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Topical preparations and their use in dermatology

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Summary

The challenges of everyday clinical routine require dermatologists to have a basic knowledge of the composition of topical preparations as well as the regulatory background associated with their prescription. Proper selection, prescription, and application of topical preparations, depending on the respective indication, are key to professional and responsible medical practice. Problems commonly arise with respect to regulatory classifications (medicinal products, medical devices, or cosmetics), eligibility for reimbursement by the statutory health insurances (GKV), and insufficient declaration of vehicle systems. Apart from selecting the appropriate active substance and its proper concentration, choosing a suitable pharmaceutical (galenic) formulation – and thus utilizing the intrinsic effects thereof – is pivotal in enhancing the intended therapeutic effects. When prescribing individual formulations, dermatologists should, to the greatest extent possible, always resort to standardized extemporaneous preparations. Given the multitude of potential ingredients available for pharmaceutical formulations as well as the complexity resulting therefrom, arbitrary changes in quality or quantity of individual components are associated with a high risk of instability, thus jeopardizing safety and the rationale behind any given formulation. Optimal use of topical preparations also requires basic knowledge in pharmacokinetics as well as evidence-based treatment planning.

Introduction

The professional use of topical preparations is one of the core competencies in dermatology.

Given that the vast majority of pathological skin conditions can be adequately treated by topical preparations, such preparations are the most commonly prescribed agents in dermatology. The professional use of topical preparations in various indications is one of the core competencies in dermatology. Based on pharmacological and dermatopathological knowledge, such competency has to be learned by gathering experience in various individual treatment situations [1]. The present article therefore aims to summarize essential knowledge-based aspects in accordance with the current state of technology.

Regulatory categories

From a regulatory perspective, topical agents are divided into the categories medicinal products, medical devices, and cosmetics.

From a regulatory perspective, topical agents are divided into the categories medicinal products, medical devices, and cosmetics (Figure 1). Assignment to a category is determined by the composition, quality, and purpose of a given preparation. The basic requirements of medicinal products (both finished medicinal products

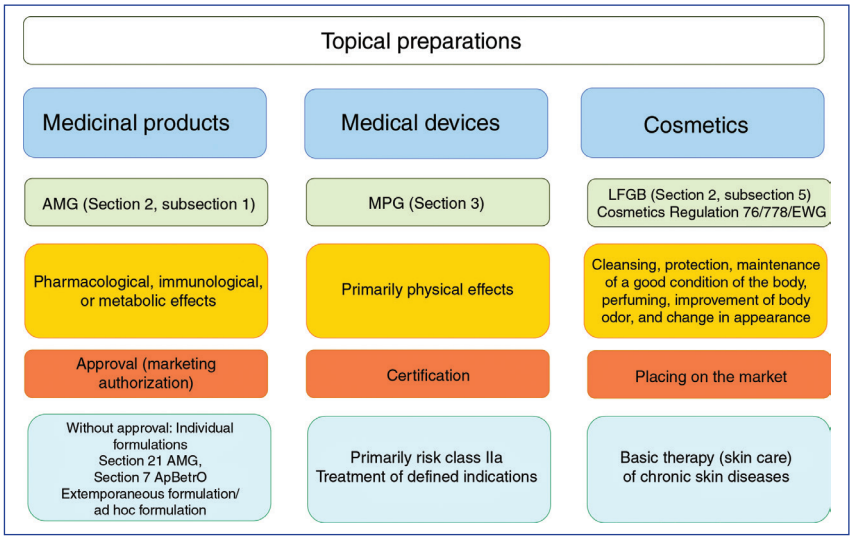

Figure 1 Summary of regulatory categories of topical preparations, their therapeutic benefits and characteristics, as well as relevant national laws. AMG, Medicinal Products Act; MPG, Medical Devices Act; LFGB, German Food and Feed Code; ApBetrO, Ordinance on the Operation of Pharmacies.

