



# Secundum Artem

Current & Practical Compounding  
Information for the Pharmacist.

## COMPOUNDING FOR DERMATOLOGY PATIENTS

### GOALS AND OBJECTIVES

**Goal:** To provide compounding pharmacists with supportive information on the treatment of dermatological disorders and the use of various extemporaneously compounded preparations.

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

1. Discuss the structure of the skin and the function of the various layers.
2. Define the general classes of dermatological disorders.
3. List some of the more common dermatological disorders and some preparations often used in their treatment.
4. Explain some of the techniques used in compounding dermatological preparations, especially ointments, creams, pastes, gels and sticks.

### INTRODUCTION

It has been estimated that about 5% of the population suffer from a chronic skin, hair or nail condition; it is also estimated that over half of individuals over 65 years of age suffer from skin conditions such as seborrheic dermatitis, fungal infections and neoplastic growths.<sup>1</sup> The skin is a remarkable organ, subjected to the extremes of the external environment and altered by the internal environment (the physiological processes occurring within the body), but responding with amazing resiliency.

### THE SKIN

The skin is the largest organ in the body, averaging about 1 to 2 mm in thickness with the thickest skin on the palms and soles and the thinnest on the eyelids and scrotum. The skin is the envelope that wraps our bodies, keeps all the pieces together and serves numerous functions. It may be light or dark, smooth or wrinkled, but it helps define how we appear to others. This body covering, the skin is composed of the epidermis, dermis and the hypodermis.

### Epidermis

The epidermis (0.075 to 0.15 mm thick) is composed mostly of compact, avascular stratified squamous epithelial cells. There are actually five layers to the epidermis (from the innermost to the exterior); the stratum germinativum, stratum spinosum, stratum granulosum, stratum corneum and the stratum lucidum. The lowest layer, the basal cell layer (stratum germinativum) is where new cells (keratinocytes) divide and move upward. The keratinocytes change from living cells to dead, thick-walled, flat, non-nucleated cells containing keratin as they move towards the skin surface. This layer is especially important in laying down new granulation tissue in conditions such as wounds, ulcers, etc. The next layer, the stratum spinosum contains keratinocytes, melanocytes and melanin granules, important for skin pigmentation. Changes in this region can alter skin coloring. Next, the stratum granulosum, containing several thicknesses of flattened polygonal cells, are rich in keratohyalin. The stratum lucidum, a translucent, thin area, (in the palms and soles) is a narrow band of flattened, closely packed cells. The surface layer, the stratum corneum, is composed of flat, scaly, dead (ker-

atinized) tissue normally exposed to the environment. The stratum corneum cells are constantly being shed (desquamated) and are replaced by new cells generated by the mitotic process deeper down in the basal cell layer. Actually, the newer cells push the older cells closer to the surface and the cells become flattened, lose water, and are compressed as they move towards the surface. From basal cell formation to desquamation, the complete cycle, ranges from 28 to 45 days. The stratum corneum is about 15-20 cells thick; therefore, approximately 0.5 to 1 cell layer per day is sloughed off the body.

The stratum corneum, where most inflammations and disorders occur, maintains its flexibility because of its water content which is normally between 10 and 20%. This flexibility is influenced by humidity, temperature, surfactants, and physical or chemical trauma. The keratin can actually absorb several times its weight in water and retain it to maintain the flexibility and integrity. Water is important to the skin! Oleaginous vehicles are occlusive and aid in retaining the moisture in the skin. The stratum corneum is primarily lipophilic.

### Dermis

The dermis (about 1 to 4 mm thick), or basement membrane separates the epidermis from the lower fatty layers and actually physically supports the epidermis. The dermis is composed mainly of collagen and elastin embedded in a mucopolysaccharide substance containing fibroblasts and mast cells. The dermis also contains a network of nerves, lymphatic and blood vessels, supplying hair follicles, sebaceous glands and sweat glands. It is this layer where the cutaneous sensations occur, for example, itching from the upper region, stinging from the middle region and pain in the region closest to the subcutaneous fat. The dermis contains the papillary and reticular layers. The former is rich in blood vessels and appears to aid in bringing nutrients to the avascular epidermis. The lower portion, the papillae, contains coarser tissue that connects the dermis with the hypodermis. Altered pain perception can occur when this layer is damaged, or even destroyed.

