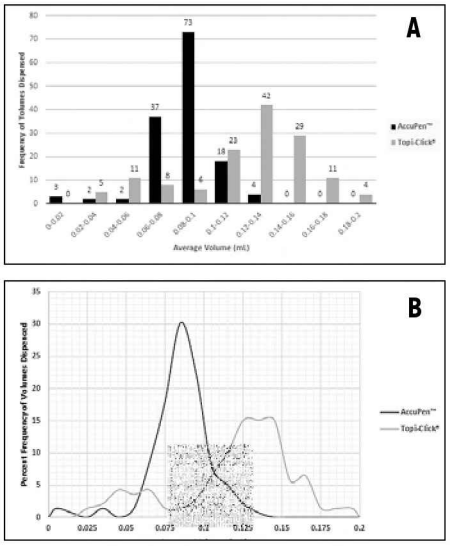


Figure 15.13 Average volumes of cream dispensed per actuation: (A) within a range of volumes, and (B) by percentages of volumes.

Unguator® jars (Fig. 15.14) are convenient in that the compounded preparation can be mixed directly in the container, then stored and cleanly dispensed from the same container. A device such as the Exact Dose dispenser can be attached to the jar, allowing for a measured dose of preparation to be dispensed with accuracy. This device involves a small chamber with a stopper inside. The bottom of the Unguator® jar is pressed upward until the dispenser cap is filled with ointment and the small stopper moves to the top of the chamber. The chamber is then rotated 180° and the bottom of the jar is pressed until the ointment is fully expelled. At the same time, the stopper is moved to the top of the chamber once again and a dose of ointment is primed for the next use.

Figure 15.14 Unguator® jar with the Exact Dose dispenser.

Observing Preparations for Evidence of Instability

USP–NF Chapter <1191> notes that, "the primary indication of instability is often either discoloration or a noticeable change in consistency or odor." For ointments, excessive "bleeding" (i.e., separation of excessive amounts of

liquid) and formation of granules or grittiness are other possible indicators of instability.[16] Chapter <1151> Pharmaceutical Dosage Forms states that creams usually require the addition of a preservative(s) unless they are compounded immediately prior to use and intended to be consumed in a relatively short period of time.[17]

In a more general sense, instability of the various dermatological preparations can be identified by a separation of components, discoloration, development of rancid odor, dryness, crystal growth, shrinkage resulting from water loss, and gross microbial contamination. Anhydrous preparations tend to be relatively more stable than hydrous products. The default beyond-use dating of Chapter <795> indicates that nonaqueous preparations have a 6 month beyond-use dating if all ingredients have expiration dates longer than that period of time. For topical preparations containing water, the beyond-use dating is 30 days.[18]

Ointments are susceptible to contamination by *Pseudomonas aeruginosa* and *Staphylococcus aureus*. Dermatological preparations are not required to be sterile, but the use of preservatives may be justified because of the potential contamination. Preservatives commonly used in ointments are methylparaben and propylparaben, benzoic acid, benzyl alcohol, quaternary ammonium salts (e.g., benzalkonium chloride), thimerosal, and sorbic acid.[19] Preparations that contain water support microbial growth to a greater extent than those that have little moisture, thereby creating a greater need for preservation. The preservative should be concentrated in the aqueous phase of the ointment because most bacterial growth will occur in that phase. If a preservative partitions into the oil phase of the ointment, additional preservative may be necessary.

Ointments are best packaged in tubes or in syringes, if feasible. Such packaging leaves minimal space for air, and the product can be kept clean during administration. Syringes can be filled by drawing the softened ointment into the barrel using the plunger, or by removing the plunger and filling the barrel. A problem might occur when the plunger is re-inserted into the barrel; it might expel ointment from the syringe. This can be avoided by placing a straightened paperclip down the inside of the barrel and then inserting the plunger. The paperclip will allow air to escape from the barrel until the plunger touches the ointment. The paperclip then can be removed and the seal between the barrel and the plunger is reestablished.

Ointment jars, although widely used, expose the preparation to air when opened and to microbial contamination, particularly when ointment is removed with the fingers. One way to lessen contamination is to use an implement similar to a tongue depressor to remove the required quantity of ointment from a jar for application. Pharmacies that prepare large quantities of ointments often use plastic tubes and a tube sealer.

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Formulation Record 1

Note: The purpose of this lab is to use contemporary compounding equipment for dermatologicals and investigate the influence of the equipment on the particle size and texture of a preparation. You will make a large batch of a urea 20% (200 gm) on a pill tile, then use part of it in the Unguator® (50 gm) and part in an ointment mill (120 gm). You will then evaluate the urea particle size in each preparation using microscopic techniques. You will also package 20 gm of the ointment in an ointment tube and use a heat sealer to seal the tube.