and individual formulations) are formulated in the Medicinal Products Act (The Drug Law) (AMG): efficacy, safety, and pharmaceutical quality. Finished medicinal products are subject to an approval (marketing authorization) process (Section 22, subsection 2, number 3 of the AMG) in which evidence of the abovementioned quality criteria has to be provided. While individual formulations are not subject to such an approval process pursuant to Section 21, subsection 2, number 1 AMG, they are, however, subject to a mandatory plausibility check by the pharmacist prior to being put into circulation (Section 7 ApBetrO (Ordinance on the Operation of Pharmacies), Section 8 AMG). In this context, a distinction is made between standardized, quality-tested formulations (extemporaneous formulation) and ad hoc formulations [2]. When having the choice between finished medicinal products and individual formulations, the latter should only be preferred if the active ingredient (or ingredients) contained therein or its desired dosage is not available in suitable finished medicinal products, or if equivalent individual formulations are less expensive. Pursuant to Section 5 AMG, individual formulations must not be used to place unsafe medicinal products on the market. Pursuant to Section 3 Medical Devices Act (MPG), medical devices must have predominantly physical, non-medicinal primary effects for a defined indication. They, too, do not require market authorization, but are certified (CE label) following a conformity assessment process. According to their characteristics, medical devices are classified into risk classes based on their purpose and duration of use. Semisolid topical preparations for external application usually belong to risk class 2a. The quality of the ingredients of medical devices (in the case of topical preparations, better referred to as medical products) does not necessarily comply with AMG requirements, so their use in individual formulations is not generally permissible. Cosmetic products pursuant to Section 2, subsection 5 of the German Food and Feed Code (LFGB) are subject to the Cosmetics Directive 76/778/EWG, and are applied for protection, maintenance of a good condition, perfuming, changing in appearance, or improving body odor. They are placed on the market following a safety assessment by a responsible

individual. The quality of cosmetic products does usually not meet the quality criteria of the AMG, and thus precludes their use in individual formulations. Only if a manufacturer of cosmetic products provides written evidence of qualitative, quantitative, and manufactural conformity with the AMG, may the requirements of the Ordinance on the Operation of Pharmacies (ApBetrO) and of the AMG be met.

Pursuant to Section 12 of the Germany Social Code (SGB) Book V, prescription of a medicinal product has to be efficient, sufficient, and appropriate, and must not exceed what is necessary. The efficiency precept is reflected in the Medicinal Product Directive (AM-RL), which is passed by the Federal Joint Committee (G-BA). In this context, relevant limitations and exclusions with respect to prescriptions include inefficient medicinal products pursuant to Appendix III of the AM-RL, medicinal products that improve quality of life (live style medication) pursuant to Section 14 of the AM-RL, as well as medicinal products for the treatment of minor health disorders (minor ailments) pursuant to Section 13 of the AM-RL. In addition, therapeutic suggestions issued by the G-BA have to be noted [3].

Off-label use – the use of a finished medicinal product in a non-approved indication and mode of application, or at a non-approved dosage or dosing interval or patient age – is not against regulations if and only if: 1. the non-approved medicinal product is effective and safe based on current scientific knowledge, 2. an equivalent alternative is not available or does not appear to be safer, 3. failure to treat would be riskier. Here, the prescribing physician has a special obligation to inform the patient. Prior to treatment, it is recommended that a statement be obtained from the competent insurance company declaring that the costs will be covered.

The therapeutic effects of topical agents are determined by the choice of the active ingredient(s), their concentration, and the choice of the galenic base.

