

Dermatological pharmacology: topical agents

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Abstract

Topical therapies constitute an important aspect of dermatological treatments. This article covers the principles of topical treatments, the vehicles used and a number of commonly used topical agents, including corticosteroids. Indications for use and common adverse effects of these topical agents are outlined.

Keywords Brimonidine; calcineurin inhibitors; corticosteroids; creams; imiquimod; ingenol mebutate; ivermectin; ointments; rapamycin; retapamulin; retinoids; topical treatments; vitamin D analogues

Principles of topical therapy

Topical therapy allows direct delivery of drugs to the skin with minimal risk of systemic adverse effects. Challenges include poor concordance related to the inconvenience of regular topical applications.

The effectiveness of topical drugs depends on their ability to penetrate the epidermis. This is influenced by the choice and concentration of the drug, vehicle or base, and the age and degree of hydration of the skin:

- substances enter aged skin more easily, but clearance into the circulation is slower because of changes in the dermal matrix and reduced vasculature; therefore the skin may be more susceptible to both the beneficial and the adverse effects of topical medication
- use of emollients to increase skin hydration before applying topical agents such as corticosteroids can increase their penetration fivefold; occlusion of the skin also increases drug penetration
- the specific condition and body site to be treated is also important; for example, absorption is greater at flexural sites, so less potent corticosteroids should be used.

Vehicles

An understanding of the available vehicles is important for effective prescribing of topical therapies. Vehicles hydrate the

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Key points

- Topical therapy allows direct delivery of drugs to the skin with minimal risk of systemic adverse effects, and is widely used to treat a range of dermatological conditions
- Topical corticosteroids should be applied once or twice daily; the quantity applied can be assessed by the fingertip unit concept
- New treatments for rosacea include topical brimonidine gel and ivermectin cream
- Ingenol mebutate is a novel topical treatment option for actinic keratosis
- Rapamycin solution is a topical agent that can be used to manage patients with facial angiofibromas
- Use of topical therapies in the elderly is associated with increased challenges; instructions should be simple, clear and in writing, specifying the amounts and duration of specific treatments

skin, can have an anti-inflammatory effect and help the active drug penetrate the skin, as follows.

- **Creams** are water-based products with a cooling and emollient effect. They contain preservatives to prevent bacterial and fungal growth, but the preservatives can lead to sensitization and allergic contact dermatitis. Creams are less greasy than ointments and are cosmetically better tolerated.
- **Ointments** contain no water; they are oil-based products providing an occlusive layer over the skin surface that helps to retain water. This hydrates dry and scaly skin and enhances absorption, and they are therefore useful in chronic dry conditions. They contain no chemical preservatives.
- **Lotions** are watery suspensions that can be used over hairy and large body surface areas. They have a drying, cooling effect.
- **Gels** are watery suspensions of insoluble drugs such as corticosteroids, salicylic acid and retinoids. Gelling agents are added to aid their absorption.

Topical agents

A list of common topical agents is shown in [Table 1](#).

Emollients

The term 'emollient' covers a diverse range of products, including soap substitutes, bath additives, creams, ointments and even aerosol spray products. They are important in the management of itchy, dry skin conditions, giving symptomatic relief, and can reduce requirements for topical corticosteroids. Their effects are temporary, and frequent applications are needed even after initial clinical improvement. The choice of emollient is

Topical agents

| Agent | Indications | Adverse effects |
|------------------------|---------------------------------------|--|
| Corticosteroids | Inflammatory dermatoses | Striae, telangiectasiae, bruising, allergic contact dermatitis, depigmentation, worsening of infection, rebound phenomenon, suppression of hypothalamic–pituitary–adrenal axis |
| Emollients | Xerosis, atopic dermatitis, psoriasis | Folliculitis |
| Retinoids | Psoriasis, acne, photodamage | Skin irritation, erythema |
| Vitamin D analogues | Plaque psoriasis | Skin irritation, pruritus, erythema, hypercalcaemia |
| Coal tar | Plaque psoriasis | Skin irritation, staining, folliculitis, skin cancers |
| Dithranol | Plaque psoriasis | Skin irritation, staining |
| Calcineurin inhibitors | Atopic dermatitis | Skin irritation, burning, erythema, infections, alcohol intolerance |
| Retapamulin | Impetigo | Skin irritation, pain, erythema, pruritus |
| Brimonidine | Rosacea | Facial flushing, skin irritation, burning |
| Ivermectin | | |
| Imiquimod | Actinic keratosis | Inflammation, pain, crusting |
| Ingenol mebutate | | (rarely flu-like symptoms such as fever, headache and muscle pain with imiquimod) |
| Rapamycin | Facial angiofibromas | Skin irritation, burning |

Table 1

guided by the nature of the condition, its severity and patient preference. Emollient creams, ointments and sprays are best applied after a bath or shower. Many emollients contain preservatives and other additives, and sensitization can rarely occur.

Topical corticosteroids

Topical corticosteroids are classified according to their potency (Table 2). The cutaneous effects of topical corticosteroids include

Topical corticosteroids

| Potency | Corticosteroid | Risk of skin thinning with long-term use |
|-------------|-------------------------|--|
| Mild | Hydrocortisone | Low |
| Moderate | Clobetasone butyrate | Some |
| | Triamcinolone acetonide | |
| Potent | Betamethasone valerate | High |
| | Mometasone furoate | |
| Very potent | Clobetasol propionate | Very high |

Table 2

vasoconstriction, reduced dermal blood vessel permeability and inhibition of phospholipases, fibrin and kinins. In addition, inhibition of phospholipases causes blockage of the arachidonic acid pathway, which leads to a cascade of inflammatory mediators. Anti-inflammatory effects thus occur, and corticosteroid-responsive conditions such as eczema usually exhibit clinical improvement within 2 weeks of starting treatment with a potent agent. Inflammatory skin conditions involving delicate skin on the face, flexures or genitalia require a mild or, at most, moderately potent corticosteroid. In contrast, palms, soles and markedly thickened skin (e.g. from chronic scratching) often require a potent or very potent agent.

Corticosteroids should be applied once or twice daily. The quantity applied can be assessed using the 'fingertip unit' (FTU) concept – an amount of cream or ointment the length of an adult fingertip is about 0.5 g and is sufficient to treat 300 cm² of affected skin (Figure 1).¹ A single application for one adult arm or leg, for example, is 3 FTU or 6 FTU, respectively.

Failure to respond to topical corticosteroids can occur as a result of incorrect diagnosis, skin infection/infestation, contact allergy, poor compliance or inadequate application of treatment. Undertreatment through use of too weak or inadequate amounts of topical corticosteroids is a significant problem; it is more often seen in clinical practice than overtreatment through long-term use of potent agents. The risk of adverse effects increases with corticosteroid potency.

Topical retinoids

Topical retinoids belong to a unique group of drugs that are widely prescribed for skin conditions, including acne, psoriasis and photodamage. The first topical retinoids were synthetic derivatives of vitamin A. Newer compounds such as adapalene have different structural configurations, but also act via nuclear retinoid receptors. Adverse effects of topical retinoids include skin desquamation and erythema, producing mild irritant dermatitis.

- **Adapalene** is a topical retinoid drug used for acne. It is less irritant than other retinoids, and is effective in both comedonal and inflammatory acne.



Figure 1 Demonstration of one fingertip unit, which is sufficient topical corticosteroid to apply to two 'handprint areas' of involved skin.

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