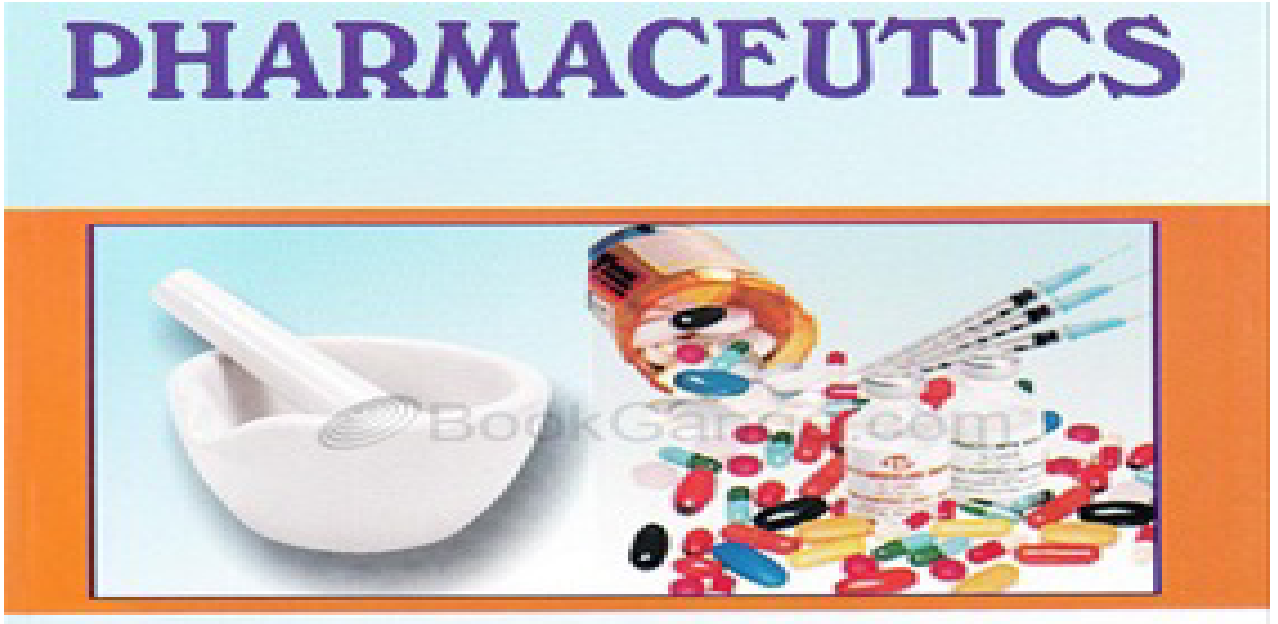

Semisolid dosage forms 2018

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MSc. Phar.Sci. (Pharmaceutics)

Semisolid

- A state of matter inbetween solid and liquid. It's neither solid nor liquid.
- It has some properties of solid e.g. trexture and melting
- It also has some properies of liquids such as spreadability& container volume shape

Types, definition & uses of S.S. dosage forms

Ointments, creams, and gels are semisolid dosage forms intended for topical application. They may be applied to the skin, placed on the surface of the eye, or used nasally, vaginally, or rectally. Most of these preparations are used for the effects of the therapeutic agents they contain. The unmedicated ones are used for their physical effects as protectants or lubricants.

Topical preparations are used for both local and systemic effects. Systemic drug absorption should always be considered when using topical products if the patient is pregnant or nursing, because drugs can enter the fetal blood supply and breast milk and be transferred to the fetus or nursing infant.