The therapeutic effects of topical agents are determined by the choice of the active ingredient(s), their concentration, and the choice of the galenic base. The physician's therapeutic authority to select an appropriate galenic base – in accordance with the indication and the individual skin condition – is limited by legal regulations that facilitate the substitution of medicinal products with the same active ingredient. Without active use of the aut-idem rule, the pharmacist is required to replace the prescribed medicinal product – pursuant to Section 129 SGB V in accordance with the Pharmaceutical Market Reorganization Act (AMNOG) – by a medicinal product containing the same active ingredient for which there is a discount agreement between health insurance companies and pharmaceutical companies. If there is no discount agreement, the pharmacist is required to provide the prescribed medicinal product or one of the three least expensive medicinal products containing the same ingredient. With regard to package size, the pharmacist is not required to observe the exact amount but only the same package size indicator: N1, N2, or N3.

Ingredients of topical preparations

The composition of a medicinal preparation is based on the physicochemical properties of the active ingredient (including its solubility, molecular weight, pH stability), the intended indication-adjusted manner of application and the viscosity depending therefrom (for example, widespread application, scalp, nail apparatus, mucous membranes, face, palms, soles), the possibilities of using ingredients in accordance with regulatory requirements (for example, pharmaceutical law, patent law), as well as the requirements imposed by packaging and stability considerations (for example, microbiological, chemical, or organoleptic stability) [4]. Apart from the medicinal ingredient itself, the adequate solvent plays a crucial role. The selected vehicle system consists of specific components in accordance with the pharmaceutical (galenic) concept, and is – depending on therapeutic

requirements – supplemented by other ingredients such as preservatives, bodying agents, antioxidants, dyes, and buffers [5, 6]. The many partial aspects involved in the overall composition of a suitable, well-balanced, and stable preparation are by no means trivial. Conceiving such a preparation – frequently also on an empirical basis – requires comprehensive experience and is one of the core competencies of pharmacists.

Quality criteria of medicinal preparations

Today, medicinal products, medical devices, and cosmetics are validated and manufactured according to high quality standards.

In general, topical preparations, irrespective of the regulatory category they are assigned to, have to meet defined quality criteria. Given the high quality standards required for medicinal products in particular, pharmaceutical companies are forced to bear considerable costs in the development of finished medicinal products. Nevertheless, medical devices and cosmetics, too, are validated and manufactured according to high quality standards. However, one of the prerequisites in the manufacture of medicinal products is that all ingredients must be characterized by particularly high purity and quality (pharmaceutical grade), and may only be obtained from certified suppliers. In addition, the manufacture process also requires certified and (repeatedly) quality-assured processes, which likewise may only be provided by certified manufacturers with specially trained personnel. Each batch of the final preparations undergoes testing for chemical, physical, and microbiological stability before being released. For this purpose, stress tests are conducted, and the in-use and storage stability are determined [7]. The quality requirements of the AMG also apply to individual formulations. Given that the quality assessment of ad hoc formulations is usually solely based on a plausibility check done by the pharmacist, the most relevant quality flaws are to be expected in this context. Against this background, ad hoc formulations should, if possible, be avoided. Since extemporaneous formulations are standardized in terms of quality, the aforementioned concerns do not apply here.

Basic principles of cutaneous pharmacokinetics

Pharmacokinetics are determined by the interaction of physicochemical characteristics of the active ingredient, characteristics of the vehicle system, and the condition of the skin.

Pharmacokinetics (PK) of topical agents are determined by the interaction of physicochemical characteristics of the active ingredient, characteristics of the vehicle system, and the condition of the skin. Consequently, the use of different pharmaceutical (galenic) concepts in the form of different vehicle systems has an impact on PK. At the same time, this shows that the indication on which the application is based as well as the individual skin condition play a crucial role. The selection of an appropriate preparation can therefore only partly be based on pharmacodynamic criteria. Vehicle properties, its intrinsic effects, and the acuteness of the indication – thus individual pathological circumstances – also have to be taken into account [8].

Following epicutaneous application of a topical agent, the active ingredient dissolved or suspended therein as well as other ingredients are released (liberated) from the preparation.