### Hypodermis

The subcutaneous tissue, called the hypodermis is composed of loose connective tissue and adipose tissue. This layer aids in thermal control, holds nutrients and provides cushioning and/or padding. Burns extending into this area require close monitoring of the patient, depending upon the extent of involvement.

### PURPOSE OF THE SKIN

The skin, the largest organ in the body, is the protective barrier between the body and the environment. The skin works to protect the body from chemicals and pathogenic organisms; its functions are dependent upon, and in association with, age, immunologic status, underlying disease states, use of oral/topical medications and the preservation of an intact stratum corneum.

In addition to protection, the skin also serves for temperature control, pigment development, water regula-

tion/moisture loss and even vitamin synthesis.

The skin can be challenged by wounds, burns, chafing, drying, internal physiological disorders, chemicals and bacteria, resulting in alterations and may involve the different skin layers. Commonly encountered dermatologic disorders include general classes of dermatitis and dermatoses. Specifically, allergic skin diseases include urticaria, atopic dermatitis (eczema), allergic contact dermatitis and photoallergic reactions. Others include insect bites/stings, acne, burns (including sunburn), minor wounds, skin infections, cancer, skin ulcers, hyperpigmentation, photoaging, lice infestation and even hair loss. Only a few, however, will be discussed here.

### DEFINITIONS OF SKIN PROBLEMS

Dermatitis is used as a term to describe a number of conditions that are inflammatory and are generally characterized by erythema. The term literally means an inflammation of the skin. Dermatitis can be characterized by various skin appearances, such as a macula, wheal, subcorneal blister, intradermal blister, subepidermal blister, pustule, papule, rhagades, ulcer, squama, keratosis, scab (crusta), scar (cicatrix) and mucous membrane.<sup>2</sup> Treatment of dermatitis can include anti-inflammatory agents, antibiotics, antifungals, corticosteroids, anesthetics and others.

Dermatosis is a nonspecific term used for any cutaneous abnormality or eruption. It includes many disorders and literally means, a disorder of the skin. Treatment depends upon the specific problem and the portion of the skin involved.

Eczema is a generic term for inflammatory conditions of the skin, particularly with vesiculation in the acute stage, typically erythematous, edematous, papular and crusting; followed by lichenification and scaling and occasionally by duskiness of the erythema and, infrequently, hyperpigmentation; often accompanied by sensations of itching and burning; the vesicles form by intraepidermal spongiosis. Eczema is treated by anti-inflammatories, antibiotics, antifungals, corticosteroids, anesthetics and other agents.

### DISEASES OF THE SKIN AND THEIR TREATMENT

#### Acne

Acne vulgaris is characterized by comedones and other lesions, including scars and occurs throughout adolescence. Acne affects all skin layers even into the subcutaneous areas. The treatment objective is to clear the lesions, prevent scarring and minimize psychological distress. Acne is often treated by drying agents, proliferative agents, antibiotics, anti-inflammatory agents and others. A sample formulation often used is as follows;

Rx - Nicotinamide 4% Acne Gel	
Nicotinamide	4 g
Carbomer 934	1 g
Methylparaben	50 mg

Propylparaben		10 mg
Triethanolamine	qs	
Purified water	qs	100 mL

Accurately measure each ingredient. Dissolve the nicotinamide, methylparaben and propylparaben in about 95 mL of purified water. Disperse the carbomer 934 in the solution slowly so as to not form lumps. Add sufficient purified water to make 100 mL. Add triethanolamine dropwise to the desired viscosity. Package and label.

### Psoriasis

Psoriasis is a chronic disease characterized by epidermal hyperplasia and a greatly accelerated rate of epidermal turnover. It was discussed in a special *Secundum Artem* (Volume 9, Number 4- *Compounding for Patients with Psoriasis*). This can be found online at [www.paddocklabs.com](http://www.paddocklabs.com).

### Skin cancers

Skin cancer rates appear to be increasing but can be treated if caught early. An easy-to-apply sample formulation that has been used for treating certain small skin cancers is the following.

#### Rx - Fluorouracil 5% Medication Stick

Fluorouracil	5 g
Polybase	95 g

Accurately measure each ingredient. Melt the Polybase using low heat to about 60-65° C. Incorporate the fluorouracil, cool, and package into medication stick containers.

