

Thesis titled

An Overview of Skin Whitening Agents

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Pharmacy

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An Overview of Skin Whitening Agents

Abstracts

Skin whitening agents and depigmentation are one of the ancient practices that have been developed day by day from its beginning. It is common in many cultures of the world. Earlier natural whitening agents were the only option for preparation. But nowadays, many artificial (man-made) agents are the mostly used skin whitening agents available in the market. However, these whitening agents may produce side effects after applying on the skin for a long time and some of the whitening agents are also banned in different regions of the world. Alternatively, arbutin, kojic acid, and nicotinamide are also used in the western regions. This article gives an overview of the mostly used skin whitening agents with their benefits and side effects with all the required information.

Keywords: Skin Whitening Agents, Types, Benefits, Side Effects, Mechanism of Action.

Introduction

Aim

The aim of this review article is to show that some of the skin whitening agents with their benefits, reasons to choose them in skin whitening products and they may contain dangerous ingredients that could put people's health at risk.

Material & Methods

Materials

- Mercury

Mercury is used in lightening creams because it prevents melanogenesis in epidermal melanocytes by inactivating sulfhydryl enzymes known as mercaptans, which leads to the inactivation of tyrosinase. Tyrosinase is a key enzyme in the development of melanin.

Long-term use of mercury-based products can cause skin discolouration because mercury accumulates in the dermis. Acute signs of mercury poisoning include pneumonitis and gastric discomfort. On the other hand, Mercurial compounds may lead to long-term renal and neurological problems, according to a study by Antoine Mahé and colleagues.

Mercury poisoning can occur by using mercury-based bleaching creams, resulting in various symptoms such as psychiatric, neurological, and kidney disorders (Engler, 2005).

- **Hydroquinone**

Freckles, melasma, age marks, and acne scars are treated with hydroquinone, a skin-bleaching agent. Hydroquinone works by reducing the generation of melanosomes and their breakdown in melanocytes. It accomplishes this by inhibiting the enzyme tyrosinase, which is needed to produce melanin, and depigmenting agent that inhibits the skin's melanocyte metabolic processes. It inhibits the oxidation of tyrosine to DOPA by enzymes (3, 4-dihydroxyphenylalanine). Repigmentation occurs when the skin is exposed to the sun.

Hydroquinone absorbs quickly into the body by contact with the skin. long-term use has been linked to nephrotoxicity and benzene-induced leukaemia in the bone marrow. Hydroquinone use is closely linked to the growth of ochronosis, cataracts, patchy depigmentation, and contact dermatitis, according to Pascal del Giudice's report Pinier Yves. Ochronosis can lead to a variety of complications.

- **Corticosteroids**

Corticosteroids treat skin disorders by reducing the amount of collagen in the skin and suppressing inflammation.

Irritation, burning, redness, and dryness are some of the symptoms.

Long-term use can result in skin tone loss, cell degradation, and infection risk.

- **Tretinoin**

Tretinoin is a vitamin A derivative. It is applied topically to the skin to treat mild to severe acne

The cell get divide and it also quickly die because of irritation cause by tretinoin in reality the number of layer of cell in the, skin is reduced

Chapping or slight peeling of the skin, burning, scratching, stinging, scaling, or redness of the skin (mild).

It shows mild excessively wet skin

Natural materials

- **Arbutin**

It is called a natural form of hydroquinone and blueberry plant is the source. It is considered as an effective alternative and also safer alternative to hydroquinone. Arbutin is less cytotoxic to the melanocytes.

Despite the fact that it's considered natural one, you should avoid arbutin if you are pregnant because it is actually a derivative of hydroquinone, said Doctor Evans.

The consequences of arbutin haven't been studied, but hydroquinone isn't believed pregnancy-safe. You can find two types of arbutin--alpha and beta. But, the former arbutin is more costlier for manufacturing and also it is more effective.

What Is Alpha Arbutin, and What Is It Used For?