In understanding pharmacokinetic principles, three functionally overlapping processes are of importance (Figure 2). Following epicutaneous application of a topical agent, the active ingredient dissolved or suspended therein as well as other ingredients are released (liberated) from the preparation. Only that particular proportion of the ingredient(s) may potentially become bioavailable to the skin. The liberation rate depends on the composition of the vehicle, the physicochemical properties of the (active) ingredient(s), as well as the properties of the skin (acceptor). With respect to a defined indication, said acceptor properties differ inter- and intraindividually, and may also change over the course of the healing process. Therefore, the bioavailable proportion of a given topical agent that is potentially

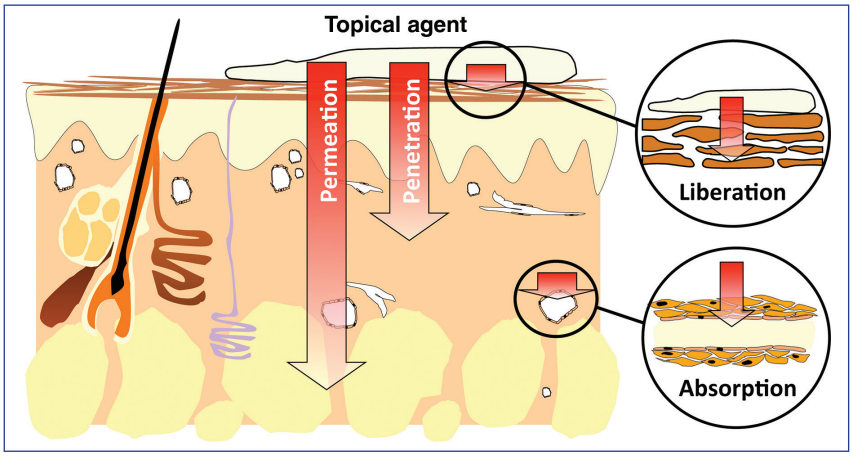

Figure 2 Basic concepts of cutaneous pharmacokinetics describing the interaction between active ingredient and skin following epicutaneous application.

Liberation of the active ingredient is followed by a distribution process within numerous microcompartments.

Fick's laws of diffusion

The permeation rate signifies that proportion of the active ingredient that has passed through any given or all skin layers; the process itself is referred to as permeation.

Intercellular passage is the most important route.

available to exert the desired therapeutic effects also varies. In this context, the composition and condition of the stratum corneum are of particular importance, given its role as boundary layer and thus immediate acceptor of drug uptake. In the pharmacokinetic context, this property of the stratum corneum is also referred to as "reservoir function". With regard to the application of semisolid preparations, transfer of ingredients from the preparation into the stratum corneum has to take place within a few minutes before any residues (of the topical preparation) are removed from the skin surface by clothing or otherwise. Liberation of the active ingredient is followed by a distribution process within numerous microcompartments of the various skin layers – a process referred to as penetration. The most important factors impacting this physical distribution process are described in Fick's laws of diffusion. Here, concentration differences, diffusion surface, diffusion distance, and diffusion properties of individual compartments (diffusion coefficient) play a key role [9]. In addition, thermodynamic activity and convection processes as a function of the hydrodynamic pressure gradient (Hagen-Poiseuille's law) are also of importance. The permeation rate signifies that proportion of the active ingredient that has passed through any given or all skin layers and has subsequently diffused into deeper tissue layers; the process itself is referred to as permeation. Given that the active ingredient passes through vascularized tissue layers, proportional elimination occurs either through absorption via the microvascular system or through enzymatic degradation by various sessile cell types.

Various routes are available for the diffusion process, in particular for the passage through the stratum corneum (Figure 3). The most important route is intercellular passage, which is marked by a hydrophilic and a lipophilic route. The former utilizes the hydrophilic head groups of ceramides and interacting water molecules (in a membrane-like molecular arrangement) for diffusion. In the latter, flexible lipophilic side chains of ceramides serve as matrix for penetration.