FEATURES AND USE OF DERMATOLOGIC PREPARATIONS

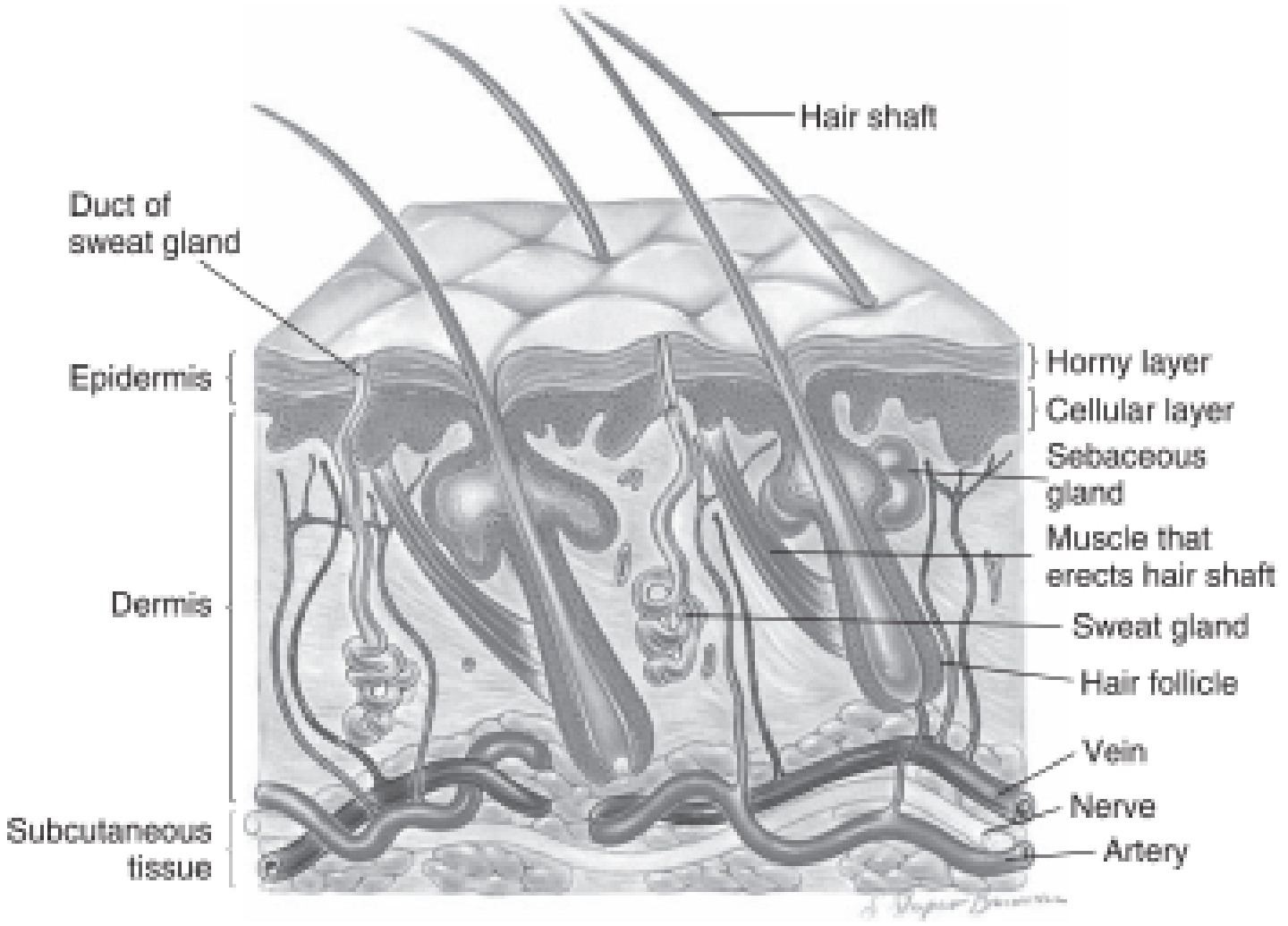

FIGURE 10.9 Stratified organization of the skin. (Reprinted with permission from Bickley LS, Szilagyi P. Bates' Guide to Physical Examination and History Taking. 8th Ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2003.)

The skin is divided histologically into the stratum corneum (the outer layer), the living epidermis, and the dermis, collectively a laminate of barriers protecting against permeation by external agents and loss of water from the body. Blood capillaries and nerve fibers rise from the subcutaneous fat into the dermis and up to the epidermis. Sebaceous glands, sweat glands, and hair follicles originating in the dermis and subcutaneous layers rise to the skin's surface (Fig. 10.9). The stratum corneum is the desquamating horny layer, a 10- to 15-μm thick layer of flat, partially desiccated, dead epidermal cells (8, 9). The stratum corneum is composed of approximately 40% protein (mainly keratin)

and 40% water, with the balance being lipid, principally as triglycerides, free fatty acids, cholesterol, and phospholipids. On the surface is a film of emulsified material composed of a complex mixture of sebum, sweat, and desquamating epidermal cells.

The film covering the stratum corneum varies in composition, thickness, and continuity as a result of differences in the proportion of sebum and sweat produced and the extent of their removal through washing and sweat evaporation. It offers little resistance to drug penetration. Hair follicles and gland ducts can provide entry for drug molecules, but because their relative surface area is so minute compared to the total epidermis, they are minor factors in drug absorption.

The stratum corneum, being keratinized tissue, behaves as a semipermeable artificial membrane, and drug molecules can penetrate by passive diffusion. The rate of drug movement across this skin layer depends on the drug concentration in the vehicle, its aqueous solubility, and the oil–water partition coefficient between the stratum corneum and the product's vehicle (10). Substances with both aqueous and lipid solubility characteristics are good candidates for diffusion through the stratum corneum. Once through the stratum corneum, drug molecules may pass through the deeper epidermal tissues and into the dermis. If the drug reaches the vascularized dermal layer, it becomes available for absorption into the general circulation.

7 In treating skin diseases, the drug in a medicated application should *penetrate* and be *retained* in the skin for a while. Drug penetration into the skin depends on a number of factors, including the physicochemical properties of the medicinal substance, the characteristics of the pharmaceutical vehicle, and the condition of skin itself. Normal unbroken skin acts as a natural barrier, limiting both the rate and degree of drug penetration.

Such penetration (percutaneous absorption) should be enough to reach epidermis or dermis but limited to not reach subcutaneous layer where the drug is absorbed to blood causing undesirable adverse effects

However, if systemic effect is desired, penetration through the skin layers till it reaches blood should be achieved. This is called TRANSDERMAL delivery (TRANSDERMAL absorption) and will be discussed in "Advanced drug delivery systems"

OINTMENTS

Ointments are semisolid preparations intended for external application to the skin or mucous membranes. Ointments may be medicated or not. Unmedicated ointments are used for the physical effects they provide as protectants, emollients, or lubricants. *Ointment bases*, as described, may by used for their physical effects or as vehicles for medicated ointments.

Types of ointments

Ointments are classified pharmaceutically according to type of Ointment bases.

OINTMENT BASES

Ointment bases are generally classified by the USP (2) into four groups: (*a*) oleaginous bases, (*b*) absorption bases, (*c*) water-removable bases, and (*d*) water-soluble bases.

Note: Pharmaceutically, a base is a semisolid vehicle comprising the largest proportion in the semisolid dosage form.

Oleaginous Bases

Oleaginous bases are also termed *hydrocarbon bases*. On application to the skin, they have an emollient effect, protect against the escape of moisture, are effective as occlusive dressings, can remain on the skin for long periods without drying out, and because of their immiscibility with water are difficult to wash off. Water and aqueous preparations may be incorporated, but only in small amounts and with some difficulty. Petrolatum, white petrolatum, white ointment, and yellow ointment are examples of hydrocarbon ointment bases.

When powdered substances are to be incorporated into hydrocarbon bases, liquid petrolatum (mineral oil) may be used as the levigating agent.

Name	Synonyms
xxxxxx	Paraffin wax= White wax = hard paraffin
xxxx	Liquid paraffin= paraffin oil= Mineral oil
Petrolatum	Yellow soft parrafin = Yellow petroleum. Jelly= Vaseline
White petrolatum	White soft paraffin = White petroleum jelly = White Vaseline

Petrolatum, USP, is a purified mixture of semisolid hydrocarbons obtained from petroleum. It is an unctuous mass, varying in color from yellowish to light amber. It melts at 38°C to 60°C and may be used alone or in combination with other agents as an ointment base. Petrolatum is also known as yellow petrolatum and petroleum jelly. A commercial product is Vaseline (Chesebrough-Ponds).

