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Study on the application of *Aloe vera* in cosmetology and clinical treatment of skin diseases



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ARTICLE INFO	A B S T R A C T
Keywords: Aloe vera Cosmetology Dermatosis Clinical application	The medicinal value of <i>Aloe vera</i> (AV) has been continuously explored and utilized in recent years, becoming a research hotspot. Some basic studies have found that AV had cosmetic effects such as whitening, sun protection, antioxidant, anti-aging, and moisturizing. Some clinical trials have found that AV had medical effects such as antibacterial, anti-damage, and promoting wound healing. In this work, we summarized the indications and therapeutic efficacy of AV in cosmetology and clinical treatment of dermatosis, in order to provide certain inspiration for the development of new AV-based skincare products and new medicines for skin diseases.

1. Introduction

Aloe vera (AV) originates from South Africa and belongs to the *Liliaceae* family. There are more than 400 species, of which only a few have medicinal value, such as AV, *Aloe ferox* Miller, and *Aloe arborescens*. Among them, AV (also known as *Cape Aloe*) is considered to have greater development potential and the most widely studied by researchers.¹ In China, the unique variety is Yuanjiang Aloe, also known as Chinese Aloe, which has the characteristics of fast reproduction, vigorous growth, and rich active ingredients. Studies have found that AV contained more than 160 kinds of chemical components, including polysaccharides, organic acids, amino acids, proteins, cellulose, vitamins, minerals, bioactive enzymes, anthraquinone compounds, flavonoids, and trace elements.²

As a natural plant, AV had reliable safety and was widely used for a long time. Cai et al. summarized the effects of AV on anti-tumor, diabetes treatment, and immunity, as well as the benefits of AV on the skin such as bactericidal and anti-inflammatory, promoting wound healing, antioxidant and anti-aging.³ It could effectively treat dermatological diseases such as acne vulgaris in clinical practice, skin ulcers, skin itching, and allergic dermatitis. The effect was better when it was used in combination with some drugs.^{4–6} Moreover, AV had the following effects in various types of beauty cosmetics: whitening, sun protection, anti-aging and antioxidant, moisturizing, and regulating water and oil balance. And it had a long history of beauty applications. Relevant literature reported that as early as the 14th century BC, Egyptian Queen Neferti began using AV for cosmetology.⁷ At present, AV products include gel, lotion, powder,

and masks, which have been used commonly in daily life.

However, due to individual differences and lack of standardization of dosage and usage, some patients still had doubts about the efficacy of AV, and the mechanism of AV in treating some skin diseases was still unclear up to now. The research and development of new AV medicines still face great obstacles. In this work, we provided a compilation and summary of the clinical applications of AV in cosmetology and dermatosis, aiming to further explore its effective components and mechanisms in this field, thereby tapping into its medicinal value and development potential more comprehensively, facilitating its broader application in skincare and dermatosis treatment.

2. AV in cosmetic applications

2.1. Whitening

Melanin is produced by oxidation of L-tyrosine through a series of enzymatic reactions.⁸ The principle of whitening is to control the key enzymes required at various stages of the melanin synthesis, reduce the generation of melanin, and inhibit the transfer and redistribution.⁹ Studies have shown that plant extracts rich in flavonoids have a strong inhibitory effect on tyrosinase.¹⁰ AV was rich in flavonoid substances, thus, it had great potential for application in the development of whitening skincare products. Kahramanoğlu et al. analyzed the phytochemical characteristics of the following *Aloe* species: *Aloe arborescens* Mill, *Aloe ferox* Mill, *Aloe greenii, Aloe mutabilis, Aloe saponaria* and AV. It was

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found that AV showed the highest content of flavonoid and antioxidant capacity, which suggested AV would be more likely to be developed in whitening skincare products in the future.¹¹ Xu et al. found that AV gel could effectively inhibit the production of pigments through clinical trials. At the same time, it could also form a membrane on the epidermis to reduce the damage of ultraviolet (UV) rays to the skin.¹² Tyrosinase was the key enzyme in the process of catalyzing tyrosine to produce melanin. Research has found that AV extract can bind to tyrosinase and enzyme substrate complexes, causing the enzyme to lose its activity, and thus inhibiting the production of melanin.^{13,14} Additionally, aloesin is also a competitive inhibitor of tyrosine, which could inhibit the hydroxylation and oxidation activity of tyrosinem, and its conversion to melanin was reduced soon afterwards. Choi et al. studied the inhibition activity of aloesin on melanin deposition caused by UV, and found that aloesin inhibited melanin formation in a dose-dependent manner.¹⁵ Furthermore, research has found that aloesin in AV had the activity of inhibiting tyrosinase, which presented in the epidermis and mucilage, while the pulp had no inhibitory effect on tyrosinase.¹⁶ These studies indicated that aloesin in AV had a whitening effect.

2.2. Sun protection

Medium-wave ultraviolet rays (UVB) (290–320 nm) in sunlight can damage the dermal connective tissue of the skin. Keratinocytes are particularly sensitive to UVB, leading to the release of inflammatory factors such as TNF- α and IL-10, triggering a series of signal transductions afterwards and resulting in skin aging ultimately.¹⁷ UV rays can also activate tyrosinase in the basal cells of skin, which then catalyzes the production of melanin, leading to pigmentation spots and thereby deepening skin color.¹⁸ Some commercially available products contain organic sunscreens, which absorb UV rays of specific wavelengths through their specific structures (such as chromophores) to achieve the purpose of sun protection. However, organic compounds are prone to residual accumulation on the skin, which can cause skin allergies and pose a risk of carcinogenesis. Therefore, green and safe sunscreen products based on natural plants will be more attractive.

