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GALENIC EXCIPIENTS AND VEICLES IN DERMATOLOGY: PRINCPLES, CHEMISTRY, CLASSIC USE AND FORMULATION

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ABSTRACT

The aim of this work is to evaluate the excipients and veicle commonly used in galenic dermatology
With an pharmaceutical – chemical point of view.
It is a real complex world: products form mineral, animal or vegetal origin or also syntetic.
The hystoricsl use of remedies in dermatological condition is very ancient in the humanity history and since today the term GALENIC is used in the modern pharmacy setting.
The efficacy ot the therapy is related not only to the various AIPs used but also to the excipienst or veicle employed as well as the Pharmaceutical form choosed by the dermatologist or the pharmacist.
Efficacy, safety and tollerability are the key factors for acute or prolonged therapy : for adults or children.
The chemical stability and the microbiological aspects complete the profile for a good galenic product.
The characteristics of the some **pharmaceutical or cosmetic** topical form and their composition are reported : classic formulation are then submitted to clarify some useful concepts.

KEYWORDS: physiology, anatomy, dermatology, topic, cosmetics, cream, ointment, gels, lotions, paste, powders, topical solutions, odontoiatry malignancy, APIs, veicle, bases excipeints, technical pharmaceuticals, galenic laboratory, safety.

INTRODUCTION

Between the various and complex funciton of the skin it is possible to see :

Protective barrier from the environment, tempertaure regulation, immune function, excretory functions eletrolite and liquid (sweat)**,** methabolic functions, hormonal function (vit E and cholicalciferol), neuroception(sensorial for temperature, tactile, pain), social and relation funcion, psicological implication.

Under an anatomic point of view : the skin is composed of 2 tissue (**one superficial- epitelial named epiderma) and one internal (connective named derma).**

Below the derma there is lypid layer – subcutaneous.

Epidermide and derma are separated by an juntionem membrane- basal membrane anchored to the derma with collagen fibrill.

Epidermide is an epitelia squamous pluristratified. Thickness from 70-120 micron according the various site.

The more deep layer is named basal layer or germinative, upper there are then spinous layer, granular layer and corneal. The basal layer is composed by cubic or cilindic cell whit possibility to reproduce by mitose. This make possible to sobstitute the cell losted by trauma or desquamation.

From this layer a differentiation produce corneocite – cheratinizzation with lost of the nucleous.

The more external stratum corneous is made of death cells (flatted cells), poor of lipid, immersed in an extracellular matrix – gelified.

The combination of cornified cell idrofilic with intercellular material idrofobic produce a good barrier for both idrofilic and idrofobic substantie.

The epidermis have not blood vases, instead the nutritive substantie is provided by capillary of the connective tissue and by the diffusion of the interstital liquid of the intercellular space.

The composition of the corneum strate : water 15-20 % (instead the intere body have 55%) a low level and rich in protein 80% (intere body 20%), and keratin is the major component. The lipids are represented especially by ceramide.

Between germinal cell of epidermid there are the melanocite responsible of the pigmentation of the skin in order to protect from solar radiation and the Lanherans cell – immunitary role.

Thus cells are APC - antigen presentating cell, and involved with allergy process.

Derma : it differentiate because have few cell inside. It is made of a matrix of connective tissue :Especially fibrous protein like collagene 70% and elastine 4% and a fundamental substantia mucopolisaccarides: jaluronic acid and condroitin sulfate. This confer elasticity and mecanical resistence to the skin.

Ipoderma : below derma, tichness vary according the various site of the body. In this layed the adipocite store the TG for energetic scope. This layer act as termoregulator for the body.

Annexial – skin appendages: hair, sebaceum gland, apocrine gland (exclusively in inguinal and anxillary) and sudoripare gand. The sebacea gland produce sebum – lipidic material instead sudoripare gland produce a liquid aqueosus relevant for the termoregulation.

Nails – this can be affeted by micotic or bacterial pathology.

Mucose : multistratified, coated with mucus (water dispersion of protein – mucine.Below mucose there is the basal lamina that connect with a layer of connective tissue. Hard palate is of keratinized epitelia.

To be clarify is that the site of application of topical therapy are the skin but also external mucose of the genital organ.

According article Anatomy, Skin (Integument), Epidermis

Hani Yousef; Mandy Alhajj; Adegbenro O. Fakoya; Sandeep Sharma. Last Update: June 8, 2024.

“The skin is the **largest organ** in the body, covering its entire external surface. The skin has 3 layers—the epidermis, dermis, and hypodermis, which have different anatomical structures and functions. The skin's structure serves as the body's initial barrier against pathogens, ultraviolet light, chemicals, and mechanical injury. This organ also regulates temperature and the amount of water released into the environment.

Skin thickness varies by body region and is influenced by the thickness of the epidermal and dermal layers. Hairless skin in the palms of the hands and soles of the feet is the thickest due to the presence of the stratum lucidum, an extra layer in the epidermis. Regions lacking this extra layer are considered the thin skin. Of these regions, the back has the thickest skin because it has a thick epidermis. The skin's barrier function makes it susceptible to various inflammatory and infectious kinds of conditions. Wound healing, sensory changes, and cosmesis are significant surgical concerns. Understanding the skin's anatomy and function is crucial for managing conditions across all medical fields.”

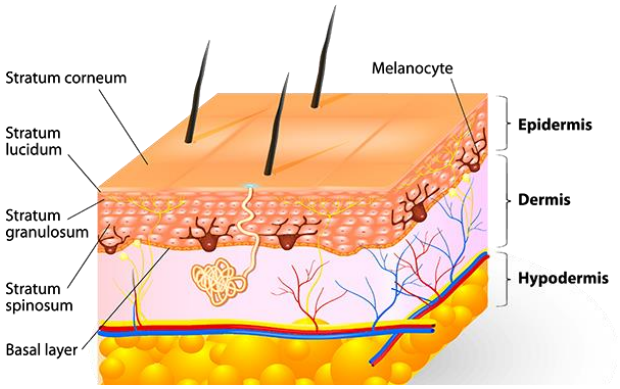


Fig n 1 the layer of the human skin.

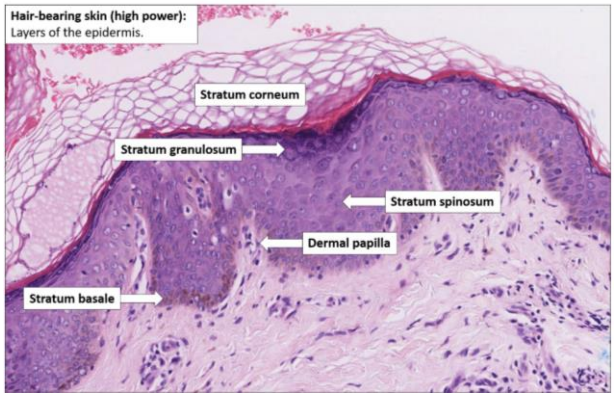


Fig n 2 normal skin hystology from https://medicine.nus.edu.sg/pathweb/normal-histology/skin/

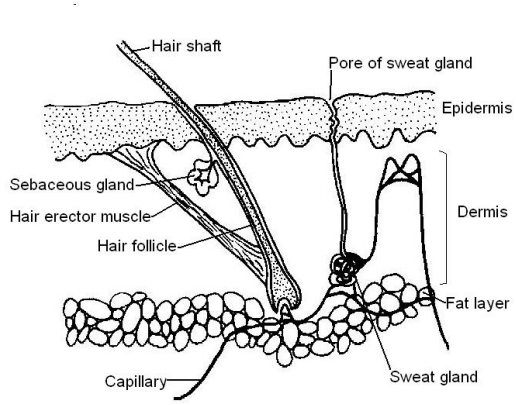


Fig n 3 skin appendages.

Nurs Clin North Am. 1999 Skin anatomy, physiology, and pathophysiology A B Wysocki.
"The skin has two layers, the epidermis and dermis, separated by a basement membrane zone."

And in Basic Science January 2022 Physiology of the skin Gerard McKnight · Jasmine Shah · Rachel Hargest
DOI: 10.1016/j.mpsur.2021.11.005

It is possible to verify that :
"The skin is the main interface between the individual and the environment. It has essential physiological functions which allow the individual to live safely, even under changing external conditions which might pose potential threats. The most important function of the skin is protection against various forms of noxious stimuli including physical and chemical trauma, micro-organisms and radiation. The skin and its appendages like as hair are also vital for thermoregulation. Many modalities of sensation are mediated via the skin allowing the individual to recognize the context of their relationship to the environment. The skin is a significant water storage organ, particularly in hypodermis layer. Although it mainly acts as a barrier, the skin does have some ability to absorb various substances, particularly lipophilic compounds.

Emotions like as fright, anger or joy can be expressed via the skin, due to changes in blood supply, the position of hairs, or movements of those muscles which insert directly into the skin. Synthesis of vitamin D occurs in sun-exposed skin and is the major site of production in the normal health. It is important for surgeons to understand the functions of the skin in order to recognize when clinical problems occur and to appreciate how patients with disordered skin physiology are likely to respond to an traumatic or surgical injury."

Between the advantages of a topical therapy there is the possibility to have high concentration of a drug in a specific site whit a minimal exposure to other organ.

In article Skin Structure, Physiology, and Pathology in Topical and Transdermal Drug Delivery by Sofia Brito, Moonki Baek, Bum-Ho Bin
Pharmaceutics
https://doi.org/10.3390/pharmaceutics16111403 October 2024

"Drug Diffusion Through the Skin
The drugs absorbtion is a **passive diffusion process.**
Effective drug penetration requires passage through the **stratum corneum, the outermost layer** of the epidermis. There are primarily 2 established pathways by which pharmacological agents can penetrate this barrier"

Skin permeability and penetration way: the skin has a good barrier property, especially the corneum strate.

This oppose to the exchange with external. The stratum corneum is the rate limitanting barrier to the drugs penetration. The penetration is a function inverse proportional to the tickeness of the stratum corneum.

There is also a **regional difference in the Drugs penetration** : high in mucose, scrotum and in decreasing way : face chest and back, upper and lower arm and legs, since dorsals hands and feet.

Essential oil or other great penetranting component can produce irritation or allergy.

The overcoming of this barrier imply factors related the skin (there are body regional differences), the APIS charcteristics, and the formulation the veicle efficiency depend on the kind of preparation (cream ointement,gels or other) and by the excipients used
The drug can pass trought the corneous layer in 3 way
1) Intracellular – corneocite, 2) intercellular trought extracellular matrix, 3) annexial way trought
Hair follicules or sweat or sebaceous galnd ducts

The annexial way is elective way for the idrofile drugs, even if is is only 0,1% of the skin surface.

The intercellular route is the preferential way for the liposoluble APIs.

An excessive lipofile drug can be accumulated in the corneum strate and obstaculate the passage to the more deep layer more polar.

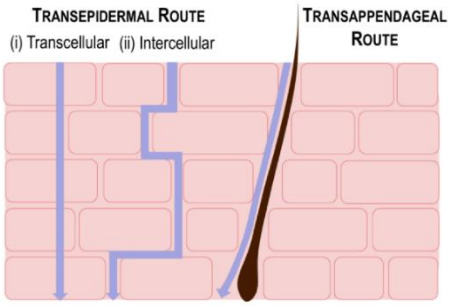


Fig n. 4 Scheme depicting the routes of drug diffusion through the skin. Each pathway is represented by a purple arrow below each label. From S. Brito et al.

Percutaneous absorbtion:
APIs + veicle --→ skin diffusion transepidermal -→ 1) diffusion to corneum strate
Or 2) via annexial (trough gland eccrine and pilosebaceum units)
All this two way produce an→ permeation epidermide and derma → capillare absorbtion → systemic circle (this last can provide or a pharmacological sytemic action but also a systemic toxiciy).

Factors that can influence the drugs percutaneous absorbtion
1) Thickeness of the corneum strate, this vary in the different skin site: minimun behind the hear an maximum in the hand palm.
In newborn the skin barrier is not completed and so the permeability is high.
2) hydratation of the stratum corneum
3) chemico-physical characteristic of the drugs, the skin is a lipofile barrier, easy penetration of apolar molecule. Partitition coefficient W/0 and ionization grade, PH of the formulation
4) APIs concentration gradient, ripartition coefficient veicle -skin and ionization grade of the APIs
5) the way of application
The use of excipients that increase solubility of the drugs generally increase the gradient of concentration and the diffusion velocity.

The ionization increase the idrofilic properties.Other substantie can improve the absorbtion like fat acid long chain, sulfoxide and organic solvents.

Physical methods to increase drug penetration: ionophoresys, low level of electric current application.

Other methods
the use of prodrugs to increase penetration, like betametason valeranate, more active then simlply betametason becase it is more lipfolile, then after absorbtion is coverted by esterase in the free molecule.

Permeability : to be considered that SC is little permeable to the water. Alchools : can penetrate and extract lipids, Polialchool like glicerin are held back into SC. Oranic solvents : like DMSO, esane, cloroform, etere can destroy the skin barrier. Salts : SC is not permeable.
Tensioactives: this excipients weaken the SC barrier and permitt to other products to permeate.
Lipids : oil, fats, wax not permeate, cholesterol and phitosterole yes trouh the transfollicular way
Essential oil : very penetranting.
To be considerd for the dermatological topic products : the dosage form and the delivery suystems.
Drug stability, intended use, site of application,products type**.**
The drugs release from a veichle depends on : drugs concentration, stability of the APIs in the veicle, APIs partition's between the veicle and the skin. Veicle that increase hydratation and skin permeability :
Occlusive, lipofilic, emulsion W/O. Solvents like alchool can dissolve skin lipids.

Promotor of absorbtion: alchols, long chain fatty acid, sulfoxide, solvents.
The application of electric current increase penetration of drugs (ions)- a Physical effect

Related the choosing of the bases and veicle
In some condition even if a drugs absobtion is superior using an hydrocarbon base it can be more useful to use a less occlusive veicle.
In other situation it can be increased the percutaneous absorbtion and activity can using an hydrophilic bases.

In Indian J Dermatol. 2016
On the History of Classification in Dermatology Amiya Kumar Mukhopadhyay
"Since the early days of cutaneous medicine, naming of the entities had remained a confusing subject. Earlier texts of all ancient civilisations are almost similar in this topic. The Biblical controversy regarding the actual translational meaning of the original Hebrew term Zara 'at has become a centre of controversy amongst many research scholars of medical history. Similar debate exists about the Ayurvedic term Kustha-- whether it meant leprosy or stood for a number of skin affliction is a matter of controversy. A scientific and rational classification system was, needed. The process started with Galen and traversed a long path and ultimately with the eight orders classification system proposed by Robert Willan in the early part of the nineteenth century resolved the issue**."**

Skin common disorders: this can vary form common acne since to the dangerous melanoma cancer.

acute and chronic dermatoses, **infectious** dermatoses, **autoimmune, bullous** disorder**.**

Major classifications of skin diseases
Inflammatory/Dermatitis: Atopic dermatitis (eczema), contact dermatitis, seborrheic dermatitis, psoriasis, lichen planus.
Infections: Bacterial (boils, impetigo), viral (warts, herpes), fungal (candidiasis), parasitic (scabies).
Autoimmune/Connective Tissue: Lupus, dermatomyositis, scleroderma.
Genetic/Congenital: Ichthyosis, Epidermolysis Bullosa (fragile skin).
Pigmentation Disorders: Vitiligo, albinism.
Appendage/Hair/Nail: Acne, alopecia.
Vascular Lesions: Angiomas, pyogenic granulomas.
Drug Eruptions: Adverse skin reactions to medications
Neoplasms (Skin Cancers): Melanoma, basal cell carcinoma (BCC), squamous cell carcinoma (SCC), seborrheic keratosis.

The WHO ICD-11 Classification of Dermatological Diseases: a new comprehensive online skin disease taxonomy designed by and for dermatologists
J.M.L. White, H. Lui, C.G. Chute, R. Jakob, R.J.G. Chalmers July 2021 https://doi.org/10.1111/bjd.20656 view metrics.

"In May 2019, the World Health Assembly officially adopted the 11th Revision of the International Classification of Diseases (ICD-11)."

it is relevant to verify the stage of the disease in example
J Pediatr Pharmacol Ther. 2024 doi: 10.5863/1551-6776-29.6.587
Atopic Dermatitis: A Review of Diagnosis and Treatment Jack Jeskey, Christine Kurien, Henry Blunk, Kiran Sehmi, Sathya Areti, Delena Nguyen, Robert Hostoffer
"Eczema is a wastebasket term for acute dermatitis that is characterized histologically by spongiosis or intercellular edema. The microscopic findings of AD are nonspecific and share many features with other eczematous rashes. Histology is more useful in characterizing the chronicity of eczematous lesions as **acute, subacute, or chronic.** if the diagnosis remains unclear, skin biopsy can also aid in excluding other inflammatory dermatoses."

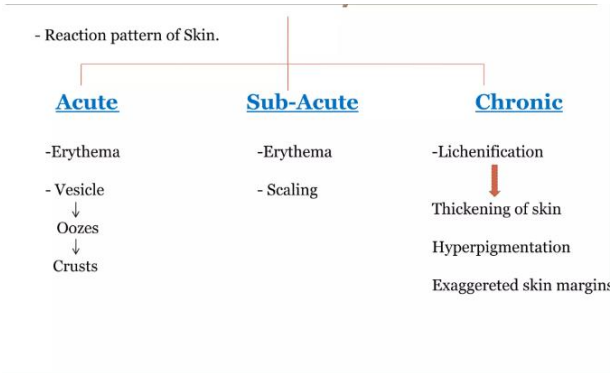


Fig n 5 dermatitis-eczema.

Acute disorder can include: urticaria, acute eczema, eritema multiform in eczema patch of skin become inlflamed, itchy, red, craked and rough (different kind allergic contact dermatitis, atopic, drug related, photoeczematous primary irritant dermatitis.
Chronic disorder: psoriasis, lichen planus, lichen simplex chronicus.
Bullous disorder like phenphigus, bolloid phemphigus, dermatitis herpetiform.
Infectious conditions : by fungi, bacteria and viruses
Parassitic conditions : scabia, pediculosis and other
Tumors: premalign epithelial lesions, malignant epidermal lesion, melanocitic proliferation.
Eczema cause: sensitization from contact whit plants, chemicals, metals, dyes for hair or clothes, nikle form jewelery (vescicle, and bullae, itching, scaly crusts form by the ruptured lesion, oozing plaques).
Scratching cause the lesion to burst and ooze with spread of the condition. Therapy: hydratanta, topical corsticosteroids and other products.
Urticaria: vasculare reaction of the skin to an allrgen, wheal (round elevation lesion, red edge and pale center, extremely itchy (involved hystamine release with vasodilatation and edema). Caused by Mast cell deranulation : after the antigen + Ige antibodies. Often caused by food, allergenes, pollens virus or stress conditions. Therapy used : steroids, antihystamines, topical therapy.
Penfigus: autoimmune disorder, uncommon, blistering disorder. Due by the loss of the normal intercellular attachements within the epidermis and the squamous mucosal epithelium.
It is an hypersentitivity reaction type 2 : IGG autoantibodies + intracellular desmosomal skin protein and this phenomena disrupt the adhesive function.
Psoriasys: the name comes from psora (itching), chronic inflamatory hyperproliferative condition.

Papulo squamosus (eritematosus papule and plaques, with overlying silvery scale), idiopatich, immune T cell are involved. Epiedmiology about 2% of the population (prevalence). Precipitantin factors : trauma, stress, climate change, infections, some drugs. Lesion often in the extensor surface (knee, arms, legs, sacral and gluteal, scalp, nail). Initially : red spots, dry swollen inflamed patches, covered with silver white flakes, rasied and thin skin.

The lesion seem caused by : tissue injury, trauma, T CELL release of cytokine IL 12, IL 23, TNF, interferon.
With keratinocyte proliferation, great inflamation, vessel diatated, erithema, plasma protein and leucocite agregate. The keratin production is increased, parakeratosys whit retain nuclei, death of the keratinocite and desquamation. The basal stratum become weak and other layer become thikened, the stratum corneum cell not adhere properly.

Other conditions : skin rash and pruritus, mounth conditions, palm and sole conditions, nail disease Nappy rash, acne, skin pigmentation.

Pathology like bacterial and fungal infections, parassites, psoriasis, eczena dermatitis, skin ulcers and other conditions seen need the right therapy.

Editorial J Pers Med. 2022 doi: 10.3390/jpm12091370 Skin Inflammation—A Cornerstone in Dermatological Conditions Mircea Tampa, Monica Neagu, Constantin Caruntu, Carolina Constantin, Simona Roxana Georgescu.

"Although the 5 cardinal signs of inflammation (calor, dolor, rubor, tumor and functio laesa) have been described since ancient times, there are still many questions surrounding the inflammatory process. The triggering factors, the signaling pathways, and roles of the molecules and cells involved remain to be fully elucidated, even today. ISDs represent a puzzle with many missing pieces, but we know that inflammation remains the cornerstone of their pathogenesis."