White Petrolatum, USP, is a purified mixture of semisolid hydrocarbons from petroleum that has been wholly or nearly decolorized. It is used for the same purpose as petrolatum, but because of its lighter color, it is considered more esthetically pleasing by some pharmacists and patients. White petrolatum is also known as white petroleum jelly. A commercial product is White Vaseline (Chesebrough-Ponds).

Yellow Ointment, USP. This ointment has the following formula for the preparation of 1000 g:

Yellow wax	50 g
Petrolatum	950 g

Yellow wax is the purified wax obtained from the honeycomb of the bee *Apis mellifera*. The ointment is prepared by melting the yellow wax on a water bath, adding the petrolatum until the mixture is uniform, then cooling and stirring until congealed. Also called simple ointment, it has a slightly greater viscosity than plain petrolatum.

White Ointment, USP. This ointment differs from yellow ointment by substitution of white wax (bleached and purified yellow wax) and white petrolatum in the formula.

Both are called Simple Ointment USP

To prepare 1000 g

White wax. 50 g

White petrolatum. 950 g

Absorption Bases

Absorption bases are of two types: (*a*) those that *permit* the incorporation of aqueous solutions resulting in the formation of water-in-oil (W/O) emulsions (e.g., *hydrophilic petrolatum*), and (*b*) those that *are* W/O emulsions (syn: *emulsion bases*) that permit the incorporation of additional quantities of aqueous solutions (e.g., lanolin). These bases may be used as emollients, although they do not provide the degree of occlusion afforded by the oleaginous bases. Absorption bases are not easily removed from the skin with water washing, because the external phase of the emulsion is oleaginous. Absorption bases are useful as pharmaceutical adjuncts to incorporate small volumes of aqueous solutions into hydrocarbon bases. This is accomplished by incorporating the aqueous solution into the absorption base and then incorporating this mixture into the hydrocarbon base.

Hydrophilic Petrolatum, USP, has the following formula for the preparation of 1000 g:

Cholesterol	30 g
Stearyl alcohol	30 g
White wax	80 g
White petrolatum	860 g

It is prepared by melting the stearyl alcohol and white wax on a steam bath, adding the cholesterol with stirring until dissolved, adding the white petrolatum, and allowing the mixture to cool while stirring until congealed.

Lanolin, USP (Anhydrous lanolin) obtained from the wool of sheep (*Ovis aries*), is a purified waxlike substance that has been cleaned, deodorized, and decolorized. It contains not more than 0.25% water. Additional water may be incorporated into lanolin by mixing. *Modified Lanolin, USP*, is lanolin processed to reduce the contents of free lanolin alcohols and any detergent and pesticide residues.

Water-Removable Bases

Water-removable bases are oil-in-water emulsions resembling creams. Because the external phase of the emulsion is aqueous, they are easily washed from skin and are often called water-washable bases. They may be diluted with water or aqueous solutions. They can absorb serous discharges. Hydrophilic Ointment, USP, is an example of this type of base.

Hydrophilic Ointment, USP, has the following formula for the preparation of about 1000 g:

Ingredient	***Amount (grams)***
Methylparaben	0.25
Propylparaben	0.15
Sodium lauryl sulfate	10.00
Propylene glycol	120.00
Stearyl alcohol	250.00
White petrolatum	250.00
Purified water	370.00

The stearyl alcohol and white petrolatum are melted together at about 75°C. The other agents, dissolved in the purified water, are added with stirring until the mixture congeals. Sodium lauryl sulfate is the emulsifying agent, with the stearyl alcohol and white petrolatum constituting the oleaginous phase of the emulsion and the other ingredients the aqueous phase. Methylparaben and propylparaben are antimicrobial preservatives.

Water-Soluble Bases

Water-soluble bases do not contain oleaginous components. They are completely water washable and often referred to as greaseless. Because they soften greatly with the addition of water, large amounts of aqueous solutions are not effectively incorporated into these bases. They mostly are used for incorporation of solid substances. Polyethylene glycol (PEG) ointment, NF, is the prototype example of a water-soluble base.

Polyethylene Glycol Ointment, NF PEG is a polymer of ethylene oxide and water represented by the formula $H(OCH_2CH_2)_nOH$, in which *n* represents the average number of oxyethylene groups. The numeric designations associated with PEGs refer to the average molecular weight of the polymer. PEGs having average molecular weight below 600 are clear, colorless

liquids; those with molecular weight above 1,000 are waxlike white materials; and those with molecular weight in between are semisolids. The greater the molecular weight, the greater the viscosity. The NF lists the viscosity of PEGs ranging from average molecular weight of 200 to 8,000.

The general formula for preparation of 1,000 g of PEG ointment is

PEG 3350	400 g
PEG 400	600 g

Combining PEG 3350, a solid, with PEG 400, a liquid, results in a very pliable semisolid ointment. If a firmer ointment is desired, the formula may be altered to contain up to equal parts of the two ingredients. When aqueous solutions are to be incorporated into the base, substitution of 50 g of PEG 3350 with an equal amount of stearyl alcohol is advantageous in rendering the final product firmer.

SELECTION OF THE APPROPRIATE BASE

Selection of the base to use in the formulation of an ointment depends on careful assessment of a number of factors, including the following:

- Desired release rate of the drug substance from the ointment base
- Desirability of topical or percutaneous drug absorption
- Desirability of occlusion of moisture from the skin
- Stability of the drug in the ointment base
- Effect, if any, of the drug on the consistency or other features of the ointment base
- Desire for a base easily removed by washing with water
- Characteristics of the surface to which it is applied

For example,

* oleaginous is prefered for non-oozing dry scaly skin,
* emulsion ointment for oozing skin at area needs easy washing by water e.g. face, neck
*absorption ointment for oozing skin at area not require easy washing by water e.g.leg ,
*water soluble ointments for non-oozing hairy or in contact skin.

Q. What type of ointment is preferred for
a. Nasal b.ophthalmic. c. Otic

Used for dry or wet Skin				
Drug release slowOr rapid				
Emollient or Not				
Can incorporate. Or absorp water or Not				
Occlusive Or not				
Percut. Absorption High or low				
Spreadability High or low				
Water washable or not				
Hydrophilic Or phobic				
Type of ointment/oint. Base	Olegen.	Absorpt.	Water removable	Water soluble

PASTES

Pastes are semisolid preparations intended for application to the skin. They generally contain a larger proportion of solid material (such as 25%) than ointments and therefore are stiffer.