In recent years, studies have shown that AV was a broad-spectrum natural sunscreen that could effectively reduce the damage of UV radiation to the skin.¹⁹ He et al. used AV flower extract to treat the Mela-Kutis® 3D melanin skin model. The UVB stimulation group and the model group were compared in terms of apparent chromaticity, L* value, and melanin content. It was found that AV flower extract showed a better protective effect.²⁰ Ma et al. added TiO₂ and fresh AV juice to the emulsion formula to create a moisturizing product that combined physical and chemical sunscreen, and found that it had good performance after being detected by UV spectrophotometer.²¹ Aloin, the main anthraquinone in AV, which could reduce the photodamage caused by UVA (320-420 nm) and UVB.²² Reuter J et al. applied AV gel and 1% hydrocortisone to the UVB-irradiated areas on the back of the test volunteers, and the results showed that the AV gel significantly reduced the erythema induced by UV light after 48 h.²³ There was also research found that AV gel contained small molecular immunomodulators, and it could prevent UVB-induced immune suppression in the skin by restoration of UVB-induced damages on epidermal Langerhans cells (LC), ultimately, it was beneficial to restore the function of LC as helper cell.²⁴ Existing studies have found that anthraquinone substances in AV were mainly concentrated in the leaves, while the roots and stems contained almost no anthraquinone, which provided a direction for the extraction of effective sunscreen ingredients from AV in the future.²⁵ Song et al. found that aloin could inhibit the secretion of inflammatory factors TNF- $\!\alpha$ and IL-10 caused by UVB, alleviate inflammatory reactions, and also reduce skin inflammatory damage caused by UV rays.¹⁷ In order to better exert the photoprotective effect of AV, Roshini et al. prepared solid lipid nanoparticles of AV as carriers for sunscreen formulations, which could continuously and stably release the effective sunscreen components of AV.²⁶ AV can not only inhibit the proliferation of melanocytes and reduce

skin pigmentation, but also decrease the damage of UV rays to the human immune system and reduce the possibility of skin cancer,²⁷ hence, AV could effectively resist the damage of UV rays to the skin. There were also many commercial sunscreens with AV as the main ingredient. However, based on the current research, the wavelength range of UV rays absorbed by current AV sunscreen products was still limited at present. In consideration of the mild and safe properties of AV, developing a broader spectrum of AV sunscreen products has great research potential in the future.

2.3. Anti-oxidation and anti-aging

Skin aging is mainly caused by oxidative damage induced by reactive oxygen free radicals (ROS). Excessive ROS can induce excessive oxidative stress, leading to biomolecule denaturation and cell death.²⁸ For example, hydroxyl free radicals can cause oxidative damage to adjacent biomolecules.²⁹ When the body's antioxidant defense system declined, free radicals couldn't be cleared in time and accumulated gradually, leading to cell damage and skin aging ultimately.³⁰ Therefore, removing reactive ROS and inhibiting oxidation is one of the means of anti-aging.

In the late years, research on the anti-aging and antioxidant abilities of AV has been a popular topic. AV had also been proven to have the ability of scavenging ROS, inducing antioxidant proteins, and protecting deoxyribonucleic acid and superoxide dismutase. AV contains numerous antioxidant constituents like ascorbic acid, carotenoids, flavonoids, α -tocopherol, and tannins, which can scavenge free radicals.³¹ Chen et al. found that aloin had a good effect in scavenging superoxide anion free radicals.³² Through oxidative hemolysis inhibition, thiobarbituric acid reactive substances formation inhibition (TBARS), β-carotene bleaching inhibition (β-CBI) tests, and Pearson analysis, Añibarro-Ortega et al. found that the anti-hemolysis and β -carotene antioxidant capacity were strongly correlated with the flavonoid content in AV, and the TBARS inhibition capacity was closely related to the malic acid content.³³ Jiang et al. prepared acetylated, phosphorylated, and carboxymethylated aloe polysaccharides, and then measured the antioxidant activity of AV polysaccharides and their derivatives in vitro. They found AV polysaccharides and their derivatives showed good activity in superoxide anion radical scavenging rate, hydroxyl radical scavenging rate, anti-lipid peroxidation, and DPPH radical scavenging ability. Preliminary structure-activity relationship studies showed that phosphorylated AV polysaccharides (AVP) had the best antioxidant activity in vitro, which was at the same level as that of the positive control (vitamin C).³⁴ Mohammad M. Fares et al. prepared MO/AV microemulsions, and they experimentally demonstrated that MO/AV microemulsions have strong ROS scavenging capacity and high sun protection factor (SPF) values (SPF 40), indicating that they could effectively resist oxidative stress and effectively dissipate UV radiation, and the successful manufacture of this product was the cornerstone of the fight against skin aging.³⁵ AV is rich in hyaluronic acid, and it has the ability to stimulate collagen synthesis via induction of fibroblasts in the dermis. The increased production of collagen makes skin smoother, reduces wrinkles, and improves skin elasticity and longevity.³⁶ It has also been found that the dendritic AV fermented by Lactobacillus plantarum exhibited more significant anti-wrinkle ability than before fermentation, which might be related to the decomposition of macromolecular polysaccharides into small molecules during the fermentation process, making it easier for them to enter fibroblasts and exert their effects.³⁷ Other research showed that fermentation of AV considerably reduced the production of pro-inflammatory factors TNF- α and IL-1 β and significantly increased the yield of the anti-inflammatory factor IL-4 in animal serum.³⁸ The abundant carbohydrates and amino acids in AV had the function of repairing collagen. Then, collagen could maintain the elasticity and firmness of the skin, decompose the aging elastic fibers, and promote the restoration and regeneration of its own tissues, thereby delaying the aging of the skin.

