Drugs and the skin

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The main reference: Bennett et al (editors). Clinical pharmacology, Edinburgh …, Churchill Livingstone, Eleventh edition

Drug absorption through the skin is determined by the:

- **type of vehicle** in which the drug is presented
- **physicochemical properties** of the drug (lipid-soluble vs water soluble)
- **degree of hydration of stratum corneum** (hydration increases diffusion)
- **site of application:** absorption is low in sole of foot and palm of hand
- **state of skin**: in damaged skin (as by inflammation, burn,..) absorption increases
- **occlusive dressing** can increase absorption by 10-folds (e.g. impermeable plastic membrane, plastic pants for babies)

Topically-used substances for skin diseases

1. Keratolytic agents: used to destroy unwanted tissue e.g. warts, corns. Examples: salicylic acid and trichloroacetic acid. Resorcinol and sulphur are mild keratolytic agents used in acne.

2. **Dithranol** (Anthraline) has anti-proliferative and anti-inflammatory effects on psoriatic and normal skin

3. Tars: are mildly antiseptic, antipruritic, and inhibit keratinization, used in psoriasis.

4. Zinc oxide: provides mild astringent, barrier and occlusive actions. Calamine; is a basic zinc carbonate; its pink color is due to added ferric oxide. It has a mild astringent action.

5. Psoralins (occurs naturally in some fruits and vegetables such as common fig, celery, …) e.g. methoxsalen; are used to induce photochemical reactions in the skin.

Topical or systemic administration of psoralens with subsequent exposure to ultra-violet light type A (UVA)(called PUVA therapy), results in an erythematous reaction; melonocytes are activated and pigmentation occurs over the following week; used to treat depigmenting conditions e.g. vitiligo.

In addition, in presence of UVA, psoralen interacts with DNA to inhibit its Synthesis, and, therefore, used in severe psoriasis.

Psoriasis

In psoriasis, there is increased epidermal proliferation (x10), inflammation of epidermis and dermis and increased number of cells containing abnormal keratin.

Drugs are used in treatment of psoriasis to:

a) dissolve keratin (keratolysis)
b) inhibit cell division

Drugs used in treatment of psoriasis include:

Emollient such as aqueous cream.
Elimination of proliferating cells e.g. dithranol (antimitotic).
Tar is an alternative to dithranol, but less effective.
Topical adrenal corticosteroids
Vitamin D derivatives e.g. calcipotriol (inhibits cell proliferation and encourage cell differentiation).
Vitamin A derivatives e.g. acitretin (inhibits psoriatic hyperkeratosis, it is teratogenic like other vitamin A derivatives)
UVB light
Psoralen followed by UV light (PUVA)
Ciclosporin
Folic acid antagonists e.g. methotrexate

Topical Adrenal Steroids in Psoriasis: Occlusive therapy can be very effective, but rebound may be severe following withdrawal
Systemic corticosteroids should be avoided in psoriasis because high doses are needed to suppress the disease, which is liable to recur in a more severe form when treatment is withdrawn.

Acne vulgaris

Acne vulgaris results from disordered function of pilosebaceous follicle where. Abnormal keratin and sebum form debris that plugs the mouth of the follicle(Sebum production is androgen dependent). The debris is colonized by bacteria (propionibacterium acnes). Bacterial action releases inflammatory fatty acids from the sebum resulting in inflammation

Treatment of acne

1. **Mild keratolytic (peeling) agents** to unblock pilosebaceous ducts e.g. benzoyl peroxide, sulfur, salicylic acid, azelaic acid
2. **Systemic or topical antimicrobial drugs** such as tetracyclines (e.g. doxycycline) and erythromycin (systemically) and clindamycin (topically). They are used over months. Benefit is due to suppression of

bacterial lipolysis of sebum, thus, inhibiting the generation of inflammatory fatty acids.

3. **Vitamin A (retinoic acid) derivatives** reduce sebum production and keratinization

   Tretinoin (Retin-A) is applied topically (but not with other keratolytics). It should be avoided in sunny weather and in pregnancy. Benefit is seen in weeks. Isotretinoin orally is highly effective. But it is a serious teratogen. Women of child-bearing potential should be pregnancy tested before treatment and use contraception for 4 weeks before, during and for 4 weeks after cessation.
4. **Hormone therapy** to reduce androgen production or effect, by using: estrogen, antiandrogen (cyproterone), combination of estrogen and cyproterone.

Skin lightening agents

Hydroquinone

Hydroquinone is used to inhibit melanin production.
Topical hydroquinone comes in 2% to 4% (or more) alone or in combination with tretinoin 0.05% to 0.1%.
They are used to prevent sun- or hormone-induced melasma.
It can only disrupt the synthesis of melanin hyperpigmentation.
It has been banned in some countries (e.g. France) because of fears of a cancer risk.

Hydroquinone can be **irritant**, particularly in higher concentrations of 4% or greater and particularly when combined with tretinoin. A corticosteroid can be included with them as an antiinflammatory.

Antiseptics

Antiseptics are antimicrobial substances that are applied to living skin to reduce the possibility of infection
Disinfectants destroy microorganisms found on non-living objects

Examples of antiseptics

Alcohol, Benzalkonium (used e.g. in antiseptic towels), Boric acid (used e.g. in eyewashes), Chlorhexidine, Hydrogen peroxide, Iodine (Povidone-iodine), Phenolic compounds

Alcohols

The most commonly used is ethanol (60-90%). One use is to disinfect the skin before injections are given.

Chlorhexidine
is effective on both Gram-positive and Gram-negative bacteria.
The mechanism of action being membrane disruption.
Chlorhexidine is also useful against fungi and enveloped viruses.
Chlorhexidine is harmful in high concentrations, but is used safely in low concentrations in many products, such as mouthwash and contact lens solutions

Hydrogen peroxide
Used as a 6% solution to clean and deodorize wounds and ulcers. The strong oxidization may cause scar formation and delays healing. Gentle washing with mild soap and water or rinsing with sterile saline is a better practice.

Iodine
Tincture of iodine (alcoholic solution) and Lugol's iodine solution are no longer recommended to disinfect minor wounds because they induce scar tissue formation and delay healing.

Povidone-iodine (a complex of povidone, a water-soluble polymer, with triiodide anions, containing about 10% of active iodine) are better tolerated, don't negatively affect wound healing, and leave no persistent effect.
The great advantage of iodine antiseptics is their wide range of antimicrobial activity, killing all principal pathogens and, if given enough time, kill even spores.

Phenol (carbolic acid) compounds
Phenol is germicidal in strong solution, germistatic in weaker solutions. They are used for pre-operative hand cleansing and in the form of a powder as an antiseptic baby powder. Also used in mouthwashes and throat lozenges, where it has a painkilling effect as well as an antiseptic one.