

Review on Phytochemical, Pharmacological and Marketed Product of Alovera Extract

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ABSTRACT

Aloe vera has historically been utilised for the treatment of skin injuries (such as burns, cuts, insect bites, and dermatitis) and digestive issues due to its anti-inflammatory, antibacterial, and wound-healing attributes. The research on this medicinal plant focusses on substantiating traditional applications and elucidating the mechanism of action, as well as identifying the chemicals responsible for these effects. Similarly, novel effects have been explored for Aloe vera and its active constituents, particularly emphasising its potential as a cytotoxic, antitumoural, anticancer, and antidiabetic drug. Over the past six years, the majority of pharmacological research has comprised in vitro and in vivo trials. In vitro research predominantly focus on antibacterial, anti-inflammatory, cytotoxic, antitumor, anticancer, and skin protective effects. It is particularly important to highlight that various in vitro studies assess the preventive effects of Aloe vera in bone disorders, including osteoporosis. The findings on bone protection are encouraging; however, it is essential to do further studies with experimental animals and humans. In vivo studies are designed to assess cardioprotective effects, cytotoxicity, antitumor and anticancer activities, as well as skin protection efficacy. Clinical trials are constrained in comparison to in vitro and in vivo testing, concentrating mostly on digestive and dermal protective effects. Furthermore, these clinical trials have solely utilised Aloe vera, excluding its isolated components; hence, it would be pertinent to investigate the therapeutic effects of significant metabolites across various human diseases and illnesses. Research over the past six years has concentrated on the principal active compounds: aloe-emodin, aloin, aloesin, amodin, and acemannan. Aloe-emodin and aloin have been the most extensively researched among these compounds. Aloe-emodin has emerged as a potential drug with antibacterial, antidiabetic, cytotoxic, cardioprotective, and bone protective properties in in vitro investigations, as well as anti-inflammatory and skin protective effects in in vivo research. Aloin shown efficacy in inflammatory processes and bone illnesses (in vitro studies) as well as in cancer and cardiovascular diseases (in vivo studies). The encouraging outcomes of fundamental research promote an increased number of clinical trials to evaluate the therapeutic application of Aloe vera and its primary constituents, especially regarding bone protection, cancer, and diabetes.

Keywords- Aloe, Herbal plant, Pharmacological activity, Nutraceutical.

I. INTRODUCTION

Aloe species (family Asphodelaceae) have been extensively utilised for ages in the treatment of numerous illnesses, as well as for aesthetic and cosmetic purposes. The Aloe genus includes more than 430 species, such as *A. vera* and *A. ferox*, among others. These species have demonstrated pharmacological activity such as anti-inflammatory, immunomodulatory,

antibacterial, antifungal, antiviral, antiproliferative, antidiabetic, laxative, wound healing, moisturising, anti-aging, and skin protective effects [3–5].

Aloe species are progressively integrated into various cosmetic items, health beverages, foods, and drinks owing to the advantageous biological activities of the phytochemicals predominantly present in the leaves. The phytochemicals comprise polysaccharides, flavonoids, carbohydrates, coumarins, tannins,

chromones, alkaloids, anthraquinones, organic compounds, pyrones, phytosterols, anthrones, sterols, vitamins, proteins, and mineral components [2, 5, 6]. The concentration variation of these chemical elements depends on the plant part utilised, extraction method, solvent, growth stage, and plant origin. While advantageous, several phytochemicals may be linked to harmful effects [7].



Fig: 1 Aloe vera plant

Numerous researchers have identified potential toxicities and dangers linked to some plants and vegetables, specifically hepatotoxicity, nephrotoxicity, and carcinogenicity [8, 9]. Consequently, the toxicity assessment of medicinal plants has emerged as a primary priority to ensure their safe application [10, 11]. This research examines the phytochemistry and toxicity of *A. vera* and *A. ferox*, the two commercially significant species of *Aloe*. This study will facilitate the standardisation and quantification of phytochemicals in *Aloe* species. It will also raise awareness among locals regarding the hazardous effects potentially linked to the medicinal usage of these species and future human studies [12-13]