Great information are provided by the hystology of the various lesion to undesrtand the patological movens :

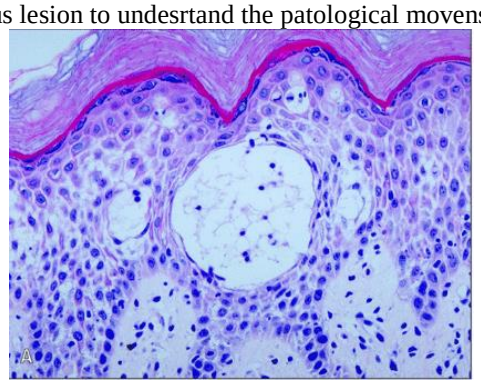


Fig n 6 Acute spongiotic dermatitis with infiltration of upper dermal inflamatory cell From DOI:10.5021/ad.2011.23.S1.S88

Ramesh H, Somashekhar S, Kanathur S. Lichens in dermatology. Indian J Dermatol Venereol Leprol 2023
"lichen" is derived from the Greek word, "leichen" which means tree moss. These are small green/grey or yellow plants that grow on trees/rocks/roofs and walls and are usually found in damp and shady places.

Hippocrates (460–371 BC), who was among the first to use the term lichen, described it like as "an eruption of a papulae. Clinically, lichen means a flat-topped papule and lichenoid means "lichen planus-like morphology". However, histologically the definition of lichenoid is a pattern of histopathological changes, where there is a band-like infiltrate consisting predominantly of mononuclear cells that obscure the dermo-epidermal interface. The word "lichenification" is used to describe lesions with hyperpigmentation, skin thickening and exaggerated skin markings. There are numerous skin conditions that are associated with the term "lichen" or "lichenoid" in dermatology."

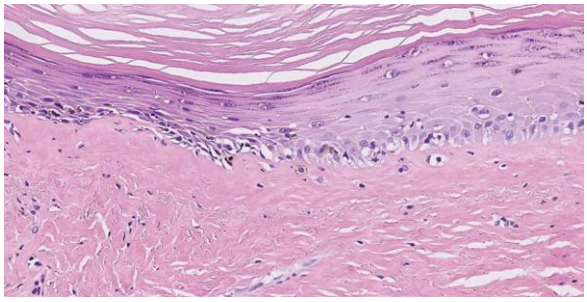


Fig n 7 Lichen sclerosus: typical histological features. Thinning of epidermis, hyalinised band of collagen, and lymphocytic infiltrate. From F.M. Lewis.

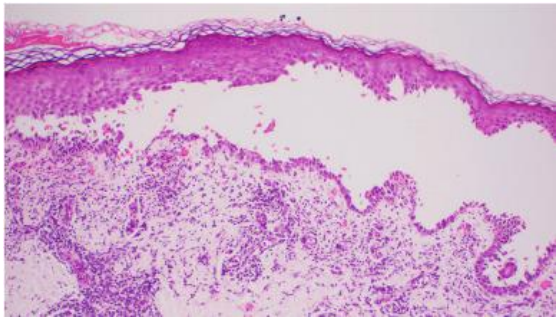


Fig n 8 from Pemphigus vulgaris. A ruptured suprabasal blister is seen and a single layer of intact basal cells remains. (H&E, low magnification). From R.C. Saal.

Dermatopathology (Basel). 2021 doi: 10.3390/dermatopathology8020017
Ichthyoses—A Clinical and Pathological Spectrum from Heterogeneous Cornification Disorders to Inflammation Dieter Metze, Heiko Traupe, Kira Süßmuth

"Ichthyoses are inborn keratinization disorders affecting the skin only (non-syndromic) or are associated with diseases of internal organs (syndromic). In newborns, they can be life-threatening. The identification of the gene defects resulted in reclassification and a better understanding of its pathophysiology. Histopathologic patterns include an orthohyperkeratosis with a reduced or well-developed stratum granulosum, hyperkeratosis with ortho- and parakeratosis with preserved or prominent stratum granulosum, and epidermolytic ichthyosis."

Fundamental is the clinical presentation for diagnosys and therapy :

Fig n 9 Fungal infection- to be use antimicotic local therapy.

Home Atlas of PET-CT Chapter
Malignancies in Dermatology Chapter, 07 February 2019

Stefano Fanti, Mohsen Farsad, Luigi Mansi, Paolo Castellucci
"Cutaneous melanoma represents about 5% of all malignant tumors and its incidence has increased in recent years. Melanoma is aggressive due to its ability to metastasize in early stages of the disease. Early diagnosis is essential for a better prognosis."

Fig n 10 Melanoma.

From Mayo clinic : "Signs that may indicate melanoma
Some moles aren't typical. They may have certain characteristics that indicate melanomas or other skin cancers. Characteristics may include:
Asymmetrical shape. Look for moles with unusual shapes, such as two very different-looking halves.
Changes in color. Look for growths that have many colors or unusual color patterns.
Changes in size. Look for new growth in a mole larger than 1/4 inch (about 6 millimeters).
Changes in symptoms. Look for changes in symptoms, such as new itchiness or bleeding.
Unusual border. Look for moles with unusual, notched or scalloped borders."

A review of sunscreen in the prevention of skin cancer
John P Micha, Randy D Bohart, Bram H Goldstein
https://doi.org/10.1177/10781552251327596

"sunscreen reduces the incidence of melanoma and non-melanoma skin cancers although deriving the intended effect is contingent upon the type of sunscreen and to the adherence to the recommended guidelines."

Aim of this work is to verify the topical therapy with a special focus on the pharmacutical forms and the excipients – veicle to be used. Semisolids preparation can act on the surface of the skin instead ointments can act on the more deeply skin layers. The choose depend also on various factor like : kind of the skin, and the kind of action needed :
Epidermic ointments are used to treat infection from fungus or yeast on the surface of the skin. skin's deeper layers. **Diadermic** ointments penetrate to the deeper layers (**hypodermis**) of the skin and has a systemic effect (eg: nitroglycerine).

The veicle must to be choosen related the various APIs needed ant their chemical caracteristics like solubility compatibility with the same APIs, the specific target to be treated (skin, skin folds, scalp), not irritant, easy application and removal, good washable properties if possible, aspects.

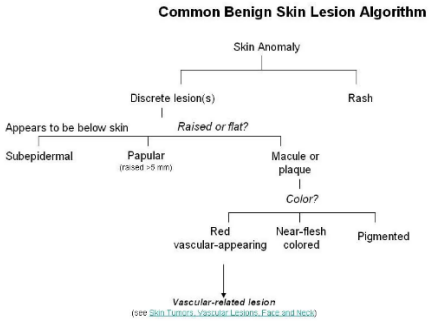


Fig n. 11 from Mescape.

The skin lesion can be primary or secondary (evolution from primary lesion)-**Common Primary Skin Lesions** (appear for the first time as sign of disease) from Fitzpatrick TB, et al.
Macule Circumscribed area of change in normal skin color, with no skin elevation or depression; may be any size –Staines.
Papule: little Solid, raised lesion up to 0.5 cm in greatest diameter, palpable.
Nodule Similar to papule but located deeper in the dermis or subcutaneous tissue; differentiated from papule by palpability and depth, rather than size, palpable, bigger then papule, diameter > 1 cm.
Plaque Elevation of skin occupying a relatively large area in relation to height; often formed by confluence of papules (one or more)
Skin weals: raised, pruriginous short duration, less then 24 h., in example urticaria reaction.
Pustule Circumscribed elevation of skin containing purulent fluid of variable character (i.e., fluid may be white, yellow, greenish or hemorrhagic)
Vesicle Circumscribed, elevated, fluid-containing lesion less than 0.5 cm in greatest diameter; may be intraepidermal or subepidermal in origin.
Bulla Same as vesicle, except lesion is more than 0.5 cm in greatest diameter.

About thickeness
1) flat: macula, patch 2) palpable :papule plaque, vescicle, bulle, pustule, nodule, tumor, wheal.
Secondary lesions: scale, crust, exscoraiation, fissure, erosion, ulcer, scar, atrophy.
Scales: residual of stratification of the corneum strate. (psoriasi), **Crusts:** accumulation of dry exudatewen the liquide dry, **Erosions:** lost of surface of epidermide without involving the derma.
Ulcers: lost of substantia more deep that involved also the derma, This not heal in autonomous way.
Scars: results of lesion that involve tissue repair with formation of new tissue, **Atrophy** : thinning of the skin, it becomes more shiny and thin, **Lichenification**: tickening with alteration of the trama, due by chroonic rubbing.

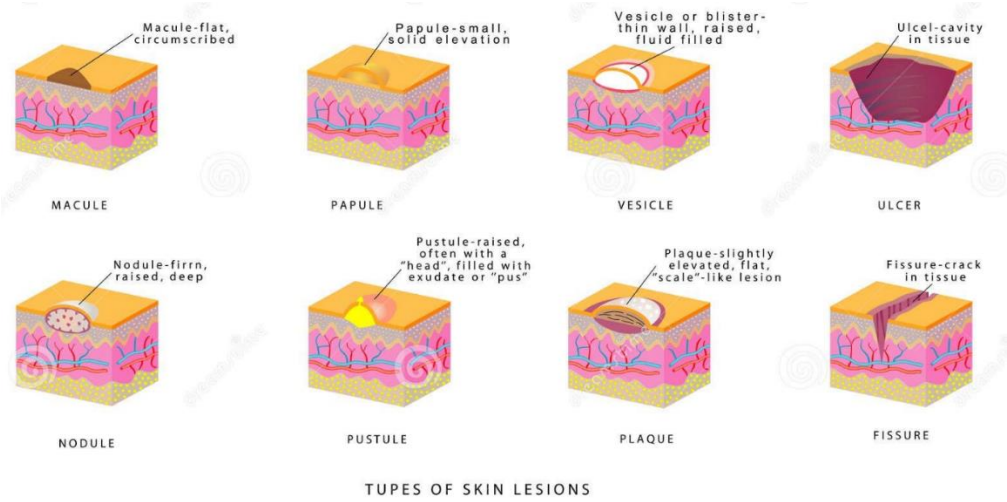


Fig n. 12 Skin lesions.

Fig n 13 from Sirawit Saiwaeo et al Human skin types differ [23], with each having its own unique characteristics and care needs. The three main skin types include normal, oily, and dry skin.

Kind of skin
sebostatic – with idrolipidic film reduced
seborroic – abundant film idrolipidic

Kind of lesion
wet lesion, with exudate, typical of acute conditions. To be used aqueous veicle.
Dry lesion: dry skin, typical in chronic condition like chronic eczema, proriasys.
To be used emollients- oleaginous veicle.
Zone rich of hair it is better to use aqueous formula.
Sensible skin: avoid alchoolic excipients

Int J Womens Dermatol. 2018 Jun 22; doi: 10.1016/j.ijwd.2018.03.002
Male versus female skin: What dermatologists and cosmeticians should know
S Rahrovan, F Fanian, P Mehryan, P Humbert, A Firooz

"sebum content is higher in men because sebum is highly influenced by sex hormones. Also, skin pigmentation and thickness are significantly higher, facial wrinkles are deeper, and facial sagging is more prominent in the lower eyelids of men, there is no significant difference in skin elasticity between the sexes."

Adv Wound Care (New Rochelle). 2015 doi: 10.1089/wound.2015.0642
Skin Physiology of the Neonate and Infant: Clinical Implications Teresa Oranges, Valentina Dini, Marco Romanelli.

"During the barrier development, impaired skin function makes the skin vulnerable to chemical damage, microbial infections, and skin diseases, possibly compromising the general health of the infant. Preterm newborns, during the first weeks of life, have an even less developed skin barrier and, therefore, are even at more at risk. It is extremely important to evaluate the risk of infection, skin breakdown, topical agent absorption, and risk of thermoregulation failure."

Anatomy, Skin (Integument), Epidermis
Hani Yousef; Mandy Alhajj; Adegbenro O. Fakoya; Sandeep Sharma. 2024.
"Skin thickness varies by body region and is influenced by the thickness of the epidermal and dermal layers. Hairless skin in the palms of the hands and soles of the feet is the thickest due to the presence of stratum lucidum, an extra layer in the epidermis. Regions lacking this extra layer are considered thin skin. Of these regions, the back has the thickest skin because it has a thick epidermis. The skin's barrier function makes it susceptible to various inflammatory or infectious conditions. Wound healing, sensory changes, and cosmesis are significant surgical concerns. Understanding the skin's anatomy and function is crucial for managing conditions across all medical fields."

Pityriasis Rosea
Graham Litchman; Pragya A. Nair; Hasnain A. Syed; Jacqueline K. Le. 2024.
“Pityriasis rosea, also known as pityriasis circinata, roseola annulata, and herpes tonsurans maculosus, is an acute self-limiting papulosquamous disorder. The hallmark features of this condition include the development of a slightly raised, oval-shaped scaly patch called a "herald patch," followed by the emergence of multiple clusters of similar scaly oval patches within 2 weeks. These clusters typically distribute in a "Christmas tree" pattern on the trunk and proximal extremities. (PR) can sometimes be difficult to manage because of factors including variations in the clinical manifestation of the condition and acknowledging instances where the typical herald patch may be absent. The exact cause of PR is unknown; features like seasonal variation and community clustering suggest that it is an infectious disease. Infections like viruses, bacteria, and spirochetes, as well as noninfective causes like atopy and autoimmunity, are known causes of PR. Upper respiratory tract infections that precede PR suggest that streptococcus plays a role in developing this condition.Reactivation of latent human herpesvirus infections have been identified as possible etiologic agents.”

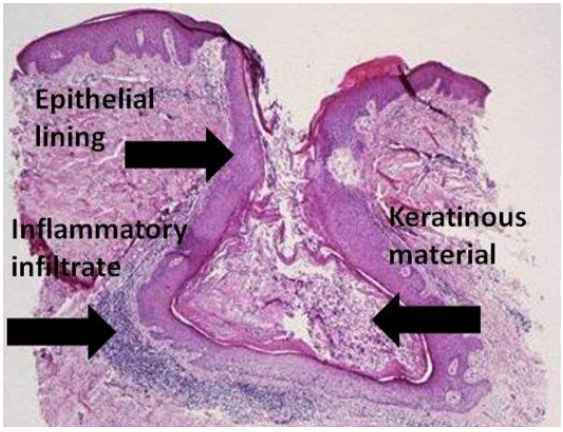


Fig n 14 acne vularis comedone from Graham Library of Digital Images, Wake Forest University Department of Dermatology. © 2009.

https://www.nysora.com/musculoskeletal/skin-and-subcutaneous-tissue/
“In regions that are not subject to the pressure, the epidermis is thin and hairy, whereas palms of the hands and soles of the feet), the skin is hairless and may thicken to an even greater extent as a result of a hypertrophied stratum corneum.”

Cutaneous Manifestations of Diabetes Mellitus Michelle Duff, Olga Demidova, Stephanie Blackburn, and Jay Shubrook
“diabetes is the most common endocrine disorder, affecting 8.3% of the population
(1). Skin disorders will be present in 79.2% of people with diabetes (2). A study of 750 patients with diabetes found that the most common skin manifestations were the cutaneous infections (47.5%), xerosis (26.4%), and inflammatory skin diseases (20.7%)

(2). Individuals with type 2 diabetes are more likely than those with type 1 diabetes to develop cutaneous manifestations. The Cutaneous disease can appear as the first sign of diabetes or may develop at any time in the course of the disease”

Epidermal thickness in healthy humans: a systematic review and meta-analysis
D.A. Lintzeri, N. Karimian, U. Blume-Peytavi, J. Kottner 2022 https://doi.org/10.1111/jdv.18123

“the epidermis tends to become thinner by ageing and does not seem to be influenced by sex.”

Between common therapeutic agent used in topical tehrapy it is possible to see :
antibiotics, antivirals, antimicotic, antiparassite, antiseptis, antinflamatory, antistamicis, corticosteroids, emollient, keratolitics, astringents, retinoids, acne treatements, local anaestetics, antiprurictis, 5 FU, immunosuppressive, sun protection and many other are also required properties like hydratant, protective action, keratolitic, occlusive and so on Of interest to verify the study program : from https://www.fpharm.uniba.sk/uploads/media/Lectures_2025.pdf

DEPARTMENT OF GALENIC PHARMACY - PHARMACEUTICAL TECHNOLOGY 2 -PROGRAM :
“Semi-solid preparation for cutaneous application. Skin, its anatomy and physiology. Biogalenical aspects of topical preparations. Liberation, penetration, absorption of drugs from semi-solid preparations. Ointments, creams, pastes. Bases for ointments, creams, and pastes. Production of semi solid preparations (solution, emulsion, suspension systems). Polymers as pharmaceutical excipients. Gels and gel structure. Viscosity, apparent viscosity, rheology.”

Between the topical pharmaceutical form for dermatology is possible to classify in liquid, semisolid an solid preparation.

Related the chemico physical properties of this topic semisolid and liquid preparation are relevant the reologgy property, viscosity (for spreadability)

Dermatologic semisolid preparation
this preparation play 3 principal role :
1) **protection of the skin from the external environmenmt**
2) **promote the skin hydratation**
3) **carry the APIs to the skin for an topic or systemic action**

This are **Disperses systems** : a phase dispersed and a phase dispersant- gelificant. They have **pasticity property** : they can be spreaded on the skin.

Paste, Cream idrophile, idrofobe, Ointment: idrofilic, lipofile, Gels. The Liquid preparations: to be applied to the skin, hair, nails (APIs + veicles), This can be **solutions, suspension emulsions**, Sterile if to be used in damaged skin, other Shampoo, skin foams, lotions, liniments, aereosols.

Unguenta definition
Semisolid preparations to be applied to the skin or to mucose surfaces in order to produce a topical action or APIs transdermal penetration or to provide emollient and protective action. (IT FU XII ED)

In example antiseptics (**surface action**) or Local anaestetics (**more deep action**)
Factors involved absorbtion : chemico-physical properties of the APIs and excipients used. Kind of formulation, PH, zone of application, skin state, skin hydratation, occlusivity of the preparation Way of application.

Effect of the preparate on the skin
Acqueous preparation: dry of the skin, Idro alchoolic : hard skin drying, delipidization, irritation
Emulsion O/W :controlleed drying, using poliole that reduce water evaporation
Emulsion W/O :emollient, occlusive, Powders: drying, Paste : drying

Excipients – bases -veicle: general classification
1) Oleaginous bases or hydrocarbon: **emollients**, avoid escape of moisture, are occlusive, difficult to wash out and are persistent (petrolatum, white and yellow ointment USP), restore skin idratation.
It can be used mineral oil to levigate and incoroporate powders inside.
Vaselin Advantages :Long-lasting emollient effect, Inert, stable, non-reactive,Good for protecting the dry skin. Limitations: Poor drug release, occlusive.
Greasy feel with reduces patient compliance, Common Formulations : White petrolatum-based skin protectants Paraffin-based burn creams.
Plastibase :gelled oil veichle, Plastibase is composed of a mixture of high molecular weight polyethylene and mineral oil (liquid paraffin), creating a pliable, stable, and inert semi-solid ointment base used for topical pharmaceutical and cosmetic products. The polyethylene gives it structure, while the mineral oil acts as a plasticizer.

2) Absorbtions bases (emulsion) : emollients, various grade of occlusive properties, greasy properties whran applied, difficult to be removed.
The anydrous ones can be used when water presence can cause instability of APIS (antibiotics)

Hydrophilic petrolatum USP (its variation can adsorb three times in its weight of water and it is useful when necessary to incorporate water soluble APIs in an oleaginous base like in ophtalmic ointment of tobramycine sulphate)

Lanolin USP, anydrous, from wool of sheeps, purified (cleaned, deodorized, decolorized), it can incorporate water.

Modified lanolin USP: reduced level of lanolyn alchools and pesticide or detergents residues.

(In the market there are lanolin niplle cream). Advantages: Can incorporate aqueous solutions, More hydrating than the hydrocarbons base. Some drug release capability. Limitations: Greasy, not easy water-washable, Can become rancid (especially natural oils like lanolin). Between Common Uses : Anti-inflammatory ointments. Anhydrous lanolin-based formulations for dry eczema.

3) Water removable bases : O/W emulsion**, cream** (commonly used), this can be diluited with water.
This bases can contain preservatives, antioxidants, chelanting agent for metals, buffers, humectants like glicerin or propilen glicole, emulsifier to increase the stability and the efficacy.
Advantages :Good patient acceptability, Easier to apply and remove, Can be used on moist lesions, refrescing It can be used in acute and in hair zone.
Limitations: Less occlusive, required preservatives to avoid microbial growth.Common Uses: Hydrocortisone creams, Antibiotic preparations. **Hydrophilic ointment USP** O/W emulsion.

Vanishing cream : water removal bases, O/W emulsion that contain lare amount of water and humectant an excell of stearic acid help to provide a thin film when water is evaported.