The pharmacodynamic properties of an active ingredient and the dermatological indication to be treated determine (galenic) target compartments, which are essential with respect to optimizing the concentration-time profile of the active ingredient, thus the effectiveness and dynamics of the diffusion process. Optimal use of the therapeutic efficacy of a preparation therefore requires an indication-based approach. In this context, indication should be understood as the entirety of the

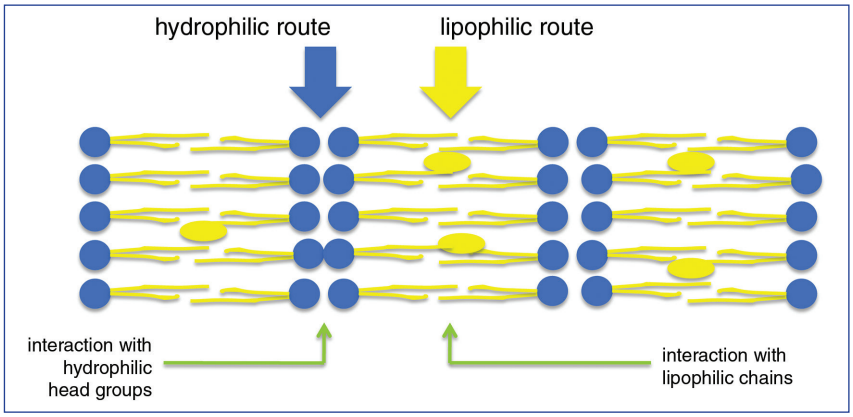

Figure 3 Illustration of relevant pathways of the intercellular diffusion route into and through the stratum corneum.

diffusion environment of the diseased skin including chemical and physical factors, and not primarily as a medical indication. Knowledge about the structural makeup of the skin, the molecular arrangement of individual layers, and the clinical changes associated with a specific indication (hence, the diseased skin) belongs to the core competencies of dermatologists. From this arises a particular responsibility with regard to evidence- and quality-oriented application as well as with regard to residency training and continued medical education, both in the specialist and interdisciplinary context.

Pharmaceutical (galenic) concepts

Intrinsic effects of the base through its direct interaction with the skin

Vehicle system in accordance with the therapeutic objective (indication).

The multitude of pharmaceutical formulation variants, including officinal bases, require special knowledge, which is one of the core competencies of pharmacists.

As regards the differentiation of multiphase systems, the following categories have been tried and tested: ointments, creams, gels, and pastes.

On principle, anhydrous systems are subsumed under the term ointment.

Not only does the pharmaceutical concept of a topical preparation play an essential role in determining the cutaneous bioavailability of a medicinal or cosmetic ingredient, it also determines the intrinsic effects of the base through its direct interaction with the skin. The selection of a specific pharmaceutical concept is primarily based on the physicochemical properties of the active ingredient(s), on their pharmaceutical target compartments, and on the intended intrinsic effects of the vehicle system in accordance with the therapeutic objective (indication). As regards the prescription of finished medicinal products, the actual pharmaceutical concept can neither be derived from the summary of product characteristics (SPC) nor from the information provided on the packaging. Labeling regulations of medicinal products (pursuant to the AMG) do not require pharmaceutical companies to declare the pharmaceutically correct formulation type. Since even specialists have a hard time identifying the exact pharmaceutical concept of any given topical preparation from merely reading the packaging label, it comes as no surprise that pharmaceutical laymen are frequently unable to name the type of formulation used. When choosing a particular finished medicinal product, the prescribing physician therefore faces the problem of not being able to sufficiently take the intrinsic effects of the vehicle system into account.

Understanding the multitude of pharmaceutical formulation variants, including officinal bases, requires special knowledge, which is one of the core competencies of pharmacists. Dermatologists should use a pragmatic and thus simplified categorization primarily based on practical relevance in the clinical context. In our experience, the following categories have been tried and tested as regards the differentiation of multiphase systems: ointments, creams, gels, and pastes.

