

A REVIEW ON EFFICACY OF ALOESIN IN THE TREATMENT OF HYPERPIGMENTATION**Nwachukwu precious, Saurabh Sharma*, Priyanka Saharan, Sandip Prasad Tiwari****Faculty of Pharmacy, Kalinga University, Naya Raipur, Chhattisgarh India (492101)***Corresponding Author's E mail: saurabh.sharma@kalingauniversity.ac.in

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ABSTRACT

Hyperpigmentation is a common dermatological condition characterized by darkening of the skin due to increased melanin production. Aloesin, a natural compound derived from Aloe vera, has garnered significant attention for its potential therapeutic effects in treating hyperpigmentation. This review aims to comprehensively evaluate the efficacy of aloesin in the treatment of various hyperpigmentation disorders, including melasma, post-inflammatory hyperpigmentation, and solar lentigines. Aloesin exhibits its anti-hyperpigmentation properties through multiple mechanisms. Primarily, it inhibits tyrosinase, a key enzyme in melanogenesis, thereby reducing melanin synthesis. Additionally, aloesin demonstrates antioxidative properties, which further contribute to its protective effects against UV-induced skin damage and subsequent pigmentation. The review also highlights the limitations of current research, including small sample sizes and short study durations. Furthermore, the variability in aloesin concentrations and formulations across different studies complicates the direct comparison of results. Future research should focus on long-term clinical trials with standardized formulations to better assess the sustained efficacy and safety of aloesin. In conclusion, aloesin emerges as a promising agent in the treatment of hyperpigmentation, offering a natural and safer alternative to conventional therapies. This review underscores the need for further research to optimize its clinical application and establish standardized treatment protocols.

Keywords: Melanogenesis, Hyperpigmentation, Antioxidant, Tyrosinase

INTRODUCTION

Hyperpigmentation can be defined as the over production of melanin in specific skin regions usually the arms, face, neck or other places which usually gets exposed to the sun, leading to a darker patch or spot. Asides from sun exposure, other causes of hyperpigmentation are hormone fluctuation, inflammation, trauma or skin disorders like melisma or post- inflammatory hyperpigmentation^{1,2}. A series of metabolic events takes place in the melanocyte (a specialized skin cell that produces the protective skin-darkening pigment, melanin) when UV light penetrates the skin. This metabolic event

causes the build-up of melanin in the epidermis. Melanin production is very important to the body as it shields the deeper layer of skin from harm. Usually, hyperpigmentation is confused with tanning but while both are similar, they are not the same. Hyperpigmentation often appears as dark patches or spots on the skin and affects any part of the body but usually the face, neck, hands are other areas exposed to the sun while tanning results in a more uniform darkening of the skin, giving it a sun-kissed appearance.

Also, hyperpigmentation can be caused by other factors other than sunlight but tanning is strictly caused by exposure to sunlight. Recently, there are a lot of treatments for hyperpigmentation and most are synthetic treatments. This article will focus on a chemical constituent of aloe vera known as 'aloesin', which is said to exhibit depigmenting qualities. Aloe vera is a succulent plant which is made up of three layers³.

- i. The interior transparent gel which is made of sterols, vitamins, amino acids, glucomannans and 99% water.
- ii. The bitter yellow sap or middle layer of the latex containing glucosides and anthraquinones.
- iii. The rind which is a thick layer of 15-20 cells that serves as protection There are about 75 potentially active substances in Aloe vera which includes Vitamins, Anthraquinones, Polysaccharides, Enzymes, Glycoproteins, Minerals, salicylic acid, Amino acid, Sterols.

Methods of isolation of Aloesin from Aloe vera

Aloesin present in aloe vera is extracted directly from the plant's leaves. The gel is carefully gathered and processed to guarantee its quality and purity using various materials like; the fresh aloe vera itself, ethanol, distilled water, blender, fine mesh strainer, solvent evaporator and so on^{4,5}.

The various methods listed here are used according to the procedure which is to be used, the researchers' choice and the equipment available.

1. Solvent extraction is mostly used these days for the isolation of aloesin. This method is simple to use and less costly but it can pose some disadvantage to the environment and public health due to the use of organic solvents. It is also time consuming and the extract may not have high-purity⁶.
2. Ultrasound Assisted Extraction makes use of ultrasonic waves hence its name and because of this wave, the effectiveness of extraction is increased compared to the first method. It is quicker than

Saurabh et al. A Review on efficacy of aloesin in the treatment of hyperpigmentation the conventional techniques and frequently uses less solvent. This method is costly to operate and causes chemicals which are susceptible to heat to degrade ⁷.

3. Extraction Assisted by Enzymes is also a technique use for the isolation of aloesin. It increases aloesin release by disintegrating the cell membrane of plants using certain enzymes. By using this gentle technique instead of the harsh chemicals, aloesin's yield and purity can be increased and it is beneficial to the environment. Its downside is that the enzymes used can be expensive and each enzymes requires precise conditions to be met ⁸.

How does aloesin work on a skin affected by hyperpigmentation?