4) Water soluble bases: PEGs based, not irritant, inert, identified with a number related the Molecular weight. This are anydrosus and non occlusive, this can obstacolate the percutanoeou absortion of APIs because dehydrate the stratum corneum.

PEG 400 is liquid instead PEG 6000 is solid. The **Polyetilen glicole ointment NF** is a mix of high and low molecular weight PEG. Advantages: stable with many APIs and Non-greasy, good for scalp use. Limitations : it Can be drying or irritating, With a Poor emollient effect.
Common Uses :PEG-based ointments for mucosal and rectal delivery.

Antiseptic gels, lipofilic like vaselin silicons, fats. This not incorporate water. Can incorporate water lanolin, hydrofile vaselin, lanovaseline.
Hydrofilic like PEG.

Other cathegories of exipients
gelifiers, suspending agents, agar, pectine, gelatin, Hydrocolloides : metilcellulose, CMC, gums
Emulsionants : anionic, cationic, non ionic, useful to reduce interface tension between two phases
Thickening agents : increase viscosity like petrolatum, beeswax, xanthum gum
Solvents : water, alchhol, etere, aceton. This increase solubiliti of the APIs
Cosolvents: propylen glicole
PH modifier : buffer
Penetration enhancers : propylen glicole, urea, DMSO (they increase hydratation of the stratum corneum or trought keratolitic effect)
Physical enanchers : using ionophoresis, ultrasound or other. This alter the architecture of the SC
Stabilizer: preservants, antioxidant, chelants (EDTA, acid citric)
Lubricants : magnesium stearate

From COMPREHENSIVE REVIEW OF OINTMENT BASES:TYPES, PROPERTIES, AND APPLICATIONS
A.S. KONDRATIUK, V.L. BILOUS
Palladin Institute of National Academy of Sciences of Ukraine, Kyiv 2024

“Chelating Agents
In ointment bases, chelating agents play a crucial role in enhancing the stability and efficacy of the formulation. Their primary function is to bind metal ions, such as iron, copper, or calcium, which may be present as impurities in the base or packaging.

By forming stable complexes with these metal ions, chelating agents prevent oxidation processes that could degrade active ingredients or the base itself. They improve the chemical stability of sensitive components, such as vitamins, antioxidants, and preservatives, and enhance the efficacy of preservatives by preventing metal ions from interfering with their antimicrobial action.

Common examples of chelating agents include ethylenediaminetetraacetic acid (EDTA) and its salts, citrates (like citric acid), and phosphates. Overall, chelating agents help maintain the integrity of the ointment base, prevent undesirable chemical reactions, and prolong the product’s shelf life.”

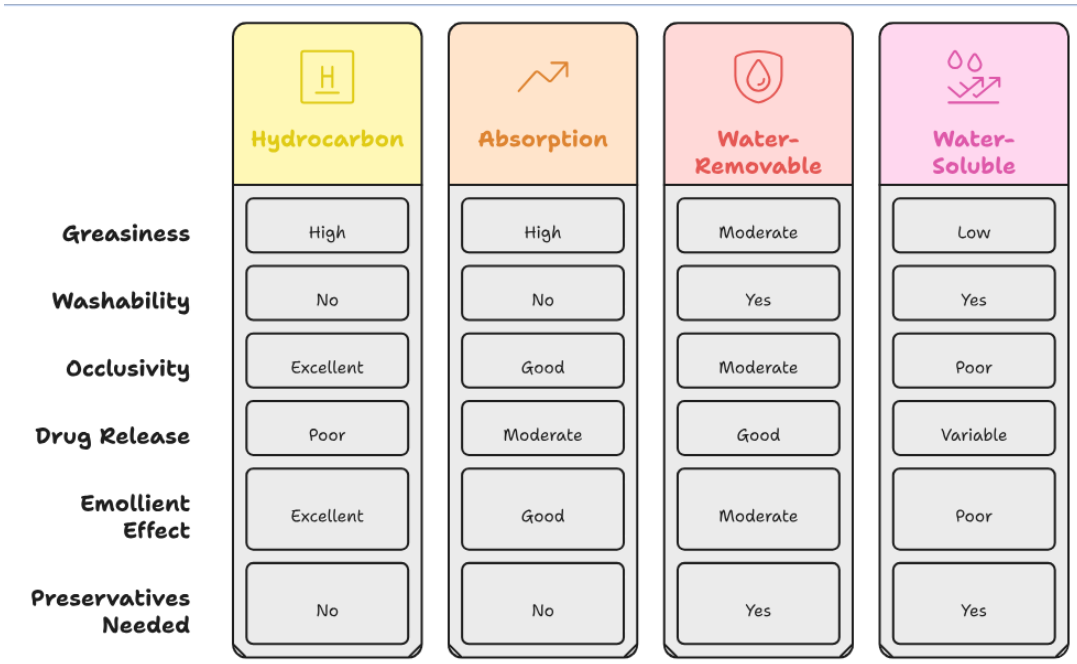


fig n 15 from https://www.pharmanow.live/pharma-manufacturing/ointment-base-types-guide R.Warang

the pharmacologic properties of some APIs change according the excipients used: if incorporated in powders salicilic acid results in keratolytic instead in ointment keratoplastic and at high concentration keratolytic and at low keratoplastic.

Basis and skin penetration
oleaginous : poor penetration
A/O dermic penetration
O/A in all skin
The APIs must to be in solution to be absorbed and not to be soluble in the veicle. The occlusion can favorite infections bacterical or fungine. The > penetration of the APIs is obtained with occusive bases

Topical vehicle potency (drug delivery efficacy)
generally sequences from highest to lowest as: Ointments > Creams > Gels > Lotions > Solutions/Foams/Sprays,

primarily due to differing occlusive properties and ability to enhance the drug penetration. Ointments are most potent (occlusive), while solutions and sprays are least potent (non-occlusive).

The choice of the vecile depends on : anatomical stite (scalp, face) and according the skin condition to be treated (dry or exudative)

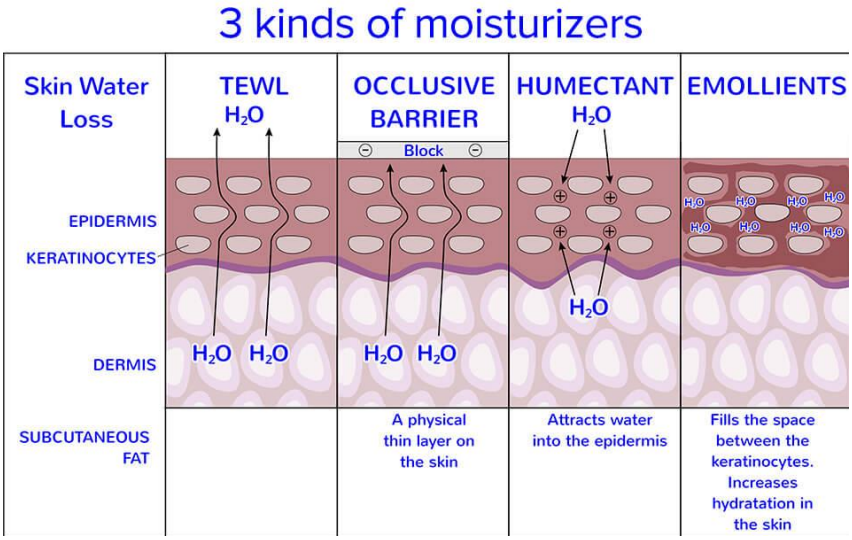


Fig n 16 Kinds of Moisturizers.

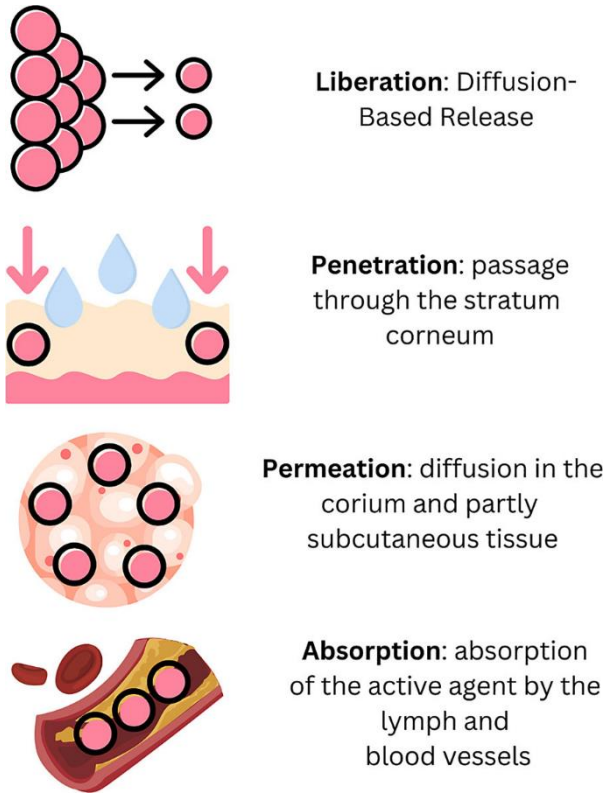


Fig n 17 from https://doi.org/10.1159/000541418 Major steps in active transport of a drug. The figure depicts the four major steps involved in active transport of an agent from penetration into skin to systemic absorption.

Fig n 18 from https://pharmaeducation.net/difference-between-ointment-cream-paste-gel/

TABLE 1.

Characteristics of Major Drug Delivery Vehicles

Vehicle	Composition	Advantages	Disadvantages
Ointment	Homogenous, semi-solid preparation with a high viscosity	• Occlusive effect for increased hydration • Can be used on thickened skin lesions	• Greasy or messy application • Insoluble in water, thus difficult to wash off
Cream	Emulsion of oil and water in variable proportions	• Occlusive effect for increased hydration • Can be used on thickened skin lesions	• Less hydrating and less occlusive than ointments • May feel oily due to thick consistency
Solution	Clear and homogenous liquid composed of one or more solutes dissolved in an aqueous, non-aqueous or hydroalcoholic solvent	• Simple formulations • Easily spreadable • Ease of application to hair-baring areas • Little impact on cosmesis	• No occlusive, hydrating or emolliating properties • May cause stinging, dryness or irritation (due to alcohol base)
Gel	Semisolid emulsion formulated as a colloidal dispersion in an aqueous or alcohol base	• Stabilizing properties for active ingredients • Cooling effect on application • Quick drying • Ease of use on hair-baring and non-hair baring areas • Little to no impact on cosmesis	• Little to no occlusive effect • Little hydration • Low side effect profile (burning, itching, redness of skin)
Foam	Pressurized liquids with a propellant that produce a liquid or semi-solid product on valve actuation	• Enhanced absorption of drug • Application advantages (minimal residue, quick drying, spreadable) • Ease of application, especially to hair-baring areas • Little impact on cosmesis	• No occlusive effect • Little to no hydration • May result in burning or stinging on abraded skin

Fig n 19 from j. Rosen BA et al.

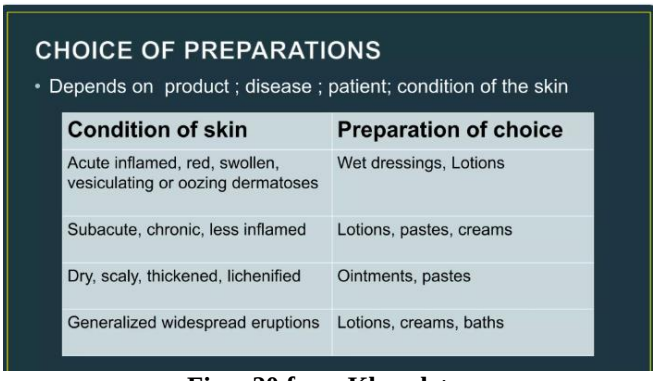


Fig n 20 from Khezaleto.

To be avoided
for the face the use of strong keratolitic, alchool, fenol, antralin, mentol.
for hair scalp: avoid shake lotion, not water washable ointments, paste.
pubic area: avoid shake lotion.
intertriginous area : avoid paste and ointment.
axilla area: avoid macerating greases.
external ear canal: to be avoided paste and shake lotion.

Pharmaceutical topical form
A)"**Creams** are opaque, viscous, relatively soft, consistently spreadable, semisolid emulsion dosage forms that often comprise more than 20% water and volatiles and normally less than 50% hydrocarbons, waxes, or polyols as the vehicle for the drug substance. Drug substances delivered in creams, intended for external application to the skin or to the mucous membranes. Creams are either a water-in-oil (W/O) emulsion for example cold cream (fatty cream as in the European Pharmacopoeia) or as an oil-in-water (O/W) emulsion, for example, Betamethasone Valerate cream."
Becauste the cream have not unpleasant odour but some APIs yes it can be used whit essential oil.
In cream W/O to prevent microorganism can be used antiseptics.

B) Ointments are semisolid dosage forms that comprise less than 20% water and volatiles, and more than 50% hydrocarbons, waxes, or polyols as the vehicle. Active pharmaceutical ingredients delivered in ointments intended for only local or for systemic absorption".
Used for skin and mucous membrane.
This can be **medicated or not** (this last use physical properties as protectants, emollients, lubricants.
The bases ointment are classified as: oleaginous, absorbtion, water removable and water soluble bases.
The Idrofobic are Used for dry skin and on lesion, are emollient and provide hydratation.
They have more percistence then cream or lotion, **occlusive** and not washable with water.
Vaselin, paraffin, vegetal and animal oil, wax.

Fig. n 21 paraffin wax.

The ones that can adsorbe water are : lanolin, lanolin alchool, monoglicerides, sorbitan estere.
The idrofilic ointment : are water soluble, it can adsorbe water, **non occlusive** (PEG based)
Oftalmic ointment: vs colliria show more time of residence in the site of action, more biodisponibility
Needed night subminitration because produce blurred vision.

Preparation: to disperse the API sinto the veicle in uniform way.
Two kinds: **officinal and magistral**, Two methods : **incorporation** or by **fusion**
Are used mortare and peste or non absorbent slab -plate and spatula. Baigne marie if needed to fuse the base. It can be used or glass or porcelan plate or non adsorbent parchement paper (this to avoid the celaning of the plate after the use)
In other situation it can be used ointment mill, electronic devices (like UNGUATOR or other)

Fig n 22 device for ointment production.

If the component used react whit metal of the spatule like iodine it is needed to use an hard rubber one.
They can be preparate trought : **mixing, solution, chemical combination**
The ointment is produced by spatulation, working togheter APIs and excipient since uniform composition. The veicle is placed on a zone of the plate and the powder to be incorporated near.

A little amount is mixed using the **geometric diluition methods**. The powder befor must to be reduced in size to avoid to be gritty in the final products. It can be used a leviganting agent to facilitate the operation (similar quantity to the powder) Mineral oil for bases in which oil are the external phase or glicerin if water is the external phase If the APIs is not soluble in the veicle it must to be solved before in little amount of other right solvent Then incorporate with the rest of excipient (are used vaselin oil or glicerin), in example cantharidin ointment.
It is needed global compatilbility with all component.

The powder can be dissolved in water or alchool. To be remebered that olny litte amount of water can be incorporated in an oleaginous ointment.If necessary it mus to be added the little amount of the idrofilic solution with and equale volume of Idrofobic liquid. The mortar and pestel are better to be used when high amount of

liquid ar to be used or it is needed to work gummy materials, In example using Camphora it is needed pulverization by intervention : using a solvent and after the pulverization waiting the evaporation of the solvent.

The fusion methods : one or more component are melted together mixing and then cooled (also congealed). Used for medicate or not medicated ointment that use beeswax, solid paraffin, high molegular PEGS that not permitt easy myxing without fusion.

Gelifier to be used : bees wax, spermaceti, cetilpalmitate, cetostearilic acid, solid paraffin.

The heat lable component must to be added only whe the temperature allow this operation in order to avoid incativation.

The emulsion ointment are prepared : waxes and oil are fused at 70 grades and the water soluble component (heat stable) are dissolved and then heated at the same tempertaure, then this last is added to the fused oleous phases, mixed mcanically, the temperature must to be manteined for 5-10 minutes, after this cooled.

Requirement for ointments: According USP : test for microbial content (not reuired sterility), minimum fill (net weight of content vs in label indicated), packaging, storage, labeling and test for sterility (ofthalmic ointment)

To prevent microbial growth are used preservatives (methylparaben, propylparaben, phenols, benzoic acid, sorbic acid, and quaternary ammonium salts), in example betametasone valeranate ointment require for USP : test of absence of staphilococcus aureus and Pseudomonas aeruginosa that can infect damaged skin of some patients.

For this reason a re requested test for the raw materials, water of needed quality (sterile in example for oftlalmic use), control in process, final control.

the products for rectal, urethral, or vaginal use must to be controlled for yeasts and molds.

Pakaging : in large-mouth ointment jars (clear or opaque glass or plastic) or in metal or plastic tubes.

Ophthalmic preparation, nasal, vaginal, or rectal semisolid products are almost always packaged in tubes or syringes. Well-closed containers to protect against the contamination and in a cool place to protect against product separation in heat. When it is required, light-sensitive preparations are packaged in opaque or light-resistant Container.

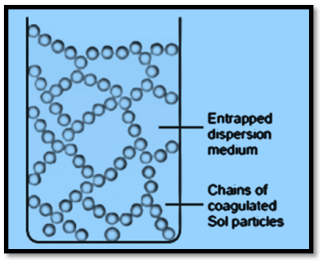
The producers test also for viscosity and in vitro drug release to veryfy the lots uniformity

C) Gels are usually clear, transparent, semisolid dosage form containing the solubilized active substance.

According to USP, gels are semisolid preparations that contain dispersions of small or large molecules in an aqueous-based vehicle rendered jelly-like through the adding of a gelling agent. A gel is an intermediate state of matter that has both solid and liquid components. This can be used for hair zone.

Gels may be formed by dispersing the gelling agent in the continuous phase (for example by heating starch), by crosslinking the dispersed phase gelling agent, by changing the pH (as for Carbomer co-polymer), or by reducing the continuous phase by heat or vacuum (as for gels formed with sucrose)

Gelification point: gelifier concentration below with the gel not form



Fi. n 23 Gel structure.

D) Pastes are thick, stiff, semisolid dosage form in which is high concentration of insoluble powder substances (20% to 50%) finely dispersed in a fatty or aqueous base.

The solid particle must to be pulverized to avoid skin irritation. According to USP, Pastes are semisolid preparations of stiff consistency and contain a high percentage (20%–50%) of finely dispersed solids. Pastes are intended for application to the skin, mucous membranes, oral cavity. Generally, pastes do not flow and thus can function as protective coatings and occlusive at normal body temperature.

There are two kind : **paste with liquid binder or semisolid.**
And every of this group can be divided in paste with **oleous binder** or with **acqueous binder.**

Use: protective (are occlusive), absorbe sierous substantie, solar radiations, coagulation plate, local antiseptic properties. Protective : ZN OXIDES, based, with Titanium bioxide as solare radiation protective, boric acid ans sulfur based as antiseptic.

Acqueous paste are used in fat veicles intolerance, in example in subacute edematoses after reression, exudation. Absorbent are used fo exudant lesion.

Fat paste: for superficial lesion, subacute/acute (eczematose) in inflitrative phase.

Can be incorporated keratoplastic, keratolitic, emollient, reducing APIs. Application: with brush,gauze pad, with the hands. It must to be applied in thin layer, for detersion are used water lukewarm.
Fat paste: are greasy, needed bandages, gauze plus elastic bandages, for detersion are used oils
Hoffman paste, for bedsores, Zno 49 gr, olive oil 49 gr, boric acid g 2
Anticzematous paste : Zinc precipitate, Zic oxide, sterilized clay, olive oil, anidre lanolin, vaselin.
Total screen paste : Zinc oxide, titanium bioxode, lanovaselin.

E) Lotions are pourable, an emulsified liquid dosage form intended for external use. They are usually prepared by dispersing or dissolving the API into the more appropriate phase (oil or water), adding suitable emulsifying or suspending agents and finally mixing the oil and water phases to make a uniform fluid emulsion. In example for hair site like scalp, this are not occlusive.
According to BP, Lotions are Liquid preparations for the cutaneous application that are intended to be applied to the unbroken skin without friction. Lotions in suspension to mix, solvents : water or alchoolic plus little % of powderes and glicerin.
Metilcellulose is added to produce the suspension. After the evaporation the powders join to the skin.
For subacute eczema (phase after exudation). Refresching action, drying, In example this can incorporate liquid tar, sulfur, salicilic acid, ittiol, resorcin
Shake lotion: zinc oxide, talc, glicerin isopropilic acid.

Ointment	Cream	Paste	Gel
Hydrocarbon based greasy semisolid	Mostly water-based where drugs are loaded in O/W or W/O emulsion	It is basically an ointment where a high percentage of insoluble solids are added	The liquid phase is trapped within a three-dimensional polymeric matrix
Translucent to opaque	Opaque	Opaque	Transparent
Greasy	Less greasy	Less greasy	Non-greasy

2.2.1. Ointments

Fig n 24 from DOI:10.3390/molecules26195905

Fig n. 25 from D.Lee Cream Preparation.