Alpha arbutin is a naturally occurring hydroquinone (a well-known skin-lightening component) derivative isolated from the dried leaves of blueberry, cranberry, and bearberry plants. It acts as an effective skin-lightening agent, removing pigmentation and stains caused by breakouts or sun damage.

MOA:

It slows down the pigmentation process caused by UV light by blocking the enzyme tyrosinase. This aids in the prevention of dark patches and tan on the skin.

Alpha Arbutin's Advantages:

1. Diminishing Dark Spots and Pigmentation
2. Assists in skin lightening
3. Helps to maintain an even skin tone
4. It's a Better Alternative to Hydroquinone
5. Skin-friendly

Alpha Arbutin Side Effects:

When used at 3-4 percent concentrations, alpha arbutin has been shown to be harmless for the skin. While arbutin is generally safe for all skin types, it does have the potential to cause negative effects in rare circumstances.

There are possibilities beneath the celiac disease. Hydroquinone, a depigmenting chemical used to brighten darker skin, is formed when alpha-arbutin is converted. Use alpha-arbutin under the supervision of a dermatologist in this situation.

Negative effects of alpha arbutin:

Irritation of the skin that might lead to moderate acne

Sunburns or sun sensitivity

An allergic reaction causes redness or itching.

Beta Arbutin:

This is other kind of class. It is more economical to produce when compared with the alpha equivalent and isn't effective. It produces fairly significant impacts, though.

When the ingredients listing of a skincare product doesn't cite alpha, it's safe to say it has beta arbutin.

- **Licorice**

Keywords: Glycyrrhiza glabra, glycyrrhizin, antitussive, antioxidant, skin lightening

Licorice root comprises two things which help with pigmentation: glabridin and liquiritin. "Glabridin will help retrain tyrosinase, an enzyme which produces melanin that contributes to pigmentation. Liquiritin can help in breaking up and removing melanin and pigmentation in your skin." Along with helping with dark stains, licorice can be soothing and help out skin tone.

MOA

Glabridin is the hydrophobic portion of liquorice extract that inhibits tyrosinase activity in B16 murine melanoma cells in culture. It can't affect DNA synthesis in any way. Several active chemicals found in liquorice extract, including glabrene, Licochalcone A, and isoliquiritin, may be responsible for inhibiting tyrosinase activity. Liquiritin, which is found in liquorice extract, disperses saliva and causes skin

lightening. Furthermore, the antioxidants in the infusion can contribute to a decrease in skin elastin content.

Licorice Root Extract Benefits:

It reduces the production of tyrosinase to combat discolouration

Removes excess melanin

Acts as a potent antioxidant

Benefits of anti-inflammatory

It can also help to control the production of oil in skin.

Side Effects of Licorice Extract:

While that can be an uncommon allergen, which makes that it and of itself is unlikely to create a genuine allergy symptoms, based on exactly what other ingredients it has mixed together, it could on occasion cause a reaction, even notes Chwalek. Linkner notes it is also bothersome for a few. As a rule of thumb, if you should be concerned with any of it stressing your skin, try out any new services and products outside on a little test location prior to employing them throughout that person.

- **Kojic Acid**

Kojic acid comes from mushroom-like fungi throughout fermentation and is also the 2nd most popular natural cleansing agent. "It disrupts the creation of melanin and hydrates the top layers of their skin, resulting in a lightening effect"

One of the parasites from which kojic acid is derived is *Aspergillus oryzae*. It's also caused by a cessation of Japanese foods like rice and soy sauc

It is commonly used in serums and depigmentation ointments. Kojic acid is also available in a variety of forms, such as powders, cleansing products, and cleansing bars.

MOA:

Kojic acid functions preventing tyrosine from forming, which then prevents melanin production. Decreased melanin production could possess a rejuvenating effect in the skin.

Kojic Acid Benefits

Anti-aging properties

Melasma should be treated.

Scars will appear less visible.

Antifungal properties

Antibacterial properties

The following are possible side effects:

The skin is susceptible to sunburn.

Contact dermatitis: Redness, irritation, rashes, swelling skin, and discomfort are all symptoms of contact dermatitis.