On principle, anhydrous systems are subsumed under the term ointment. These are divided into lipophilic ointments (here, lipophilic active ingredients may be incorporated), anhydrous absorption bases (here, the addition of water results in a cream), or hydrophilic ointments (here, hydrophilic substances may be incorporated). Creams, on the other hand, are classic three-phase systems consisting of an aqueous, an oily, and an emulsifying phase. Depending on the continuous (outer) phase, a distinction is made between hydrophilic creams (oil-in water type), lipophilic creams (water-in-oil type), and amphiphilic creams (bicontinuous creams, with oil-in –water and water-in-oil components). 'Quasi emulsions' may be distinguished as a special variant; they are also known as cold creams. These are stable, at room temperature highly viscous, lipophilic ointments in which (without the addition of emulsifiers) water droplets have been incorporated. Upon application and melting of the ointment, these droplets are released onto the skin, evaporate, and thus convey a cooling effect. Gels represent another therapeutic option. They consist of a matrix builder that specifies a three-dimensional structural framework (for example, starches), which – dispersed in water or oil – results in a semi-solid preparation of variable viscosity. While pastes also possess certain practical relevance, their importance has declined considerably. The term paste refers to systems that contain an insoluble (particle) component (frequently zinc oxide) suspended in ointment/oil or cream.

Creams are three-phase systems consisting of an aqueous, an oily, and an emulsifying phase.

Gels are composed of a matrix builder, which – dispersed in water or oil – results in a semi-solid preparation of variable viscosity.

Pastes contain an insoluble (particle) component suspended in ointment, oil or cream.

In addition to these "classic" vehicles, basic knowledge of more modern vehicle systems – with a colloidal phase – is useful. Liposomes are usually aqueous phases surrounded by a lipid membrane (bilayer); their molecular arrangement can be modified (lamellar structures). Microemulsions are Newtonian fluids that, in addition to an aqueous and oily phase, also contain an emulsifier/co-emulsifier mixture, and thus have particular thermodynamic properties. Finally, nanoparticles represent the smallest particles (mostly polymers) that – as porous particles – either absorb liquids like a sponge or encapsulate liquid droplets.

Modern vehicle systems have a colloidal phase.

Liposomes

Microemulsions

nanoparticles

The choice of a pharmaceutical (galenic) concept is primarily based on the requirements of the physicochemical properties of the active ingredient to be applied. Finally, the intrinsic effects of the vehicle system with respect to the clinical condition of the skin are only of secondary importance. However, there are clinical treatment scenarios in which medicinal products with suitable active ingredients should not be applied because the intrinsic effects of the vehicle can be expected to cause the preparation to be ineffective or even deteriorate the skin condition. This is true, for example, for lipophilic ointments containing calcineurin inhibitors or corticosteroids; such preparations are not useful and even counterproductive in the treatment of highly exudative acute (or hyperacute) forms of dermatitis.

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Combination preparations

The fixed combination of active pharmaceutical ingredients in topical preparations is suitable for only a limited number of clinical treatment scenarios. From a pharmaceutical point of view, optimization of a preparation exclusively in terms of the physicochemical properties of an active ingredient is possible. Combination preparations therefore always represent a pharmaceutical compromise. Arguments in favor of a fixed combination of two (rarely more) active pharmaceutical ingredients include clinical efficacy through additive effects in certain indications as well as improved patient adherence to treatment. Exemplary indications for advantageous fixed combinations include inflammatory cutaneous mycoses (antifungal agent

The fixed combination of active pharmaceutical ingredients in topical preparations is suitable for only a limited number of clinical treatment scenarios.