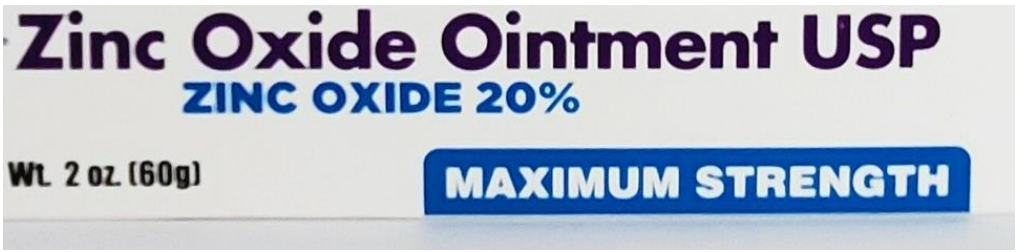


Fig n 26 ZINC OXIDE ointment.

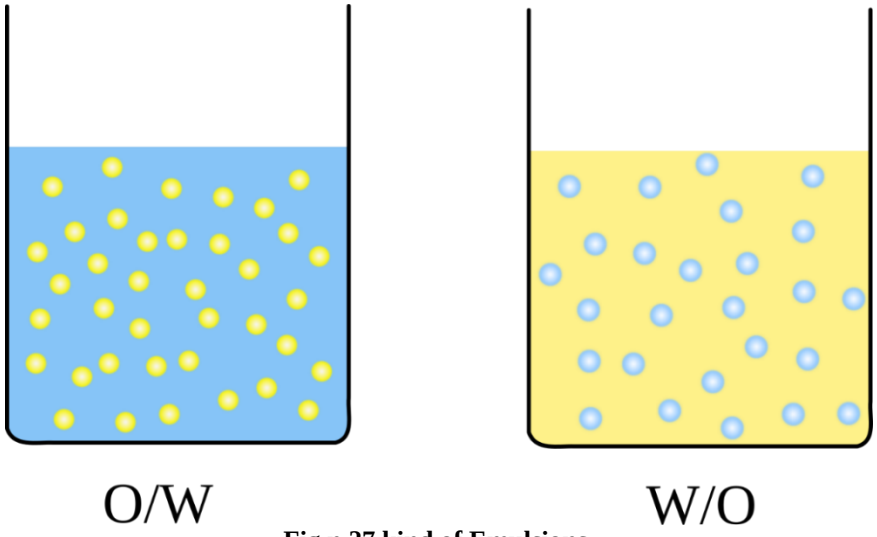


Fig.n 27 kind of Emulsions.

Topics of interest in this work are : pomate,creams, ointment, solutions, powders, paste, emulsions (A/O and O/A), gels.

Characteritics of the preparation : occlusive, non occlusive, hydatant, lenitive, emollient, protective esfoliant, keratolitic.

Emulsion preparation
crusching of one of the two phases to bring it id dispersion into the other with a mechanical force and using emulsionants (to orienting the emulsion and to stabilize it) for reduce the superficial tension (reduce the amount of energy needed for the process) mortar and pestel, immersion mechanical crusher.

Other topical products of interest
Solutions, lotions, tincture
with solvents: acqueous, idroalchoolic, alchoolic, for diluition of acids, alcali, colorants plant infuse the solution can be transparent (lotions) or coloured (tincture)
action: on skin surface, refreshing, anti exuding, astringent, antiseptic, rubefacient
Way of use: touches, brush strokes, skin friction, footbath, sitz bath, medicated bath, compress in example starch 100-300 gr in 200 ml water at 35 grades, for eczema, ittiosys, psoriasis other examples: potassium permanganate sol 0,1 -0,25 ,antiseptic for dermatoses bullous, burns, ulcers alcaline baths with calcium carbonate sol. or with sodium bicarbonate, calming : oatmeal + bran+starch sulforous, anti septics potassium permanganate sol diluited, tincture colourants : rapid evaporation (if used alchool, etere, cloroformium) not to e used in dermatoses irritable, not very liked because this can deface.

glicerolates: gelatinous, idrosoluble, transparent, glicerine and powders in example starch glicerolate : water, wheat starch, glicerin; it must to be always fresh because easy alterable. Used as decongestant, emillient, refreshiong, surface sedative. Not to be used on exudative skin or with erosion.

Balsams: oleoresin, mix of natural resins and essential oils. Liquid/semisolids, coloured or not if purified Insolubles in water, they solve in alchool etilic. this are protective, astringent, sedative low antiseptics, cicatrizzant. Balsam copaive for scabies or psoriasis. Balsams PERU' from a three of south america for ragades niplles, ulcerated chilblains. Balsam Tolu : for psoriasis, cloudy sores, tongue ulcer.

Suspension
Topical emulsion: bifasic system, O/A idrofile cream, under make up or vanishing and A/O like lanolin hydrate and idrofobe cream or reidratant. Phase dispersed /disperdent
It is increased the surface contact of the dispersed phase, are used tensioactives -emulsionants
Liquid -semisolid of substantie not soluble between them in example fats animal or vegetal and water
This have detergent action
The emulsionant must to be inhert, non toxic, not irritant, not allergizant, resistance to PH variation
The stability of the emulsion depends on : concentration of the disp. phases, temp, electrolite add, preservants.

Emulsionants : can be divided in anionic, cationic, not ionic The anionic with water ionize anf the lipofile group become negative.
In example soaps inorg/organic sodium stearate, cetilic alchool
Cationic: detergent, disinfectants 0,05- 1%, bactericide
Non ionic: more diffused, are neutral, stable, often not toxic, polisorbate 80 tween 20 Span, PEG.
Are incompatible with Arg entum salts and tannine
Like sorbitan, CLT, glicerol monostearate
Milks and creme This have variable viscosity

Emulsion W/O

Cold cream, gives refreshing sensation, water about 40%, after its evaporation reman the fat part on the skin. Cold cream BP: borax, white wax, spermaceti, water, almond oil. Can incorporate APIs, for lesion also exudative phase. If too high concentration of salicilic acid, tannic acid can break the emulsion.

In example Ceratum refrigerans galeni: beeswax 13 gr, sweet almond oil 54 gr, rose water g 33

Preparation : heat the water rose at 70 grades into the oleous phase fused berfore, mixing since gelification then cool.

Today in modern formula are added oil and tensioactive.This are "**night creme"** emulsion W/O.

Emulsion O/W: day cream or dry or evanescent, rapid water evaporation, refresching, rapid penetration transcutaneous of particles. The water is the great part the rest is the fat part

In example for scalp seborrea

Salicilic acid/sulphur preciptate/trietanolamin

Carbowax

Cera lanetta : mix of mono e diglicerides plus low parts of fatty acids and soaps. This can be used at PH 2-12 (advantages). It is inert, low dirty property, easy to apply, easy removable, good tollerability and can incorporate APIs

Cream W/O: cosmetic use, nutritive cream, night cream.

Cream O/W not dirty property, water washable, this can mix with sebus, sweat, skin dirt.

This can penetrate in glandular outlets and hair follicules and can veiculate antibiotics – anti micotics for piodermitis and micosis also in hair zone. Useful for acne seborrea, can veiculate salicilic acid or sulphur.

Alone this can be used to **protect from the cold, vs solar radiations, barrier cream**

This are less suitable for dermathoses, croust, exudated.Indicated for the scuamous form

Baths: the body or its part are immerged, used for widespread less excudative lesion.

Two type : general **cleansing bath** to remove dirt, debris, crust and scales or adherent remains of the medication and **medicated bath** : k permanganate solution for exudative vescicular bullous eruption Infected dermatoses.

Wet compresses : for wet, exsudative condition, acute eczema, stasis ulcer and other

Two type **open or closed** (permitt or not permitt water evaporation)

Lotions : are emulsion or fluid suspension

Foam : three-phasic, composed by oil, organic solvents and water, if used for burns or opern wound this must to be sterile

In pressurized contaniner, with hydrocarbon propellent

Stable foam or quick breaking. Used for steroids, local anhestetics and other drugs.

The alchool contained help in the drugs penetration. Are easy for applications spread and remove.

Sprays : Apis in solution with a propellent (used for steroids also) advantages not required direct contact, easy use, the part not used remain not contaminated. Disvantages high costs and risk of air pollution.

Paints: acqueous idroalchollic or alcholic, applied with brush, the alchool evaporate then

Liquide, they dray rapidly, leave a covering layer

Veicle insoluble, volatile solvent, eter or clorophormio plus APIs, preservants like nipagin to avoid mold

Can be sensitivier

Collodium : nitrocellulose 5% in eter or alchool

Elastic collodioum: ricin oil, that is less drying, and easy removable.

Applied with brush strokes

can be added APIs like salicilic acid to soften iperkeratosic lesion or callosity

collodium callifgo: salicilic acid/lactic acid/ elastic collodium

coaltar, cignolin, cade' oil that are reducing.

ittiole : antiflogistic

for psoriasis: colatar/etere also for hair zone, because it is a pure catrame it must to be applied only few days.

For liche ruben planus: corrosive sublimate, cresoto, fenic acid, collodio

Paints with adracantum gum

Benzoic acid, gum adracant, glicerin, water

Idrosoluble paints: gelatin, casein plus APIs idrosoluble

Rapidly dry, permeable, easy removable with water

Glues and gelatin: with ZnO, this are mix of glicerin, gelatin, powder, water

This are solid at room temperature and are Protective, for infiltrating eczema after the acute phase, for stasis eczema and lichen ruben planus. Not for exudative lesions and piodermitis

Gelatin Zinc hard of Unna: Zno, gelatin, glicerin, water, can be added salicilic acid or canphora

By fusion. Today animal gelifier are sobstituted by the syntetic : PVP and cellulose estere

Used also gel bentonite.

Lotion calamin: calming, composition: glicerin, calamin, ZnO, gel bentonite, sol calcium idroxide

Calamin is a mixture of ZnO plus 0,5% ferrum oxide (III)

Stiks : like styptic pencil.

Transdermal patch, adesive, the drug is delivered in kostant way.

There is a reservoir of the drug, a membrane and adesive layer.

Microsponges: composed by porous beads, inhert, when applied release slowly the APIs.

Liposome: acqueous phase sorrounded by a lipid capsule, this delivery the drug by fusion with the bilayer of the cells, diffusion or endocitosys, used in cosmetic to avoid irritation vs other topic substantie.

In emulsion Are used **tensioactive**s to reduce interfacial tension betweeh two liquid immiscible, reduce the work needed to produce the emulsion, this procuce an stable film around the dispersed phase.

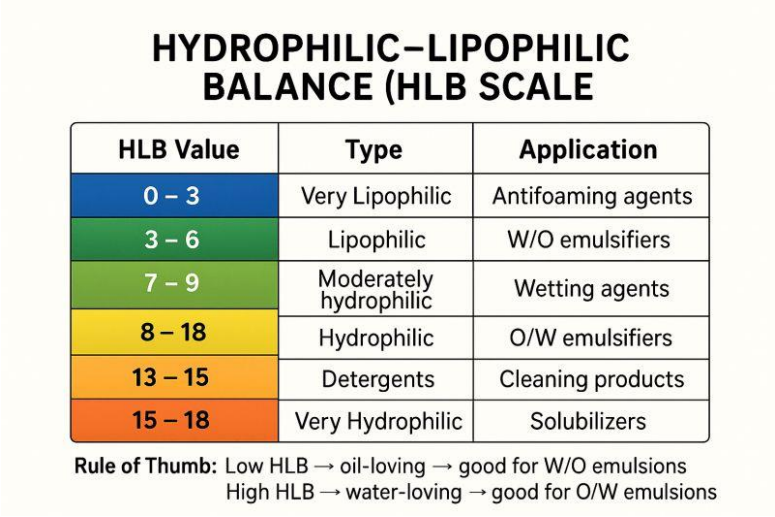


Fig n. 28 from T. Hsan use of tensioactive based on HLB needed.

Stability of the emulsion :
creamin, coalescence, phase inversion, chemical deradation (like tretionin degradation)

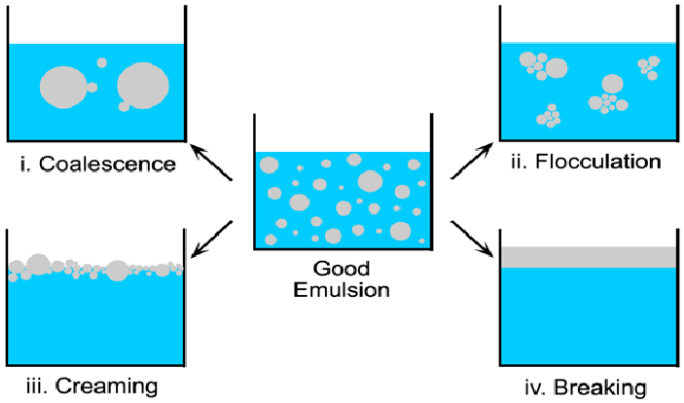


Fig. n. 29 from A Naaved.

For the semisolid dermatologic preparation are requestd a Topic action or transdermic release of APIs or must to be protective or emollient for the skin.

The skin absorbtion depend on
1. bases distribution on the skin,
2. Capacity of the base to release the APIs
3. effect of the base on the skin

Excipients and veicles characteristics : not toxic fot the skin, removable, good APIs compatibility, good oranolectic characteristics.

the bases are classify: lipofilic, that can absrorb water, emulsifier, idrosolubles

Fig n 30 from https://alazharpharmacy.com/documents/level-2/semester-2/pharmaceutics-1/chapter-3-ointment.pdf

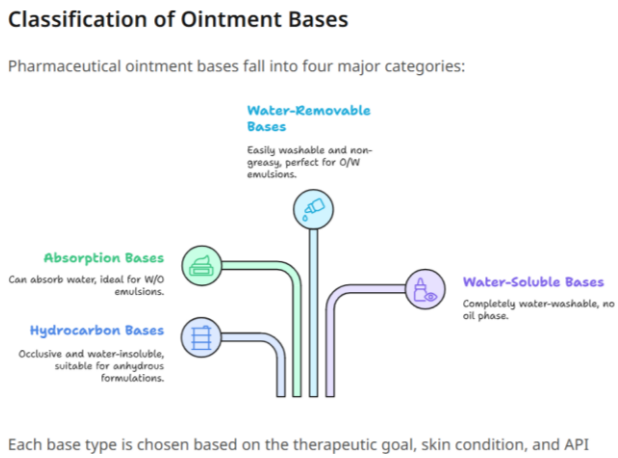


Fig n 31 from https://www.pharmanow.live/pharma-manufacturing/ointment-base-types-guide

Examples of topic therapy in use
corticosteroids for eczema – psoriasis, antibacterial for acne, antivirals for herpes,citostatics for skin neoplasia, retinoids in acne, catrame for psoriasis, psoralen photo sensib. In Psoriasi.

Target
skin surface like protectives in ex films for radiation, irritant liquid, insects antipermabilizants: to reduce disidratation.
annexes: anti traspirant, antibiotics, anti micotics, for infectious of the hasir bulble hydratants if too much dry, for patological tickening.
corneum strate : kerratolytics, idratants
epidermic/derma: fans, local anhestetics, anti cancer (cancer stasrt in the basal layers) local anhestetic must to reach the nerve
TTS : plasters for systemic use.

BASIS : characteristics and products examples
Absorbent water bases: simply (lanolin) **composite** (lanolin anhydrous, complex bases with lanolin alternative bases to lanolin), basis with idrofobic tensioactive (lanolin alchool and cholesterol).
It can be added to the vaselin tensioactive liposoluble like 3 % of sorbitan stearate – span 60
Raw material : tensioattive lipofile (lanolin, lanolin alcool, cholesterol, superior alifatic alchool)
Hydrophilic bases: macrogol unuenti base FU, idrogel (gel idrofiliC)
Raw material : polialcols (glicerin, propilen glicol, polietilenglicol PEG)
PEG : polimer of etliene oxide and water
Idrocolloidi CMC, HEC
Polimers of sintesis carbomers, polimers acrilic acid
This are water soluble, not miscible with liq oleous, can be removed with water.
Peg can be **liquid** (low molecular weight) or **solid** (high MW)
lipofilic bases : semply (vaselin) or composite (vaselin modified lipogel or idrofobe gel)
Raw materiale for lipofile bases examples :
hydrocarbons : paraffin liquid and solid, vaselin

Fig n. 32

glicerides (vegetal, animali), mono -di-trigliceride, natural or semi sysntetic /sysntetic
fatty acids : stearic acid
fatty acid estere isopropil miristate
bees wax (solid), carnauba, spermaceti, cetile palmitate

Fig n 33 bees wax -purified from honeycomb of Apis mellifera.

fat alcools : alcol cetilico, stearilico, cetostearilico(alcool at long chain)
vegetal oils : almond oil, jojoba oil
burro karite' : triglicerides (nutrient and idratant properties).
silicons polimer, syntetic, liq or solid (depending on the different R- chain)

Emulsifier basis W/O (can incorporate little amount of water with mechanical action) and **O/W** (this can incorporate little amount of oleous liquid by mechanical action)

Vaselin : idrofobe, hydrocarbon petrolate derivate, from rectification of petroleum, it is purified and decolored. it can be liquid (paraffin) or semisolid (withe vaselin)
It can incorporate max 20% oleous liquid with out change its characteristics, Instead with **Modified Vaselin** it can be incorporate since 25% oleous phase
Lipogel : gel idrofobi lipofilic base, this are liquid oleous gelified with paraffin, beeswax, glicerides at low medium temperature. (15-25%)
This are prepared with fusion (bain marie) and cooling
Lipofilic Excipients that can incorporate water : lanolin, hydroenated lanolin, beeswax
The make possible incorporation in this products must to be added an tensioactive.
Lanolin : fron sheep wool, it is a far scheep, this can incorporate water and make possibe to produce emulsion W/0 (composition alcools and steroles)

Fig n. 34 lanolin.

Hydratated lanolin : EU Ph. Composition 75% lanolin and 25% water (lanolin is melted and incorporated the water mixed then cooling)
Lanolin alchool : are less allergizant then lanolin
Alternative bases of lanolin : are used vaselin added with tensioactives liposoluble
Sorbitan stearate – spans 60 3%
Complex bases with lanolin : mixture of vaselin and lanolin (lanolin 10-50%), more easy to use, it can incorporate more water
Creams: if thee API is water soluble it must to be add in the acquous phase, if it is soluble in oleous phase it must to be add in the oleous phase.
This can be or W/O or O/W.
The **W/O** make more greasy (used tesioactive HLB between 4-7 generally), are occlusive.
Hydratant at long term
O/W, low greasy, rapid hydratation, easy removable. They can be prepared at room temperature or heating.
Lidocain cloridrate : water soluble, must to be added to the acqueous phase intead if used Lidocain base must to be added to the oleous phase

From SIFAP : Cream production - bases preparation
“Usare sempre acqua depurata bollita di fresco o appena preparata. Le creme vengono generalmente preparate secondo il metodo della fusione. La fase grassa e i componenti lipofili vengono portati alla loro temperatura di fusione; separatamente l’acqua e i componenti idrofili vengono scaldati fino al raggiungimento della medesima temperatura. Le due fasi (alla stessa temperatura) vengono unite e miscelate sino a raffreddamento, eventualmente reintegrando l’acqua evaporata.

Preparartion of medicated creams
- Nel caso si disponga di una crema base, sciogliere i principi attivi direttamente nella crema oppure meglio in solvente adatto (acqua, alcool, glicerina se crema idrofila, olio di vaselina se crema lipofila).
a) Preparazione a caldo. Si esegue quando il principio attivo è termostabile si scioglie a caldo insieme alla fase in cui è miscibile e, poi, si uniscono le due fasi sotto agitazione.
b) Preparazione a freddo. Si esegue quando il principio attivo è termolabile. Nel caso sia insolubile, lo si polverizza finemente, eventualmente lo si umetta (se insolubile) con un eccipiente fluido e, quindi, lo si incorpora a freddo nella crema base. Quando il principio attivo è solubile in un solvente compatibile con la base lo si solubilizza nella minima quantità di solvente prima di unirlo alla base stessa.
- Procedere al confezionamento.
- Determinare la data limite di utilizzazione e le eventuali modalità di conservazione, entrambe da indicare in etichetta.
- Compilare la documentazione secondo quanto previsto nelle procedure delle preparazioni magistrali e officinali”

Cold cream: used for chilblain, hand cream, composition wax alba, spermaceti, liquid paraffin almond oil an other excipients.

Cold cream, also known as ceratum refrigerans, is an emulsion of water and certain fats, usually including beeswax and various scent agents, designed to smooth skin and remove makeup. Cold cream is a water-in-oil emulsion (emulsion of small amount of water in a larger amount of oil), unlike the oil-in-water emulsion of vanishing cream, so-called because it seems to disappear when applied on skin. The name "cold cream" derives from the cooling feeling that the cream leaves on the skin. Variations of the product have been used for nearly 2000 years.

