Dermatologic pharmacology :

i) Drugs for microbial infections :

1) Bacterial infections .
Topical Antibacterial Agents :
against Gram (+) :
Bacitracin , Gramicidin.
Against Gram (-) :
Polymyxin B , Neomycin , Gentamicin.

Topical Antibacterials in Acne :
Clindamycin , Erythromycin, Metronidazole , Sodium sulfacetamide.

2) Topical Antiviral Agents :
Acyclovir , Valacyclovir , Penciclovir , Famciclovir.

3) parasitic infections :
Ectoparasiticides :
Permethrin , Lindane, Crotamiton , Sulfur, Malathion.
Drugs for Leishmania:
Sodium Stibogluconate , Amphotericin B , Miltefosine , Pentamidine .

4) Fungal infections :
topical :
Azole Derivatives , Ciclopirox Olamine. Naftifine and Terbinafine ,Tolnaftate, Nystatin and amphotericinB
oral :
Azole Derivatives , Griseofulvin , Terbinafine

ii)drugs interfere with the immune system :

Immunomodulators :
Imiquimod , Tacrolimus , Pimecrolimus.

Drugs for Psoriasis :
Acitretin , Tazarotene , Calcipotiene , Biologic Agents : Alefacept, Etanercept .

iii) Drugs interfere with the inflammatory rxn :

Anti-inflammatory Agents :
Topical Cortcosteroids , Tar compounds

iv) Drugs for skin disorders :

Agents affecting Pigmentation :
- hydroquinone, Monobenzone , Mequinol.
- Trioxsalen , Methoxsalen.

Sunscreens and Sunshades :

Acne Preparations :
Retinoic Acid and Derivatives , Isotretinoin(Accutane) , Benzoyl Peroxide, Azelaic Acid .

Keratolytic and Destructive Agents :
Salicylic acid , Propylene Glycole , Urea , Podophyllum Resin and Podofilox , Flurouracil , Nonsteroidal Anti-inflammatory Drugs(NSAIDs) , Aminolevulinic Acid .

Antipruritic Agents :
Doxepine , Pramoxine

Trichogenic Agents :
Minoxidil (Rogaine) , Finasteride (Propecia)

Antitrichogenic Agent :
Eflornithine.

i) Drugs for microbial infections :

1) Bacterial infections :

Topical Antibacterial :

- against the Gram(+) :
Bacitracin , Gramicidin.

-against the Gram (-) :
Polymyxin B , Neomycin , Gentamicin

Topical Antibacterial in Acne :

- Clindamycin.
10% absorbed , so possibility of Pseudomembranous colitis.
- Erythromycin
- Metronidazole
- sodium sulfacetamide

Antilepromatous Drugs :

Dapsone and Sulphones :

Related to sulphonamides.
Inhibit folate synthesis.
Resistance develops.
Combined with Rifampin and Clofazimine.
Also used for Pn. Jeroveci in AIDS patients.
Well absorbed and distributed.
Retained in the skin, muscle, liver and kidney.

Side effects :

Hemolysis, particularly in G-6-PD deficiency.
GIT intolerance
Fever, Pruritus, Rashes.
Erythema Nodosum Leprosum : suppressed by steroids or thalidomide.

Rifampin :
Discussed with antituberculous drugs.

Clofazimine :

Binds to DNA.
Stored widely in RES and skin.
Released slowly from storage sites, t 1/2 = 2 months.
Given for sulphone- resistant or intolerant cases.
Causes skin discoloration (red-brown to black) and GIT intolerance.

2) Viral infections :

#Topical Antiviral :

Acyclovir, Valacyclovir , Penciclovir, Famciclovir.
- they are synthetic Guanine analogs .
- used against HSV .
- Ointments and creams are useful for recurrent orolabial HSV.

3) parasitic infections :

Ectoparasiticides :

- Permethrin :

- against Pediculus humanus, Pthirus pubis, and Sarcoptes scabiei .
- in cases of Pediculosis: cream applied for 10 minutes and then rinsed off with warm water.
- in cases of Scabies: cream applied for the whole body for 8-14 hours.