Pastes can be prepared in the same manner as ointments, by direct mixing or the use of heat to soften the base prior to incorporating the

solids, which have been comminuted and sieved. However, when a levigating agent is to be used to render the powdered component smooth, a portion of the base is often used rather than a liquid, which would soften the paste.

Among the few pastes in use today is zinc oxide paste (Lassar's Plain Zinc Paste), which is prepared by mixing 25% each of zinc oxide and starch with white petrolatum. The product is very firm and is better able to protect the skin and absorb secretions than is zinc oxide ointment.

CREAMS

Pharmaceutical *creams* are semisolid preparations containing one or more medicinal agents dissolved or dispersed in either a W/O emulsion or an oil-in-water emulsion or in another type of

Note : Many references consider Emulsion ointments as O/W cream . Therefore, Hydrophilic ointment USP is an example of O/W cream

Example of O/W (aqueous) Creams

30. a

Vanishing cream

Stearic acid	15	g
Cetyl alcohol	0.5	g
Propylene glycol	3	g
KOH	0.5	g
NaOH	0.1	
	8	
Glyverin	5	g
Preservative & perfume	q.s.	g
Water Ad.	100	

Example of W/O (Oily) Creams

Cold cream

Bees wax	2	g
Borax	2	g
Almond or paraffin oil	50	g
Lanolin	0.5	g
Preservative & perfume	q.s.	g
Water (or rose water) ad.	100	g

30. c

Creams find primary application in topical skin products and in products used rectally and vaginally. Many patients and physicians prefer creams to ointments because they are easier to spread and remove. Pharmaceutical manufacturers frequently manufacture topical preparations of a drug in both cream and ointment bases to satisfy the preference of the patient and physician.

O/W creams are preferred for skin/mucous membranes areas that are wet or oozing or need easy washing by water e.g. face, neck, palm, nipples, nasal, vaginal, rectal, otic, mouth.hairy or scalp

GELS

Gels are semisolid systems consisting of dispersions of small or large molecules in an aqueous liquid vehicle rendered jellylike by the addition of a *gelling agent*. Among the gelling agents used are synthetic macromolecules, such as carbomer 934; cellulose derivatives, such as carboxymethylcellulose or hydroxypropyl methylcellulose;

Note: Hydrogels are the most common
Hydrogel: water or water+alcohol is the vehicle.
Organogel: non-aqueous vehicle : an alcohol or a mixture
Oleogel: non-aqueous vehicle : oil.
Emugel: vehicle is O/W emulsion

and natural gums, such as tragacanth. Carbomers are high-molecular-weight water-soluble polymers of acrylic acid cross-linked with allyl ethers of sucrose and/or pentaerythritol. Their viscosity depends on their polymeric composition. The NF contains monographs for six such polymers, carbomers 910, 934, 934P, 940, 941, and 1342. They are used as gelling agents at concentrations of 0.5% to 2.0% in water. Carbomer 940 yields the highest viscosity, between 40,000 and 60,000 centipoises as a 0.5% aqueous dispersion. Gels are sometimes called *jellies*.

Single-phase gels are gels in which the macro-

Single-phase gels are gels in which the macromolecules are uniformly distributed throughout a liquid with no apparent boundaries between the dispersed macromolecules and the liquid. A gel mass consisting of floccules of small distinct particles is termed a *two-phase* system, often referred to as a *magma*. Milk of magnesia (or magnesia magma), which consists of a gelatinous precipitate of magnesium hydroxide, is such a system. Gels may thicken on standing, forming a thixotrope, and must be shaken before use to liquefy the gel and enable pouring.

In addition to the gelling agent and water, gels may be formulated to contain a drug substance, solvents, such as alcohol and/or propylene glycol; antimicrobial preservatives, such as methylparaben and propylparaben or chlorhexidine gluconate; and stabilizers, such as edetate disodium.

Medicated gels may be prepared for administration by various routes, including the skin, the eye, the nose, the vagina, and the rectum.

Gels (Hydrogel or emugels) have cool and lubricating effects and faster drug release than most other semisolids and therefore are most preferred for hairy areas, mucous membranes and face.

Glycerogelatins are plastic masses containing gelatin (15%), glycerin (40%), water (35%), and an added medicinal substance (10%), such as zinc oxide. They are prepared by first softening the gelatin in the water for about 10 minutes, heating on a steam bath until the gelatin is dissolved, adding the medicinal substance mixed with the glycerin, and allowing the mixture to cool with stirring until congealed.

Glycerogelatins are applied to the skin for the long term. They are melted before application, cooled to slightly above body temperature, and applied to the affected area with a fine

Preparation of S.S. dosage forms

All semisolid dosage forms can be prepared by one of the following methods:

1. Incorporation: the drug and excipients are added to already prepared base.

2. Fusion: ingredients of the base is heated /melted then drug and excipients are added to melted mass and the preparation left to congeal at cold.

Incorporation

The components are mixed until a uniform preparation is attained (Fig. 10.1). On a small scale, as in extemporaneous compounding, the pharmacist may mix the components using a mortar and pestle, or a spatula may be used to rub the ingredients together on an ointment slab (a large glass or porcelain plate or pill tile). Some pharmacists use nonabsorbent parchment paper to cover the working surface; being disposable, the paper eliminates cleaning the ointment slab. If using an ointment parchment pad, it is best to not allow too long a contact of the ointment with the parchment, as it may soften and tear.

Others will use an ointment mill, an electronic mortar and pestle, or a device called an "Unguator" which allows a pharmacist to place the ingredients in a plastic ointment jar with a special lid that allows for a mixing blade to be used to mix the ingredients in the dispensing container. These devices can be controlled manually or via computer software. See Figures 10.2 to 10.4.

