Organic Aloe Vera extracts

Aloe vera has been used for medicinal purposes in several cultures for millennia: Greece, Egypt, India, Mexico, Japan and China. Egyptian queens Nefertiti and Cleopatra used it as part of their regular beauty regimes. Alexander the Great, and Christopher Columbus used it to treat soldiers' wounds. The first reference to Aloe vera in English was a translation by John Goodyew in A.D. 1655 of Dioscorides' Medical treatise De Materia Medica. By the early 1800s, Aloe vera is in use in the United States, was successfully used to treat chronic and severe radiation dermatitis.

A.vera/olive oil cream was at least as effective as betamethasone 0.1% in the treatment of sulfur mustard-induced chronic skin complications and might serve as a promising therapeutic option for the alleviation of symptoms in mustard gas-exposed patients.

Uses based on scientific evidence: These uses have been tested in humans or animals. Safety and effectiveness have not always been proven.

Conditions: Seborrheic dermatitis, psoriasis vulgaris, genital herpes, skin burns, wound healing (results of aloe on wound healing are mixed with some studies reporting positive results), pressure ulcers, mucositis, radiation dermatitis

 Yunes Panahi, Seyyed Masoud Davoudi, Amirhossein Sahebkar, Fatemeh Beiraghdar, Yahya Dadjo, Iraj Feizi, Efficacy of Aloe vera/olive oil cream versus betamethasone cream for chronic skin lesions following sulfur mustard exposure: a randomized double-blind clinical trial <u>Cutaneous and Ocular Toxicology</u> Vol 31(2), 2012, 95-103 |

2. <u>KOJO ESHUN & QIAN HE</u> Aloe Vera: A Valuable Ingredient for the Food, Pharmaceutical and Cosmetic Industries—A Review <u>Critical Reviews in Food Science and</u> <u>Nutrition 4</u>4(2), 2004 -91-96 19. West DP, Zhu YF. Evaluation of aloe vera gel gloves in the treatment of dry skin associated with occupational exposure. Am J Infect Control. **2003**;31:40–2.

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Research Articles ALOE GEL

Yunes Panahi, Seyyed Masoud Davoudi, Amirhossein Sahebkar, Fatemeh

<u>Beiraghdar, Yahya Dadjo, Iraj Feizi,</u> Efficacy of *Aloe vera*/olive oil cream versus betamethasone cream for chronic skin lesions following sulfur mustard exposure: a randomized double-blind clinical trial <u>Cutaneous and Ocular Toxicology</u> Vol 31(2), 2012, 95-103 | *Background*: Chronic pruritic skin lesions are among the common late complications of sulfur mustard intoxication. In the present randomized double-blind clinical trial, therapeutic efficacy of *Aloe vera*/olive oil combination cream in the alleviation of these lesions was evaluated and compared to that of betamethasone 0.1% cream.

Methods: Sixty-seven Iranian chemical warfare-injured veterans were randomized to apply *A. vera*/olive oil (n = 34, completers = 31) or betamethasone 0.1% (n = 33, completers = 32) cream twice daily for 6 weeks. Evaluation of pruritus severity was performed using a pruritic score questionnaire and visual analogue scale (VAS).

Results: Both treatments were associated with significant reductions in the frequency of pruritus (p < 0.05), burning sensation (p < 0.01 and p < 0.001 in *A. vera*/olive oil and betamethasone group, respectively), scaling (p < 0.01 and p < 0.05) and dry skin (p < 0.001) at the end of trial. Fissure and excoriation were only reduced in the *A. vera* group (p < 0.05). The change in the frequency of hyper- and hypopigmentation lesions, blisters, erythema and lichenification did not reach statistical significance in any of the groups (p > 0.05). Mean pruritus (p < 0.05) and VAS scores (p < 0.01 and p < 0.05) were significantly decreased by the end of trial in both groups. The rate of improvement in the pruritus severity [defined as being classified in a less severe category (mild, moderate and severe)] was found to be comparable between the groups (p > 0.05).

Conclusion: A. vera/olive oil cream was at least as effective as betamethasone 0.1% in the treatment of sulfur mustard-induced chronic skin complications and might serve as a promising therapeutic option for the alleviation of symptoms in mustard gas-exposed patients. <u>KOJO ESHUN & QIAN HE</u> Aloe Vera: A Valuable Ingredient for the Food, Pharmaceutical and Cosmetic Industries—A Review <u>*Critical Reviews in Food Science and Nutrition* 4</u>4(2), 2004 - 91-96

Amar Surjushe, <u>Resham Vasani</u>, and <u>D G Saple</u> ALOE VERA: A SHORT REVIEW, <u>Indian</u> <u>J Dermatol</u>. 2008; 53(4): 163–166.

Aloe vera is a natural product that is now a day frequently used in the field of cosmetology. Though there are various indications for its use, controlled trials are needed to determine its real efficacy. The aloe vera plant, its properties, mechanism of action and clinical uses are briefly reviewed in this article.

Keywords: Aloe vera, health and beauty, skin

Introduction

The Aloe vera plant has been known and used for centuries for its health, beauty, medicinal and skin care properties. The name Aloe vera derives from the Arabic word "Alloeh" meaning "shining bitter substance," while "vera" in Latin means "true." 2000 years ago, the Greek scientists regarded Aloe vera as the universal panacea. The Egyptians called Aloe "the plant of immortality." Today, the Aloe vera plant has been used for various purposes in dermatology.

