Mini Review

Compounded Topical Medications for Diseases of the Skin: A Long Tradition Still Relevant Today

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Compounded medications remain an important component of the physicians' armamentarium. As the volume of scientific information taught in medical school increases, the time devoted to teaching traditional treatments can at times become limited. This succinct manuscript will focus on introducing the reader to this therapeutic option and highlight some of the compounded treatments used in the management of skin diseases.
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INTRODUCTION

Medical students, residents, and physicians early in their careers may have limited exposure to medical compounding. Compounded medications can be individualized and are very useful for individuals with sensitivity to ingredients of commercially available products. Sometimes compounded medications are the only way someone can receive a treatment that has been deemed insufficiently profitable by pharmaceutical companies. Compounding not only allows physicians to individualize treatment, but also connects physicians with the traditions of our profession. This manuscript is intended as an introduction to compounding for the medical student and young physician and will focus on compounded treatments used in skin care.

BACKGROUND

Healers have always sought ways of creating treatments uniquely suited to the problems confronted in their patients. Compounding has ancient roots, with healers in hunter-gatherer societies creating special concoctions. The Chinese Emperor ShenNung studied the health aspects of herbs and roots around 2000 BC, and Cladius Galen (130-200 AD) mentioned compounding and natural formulas in his writings (1). Pharmacists and chemists opened the first shops considered to be precursors of our modern drugstores at around 700 AD.[1,2] In the 1800s pharmacists created crude extracts like opium by using natural plant sources and extracted active ingredients using water or alcohol. The isolation of medications from raw materials gave birth to modern pharmaceuticals. Pharmacists were trained to compound preparations but could only do so on a small scale. Industrialization and improved understanding of chemistry allowed for production to occur on a much greater scale in the eighteen and nineteen hundreds.

The practice of pharmacy was not regulated at the beginning of the 19th century.[2] Most pharmaceuticals were imported or made by the people who used them. As the population grew, the University of Pennsylvania offered a course for pharmacists in 1821 and the Massachusetts College of Pharmacy began offering courses in 1823.[2] These courses were voluntary.[2] The practice of pharmacy was well-organized in Europe, but it was not until 1905 that New York State required registered licensed pharmacists to be college graduates.[2] With increased training in chemistry and physiology, pharmacists and physicians broadened the arsenal to include named formulas such as Gentian Violet solution, Whitfield's ointment, Castellani's paint, potassium permanganate soaks, and a wide variety of creams and ointments. Compounded medicines became an integral part of many practices and personalized medicaments were used for a variety of disorders.

Today, compounded medications remain popular. Problems with infection secondary to contaminated compounded medications for injection have led to increased regulation and restriction of compounding pharmacies.[3,4] The move towards restrictive formularies and the use of generic medications to cut costs has also adversely affected access to compounded medication. Nonetheless, compounding remains an important resource for patient care.[5]

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DISCUSSION

Because manifestations of skin diseases are often easily accessible through careful inspection, and because photographic documentation allows for easy documentation of changes in the skin, dermatologists are well aware that treatments useful for one patient with a particular skin disorder may not be as effective in another patient with the same disorder but with a different presentation or a disorder in a different state of progression. Unlike situations in which a simple algorithm may apply where patients have the same set of symptoms and are expected to respond the same way to a given drug, peoplesuffering from skin disorders can readily be shown to respond differently. Medications should be adjusted to fit the patient's needs whenever possible.