Anfifilic cream : intermediate properties, This can incorporate water and oil solution
Composition : vaselin, triglicerides, cetostearilic acid, PEG, propilen glicol, water
Cream BASE – with polisorbate, prepared heating at 70 grades
Cream with stearate

Fig n. 35 mortar and pestel.

Ointment
according FU I "preparazione semisolide per applicazione cutanea costituite da una base monofasica in cui possono essere disperse sostanze solide o liquide"
they can be **idrofile** (if used idrofilic bases), **idrofobic** (if used lipofilic bases) this are occlusive or that can emulsionate water.

can contain fats animals or vegetal, or sature alifatic idrocarbon llike vaselin and paraffin this are greasy, can be added APIs.

The fats are triglicerides of fatty acid, carboxilic acid sature or insatured and mineral fats to be used for chronic, dry, brittle, lichenificate dermatoses using an emulsionant agent in an idrofobic ointment we can obtain a cream (W/O or O/W) generally require less preservatives because no water conten or reduced disavtages: difficult to spread and wash, decreased evaporation loss, not to be used in acute weeping lesion and intertriginous area.

true fats: **vegetal** oil, triglicerides of oleic acid and fatty acid sature or insature of various chain lenght and free fatty acid sweets almond oil, emollient, but easy rancidity.

olive oil, sesame oil (more refresching), peanuts oil, castor oil, cotton seeds,sunflower oil, linum, cocoa butter.

Animal origin fats: pig suet, spermaceti from whale, bees wax, lanolin from sheep's whool (very idrofile)
Hydrated lanolin can contein since 25% of water, low rancidity.
This can contain impurity from the chemical process used in production that can cause sensibilization good excipient, greasy, softener, good for subacute /chronic lesion, ipercheratosic / xerodermic with dry skin Often is associated to vaselin
Eucerin : 5 part of cholesteric alchool of lanolin plus 95 part of vaselin
The suet can be added of benzoin 2% to reduce rancidity
Wax white or yellow, greasy, pleasant odour
Cera lanette: used for emulsion O/W, alchool cetilic and sulforic ester of fatty alchool sup.

Mineral fats: paraffinic hydrocarbon from fractionated petroleum distillation, mixture of various satured hydrocarbure (high fusion poin 44-55 grades)
Vaselin: greasy, insoluble in water, not go rancid, yellowish
White vaselin is more purified, it can have impurity that can produce sensibilization
Are in fact used additives to withening
Vaselin oil: emollient, good tollerated, easy spreadable also for wide zone.
It is used to remove residues of other fats un the skin (necessary to consider that a prolonged use ca be acantogen).
Fat excipients classification: covering agent, protective, refrescing, absorbent, cosmetics, penetranting agent Natural or syntetic (carbowax, silicon gel)
Other classification: silicons, alifatic sature hydrocarbure, fats, wax, emulsions, mucillagines, polietilenoxides.
Ointment action: differently to te paste the ointment are waterproof, occlusive and irritants
They make possible easy absortion of the APIs in deeply.
They have indication for dry lesions and ipercheratosic, they increas the scuame detachement
Can be incorporated keratolitics and softeners useful for high ipercheratosys like salicilic acid, resorcin, urea
contraindication: lesion in exudation, vesciculating, erosion cbecause cam aggravate.
To be applied in thin layer, frictioning in limited area.
They have dirty properties.
Before a new application remove with olive oil previous application (or almond oil or vaselin oil)

Production in the galenic lab
two methods or by **fusion or by mechanical embedding** (mixing, shredding, smoothing)
APIs soluble in the base : mixing (liquid), semisolid - solid mixing previous solubilization in solvent miscible with the base.

If Insolubel APIs : emulsion / suspension. Solids : is needed dimension reduction.

Mixing : geometric diluition method
The idrofobe ointment are Prepared using plate and spatula, smooth the API with a little part of the base or in a liquid soluble in the base. It can be fused with a baine marie a little portion of the base or the use of an mineral oil. The rest of the bases is then added with the geometric diluition method.

Fig n. 36 fusion of veicle with a Baine maire. From N. Backstrom.

Fig n. 37 industrial pakage process.

For the ointment that absorbe water it must to be first prepared a solution- suspension of the API in water using mortar and pested then incorporate in the fused bases, and after mixing and cooling the preparation is done.

For the idrosoluble ointment the APIs can be dissolved in little part of water and mixed in mortar and pestel.

Insoluble poweder can be smoothed with PEG 300, licerin, propilen glicole and mixed.

Pay attention : even if the APIS have a good solubility inethilic alcool it can produce irritation

If used volatile substantie (like mentol) it is necessary to reduce the emperature if used method by fusion.
Heat with baign marie, not prolonged and after the APIs add in is necessary to reduce the temperrature.
Add the APIs after the cooling of the fused bases
The fusion method is better when the APIs is witha a slow soluble in the medium.
If the API is a powder it must to be reduced to a fine powder, after the drug add wait its solution
If drugs insoluble in the bases : if liquid (emulsion used), if semisolid (emulsion) and if solid (dissolution, suspension or emulsion)
If insoluble APIs it is before smoothed in a marble plate or in an mortar in a liquid in which is not soluble
In this way is obtained an lipofilic suspension to be mixed to the cooled ointment.

Gelifier for ointment by fusion :
beeswax (under 10% is semiliquid and over 25% is difficult to spread) yellow type with impurities and white spermaceti (from cachalot), cetilpalmitate, cetostearilic acid, glicerol distearate to be used at 15-25% solid paraffin. Tensioactives: lanolina 10-30%, lanolin alchool 1-2%.

GELS : two types LIPOGEL and IDROGEL, water based or alchoolic
LIPOGEL : oleous liquide gelified with silica gel, beeswax, polimeric substantie
IDROGEL : they dry rapidly, water gelified with hydrocolloides (CMC, HEC, metilcellulose, carbopol, sodium alginate)
Inorganic : bentonite, allumine idroxide

Fig n 38

CARBOPOL change its properties accordinf the medium PH
Carbomer 1-2 % thys have an high content of -COOH (curled up), in basic environment become linerar, max of viscosity at ph= 7 (sodium hydroxide and the more used trietanolamine).
If added alchool more then 30% there is reduced viscosity, in order to increase viscosity it can be added glicerin.

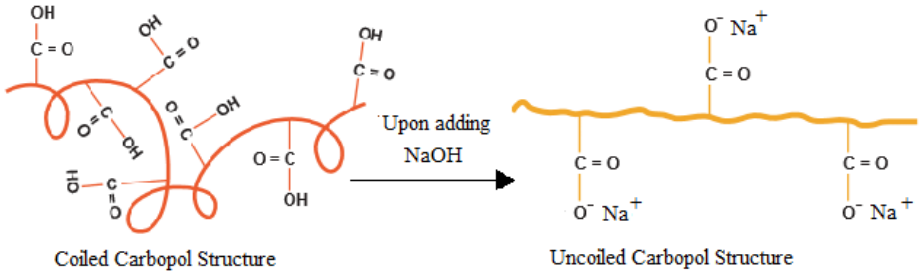


Fig n. 39 Carbopol strucure if changed PH from DOI:10.22159/ijpps.2018v10i10.23071

SEPIGEL – idrogel Poliacrilamide. This gel are produced trought copolimerizzation of acrilamide, that is water soluble, with an agent that produce cross binding providing a tridimensional reticule (used 'N,N'-metilene bisacrilamide (BIS).

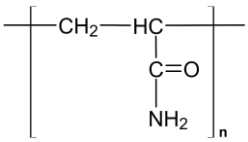


Fig n 40 monomeric unit of polyacrilamide.

Sodium alginate: at concentration more then 2,5% and with calcium ions at PH 5-10 produce stable gel.
Gelatin: produced using hot water then cooling, it can be wet the gelatin with 3-5 parts of alchool or propilen glicole before add water.
Metil cellulose: used at concentration sice 5%, dispersed in water at 80 grades, under mixing, then cooling Stability – conservation: water gels need preservants like parabens 0,1% to avoid microorganism growth If present alchool this help in the preservation.
Idrofobic gels : mix of oils with added solids like colloidal silica (if anidrous the gel produced is trasparent, if hydrated the gel become opaque)
The gels are prepared by mixing, if the recipienti s not perfectly dryed the gel obtasined can be opaque.
It can be used : humetctans, preservants, antioxidant, chelants, cosolvents for the APIs
Humectants: are hygroscopic substantie, and draws the water in the corneum stratum : glicerol, PEG, sorbitol (liquid), urea, glicolic acid, lattic acid, used also to prevent skin dehydratation.
Lipids : avoid the lost of humidity, squalene, vegetal TG, hydrocarbon derivates, silicons, wax, lanolin.
Botanic exctracts : aloe vera gel, betulla alba (hydratants, little barrier function, keratinocite differentiation effect)
Antioxidants: vit. E, BHT, BHA Tensioactives : example ricin oil etossilate, used in example to modify an oleous liquiq in an washable liquid, olea europea extract, other products fucus vescicolous extract, algae, from atlantic, pacific and baltic sea, promote contraction collagen gel with fibroblast and modify the mechanical property of collagen gel improving elasticity.
PASTE: semidolid preparations, for skin treatement, charcterized by great amount of powders dispersed in the base (30-60% in weight), generally are protective (film), also some antinflamatory.
2 kinds: acqueous paste or fat paste
This can be absorbent, for exudant area, also for hair zone, refresching, occlusive.
In example Zinc oxide, talc, caolin, starch, calium carbonate, and can contain APIs like sulphur, resorcin and other.
There are 2 kinds : paste with **liquid binder** (oleous or water) and with **binder semisolid** (oleous or water)
The paste with liquid binder are suspension (a solid dispersed in a liquid) the powder produce a reticulation structure (semifluid). The acqueous paste can be thin (drying) or soft (refresching) with fat veicle.
Thin paste : powders (about 60 %) plus liquid(water and glicerin). This are porous and facilitaste the skin perspiration., absorbe exudate, anti maceranting, refrescing, In example water based paste : Zinc oxide, talc veneto, glicerin and second water of lime. Thin paste : Refresching powdere/water sol/fats
In example this paste of UNNA : Zinc oxide, prepared crete, linen oil, second water of lime
Oil paste : zinc oxide, veneto talc, second water of lime, olive oil.
It can be added also precipitated sulphur 2-5%, low antiseptic, keratoplastic or acetale alluminium 1% -2,5% Slihtly acid, For diaper dermatitis.
Advantages: not produce crust, more protetcive action, more lenitive.
Fat paste: are refrescin, fattening, provide more penetration of the APIs incorporated, not hinder perspiration and are less irritabt then pomate. This cuase dirty and often need thick bandage.

Binder oleous
HOFFMAN PASTE : ZN OXIDE 50% and 50% OLIVE OIL also with 3% boric acid.
The boric acid in pediatry for topic therapy must not overcome 3% because toxic (to be avoided in new born and below 2 year)
Acueous binder : water paste PASTA ALL'ACQUA : zinc oxide, talc, glicerin, depurated water (ana 25%)
Used in newborn and children as absorvent, iriitiation by diaper.
When evaporate the water th powder and glicerina act.
Preparation : smooth in mortar with pestel powder plus glicerin then add water.
It can be used oil for the smoothing
Paste that require a liquid base - water need the use of humectant like glicerol

Lassar paste Zinc oxide 25 g, Acid salicilic 2g,Starch 25g, White vaselin q.b. to 100 g.
Smooth the salicilic acid with liquid paraffin, then incorporate this suspension into the vaselin.
Incorporate the other powders previously mixed inthe vaselin ointment.
Powders: mixture of finely divided drugs or chemicals in dry form, classify as bases powders or medicated.
APIs + excipients (powder bases)
This can be of **mineral, or animal or vegetal origin** (**simply or composed**)

Inert or active
This have **surface properties**, duration of action limited, if more finesse is more active because increase the absorbtion surface.
Bases powders generally have : **absorbtion, astringent, protective or lubrificant actions.**
This can be used for folds (no talc in exudative phases, no starch in intetriginous zone if candida infectious)
If to be applied in **open wound or in damaged skin must to be sterile**
If multidose are used specfic spreader powder or pressurized system.
Requirements: adeguate finesse, to avoid ittitation on the skin, agregate absence, skin adfesiveness.
Smootheness to be easy applied. This can be **organic or inorganic**
Talc (Magnesium silicate hydrate lipofil, caolin, starch, silica (absorbent), stearate (smoothness), zinc oxide (astringent), titanium oxide. Talc can absorbe oil and have lubrificant property
Other action of the various powders are **cooling effect, prevents frictions, absorbe moistures, covering property**, also used in intertriginous area and on feet
Adeverse effect can be : **irritation, crusting, inalation by the user**
The insoluble powder must no to be used in open wound.
Previous application must to be washed off.
Example of mineral powder : Zinc oxide powder, Bentonite, CaCO3, mg carbonate
To be take in consideration **rare case of granuloma**.
Talc : silicate hydrate of Mg
Caolin: silicate of Al

This can have Ph tending to alcaline
Vegetal powders: starch rice or oats, derivate of cellulosa CMC, adragant gum (mucillagin in water)
The vegetal powder can decompose, and in skin folds can produce bacteria growth.
Animal origin powders: gelatin from bones
Inorganic powder: are less alterable
Fat powders: when is needed more adhesionto the skin : lanolin, zinc oxide, talc veneto
Low antiseptic action.
Between powders use: inflamatory form (eritematous phase or edematouse) but in absence of exudation to avoid crust formation.
Are used with dab, gauze, perforated jar, it can be wrapped the zone of application with thin canvas.
To be remembered that penicillin and salicilic acid inactivated if mixed togheter.
Penicillun is sensitizing
Shampoo: for greasy hair, with dandruff, dry hair, normal hair, delicate shampoo, medicated (ketoconazol shampoo)
Dry shampoo: component used clay, starch rice, mais, talc, used for cosmetics when few time is requested to revive hair vs the washing procedure. The dry powder hekpin absorbe sebo and dirty.
It can be used also vegetal extracts like betulla alba, achillea millefolium (effect on blood circulation), matricaria chamomilla (lenitive), capsicum annum (rubefacent), salvia officinalis(high level of fenolic coefficent in the essential oil), thymus vulgaris, urtica dioica in dandruff.
Emulsions : A/O and O/A
Used also **antioxidants** BHA, BHT, ascorbic acid and **preservatives** like parabens, sodium benzoate, clorure benzalconium
This can be applied to the skin or mucose,to veicle antinflamatory drugs, to treat burned skin, or in cosmetics like hydratants, protectants vs UV.
Solutions
water based solution : in example tricloroacetic acid 50% to treat for corns and warts.

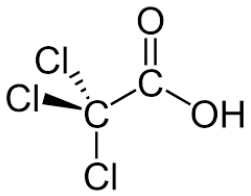


Fig. n 41 Tricloroacetic acid.

Iodine tincture
Minoxidil 2% solution From Mayoclinic : applied to the scalp to stimulate hair growth in adult men and women with a certain type of baldness(The exact way that this medicine works is not known).
Oleous solutions : veicle olive oil, almond oil, peanuts oil
Glicerites: glicerin, skin protectant, Moisturizes.
Collodions: non acqueous, col of cellulose nitrate with ether and ethanol.
(After application this provide a thin film that make possible after evaporation the APIs remain in contact with the skin) in example acid salicilic to treat warts.
Liniments: non aqueous sol, in oil and alcholic sol. of soap (trought rubbing or massaging) used for astringent, analgesic, calming, for irritable dermatosis, acute eczema
Oleo calcarea liniment: sweet amlond oil /calce water, for diaper baby irritation
It must to be well mixed before the use
Liniment benzoile benzoate: anti parassitic
In severe bollous dermatosys and burns of II grade can be used oleo calcarea liniment mixed with lassar paste 1:1 with baigne marie.

Shake lotions, tend to sediment, needed to shake before use in ex calamine lotion
Poultices – cataplasm (in past based on meals, herb, plants, and seed) in example flax seed for skin in dermatosi with itch. this flax seed is added to hot water mixing.
Solids fluidizabler with increase of temperAture, to be applied on the skin
Metallic soaps Pb et other or by mixture of resins, wax, fat bodies
They can incorporate APIs like salicilic acid, ittiole, coaltar
For localized iperkeratosis (palmo-plantar), psoriasis
Ditranol/catrame/ salicilic acid / poultices oleous of Pb
Other example cataplasm of clay to reduce joint effusions
To be remembered thart the galenic preparation are inflamable if alchool based in high concentration

Exipients in FU and EP 8 edition :
1) Tensioactives/ emulsionant: cetostearilic alchool, lanolin alchool, calcium stearate, gliceride polyglicosilate.
Etilen glicole monostearate or stearate, macrogol derivates, sodium lauril sulfate, sorbitan palmitate, zinc stearate polisorbate 20/40/60/80
2) lipids: alchool cetostearilic, lanolin, hydrogenated lanolin, vegetal oil, liquid paraffin, triliceride saturated, oils, animal fats, vegetal butters, stearic acid, isopropil palmitate, squalene, jojoba oil, wax.
3) reologic agents: alginic acid, bentonite copovidon, cros caramellose sodium, etilcellulose, arabic gum, adragant gum, guar, idrossietilcellulose, macrogol, metilcellulose, carbomer, gelatin.

Other
Protective, Hydratants- hemollients, Drying, Antimicrobials- anti mycotic- anti parassyte, Keratolitics Astrintents, Anti exuding, Antiitching, Occlusive- cover agent, Stabiliziers, Colourants, Keratoplastic Revulsive, Anti seborroich, detergent to clean the skin, deodorants - antiperspirants, depilators photo protective.
Occlusive agents: paraffins, wax, mineral oil, petrolate, lanolin
This increase the APIs absorbtion.
Used for ulcer and dermatitis, pay attention to allergy.
Anti aging: protect from free radicals, improving hydratation and microcircle to provide better tissue oxigenation, increase production of ialuronic acid, collage, elastin, depigmentant.
Product : protective vit E, ginko biloba, fish cartilagin, vitis vinifera, asiatic centella, Zinc or to improve microcircle like borragin oil, ginko biloba Solar filter
Antioxidants, hydratants, hemollients, anti free radicals
Used glicerol, ialuronic acid, malva extracts (mucillagines), urea, alfa idroxiacid of fruit, allantoin.
Alfa idroxiacids of fruit : from lemon, orange, mirtillo, ananas, lactic acid, licolic acid, apple, papaya Salicilic acid, vit A, D- pantenol
Antioxidants: resveratrol, vit C, olea europea

Controls for semisolids preparations
in the galenic lab. Pharmacy : verify of the procedure followed, aspect, amount to be dispensed, verify held of the primary container, right labeling other control : title in APIs (TLC, HPLC, CG)
stability (stabile viscosity during the time, ph variation, unpleasant odour, creaming for emulsion)
verify under physical stress cycle temperature high and after cooling (5-45 grades)
microbial contamination: under pharmacopeia limits for this kinds of products- verify unpleasant odour, or mold presence. Sterile chek – only if request by the product mass or volume releasable – for dose unic product particle size if requested.
technological controls: aspect, omoeneous and uniformity, loss of water, loss at dry, reological parameter – viscosity, PH allergizant power.
Skin sensation, greasy, consistency, spread property, allergy reactions, biodisponibility.

Semisolid galenic topic preparation microbiological requirement
total count of living aerobic microorg. No more then 10^2 aerobic bacteria and fungi for gr or ml.
No more then 10 enterobacteria or other gram – for gr or ml.
Absence of pseudomonas aeruginosa and staphilococcus aureus.

Stability of semisolid topic preparation
30 days (expiry data) in absence of specific indication about he stability of the products
This limits can be reduced (in cream withour preservants- antioxidants) or increased if available specific data.
For non acqueous preparation (anidrous ointmenet) the expiration data can be no more then 25% of the more short period of expiration of the component used; but no more then 6 month.

The information related the stability of the APIs can be obtained whit the verify of this stability during the time (accelerated satbility proof) or from official texbook or literature.

About tollerability
surfactants both cationic and anionic can damage the stratum corneum depending on their concentration and duration of use. The non ionic sufactants are more tollerated.
Parameter to be avlued : stability of the APIs, and other components, loss of water and volatile components
omogeneous distribution of the phases, distribution of the dispersed phase, reologic characteristic
Physiologi c PH, skin sensation, allergy, biodisponibility.
The most used preservative antimicrobial and antioxidant are : sono: parabens, quats, alogenate phenols
Clorexidin, imidazolinidil uree, organic derivates of mercury, benzoic acid and sodium benzoate sorbic acid

and e K sorbate, BHA and BHT, tocoferols, gallic acid estere, citric acid, tartaric acid
Acceptability consideration : consistency and spreading properties.
Even if a drugs activity can be superior using an hydrocarbon base the patient acceptability can be low due by its greasy property.
The PEG bases (because water soluble) can be appreciated byt its use in an traumatize tissue can produce irritation.