2.4. Hydration and moisturization

Maintaining adequate moisture in the skin helps delay aging and keep the skin smooth. When the skin is dehydrated, it may lead to metabolic disorders and an increase in the forces between molecules and cells, causing the skin to become harder. As desmosomes were not completely hydrolvzed, keratinocytes will adhere and form scales on the skin surface.³⁹ At this time, it was significant to moisturize the skin in a timely manner. AV contains amino acids, organic acids, and various trace elements, which are natural components of the skin's hydration factors, which absorb moisture from the air. AVP contained in AV also plays an important role in moisturizing, due to its polar groups such as hydroxyl and carboxyl groups which could form hydrogen bonds to bind a large amount of water. On the other hand, the dense network structure formed by the polysaccharide could also reduce the evaporation of water.⁴⁰ Zang M et al. prepared the PVP/CNF/AV nanofiber composites, which were particularly suitable for mask applications. In this composite, AV powder and cellulose nanofibers played a synergistic role to enhance the overall properties of the composites, including the improvement of nanofiber morphology, mechanical properties, and biocompatibility. Mucous AV gel easily penetrated the skin and prevented moisture loss and enhanced skin moisture. What's more, the contained polysaccharides enhanced the water absorption and retention capacity of nanofiber composites.⁴¹ In addition, AV is rich in hyaluronic acid, which is an excellent moisturizing ingredient filled in the dermis and serves as a water source for the entire moisturizing system. Mao et al. prepared a hyaluronic acid lotion using bacterial cellulose film as a carrier, and they found that it had a high absorption efficiency of hyaluronic acid lotion on the skin, with a very low water loss rate and good moisturizing performance.⁴² Tanaka M et al. had found that AV sterol could stimulate collagen and hyaluronic acid production in human dermal fibroblasts. Subsequently, they performed a trial to evaluate the effects of oral AV sterol supplementation, and the result showed that collagen content in the dermis increased with AV sterol intake, but also the continued AV sterol ingestion contributed to maintaining healthy skin.43 Zhang et al. measured the moisturizing properties of Kusola AV macromolecular gel and found it significantly increased the expression of AQP-3 protein and ZO-1 protein in keratinocytes related to active moisturizing and water-locking barrier. This study further validated that AV extract had a very good moisturizing efficacy on the skin, and the higher its content, the better the moisturizing performance.44 These above studies demonstrate that AV had a good moisturizing efficacy, and its natural moisturizing factors, hyaluronic acid, and other substances extracted from it could serve as effective components of moisturizing skincare products.

3. AV in the treatment of skin diseases

3.1. Acne vulgaris

Acne vulgaris is a chronic inflammatory skin disease that occurs in the sebaceous glands of the hair follicles,⁴⁵ and its onset is closely related to hormone imbalance, irregular diet and rest, bacterial infection, decreased immunity, and other factors.⁴⁶ Commonly used treatments in clinical practice include topical or oral antibiotics (such as metronidazole, erythromycin), oral anti-androgen drugs, acid scrubbing (such as retinoic acid), red-blue light irradiation therapy, chemical peeling, and fire needles.⁴⁷ Propionibacterium acnes in the sebaceous glands of hair follicles is closely related to the formation of acne. Acne patients have the problems of blockage of hair follicle sebaceous gland ducts and a large amount of lipid secretion from sebaceous glands, which provide a suitable environment for the reproduction of lipotrophic and anaerobic Propionibacterium acnes, resulting in abnormal proliferation of Propionibacillus acnes and other microorganisms in hair follicles, thus resulting in skin inflammation.^{48,49} Therefore, inhibiting the growth of microorganisms such as Propionibacterium acnes, was one of the effective means of treating acne.

Studies have shown that AV contains guinones (emodin, aloin, etc.), polysaccharides, tannin compounds, and other substances with strong bactericidal and anti-inflammatory functions, which can kill harmful facial flora such as Propionibacterium acnes and Staphylococcus aureus, and then it can reduce damage to the skin surface and alleviate acne symptoms. The main mechanisms of bacteriostasis of anthraquinones include inhibiting the synthesis of bacterial protein and hereditary substance and destroying bacterial cytoderm and biomembrane.⁵⁰ AV could kill pathogenic bacteria by regulating immune function and enhancing immunity.⁵¹ Flavonoids achieved an antibacterial effect by inhibiting the function of nucleic acid synthesis, cytoplasmic membrane function, energy metabolism, biomembrane formation, and the function of cell membrane porins.⁵² Tannins inactivated microbial adhesins, enzymes, membrane transporters, etc. through non-specific binding with proteins.⁵³ By utilizing the cold dispersion method and Design Expert 11 for precise optimization, Rana T et al. merged clindamycin phosphate and AV to develop an anti-acne cream. Through the antimicrobial experiments in vitro, they found that the anti-acne cream showed a stable and better antibacterial and anti-inflammatory effect on Propionibacterium acnes, when compared to the use of clindamycin phosphate and AV gel alone. Besides, they also found that AV gel had a stronger inhibitory effect on pathogenic bacteria of acne than traditional antibiotic treatment.⁵⁴ Li et al. found that the antibacterial rate of AV gel against Propionibacterium acnes increased with the prolongation of the using time and the increased concentration of AV gel.⁵⁵ The anti-inflammatory effect of AV gel might be related to reducing neutrophil aggregation and inhibiting the production of inflammatory factors TNF- α and IL-6. Hajheydari Z. et al. Recruited 60 testees with mild to moderate acne vulgaris for the trial, and found that the combination of tretinoin (TR) cream (0.05%) and AV had good tolerability on the testees, which was significantly more effective than TR and excipients in the treatment for the examinees, which illustrated the potential of AV in the clinical treatment of mild to moderate acne vulgaris.⁵⁶

