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Secundum Artem

Current & Practical Compounding Information for the Pharmacist.

BASICS OF COMPOUNDING FOR ACNE

GOALS AND OBJECTIVES

Goal: To provide pharmacists, pharmacy students and pharmacy technicians supportive information on the basics of compounding solutions for the prevention and treatment of acne.

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

1. Explain the causative factors related to acne.
2. Discuss the basic treatment regimens for acne.
3. Describe the various lifestyle factors that can cause acne.
4. List various compounded formulations that are being used in the treatment of acne.

Introduction

Acne is an inflammatory follicular, papular, and pustular eruption involving the pilosebaceous apparatus.[1] There are many types of acne with acne vulgaris the most common. Acne vulgaris is an eruption, predominantly of the face, upper back and chest, composed of comedones, cysts, papules and pustules on an inflammatory base. Acne occurs in almost all individuals at some time or another and is one of the most widespread medical conditions in the world, yet there is no cure. It has been said that there is no single condition that causes more psychic trauma, maladjustment, general insecurity, feelings of inferiority and other psychic suffering than acne vulgaris.[2]

The incidence is approximately 85% between the ages of 12 and 24 years. It typically occurs in males aged 16 to 18 and in females about a year earlier. In the mid-teen years, papular lesions generally occur and nodular lesions in the late teens. By the mid 20s, it generally clears in males but may persist into the 30s in women and worsen during menopause.[3,4] In the US, it is estimated that 60% of the teenagers use OTC products to treat acne.[5]

Acne formation

Acne is related to hormones, sebum, follicle fallout, bacteria and inflammation and begins in the pilosebaceous units (hair follicle and associated sebaceous glands) in the dermis. These units are made up of a hair follicle, sebaceous glands and a duct (pilosebaceous duct) connecting it to the skin surface through which the hair shaft passes. Epithelial tissue forms the lining of this shaft. During normal operation, the sebaceous glands produce sebum that passes to the skin surface through the ducts spreading over the skin to minimize water loss and to maintain skin and hair hydration. Sebaceous glands are more common on the face, back and chest, where acne most often occurs.

During prepuberty, there is relatively little activity from the sebaceous glands. However, as both males and females approach puberty, androgenic hormones increase and, as a result, sebaceous glands are stimulated.

During puberty, an increase in androgens is closely related to four processes involved in acne development, including (1) an abnormal keratinization of cells in the pilosebaceous duct, (2) and increase in sebum production, (3) an accelerated growth of *Propionibacterium acnes*, and (4) the occurrence of inflammation.[4,6]

With an increase in keratinization of cells shed in the duct and an increase in their cohesiveness, an obstruction of the follicle occurs, rather than the normal migration and removal of the cells from the skin surface. The entrapped and keratinized cells cause the follicle to expand and form a microcomedo, which is the beginning of the acne lesion. As the process continues and additional cells and sebum accumulate, the

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microcomedo enlarges and becomes visible as a closed comedo, or whitehead and becomes visible as a small, pale nodule just beneath the skin surface. This lesion is the precursor to further development.

As the lesion progresses and additional material accumulates, the plug is pushed towards the surface resulting in an open comedo, or blackhead. The color of the blackhead may be due to the presence of melanin in the plug. In the duct, *P. acnes*, an anaerobic rod and the primary microorganism found in the duct, undergoes accelerated growth. Through lipase production and the breakdown of the sebum to free fatty acids, an inflammatory reaction occurs, contributing to inflammatory acne lesions and localized tissue destruction.

As the plug grows and the inflammatory processes continue, inflammation of the duct wall develops resulting in a disruption of the epithelial lining and lymphocyte infiltration. If the follicle ruptures, spontaneously or by squeezing or picking, a severe inflammatory reaction can occur. During squeezing or picking, the contents of the plug can be discharged into the surrounding tissue resulting in abscesses that may result in scars or pits after healing. Inflammatory acne, with pustules or purulent nodules, are more likely to cause scarring than noninflammatory acne.