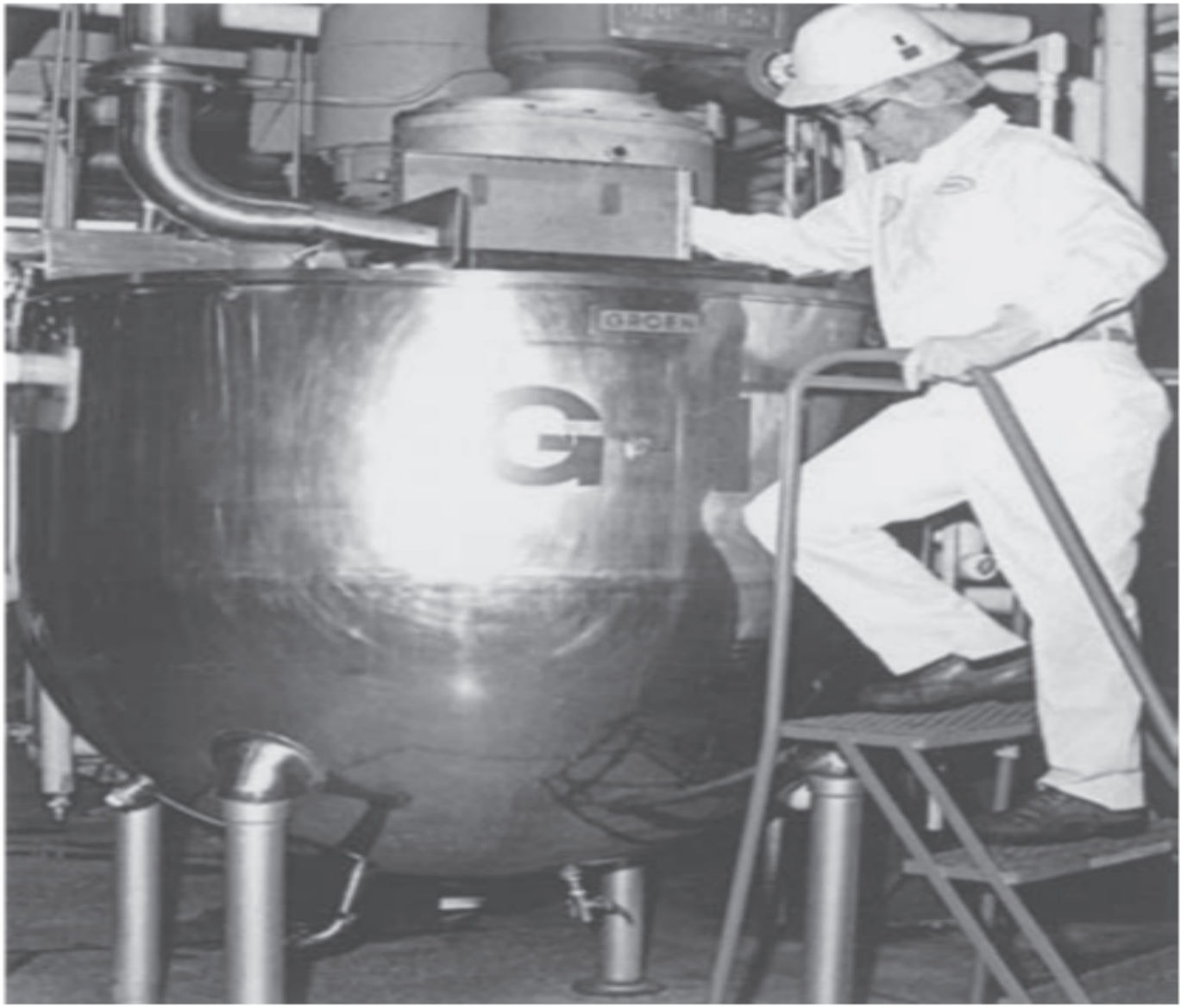

FIGURE 10.1 Creams and ointments in batch sizes up to 1,500 kg are manufactured in this stainless steel tank, which has counter sweep agitation and a built-in homogenizer. (Courtesy of Lederle Laboratories.)

FIGURE 10.2 Unguator Model B-R Electronic mortar and pestle. (Courtesy of Health Engineering Systems.)

Incorporation of Solids. When preparing an ointment by spatulation, the pharmacist works the ointment with a stainless steel spatula having a long, broad blade and periodically removes the accumulation of ointment on the

large spatula with a smaller one. If the components of an ointment react with metal (as does iodine), hard rubber spatulas may be used. The ointment is prepared by thoroughly rubbing and working the components together on the hard surface until the product is smooth and uniform. The ointment base is placed on one side of the working surface and the powdered components, previously reduced to fine powders and thoroughly blended in a mortar, on the other side. A small portion of the powder is mixed with a portion of the base until uniform. Geometric dilution is continued until all portions of the powder and base are combined and thoroughly and uniformly blended.

It often is desirable to reduce the particle size of a powder or crystalline material before incorporation into the ointment base so the final product will not be gritty. This may be done by

levigating, or mixing the solid material in a vehicle in which it is insoluble to make a smooth dispersion. The levigating agent (e.g., mineral oil for bases in which oils are the external phase, or glycerin for bases in which water is the external phase) should be physically and chemically compatible with the drug and base. The levigating agent should be about equal in volume to the solid material. A mortar and pestle are used for levigation. This allows both reduction of particle size and dispersion of the substance in the vehicle. After levigation, the dispersion is incorporated into the ointment base by spatulation or with the mortar and pestle until the product is uniform.

Solids soluble in a common solvent that wil
affect neither the stability of the drug nor th
efficacy of the product may first be dissolved i
that solvent (e.g., water or alcohol) and the solu
tion added to the ointment base by spatulatio
or in a mortar and pestle. The mortar and pestl

method is preferred when large volumes of liquid are added, because the liquid is more captive than on an ointment slab.

For incorporating a gummy material, such as camphor, pulverization by intervention can be used. The material is dissolved in a solvent and spread out on the pill tile. The solvent is allowed to evaporate, leaving a thin film of the material onto which the other ingredient or ingredients are spread. The material is then worked into the ingredients by trituration with a spatula.

Incorporation of Liquids. Liquid substances or solutions of drugs, as described above, are added to an ointment only after due consideration of an ointment base's capacity to accept the volume required. For example, as noted previously, only very small amounts of an aqueous solution may be incorporated into an oleaginous ointment, whereas hydrophilic ointment bases readily accept aqueous solutions.