3.2. Skin itching

Skin itching can be caused by a variety of reasons. The local skin itching caused by dry skin is mainly due to the decrease in the moisture holding capacity of the skin stratum corneum and excessive water loss. The skin barrier has the function of regulating the moisture holding capacity of the stratum corneum. Timely protection of the skin barrier and elimination of the causes of skin dehvdration can partly relieve the itching symptoms.⁵⁷ As mentioned above, AV has natural moisturizing factors, which can absorb moisture from the air, repair collagen in the skin promptly, thereby protecting the skin barrier and relieving itching caused by dry and dehydrated skin. During the allergic reactions, mast cells mediated the occurrence of inflammatory reactions by producing IL-4 and IL-6, causing itching symptoms. Aloe emodin (one kind of quinone anthracene derivative) was a mast cell degranulation inhibitor, which could effectively inhibit the itching symptoms caused by allergic dermatitis.⁵⁸ Atopic dermatitis was a chronic pruritic dermatitis that caused skin itching and swelling. Chen studied atopic dermatitis in rats with AVP intervened, and the results showed that AVP improved the damage caused by atopic dermatitis on the back skin of rats. It was speculated that AVP might alleviate inflammation and reduce itching symptoms by inhibiting Th17 cell immune response, lowering IgE levels, and inhibiting the NF-kB pathway.⁵⁹

3.3. Skin ulcers

Skin ulcers refer to the symptoms of local skin tissue defects caused by different reasons such as burns, scalds and external trauma. Clinically, recombinant bovine basic fibroblast growth factor (rb-bFGF) is suitable for the treatment of acute and chronic ulcers, trauma, and so on. As an exogenous growth factor, rb-bFGF can promote the expression of endogenous fibroblast growth factor, accelerate the growth rate of

granulation tissue, and promote angiogenesis.⁶⁰

Currently, research has indicated that AV could treat pain, erythema, and exudation caused by ulcers, as well as reduce the size of wounds. It could promote the secretion of growth factors such as EGF and VEGF in wound tissues, and also reduce inflammatory factors such as TNF-α and IL-16. It might regulate the expression of cytokines through various pathways such as NF-KB inflammatory pathway and PKC signaling pathway to accelerate wound healing.⁶¹ Other studies have shown that AV could inhibit the production of prostaglandin E2 and increase the infiltration of leucocytes, afterwards, the inflammation was reduced and the wound was healed consequently.⁶² Aloe glycoside and calcium isocitrate in AV could promote the discharge of dirt in the body, soften blood vessels, purify blood, and promote blood circulation.⁶³ Apigenin (a flavonoid in AV) could increase the tissue oxidation at the site of the wound and promote the contraction and closure of the wound by inducing apoptosis.⁶⁴ AVP could promote the production of epidermal growth factor and accelerate the repair of damaged endothelial cells.⁶⁵ Zheng et al. wrapped the foot wounds of diabetic rats in the experimental group with spinning varn soaked in 10% AVP solution. After 14 days of continuous treatment, it was found that it had a higher wound healing rate, lower levels of inflammatory factors (IL-1, TNF- α), and higher levels of fibroblast growth factors (bFGF, PDGF-BB) in the experimental group.⁶⁶ Chen et al. found that AV freeze-dried powder had a more significant effect on wound repair in rabbits than Yunnan Baiyao (a famous Chinese medicine), and was at the same level as rhEGF in promoting wound healing.⁶⁷ Liang et al. found that Aloe gel treatment might promote wound healing and alleviate scars by up-regulating the expression of miR21, miR126 and miR210, meanwhile, down-regulating the expression of miR29a and miR155 in wound granulation tissue.⁶⁸ AV-containing hydrogel dressings increased the absorption of wound exudate and its mechanical properties.⁶⁹ Baljit Singh et al. explored the biological activity of AV and soralen glue (SG), and then they prepared AV-SG hydrogel porous wound dressing, which was proved to have good antioxidant activity. When loaded with antibiotics, it could achieve better bactericidal and anti-inflammatory effects through slow release, while the dressing could keep the wound moist, which was conducive to better wound healing.⁷⁰ Jeirani Khamene et al. fabricated PVA/BC/G-C₃N₄/Ca/AV nanofibers. Compared with traditional dressings, the biocompatibility, antimicrobial activity, and mechanical strength were improved overall, providing a better treatment option for chronic wounds, especially diabetic ulcers.⁷¹ These above experiments showed that AV could effectively promote the production of epithelial cells in wounds and accelerated the healing of ulcer wounds. Further, for the treatment of burns and scalds patients, the arbutin in AV could also prevent scarring of muscle tissue and restore the skin tissue to its original state.⁷² In recent years, the development of new dressings using AV as raw material has become a popular research direction in wound care. Wei et al. prepared Gel/CMCh/AV hydrogel with gelatin and carboxymethyl chitosan as raw materials and AV as anti-inflammatory components. In the antibacterial test, it was found that the gel had great antibacterial activity against Escherichia coli and Staphylococcus aureus, and also the gel had excellent biocompatibility with HFF-1 cells. Moreover, Gel/CM-Ch/AV hydrogel showed rapid and sustained release of levofloxacin hydrochloride, showing its potential as a wound dressing. Therefore, it can be used for wound care to promote wound healing.⁷³ In Xi's work, aloin and carbon nanoparticles were used as raw materials to improve polymeric hybrid hydrogels. Aloin was a natural antibiotic, which could achieve a double antibacterial effect when combined with near-infrared-light (triggering photothermal/ROS route). What's more, aloin had the ability to promote wound healing through TGF-\beta1/Smad signaling pathway, and this new dressing could achieve a better wound care effect.74