Acne is characterized by whiteheads, blackheads, acne pimples and acne blemishes. Closed or open comedones, (whiteheads and blackheads) are characteristic of noninflammatory acne. Typically, a patient with acne will experience a combination of open and closed comedones, papules and pustules, typically on the face, chest and back but are not limited to these areas. Pimples are characteristic of inflammatory acne and are small, prominent, inflamed elevations of the skin. They may rupture to form papules, which are inflammatory lesions appearing as raised, reddened areas on the skin. Pustules are small round lesions that are clearly inflamed and contain visible pus. They may appear red at the base with a yellowish or whitish center. If the area continues to penetrate into surrounding and underlying tissue and produce necrotic, purulent nodular lesions known as cysts, they may lead to pitting and scarring if left untreated.

Scarring is a visible sign of tissue injury and repair when the tissue cannot be restored to its former state. Scars can be caused by increased tissue formation and/or by tissue loss. They can be of several types, including soft, ice-pick, depressed fibrotic, atrophic macules and follicular macular atrophy scars. Some scarring can be treated with topical resurfacing agents, such as retinol, or microdermabrasion.

ACNE CLASSIFICATION

Acne has been classified into the following categories.

- Grade I (Comedonal acne) consists of comedones only; less than about 10 on the face, none on the trunk, no scarring and noninflammatory in nature.
- Grade II (Papular acne) is described by 10-25 papules on the face and trunk with mild scarring and the presence of inflammatory lesions, less than 5 mm in diameter.
- Grade III (Pustular acne) consists of more than 25 pustules with moderate scarring.
- Grade IV (Severe or persistent pustulocystic acne) consists of nodules or cysts with extensive scarring and inflammatory lesions over 5 mm in diameter. Also, recalcitrant severe cystic acne characterized with extensive nodules and/or cysts.

VARIABLES INVOLVED

There are a number of contributing factors to acne, including environmental, physical, emotional, cosmetic use and heredity. Environmental factors, such as high humidity and heat and other conditions that cause frequent and prolonged sweating can exacerbate acne. Tight fitting clothes that restrict air movement and prevent evaporation of skin moisture also increase skin hydration and contribute to acne. Also, acne can be aggravated by headbands, helmets and friction-producing devices or positions such as resting the chin or cheek on the hand often and for long periods of time. Also, exposure to dirt, cooking oils/vapor/smoke or industrial chemicals such as petroleum derivatives can cause occupational acne.

Acne resulting from cosmetics is usually of the closed, noninflammatory type and is more common in women. Products that contain oils (lanolin, mineral oil, cocoa butter) are comedogenic, being occlusive and plugging the folicles exacerbating or even initiating acne. Hair spray can occlude the pilosebaceous gland and cause acne.

Emotional factors contributing to acne may include severe or prolonged periods of stress or other emotional extremes, but will not cause acne.

Hormonal factors are evidenced by premenstrual flare-ups. Androgenic progestins, as in some oral contraceptives, are contributors to acne, as are some cyclic progestins used in menopausal hormone replacement therapy.

Some medications can exacerbate pre-existing acne but will not actually cause a true acne. Drugs that may contribute to or induce acne eruptions include corticosteroids (systemic and topical), androgens, azathioprine, bromides, contraceptives with a high progestin level, corticosteroids, dantrolene, disulfiram, ethionamide, haloperidol, halothane, iodides, isoniazid, lithium, phenytoin (and other hydantoins), quinine, rifampin, thyroid preparations and trimethadione.

TREATMENT

Acne usually resolves by the mid 20s. Class 2 to 4 acne may produce scarring but this can be minimized if properly treated. One of the long-term primary goals in prevention of acne is to keep the pilosebaceous ducts open and avoid physical irritation of the skin and oil-based cosmetics and cleansers. Nonpharmacologic therapy can include cleansing the skin to remove excess sebum, minimizing exacerbating factors (tight clothes, irritation, etc.) and not picking or squeezing the lesions.

Only Grade I (noninflammatory) acne is appropriate for self treatment with higher grades requiring professional care. Nonpharmacologic measures include cleansing the skin and avoiding factors that contribute to acne. Some topical mild irritants can aid in unblocking pilosebaceous ducts.