Toxicity of the topical products: this can befor the various Apis: allergy, irritation, phototoxicity, acne induction, malignance (very rare), systemic toxicity, teratogenicity drug interaction, hypotalamic, pituitary adrenal axix suppression.

Instruments: mortar and pestel, plate, spatule, electric mills, mixer, baigne marie, balance For the emulsion are needed: mechanical mixer, homogenizer, ultrasound device, mills for colloids, heater for dry sterilization, mixer for emlusion.

Operation: weighing Apis and exipients,reduzing size of the powders, solubilization of the APIs if needed fusion veicle if needed, mixing, Smooth, cooling, filling, final testing (sterile operation if needed)

Measure unit : W/W, W/ V, parts (in example 1 part in 1000 parts for liquids)

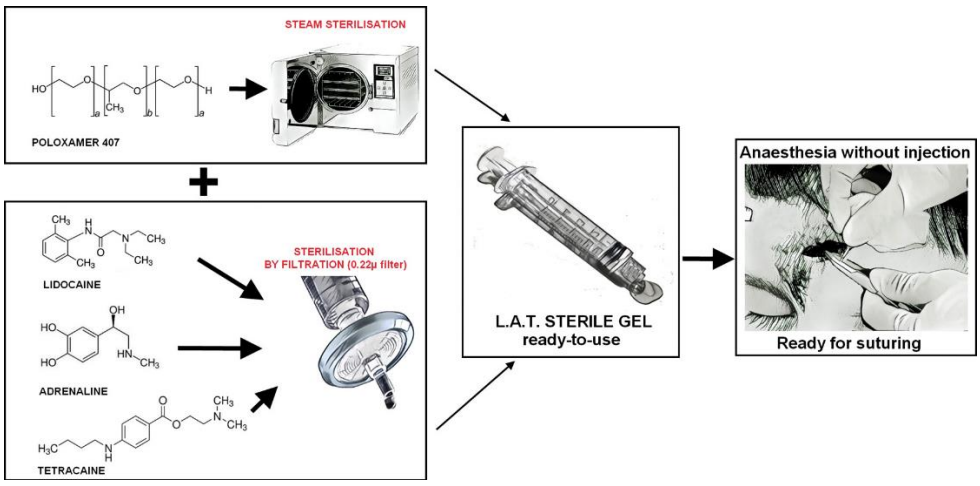


Fig n. 42 lat gel – sterile filtration from https://doi.org/10.1016/j.ejps.2019.104962 gel for dermatologic emerencies in children, Anestetic properties for little wounds (scalp et other)

Accordin Jadhav NR et al
"Talc is a stable material and hence it can be sterilization by heating at 1600C for not less than
an hour. It may also be sterilized by exposure to the ethylene oxide or gamma irradiation."

Control of the raw materials and APIs: technical sheet -certificate of analysis and safety sheet.
Risk evaluation: if used heating systems, electrical devices, mecanical mills.
Documentation : working sheet, mainteniance verify of the instrument used, updating course of the galenic pharmacist
Packaging: this must to be compatible for the products to be filled. (tested at room temperature or in accelerate conditions like 40-50 grades)

It contained water or volatile component there is the need for an hermetically closed container and if sterile with an inviolable closyng system. Generally this must to be light in weight, inexpensive, convenient for the use, compatible with most formulative components, provide greater protection against external contamination and environmental conditions than jars.

The tubes can be of alluminium or plastic made. The aluminium is covered with epoxy resin,vinyl, or lacquer to prevent interacrion beteen the content and the tube. The tube can be of HDPE, LDPE, PP, PET with various layers. Plastic are better the metals for compatibility with the content.

During the filling of the jare it is necessary to avoid intrapping of air inside paking the ointment at the bottom of the container. If used fusion method the jare must to be filled and then froze it to avoid stratification of the various different component. In pharmaceutical industry is used also pressure force to fill the right amount.

Labeling: pharmacy name, preparation data (APIs concentration, and excipients), date of preparation, expiry data, conservation modality, use external indication, precaution and other needed.

Cosmetic cream
cleansing cream, cold cream, night cream, moisturizing cream, foundation cream, vanishing cream, all purpose cream, massages cream, hand and body cream, self tanners, solar filters.
Lotions : cleansing lotions, sunscreen lotion.

Powders, face powders, talcum powder, body powder.

Emulsions
shampoo, balm and other like skin colorants lipstiks, rouges, skin care products shampoo according FU are liquid - semiliquid preparation to be applied to the scalp and the rinsed with water. This contain tensioactives.

Acute dermatoses inflamatory : whit component erithema- edematous, also vescicolous (eczema): can be evaluated by the physician aqueous sol. Cold of antinflamatory, astringent, anti exudants like alluminium acetate, nitrate of Ag, boric acid, permanganate K diluited solution, ipoclorite diluited solution.

Are used permanent repeated compresses
In **acute form** are generally controindicated the powders that could produce crust and the greasy ointments (not permeable to perspiration), this can increase flogosys with reabsorbtion of substantie produced by the inflamatory process.
Subacute lesions: sol/powders
Pasts thin or greasy, liniments, some tincture, lotions, emulsions, glicerolate
Chronic lesions: also infiltrative, can be evaluated greasy paste, ointment, balsam, emulsion.
For **ipercheratose** : emulsions, lanolin, licerolate, urea, salicilic acid resorcin. (see G.Leigheb)
To be considered thar the increase of an APIs can both increase efficacy and toxicity since caustic reaction in some case.

Other conditons that can be considered :
kind of lesions
wet, exudated, acute (aqueous veicle)
dry, no exudate, chronic (veicle oleous, emollient)
skin with hair : aqueous veicle
sensible skin : not alchoolic

Reported use of interest (old, obsolete or in use): from texbooks, literature some examples
Astringent, decongestionants, anti exudative
saline solution 0,9%, sol ringer locke
infusion of malva and chamomilla, cold for dermatoses eritemo edematous acute in delicate zone like face and genital.
Argentum nitrate pencils, caustic, coagulant, for ipertrofic lesion, in vegetation, to arrest iperplasia of granulation tissue in ulcers or wouds.
Sol 1-2% antiseptics and reepitelizant, it is irritant, to be used only in little lesion, astringent, decongestionant per eczema exudant and ulcer.
Patients repots mild burning, this product coloration brown black of th skin and linen indelebile.
Argentum proteinate: 8% of Ag, antiseptic and astrinent, less irritant of AGNO3, more diffusible in tissue
Sol in water 0,25-1,25%
Use also for anal pruritus, emorrohides, proctites

Lime water: water sol of CA(OH)2, atringent, antiexudant, degreasing, antiseptic.
Alluminium acetate: 1-3%, well tollerated, antiseptic, astringent, lenitive, dcongestionant
For compresses, pediluvi
For lesion exudants, ulcerative, wounds, antinflamatory, anti maceration in hyperhydrosis and macerant plantar sweat.
Pb acetate: antiseptic, astringent, use on skin not dis epitelizated.
Water Dalibour: for compresses astringent and antiseptic
Copper sulphate/ZNSO4/ canphor water, used diduited
KMNO4: to be mantained shelter from light, Energic oxidant
Dil 0,25-1 ‰ for skin lesion, 1:7000 for mucose lesion(irrigation uretral)
Used for bath, pediluvi, septic ulcers, maceratin folds, burnst, plantar hyperydrosis
If too high conc can cause intollerance since toxicity, color also in brown skin.
Can cause micro burn if cristals not good solved
Incompatible with peroxide of hydrogen, alchool etilic, ferrose salts.

Boric acid: sol in water, ETOH, glicerin, weak anti septic and antimicotic
Antimicrobial, low irritant, decongestionant used for inflamatory dermatoses localized
Eyelids 2-4% compresses, ulcus cruris
No for wide zone to avoid toxicity in children, obsoltete the incorporation of boric acid in ointment and powders

Talc- borate : acid boric, talc
To be used with caution in infants, can cause also fatal intoxication with renal failure
Research article, 2015
Safety Assessment of Talc as Used in Cosmetics
Monice M. Fiume et al
https://doi.org/10.1177/10915818155867
“Talc is used as a dusting powder, alone or with starch or boric acid, for medicinal and toilet preparations”

Regulatory Toxicology and Pharmacology 2021
Toxicity of boric acid, borax and other boron containing compounds: a review
Niels Hadrup, Marie Frederiksen, Anoop K. Sharma
“One male infant aged 27 days who had been treated for dermatitis with borated talc followed by boric acid powder for 7 days was hospitalised with gastroenteritis after having vomited all feedings for 3 days. His symptoms also included erythematous patches on several body parts, and subsequent excoriation of the skin. The blood and urinary levels of boric acid were 8.8 mg B/L and 49 mg B/L, respectively.”
Clorooxidants: sol, antiseptics, clorine based, for wounds, burns, scores.
Short durate of action, to be prepared in estemporaneous way Can be tissue irritants if on damaged tissue, because is alkaline.

Ipoclorite: antiseptics, decongestionant, detergent fo skin lesion at opportune diluition
Sodium ipoclorite concentratec 16-30 clorimetric grades water of Javel Or diluited 4,5 -5% active clore sol Dakin, the caustic soda is nerutralized with acid boric Sol Carrel dakin
Uses of ipoclorite : antiseptic, for lacerated wounds, fistulas lesion, ulcers, burnst, exudative dermatoses especially if ovelapping of germe.
It has deodoring property for process macerative, necrotic, gangrenotic
Cloramine: it decomposes on air, alkaline sol, used at 0,1-4%, can produce skin intollerance
Are added NACL 0,5% to correct its ipotonic properties.
This solution are incompatible with acid sol.
Electrolitic chloro-oxidant: cl active 1,1%, develop O2 rising, it is ipertonic NACL(18%)
To be protected by light to avoid decomposition.
It is not caustic, the ipoclorose acid produced is bacteri-sporicide.
Sol isotonic at 5% used for skin detersion, ulcer, exudant dermatitis
Ipertonic sol 5-10% is used for necrotic tissue with torpid granulation, II grades burns with flittene
Oranic colorants: diluited idroalchoolic solutions Antiexudants anti macerants, anti septic, anti micotics for superficial lesion.
This dye the skin and linen, Some delays cicatrization
Gentiana violet: 0,1-1% sol water /glicerol for gram + and candida (intertrigo), can cause local intollerance.
Malachite green: similar effect
Basic fucsine, antimicotic, colour of red, in example
Tintura rubra Castellani, irritant due by fenol, aceton, resorcin especially if used in scrtotum or in axillary cables.
Merbromin: sol 2% brush strokes, it is antiseptice because contain HG and BROME
Keratoplastic, drying, antisecretive
Low toxic used for continous solutions of skin and mucose, intertrigo,burns.
Colour of red, can be decoloured usin sodium ipoclorite sol.
It is not compatible with acid, ETOH, local anestetics
Eosin 0,5-3%, used for submammary folds, area interlutei, inguinal in babys and for pseudomucose genitals
Action: reducing, cheratolitic, for infiltrative dermatoses-likenification and iperkeratotic psoriasis superficialadded to UV
It is photosensibilizant
Rare irritation due by its impuruity
Metilen blue: sol in water, low in ETOH, dye in blue, it can be removed using sol of sodium ipoclorite plus cloridric acid diluited. Not compastible with reducing agents, oxidants, and iodure
Weak antibacterial antimicotic, also used as mouthwash 0,5-2%
Antiseptics: bacteriostatics – cide at adeguaste conc.
Quats: antiserpsys cutis, piodermitis, action vs gram +, coniugation with azotate bacterial compounds with denaturation, this cam produce sensibilization, use at 1-2%
As benzalconium clorure, detersive cationic
Fenol and derivates: from fossil catrame, also syntetic
Sol in water, ETOH, glicerol, etere, oils, fats
It is caustic, whaitwash the skin when used, incompatilble with alcali, KMNO4, oxidants, alogens, canphor resorcin.
Good anti septic on the putrefactive germ, not efficacy on the spore. Can be used for wounds, ulcerated lesion, decubitus, antipruritic, local anestetic 1-5% Epidermolitic, for peeling for cicacitral exitus of acne.
No for compresses because it can cause necrosis, If systemic absorbtioncan cause toxicity : cefalea, SNC toxicity, ipotermia, coma Ex Castellani tincture.
Picric acid: fenol nitroderivate, topic antiseptic keratoplastic, analesic for burns, eczema, erisipela, insects puncture, chilblains.
It is toxic, not to be used in children or on vaste area, if systemic absorbtion renal zone pain, red brown urine
Sol idroalchollic 5: 1000
Cliochinolo: insolube in water – etanol, soluble in cloroform.

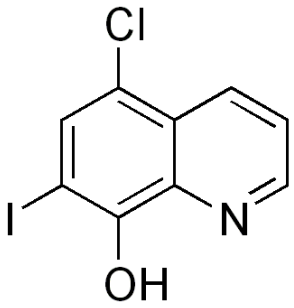


Fig. n Cliochinol.

Jellowish powder
Cream, ointment 3%, powder composite 20%
Antiseptic, antimicotic, can give skin sensibilization.
Esachlorofene: antibacteric in pomate 1%, soap solution 0,25%, for surgery antisepsy, can give skin reactions, allergy. Used to prepare soaps, deodorants, germicide, inib decomposition of bacteria organic substantie.

iodine and derivates
sol acueous, etoh, glicerin, etere, if concentrated is caustic (uset to treat wards), if dil antiseptic, revulsive, irritants, it was prescribed diluited for alopecia, it can give systemi absorbtion iodio tincture and sol iodo-iodurate lugol antibacterc, antimicotic, also mouthwash, brusch strokes for tonsils, gargles.

PVP – IODINE: 9-12 % of iodine, antiseptic, disinfectant with iodine disp, 0,1 -1%.

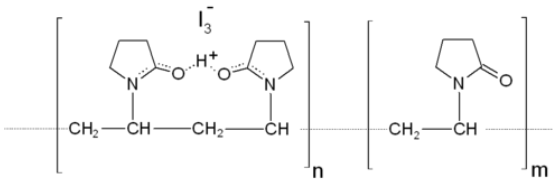


Fig n 43 PVP-iodine.

Water solution, cream, shampoo

Mercurium and derivates: to pay attention to absorbtion skin – mucose, renal elimination, intestinal saliva, sweat

Anti luetic, antipratssite, antiseptic, antipsoriasis, bacterisostatic

The inorganic compound are sobstituted with organic ones : are more active and less toxic

Are inactivated by solforate products

White precipitate : clorure of mercurammonio; Corrosive sublimate : biclorure of mercurium

Tox, it was used for pitiriasis versicolor and aopecia

Jellow precipitate : jellow oxide of HG, caustic, astringent, antiseptic, used for impetigo

Antimicotics: (not azole or other pharmacological APIs) kmno4 sol, corrosive sublimate, boric acid sol, clorooxidants, gentiana violet, fucsina, eosin, green brillant – Tinctura rubra Castellani, iodio tinture (irritant in delicate site or in infiammatory lesion), alchool iodate 1-2% for surface mucosis and scalp, pytiriasys versicolor, epidermophytes, scalp ringworm.

Iodine must not to be mixed with HG to avoid formation of HGI, very irritant.

Sulphur: antimicotic trought H2S production, oxidative action.

Powder 1-5%, pomate, paste 2-5%

Sulfosalicilic pomate: salicilic acid/sulphur precipitate/vaselin

sodium iposolfite plus an acid sol it was used for pytiriasys versicolor, If too much high sulphur concentration it is irritant Sulphur have aslo kerastolitic, reduxing, antiseborroic properties.

Salicilic acid: keratolitic and Benzoic acid, topical anti micotics

Fat acid insature, propionic acid caprilic acid. Withfield oinment : salicilic acid, benzoic acid, vaselin, lanolin.

Some antimicotics are dirty and not appreciated by the patients. Also are not covered activity vs all micetes (are better imidazolic molecule)

Cheratolitics: salicilic acid, to be dissolved in hot water / etoh, cloroform / oil Bacteriostatic, fungicide, fotoprotectors.

It is not compatible with lime water, resorcin, ferrum salts because precipitate, calcium carbonate neutralize it

0,5-1% cheratplastic, 2-3% cheratolitic.

Used also for friction to the scalp, acne, seborroic styate, scaly dermatosis, psoriasis, ipercheartosic eczema for ipercheratose palmo-plantar the concentration needed if greater since 10-15%.

Salicilic vaselin: it can be added urea (emollient), not to be used in wider skin zone because increase the systemic absorbtion with acidosis.

Resorcin: soluble in water/etoh/etere/fats, little caustic for mucose, skin irritant it was used as antiseptic, keratolitic, reducing for psoriasis, acne, varicose ulcer inferior arts, anal fistule it reactivate the repair process sol. Alchoolic or paste 0,5-3% antiseborroic, at low conc keratoplastic it must to be prescribed at low conc to test tollerability, then increase the conc.

Paste 20-50% strong keratolitic to provide exfoliationof infiltrative lesion of acne (a chemical peeling)

To be avoided fat excipient becausa increase the resorcin absorbtion with more systemic tox.

Not to be used in wide sone

Ex lotion salicilic/ resorcinata: salicilic acid/resorcin / ricin oil, alchool.

Keratoplastics: reepitelizant, cicatrizant, before is needed detersion, and antisepsi.

Sulphur, merbromin, resorcin, AGNO3 (to reepitelization of ulcers).

Tolu' balsam, from a tropical tree, it is an oleous resin, API cinnamoin, liq siruppous red- brown

Acid, insoluble in water, sol in etoh, cloroform, fat oil

It was used for Antiscabbia, reepitelizating, for nipple ragads, scalp friction

It can give skin sensibilization.

Dermatole: sottogallate of Bismute 10-20% for bullous dermatose, penfigo, sprinkler powder Weak antiseptic.

Emollients: this prtoduct hydrate, make more soft corneum stratum

Oil, fat bodies, vaselin, occlusive, they oppose to water evaporation

Lasnolin, partial occlusive, prevent dry skin

Lubrificant, reduce desquamation, inrease softeness, this are hydratant b, igroscopic

Hydrated lanolin: 22% water

Powders in acqueous sol.

Starch baths. Alcaline baths, sulphorous baths

Starch glicerolate

This products are suitable for ittiosis, eczema iperkersatoses, seborroic, psoriasis, dermatoses with marked keratinization

This can incorporate APIs.

Urea: sol water/ etoh, insoluble in etere, fat bodies, incompatible with nitric acid, produce precipitation, alcali for decomposition

Urine have cicatrizant property.