### Skin ulcers

Skin ulcers may occur anywhere over the body but especially where the skin is subjected to constant rubbing or irritation. Decubitus ulcers in hospice patients and those confined to a bed are all too common. If malodorous, metronidazole topical solutions can be used, as follows;

#### Rx - Metronidazole 1% Topical Solution

Metronidazole		1g
Hydrochloric acid 10% solution		1.5 mL
Propylene glycol		10 mL
Methylparaben		100 mg
Propylparaben		50 mg
Purified water	qs	100 mL

Accurately weigh/measure each ingredient. Add the metronidazole to about 50 mL of purified water, followed by the hydrochloric acid 10% solution. Mix the parabens with the propylene glycol and add to the metronidazole solution. Add sufficient purified water to volume and mix well.

The following preparation has been effective in many cases to increase granulation from the lower tissues and enable the ulcer to fill in and heal, while making the patient much more comfortable.

#### Rx - Ketoprofen 2%, Lidocaine 2%, Phenytoin 2% and Misoprostol 0.0024% in Dermabase

Ketoprofen		2 g
Lidocaine HCl		2 g
Phenytoin		2 g
Misoprostol		2.5 mg
Dermabase	qs	100 g

Accurately weigh/measure each ingredient. Mix the ketoprofen, lidocaine HCl, phenytoin and misoprostol with a small quantity of propylene glycol to form a paste. Geometrically, add sufficient Dermabase to 100 g and thoroughly mix.

### Lice/Scabies

Lice/scabies is usually treated by scabicides and even insecticides. It is really a problem during the school terms when young children go back to school and tend to spread the lice. It has been occurring almost at epidemic levels in recent years and some of the routine commercial products are not effective. The following preparation, has been used quite effectively.

#### Rx - Malathion 0.5% Lotion for Head Lice

Malathion		500 mg
Isopropyl alcohol 70%		68 mL
Lavender oil		30 drops
Bay and/or pine oil		3 drops
Ethyl alcohol 95%	qs	100 mL

Caution: Due to fumes, this should be prepared in a well-ventilated area or under an exhaust hood. The compounder should wear disposable gloves to prevent retention of odor on the hands. Accurately weigh/measure each ingredient. Disperse the malathion in the isopropyl alcohol; add fragrances and bring to volume with ethyl alcohol and mix well.

### Insect Bites/Poison Ivy

Spring and summer bring a great increase in the incidence of insect bites and stings, as well as exposure to poison ivy, sumac and oak. Preparations used in treating these disorders often incorporate anesthetics in either sprays, creams or gel forms.

#### Rx - Lidocaine 2% Anesthetic Gel

Lidocaine		2 g
Carbomer 934		2 g
Ethanol 95%		90 mL
Triethanolamine	qs	
Purified water	qs	100 mL

Accurately weigh/measure each ingredient. Dissolve the lidocaine in the ethanol. Disperse the carbomer 934 in the lidocaine:ethanol solution. Add the purified water and mix well. Add a few drops of triethanolamine to thicken the gel. Package and label.

Other preparations are more complex and incorporate anti-inflammatory/corticosteroids, antihistamines, and other antipruritics in various dosage forms, such as the following gel.

#### Rx - Insect Bite/Sunburn Gel

Hydrocortisone	1 g
Pramoxine HCl	1 g
Diphenhydramine HCl	2 g
Menthol	300 mg
Camphor	300 mg
Benzyl alcohol	1.6 mL
Hydroxypropyl cellulose	2 g
Propylene glycol	10 mL
Alcohol 70%	60 mL
Purified water	qs 100 mL

Accurately measure each ingredient. Mix the alcohol with about 20 mL of purified water. Add the hydrocortisone, pramoxine HCl, diphenhydramine HCl, menthol, camphor and benzyl alcohol and mix well. Mix the hydroxypropyl cellulose with the propylene glycol and add to the drug solution. Add sufficient purified water to volume, package and label.

#### Hyperpigmentation

Hyperpigmentation can be related to the activity occurring in the region of the stratum spinosum, resulting in several different pigmentation disorders. Hyperpigmentation can be treated with bleaching agents, such as hydroquinone, generally applied two to three times daily. A sample preparation that has been used is as follows;

#### Rx - Bleaching Cream

Retinoic acid	100 mg
Triamcinolone	100 mg
Hydroquinone	4 g
Butylated hydroxytoluene	400 mg
Castor oil	4.5 g
Vitamin E acetate liquid (1 IU/mg)	1.75 g
Polysorbate 80	1 g
Propylene glycol	10 mL
Sodium ascorbate	3 g
Citric acid	1 g
Dermabase	qs 100 g

Accurately weigh/measure each ingredient. Triturate the retinoic acid and triamcinolone with a small quantity of the propylene glycol. Add the hydroquinone powder and mix well. Incorporate the sodium ascorbate and citric acid. Add the butylated hydroxytoluene, polysorbate 80, castor oil and vitamin E acetate and mix well. Incorporate into the emulsion base and mix until smooth and homogenous. Note: Use mixing techniques that minimize incorporation of air into the product. This preparation is more stable when packaged to minimize contact with air, such as in a large syringe.