Inflammatory acne (Grades II through IV) can require both OTC and Rx products, including oral and topical antibiotics and retinoids and exfoliants. Often-used active ingredients include benzoyl peroxide (2.5 to 10%), salicylic acid (0.5% to 2%), sulfur (3% to 8%) and a combination of sulfur (3-8%) with either resorcinol (2%) or resorcinol monoacetate (3%), glycolic acid, retinoic acid (0.01% to 0.1%) and various antibiotics, such as tetracycline and erythromycin. Dosage forms include solutions, suspensions, sprays, lotions, gels, creams, cleansers, masks, soaps and bars.

Benzoyl peroxide is a local irritant and causes irritation and desquamation when applied. It prevents closure of the pilosebaceous orifice. It's irritant action increases the rate of turnover of the epithelial cells lining the follicular duct and increases sloughing. Benzoyl peroxide also is an oxidizing agent and has bactericidal and bacteriostatic action that may inhibit *P. acnes* from growing, thus reducing the formation of irritating free fatty acids. Benzoyl peroxide also has irritant, drying and sensitizing effects.

Salicylic acid is a mild keratolytic used as a safe and effective agent in preventing and clearing both comedones and inflam-

matory lesions of acne. It increases the rate of desquamation of the epithelial layer of skin.
Sulfur is a keratolytic in 3 to 10% concentrations and is generally applied as a thin film one to three times daily. Sulfur preparations do have a noticeable color and odor.
Resorcinol and resorcinol monoacetate in concentrations of 1% to 2% have been used.
Combinations of sulfur and resorcinol act primarily as keratolytics, encouraging cell turnover and desquamation.
Glycolic acid (hydroxy acetic acid, hydroxyethanoic acid) is used as an agent to enhance desquamation or peeling of the skin, depending upon the concentration.
Retinoic acid (tretinoin, Vitamin A acid) is a skin irritant. It is used primarily in the treatment of acne vulgaris in which comedones, papules and pustules predominate. It is generally applied as a cream, gel or alcoholic solution in concentrations ranging from 0.01% to 0.1%. The skin is thoroughly cleansed to remove oiliness about 15-30 minutes prior to application of the tretinoin, once or twice daily.
Tetracycline hydrochloride is a broad spectrum bacteriostatic antibiotic that is used topically in concentrations of 0.2% solution for acne. It is also used orally at a dose of 250 mg twice daily for systemic treatment of acne.
Erythromycin is a macrolide antibiotic that is primarily bacteristatic against a broad range of bacteria. Erythromycin is used orally and topically (2%) in the treatment of severe acne.
Ethyl and isopropyl alcohol are often used as vehicles and will evaporate rapidly after application to the skin. This results in a film of the active drug remaining on the skin surface to exert its effect.
Dosage form selection should include those delivery systems that are noncomedogenic. Gels tend to be most effective but some patients may need the less drying lotions or creams for dry or sensitive skin or for use during dry winter weather. Gels containing only water tend to be slow to dry; the addition of ethyl or isopropyl alcohol to the gel hastens their drying to a film. Gelling agents should not leave a sticky film and should be thin and colorless, thus eliminating the need for coloring to blend the product to the color of the skin. Generally, gels can be recommended for those with darker complexions and creams for those with fair complexions.

Examples of Compounded Preparations for Acne

Creams

Rx - BENZOYL PEROXIDE 10% CREAM

Benzoyl peroxide		10 g
Benzyl alcohol		10 g
Polysorbate 80		4 g
Hydrophilic ointment	qs	100 g

METHOD OF PREPARATION
1. Calculate the required quantity of each ingredient for the total amount to be prepared.
2. Accurately weigh / measure each ingredient.
3. Mix the benzoyl peroxide with the benzyl alcohol.
4. Using low heat, melt the hydrophilic ointment and add the polysorbate 80.
5. Add the benzoyl peroxide and benzyl alcohol mixture and mix well.
6. Cool with stirring, package and label.

STABILITY
A beyond-use date of 6 months can be used for this formulation.[7]

Gels

Rx - BENZOYL PEROXIDE 10% GEL

Benzoyl peroxide		10 g
Propylene glycol		5 g
Benzyl alcohol		5 mL
Carbomer 940		0.75 g
Trolamine		0.7 mL
Ethanol 95%		55 mL
Purified water	qs	100 mL

METHOD OF PREPARATION
1. Calculate the required quantity of each ingredient for the total amount to be prepared.
2. Accurately weigh / measure each ingredient.
3. Dissolve the benzoyl peroxide in the benzyl alcohol.
4. Add the propylene glycol with rapid mixing; then add the carbomer 940.
5. Slowly add about 40 mL of purified water and mix until uniform.
6. Slowly add the alcohol, followed by the trolamine and mix well.
7. Add sufficient purified water to volume and mix well.
8. Package and label.