Arguments in favor of a fixed combination of two (rarely more) active pharmaceutical ingredients include clinical efficacy through additive effects or improved patient adherence.

plus corticosteroid), highly inflammatory staphylococcal skin infections (antibiotic/antiseptic agent plus corticosteroid), papulopustular acne (benzoyl peroxide plus clindamycin/adapalene or clindamycin plus tretinoin), or plaque-type psoriasis (corticosteroid plus calcipotriol/salicylic acid or anthralin plus salicylic acid). In addition to finished medicinal products, extemporaneous formulations, too, offer the possibility of combination therapy. When selecting suitable combination partners, however, pharmaceutical incompatibilities and interactions, which are not trivial and require special knowledge, have to be considered. The use of nonspecific polyvalent preparations indiscriminately applied to a skin lesion without clear indication should be avoided. Such sweeping therapeutic approaches using preparations that, among others, contain corticosteroids, antibiotic/antiseptic agents, antifungal agents, and local anesthetic agents do not meet the requirements of professional treatment. They are inefficient and pose undue risks through specific and nonspecific adverse effects. Sequential use of monopreparations, too, allows for the implementation of a combined therapeutic concept. At least a 30-minute interval should be observed between individual applications in order to reduce the risk of interaction between active ingredients in ointment residue or in the skin.

The indiscriminate use of nonspecific polyvalent preparations without clear indication should be avoided.

Treatment planning

In order to be able to optimize a therapeutic intervention according to medical, economic and practical aspects, conceptual planning is necessary and useful. This approach is of particular importance in the case of severe and chronic diseases. Here, depending on the acuteness of the disease, differentiation between induction and maintenance therapy has proven to be successful. Through evidence-based selection of individual therapeutic components, both the pathogenesis of a particular disease as well as the circumstances of an individual patient can thus be taken into account [10]. The planning process includes various pharmacological, physical, physiotherapeutic, cosmetic, as well as possibly other options. When using medicinal products for topical application, not only the choice of a suitable vehicle system but primarily also the dosage of the preparation plays a crucial role. The active ingredient in finished medicinal products usually comes in only one concentration (rarely two). Variable dosage may primarily be achieved by adjusting the amount applied or the application frequency, if this is covered by the indication for which the preparation is approved. In certain patient groups in particular, off-label use is beneficial, and may offer an additional chance for curative treatment. Certain requirements have to be met for off-label prescription, including informed written consent. Otherwise, extemporaneous formulations are an excellent option to modify both the application interval as well as the initial concentration of the active ingredient (within pharmaceutically defined limits). In this regard, there is a selection of active ingredients that are marked by a different potency (for example, corticosteroids) or by different modes of action (for example, antiseptics, antibiotics). In this context, it is important to provide patients with written instructions for use (Section 2, subsection 1, number 7, drug prescription regulation [AMVV]), which serves as a substitute for the missing package insert. Moreover, such instructions are required to render the physician's therapeutic concept plausible to both the patient and the pharmacist, and to prevent misuse. For this purpose, there are tear-off pads or digital templates with prepared information available in the NRF (formulary of extemporaneous formulations, issued by the National Association of Pharmacists). Supplemented by individual handwritten notes, they provide a timesaving tool in everyday practice. A structured, evidence-based therapeutic concept, weighing of existing treatment options, mentioning possible adverse effects,

In order to be able to optimize a therapeutic intervention according to medical, economic and practical aspects, conceptual planning is necessary and useful.

The planning process includes various pharmacological, physical, physiotherapeutic, cosmetic, as well as possibly other options.

In finished medicinal products, variable dosage may primarily be achieved by adjusting the amount applied or the application frequency.

Extemporaneous formulations are an excellent option to modify both the application interval as well as the initial concentration of the active ingredient.

It is important to provide patients with written instructions for use.

The communication between doctor and patient has a decisive impact on patient adherence and, consequently, therapeutic success.

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and the inclusion of patient-specific treatment aspects form the basis of the informed consent discussion with the patient. Such communication marks the basis of a trusting doctor-patient relationship, which has a crucial impact on patient adherence and, consequently, therapeutic success [11].