II. CHEMICAL CONSTITUENTS

Aloe comprises two categories of Aloins: nataloins, [14] which produce picric and oxalic acids upon reaction with nitric acid and do not exhibit a red colouration; and [15] barbaloins, which yield aloetic acid ($C_7H_2N_3O_5$), chrysammic acid ($C_7H_2N_2O_6$), picric, and oxalic acids when treated with nitric acid, resulting in a reddened solution. The second category can be categorised into a-barbaloins, derived from Barbados aloes and reddened in cold conditions, and b-barbaloins, sourced from Socotrine and Zanzibar aloes, which are reddened by standard nitric acid when heated or by fuming acid in cold conditions. Nataloin produces vibrant yellow scales. Barbaloin crystallises into yellow prisms. [16] The plant generates a minimum of six

antimicrobial compounds, including lupeol, salicylic acid, urea nitrogen, cinnamic acid, phenols, and sulphur. These chemicals are classified as antiseptics because of their efficacy in eradicating or managing mould, bacteria, fungi, and viruses, which accounts for the plant's capacity to combat many internal and external illnesses. Lupeol and salicylic acid found in the juice are two highly powerful analgesics. [17] It comprises a minimum of three anti-inflammatory fatty acids, cholesterol, campesterol, and β -sitosterol. These are highly effective in the treatment of burns, cuts, scrapes, abrasions, allergic reactions, rheumatoid arthritis, rheumatic fever, acid indigestion, ulcers, and various inflammatory conditions of the digestive system and other internal organs, including the stomach, small intestine, colon, liver, kidneys, and pancreas. β -sitosterol is a potent anti-cholesterol agent that aids in reducing detrimental cholesterol levels, elucidating its numerous advantages for cardiac patients. *Aloe* juice contains around 23 polypeptides that assist in regulating a wide range of immune system diseases and disorders. [18] Polypeptides, along with the anti-tumor drugs *Aloe emodin* and *Aloe lectins*, are currently utilised in cancer treatment. [19]

Anthraquinones

Twelve distinct anthraquinone varieties are found in *Aloe Vera* sap: Aloin, Isobarbaloin, Anthracene, Emodin, [20] Ester of Cinnamic acid, Chrysophanic acid, Barbaloin, Anthranol, Aloetic acid, *Aloe Emodin*, Ethereal oil, and Resistannol. They function as natural laxatives, analgesics, and pain relievers, possessing potent antibacterial, antifungal, and virucidal activities. [21][22]

Amino Acids

Amino acids serve as the fundamental components of proteins, which synthesise and restore muscle tissue. The human body necessitates 22 amino acids, of which 8 are essential. *Aloe Vera* supplies 20 of the 22 necessary amino acids and 7 of the 8 essential amino acids. These are amino acids. [23][24][25]

Enzymes

Enzymes are natural protein molecules that possess specialised catalytic activities in biochemical reactions, produced by all living creatures, including microbes, plants, animals, and humans. [26][27] Enzymes, like all proteins, are made of amino acids; yet, they uniquely promote biological reactions without suffering any alteration themselves. The key enzymes in *Aloe Vera* are Peroxidase, Aliiase, Catalase, Lipase, Cellulose, Carboxypeptidase, Amylase, and Alkaline Phosphatase. [28][29]

Vitamins

Aloe Vera comprises many vitamins, including Vitamins A, C, and E, which are essential antioxidants that counteract harmful free radicals in the body. [30][31][32] Vitamin B and Choline are involved in energy production, amino acid metabolism, and muscle mass development. Vitamin B12, which facilitates the

creation of red blood cells, and Folic acid, which aids in the development of new blood cells.

Minerals

Aloe Vera contains the following minerals: **Calcium:** [34](essential for proper bone and teeth density). **Manganese:** (a component of enzymes necessary for the activation of other enzymes). **Sodium:** [35] (ensures that the body fluids do not become too acidic or too alkaline). **Copper:** (enables iron to work as oxygen carriers in the red blood cells). **Magnesium:** (used by nerves and muscle membranes to help conduct electrical impulses). **Potassium:** [36] (regulates the acidic or alkaline levels of body fluid). **Zinc:** (contributes to the metabolism of proteins, carbohydrates and fats), **Chromium:** (necessary for the proper function of insulin, which in turn controls the sugar levels in the blood). **Iron:** [37] (controls the transportation of oxygen around the body via the red blood cells).