When it is necessary to add an aqueous preparation to a hydro*phobic* base, the solution first may be incorporated into a minimum amount of a hydro*philic* base and then that mixture added to the hydrophobic base. However, all bases, even if hydrophilic, have their limits to retain liquids, beyond which they become too soft or semiliquid.

Alcoholic solutions of small volume may be added easily to oleaginous vehicles or emulsion bases. Natural balsams, such as Peru balsam, are usually mixed with an equal portion of castor oil before incorporation into a base. This reduces the surface tension of the balsam and allows even distribution of the balsam throughout the base.

Ointment or roller mills can be used to force coarsely formed ointments through stainless steel or ceramic rollers to produce ointments uniform in composition and smooth in texture (Fig. 10.5). Small ointment mills also find use in product development laboratories and in small-batch manufacture or compounding.

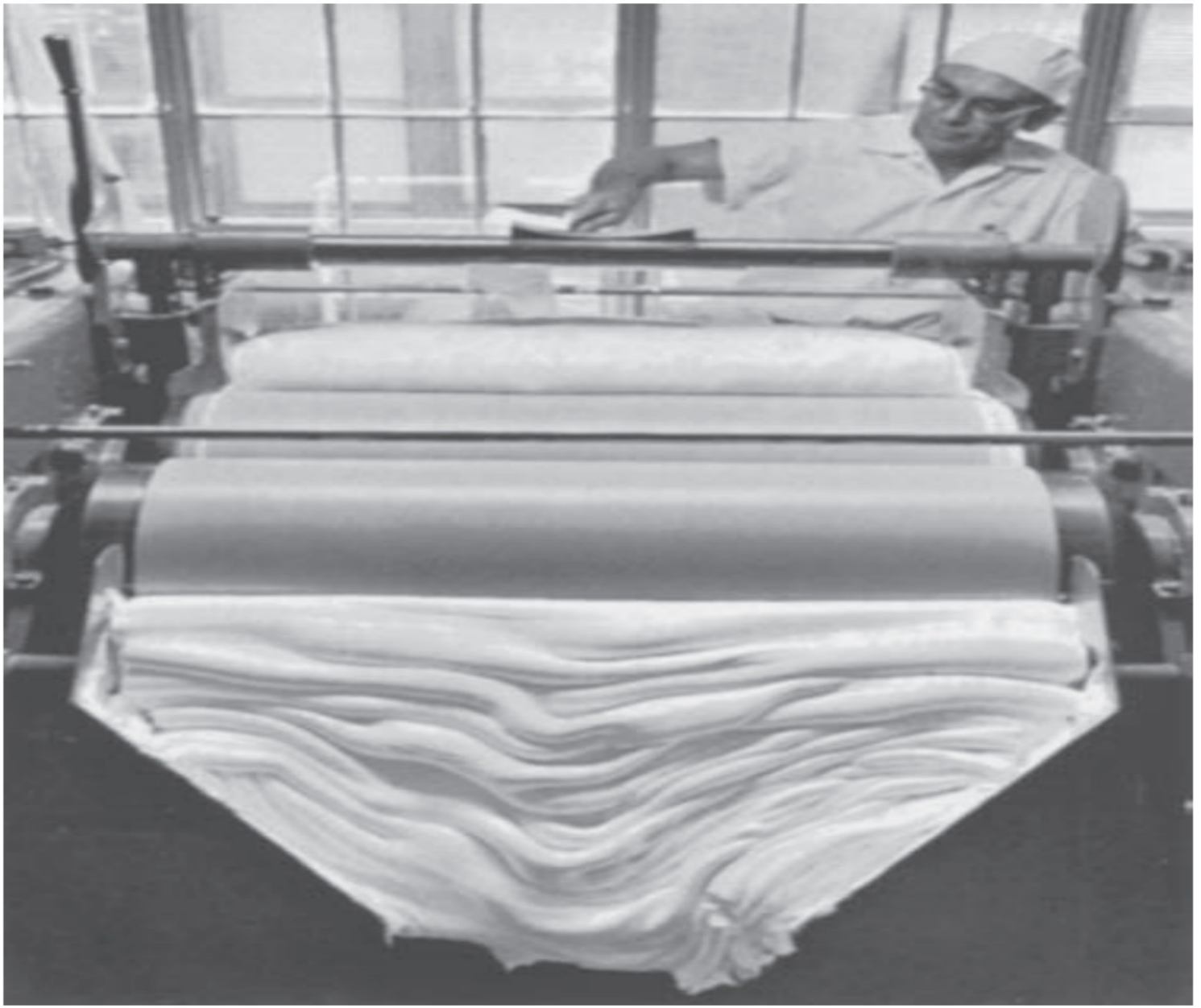

FIGURE 10.5 Day ointment roller mill. Standards of fineness and smoothness require that no grains of material be visible under a 10-power microscope after passage through this machine. (Courtesy of Eli Lilly and Company.)

Fusion

By the fusion method, all or some of the components of an ointment are combined by being melted together and cooled with constant stirring until congealed. Components not melted are added to the congealing mixture as it is being cooled and stirred. Naturally, heat-labile substances and any volatile components are added

last, when the temperature of the mixture is low enough not to cause decomposition or volatilization of the components. Substances may be added to the congealing mixture as solutions or as insoluble powders levigated with a portion of the base. On a small scale, fusion may be conducted in a porcelain dish or glass beaker. On a large scale, it is carried out in large steam-jacketed kettles. Once congealed, the ointment may be passed through an ointment mill (in large-scale manufacture) or rubbed with a spatula or in a mortar to ensure a uniform texture.

Medicated ointments and ointment bases containing components such as beeswax, paraffin, stearyl alcohol, and high-molecular-weight PEGs, which do not lend themselves well to mixture by incorporation, are prepared by fusion. By this general process, the materials with the highest melting points are heated to the lowest required temperature to produce a melt. The additional materials are added with constant stirring during cooling of the melt until the mixture is congealed. In this way, not all of the components are subjected to the highest temperature. Alternative methods entail melting the component with the lowest melting point first and

adding the remaining components in order of their melting points or simply melting all of the components together under slowly increasing temperature. By these methods, a lower temperature is usually sufficient to achieve fusion because of the solvent action exerted by the first melted components on the others.

melted components on the others.