Summary and outlook

The most frequently prescribed medicinal products in dermatology by far, topical preparations are still of paramount importance in the treatment of skin disorders. Used in the context of basic therapy (skin care), cosmetic products and medical devices (products) are employed particularly frequently in inflammatory dermatoses. By defining quality standards, innovative extemporaneous formulations are becoming increasingly available for the treatment of skin diseases, thus complementing the wide spectrum of established formulations and finished medicinal products in particular. Given our growing understanding of the molecular structure of the stratum corneum, the function of the epidermal barrier, and the interaction between modern vehicle systems and the skin, further developments in topical therapy are to be expected in the years to come. These advances will primarily involve the development of new indications for existing topical agents, the establishment of systemic agents in topical therapy, and the increased use of colloidal drug carriers as well as transdermal systems.

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Fragen zur Zertifizierung durch die DDG

1. Welche Arzneimittel werden von Dermatologen am häufigsten verordnet?
a) Biologika
b) Impfstoffe
c) Topika
d) Immunsuppressiva
e) Antihistaminika

2. Wie ist ein Medizinprodukt definiert?
a) überwiegend physikalische Wirkung
b) immunologische Wirkung
c) metabolische Wirkung
d) pharmakologische Wirkung
e) kosmetische Wirkung

3. Welches ist kein typischer Inhaltstoff eines Topikums?
a) Öle
b) Puffer
c) Konservierungsstoff
d) Emulgator
e) Geschmacksverstärker

4. Welcher Prozess ist für die Pharmakokinetik von Topika unbedeutend?
a) Penetration
b) Annullation
c) Liberation
d) Absorption
e) Permeation

5. Welches ist die bedeutendste Kraft, die einen Wirkstoff in die Haut transportiert?
a) Osmolalität
b) Zentrifugation
c) Dampfdruck
d) Diffusion
e) Suggestion

6. Welches Vehikelsystem enthält definitionsgemäß kein Wasser?
a) Creme
b) Salbe
c) Paste
d) Gel
e) Lösung

7. Welche Fixkombination ist keine akzeptierte Therapieoption?
a) Minoxidil + 17-alpha-Estradiol
b) Clindamycin + Benzoylperoxid
c) Azol + Glukokortikoid
d) Salizylsäure + Glukokortikoid
e) Betamethason + Calcipotriol

8. Was versteht man unter einer Magistralrezeptur?
a) eine Rezeptur aus der traditionellen chinesischen Medizin
b) in der Apotheke hergestellte Kapseln
c) Cremegrundlagen für die Köperpflege
d) Rezepturen mit bedenklichen Arzneistoffen
e) standardisierte Rezepturen aus Arzneibüchern und einschlägiger Fachliteratur

9. Welche Maßnahme führt nicht zu einer Dosissteigerung eines topischen Glukokortikoids?
a) mehr Volumen der Zubereitung auftragen
b) häufigere Anwendung der Präparation
c) Erhöhung der Konzentration des Glukokortikoids in der Zubereitung
d) Kombination mit Harnstoff
e) Vortherapie mit wirkstofffreier Salbe

10. Was muss man einem Patienten mit einem Rezept für eine Magistralrezeptur mitgeben?
a) Adresse einer geeigneten Apotheke
b) Herstellungsvorschrift für den Apotheker
c) Anwendungshinweise (Gebrauchsinformation)
d) Kühlakkus
e) Probenmuster der Rezeptur

Liebe Leserinnen und Leser,
der Einsendeschluss an die DDA für diese Ausgabe ist der 18. Dezember 2016. Die richtige Lösung zum Thema „Clinical Management of Pruritus“ in Heft 8 (August 2016) ist: (1b, 2c, 3c, 4d, 5b, 6a, 7c, 8e, 9a, 10d).

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