3.4. Radiation dermatitis (RD)

Dermatitis is a common skin disease that could cause skin swelling

and irritation, and there are many causes and manifestations for its occurrence. Exposure to ionizing radiation during radiation therapy may lead to the production of large amounts of free radicals in body. These free radicals can damage and break DNA, resulting in acute inflammatory reactions in the skin, which is known as radiation dermatitis (RD). It aggravates the pain and psychological pressure to patients for receiving radiotherapy.⁷⁵ Reasonable prevention and relief of RD symptoms is an important part of improving the life quality of patients and the treatment effectiveness.

Traditional Chinese medicine diagnosis considered that RD was caused by the invasion of heat toxins into the body.⁷⁵ AV was cold in nature and could clear away heat, detoxify, cool blood, and relieve pain. In Hu et al.'s meta-analysis on the use of AV gel to prevent RD (including 735 cancer patients undergoing radiotherapy), it was validated that AV gel could effectively prevent the development of severe RD (the incidence rate of severe RD in the intervention group, and there was a statistically significant difference compared with the control group, P <0.05).⁷⁶ However, in the evaluation study of the effectiveness of preventing mild to moderate RD and reducing the incidence rate of RD, there was no statistical difference between the intervention group and the control group. Nonetheless, due to limited research conditions, further validation is still required through more samples and comprehensive studies. Zhu et al. conducted a group experiment on 120 nasopharyngeal cancer patients with RD and found that the new rehabilitation drug (made from EGF extracted from Periplaneta americana) combined with AV was more effective at high radiation doses, when compared to the use of growth factors alone. There were more first-time RD cases but fewer severe RD cases, proving the effectiveness of AV in the treatment of RD.⁷⁷ Medical radiation protection spray can reduce the damage caused by RD, whose components are superoxide dismutase (SOD), vitamin B_{12} , and potassium sorbate. They can accelerate skin tissue repair by removing negative oxygen ions from the skin surface.⁷⁸ Zhu et al. found that the treatment of using fresh AV juice combined with medical radiation protection spray was more effective in preventing and treating RD and relieving pain than using anti-radiation agents alone.⁷⁹ In Lu et al.'s work, the results showed that the cure rate of the AV treatment group was higher than that of the control group (sham irradiation treatment).⁸⁰ It was speculated that the mechanism of AV gel promoting RD wound healing was related to fibroblast growth factor and endothelial cell growth factor. The above clinical trials and animal experiments indicated that AV was suitable for the treatment of RD patients, as it could accelerate RD wound healing, reduce the incidence of severe RD, relieve pain, and improve the life quality of these patients. The therapeutic effect was more significant when used in combination with other medicines.

4. Discussion

The skin is the first immune barrier of the body against external pathogens and plays an important protective role. With the continuous development of the society, people are increasingly paying attention to skin health issues. When choosing external skin medicines, there is a growing preference for natural medicinal products. The compendium of "Materia Medica" explained that AV was cold in nature, and also, it had effects in killing parasites, clearing heat, and relieving pain. In recent years, with the development of related research on AV, its medicinal value has been developed and utilized continuously. In this work, the effective ingredients of AV and their pharmacological effects were discussed point by point. In summary, components such as aloin, emodin, mucopolysaccharide, hyaluronic acid, flavonoids, and other ingredients in AV were valuable in cosmetics or treatment of skin diseases, and could be used for the development of new skin care products and skin medicines (the summary diagram was shown in Fig. 1). In terms of the cosmetics industry, AV had the effects of whitening, sun protection, antioxidation, anti-aging, and moisturizing. While, in the treatment of skin diseases, it had the effects of treating common acne, skin itching, skin ulcers, and radiation dermatitis. In clinical practice, it could usually



Fig. 1. The summary diagram of ingredients-cosmetic/clinic uses-mechanism of Aloe vera in cosmetology and skin diseases treatment.

achieve better therapeutic effects when used in combination with other medicines. However, its active ingredients, efficacy, and mechanism for disease treatment have not yet been explored fully, and more in-depth exploration is still needed hereafter. Looking forward to the future, AV has broad prospects of development and application in cosmetology and skin disease therapy.

CRediT authorship contribution statement

Jiajun Zhu: Writing – original draft, Software, Investigation. Yuanru Zheng: Validation, Funding acquisition, Conceptualization. Yanhui Ge: Writing – review & editing, Supervision, Project administration, Funding acquisition, Conceptualization.

