Agents Affecting Pigmentation

Depigmenting Agents

They are used to reduce hyperpigmentation of the skin.

A. Tyrosinase inhibitors:

- Hydroquinone, mequinol and monobenzone
- Arbutin
- Kojic acid
- Licorice extract
- Vitamin E

B. Melanocyte-cytotoxic agents:

- Azelaic acid

C. Other agents:

- Alpha-hydroxy and beta-hydroxy acids
- Resorcinol peels
- Vitamin C
- Tretinoin
- Sunscreens

A. Tyrosinase inhibitors:

- **Tyrosinase activity is thought to be a major regulatory step in melanogenesis.**

Hydroquinone, Monobenzone, & Mequinol

- **Topical hydroquinone and mequinol usually result in temporary lightening.**
- **Topical monobenzone causes irreversible depigmentation.**
- **They are used as skin lighteners as drugs. They are also natural ingredients in many plant-derived products e.g., vegetables, fruits, grain, coffee.**

Mechanism of action:

1) **Inhibition of the enzyme tyrosinase by about 90%, thus interfering with the biosynthesis of melanin.**

2) **Reversible inhibition of cellular metabolism (affect DNA and RNA synthesis).**

3) **In addition, monobenzone may be toxic to melanocytes, resulting in permanent loss of these cells.**

- **Indications:**
  1. **Melasma**
  2. **Post-inflammatory hyperpigmentation**

- **May be used alone or in combination with other agents such as tretinoin, glycolic acid, Kojic acid and azelaic acid.**

Adverse reactions:

1) **Exogenous ochronosis:**
   - **Asymptomatic blue black macules in areas of hydroquinone application.**
   - **It occurs due to inhibition of homogenistic acid oxidase enzyme in skin → local accumulation of homogenistic acid that then polymerizes to form ochronotic pigment.**
   - **It is more common in patients with *dark skin* types.**
   - **To limit this adverse effect, it is prudent to use it in four-month cycles only, alternating with Kojic acid, azelaic acid or others.**
2) **Monobenzone may cause hypopigmentation at sites distant from the area of application (some percutaneous absorption of these compounds).**
3) **Both hydroquinone and monobenzone may cause local irritation.**
4) **Allergic contact dermatitis may occur.**

Arbutin

- It is a naturally occurring β-D-glucopyranoside that consists of a molecule of hydroquinone bound to glucose.
- It is present in the leaves of pear trees.
- Mechanism of action:
- It causes a reversible inhibition of melanosomal tyrosinase activity.

Kojic acid

- **Kojic acid is a *fungal metabolite* commonly produced many species of Aspergillus, Acetobacter and Penicillium.**
- **It is used as a *food additive* for preventing browning and to promote reddening of unripe strawberries.**

Mechanism of action:

- **It suppresses tyrosinase activity, mainly by chelating copper, resulting in whitening effect of the skin.**

Directions of use:

- **Twice daily application for two months. It can be used alone or in combination with glycolic acid 10% or hydroquinone 4% (give good results).**

Licorice extract

- **Glabridin is the main ingredient of licorice extract that can affect skin.**
- **Glabridin inhibits tyrosinase activity.**
- **It is better used in combination with other agents.**

Vitamin E

- **Oral intake of vitamin E is effective for the treatment of facial hyperpigmentation especially in combination with vitamin C.**
- **Mechanism:**

1. **It inhibits tyrosinase enzyme.**
2. **It has anti-oxidant action.**

B. Melanocyte Cytotoxic Agents

Azelaic acid

Mechanism of action:

- **It has anti-proliferative and cytotoxic effects on melanocytes.**
- **Azelaic acid 20% is an excellent alternative for patients who cannot tolerate hydroquinone.**
- **Good result is obtained if combined with glycolic acid 15%.**

C. Other Depigmenting Agents

Alpha hydroxyl and beta hydroxy acids:

e.g., glycolic acid

- **Used as chemical peel in 20-70%**

Mechanism of action:

1. **Diminish corneocytes cohesion → faster desquamation of the pigmented epidermis (with hope that the new epidermal cells will contain less pigment).**
2. **It increases keratinocytes turnover rate.**

Directions of use:

- **The use of topical hydroquinone pre- and post-peel decreases the chances of aggravating the post-inflammatory pigment alteration.**

Resorcinol peel:

Uses:

1. **Acne vulgaris**
2. **Melasma**
3. **Freckles**

- **It should not be used in dark skin.**

Vitamin C:

- **Topical: magnesium L-ascorbyl-2-phosphate.**
- **Oral: used as antioxidant.**

Tretinoin:

- **It is used as adjuvant in treatment of pigmentary disorders.**
- **Mechanism: it inhibits induction of tyrosinase.**

Sunscreens: very important

- **Sun protection plays a role in the treatment of pigmentary disorders.**
- **It should be a part of any skin lightening regimen.**

Pigmenting Agents

Trioxsalen & Methoxsalen

- Trioxsalen and methoxsalen are psoralens used for the repigmentation of depigmented macules of vitiligo.
- With the development of high-intensity long-wave ultraviolet fluorescent lamps, photochemotherapy with oral methoxsalen for psoriasis and with oral trioxsalen for vitiligo has been under intensive investigation.

Mechanism of action:

- Psoralens must be photoactivated by long-wavelength ultraviolet light in the range of 320–400 nm (ultraviolet A [UVA]) to produce a beneficial effect.
- Psoralens intercalate with DNA, and with subsequent UVA irradiation, cyclobutane adducts are formed with pyrimidine bases.
- Both monofunctional and bifunctional adducts may be formed, the latter causing interstrand crosslinks.
- These DNA photoproducts may inhibit DNA synthesis.

Adverse effects:

- The major long-term risks of psoralen photochemotherapy are cataracts and skin cancer.


Thank You