# Importance of Vehicles in Topical Treatment of Fungal Infections

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**KEYWORDS**

• Vehicle • Topical • Antifungal • Adherence

**KEY POINTS**

- Compared with systemic treatment, topical drug delivery provides 2 notable benefits in the management of skin diseases. First, medication can be efficiently deposited directly to the site of disease activity, potentially optimizing therapeutic response. Second, topical drug application generally results in little to no plasma concentration of the active drugs.
- The issue of secondary formulations may have therapeutic implications. Chemical and physical changes occur from the moment a formulation is applied to skin. For example, if a water-insoluble active molecule is formulated into an aqueous vehicle, as the water evaporates on application, the active molecule and its solvent are left on the skin, providing a higher effective concentration of active.
- Certain dosage forms may be better suited for use at certain anatomic sites. For example, an ointment is not ideal for application to the hairy scalp. Another consideration is the spreadability of a formulation.
- Of particular relevance to podiatric medicine, the emergence of topical treatments for toenail onychomycosis represents an especially interesting development in new vehicle formulation.
- A combination of 3 primary considerations may influence the selection of a particular topical formulation in the clinical setting: (1) anticipated efficacy; (2) supportive effects of the vehicle formulation; and (3) practical, patient-based considerations.

Topical drug therapies are commonly used to manage dermatologic diseases and their manifestations in the skin, hair, nails, and mucous membranes. Compared with systemic treatment, topical drug delivery provides 2 notable benefits in the management of skin diseases. First, medication can be efficiently deposited directly to the site of disease activity, potentially optimizing therapeutic response. Second, topical drug

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application generally results in little to no plasma concentration of the active drug, hence it is associated with low risk for systemic exposure and associated potential systemic side effects.

The modern pharmacologic landscape offers several topical dosage forms and many formulation bases, each with its own potential benefits. In many cases, the same active drug is available in several different dosage forms (**Box 1**), offering prescribers the ability to tailor treatment to the patient's unique presentation and needs. In the clinical setting, prescribers must identify the topical drug formulation that is best suited to the presentation of the disease and most likely to encourage therapeutic adherence. This process is best done with an understanding of topical drug delivery, vehicle formulation, and patient behaviors.

## TOPICAL DRUG DELIVERY BASICS

Most topically applied drugs are metabolized in the epidermis. The enzyme-rich skin is the largest drug metabolizing organ. Biotransformation of compounds often occurs in the epidermis, presenting both challenges and opportunities to formulators. Epidermal biotransformation could render a drug ineffective before it reaches its target or, in the case of some prodrugs, synthesize a biologically inactive molecule to an active form.[1]

Although topical drug application seems intuitive in the management of dermatologic diseases, topical drug delivery is no easy task. The epidermal barrier serves an important function: it prevents entry of chemicals, allergens, and other toxic elements into the body because these are all perceived as foreign bodies, including drugs.[2] Because of the action of the epidermal barrier and its general efficiency, the amount of topical drug that bypasses the epidermal barrier and is absorbed by the skin is typically minimal. This barrier function remains the case, even though impairment of epidermal barrier function is a characteristic of many common dermatoses.[3] The barrier is frequently impaired enough to cause symptoms or allow entry of pathogens, but not enough to facilitate drug delivery.

Faced with this reality, topical drug formulators must engineer delivery vehicles that either bypass or override the barrier. This engineering may be done in various ways, and the approach depends to large extent on the active agent to be delivered. Characteristics such as the size, charge, solubility, and lipophilic or hydrophilic nature of the molecule influence the development process, with the ultimate goal of developing

**Box 1**
**Topical dosage forms**

*Eight topical dosage forms recognized by the US Food and Drug Administration (FDA)*

Solution

Suspension

Lotion

Paste

Gel

Ointment

Cream

Other (includes foams, aerosols, powders, patches, and so forth)