Aloesin (C₁₉H₂₂O₉), a natural phenolic compound found in aloe vera. Its chemical structure is made up of a chromone core with a C-glucosyl linkage, contributing to its biological activity. The unique structure of aloesin is what makes it able to interact with the various pathways, making it useful in the management or mitigation of hyper pigmentation ⁹.

Interaction with Tyrosinase Activity

Tyrosinase is an essential enzyme for the formation of melanin. It causes tyrosine to oxidize to DOPA and then Dopaquinone, which is how melanin is produced. Tyrosinase is inhibited competitively by aloesin, which binds to the enzyme's active site and stops tyrosine from oxidizing. Tyrosinase activity is thereby reduced, which lowers melanin synthesis and lightens the hyper pigmented area. Studies have indicated that aloesin demonstrates a dose-dependent inhibition of tyrosine hydroxylase and DOPA (3, 4-dihydroxyphenylalanine) oxidase activities of tyrosinase from the natural melanocytes gotten from normal human ¹⁰.

Interaction with Melanocytes:

The specialized cells known as melanocytes are in charge of producing melanin. Research has demonstrated that aloesin has the ability to regulate melanocyte's function and activity. At the cellular level, aloesin inhibits melanin formation by decreasing tyrosinase activity in melanocytes ¹¹. Aloesin has been shown in some circumstances to also cause melanin death which adds to its depigmenting properties ¹².

Reduced Inflammation:

Hyperpigmentation, especially post-inflammatory hyperpigmentation, is known to be triggered by inflammation. Because of its anti-inflammatory qualities, aloesin helps lessen skin inflammation and

the chance of hyperpigmentation that follows. Aloesin helps in the preservation of the skin homeostasis and stops hyper pigmented lesions from getting worse by preventing the synthesis of pro-inflammatory cytokines and mediators ¹³⁻¹⁴.

Inhibition of UV-induced Melanogenesis:

Research has proven that aloesin blocks UV-induced melanogenesis by interfering with the signaling pathways that UV light activates. Among these are the blockage of the cAMP pathway, which has part in the activation of melanogenesis, and the downregulation of MITF, a critical regulator of melanogenic enzymes ¹⁵.

There have been several challenges faced in the utilization of aloe vera {aloesin} as a depigmenting agent and some of them are;

- a. Studies on aloesin's effectiveness in treating hyperpigmentation shows inconsistent results and variability, questioning its efficacy compared to other proven therapies like hydroquinone or retinoid.
- b. Formulation challenges and stability: Aloesin's stability in topical formulations is problematic due to factors like pH sensitivity, light exposure, and interaction with other substances. ⁽¹⁶⁾
- c. Skin penetration and bioavailability: Limited penetration and bioavailability of aloesin can compromise its therapeutic activity in targeting pigmented cells. ⁽¹⁷⁾
- d. Skin safety and adverse effects: Aloesin may cause allergic reaction, skin sensitivity or other adverse effects potentially limiting its use.
- e. Quality control and standardization: Issues with aloesin's purity and extraction methods can affect the consistency and efficacy in skin care products. ⁽¹⁸⁾
- f. Lack of comprehensive clinical trials: The absence of well-designed clinical trials specifically assessing aloesin's safety and effectiveness in treating hyperpigmentation hinders understanding of its potential ¹⁹.

Other limitations are: limited comparative study, variability in study design, imprecise mechanism of action, and depth of pigmentation.

Scope for further work

In as much as aloesin has a lot of advantages, there are still some limitations which must be addressed.

To improve aloesin's skin penetrating properties, future research should concentrate on enhancing the formulation and delivery techniques like the utilization of Nano encapsulation, micro emulsion, penetration enhancers, pH adjustment and the use of targeted drug delivery system that releases aloesin at a particular depth or within melanocytes where melanin production occurs.

To be able to conclusively evaluate the clinical significance and safety profile of aloesin, larger- scale clinical trials with a varied population type and size would be important ²¹. To also boost the depigmenting effect of aloesin, it might be important to investigate more combination therapies that combines aloesin with other depigmenting agents given how arbutin + aloesin produced a better effect. More of these kinds of formulations should be formulated. In addition, understanding aloesin's mode of action and determining the possible molecular targets depends on further scientific investigations that clarifies the precise processes by which it prevents melanin formation.

CONCLUSION

The majority of the most widely used depigmenting products on the market today are recognized to have negative side effects and to be harmful to melanocytes. Compared to melanocytotic substances, inhibitors like aloesin which inhibit tyrosinase activity the enzyme that limits the rate at which melanin is produced have the capacity to be safer. Whereas, it has been demonstrated that kojic acid, a well-known tyrosinase inhibitor, is extremely skin- sensitive, and incidents of contact allergic dermatitis have been documented. The current study discovered that aloesin therapy inhibits UV-induced hyperpigmentation in a dose-dependent way. An additional effect was seen after co-treatment with 100 mg of arbutin and aloesin per g vehicle. We draw the conclusion that aloesin has a therapeutic impact on pigmentation suppression through its inhibitory effect on the tyrosinase activity. The difficulties in the outcomes in in-vitro and in-vivo studies highlight the difficulties in converting promising molecules into practical therapies.

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