Lignin

This cellulose substance is found in the gel has no known medical properties except it posses the property of penetrating the human skin.[38][39]

Saponins

These produce soapy lathers when combined and stirred with water. They have been utilised as detergents, surfactants, and possess antibacterial characteristics.[40][41]

Sugars

Aloe Vera comprises both monosaccharides, including glucose and fructose, and polysaccharides. Polysaccharides represent the most significant category of carbohydrates. They facilitate optimal digestion, regulate cholesterol levels, enhance liver functions, and promote bone fortification. [42][43]

Sterols

Sterols serve as significant anti-inflammatory agents. *Aloe Vera* contains Cholesterol, Sitosterol, Campesterol, and Lupeol. These sterols possess antibacterial and analgesic effects. They possess analgesic characteristics akin to those of aspirin.[43][44]

III. PHARMACOLOGICAL ACTIVITY

Wound Healing Properties: Wound healing is a dynamic process that transpires in three phases. The initial phase involves inflammation, hyperaemia, and leukocyte infiltration. The second phase involves the excision of necrotic tissue. The third phase of proliferation involves epithelium regeneration and the development of fibrous tissue.

Numerous researches have indicated that the active constituents for wound healing may include tannic acid and a specific polysaccharide.[45][46] Other researchers have reported that glucomannan, a mannose-rich polysaccharide, and gibberellin, a growth hormone, interact with growth factor receptors on fibroblasts, thereby stimulating their activity and proliferation, which significantly increases collagen synthesis following topical and oral administration of *Aloe vera*. [47][48] *Aloe gel* not only enhanced the collagen content of the wound but also altered the collagen composition and elevated the degree of collagen cross-linking. Acemannan, regarded as the primary functional component of *Aloe vera*, consists of an elongated chain of acetylated mannose (mucopolysaccharides). [49][50] This intricate carbohydrate expedites wound healing and mitigates radiation-induced dermal responses.

Macrophage: Activating potential acemannan may stimulate the release of fibrogenic cytokines. Direct binding of acemannan to growth factors and their stabilization may lead to promotion of prolong stimulation of granulation tissue. [51]

Beauty care properties: Aloin and its gel serve as a skin tonic for combating acne. *Aloe vera* is utilised for alleviating skin irritation and maintaining moisture to prevent dryness of the scalp and skin in severe, arid conditions. *Aloe vera* can also serve as a moisturiser for oily skin. Research indicates that *Aloe vera* enhances the skin's hydration capacity, facilitates the exfoliation of dead skin cells, and possesses efficient permeation properties that assist in the delivery of beneficial chemicals through the skin. Each of these qualities renders *Aloe vera* an optimal component in cosmetic and dermatological formulations. *Aloe vera* is presently one of the most significant components in the cosmetics sector, employed in approximately 95 percent of the dermatologically beneficial extracts produced globally. *Aloe sugars* are utilised in moisturising formulations. Combined with carefully chosen essential oils, it serves as an exceptional skin-smoothing moisturiser, sunscreen, and a variety of beauty items. Maharishi Ayurveda advocates the use of *Aloe vera* for many dermatological issues due to its calming and cooling properties.[52]

Skin and Body Anti- Aging Properties: The invaluable oligo-elements present in *aloe juice*, manganese and selenium, constitute the enzymes superoxide dismutase and glutathione peroxidase, recognized as powerful antioxidants and cellular anti-aging agents [53]