In preparation of ointments having an emulsion base, the method of manufacture often involves both melting and emulsification. The water-immiscible components such as the oil and waxes are melted together in a steam bath to about 70°C to 75°C. Meantime, an aqueous solution of the heat-stable, water-soluble components is prepared and heated to the same temperature as the oleaginous components. Then the aqueous solution is slowly added, with mechanical stirring, to the melted oleaginous mixture. The temperature is maintained for 5 to 10 minutes and the mixture is slowly cooled and stirred until congealed. If the aqueous solution is not at the same temperature as the oleaginous melt, some of the waxes will solidify on addition of the colder aqueous solution to the melted mixture.

MICROBIAL CONTENT

With the exception of ophthalmic preparations, topical applications are not required to be sterile. They must, however, meet acceptable standards for microbial content, and preparations prone to microbial growth must contain antimicrobial preservatives. Preparations that contain water tend to support microbial growth to a greater extent than water-free preparations. Among the antimicrobial preservatives used to inhibit microbial growth in topical preparations are methylparaben, propylparaben, phenols, benzoic acid, sorbic acid, and quaternary ammonium salts.

Pharmacopeial (quality control) specification requirements

MICROBIAL CONTENT

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Microbial limits are stated for certain articles in the USP. For example, Betamethasone Valerate Ointment, USP, must *meet the requirements of the tests for absence of Staphylococcus aureus and Pseudomonas aeruginosa*. These particular microbes have special importance in dermatologic preparations because of their capacity to infect the skin, which for patients being treated for a skin condition, is already compromised.

MINIMUM FILL

The USP's *minimum fill* test is determination of the net weight or volume of the contents of filled containers to ensure proper contents compared with the labeled amount.

ADDITIONAL STANDARDS

In addition to the USP requirements, manufacturers often examine semisolid preparations for viscosity and for in vitro drug release to ensure within-lot and lot-to-lot uniformity (3, 4). In vitro drug release tests include diffusion cell studies to determine the drug's release profile from the semisolid product.

PACKAGING, STORAGE, AND LABELING

Ointments and other semisolid preparations are packaged either in large-mouth ointment jars or in metal or plastic tubes. Semisolid preparations must be stored in well-closed containers to protect against contamination and in a cool place to protect against product separation in heat. When required, light-sensitive preparations are packaged in opaque or light-resistant containers.

In addition to the usual labeling requirements for pharmaceutical products, the USP directs the labeling for certain ointments and creams include the type of base used (e.g., water soluble or water insoluble).

Tubes used to package topical pharmaceutical products are gaining in popularity. They are light in weight, relatively inexpensive, convenient for use, and compatible with most formulative components, and they provide greater protection against external contamination and environmental conditions than jars (5).

mental conditions than jars (3).

Ointment tubes are made of aluminum or plastic. When the ointment is to be used for ophthalmic, rectal, vaginal, aural, or nasal application, they are packaged with special applicator tips. Tubes of aluminum generally are coated with an epoxy resin, vinyl, or lacquer to eliminate any interactions between the contents and the tube. Plastic tubes are made of high- or low-density polyethylene (HDPE or LDPE) or a blend of each, polypropylene (PP), polyethylene terephthalate (PET), and various plastic, foil, and/or paper laminates, sometimes 10 layers thick.

Filling Ointment Tubes

Tubes are filled from the open back end of the tube, opposite from the cap end (Fig. 10.6). Ointments prepared by fusion may be poured while still soft but viscous directly into the tubes with caution to prevent stratification of the components. On a small scale, as in the extemporaneous filling of an ointment in the pharmacy, the tube may be filled manually (Fig. 10.7) or with a small-scale filling machine (Fig. 10.8). The filled