- Lindane(Hexachlorocyclohexane) :

- 10% absorbed and concentrated in fatty tissues.
- Can cause neurotoxicity and hematoxicity.

- Crotamiton.

- Sulfur.

- Malathion.

drugs for Leishmania :

* Leishmania species:

L.tropica causes: Cutaneous leishmaniasis or oriental sore.
L. brazeliensis causes: Mucocutaneous leishmaniasis.
L. Donovani causes: Visceral leishmaniasis

- Sodium Stibogluconate :
Pentavalent antimonial

- mechanism of action :
Binds to SH groups on proteins.
Typical preparations contain 30% to 34% pentavalent antimony (الإثمد) by weight as well as m-chlorocresol added as a preservative.
Also, inhibits phosphofructokinase

- pharmacokinetics :
Local, IM or slow IV, irritant.
Given for 20-28 days.
Drug of choice for all forms of leishmaniasis.
Resistance is increasing, especially in India.

- side effects :

Cough, V, D, myalgia, arthralgia, ECG changes, Rash, Pruritus.

Amphotericin B :

Antifungal agent, difficult to use, and toxic.
Alternative therapy for visceral leishmaniasis, especially in areas with high resistance.

Miltefosine :

used for : For visceral leishmaniasis.
Given : orally, for 28 days.
Causes : V & D, hepatotoxicity, nephrotoxicity, and it is teratogenic

Pentamidine :

mechanism of action :
Inhibits DNA replication. Also, DHF reductase inhibitor .
Binds avidly to tissues, not the CNS.

Given :
IM or IV injection and Inhalation .

used for :

Leishmaniasis:
Alternative to Na stibogluconate .

Pneumocystis jiroveci:
Treatment and prophylaxis of patients who cannot tolerate or fail other drugs.

Trypanosomiasis:
For early hemolymphatic stage .

Adverse Effects :
Rapid Infusion: Hypotension, tachycardia, dizziness.
Pain at the injection site.
Others: Pancreatic, Renal, and Hepatic toxicity.

4) Fungal infections :

Topical Antifungal :

- Azole Derivatives :

-used against :
dermatophytes (epidermophton, microsporum, and trichophton)
yeasts , including Candida albicans and Pityrosporum orbiculare .

- Ciclopirox Olamine.
- Naftifine and Terbinafine .
- Tolnaftate.

- Nystatin and amphotericin B :
- used Only for Candida albicans.
-Available as topical preparations, oral suspension, or vaginal tablets

Oral Antifungal :

- Azole Derivatives :
Fluconazole. Itraconazole. Ketoconazole.

- Mechanism of action :
Affect the permeability of fungal cell membrane through alteration of sterol synthesis.

- Affectivity against :
in systemic mycosis, mucocutaneous candidiasis, and other cutaneous infections.

- Systemic side effects :
hepatitis and liver enzyme elevations, and interactions.

- Griseofulvin :

Affectivity against epidermophyton, microsporum, and trichophton.
- Requires prolonged treatment:
4-6 weeks for the scalp.
6 months for fingernails.
8-18 months for toenails.

- Has many side effects.

Terbinafine :

Affectivity against onchomycosis.

- 6 weeks for fingernails.
- 12 weeks for toenails.

ii) Drugs interfere with the Immune system :

1) Immunomodulators :

- Imiquimod:

used For :
external genital and perianal warts.
Actinic keratosis on the face and scalp.
Primary basal cell carcinoma.

mechanism :
Stimulates peripheral mononuclear cells to release interferon- ά and to stimulate macrophages to produce interleukins-1,-6, and -8 and tumor necrosis factor-ά.

- Tacrolimus:

-Pimecrolimus.

Useful for : atopic dermatitis.

mechanism : Inhibit T-lymphocyte activation and prevent release of inflammatory cytokines and mast cell mediators .

2) drugs for psoriasis :

- Acitretin:

Related to isotretinoin.
Given orally.
Hepatotoxic and teratogenic.
Patients should not become pregnant for 3 years after stopping treatment, and also should not donate blood .

- Tazarotene:

Topical.
Anti-inflammatory and antiproliferative actions.
Teratogenic. Also, can cause burning, stinging, peeling, erythema, and localized edema of skin.