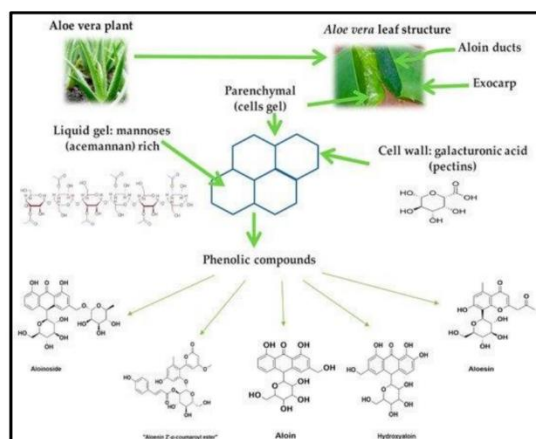


Fig: 2 *Aloe vera* phenolic compound

Their high antioxidants slow down the aging process. This helps cells to become stronger in combating the negative effects caused by oxygen and the broad spectrum radiation we are exposed to daily. [54][55] The non-essential amino acid, proline, is instead a constituent of collagen, whose role is to ensure the perfect holding capacity and elasticity of epithelial tissues. It naturally follows that the intake of the vitamins and minerals present in Aloe stimulates proper blood saturation, thus guaranteeing better oxygenation and faster expulsion of toxins. Skin becomes smoother, hydrated and more elastic, protected from free radicals and their degenerative activity, resulting in impressive / substantial anti-aging effects. [56][57]

Anti-inflammatory Action: Aloe vera inhibits the cyclooxygenase pathway and reduces prostaglandin E2 production from arachidonic acid. Recently, the novel anti-inflammatory compound called Cglucosyl chromone was isolated from gel extracts.[58][59]

Fresh Aloe vera gel: significantly reduced acute inflammation in rats (carrageenin-induced paw oedema), but not in chronic inflammation. In croton oil-induced oedema in mice, three Aloe vera gel sterols were able to reduce inflammation by up to 37%. Lupeol, the most active anti-inflammatory sterol, reduced inflammation in a dose dependent manner.[60]

Anti-ulcer Activity: It stops bleeding, damage and leakage of intestine walls and rebuilds protective mucosa lining.⁶⁰

Gastroprotective activity: The plant was more active as a gastroprotective agent at lower concentration against mucosal injury. Aloe vera acts as a healing agent inside the digestive tract. It encourages the release of pepsin a gastric enzyme necessary for digestive process. ⁶¹

Atherosclerosis and coronary heart disease: The ingestion of aloe gel may have beneficial effect by lowering serum cholesterol, serum triglycerides and serum phospholipids, which when elevated, seem to accelerate the deposition of fatty material in the large and medium sized arteries, including the coronary arteries, including the coronary arteries of the heart.⁶²

Hypolipidemic activity: The administration of Processed Aloe vera gel lowered triacylglyceride levels in liver and plasma. Aloe vera gel helps rebalance the blood chemistry in a way that it lowers cholesterol naturally.⁶³

Antifungal activity: Leaf pulp and liquid fraction of *Aloe vera* act against plant pathogenic fungi.⁶⁴

External Skin Care: Aloe vera heals the skin in several ways.

Cures cuts: It promotes healthy healing of minor cuts, scrapes, scratches and wounds. It seals off the injury and helps the formation of new skin cells.

Heals burns: It helps the formation of new skin cells and hastens healing. It promotes healthy tissue growth by reducing inflammation and killing bacteria that thrive on damaged skin cells. Its cooling effects offer instant relief from burns and prevent blistering.

Alleviates Allergy: It is proven that the pulp of aloe vera relieves itching due to allergies and insect bites as well as aids in healing. Aloe vera is used on blisters, sores, rashes, fungal infections etc.

Skin disease treatment: Aloe vera is reputed to be effective in the treatment of seborrhea, herpes, red spot, eczema, psoriasis, warts etc.

Reduces stretch marks: Pregnant women use aloe vera gel and lotion to make stretch marks disappear.

Enhances beauty: It gives a glowing effect to dry skin. It reduces acne and sunburn. It lessens wrinkles and overall gives the skin a healthy touch.

Scalp and hair care: Aloe vera is good for hair and scalp acting as a natural hair conditioner. It makes the root of the hair stronger and reduces hair-fall. It revitalizes dull hair, giving them a natural sheen.

Industrial processing of aloe vera leaf gel: Industrial processing of Aloe vera leaf gel includes the following steps.³⁰

Reception of raw materials: The Aloe vera leaves after harvesting were preferably transported in refrigerated vans from the field to the processing place. The leaves should be sound, undamaged, mold/rot free and matured (3-4 years) in order to keep all the active ingredients in full concentration¹. However, the composition of these active ingredients are subtly affected by seasonal, climatic and soil variations. One important factor that must be considered is the handling/treatment of the leaves after its harvesting because the decomposition of the gel matrix occurs on cutting due to natural enzymatic reactions and the activity of bacteria that are normally present on the leaves. This degradative process can adversely affect the quality of the end product. Therefore, there is a need to carefully work towards refrigerating the freshly removed leaves within 4-6 h or get the raw material directly into production.