#### Fungal Infections

Fungal infections (mycoses) can be either superficial or deep infections and can involve many different microorganisms. When the nails are involved, therapy may last from 6 months to one year; treatment of the skin is usually shorter in duration. A sample preparation for treating fungal infections of the nail is as follows;

#### Rx - Fluconazole in Dimethyl Sulfoxide (DMSO)

Fluconazole	2 g
Dimethyl sulfoxide qs	100 mL

Accurately weigh the fluconazole. Dissolve the fluconazole in the DMSO or mix the finely powdered tablets with the DMSO. If the tablets were used, filter the preparation after the fluconazole has gone into solution. Package in a bottle with a glass rod applicator.

#### Wounds

A wound is trauma to any of the tissues of the body, especially that caused by physical means and with interruption of continuity. There are many types of wounds and many involve the skin, either superficially, dermally or subcutaneously. Treatment is dependent upon the cause, location and potential for infection and further injury. A sample formula for abraded skin is the following;

#### Rx - Wound Care Mixture

Phenol	200 mg
Zinc oxide	12 g
70% Ethanol	
Calcium hydroxide solution aa qs	100 mL

Accurately weigh/measure each ingredient. Prepare 100 mL of the vehicle using equal parts of 70% ethanol and calcium hydroxide solution (lime water). Dissolve the phenol in about 75 mL of this vehicle. Sprinkle the zinc oxide powder on the phenol-vehicle mixture. Add additional vehicle to volume and mix well. Package and label.

#### FORMULATING DERMATOLOGICALS

Dermatologicals have three primary functions. They are to provide for skin hydration (emollient effect), to protect injured areas from the environment and permit rejuvenation of the skin, and (3) to provide a means of conveying a medication to the skin for a specific effect, either locally or systemically.

Formulating dermatologicals requires consideration of the flux of the drug into or across the skin, retention of the dosage form on the skin's surface, the reservoir capacity of the dosage form and the elegance/acceptability of the dosage form. When the water content of the skin drops less than about 10%, chapping occurs and the stratum corneum becomes brittle and will easily crack. This results in irritants and bacteria being able to penetrate more easily, causing dermatitis and other skin conditions. The cell cycle of 28 to 45 days must be considered because some topically applied medications may not be effective until the complete cycle ends.

Commonly prepared dermatologicals include ointments, creams, lotions, pastes, gels and sticks. Ointments are semisolid preparations that will either soften or melt at body temperature and are generally used on dry, scaly lesions, as their emollient properties will aid in rehydrating the skin. They will also adhere for an extended period of time. Ointments are general-

ly used for topical/local application of drugs, mostly for local or topical effects.

Creams are opaque, soft solids or thick liquids intended for external application, consisting of medications dissolved or suspended in vanishing cream or emulsion bases; either oil-in-water or water-in-oil. Creams are usually applied to moist, weeping lesions and have somewhat of a "drying" effect, because the exuded fluids will be miscible with the emulsion vehicles. Creams can be formulated to aid in drug penetration into or through the skin.

Lotions are fluid emulsions or suspensions for external application, including both suspension and oil-in-water dosage forms. They are generally applied to intertriginous areas where rubbing occurs, as between fingers, thighs, under the arms, etc, as they have a lubricating effect. Suspension lotions, or patting lotions, are applied by application/patting but are not rubbed in; the suspended particles may cause slight damage to the sensitive skin.

Pastes are thick, stiff ointments that ordinarily do not flow at body temperature and serve as protective coatings over areas to which they are applied; they usually contain at least 20% solids.

Gels are semirigid systems in which the movement of the dispersing medium is restricted by an interlacing, three-dimensional network of particles or solvated macromolecules of the dispersed phase. After application, the liquid evaporates leaving the drug entrapped in a thin film of the gel-forming matrix physically covering the skin.

Sticks are a convenient form for administering topical medications and are solid dosage forms that melt at body temperature, releasing their medication or providing a protective barrier.

