

Sound base – pharmaceutical and cosmetic base creams

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The treatment of medical indications and cosmetic skin problems depends on how diagnosis and skin analysis are translated into an adequate therapy with appropriate preparations. Beneficial here are base creams that allow extemporaneous preparations.

A preparation for the treatment of skin problems or for skin care purposes should be adaptable to individual skin conditions and have optimal effects. Concepts on ingredients are as individual as the tolerance of substances and the acceptance of sensory and haptic properties.

Pharmaceutics had reacted to this situation a long time ago and began to develop extemporaneous preparations (magistral preparations) before the market was flooded with myriads of ready-made products. Also individual extemporaneous preparations belong to the magistral preparations which are collected in the German Pharmaceutical Codex/New extemporaneous prescriptions formulary (DAC/NRF). Medical doctors are free to select the base creams alias cream bases, the pharmaceutical drugs and their dosage. Pharmacies are responsible for the plausibility check and the preparation.

Numerous components haven't changed over time which reflects in the unmodified compositions of the base creams. A number of examples from the pharmaceutical and cosmetic field are listed in the following.

Compositions according to manufacturers (translated from the original German declaration)

- **Allergika® base cream:** phosphoric acid, purified water, white vaseline, viscous paraffin, chlorocresol, cetomacrogol 1000, cetylstearyl alcohol, sodium dihydrogen phosphate dihydrate
- **Asche Basis® cream:** aqua, petrolatum, paraffinum liquidum, stearyl alcohol, PEG-40-stearate, benzyl alcohol, carbomer, disodium EDTA, perfume, limonene, linalool, hydroxycitronellal, citronellol, geraniol, cinnamyl alcohol
- **Audor base cream:** water, soya lecithin, jojoba oil, beeswax, vitamin E acetate, allantoin, urea, D-panthenol, propylene glycol, isopropyl myristate, octyldodecanol, citric acid
- **Base cream DAC:** glycerol monostearate, cetylalcohol, medium chained triglycerides, white vaseline, macrogol-20-glycerol monostearate, propylene glycol, purified water
- **Decoderm® base cream:** cetylstearyl alcohol, glycerol monostearate, viscous paraffin, polysorbate 40, propylene glycol, highly disperse silicon dioxide, sorbic acid, medium chained triglycerides, white vaseline
- **Dermapharm® base cream:** citric acid, diammonium hydrogencitrate, cetyl alcohol, isopropyl palmitate, cetyl palmitate, glycerol monostearate, polysorbate 60, benzoic acid, purified water
- **Dermatop® base cream:** 2-octyldodecan-1-ol, polysorbate 60, purified water, sorbitan stearate, viscous paraffin, octadecan-1-ol, myristyl alcohol, benzyl alcohol, cetyl alcohol
- **dermaividuals® base cream DVL-P:** aqua, caprylic/capric triglyceride, pentylene glycol, hydrogenated lecithin, butyrospermum Parkii butter, glycerin, squalane
- **Fabitop® base cream:** aqua, petrolatum, cetearyl alcohol, paraffinum liquidum, PEG-40 hydrogenated castor oil, pentylene glycol, polysorbate 60, propylene glycol
- **Pentravan® transdermal base cream:** aqua purificata, isopropylis myristas, acidum stearicum 50, glyceryl monostearate, polyoxy 40 stearate, isopropylis palmitas, lecithin (soy), simethicone, urea, alcohol cetyllicus, alcohol stearyllicus, kalii sorbas, acidum sorbicum, acidum benzoicum, butylhydroxytoluenum, dinatrii edetas dihydricus, carbomerum 980, acidum hydrochloricum 35 %
- **Wolff base cream medium fat:** aqua, decyl oleate, glyceryl stearate, palmitic

acid, stearic acid, cetareth-3, linoleic acid, tromethamine, cera alba, perfume, methyl paraben, sodium ethyl paraben

Today's abundance of validated magistral preparations but also the slow inclusion of new ingredients into the pharmacopoeias or comparable country-specific documentation are quite an obstacle for the adaptation of cream bases to modern ingredients:

- Ph. Eur. – Pharmacopoea Europaea (Europäisches Arzneibuch)
- DAB – German Pharmacopoeia (Deutsches Arzneibuch)
- DAC – German Pharmaceutical Codex (Deutscher Arzneimittel Codex)
- DMF – Drug Master Files der FDA (Food and Drug Administration, USA)