Name: Urea Ointment

Strength: 20%

Dosage Form: Ointment

Route of Administration: Topical

Date of Last Review or Revision: xx/xx/xx

Person Completing Last Review or Revision: YOU

Ingredient	Quantity	Physical Description	Solubility	Therapeutic Activity
Urea USP	20 g	tetragonal prism crystals, with odor of ammonia; salty taste	1 gm/mL water, 1 gm /10 mL alcohol	astringent, antiseptic
White petrolatum USP	80 g	yellowish, unctuous ointment, slightly odorous	insoluble in water and alcohol; freely soluble in chloroform, ether	lubricant, suspending agent

Equipment Required:

- Prescription balance
- Ointment slab
- 2 stainless steel spatulas

Method of Preparation:

1. Using the prescription balance, weigh urea and petrolatum. Place on pill tile.
2. Use a small portion of the petrolatum as a levigating agent, and levigate the urea to form a smooth paste.
3. Using geometric dilution, incorporate the levigated urea into the remaining petrolatum.
4. Package 20 gm of the finished preparation in an ointment tube.
5. Use 50 gm of the finished preparation for the Unguator.
6. Use the remainder of the finished preparation for the ointment mill.

Description of Finished Preparation:

Thick, unctuous ointment with a gritty appearance (on pill tile).

Quality Control Procedures:

Weight of final preparation.
Microscopic examination.

Packaging Container:

An ointment tube, 4 oz ointment jar, 100 gm Unguator jar.

Storage Requirements:

Can be stored at room temperature.

Beyond-Use Date Assignment:

USP <795> Guidelines: Nonaqueous formulations: The beyond-use date is not later than the time remaining until the earliest expiration date of any ingredient, or 6 months, whichever is earlier.

Label Information:

For External Use Only

Source of Recipe:

The Pharmaceutics and Compounding Laboratory website: http://pharmlabs.unc.edu

Literature Information:

Applied Pharmaceutics and Contemporary Compounding, 2nd ed., chap. 15, "Dermatological Formulations: Ointments and Pastes."

Formulation Record 2

Note: The purpose of this lab is to demonstrate the techniques of incorporating a powder into an ointment.

Name: Hydrocortisone Ointment

Strength: 2.0%

Dosage Form: Ointment

Route of Administration: Topical

Date of Last Review or Revision: xx/xx/xx

Person Completing Last Review or Revision: YOU

Ingredient	Quantity	Physical Description	Solubility	Therapeutic Activity
Hydrocortisone USP, micronized	2%	white, amorphous powder, odorless	0.28 mg/mL in water 15.0 mg/mL in ethanol	anti-inflammatory glucocorticoid
Glycerin USP	s.a.	clear, very viscous liquid sweetener, solvent	miscible with water	sweetener, solvent, levigating agent
Calamine USP	4%	pink, amorphous powder, odorless	insoluble in water; almost completely soluble in mineral acids	used as visual aid, topical protectant, astringent
Emollient Cream	qs 60 gm	white, moist appearing cream, smooth texture, particle free	NA	cream base

Equipment Required:

- Prescription balance
- Ointment slab
- 2 stainless steel spatulas

Method of Preparation:

1. Using the prescription balance, weigh hydrocortisone and calamine. Place on ointment slab.
2. Levigate the powders with glycerin to form a smooth paste.
3. Using geometric dilution, incorporate the levigated powders into the base. Use two stainless steel spatulas.
4. Package in ointment jar. Provide a professional finish.

Description of Finished Preparation:

Uniform, lightly pink cream with no visible particles; spreads easily without a gritty texture

Quality Control Procedures:

Observations for uniform consistency.
Weight of final preparation.

Packaging Container:

Package in 2 oz. plastic ointment jar.

Storage Requirements:

Store at room temperature.

Beyond-Use Date Assignment:

USP <795> Guidelines: Nonaqueous formulations: The beyond-use date is not later than the time remaining until the earliest expiration date of any ingredient, or 6 months, whichever is earlier.

Label Information:

External Use Only

Source of Recipe:

The Pharmaceutics and Compounding Laboratory website: http://pharmlabs.unc.edu

Literature Information:

Applied Pharmaceutics and Contemporary Compounding, 2nd ed, chap 15, "Dermatological Formulations: Ointments and Pastes."

Formulation Record 3

Note: The purpose of this lab is to compound a preparation by the beaker method of making ointments.