Data availability statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

- Eshun K, He Q. Aloe vera: a valuable ingredient for the food, pharmaceutical and cosmetic industries-a review. Crit Rev Food Sci Nutr. 2004;44(2):91–96.
- 2. Sun SQ. Research progress on bioactive components and their functions of Aloe. *Chem Intermed.* 2019;18(1):166–167.
- 3. Cai JF. Research progress of pharmacological mechanism of active components in Aloe. World Latest Med. Inf. (Electronic Version). 2018;18(102):122–125.
- Sánchez M, González-Burgos E, Iglesias I, et al. Pharmacological update properties of *Aloe vera* and its major active constituents. *Molecules*. 2020;25(6):1324.
- Mansoor K, Aburjai T, Al-Mamoori F, et al. Plants with cosmetic uses. *Phytother Res.* 2023;37(12):5755–5768.
- 6. Ganesan P, Choi DK. Current application of phytocompound-based
- nanocosmeceuticals for beauty and skin therapy. Int J Nanomed. 2016;11:1987–2007. 7. Nie LH. Developing and using of Aloe vera. Food Res Dev. 2006;27(2):147.
- Stacey AND, Graeme JF, Bruce CB, et al. Signaling pathways in melanogenesis. Int J Mol Sci. 2016;17(7):1144.
- Zhou T, Li Y, He L. The progress on mechanisms of skin whitening. *Dermat Vener*. 2017;39(3):168–172.
- Iyda JH, Fernandes Â, Ferreira FD, et al. Chemical composition and bioactive properties of the wild edible plant *Raphanus raphanistrum* L. *Food Res Int.* 2019;121: 714–722.
- Kahramanoğlu İ, Chen C, Chen J, et al. Chemical constituents, antimicrobial activity, and food preservative characteristics of *Aloe vera* gel. *Agronomy*. 2019;9(12):831.
- Xu N, Li Z, Yue R, et al. Curative effect of aloe gel on prevention and treatment of pigmentation after dermabrasion. *Chin J Aesthetic Plast Surg.* 2015;26(3):159–161.
- Tan C, Zhu WY, Lu Y. Aloin cinnamic acid and sophorcarpidine are potent inhibitors of tyrosinase. *Chin Med J.* 2002;(12):100, 103, 153.
- Jones K, Hughes J, Hong M, et al. Modulation of melanogenesis by aloesin: a competitive inhibitor of tyrosinase. *Pigm Cell Melanoma R*. 2002;15(5):335–340.
- Choi S, Lee SK. Aloesin inhibits hyperpigmentation induced by UV radiation. *Clin Exp* Dermatol. 2002;27(6):513–515.
- Wu X, Yin S, Zhong J, et al. Mushroom tyrosinase inhibitors from Aloe barbadensis Miller. Fitoterapia. 2012;83(8):1706–1711.
- Song XZ, Xia JP, Bi ZG. Effect of tea polyphenol and Aloin on TNF-α and IL-1β secretions by cultured keratinocytes induced by ultraviolet B. Chin J Dermatovenereol Integr Tradit West Med. 2002;1(1):7–10.
- Shen JX, Shi LL, Tian HR, et al. Study on the effect of whitening, sunscreen and moisturizing of purified plant extracts. *Guangzhou Chem Ind*. 2020;48(1):77–79, 110.