Recent base creams with ingredients that comply with the German Cosmetic Regulation (KVO) but are not monographed in the pharmacopoeia or, in other words, are not adequately scientifically described, are considered to be cosmetic cream bases and, according to the German Pharmacy Operations Ordinance (Apothekenbetriebsordnung – ApBetrO), permitted for the processing of topical magistral preparations if their identity has been adequately verified, the certificate of analysis of the supplier is on hand and analytical testing has been implemented.¹

Base creams and active agents – synergy effects wanted

Still today there is a problem of relapses with extemporaneous preparations when the pharmaceutical drug is highly effective for the treatment of infections but the cream base does not support the recovery of the skin barrier. After the treatment – just to stay with this example – germs may again penetrate into the skin via the still damaged skin barrier.

By the same token it should be mentioned that corneotherapy, which was developed in the nineties and is based on the use of adequate active agent free base creams to regenerate the skin barrier, could prove clinically significant results, as e.g. in the case of atopic skin.²

³ Hence base creams in magistral preparations

¹ Schöffling U, Kosmetische Mittel als Rezepturgrundlagen, PTA heute 5;März 2016: 40-44

² Lübbe J, Evidence-Based Corneotherapy, Dermatology 2000; 200:285-286

³ Tabata N, O'Goshi K, Zhen YX, Kligman AM, Tagami H, Biophysical assessment of

should not only be active agent carriers but themselves have strong synergetic effects. With this objective in mind and to exclude counterproductive effects in the respective indications, it is essential to focus on the particular properties of a pharmaceutical or cosmetic base cream in the individual case. The following check list may be beneficial:

Base cream properties:

- The function as a **carrier** and **depot** for lipophilic, hydrophilic or amphiphilic active agents implies that the base creams are compatible with the active agents (in pure or pre-dissolved form). Manufacturers of base creams usually compile compatibility lists which are available free of charge on request.
- The **transport of active agents** via skin barrier (carrier function) either is achieved via penetration boosters or via occlusive conditions. Occlusivity obtained with petrolatum (vaseline), mineral oils, waxes and W/O emulsions based on these products however slows down the recovery of the skin barrier and leads to counterproductive swelling in the skin. On the other hand, O/W emulsions with non-biodegradable emulsifiers increase the transepidermal water loss (TEWL) and the dehydration of the skin through washout effects during skin cleansing. An alternative are indifferent lamellar base creams that are adapted to the structure of the skin barrier.
- To ensure the **tolerance** of base creams, individual allergies, sensitivities, irritations and last but not least the human psyche which reacts to sensory and haptic properties as well as packaging have to be taken into account.

In this context, the prevailing skin condition plays a decisive role. In the case of sensitive and even more of barrier disturbed skin, low molecular ingredients such as e.g. urea and hypertonic water phases of O/W emulsions can trigger a short burning sensation on the skin which usually is not tolerated by users. Furthermore, compatibility with the skin barrier and the dermal microbiome is significant for the long-term success of a treatment.

persistent effects of moisturizers after their daily Applications: Evaluation of Corneotherapy, Dermatology 2000;200:308-313

Anaesthetising substances such as the emulsifier laureth-9 which reduces the sensation of pain should not be used unless it is medically indicated in the form of polidocanol (INN).⁴ It goes without saying that comedogenic ingredients also are avoided.

- A significant criterion for base creams is the cosmetic **skin care effect** since additional skin care preparations should be avoided during the dermatological treatment in order to exclude unwanted interactions. Particularly lipid substances (oil phase) and moisturizers (water phase) should be biodegradable and compatible with the physiology of the skin. Even without active agents, the application of respective cream bases can be continued after the treatment until the skin is completely recovered. Beneficial are cream bases that can be used from dermatological therapy through to cosmetic prevention and skin care, in other words that can be enhanced with cosmetic active agents such as vitamins, vegetable oils (essential fatty acids), extracts and hyaluronic acid after the therapy.
- **Skin protection** is particularly important for hands that are permanently in contact with apparently harmless household chemicals or working substances. During the past twenty years the concept of sealing the skin ("plaster concept") has more and more been abandoned as it considerably impairs the natural recovery of the skin. The concept was substituted by a moderate skin protection - in combination with a high recovery effect during leisure and at night – which has proved to be the more efficient formula.
- The already mentioned **recovery of the skin** can be achieved with barrier-active corneotherapeutic ingredients, in other words, ingredients that in chemical and physical respect widely correspond with the natural conditions of the stratum corneum.⁵