- Calcipotiene:

Synthetic vitamin D3 derivative .

- Biologic Agents:

--Alefacept:
Immunosuppressive dimer fusion protein of CD2 linked to the Fc portion of human IgG1 .

--Etanercept:
Dimeric fusion protein of TNF receptor linked to the Fc portion of human IgG1.

iii) Drugs interfere with inflammation (anti-inflammatory drugs)

1) Topical corticosteroids :

Types :

Hydrocortisone.

Prednisolone and Methylprednisolone.

Dexamethasone and Betamethasone.

Triamcinolone.

Fluocinonide.

Absorption :

1% of hydrocortisone applied to the ventral forearm.
0.14 times of hydrocortisone applied to the plantar foot.
0.83 times of hydrocortisone applied to the palm.
3.5 times of hydrocortisone applied to the scalp.
6 times of hydrocortisone applied to the forehead.
9 times of hydrocortisone applied to the vulvar skin.

dermatologic disorders very sensitive to steroids :

Atopic dermatitis.
Seborrheic dermatitis.
Lichen simplex chronicus.
Pruritus ani.
Allergic contact dermatitis.
Eczematous dermatitis.
Psoriasis

Adverse effects :

Suppression of pituitary-adrenal axis.
Systemic effects.
Skin atrophy.
Erythema.
Pustules.
Acne.
Infections.
Hypopigmentation.
Allergic contact dermatitis.

2) Tar compounds :

used for :

Mainly for psoriasis, dermatitis, and lichen simplex chronicus.

adverse effects :

Can cause irritant folliculitis, phototoxicity, and allergic contact dermatitis.

iv)Drugs for skin disorders :

1) Agents affecting Pigmentation .
2) Sunscreens and Sunshades .
3) Acne Preparations .
4) Keratolytic and Destructive Agents .
5) Antipruritic Agents .
6) Trichogenic Agents .
7) Antitrichogenic Agent .

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1)Agents affecting Pigmentation:

#drugs to reduce hyperpigmentation:

Hydroquinone , Monobenzone , Mequinol .

- mechanism of action :

Reduce hyperpigmentation of skin by inhibiting the enzyme tyrosinase which will interfere with biosynthesis of melanin.

- Side effects :

Monobenzone may be toxic to melanocytes resulting in permanent depigmentation.

drugs for repigmentation :

- they are Psoralens (Trioxsalen , Methoxsalen).

- used for :
repigmentation of depigmented macules of vitiligo (البهاق) .

- mechanism of action :
Must be photoactivated by long-wave-length ultraviolet light (320-400nm) to produce a beneficial effect.
They intercalate with DNA.

- side effects :
Can cause cataract and skin cancer.

2) sunscreens and sunshades :

- Sunscreens :

absorb UV light.
Examples are : para amino benzoic acid (PABA) and its esters.

- Sunshades :

opaque materials that reflect light, like titanium dioxide.

Useful in :
polymorphous light eruption, lupus erythematosus, and drug –induced photosensitivity .

3) Acne preparations :

Retinoic Acid (Trertinoin) and Derivatives:

- is the acid form of Vitamin A.

- mechanism of action :
Stabilizes lysosomes, increases RNA polymerase activity, increases PGE2, cAMP, and cGMP levels, and increases the incorporation of thymidine into DNA.
Decreases cohesion between epidermal cells and increases epidermal cell turnover.This will result in expulsion of open comedones and the transformation of closed comedones into open ones.
Also, promotes dermal collagen synthesis, new blood vessel formation, and thickeningof the epidermis, which helps diminish fine lines and wrinkles.

- side effects :
Can cause erythema and dryness .
Tumerogenic in animals.

Isotretinoin(Accutane):

- used for :
Restricted for severe cystic acne resistant to standard treatment.
given Orally .

- mechanism of action :
Inhibits sebaceous gland size and function.

- side effects :
dryness, itching, headache, corneal opacities, pseudotumor cerebri, inflammatory bowel disease, anorexia, alopecia, and muscle and joint pains. Also lipid abnormalities.
It is Teratogenic.