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- Wozniak A, Paducj R. Aloe vera extract activity on human rorneal cells. Pharm Biol. 2012;50(2):147–154.
- He LY, Li X, Qian SX. Study on whitening effect of Aloe vera flower extract by 3D skin model. Flavour Fragr Cosmet. 2021;4:33–36.
- Ma YX. Preparation of a moisturizing sunscreen of Aloe. Sichuan Chem Ind. 2015; 18(3):1–3.
- Skarupova D, Vostalova J, Rajnochova SA. Ultraviolet A protective potential of plant extracts and phytochemicals. *Biomed Papers Med Faculty Uni Palacky*. 2020;164(1): 1–22.
- **23.** Reuter J, Jocher A, Stump J, et al. Investigation of the anti-inflammatory potential of *Aloe vera* gel (97.5%) in the ultraviolet erythema test. *Skin Pharmacol Physiol.* 2008; 21(2):106–110.
- Lee CK, Han SS, Shin YK, et al. Prevention of ultraviolet radiation-induced suppression of contact hypersensitivity by *Aloe vera* gel components. *Int J Immunopharm.* 1999;21(5):303–310.
- Zhang ML. The Extraction, Separation, Purification of Aloin from Aloe and its Application in cosmetics[D]. Jiangsu: Jiang Nan University; 2006.
- Rodrigues LR, Jose J. Exploring the photo protective potential of solid lipid nanoparticle-based sunscreen cream containing *Aloe vera. Environ Sci Pollut Res Int.* 2020;27(17):20876–20888.
- Stricklandf PR. Prevention of ultraviolet radiation-induced suppression of contact and delayed hypersensitivity by *Aloe barbadensis* gel extract. *J Invest Dermatol*. 1994; 102(2):197–204.
- Collins KG, Fitzgerald GF, Stanton C, et al. Looking beyond the terrestrial: the potential of seaweed derived bioactives to treat non-communicable diseases. *Mar Drugs.* 2016;14(3):60.
- Zeng XT, Shi LP, Tao HK, et al. Study on the antioxidant activity of Aloin in different varieties of Aloe. *Biol Chem Eng.* 2023;9(5):103–106.
- Syarina PNA, Karthivashan G, Abas F, et al. Wound healing potential of Spirulina platensis extracts on human dermal fibroblast cells. Exp Clin Sci. 2015;14(8):385–393.
- **31.** Hçś M, Dziedzic K, Górecka D, et al. *Aloe vera* (L.) webb.: natural sources of antioxidants a review. *Plant Foods Hum Nutr.* 2019;74(3):255–265.
- 32. Chen D, Liu WY, Bao GR, et al. ESR studies on the eliminating effect on the superoxide Anion free radical of Aloin in Aloe. *Chin J Mod Appl Pharm.* 2005;(1): 12–14.
- Añibarro-Ortega M, Pinela J, Barros L, et al. Compositional features and bioactive properties of *Aloe vera* leaf (Fillet, Mucilage, and Rind) and flower. *Antioxidants*. 2019;8(10):444.
- Jiang WM, Zhou SY. Preparation and antioxidant activity of Aloe polysaccharide and its derivatives. Storage Process. 2022;22(11):61–68, 75.
- **35.** Fares MM, Radaydeh SK. Novel mustard oil/*Aloe vera* gel microemuslions as potential biomaterials. *J Mol Liq.* 2024;397:124077.
- 36. Bukhari SNA, Roswandi NL, Waqas M, et al. Hyaluronic acid, a promising skin rejuvenating biomedicine: a review of recent updates and pre-clinical and clinical investigations on cosmetic and nutricosmetic effects. *Int J Biol Macromol.* 2018;120: 1682–1695.
- Ro HS, Jang HJ, Kim GR, et al. Enhancement of the anti-skin wrinkling effects of Aloe arborescens Miller extracts associated with lactic acid Fermentation. Evid-Based Compl Alt. 2020;(9):2743594.
- Hai Z, Ren Y, Hu J, et al. Evaluation of the treatment effect of *Aloe vera* fermentation in burn injury healing using a rat model. *Mediat Inflamm*. 2019:2020858.
- Li Q, Wu ZM. The principle and application of anti-aging cosmetics. *Chin J Aesthetic Med.* 2017;26(11):135–138.
- Kathuria N, Gupta N, Manisha, et al. Biologic effects of *Aloe vera* gel. *Internet J Microbiol.* 2010;9(2):1–6.
- Zand M, Sephvand S, khoshkhat P, et al. Preparation and characterization of poly(vinyl pyrrolidone)/cellulose nanofiber/*Aloe vera* composites as a biocompatible hydrating facial mask. *Int J Biol Macromol.* 2024;277:133846.
- **42.** Mao F, Xia QC, Han J. The research of hyaluronic acid transdermal release and moisturizing properties. *Appl Chem Ind.* 2016;45(11):2017–2020.
- 43. Tanaka M, Yamamoto Y, Misawa E, et al. Effects of Aloe sterol supplementation on skin elasticity, hydration, and collagen score: a 12-week double-blind, randomized, controlled trial. Skin Pharmacol Physiol. 2017;29(6):309–317.
- Zhang H, Wang Y, He LY, et al. Study on moisturizing effect of Aloe vera macromolecule gel. Flavour Fragr Cosmet. 2020;(4):31–35.
- Eichenfield D, Sprague J, Eichenfield L. Management of acne vulgaris: a review. JAMA. 2021;326(20):2055–2067.
- 46. Say YH, Heng AHS, Reginald K, et al. Modifiable and non-modifiable epidemiological risk factors for acne, acne severity and acne scarring among Malaysian Chinese: a cross-sectional study. *BMC Publ Health.* 2021;21(1):601.
- Wang R, Xu H, Liu Y. Current status of physical therapy of acne vulgaris. *Dermatol B*. 2023;40(4):527–532.
- **48.** Nishijima S, Kurokawa I, Katoh N, et al. The bacteriology of acne vulgaris and antimicrobial susceptibility of propionibacterium acnes and staphylococcus epidermidis isolated from acne lesions. *J Dermatol.* 2000;27(5):318–323.
- Xu XQ, Sushmita P, Ran YP. Advances on the interaction mechanism among the microbiota related to acne vulgaris. *Chin J Dermatovenereol.* 2021;35(2):222–227.
- Deng LH, Xie Z, Mai LY, et al. Advances in studies on antibacterial activity and mechanism of anthraquinone compounds. *Chin J New Drugs*. 2016;25(21): 2450–2455.