Name: Cold Cream

Strength: Base

Dosage Form: Cream

Route of Administration: Topical

Date of Last Review or Revision: xx/xx/xx

Person Completing Last Review or Revision: YOU

Ingredient	Quantity	Physical Description	Solubility	Therapeutic Activity
Cetyl esters wax	125 g	white to off-white translucent flakes, faint odor, bland taste	insoluble in water, soluble in hot alcohol, chloroform, ether, and fixed oils	texturing agent
White wax	120 g	white, soft to brittle wax, slight balsamic taste, honey-like odor	practically insoluble in water, soluble in hot alcohol, chloroform, benzene, ether	stiffening agent
Mineral oil	560 g	colorless, transparent, oil liquid, tasteless, odorless	insoluble in water and alcohol	Internal–laxative; External–emollient, texturing agent
Sodium borate	5 g	hard crystals, or granules, efflorescent in dry air	1 gm in 16 mL of water or 1 gm of glycerol; insoluble in alcohol	preservative; alkalizing agent
Purified water	190 mL	colorless, transparent, liquid, tasteless, odorless	N/A	vehicle

Example Calculations:

Specific gravity of mineral oil = 0.88

Equipment Required:

- Prescription balance
- Hot plate, thermometer
- 2 small beakers
- Glass stirring rod

Method of Preparation:

1. Using the prescription balance, weigh the solid ingredients.
2. If necessary, reduce the cetyl esters wax and the white wax to small pieces.
3. Melt the cetyl esters wax and the white wax in a beaker using a hot plate.
4. Add the mineral oil and continue heating the mixture until it reaches 70°C.
5. Dissolve the sodium borate in the purified water, which has been warmed in a second beaker to 70°C.
6. Add the warm aqueous mixture gradually to the melted oleaginous mixture.
7. Remove the resulting mixture from the heat; stir rapidly and continuously until the mixture has congealed.
8. Package in ointment jar. Provide a professional finish.

Description of Finished Preparation:

Uniform, luminescent white cream with no visible particles; spreads easily without a gritty texture.

Special Note: Preparation will not reach final form for several hours.

Quality Control Procedures:

Observations for uniform consistency.
Weight of final preparation.

Packaging Container:

Package in appropriate size plastic ointment jar.

Storage Requirements:

Store at room temperature.

Beyond-Use Date Assignment:

USP <795> Guidelines: Water containing topical preparation. 30 days.

Label Information:

External Use Only

Source of Recipe:

The Pharmaceutics and Compounding Laboratory website: http://pharmlabs.unc.edu

Literature Information:

Applied Pharmaceutics and Contemporary Compounding, 2nd ed., chap. 15, "Dermatological Formulations: Ointments and Pastes."

Formulation Record 4

Note: This lab will explore the relationship between emulsion stability and the amount of energy put into compounding an emulsion preparation. You will make two batches of the coal tar ointment, but by different methods. The first batch will be made by the ointment slab method. The second batch will be prepared using the Unguator.

Name: Coal Tar Ointment

Strength: 10% v/w Coal Tar Solution, 2% w/w Salicylic Acid

Dosage Form: Ointment

Route of Administration: Topical

Date of Last Review or Revision: xx/xx/xx

Person Completing Last Review or Revision: YOU

Ingredient	Quantity	Physical Description	Solubility	Therapeutic Activity
Coal tar solution USP	163.4 mL	almost black non-viscous liquid with strong naphthalene odor	81%–86% alcohol content; miscible with alcohol; coal tar compounds will precipitate out in water	local irritant, some keratolytic activity
Salicylic acid USP	32.7 g	white, crystalline powder	1 g/460 mL water; 1 g/2.7 mL alcohol	topical keratolytic
Polysorbate 80 NF	81.7 mL	amber colored, oily, viscous liquid	very soluble in water; sp. gr. = 1.08; soluble in alcohol	emulsifying agent
Ethyl alcohol USP	32.7 mL	clear non-viscous liquid	sp. gr = 0.82; miscible with water	solvent
Emollient cream	1357.7 g	unctuous, smooth, white cream	miscible with aqueous solutions and some oil based substances	ointment base
Total Batch Size	1634.0 g	NA	NA	NA

Equipment Required:

- Prescription balance
- Small and large stainless steel spatulas
- Ointment slab or mortar and pestle or Unguator®
- 50 mL beaker or 20 mL scintillation vial

Method of Preparation:

Ointment Slab Method:

1. Weigh the salicylic acid and emollient cream.
2. Add alcohol to the coal tar solution in a scintillation vial or small beaker.
3. Add salicylic acid and dissolve in the coal tar solution-alcohol mixture.
4. Incorporate the polysorbate 80 into the mixture from step 3.
5. Incorporate the liquid mixture from step 4 into a portion of the emollient cream.
6. Using geometric dilution, incorporate the remaining emollient cream.
7. Package in a plastic ointment jar.