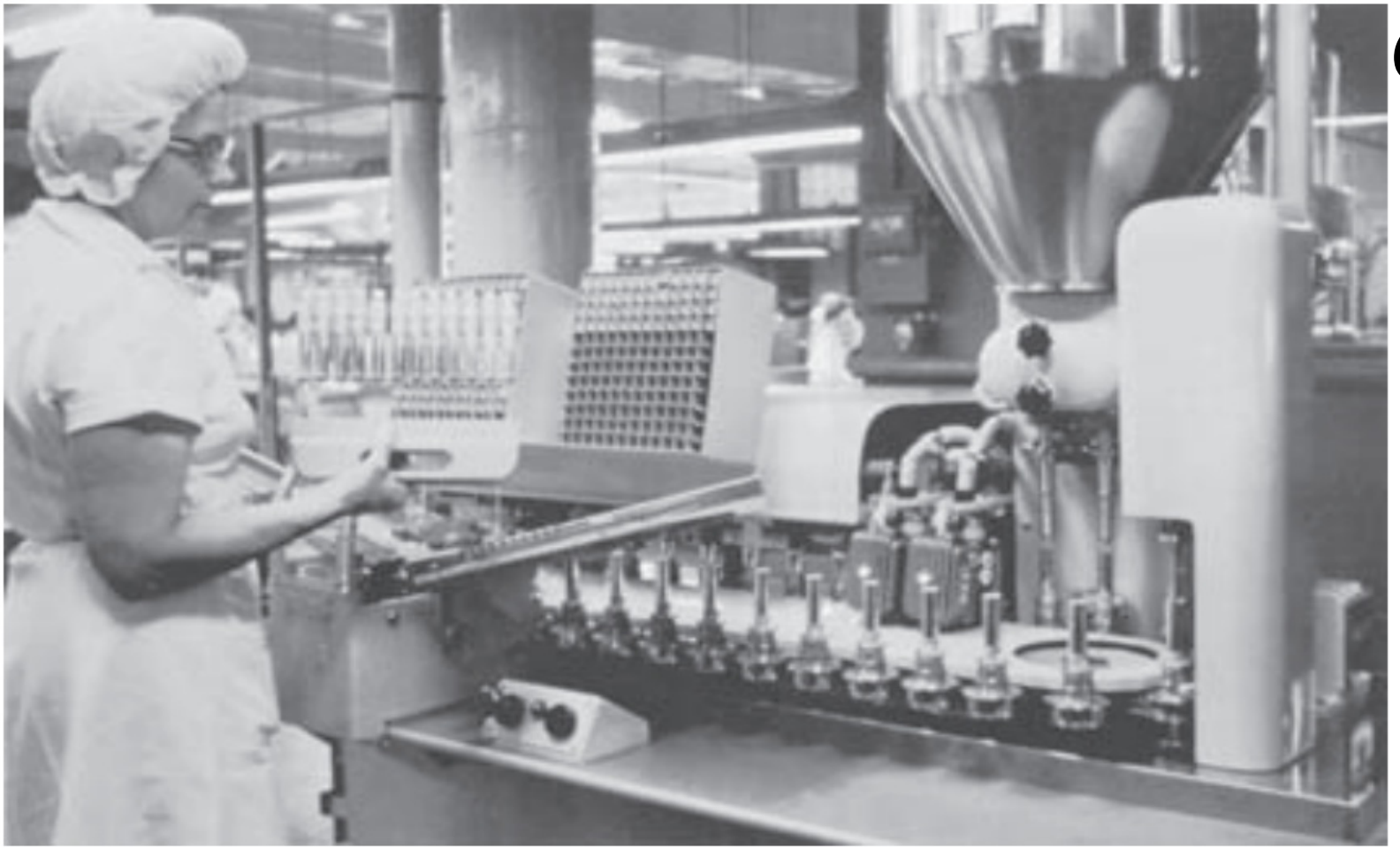

FIGURE 10.6 Arenco tube-filling machine automatically fills 125 tubes a minute with proper amount, tightens cap, orients each tube by electric eye so that label faces forward, then closes and crimps the end. (Courtesy of Eli Lilly and Company.)

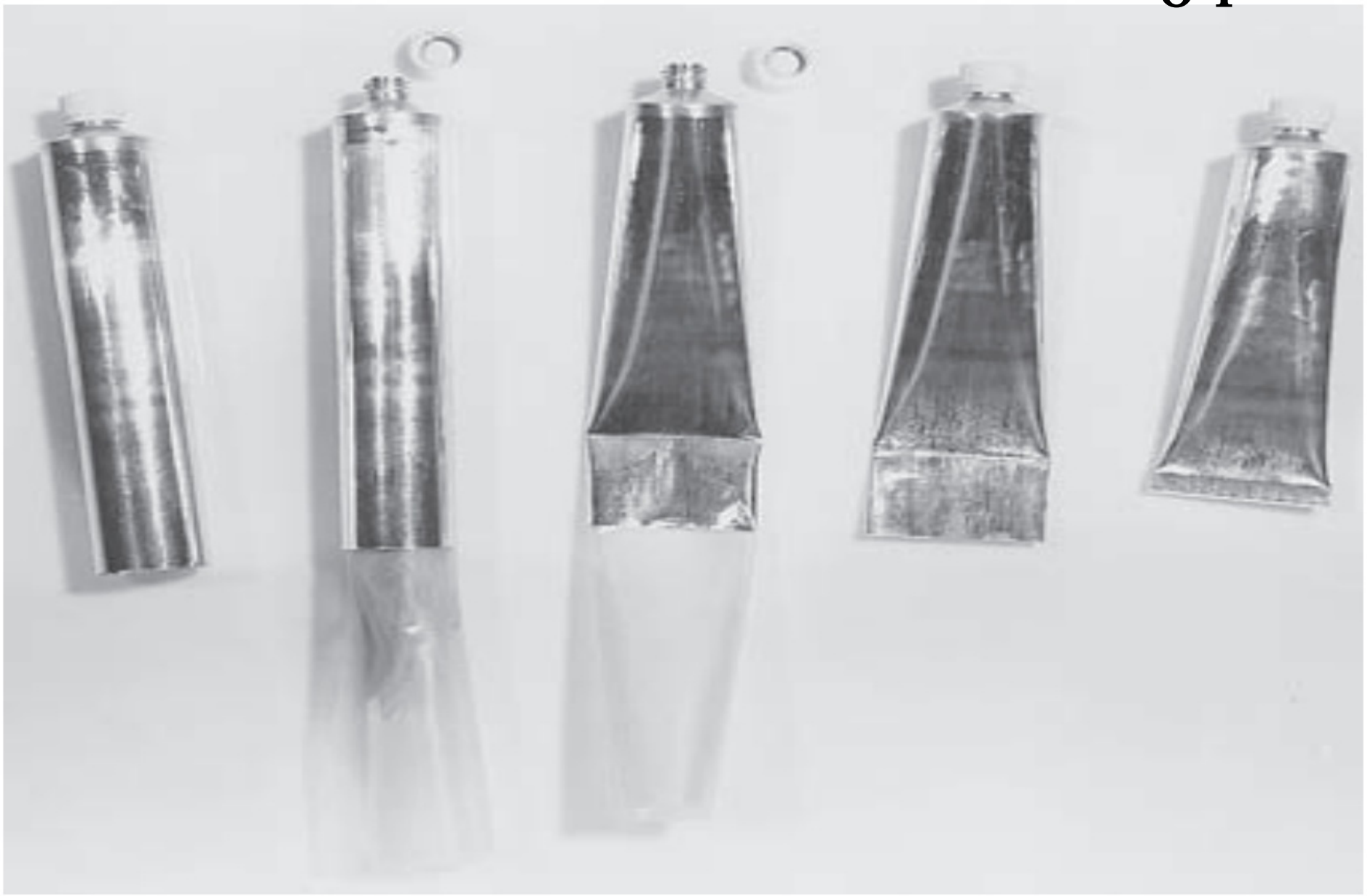

FIGURE 10.7 Steps in the manual filling of ointment tubes.

Filling Ointment Jars

Ointment jars are filled on a small scale in the pharmacy by carefully transferring the weighed amount of ointment into the jar with a spatula. The ointment is packed on the bottom and along the sides of the jar, avoiding entrapment of air.