Filleting operation: The losses of biological activity appeared to be the result of enzymatic activity after the aloe leaf was removed from the plant. In fact, it was shown that the aloe gel, once extracted from the leaf, had greater stability than the gel left in the leaf. In order to avoid the decomposition of the biological activity, the filleting operation must be completed within 36 h of harvesting the leaves. In the other hand, the anthraquinone was one important factor leading to nonenzymatic browning in aloe

Grinding/homogenization: The major steps in this process include crushing or grinding. The aloe gel fillets should be crushed and homogenized using a commercial high speed tissue crusher at room temperature (25°C). Due to the reaction of enzymatic browning, the longer the crushing/grinding time, the higher the browning index in Aloe vera gel juice. Therefore, crushing or grinding should be shortened within 10-20 min in order to avoid the enzymatic browning reaction of Aloe vera gel.

Addition of pectolytic enzyme: Enzymatic treatment of Aloe vera gel for a long duration prior to processing is detrimental to biologically active compound such as polysaccharide which is the single most important constituent in aloe. Many researches have been done on the polysaccharides. It has been reported that the enzyme treatment at 50°C and within 20 min did not induce the loss of biological activity of polysaccharide in Aloe vera gel.

Filtration: This operation influences on the stability of Aloe vera gel juice. For example, the product showed the sedimentation of particles as the filtration operation lost its control.

Addition of vitamin C and citric acid: The unpasteurized aloe gel juice was fortified with vitamin C and citric acid to avoid browning reaction, to improve the flavor of Aloe vera gel juice and to stabilize the juice. The pH of aloe gel juice was adjusted between 3.0 and 3.5 by adding citric acid to improve the flavour of Aloe vera gel juice.

Dearation: The aim of dearation step is to avoid the oxidation of ascorbic acid, which eventually improves the shelf life of the Aloe vera gel juice.

Pasteurization: Like the process of other vegetable juice, this step may affect the taste, appearance and the content of biological activity of aloe gel product. HTST (High Temperature Shot Time) treatment (at 85-95°C for 1-2 min) is an effective method to avoid the bad flavour and the loss of biological activity of the Aloe vera gel.

Flash cooling: After pasteurization, the juice is flash cooled to 5°C or below within 10-15 sec. This is a crucial step to preserve biological activity of the Aloe vera gel

Concentration: The gel obtained using the pasteurization and flash cooling methods can be concentrated under vacuum without the loss of biological activity. The concentration operation must be conducted under 125 mm mercury vacuum at temperature below 50°C and must not exceed 2 min. Higher vacuum and temperature will cause activity loss, as will extend concentration times.

Freeze or spray drying: The concentrated product can then be freeze-dried at temperature between -45 and 30°C or can be spray dried with product temperature below 60°C without the loss in biological activity.

Storage: Relative humidity and temperature are two most important environmental parameters that affect product quality. Those two parameters can also affect the amount of the volatile substances of the juice absorbed by the packaging material and consequently, affect the shelf-life of the product.

IV. QUALITY OF ALOEVERA PRODUCTS

Aloe is not just aloe because the manufacturer says so. To assure that an aloe product at a price worth paying and to achieve the desired results, it is

recommended to look for International Aloe Science Council (IASC) certification seal on literature and packaging. Another way to ascertain whether an Aloe Vera product has a high healing capacity is to find out the number of mucopolysaccharides (MPS) present. This is sometimes included on the labeling. The highest therapeutic value is found in product containing between 10,000 and 20,000 MPS per liter.³¹