STABILITY
A beyond-use date of 6 months can be used for this formulation.[7]

Rx - ERYTHROMYCIN 2% GEL

Erythromycin		2 g
Propylene glycol		24 mL
Hydroxypropyl cellulose 1500 cps		2 g
Ethyl alcohol 70%	qs	100 mL

METHOD OF PREPARATION
1. Calculate the required quantity of each ingredient for the total amount to be prepared.
2. Accurately weigh / measure each ingredient.
3. Dissolve the erythromycin in about 70 mL of the ethyl alcohol 70%.
4. Add the propylene glycol and mix well.
5. Slowly sprinkle the hydroxypropyl cellulose on to the agitated solution and stir until gelling occurs.
6. Add sufficient ethyl alcohol 70% to volume and mix well.
7. Package and label.

STABILITY
A beyond-use date of 6 months can be used for this formulation.[7]

Rx - GLYCOLIC ACID 15% GEL

Glycolic Acid 70%		21.5 mL
Methocel E4M Premium		3 g
Xanthan gum	600 mg	
Methylparaben	50 mg	
Propylparaben	25 mg	
Purified water	qs 100 mL	

METHOD OF PREPARATION
1. Calculate the required quantity of each ingredient for the total amount to be prepared.
2. Accurately weigh / measure each ingredient.
3. Heat about 70 mL of purified water to boiling and add the methylparaben and propylparaben.
4. With agitation, sprinkle on the Methocel E4M Premium and the xanthan gum.
5. Cool and incorporate the glycolic acid.
6. Add sufficient purified water to volume and mix well.
7. Package and label.

STABILITY
A beyond-use date of 6 months can be used for this formulation.[7]

Rx - SULFUR AND RESORCINOL GEL

Sulfur		5 g
Resorcinol		2 g
Propylene glycol		qs
Methylparaben		75 mg
Carbopol 940		500 mg
Trolamine		0.67 mL
Alcohol USP		12.5 mL
Purified water	qs	100 mL

METHOD OF PREPARATION
1. Calculate the required quantity of each ingredient for the total amount to be prepared.
2. Accurately weigh / measure each ingredient.
3. Dissolve the resorcinol in the alcohol and slowly incorporate the carbopol 940 by sprinkling it on with agitation.
4. Dissolve the trolamine and methylparaben in about 80 mL of purified water.
5. Combine the two liquids with mixing.
6. Make a paste of the sulfur with the propylene glycol and slowly incorporate into the gel and mix well.
7. Add sufficient purified water to volume and mix well.
8. Package and label.

STABILITY
A beyond-use date of 6 months can be used for this formulation.[7]

Ointments

Rx - RETINOIC ACID 0.2% IN PEG OINTMENT

Retinoic acid		200 mg
Butylated hydroxytoluene		800 mg
Polyethylene glycol 1540		70 g
Polyethylene glycol 300	qs	100 g

METHOD OF PREPARATION
1. Calculate the required quantity of each ingredient for the total amount to be prepared.
2. Accurately weigh / measure each ingredient.
3. Dissolve the retinoic acid and the butylated hydroxytoluene in the polyethylene glycol 300.
4. Melt the polyethylene glycol 1540 at about 55º C.
5. Add the retinoic acid and BHT solution to the melted base, mix well and allow to cool.
6. Package and label.

STABILITY
A beyond-use date of 6 months can be used for this formulation.[7]

Solutions

Rx - JESSNER'S SOLUTION

Salicylic acid		14 g
Resorcinol		14 g
Lactic acid 88%		14 mL
Alcohol, anhydrous		12 mL
Alcohol USP	qs	100 mL

METHOD OF PREPARATION
1. Calculate the required quantity of each ingredient for the total amount to be prepared.
2. Accurately weigh / measure each ingredient.
3. Dissolve the salicylic acid in about 45 mL of the alcohol USP, then add the lactic acid.
4. Dissolve the resorcinol in the anhydrous alcohol (this is a slow process).
5. Add the salicylic acid:lactic acid solution slowly with stirring and mix well.
6. Add sufficient alcohol USP to volume and mix well.
7. Package in a tight, light-resistant container and label.