Unguator Method:

1. Weigh the salicylic acid and emollient cream.
2. Add alcohol to the coal tar solution in a scintillation vial or small beaker.
3. Add salicylic acid and dissolve in the coal tar solution-alcohol mixture.
4. Incorporate the polysorbate 80 into the mixture from step 3.
5. Add the emollient cream to the Unguator jar, and then the mixture from step 4. Slightly blend the mixture with a hard rubber spatula.
6. Add the liquid mixture from step 4 into the jar, and again slightly blend with a hard rubber spatula.
7. Complete blending using an Unguator. Blend for 1.5 minutes and a rotation speed of 6.
8. Cap the mixing jar.

Description of Finished Preparation:

Gold to golden smooth, opaque cream with naphthalene odor.

Quality Control Procedures:

Preparation weight.
No signs of emulsion separation or breaking.
No change in physical appearance.

Packaging Container:

Plastic ointment jar or Unguator mixing jar.

Storage Requirements:

Room temperature; keep away from heat.

Beyond-Use Date Assignment:

USP <795> Guidelines: Nonaqueous formulations: The beyond-use date is not later than the time remaining until the earliest expiration date of any ingredient, or 6 months, whichever is earlier.

Label Information:

External Use Only

Source of Recipe:

The Pharmaceutics and Compounding Laboratory website: http://pharmlabs.unc.edu

Literature Information:

Solubility Information:

The Merck Index, 12th ed., 1996.
Remington's Pharmaceutical Sciences, 16th ed., p. 724
Allen, L. V., Jr. "Basics of Compounding with Tars," *International Journal of Pharmaceutical Compounding* 17, no. 5 (2013): 400–410.

Formulation Record 5

Name: Calamine – Zinc Oxide Ointment

Strength: 12.5% Calamine, 12.5% Zinc Oxide

Dosage Form: Ointment

Route of Administration: Topical

Date of Last Review or Revision: xx/xx/xx

Person Completing Last Review or Revision: YOU

Ingredient	Quantity	Physical Description	Solubility	Therapeutic Activity
Calamine	8.25 g	Pink powder	Insol in water and alcohol	Protective, astringent, antiseptic
Zinc oxide	8.25 g	White powder	Insol in water and alcohol	Protective, astringent, antiseptic
Mineral oil	Variable	Clear oil	NA	levigating agent
Aquaphor®	49.5 g less wt of levigating agent	Semisolid ointment base	NA	base

Example Calculations:

(for total weight = 66 g):

Calamine and zinc oxide (of each)

12.5 g / 100 g × 66 g = 8.25 g

Aquaphor: 66 g – 8.25 g calamine – 8.25 g zinc oxide = 49.5 g - weight of levigating agent

e.g., if 5 mL mineral oil used = 5 mL × 0.88 = 4.4 g (sp. gr = 0.86 – 0.905; average = 0.88)

Equipment Required:

- Prescription balance to weigh solid ingredients
- Ointment slab for mixing ointment
- 6" metal spatula to mix ointment ingredients; 4" metal spatula for scraping and packing ointment
- 5 mL–10 mL syringe to measure mineral oil

Method of Preparation:

1. Weigh the calamine and zinc oxide.
2. Draw a known quantity of mineral oil into a syringe and use as needed to levigate the powders. Determine final volume used by difference.
3. Subtract the weight of levigating agent from weight of Aquaphor.
4. Weigh Aquaphor.
5. Incorporate levigated solids into the Aquaphor using geometric dilution.
6. Transfer completed ointment into ointment jar.

Description of Finished Preparation:

Non-gritty pink ointment.

Quality Control Procedures:

- Preparation should be a well-mixed, homogenous preparation free from palpable or observable particles, but have a stiff, paste-like consistency.
- Preparation should be elegantly packaged in ointment jar with no preparation on jar lid.
- Proper amount of ointment should be in ointment jar.

Packaging Container:

2 ounce plastic ointment jar.

Storage Requirements:

Can be stored at room temperature.

Beyond-Use Date Assignment:

USP <795> Guidelines: Nonaqueous formulations: The beyond-use date is not later than the time remaining until the earliest expiration date of any ingredient, or 6 months, whichever is earlier.

Label Information:

For External Use Only

Source of Recipe:

A Practical Guide to Contemporary Pharmacy Practice (Philadelphia: Lippincott Williams & Wilkins, 1998).