The science of compounding continues to progress. Study of how materials flow (rheology) and methods of assessing absorption have led to many of the elegant products available today.[6-10] Studies on the topical use of systemic medications like clindamycin have led to useful treatments for acne.[11] Topical use of tetracycline for oral aphthous ulcers has been shown to be of benefit in randomized studies.[12] Topical medicines can be delivered in a variety of vehicles (**Table 1**), and certain vehicles are generally more appropriate for certain types of lesions (**Table 2**).Research on topical compounds has led to widespread use of selected compounds that have proven efficacious, such as topical minoxidil for the treatment of androgenetic alopecia.[13] We have listed some of the compounds that are in common usage along with corresponding references (**Table 3**). The extensive interest in cosmetics and so called "cosmeceuticals" has led to the availability of elective courses on compounding as part of some pharmacy students' curricula. More than half of pharmacy students completing such coursework indicated that it helped them counsel patients with dermatologic conditions.[25]

Although there is strong interest among physicians, patients, and pharmacists about compounded and individualized therapy, recent issues regarding infections from compounded injectables have led to increased scrutiny.[26]

If compounded medications are prepared properly in a safe and regulated environment, they can add greatly to a clinician's arsenal of therapeutics. An example of this is the use of topical mechlorethamine (nitrogen mustard) for the treatment of cutaneous lymphoma. This effective treatment for the mycosis fungoides form of cutaneous T cell lymphoma has been used with success for more than half a century. Although there was no FDA approved standardized form until recently, compounding pharmacies found stable dosage forms that could be used for patients.[27] In 2013, a topical form was approved for use. Costs vary among pharmacies, but compounded formulations of mechlorethaminecan often be most cost effective. Receiving FDA approval has facilitated insurance coverage, but it is important to note that effective medicines may sometimes not be FDA approved because of the expense involved with FDA approval process.

Recent regulations have made it more difficult for physicians to purchase compounded medications for non-patient specific office use. 503A compounding pharmacies must have a valid prescription for the medication to be compounded.[29] In-officecompounding is subject to USP 795, 797, and 800 guidelines.[30]

Clinicians and pharmacists can work together with the patient to find effective therapies for a variety of skin problems. Taking the time to find an effective treatment can be very gratifying and draw upon the curiosity and willingness to serve that has drawn us to the practice of medicine. Family physicians should be aware of the options compounded medications offer their patients.

Table 1. Common Dermatologic Dosage Forms.

Cream	An emulsion of approximately equal parts of water and oil
Gel	Semisolid emulsions most often in an alcohol base (melts at room temperature)
Lotion	Higher viscosity than solutions and tend to be emollient
Ointment	A homogenous, viscous, semi-solid preparation, most commonly of oil
Paste	An ointment in which powder is suspended.
Powder	Either the pure drug or a drug mixed with carrier such as corn starch
Shake lotion	A mixture that separates into 2-3 parts over time (often an oil mixed with water)
Solution	Of low viscosity and often have water or alcohol as its base

Table 2. Topical formulations reported for common ailments.

Skin Lesion	Recommended	Usually Avoided
Acute erythema	Shake lotion, lotion, cream	Paste, ointment
Vesicles	Shake lotion, gel, lotion	Paste, ointment
Blisters	Wet dressings, shake lotions	Paste, ointment, powder
Erosions	Wet dressings, ointment	Powder, shake lotion
Crusts	Ointment, wet dressings	Powder, gel
Chronic inflammation	Ointment	

Table 3. Examples of Topical Compounds from the Literature.

Acne	Nicotinomide4% gel [14] Spironolactone 5% gel [15]
Anesthetics (topical)	Topical piroxicam 0.5% gel [16]
Aphthous Ulcers	1 Tetracycline 250 capsule dissolved in 180 mL of water; rinse with suspension four times daily for 4 to 5 days [12,17]
Molluscum	Topical cantharidin 0.7% in an adherent film forming vehicle* [18] 5% potassium hydroxide solution [19]
Mycosis Fungoides	Mechlorethamine (nitrogen mustard) ointment, and solution [27]
Nail avulsion (medical)	Urea and salicylic acid ointment [20]
Oral Lichen Planus	Oral Lichen Planus
Psoriasis	Methotrexate 0.25% hydrophilic gel [22]
Tineapedis	Topical ibuprofen gel 10mg/ml [23]
Verrucae	Topical 0.5 or 5% fluoruracil with 17 or 40% salicylic acid [24]

**Although cantharidin is not FDA approved, this treatment is still available for individual use.*

CONFLICT OF INTEREST
None.

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