STABILITY
A beyond-use date of 6 months can be used for this formulation.[7]

Rx - RESORCINOL 3%, SALICYLIC ACID 2% & LACTIC ACID 4% PEEL

Resorcinol		3 g
Salicylic acid		2 g
Lactic acid 88%		4.6 g
Alcohol USP		50 mL
Purified water	qs	100 mL

METHOD OF PREPARATION
1. Calculate the required quantity of each ingredient for the total amount to be prepared.
2. Accurately weigh / measure each ingredient.
3. Dissolve the resorcinol in the purified water.
4. Dissolve the salicylic acid in the alcohol, followed by the lactic acid and mix well.
5. Add the two solutions together.
6. Add sufficient purified water to volume and mix well.
7. Package in an amber container and label.

STABILITY
A beyond-use date of 6 months can be used for this formulation.[7]

Rx - RETINOIC ACID 0.2% SOLUTION

Retinoic acid		200 mg
BHT		200 mg
Alcohol USP		60 mL
Polyethylene glycol 300	qs	100 mL

METHOD OF PREPARATION
1. Calculate the required quantity of each ingredient for the total amount to be prepared.
2. Accurately weigh / measure each ingredient.
3. Dissolve the retinoic acid and the butylated hydroxytoluene in the alcohol. USP.
4. Add sufficient polyethylene glycol 300 to volume and mix well.
5. Package and label.

STABILITY
A beyond-use date of 6 months can be used for this formulation.[7]

Rx - TETRACYCLINE HCL 2% TOPICAL SOLUTION

Tetracycline HCl		2.2 g
Alcohol USP		45 mL
Isopropyl alcohol anhydrous 99%		5 mL
Citric acid		100 mg
Sodium bisulfite		100 mg
Purified water	qs	100 mL

METHOD OF PREPARATION
1. Calculate the required quantity of each ingredient for the total amount to be prepared.
2. Accurately weigh / measure each ingredient.
3. Mix the alcohol USP and the isopropyl alcohol.
4. Dissolve the tetracycline HCl, citric acid and sodium bisulfite in the solution.
5. Add sufficient purified water to volume and mix well.
6. Package in a tight, light-resistant container and label.

STABILITY
A beyond-use date of 6 months can be used for this formulation.[7]

SUSPENSIONS/LOTIONS

Rx - SULFUR AND SALICYLIC ACID SUSPENSION

Sulfur	5 g
Salicylic acid	2 g
Propylene glycol	10 mL
Alcohol USP	10 mL
Methylcellulose 1500 cps	2 g
Methylparaben	50 mg
Propylparaben	25 mg
Purified water qs	100 mL

METHOD OF PREPARATION
1. Calculate the required quantity of each ingredient for the total amount to be prepared.
2. Accurately weigh / measure each ingredient.
3. Dissolve the methylparaben and the propylparaben in a mixture of the propylene glycol and alcohol.
4. Incorporate the sulfur and salicylic acid.
5. Heat about 25 mL of purified water to boiling and slowly sprinkle on the methylcellulose.
6. Add about 25 mL of ice-cold purified water to step #5 and mix well.
7. Incorporate the mixture from step #4 into the methylcellulose dispersion and mix well.
8. Package and label.

STABILITY
A beyond-use date of 6 months can be used for this formulation.[7]

Rx - ZINC SULFIDE COMPOUND LOTION (WHITE LOTION)

Zinc sulfate		4 g
Sulfurated potash		4 g
Purified water	qs	100 mL

METHOD OF PREPARATION
1. Calculate the required quantity of each ingredient for the total amount to be prepared.
2. Accurately weigh / measure each ingredient.
3. Dissolve the zinc sulfate in about 45 mL of purified water.
4. Dissolve the sulfurated potash in about 45 mL of purified water.
5. Filter each solution separately.
6. Slowly and with constant stirring, add the sulfurated potash solution to the zinc sulfate solution.
7. Add sufficient purified water to volume and mix well.
8. Package and label.

STABILITY
A beyond-use date of 6 months can be used for this formulation.[7]

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