Benzoyl Peroxide:

- mechanism of action :
Penetrates the stratum corneum or follicular openings and converted to benzoic acid within the epidermis and dermis.

- Has antimicrobial activity against P. acnes and peeling and comedolytic effects.

- Can be combined with erythromycin or clindamycin.

- Potent contact sensitizer.

- side effects :
Can cause bleaching of hair or colored fabrics.

Azelaic Acid :

- mechanism of action :
Has antimicrobial activity and inhibits conversion of testosterone to dihydrotetosterone.

4) Keratolytic and Destructive Agents :

- 7 drugs :
Salicylic acid , Propylene Glycole ,Urea , Podophyllum Resin and Podofilox, Flurouracil , Nonsteroidal Anti-inflammatory Drugs , Aminolevulinic Acid .

Salicylic acid :

- mechanism of action :
Solubilizes cell surface proteins resulting in desquamation of keratotic debris.
Keratolytic in 3-6% concentration, but destructive in higher concentrations.

- Side effects :
Can result in salicylism due to systemic absorption.
Locally, can cause urticaria, anaphylactic and erythema multiforme reactions, irritation, inflammation, and ulceration.

Propylene Glycole :

- Usually used as a vehicle for organic compounds.
- Used alone as a keratolytic agent in concentrations of 40%- 70% , with plastic occlusion, or in gel with 6% salicylic acid.

- pharmacokinetics :
Minimally absorbed, oxidized in liver to lactic acid and pyruvic acid .

- side effects :
Develops an osmotic gradient through the stratum corneum, thereby increasing hydration of the outer layers of skin.

Urea :

-properties :
Has a humectant activity, i.e. softening and moisturizing effect on the stratum corneum.
Increases water content as a result of its hygroscopic characteristics .
Decreases the unpleasant oily feel of dermatologic preparations.

- pharmacokinetics :
When absorbed, it is excreted in urine.

Podophyllum Resin and Podofilox:

- origin :
An alcoholic extract of Podophyllum peltatum(Mandrake root or May apple).
- Used for : the treatment of condyloma acuminatum and other verrucae.

- mechanism of action :
Cytotoxic activity with specific affinity for the microtubule protein of the mitotic spindle.

- side effects :
Can cause N, V, muscle weakness , neuropathy, coma , and even death.

Flurouracil :

- Used in :
multiple actinic keratosis .

- mechanism of action :
it's an Antimetabolite that resembles uracil .
it inhibits thymidylate synthetase, thus interferes with DNA and may be RNA synthesis.

Nonsteroidal Anti-inflammatory Drugs (NSAIDs) :

- 3% gel formulation diclofenac.

Aminolevulinic Acid :

- Used in :
actinic keratosis.

- mechanism of action :
After topical application(20%) and exposure to light, produces a cytotoxic superoxide and hydroxyl radicals.

5) Antipruritic Agents :

-Doxepine :

Potent H1 and H2 – receptor antagonist.
(H1 , H2 = histamine receptors) .
Can cause drowsiness and anticholinergic effects.

- Pramoxine :

Is a topical local anesthetic agent.

6) Trichogenic Agents :

- Minoxidil (Rogaine):

Designed as an antihypertensive agent.
Effective in reversing the progressive miniaturization of terminal scalp hairs associated with
androgenic alopecia.
Vertex balding is more responsive than frontal balding.

-Finasteride (Propecia):

5ά-reductase inhibitor which blocks the conversion of testosterone to dihydrotestosterne.
Oral tablets.

Can cause decreased libido, ejaculation disorders, and erectile dysfunction.

7) Antitrichogenic Agent :

- Eflornithine :

Is an irreversible inhibitor of ornithine decarboxylase. therefore, inhibits polyamine synthesis. Polyamines are important in cell division and hair growth.

Effective in reducing facial hair growth in 30% of women when used for 6 months.

Done by :

Lutfi Sowan .

قد قيل :

" لا تتردد في الرجوع إلى الله ، مهما كانت ذنوبك كثيرة ..

فالّذي سترك وأنت تحت سقف المعصية ، لن يفضحك وأنت تحت جناح التوبة " .

 # هيّا _ نتوب :)