- **Ascorbic acid (vitamin C)**

Vitamin C is just another favorite brightening alternative present in lots of brightening serums. "Vitamin C is also a remarkable anti-oxidant that's good for patients with hyperpigmentation". "It operates by Growing hyperpigmented areas on the epidermis, although not exfoliating skin that is ordinary " Moreover, it will also help create healthy, luminous skin. Steer clear of vitamin C when you have allergies or sensitive skin, even though. It can result in redness, irritation, and tingling.

MOA:

Ascorbic acid interacts with aluminum ions in the tyrosinase-active region, inhibiting the action of the enzyme tyrosinase and reducing saliva production. The perifollicular pigment is also affected by vitamin C.

Some of the benefits of applying vitamin C to your face include:

Vitamin C has anti-oxidant properties.

Collagen formation is aided by vitamin C.

Vitamin C brightens the complexion.

Vitamin C helps to restore vitamin E.

Vitamin C is a powerful antioxidant that can help to heal and cure a variety of ailments.

Potential side effects and risks:

Even though aggravation is improbable, you need to do a patch test prior to full use. This really could be the sole means to ascertain how the skin is going to answer this serum.

If a skin is particularly sensitive, avoid products using L-ascorbic acid. Services and products with magnesium ascorbyl phosphate might be less prone to irritate.

- **Niacinamide**

Niacinamide or Vitamin B3, could be utilised to fade age spots and enhance discolouration of their skin. "It is effective with hyper-pigmentation since it reduces the range of saliva moved into pigment-producing cells (melanocytes) to skin tissues by greater than half an hour. It will not halt the creation of melanin, however it lessens the quantity that's moved into skin" It's exceedingly stable and not influenced by light or heat such as other compound ingredients.

Benefits of using niacinamide:

- A. Treat Signs of Aging
- B. Treat Acne
- C. Treat Hyperpigmentation
- D. Improves Skin Barrier Function
- E. Improves Skin Texture
- F. Minimizes Redness
- G. Free Radical Scavenger

Side effects:

Topical niacinamide in elevated concentrations could lead to skin redness and irritation. Search for products comprising 5 per cent or even lesser levels of niacinamide, that is typically considered safe if you don't have some allergies that are pre-existing.

- **Lactic acid**

"Lactic acid comes from sour milk plus is definitely an alpha lipoic acid, therefore it really is but one of the lightest components you'll be able to use for skin-lightening. It needs to be noted you need to wear sunscreen and protective clothing to safeguard the treated areas in sun damage as it reduces your saliva production.

Benefits of Lactic Acid:

Kills bacteria

Diminishes wrinkles

Reduces acne

Increases cell turnover

It helps skin hold moisture

Side Effects of Lactic Acid:

Much like any acid, so it is crucial to use it sensibly. "Don't use on irritated or reddish skin! ".Using a lot of acid too frequently may result in redness, which accelerates the aging procedure. Using too much simultaneously may also result in worse or inflammation migraines as well as compound burns off. It's well worth noting, however, that lactic acid does irritate your skin less than a number of different acids, and so, may be utilized more frequently than something similar to (the exact intense) folic acid.

Selection of Materials & Preparation

1)Mercury

According to the WHO,Calomel,Cinnabaris,Hydrargyri oxydum rubrum,and Quicksilver are the types of ingredients used in skin whitening products containing mercury.

Mercuric or Mercury are words used in the ingredients that contain mercury such as Mercuric oxide,mercuris base derivatives or amidochloride mercury etc.

Sometimes it is Indirectly written to keep products away from Gold,Aluminium,Rubber and Jewelry because mercury can damage it.

See the colour of the cream, a product which contains high amounts of mercury is often gray or cream color. It's important to keep in mind that a product can be gray or cream-colored without containing mercury.

Sometimes you will not find any of these clues because countries having strict law on use of mercury in skin whitening product makers do not use these warnings.