### Other Considerations

If the drug is not incorporated as a solution into the dosage form, a very fine particle size is advantageous. Comminution of all incorporated powders is important to minimize any damage to the skin upon application.

If the skin is dry, an oleaginous ointment base (petrolatum) is recommended as a hydrated stratum corneum generally enhances drug diffusion and absorption. The cells of a well-hydrated stratum corneum are swollen, loosening the normally, tight, densely packed configuration. The hydration of the stratum corneum is increased by occlusion. Also, the additional water composition increases the absorption rate of ionized, hydrophilic drugs.

Various bases affect the hydration of the skin; for example ointments tend to enhance hydration and creams tend to be more drying over time. This is because as the area is washed or rinsed in water, the emulsifier in the cream/lotion-emulsion also can emulsify the natural body oils with their ultimate removal from the skin. The skin is then robbed of its protective natural oils, allowing water to evaporate and the skin to dry out.

Some general procedures for preparing dermatological dosage forms include the following.

1. Comminute insoluble materials to a very fine state of subdivision.
2. Levigating agents used for comminution must be compatible with the active ingredient and the vehicle.
3. Geometric dilution will enhance uniformity of distribution of the active ingredient in the vehicle.
4. Solvents with low vapor pressures, such as water, glycerin and propylene glycol should be used in place of alcohol and higher vapor pressure solvents (which will evaporate and may lead to crystallization of the drug).
5. When fusion is used and volatile substances are to be incorporated, allow the melt to cool before adding the volatile ingredients.
6. Aqueous systems should be heated for as short a time as possible to minimize water loss due to evaporation.
7. If a preparation is too stiff, decrease the proportion of waxy components and if an emulsion, increase the proportion of water.
8. For maximum preparation stability, try to keep the product anhydrous.
9. Mixing two creams/ointments can be easily accomplished in a plastic bag; this also simplifies cleanup. The preparation can easily be placed in a tube/syringe by snipping the corner off the plastic bag and squeezing the contents into the package.
10. Kitchen mixers can be used when preparing large quantities of semisolids.
11. Geometric dilution techniques will actually speed up the preparation time.
12. For ingredients that build up electrostatic charges, a few drops of a levigating agent works well.
13. Humectants can be added to cream/lotion formulations to increase their hydrating properties.
14. When preparing bases using fusion, melt the ingredient with the highest melting point first, followed by those with decreasing melting points.

### REFERENCES

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2. *Stedman's Medical Dictionary* 26th Edition. Baltimore MD, Williams & Wilkins. 1995.

### NOTES

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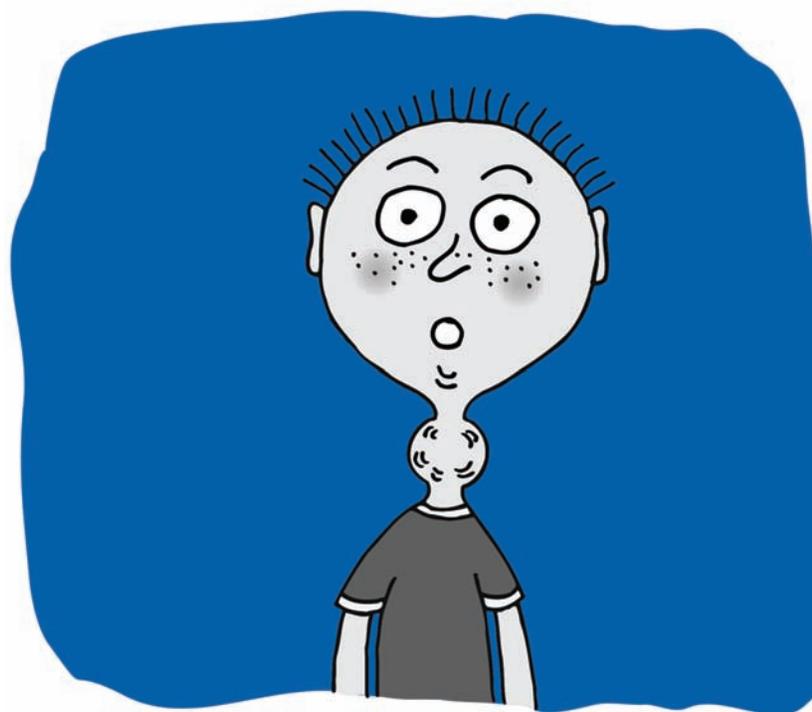
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