Hydratant and solvent for keratin because break binding -H

At 10% is bacteriostatic – fungistatic, deodorant

Emulsion O/W is ideal, not rease

Sol acqueous for pediluvi, hand bath in iperkeratosis, cream, ointment, licerolites, suspension to shake

The concentration vary from 5-40%

It is active if > 10%

It allow APIs penetration

Allantoin: cicatrizzant, emollient, softener, anti irritative, for sores and ulcers.
CLT: for alopecia sol, cream, ointment, used for ittiosis (10%) if sex linked
Reducers: they bind oxigen, for psoriasis, lichenified eczema
They stop the DNA syntesys, inibition glicolitic enzime, and the oxidative exchange
In psoriasis are increased the glicolitic enzimes, shunt oxidative, citoevolution with increase keratinocitic in germinative status.
This product reduce the inflamation, flattening of the lesion with regression
Sulphur, ittiole, vegetal catrame, minerals, calomelano, resorcin, pirogallic acid, crisarobin, antranol, cignolin.
Catrame: oleous fraction of the dry distillation of organic substantie
Use in intact skin, macerated, iperkeratoses at different dosage.
Today this product are sobstituted with cortisons and other APIs
The catrame are applied at growing dose to test the tollerability in the single patient.
This product can cause irritation, inflamation, rare allergy, photoallergy, acute papule follicolitis
Dermatitis chronic pigmantary.
Rare case of neoplasia(if patients in therapy for more then 20 year)
Wood catrame: from dry distillation of wood pinus, abete, larice, ginepro rosso, faggio Betulla, tiglio
Da conifere : this contain benzol, toluol, naftalin, fenol, cresol, pirocatechin, guaiacol Metilcresoli
Liquid viscosus dark, odour characyeristic, this can dissolve in acide water, insoluble in alcali Miscible at heat with fat substantie
Antibacteric, for chronic eczema, psoriasis
Also incorporated in shampoo
Ginepro catram: cade' oil, an essential oil, weack antiseptic, resolvent, it can be incorporated in vaselin, lanolin
Glicerolate, lotion, pomate 5-10%
Catrami from bituminous shalesfrom rests of fossil fish
If tretated with solforic acid and NH3 it can be produced ammonium sulphoittiolateor (ittiole)
This last is not photo sensibilizant, sol in water, etoh, eter, vaselin, lanolin, glicerin
Not miscible with fat oils and vaselin oil
It is irritant, antinflamatory, vasoconstrictor, antiseptics, keratoplastic 5-10% in vaselin for abscesses, pimples.
Paste, pomate 1-5% for eczema not too much active, seborroic
Meccanism of action: linked to sulphur and to its reduction power
Carbon fossil catrame: coaltar, insoluble in water, sol in cloroform, etere, benzene
For chronic eczema, psoriasis
Incorporable in paste ZNO
It can provide irritation, acute papulos follicolitis
It can be prescribed pure, sol, paste, ointment
Use for infiltrant psoriasis, acute eczema and chronic, nodular scabbia
It must to be tested for some days to verify tollerability
It is used in occlusive medication (with nylon sheets, plasters)
After various time it is necessary to rest the skin
The action it potentiated with UV, before is necessary to remove the catrame with vaselin oil
Coaltar have citostastic action, athrophying
Calomelano: clorure mercorose, insoluble in water and etoh, in contact with oranic substantie it develop sublimate corrosive
Pomate, glicerolite, poultices, as reducing vs psoriasis, depigmentant, also for delicate zone and hair region
In example calomelano/ZNO/ lanolin/vaselin
Cignolina: antralina, no for thin skin or on irritable skin, not for wide zone
Insoluble in water, sol cloroformio and fat bodies, it can stain, it can be used with occlusive medicatio, also emulsion O/W 0,1-0,4%
For psoriasis, infiltrative dermatosis, anti parassite, rubefacent, esfoliant, reducing, antimicotic.
Pirogallolo: sol in water/organic solvents, it is irritant and reabsorbent, for psoriasis it was use humidified with NH4+, used with salicilic acid, ittiole, coaltar.
Revulsive: or rubefacient, vasodilatant, erythemigenous, it was used for aerata alopecia, increase the ematic circulation, stimulation of the pilifer bulb, this give a heat sensation and burning, itching, since vescicles and bulles- vescicant.
Use also transcutaneous effect to treat condition below the skin like borsitis, sinovites, myosites, mialgia.
Black senape: from crucifere Sinapism like senape flour and lukewarm water, for pediluvi, bath, senapata papers
Capsico: solanaceea plant, from south amarica, guinea pepe, chili.
Tincture capsicum 1-3% revulsive pomate 5-10%
Jaborandi: from Paraguay, tincture lotions
Eucaliptol: australian plant, water insoluble, sol in etoh, eter, oil External use for friction, analgesic, revulsive.
Mentolo: from essential oil of mentha piperita Iperemic, fresching sensation, anti pruriginous, mild analgesic
Lotion, tincture, splinkers powders, mentolate talc
It can provide skin reaction and intollerance
Lotion like : mentole, salicilic acid, resorcine toh
Cantaridin: animal origin, from insects beetles
Water insoluble, sol etoh, cloroformio, etere, fat oil, wax, resins.
Nicotinic estere : ointment -lotions.
Other rubefacents: etere, cloroform, acetic acid fenol, resorcin, cade' oil, cloralio idrate, formol, china, iodine, pilocarpin betanaftolo, metile salicilate.
For ointment -lotion, for friction, sponging, touches
It can be added oil to reduce dryin of the product.

Antipruritics
iy was used canphora from cinnamomum, a china tree, sublimate on air, it solves in etoh.
Etere, oil, fats like canphorate oil for frictions, pomate at 10%.

Antiseptic for acne, prevention for decubite ulcers., added to revulsive in example canphor, etoh, water.
Canphor- vaselin, Chamomilla infusion, Acetate alluminium sol., Oleo calcarea liniment, Water ittiolate at 5%.
Tricloroacetic acid 5%, Cream idrate chloralio, Compresses of water and vinegar, Sponging fenic – fenic acid, etoh, glicerin, Powder mentolate or camphorata 1-3%.
Oleate : coaltar, oil cod liver, or fenol/olive oil.
Glicerolates: fenic acid, salicilic acid, tartaric acid, starch licerolate
Paste: ZNO with ittiole 5-10%
Pomate: mentol, idrate cloralio, canphora, vaselin, lanolin.
Antiseborroic: for seborroic dermatoses, in zone rich in sebaceum land like face, scalp and in person with high sebacea ipersections
Sulphur, also mild keratolitic
There are 4 syphur type :
sulphur common : not to be used in medicine, because with impurity sublimate sulphur, flower sulphur, obtained for sublimation, yellowe powder, not miscible in water, low with etoh, etere, partially in cloroform and olive oil., used for bath suphur sublimete washed: without impurity of Arsenic, because washe with NH3 dil.
Precipitated sulphur, magistero of suplhur
Sulphur it is incompatible with oxidants
It can be incorporated in lotion for seborroic alopecia and acne
If etoh solution it can be flamabe, used for friction
For eczema seborroic can be used as paste and oitment like sulpho salicilic paste.
Is some patients can be irritant in sensible skin
Other properties it was used as antiprassitic
Cadmio sulphur – selenium : antibacteric, anti seborroic, for acne, seborroic dermatitis, desquamation of the scalp (shampoo), pytitiasis versicolor 1-2%, detergent suspension.

Detergents: useful to remove death skin cells, secrections, controlling microbial flora, the agressive ones can cause dryness.

Anti acne
salicilic acid, alfa-idroxiacide, antibacterics like clorexidin, triclosan inflamatory reducers: benzoil-peroxide, retinoids (this have not the side effects of steroids)

Barrier substantie
for protection of lesive action chemical/ physical/ external for manual works when manipulating particular kind of substantie.

ZnO paste used to prevents in babies the damage by production of urea from decomposition of the urine by bacteria or the fecal irritation.

Cream idrosoluble, to protect from organic solvents like benzol, toluol, xilole, etere, etoh, lakey et other Deprived of fats and of liposoluble solvents, added cellulose, mucillagin, silicate, inert polimer.

Idroinsouble cream: fat. protect from water, acid, alcali, powder, it must to be easy spreadable, not To impede the manual work, invisible, not modifier of the substantie worked.
Easy removable, watwer, water and soaps.
This are based on resins, paraffins, lanolin, alchool, aceton and other
In example metilcellulose, paraffin, glicerin, water
Cream vanishing: O/W in example urea/ lanolin
Some commercial cream can contain nipasol /carbowax that can be allergizant
Eucerin: good barrier action like a also Cera lanette or White vaselin
Silicons, syntetic, this contain silica at high conc, can be fluid also like silicon oil or semisolid
Not irritant, can veiculate APIs, not to be mixed with soft soaps, carbowax, glicerin.
They are idrorepellents, prevent skin maceration, easy removable with water, high cost
If the conc of silica is low this not provide a good barrier action
This can be added to cacao oil, vaselin.

Photo protectors- sunscreen-tanning
In sunscreen product the radiation to be eliminate have a about 2900 angstroms : are used powders like ZNO, Titanium bioxide. bismute carbonate, barium sulfate that act as phisical screen
Other products vs the UV eritemigen about 3200 angstrom.

Photoprotective substantie : it was used vit H1 acid. para-mono-benzoic and reivates, salicilic acid, metile salicilate, lotion,cream, pomate.
This filter radiation providing a good tan.
This product degradates rapidly and afet 1 hour of exposition is reduced about 50% of efficacy
Derivate antranilic -cignolin, Chinin oleate, Cinnamic acid, Diazole, gallic acid, tannine 5-20% antiistaminic (to be avoided to prevent sensibilization)

Anti sun products
especially emulsion O/W, creams, fluid milk, spray
solar filters: physical (bumper) or chemicals(absorbent)
ferrum oxide or magnesium, copper clorure, ZnO, Titanium bioxide, Sio2, talc, zinc stearate, allumine idroxide
ic cosmetics for face are added coloured pigments like ferrum oxide to mask the white effect of the Titanium bioxide effect
pigmentant local or general action (os)
vitamins : C, alfa tocoferol, carotenoids
lipids: karite' butter, avocade oil
calendula
derivated of aminobenzoic acid – FOR UVB

salicilic acid derivate – UVB
cinnamic acid derivate - UVB
canphor derivate -UVB
UVA- benzofenone and di- dibenzoilmetane derivate
MOA mecc. Of action : photosensibilizzation with UV about 3600 A.
Increase the skin responce to UVA that have > wavelenght
It is needed a gradual approach, from initial eritema then pimentation.
Action due by formation of free radicals, fruocurarin
Psoralen from ficus Carica
Meladinin from an Egipt plant
5- metossipsoralen from bergamotto
Derivate furocumarinic 8 -TMP
Metossalene
Active after about 30 minuts of oral absuntion, are used UV (not solare radiation because more active) the toxicity limited the selection of the patient.
Contraindicated in diabetic, epatopaty, Possible carcinogenic action due to the crosslink between DNA molecule, Cataract, nevus.

Depigmentant: for cloasm, ipercromia localized by chemical -physical cause
This are palliative because not correct the causes.
Ex sublimate corrosive, ZNO, wool fat, vaselin, peroxide of hydrogen 12 vol
Cream oxigenate with sublimate
Glicolic acid
Alfa tocoferol
Ascorbic acid
Pomate -paste esfoliant with sulphur or resorcin
Calomelane pomate
Sottonitrate of bismute
For hair decoloration in ipertricose are used oxidant melaninic
H2O2 (20-30 vol) with or without of NH3 little part
Lanolin, H2O2 at saturation
Idrochinon (it is an resorcin isomer) 2-4 % sol water, etoh, etere
Paste, sol alchoolic plus retinoic acid
Action on melanocite and follicular system
Inibit enzime tirosinase, inib en.z sintesis new melanin, the action is not immediate and reversible
Good for the localized situation.
Side effects : if prolonged use, burning, dolor, esantema, skin irritation, allergy
Azelaic acid: depigmentant
Deodorant-traspirant
To eliminate unmpleasant odour fro bacterical decomposition of the sweat (initially sterile)
Expecially in zone like armpits with hair, elevated PH and high umidity
The bacteria degradate TG in fat and other product acid with umpleasant odour

Depodorants
Solvents -antiseptics, that eliminate the dirty and bacteria with powder of MgO that neutralize, absorbe the aromatic acid.

Anti traspirant : acts on production and excrection of the sweat, provide coagulation of the skin surface protein with obstruction of the sudorifer duct (AL salts)

Antihyperidrotic
for foot HYperidrose : sponging of canphorated alcool, alcool iodate, salicilic alchool 2%, inhert powders like ZNO, starch, veneto talc.
for foot iperidrose : footbath with KMNO4 dil 1:10000 or 1:5000, daily, astringent
boric acid 3%, salicilic acid 3%
tannic acid 5% in alchool 70 grades
to follow the with powders
acid salicilic, talc veneto, starch
for more severe cases: KMNO4 dil at 2-3: 1000
Sponging naftolate alchool, Beta naftole, glicerin, alchool, Then powder with b naftole, starch
Alluminium salts : acetate – water, clorure and water or in etoh 70 Grades Triclosan, Zinc ricinoleate, citronelly
Glutaraldeide 10% in Na2co3 buffered (obsolete and dangerous)
In cosmetics
Alchool sesquiterpenic, active, not alter skin equilibrium
Inibitor of bacterial esterase.
Assorbitors :capture odour without acting on the sweat secretion, ZN ricinoleate, complexant
Local hemostatics: rock alum, provide a rapid bloodcoagulation, used also for zits from piogenes bacteria.
Deodorant covering: with purfum, this have only a little antibacteric property and not act on sweat production, are used essential oils, from lavender, sandalwood, pinus silveter, timus, bergamot, eucalipt, cloves.
antibacterics deodorants :clorexidin, triclosan, trietilcitrate: idrolized in etoh and citric acid that reduce PH, reducing the production of fat acid like capric, caprilic, butirric that have odour musky.
Antioxidants as antiodourants: avoid oxidation of the sweat, preventing maleodurant compounds like ammonia and mercaptan, used vit C, vit. E, BHT, BHA.
Chelants antiodourants: zinc ricinoleate, EDTA, this product are not used alone because they can not avoid all the odour but only the top notes, for this are added fragrants like timus, pinus silvestre, limon, cloves or other essential oils.

Depilatory
chemicals, to eliminate extrafollicolar part of the hair action vs cheratin, for hydrolisis disulfuric binds that link the polipeptidic chain this are toxic, ittitant for the skin, allergizants
old products :
tallium acetate, AS sulphur, selenium sodium salts, calcium sulphur, barium, sodium, stronzium in example barium sulphate, starch, ZNO

This are diluted in water, aspplied for 3-5 minutes, the washed the zone with water and added starch powder.
Today : depilatory cream with alcaline terrose salts of tioacid alifatic like tiolicolate of CA with CAOH2 And strontium, low irritants and of accettable odour.

Antiparassitic
For artropodes parassite scabbies, lice, Some are irritant, allergizant and toxic Sulphur white yellow precipitate, peru' balsam.

Anti scabies
before needed an hot bath plus comb use sulphur iposolfite sodium 40% plus HCL 2% after (in past) benzile benzoate 10-30% esacloro glicoesane 1-3% irritant, other peru balsam olive oil, fenol derivate anti pediculosis pubis, xilol, vaselin eyelash yellow precipitate, vaselin yellow piretrum.
DDT, sol, powders, low skin absorbtion, high inalation absorbtion Copper sulfate.
Anticellulite: examples mud : fucus powder,ivy, hippocastan, capsicum extracts, glicerol, nipagin depurated water.
Clay Face mask : stearic acid, trietanolamin, depurated water, bentonite, clay, titanium bioxide.

Example of common preparation : various
echografic gel, athlete foot cream, deterent milk for nornal skin, fluid cream for sensible skin, deterent milk for babies, water boric 3% (not for damaed skin or inflamated), pink honey, liquid callifigus, arnica cream hypericum perforatum cream (lenitive, cicatrizant properties, bases cream essex -urea 10%), calendula cream (lenitive, cicatrizant properties), aesculus hippocastanus cream (for venous circulation), essentials oil cream and oil like Tea three oil (reported properties antibacteric and anti fungine), propoli cream useful for acneic skin, Canfor- eucalipt- mentol ointment FU XII, cliochinol 3% cream, permetrin 5% cream sport massage creams, peeling ointment, detergent milk, after sun milk, lip stick. examples of drugs from industry : acyclovir cream miconazole cream, diclofenac gel, tretionin gel, betametason gel.

Formulations example
YELLOW PETROLATE USP : yellow wax 50 gr+ petrolatum 950.

HYDROPHILIC PETROLATUM USP : cholesterol 30gr +stearyl aclhool 30 gr+ withe was 80 gr +white petrolatum 860 gr.

ZINC OXIDE ointment : 10%m/m in adguate excipinets Zin oxide powder: absorbent, bacteriostatic, low astringent, refrescing The Zinc link protein, to be fined sift to avoid irritation.

EUCERINA ANIDRA : withe vaselin 95% + lanolin alchool 5%, used to prepare cream A/0 (eucerin cna incorporate since 50% water)

VASELIN AND LANOLIN BASE OINTMENT FU XII ED : withe vaselin 90 gr +lanolin 5 gr cetostearilic alchool 5 gr (by fusion of the all component and mix)

LANOLIN BASE OUNTMENT FU XII: vaselin 93,5 % +lanolin alchool 6% +cetostearilic alchol 0,5%.

METILE SALICILATE in cream O/A QB 100 gr : lipophilic phase 70% and 30% idrofilic (water) 100 gr – 5 gr (api) = 95 gr excipient.
95gr x0,7 (70 %)= 66,5 gr lipofilic phase (vaselin, lanolin alchool, cetostearili acid)
Mix of 3 oil : olive, sweet almond, vaselin (ana parts)

GEL BASE: for skin treatement : HEC 5 gr+ glicerole (85%) 10 gr + water qb 100 gr (boiling before the water, mixing well and rest then for 1 h in order to produce the gel.

Starch glicerolate gel : starch, glicerin, water 10:70:20 w/w, is used as a mild, non-irritating topical dressing for skin conditions like eczema and erythema.

Canphor, eucalipto and mentol ointment: Balsamic, FOR per adults. 4,0% di canphor,eucalipt essence l 2,0%, l'1% di cinecol and lo 0,5% di mentol.

Cliochinol (Vioforrmio) ointment: composition cliochinol 3 gr, olive oil 12 gr,white vaseline qb 100 gr.
Expiration time : 30 days, Antimicrobial and atimicotic API, wide spectrum, useful in skin infections (primary or secondary), used in impetigo and cronicized eczema. It is photosensibilizant, prolonged use an provide sensibilization. In children to be used in limited little surfaces.

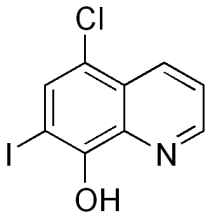


Fig n 44 Cliochinol – Vioformio.

Benzile benzoate 20% m/m in vaselin oil (or olive oil) ointment, for scabies.


Fig n 45 scabia.

Urea cream : from 2%, 5%, 10%, 20%, 30%, hydratant, antipruritic, action on the keratinocite.
Wider use in dermatology :

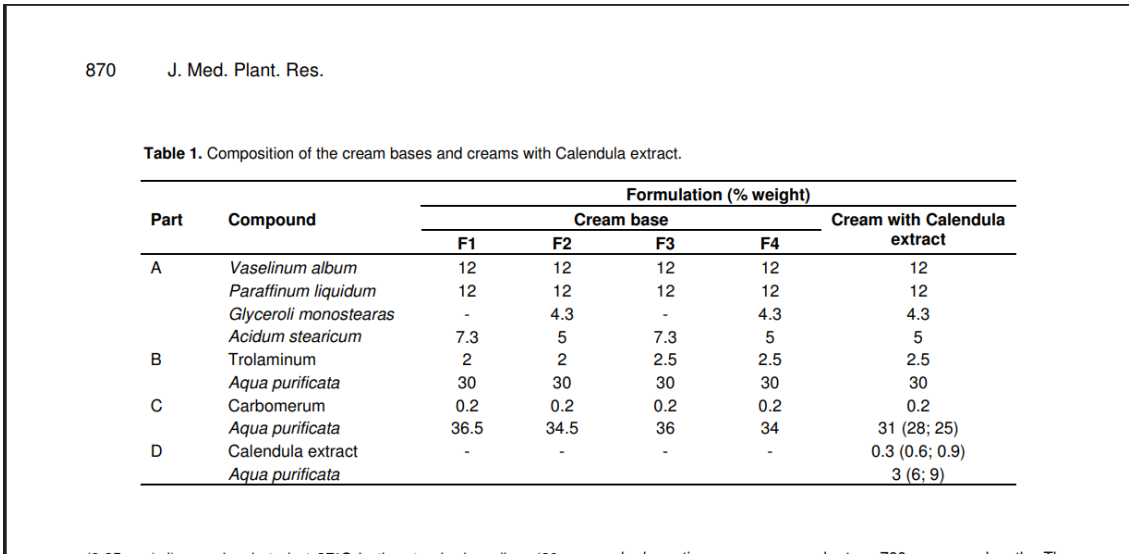
debridement in ipercheratosys lesions; dry skin, dermatitis, cheratosys, psoriasys, xerosi; ittiosi; eczema and other conditions.

iodine ointment
2% w/w iodin and 10% KI dispersed in vaselin and lanolin, Usaed as antiseptic.

Fig n 46 ictiol ointment.

Fig n 47 Permethrin 5% cream.

Metile salicilate ointment – antinflamatory il 10% w/w di metile salicilate in white vaselina.
Glicerolo gel (starch glicerolate): 70% di glicerol,85% and 10% di starch weath in depurated water a
Olea calcareous liniment: lime water 50 gr+ olive oil 50 gr, protection against skin irritations, particularly in babies' bottoms.
Oral gel antimicotic 2% miconazole composition: miconazole 2 gr, polisorbate monolaurate 3 gr, saccarin 0,3 gr, starch 10 gr, flavouring qb, alchool 96 rades 2 gr, glicerin 70 gr, nipagin 0,2 gr warer depurated qb 100 gr.
Calcium Gel 2,5 % (composition calcium gluconate, glicerin, HEC, nipagin, water) is used in the treatment of skin burns caused by Hydrofluoric acid to prevent the extraction of calcium from the wound reducing burn damage.



870 J. Med. Plant. Res.

Table 1. Composition of the cream bases and creams with Calendula extract.

Part	Compound	Formulation (% weight)				
		Cream base				Cream with Calendula extract
		F1	F2	F3	F4	
A	*Vaselinum album*	12	12	12	12	12
	Paraffinum liquidum	12	12	12	12	12
	Glyceroli monostearas	-	4.3	-	4.3	4.3
	Acidum stearicum	7.3	5	7.3	5	5
B	Trolaminum	2	2	2.5	2.5	2.5
	Aqua purificata	30	30	30	30	30
C	Carbomerum	0.2	0.2	0.2	0.2	0.2
	Aqua purificata	36.5	34.5	36	34	31 (28; 25)
D	Calendula extract	-	-	-	-	0.3 (0.6; 0.9)
	Aqua purificata					3 (6; 9)

Fig n. 48 calendula cream composition from J. Bernatoniene et al.