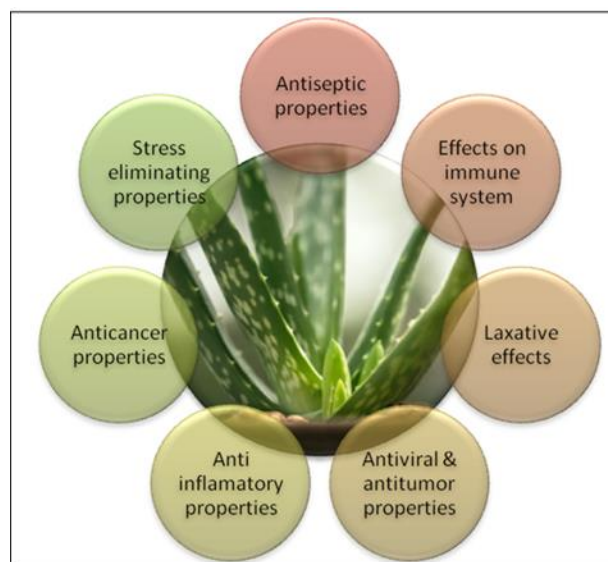


Fig: 3 Pharmacological activity of Aloe vera

V. INDUSTRIAL USES

1. Food Industry:

In the food industry, Aloe vera has been utilized as a resource of functional food, especially for the preparation of health food drinks and other beverages, including tea.⁶⁵

2. Cosmetic and Toiletry Industries:

Aloe vera gel also finds its application in the cosmetic and toiletry industries, where it is used as a base for the preparation of creams, lotions, soaps, shampoos and facial cleaners. Aloe Vera also used as moisturizer, skin caring product and healing agent in cosmetics.⁶⁶

3. Pharmaceutical industry:

In the pharmaceutical industry, it has been used for the manufacture of topical products such as ointments and gel preparations, as well as in the production of tablets and capsules³⁶. Important pharmaceutical properties that have recently been discovered for both the *A. vera* gel and whole leaf extract include the ability to improve the bioavailability of co-administered vitamins in human subjects³⁷.

Due to its absorption enhancing effects, *A. vera* gel may be employed to effectively deliver poorly absorbable drugs through the oral route of drug administration. Furthermore, the dried powder obtained from *A. vera* gel was successfully used to manufacture directly compressible matrix type tablets.

These matrix type tablets slowly released a model compound over an extended period of time and thereby showing potential to be used as an excipient in modified release dosage forms³⁸. Aloe vera also used in the preparation of nutraceuticals³⁹ and OTC drugs⁶⁷

4. Textile industry:

With the price of yarn increasing, weavers in Tamil Nadu using the aloe vera natural fibre to make colourful sarees.

5. Aloe In Global Market:

Aloe Vera being a medicinal plant and due to its extensive medicinal, nutraceutical and other uses its enjoy a great demand in the market across the globe. The major markets for Aloe Vera and its extracts are Australia, US and the entire Europe. Given the exponentially growing demand for it in the international market, Aloe Vera presents the finest commercial opportunity among the various medicinal plants. India is one among the few countries gifted with the unique geographical features essential for cultivation of Aloe Vera and other high potential medicinal plants.[68] The International Aloe Science Council is a non-profit trade organization for the Aloe Vera Industry world-wide. Aloe growers, processors, finished goods, manufactures, marketing companies, insurance companies, equipment suppliers, printers, sales organizations, physicians, scientists and researchers are all eligible for and compromise membership.[69] The common bond between the diverse group of individuals and companies is an interest in promoting Aloe Vera use in skin care products, beverages, pharmaceuticals and a wide variety of other products.[70]

VI. CONCLUSION

Aloe vera has historically been utilised for the treatment of skin injuries (such as burns, cuts, insect bites, and dermatitis) and digestive issues due to its anti-inflammatory, antibacterial, and wound-healing attributes. The research on this medicinal plant focusses on substantiating traditional applications and elucidating the mechanism of action, as well as identifying the chemicals responsible for these effects. Similarly, novel effects have been explored for Aloe vera and its active constituents, particularly emphasising its potential as a cytotoxic, antitumoural, anticancer, and antidiabetic drug. Over the past six years, the majority of pharmacological research has comprised in vitro and in vivo trials. In vitro research predominantly focus on antibacterial, anti-inflammatory, cytotoxic, antitumor, anticancer, and skin protective effects. It is particularly important to highlight that various in vitro studies assess the preventive effects of Aloe vera in bone disorders, including osteoporosis. The findings on bone protection are encouraging; however, it is essential to do further studies with experimental animals and humans. In vivo studies are designed to assess cardioprotective effects, cytotoxicity, antitumor and anticancer activities, as well

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