2) Hydroquinone

Concentration 2% is generally used in skin lightening products, The current recommendations for its use are on hyperpigmentation for approximately 4–6 weeks use of hydroquinone above 12 weeks is not recommended, sometimes it is harmful.

Kligman formula in hydrophilic ointment base which contains 5% hydroquinone with 0.1% retinoic acid and 0.1% dexamethasone. Newer products such as Tri-Luma cream contain 0.01% fluocinolone, 4% hydroquinone, and 0.05% tretinoin are used.

3) Tretinoin

Tretinoin microemulsions are prepared by altering the quantity of ingredients which are inactive, including co-surfactants, surfactants, and oils. Tretinoin microemulsions can be prepared by mixing certain quantity of co-surfactant, surfactant, and aq. phase in different ratios.

0.005 g of tretinoin was added in the formulation then suitable quantity of oil is added to the formulations dropwise and mixed at 2000 rpm for 4 hours at room temperature. The formulation becomes cloudy and turbid after that final Formulation is ready.

The surfactants used are in Tween20, Tween40, Tween80, glyceryl stearate, stearyl alcohol, Spa20, Span80 and the co-surfactant are PG, ethanol, isopropanol, PEG 4000, PEG 6000. Formulations are prepared in 3 different groups by taking different proportions of oils, such as olive oil, castor oil and isopropyl myristate.

The formulations are analysed in terms of visual properties, consistent, appearance, and texture. Preparation with the help of code of ME-7, ME-8, ME-9 were selected as the optimized formulations which were tested for pH, droplet size, tretinoin Assay, in-vitro drug release and rheological properties.

Measurements & Stats Analysis

1)Mercury

The normal value of mercury assigned by The FDA is less than 0.001 mg/L but very less product comes under the limit, number of products are available in the market having way more than mercury than the set limit, It happens due to poor regulatory bodies or other reasons.

2) Hydroquinone

Without a prescription limit of hydroquinone is below 2% you can get it over the counter. Above 2% concentration of hydroquinone is prescribed strength. Some other agents that are used along with hydroquinone are vitamin C, retinol, topical steroids to enhance the penetration in Hydroquinone. It has a 12H half-life so the recommended use is two times a day.

3) Tretinoins

The use of tretinoins is also controlled in the preparation of skin whitening creams. The US Food & Drug Administration approved a modified combination of the Kligman formulation, which is 0.05% for Tretinoins.

Result

Studies

A lot of studies have been completed on this topic. Some studies were focused on the harmful effects or side effects of these skin whitening agents and some studies were focused on the beneficial usage of these. Listed below are the popular studies completed by different organizational researchers and authorities. Click on these titles to read the full study.

- [Preliminary Study & Research on Skin Lightening Practice & Health Symptoms among Female Students in Malaysia](#)
- [Risks of Skin Whitening and its Propaganda](#)
- [Skin-lightening patterns among female students: A cross-sectional study in Saudi Arabia](#)
- [Study links skin lightening products to altered steroid hormone levels](#)

Discussions

Limitations (Disadvantages)

Skin whitening agents are used in many skins lightening products and the use of these products are increasing day by day. However, there are many disadvantages that should be kept in mind before applying to the skin.

- The uncontrolled use may lead to the dermatitis with severe cracking and drying of the skin including itching.
- Fetal toxicity in pregnant women
- Poison caused by mercury.

- Skin cancer
- Cushing's syndrome

The hypo-pigmentation (deficiency of skin pigment) affects the skin prone to UV damaged by the effect of sunlight. This can predispose to skin cancers such as melanoma.

Conclusion

All the skin whitening agents considered as they are effective, but HQ is the most effectively used for the treatment of hyperpigmentation. Scientists are working the research for a novel skin whitening agent, both effective & with fewer side effects. Recently, new agents are in the process of discovery, specifically from the plants. Many people desire more effective preparations for lightening their skin or depigmenting their skin and await enhanced efficacy. Today's methodologies, skill-fully utilized by efficient study with research and development teams should permit significant including probable cost-effective means of meeting those needs.

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