- Salah F, Ghoul YE, Mahdhi A, et al. Effect of the deacetylation degree on the antibacterial and antibiofilm activity of acemannan from *Aloe vera*. *Ind Crop Prod*. 2017;103:13–18.
- Xie YX, Yang WJ, Chen XQ, et al. Antibacterial activities of flavonoids: structureactivity relationship and mechanism. *Curr Med Chem.* 2014;22(10):2174.
- Cowan MM. Plant products as antimicrobial agents. Clin Microbiol Rev. 1999;12(4): 564–582.
- Rana T, Zaman M, Khan MA, et al. Antiacne gel containing *Aloe vera* and clindamycin phosphate: design, characterization, and optimization using response surface methodology. *Int J Polymer Sci.* 2024;(1):3353141.
- Li XM, Zhang HX, Fan Y, et al. Study on the anti-inflammatory effect of Aloe vera gel. China Surfactant Deter Cosmet. 2022;52(12):1320–1325.
- 56. Hajheydari Z, Saeedi M, Morteza-Semnani K, et al. Effect of *Aloe vera* topical gel combined with tretinoin in treatment of mild and moderate acne vulgaris: a randomized, double-blind, prospective trial. *J Dermatol Treat*. 2013;25(2):123–129.
- Jin JH, Li KY, Wang WH, et al. Establishment of xerosis-itch mice model. J Chin Pract Diagn Ther. 2020;3(3):246–249.
- Yang Y, Sun JM, You H, et al. Aloe-emodin relieves allergic contact dermatitis pruritus by inhibiting mast cell degranulation. *Immunol Lett.* 2024;270:106902.
- Chen ZH, Li X, Han L, et al. Effects of Aloe extract on IgE, IL-17 and NF-κB pathways in atopic dermatitis mice model. *Chin J Dermatovenereol*. 2019;33(6):644–650.
- 60. Han XL, Pang XJ, Lan LP, et al. Effects of recombinant bull basic fibroblast growth factor (rb-bfgf) administration on the wound healing in cleft palate patient. J Prev Treat Stomatol Dis. 2014;22(10):519–521.
- Su YY, Jin D, Zhang CJ, et al. Research progress of Aloe in promoting wound healing. Guangdong Chem Ind. 2022;49(5):62–63, 58.
- Almanza-Aranda KE, Aranda-Fonseca MG, Velazquez-Plascencia G, et al. Cytotoxic and anti-inflammatory effect of turmeric and Aloe vera in a gingivitis model. Nat Oral Care in Dental Therapy. 2020:97–109.
- Tang N, Bian K. Application of Aloe in wounds healing. Shanghai J Tradit Chin Med. 2010;44(9):72–75.
- 64. Agarwal C, Singh RP, Agarwal R. Grape seed extract induces apoptotic death of human prostate carcinoma DU145 cells via caspases activation accompanied by dissipation of mitochondrial membrane potential and cytochrome crelease. *Carcinogenesis*. 2002;23:1869–1876.
- Tabandeh MR, Oryan A, Mohammadalipour A. Polysaccharides of *Aloe vera* induce MMP-3 and TIMP-2 gene expression during the skin wound repair of rat. *Int J Biol Macromol.* 2014;65:24–30.
- Zheng YY, Shi XX, Liu DX, et al. Effect of aloe polysaccharide on wound healing of rats with diabetic foot ulcer. *Chin J Clin Pharmacol.* 2021;37(2):153–156.
- Chen K, Hu ZT, Luo BJ, et al. Promoting effects of freezing-dried Aloe barbadensis Miller powder on skin wound healing in rabbits. West China J Pharm Sci. 2009;24(3): 272–274.
- Liang YJ, Li Y, Gao YY, et al. Experimental study of using *Aloe vera* gel to treat diabetic chronic cutaneous ulcers in *Bama miniature* pigs. *J Sichuan Univ Med. Sci Ed.* 2022;53(6):953–960.
- **69.** Thomas D, Nath MS, Mathew NRR, et al. Alginate modified with *Aloe vera* gel and cellulose nanocrystals for wound dressing application: preparation, characterization and in vitro evaluation. *J Drug Deliv Sci Technol.* 2020;59:101894.
- Singh B, Singh J, Sharma V, et al. Exploring bioactive aloe-vera and sterculia gum to develop hydrogel wound dressings by graft-copolymerization. *Food Hydrocolloids Health*. 2023;4:100168.
- Khamene J, Yazdian A, Pourmadadi F, et al. Fabrication and characterization of an innovative G-C₂N₄/calcium/*Aloe vera* enriched PVA-bacterial cellulose wound dressing: a novel approach to diabetic wound management. *Inorg Chem Commun.* 2024;168:112879.
- Zhang X, Liao CJ, Jia CY. Research progress of aloe in burn wound treatment. *Chin J Inj Repair Wound Healing*, 2015;10(1):80–82.
- 73. Wei CY, Xing S, Li Y, et al. Gelatin/carboxymethyl chitosan/aloe juice hydrogels with skin-like endurance and quick recovery: preparation, characterization, and properties. *Int J Biol Macromol.* 2024;261(1):129720.
- 74. Xi J, Wu Q, Xu Z, et al. Aloe-emodin/carbon nanoparticle hybrid gels with lightinduced and long-term antibacterial activity. ACS Biomater Sci Eng. 2018;4(12): 4391–4400.
- 75. Wu XY. Clinical research on the efficacy of traditional Chinese medicine for external use in preventing radiation-induced skin damage[D]. China Academy of Chinese Medical Sciences. 2022.
- Hu M, Hu H. Effect of Aloe on preventing radiation on induced dermatitis: a meta analysis. *Chin Nurs Res.* 2019;33(10):1670–1674.
- 77. Zhu SM, Ye JZ, Yi SQ, et al. Application study of Kangfuxin Liquid combined with fresh Aloe in preventing and treating radiation dermatitis in patients with nasopharyngeal carcinoma. *Pract Clin Med.* 2022;23(3):75–78.
- Xue MF, Zhao QD, Zhang W, et al. Clinical application of anti-radiation spay combined with flamigel in prevention of postoperative radioactive skin injury of breast cancer. *Nurs Pract Res.* 2017;14(2):97–98.
- **79.** Zhu YQ, Zuo JF. Preventive effect of fresh asparagus juice combined with protective spray against rays on the radiodermatitis of patients with nasopharyngeal carcinoma. *J Clin Nurs in Pract.* 2018;4(12):150–152.
- Lu JL, Liu XP, Yang F, et al. Efficacy of Aloe gel for wound healing rate and the granulation tissue rate in the dermatitis vesicular reaction caused by radiation in rat. *J Modern Oncol.* 2006;9:1156–1158.