MATERIAL AND METHODS

With an observational point of view various literature is reported and analyzed, imaes and figure help in the general meaning.
Alla literature comes from biomedical scientific data base like Pubmed and other.
An practical local experiece is reported (PC area Hosp)
Afther all this a general conclusion is submitted to the professionals and researcher.

RESULTS

From literature
From https://www.drugs.com/monograph/boric-acid.html
"Although the topical preparations of boric acid containing a concentration of 5% or less pose no great hazard when applied to intact skin, severe poisonings and fatalities have occurred following topical application of the drug, usually when preparations (like powder, ointment, solution) containing high concentrations were applied repeatedly and/or in large amounts to wounds; to burned, abraded, denuded, or macerated skin; or to large areas of skin." (1)

Res Pharm Sci. 2015 Sep-Oct;10(5):378–387.
A comparative histological study on the skin occlusion performance of a cream made of solid lipid nanoparticles and Vaseline Hamed Hamishehkar et al.

"The water content of the epidermis is an main factor in maintaining skin smoothness and elasticity and preventing skin dryness. The Occlusive products can greatly affect skin hydration by forming a barrier on the skin following the topical administration of oil-based formulations."(2)

From
https://www.safecosmetics.org/chemicals/petrolatum/
"The primary concern with petrolatum is the potential contamination with PAHs. The National Toxicology Program considers PAHs as a class to contain reasonably anticipated carcinogens; the International Agency for Research on Cancer lists 14 PAHs as probable or possible carcinogens and one PAH as a known carcinogen. A study on Long Island, NY, found that those women with high levels of PAH-DNA adducts had a 50 percent greater risk of breast cancer. The formation of PAH-DNA adducts, an indicator of PAH exposure, is linked to cancer development. " (3)
23 July 2015 EMA/CHMP/351898/2014 Committee for Human Medicinal Products (CHMP)
Background review for sodium laurilsulfate used as an excipient.

"Reported adverse reactions to SLS in topical pharmaceutical formulations are skin irritation following an prolonged application.

The skin irritancy is thought to be due its surfactant properties, producing disruption of the cell membranes and conformational changes of proteins. In addition, disruptions of the skin barrier by several mechanisms have been described including an direct action on corneocytes leading to their swelling in size, denaturation of keratin structures via direct binding, elevation of stratum corneum pH and alteration of lipid synthesis in this layer, possibly as a result of local pH changes."(4)

J Occup Med Toxicol. 2008 Nov
Safety evaluation of topical applications of ethanol on the skin and inside the oral cavity
Dirk W Lachenmeier
"topically applied ethanol acts as a skin penetration enhancer and may facilitate the transdermal absorption of xenobiotics (carcinogenic contaminants in cosmetic formulations). Ethanol use is associated with skin irritation or contact dermatitis, especially in humans with an aldehyde dehydrogenase deficiency.

After regular application of ethanol on the skin (in the form of hand disinfectants) relatively low but measurable blood concentrations of ethanol and its metabolite acetaldehyde may occur, which are, however, below acute toxic levels. Only in children, especially through the lacerated skin, can percutaneous toxicity occur."(5)

Life (Basel). 2024 Nov Hypersensitivity to Lanolin: An Old–New Problem
Kinga Lis

"Although lanolin has significant dermoprotective properties and when applied to intact skin without inflammatory changes, it lubricates it, improves its lipid barrier, and maintains proper moisture, it can cause contact hypersensitivity when in contact with pathologically changed or damaged skin"(6)

Vahlquist, A., Gånemo, A., & Virtanen, M. (2008). Congenital Ichthyosis: An Overview of Current and Emerging Therapies. Acta Dermato-Venereologica, 88(1), 4–14. https://doi.org/10.2340/00015555-0415
"Hydration, lubrication, keratolysis and antimicrobialsThe therapeutic armature for treating ichthyoses extends from simple balneo-therapy and mechanical removal of scales to highly effective topical formulations and systemic therapy requiring an strict medical attention.

For almost types of ichthyoses, a 1 st-line therapy includes hydration and lubrication, in order to improve the bar-rier function and facilitate desquamation. This can be accomplished by creams and ointments containing low concentrations of salt, urea or glycerol, which increase the water-binding capacity of the horny layer. For ichthyoses with thick scaling and markedly increased stratum corneum thickness, addition of one or more keratolytic agents is needed to decrease cor-neocyte cohesiveness, to promote desquamation and to dissolve keratins and lipids." (7)

Table IV. *Mechanisms of action of common additives in creams and ointments*

Examples
Hydration – NaCl, urea, glycerol
Lubrication – Petrolatum and other lipids
Keratolysis – α-hydroxyacids (AHA), urea (> 5%), propylene glycol, salicylic acid, N-acetylcysteinamide
Modulators of differentiation – Retinoids, calcipotriol
Antimicrobials

from DOI: https://doi.org/10.2340/00015555-0415
Ephrem Mebratu Dagnew et al

" 423 prescriptions containing dermatological products for compounding were analyzed. female (82.1%) and aged 30-64 years (46.3%). Melasma (82.9%), acne vulgaris (68.6%), acute dermatitis (63.27%), and Rosacea (61.54%) were the four top dermatological diseases for which compounding preparations were prescribed. 56.26% contained a combination of 2 drugs. Most compounded dosage was semisolid preparations (95.98%), while 17 (4.02%) were liquids. Salicylic acid (35.39%) was the most frequently prescribed active ingredient, followed by Clobetasone (13.03%) and Betamethasone (10.01%). Vaseline (47.62%) and Nivea cream (44.3%) were the most commonly used excipients for compound preparations. Hydroquinone (4%) with Nivea cream (30gm) (17.0%), followed by salicylic acid (5%) + Betamethasone (75 g) + Vaseline (20 g) (10.6%) were the most commonly prescribed dermatological formulations." (8)

Nana Yaa T Amakye et al
"There has been an increase in uniquely named emollients between 2017 and 2021, from 109 to 126 differentkids of products. Creams and ointments remain the most recommended formulation types. Interestingly, the top 2 most recommended leave-on emollients (Dermol 500 lotion and Dermol cream) possess antimicrobial properties. However, most formularies (81% for Dermol 500 lotion, 72% for Dermol cream) listing these qualify their use by indication." (9)

Anikó Rita Marik et al
"Mean patient-assessed mSSS at the baseline was 6.6 ± 1.9 and was significantly improved overall and in the ointment and suppository groups individually by -4.6 ± 2.0, -4.4 ± 1.8, and -4.8 ± 2.2, respectively ($p < 0.0001$). Investigator-assessed mean baseline symptom score was 18.1 ± 3.9 and improved by -7.1 ± 4.5, -6.9 ± 5.4, and -7.3 ± 3.5, respectively ($p < 0.0001$). Investigator-assessed symptoms of pressure sensitivity, swelling, and discharge were improved to the greatest extent. Hemorrhoid grade was improved in the 38% of patients at the end of treatment. Compliance with treatment was 97.4% and patient satisfaction with application and onset of action was high (81.3% and 76.2%, respectively). Both the ointment and the suppository were well tolerated. "(10)

Michele Antonelli et al
"In the United Kingdom, two traditional ointment formulations of TB® are Red TB® and White TB® (Shih et al., 2015). Red TB® is recommended by the producer to soothe sore and aching muscles, and it is reported to contain camphor (11.0%), menthol (10.0%), clove oil (5.0%), cajuput oil (7.0%), as well as cinnamon oil, dementholized mint oil, yellow soft paraffin and hard paraffin (Tiger Balm Red, 2014). White TB® is recommended by the producer to relieve pain of the tension headaches, and it is reported to contain camphor (11.0%), menthol (8.0%), clove oil (1.5%), cajuput oil (13.0%), as well as dementholized mint oil, yellow soft paraffin and hard paraffin (Tiger Balm White, 2014)." (11)

Ann Allergy Asthma Immunol. 2022 Jan 20 doi: 10.1016/j.anai.2022.01.012
Optimizing Emollient Therapy for Skin Barrier Repair in Atopic Dermatitis
Peter M Elias
"Classic moisturizing products, like Aquaphor and Eucerin, are water-in-oil formulations, enriched in occlusive ingredients, such as petrolatum or lanolin. Their hydrophobic nature allows them to coat the surface of the skin with a water-repellent layer that impedes the bidirectional movement of water across the skin. By blocking the movement of water out of the skin, these agents effectively, though temporarily, trap water within the stratum corneum, ameliorating the xerosis that is characteristic of AD and other, age- and seasonally associated eczematous disorders. By improving the hydration of the stratum corneum (SC), they can dampen inflammation. It is important to note that these occlusive moisturizers are inert ingredients that do not address the underlying biochemical abnormalities in AD.

Many moisturizers also contain one or more humectants, such as glycerin, which imbibe water from the surrounding atmosphere. Because AD typically flares during winter months, when indoor humidities typically

decline drastically due to forced-air and radiant heating, humectants are often paired with an occlusive agent, such as petrolatum, to protect against further drying of the skin, which could otherwise exacerbate AD symptoms.

Many moisturizers also incorporate emollient vegetable oils, Like as coconut, jojoba or avocado oils. While these agents can impart an elegant texture to such kind of formulations, they provide no scientifically proven benefits, with 1 key exception - certain vegetable oils, such as sunflower, safflower, borage or corn oil, sea buckthorn oil, which are enriched in the essential fatty acid, linoleic acid, and/or gamma-linolenic acid. Components of these oils can: improve barrier function) enhance barrier function and reduce inflammation via activation of peroxisome proliferator-activated receptors (PPARs); and/or even provide nutritional benefits in mice and human neonates.

Allergic sensitization can occur not only in patients treated with peanut oil, but also with sunflower seed oil. Botanical ingredients are increasingly being added to moisturizers, and some of these can be beneficial. In example, chamomile contains anti-inflammatory substances, such as apigenin, which improve symptoms in AD animal models.

It should be noted that a few popular over-the-counter moisturizers also include a skin-identical or synthetic ceramide, or a ceramide mimetic. Although topical ceramides, when provided at sufficient concentrations, can improve both permeability barrier function and stratum corneum hydration, their concentration levels in most formulations is usually too low to impart measurable benefits.The term ‘ceramide’ often appears to be included in such preparations for marketing purposes. Most importantly, as described below, if the ceramide is provided without the addition of the other two key physiologic lipids at an appropriate ratio (with cholesterol and 1 or more free fatty acids), barrier function deteriorates rather than improves. Studies have shown that all three constituents must be provided together in an equimolar ratio to restore barrier function after disruption of normal skin.”(12)

REVIEW phytotherapy research
Devil's claw (Harpagophytum procumbens) and chronic inflammatory diseases: A concise overview on preclinical and clinical data
Luigi Menghini, Lucia Recinella, Sheila Leone, Annalisa Chiavaroli, Carla Cicala, Luigi Brunetti, Sanda Vladimir-Knežević, Giustino Orlando, Claudio Ferrante
First published: 04 July 2019 https://doi.org/10.1002/ptr.6395 view metrics
Luigi Menghini and Lucia Recinella equally contributed to the manuscript.
“Devil's claw (Harpagophytum procumbens) is an herbaceous plant, which can be found in the arid steppes of South Africa, particularly in the Kalahari Desert zone. As traditional medicine, devil's claw has been long used in the forms of infusions, decoctions, tinctures, powders, and extracts. The main compounds of devil's claw are iridoid glycosides, like as harpagoside, harpagide, and procumbide, which are present in the plant tubers.

Chemical constituents such as sugars (mainly the tetrasaccharide stachyose), triterpenoids (oleanolic and ursolic acid), phytosterols (primarily β-sitosterol), aromatic acids (caffeic, cinnamic, and chlorogenic acids), and flavonoids (luteolin and kaempferol) can be found in the plant.” (13)

Smith A, Matthews O. Aromatic ointments for the common cold:
what does the science say? Drugs Context. 2022;11:2022-5-6.
https://doi.org/10.7573/dic.2022-5-6
“Menthol is thought to act by signalling through the respiratory airway TRPM8 receptor, which senses cold air. This mechanism may explain why the menthol creates a sensation of eased nasal breathing, even though airflow is objectively unchanged. A similar mechanism may be considered for the interaction of menthol, eucalyptus and camphor with TRPV1 and TRPA1, which are involved in the cough response. Study works have been conducted that assessed the effects of various aromatics, namely camphor, oil of eucalyptus, oil of turpentine, cedar leaf oil, myristica oil and thymol, as single agents in only 1 study or in combination with menthol in a number of others. Menthol has been reported to have antitussive effects in induced cough models and in children with cold-associated nocturnal cough. Proprietary preparations of aromatic ointments that contain menthol, eucalyptus oil and camphor have been assessed in well-conducted clinical trials, demonstrating an clear beneficial effects in the alleviation of localized cold symptoms, including the sensation of nasal congestion, nocturnal cough and cold-associated associated sleep difficulties, whilst having no impact on objective measurements. “ (14)

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IMPACT OF TITANIUM DIOXIDE CONCENTRATION ON WHITECAST FORMATION IN DAY CREAM FORMULATION
Indah Puspita Sari,Rika Oktavia
DOI: https://doi.org/10.35472/ijcos.v3i1.2271
“Titanium dioxide (TiO_2) is widely used in day cream formulations as a physical UV ultraviolet filter due to its broad-spectrum protection and stabilizing properties.”(15)
From NIH
“tobramycin ophthalmic ointment 0.3% is a sterile topical ophthalmic antibiotic formulation prepared specifically for topical therapy of the external ophthalmic infections.

Each gram of TOBREX (tobramycin ophthalmic ointment) 0.3% contains: Active: tobramycin 0.3% (3 mg). Preservative: chlorobutanol 0.5%. Inactives: mineral oil, white petrolatum.

Tobramycin is an water-soluble aminoglycoside antibiotic active against a wide variety of gram-negative (G-) and gram-positive (G+) ophthalmic pathogens"(16)

Wien Med Wochenschr. 1997.[Viral exanthematic childhood diseases] R Allwinn 1, H W Doerr
"Exanthem is defined as multiple, inflammatory skin alteration with a hematogenic, lymphogenic or neurogenic origin. The so called exanthematic children's diseases are measles, mumps, rubella, varicella, erythema infectiosum (fifth disease) and in the past small pox."(17)

https://gpnotebook.com/pages/infectious-disease/exanthemata-bacterial
"Bacterial exanthemata include: streptococcal - scarlet fever,meningococcal, staphylococcal - toxic shock, scalded skin syndrome, scarlet fever,Lyme disease, syphilis" (18)

J Clin Exp Dent. 2013 Oct. doi: 10.4317/jced.51121
Toluidine blue staining as an adjunctive tool for early diagnosis of dysplastic changes in the oral mucosa Shambulingappa Pallagatti et al

"Prognosis of oropharyngeal squamous cell carcinoma depends on early diagnosis, despite advanced surgical techniques, the 5-year survival rate remains about 40-50%. Unfortunately, it is usually detected when it becomes symptomatic. This requires treatment which gives rise to a high rate of morbidity and mortality and early detection of oro-pharyngeal pre-malignant lesions is important to improve the survival rate and the quality of life. Since dysplasia and in situ carcinoma contain much more DNA and RNA than the normal surrounding epithelium, the use of in vivo staining, by means of toluidine blue dye, is based on the fact that it is an acidophilic dye that selectively stains acidic tissue components such as DNA and RNA. Toluidine blue TB staining is considered to be sensitive in identifying early oro-pharyngeal premalignant and malignant lesions" (19)

Experimental part
In this part is reported a practical experience Hospital departmental galenic lab PC area (covered about 280.000 citizens) and in other private pharmacy:
about 750 galenics od magistral formula prepared annually (10% topic preparation)

List of the preparation : zinc oxide crea, lassar Paste, Benzile benzoate oil and ointment, gels (lat gel), xylocain oral gel Urea cream and paste, lugol strong, vioformio cream, Tricoloroacetic acid solution, Minoxidil hair solution,Koh dermatologic solution, AlCl3 solution, sodium bicarbonate sachets for dermatological bath., acetic acid solution for dermatological wounds, hydrogen Peroxide solutions, sodium ipoclorite solutions, antiseptic hand wash gels and solution, alchool 70 grades for antiseptic use, salicilic vaseline, boric alchool 3%, eosine solutions, K permanganate solutions, Permetrine cream, toluidin solution for odontoyatry, clacium gel dermatologic antidothes, Peg 400 antidothes, DMSO solution as antidothes, arentum nitrate sol 1: 1000, boric eucerin 2%, sulpho salicilic pomate, mix of 3 oil, iodated glicerin 4%, ALA cream
Kind of use : pediatric, adult, reagents, disinfectants – antiseptics
Time of observation :from 2008 to 2025 (external laboratory from 2014 to 2019)
Quality control of the raw material : all approved
Rejection or raw materials : not reistered all, all accepted.
Non conformity (major) : not registered officially related APIs or excipients or veichle or container of final product, or due by adeverse event officially registerd by the FV. office

DISCUSSION
In this work are reported with an chemico-pharmaceutical point of view the various veicle and excipients generally used in the galenic dermatology. (it can be considered multidisciplinary focused even if are submitted basics concepts.)

This approach can be usefull for the the healthcare professionals involved in the therapy of various dermatologic condition: from physicians -dermatology prescription, since to the topic remedy provided by the pharmacist without the need of a medical order or the cosmetic use.

This is a real complex world and the hystory of the galenic (art and science) help in relevant way.

Every veicle used for compounding in pharmacy coming from the natural world (animal or vegetal) or from mineral or sysntetic world have its specific characterisctics (chemico – physical, compatibility, advantages or disvantages since also irritation if prolonged used in sensible patients).

The same the efficiency in release the APIs or the patients accettability are take in consideration.

A deep knowledge of this properties help in finding the best option for a topic treatement: efficacy, safety, technology of the preparation.

The various images and figure reported in this work help in the general meaning.

Factors to Considering in Choosing a Base: topic or percutaneous effect needed

Kind of lesion : dry or exudative, acute or chronic, primary or secondary, immunomediated, infective parassitic or since neoplasm.
API Solubility – (Water-soluble drugs may need oil-based carriers for occlusion or vice versa.)
Desired APIs Release Rate – Occlusive property needed ot to avoid : Occlusive bases offer sustained release instead creams offer faster release.
The kind of effect to be requested : keratolitic, hydratant, softner, refresching, protective reducing, antimicrobials, antiprarassitic and so on. Not irritant or sensibilizant or allergizant propersties are commonly requested.
Stability of the drug in the ointment, microbiological requirement, expiry time.
Site of Application : the Hairy areas or oozing wounds demand different textures and absorption rate.
Way of application: from the symply application to the need of bandage.
Patient Preference – Non-greasy bases often improve the global compliance.
Regulatory Considerations – Inactive ingredients must meet the pharmacopeial standards and must to be safe and not irritant. Packaging Compatibility – Some bases can react with the tubes or container materials.
Between some characteristic searched : occlusive or not, good drug release profile, emollient effect, protective, greasiness, washability, preservation need.

CONCLUSION

Topic dermatological therapy is relevant for therapeutic or cosmetic intent.

In example also in prevenction of the melanoma is recomended to protect the skin with adeguate sun screen
In the choice of the preparation it must to be considered the kind of patients, the patology and its comorbidity, the kind of skin zone to be treated, its breadth, the APIS charcteristics the excipients to be used and the kind of preparation (pharmaceutical form).

Special attention is to to be considerd for newborns and small children for their skin characteristics.

It is fundamental to know the characteritics of the various veicles and bases to be used and the preparation to be obtained : from lipofilic, to idroficlic properties, solubility of the APIs, HLB values needed, PH, fusion point, interactions (with APIs and other excipients), irritation properties, the chemical structure, the origin (natural mineral, syntetic) and all other parameter like the need to use cosolvents, preservatives or antioxidants.
APIs partition's between the veicle and the skin.

Relevant is the technique used to prepared both in the galenic pharmacy or in pharmaceutical industry.

The APIs must to be distributed in omogeneous way in the veicle.

The impurity and microbiological aspetcs and the expiration time are also fundamental for a safe use.

The preservants, antioxidants and the caractheristics of the primary container are fundamental for a right Conservation.

The condition to be treated can be acute or chronic, primary or secondary lesions, infected or not and the surface and zone to be treated can influence the choice of the specific pharmaceutical form, APIs and excipients to be used. the choice for an non occlusive or occlusive product is relevant according the kind of lesion and its stage.

The therapy can be etiologic (antimicrobials) or empiric but in every way finally it is request to be efficacy and safety.

The therapy must consider : formulation and veichle, drug concentration, frequency of application, quantity to be used, site of application, timing of application.

Even if the topic therapy is a physician competence the knowledge in this topics are useful also to other helathcare professionals like pharmacists in their galenic activity (and for products that not need a physician prescription or cosmetics).

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