- **Additives** are used for sensory and haptic purposes as well as for the stability during storage. Additives are emulsifiers, consistency agents, film-forming substances, antioxidants, complexing agents, preservatives, perfumes and dyes with partly counterproductive properties. Emulsifiers with comparatively high critical micelle concentrations (CMC) can irritate sensitive skin and trigger washout effects. Strong complexing agents such as EDTA inactivate metal-containing endogenous antimicrobial peptides (AMP) and oxidoreductases. Synthetic antioxidants such as BHT (butylated hydroxytoluene) as well as the preservatives listed in the annex of the German Cosmetic Regulation and perfumes are well-known for their allergenic properties. This should be considered in the case of a potential predisposition of the users. Subjects of some debate but less crucial are the pH-values of the cream bases, since the natural buffer of the skin rapidly reestablishes the starting values. These values usually are between pH 5.5 and pH 7.

Regulatory framework

Besides the technical properties of the base creams, also regulatory aspects are of interest. The German Pharmacies Operations Ordinance (ApBetrO) is legally binding for the **production of individual pharmaceutical preparations in pharmacies**. Individual cosmetic preparations have to be processed according to the German Cosmetic Regulation which applies for cosmetic institutes but also for pharmacies. Just to mention an example: Only recently a pharmacy had to cease its online trade activities because the labelling requirements of the German Cosmetic Regulation have not been observed.⁶

With regard to the cost reimbursement by the statutory health insurance, the competence of the pharmacists should not be questioned. In other words, the pharmacist is free to decide whether he uses a cosmetic or pharmaceutical cream base for the extemporaneous preparation. The re-assessment in the case that a cosmetic base cream was processed is not allowed though.⁷ A prerequisite is, however, that the documentation according to the German Pharmacies Operations Ordinance is

⁴ Polidocanol in kosmetischen Mitteln, Stellungnahme des Bundesinstituts für Risikobewertung (BfR) vom 15. Oktober 2003

⁵ Iwai I et al. The human skin barrier is organized as stacked bilayers of fully extended ceramides with cholesterol molecules associated with the ceramide sphingoid moiety. *J Invest Dermatol* (2012), doi: 10.1038/jid.2012.43, 1-11

⁶ VG Ansbach, Urt. v. 20.11.2012 – AN 1 K 11.02002035

⁷ Berger A, Fragen aus der Rezeptur, PTA heute online

provided and the production is GMP-compliant. In the case that adequate and equivalent pre-fabricated compounds are available, pharmacies are encouraged to offer the prefabricated compounds.

The situation is different with the **use of cosmetic base creams in the institutes**. Base creams and cosmetic active agents may only be applied as individual cosmetic preparations (active agent sera). Resulting compounds are not sold on the market but directly used in situ. Consumers can purchase cream bases and active agent sera, however, and mix them according to the guidelines of the cream base manufacturers. In particular cases, institutes can alternatively offer to mix compounds as an individual service.

Processing of base creams

A particular feature of magistral and individual cosmetic preparations is that they are processed at room temperature. The so-called cold stirring either is done manually in the provided base cream containers or separately in jars or bowls. Alternatively, automatic stirrers such as Unguator[®] or Topitec[®] are used. Pharmacies also apply conventional horse-shoe mixers and basins. During the mixing process both phase transition temperature as well as consistency of the original base creams can modify and high energy input can lead to instabilities. Hence it is essential to use stirring devices at low speed.

A further prerequisite in pharmacies is to work under aseptic conditions according to GMP standards. Unless unpreserved aqueous active agent components are used, the microbiological stability of the preparations is ensured. Aqueous solutions should either be stabilized with preservatives or alternatively with alcohols or glycols, as for instance propylene glycol. Lipophilic pharmaceuticals are added either in triturated, preferably micronised form or pre-dissolved in fatty oils.

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