History

Aloe vera has been used for medicinal purposes in several cultures for millennia: Greece, Egypt, India, Mexico, Japan and China.<u>1</u> Egyptian queens Nefertiti and Cleopatra used it as part of their regular beauty regimes. Alexander the Great, and Christopher Columbus used it to treat soldiers' wounds. The first reference to Aloe vera in English was a translation by John Goodyew in A.D. 1655 of Dioscorides' Medical treatise De Materia Medica.<u>2</u> By the early 1800s, Aloe vera was in use as a laxative in the United States, but in the mid-1930s, a turning point occurred when it was successfully used to treat chronic and severe radiation dermatitis.2

Plant

The botanical name of Aloe vera is *Aloe barbadensis miller*. It belongs to Asphodelaceae (Liliaceae) family, and is a shrubby or arborescent, perennial, xerophytic, succulent, pea- green color plant. It grows mainly in the dry regions of Africa, Asia, Europe and America. In India, it is found in Rajasthan, Andhra Pradesh, Gujarat, Maharashtra and Tamil Nadu.

Anatomy

The plant has triangular, fleshy leaves with serrated edges, yellow tubular flowers and fruits that contain numerous seeds. Each leaf is composed of three layers: 1) An inner clear gel that contains 99% water and rest is made of glucomannans, amino acids, lipids, sterols and vitamins. 2) The middle layer of latex which is the bitter yellow sap and contains anthraquinones and glycosides. 3) The outer thick layer of 15–20 cells called as rind which has protective function and synthesizes carbohydrates and proteins. Inside the rind are vascular bundles responsible for transportation of substances such as water (xylem) and starch (phloem).<u>3</u>

Active components with its properties: Aloe vera contains 75 potentially active constituents: vitamins, enzymes, minerals, sugars, lignin, saponins, salicylic acids and amino acids.

- 1. *Vitamins*: It contains vitamins A (beta-carotene), C and E, which are antioxidants. It also contains vitamin B12, folic acid, and choline. Antioxidant neutralizes free radicals.
- 2. *Enzymes*: It contains 8 enzymes: aliiase, alkaline phosphatase, amylase, bradykinase, carboxypeptidase, catalase, cellulase, lipase, and peroxidase. Bradykinase helps to reduce excessive inflammation when applied to the skin topically, while others help in the breakdown of sugars and fats.
- 3. *Minerals:* It provides calcium, chromium, copper, selenium, magnesium, manganese, potassium, sodium and zinc. They are essential for the proper functioning of various enzyme systems in different metabolic pathways and few are antioxidants.
- 4. *Sugars:* It provides monosaccharides (glucose and fructose) and polysaccharides: (glucomannans/polymannose). These are derived from the mucilage layer of the plant and are known as mucopolysaccharides. The most prominent monosaccharide is mannose-6-phosphate, and the most common polysaccharides are called glucomannans [beta-(1,4)-acetylated mannan]. Acemannan, a prominent glucomannan has also been found. Recently, a glycoprotein with antiallergic properties, called alprogen and novel anti-inflammatory compound, Cglucosyl chromone, has been isolated from Aloe vera gel.<u>7.8</u>
- 5. *Anthraquinones:* It provides 12 anthraquinones, which are phenolic compounds traditionally known as laxatives. Aloin and emodin act as analgesics, antibacterials and antivirals.

- 6. *Fatty acids:* It provides 4 plant steroids; cholesterol, campesterol, β-sisosterol and lupeol. All these have anti-inflammatory action and lupeol also possesses antiseptic and analgesic properties.
- 7. *Hormones:* Auxins and gibberellins that help in wound healing and have antiinflammatory action.
- 8. *Others:* It provides 20 of the 22 human required *amino acids* and 7 of the 8 essential amino acids. It also contains salicylic acid that possesses antiinflammatory and antibacterial properties. Lignin, an inert substance, when included in topical preparations, enhances penetrative effect of the other ingredients into the skin. Saponins that are the soapy substances form about 3% of the gel and have cleansing and antiseptic properties.

Mechanism of actions

- 1. *Healing properties*: Glucomannan, a mannose-rich polysaccharide, and gibberellin, a growth hormone, interacts with growth factor receptors on the fibroblast, thereby stimulating its activity and proliferation, which in turn significantly increases collagen synthesis after topical and oral Aloe vera.⁹ Aloe gel not only increased collagen content of the wound but also changed collagen composition (more type III) and increased the degree of collagen cross linking. Due to this, it accelerated wound contraction and increased the breaking strength of resulting scar tissue.¹⁰ An increased synthesis of hyaluronic acid and dermatan sulfate in the granulation tissue of a healing wound following oral or topical treatment has been reported.¹¹
- 2. *Effects on skin exposure to UV and gamma radiation:* Aloe vera gel has been reported to have a protective effect against radiation damage to the skin.<u>12.13</u> Exact role is not known, but following the administration of aloe vera gel, an antioxidant protein, metallothionein, is generated in the skin, which scavenges hydroxyl radicals and prevents suppression of superoxide dismutase and glutathione peroxidase in the skin. It reduces the production and release of skin keratinocyte-derived immunosuppressive cytokines such as interleukin-10 (IL-10) and hence prevents UV-induced suppression of delayed type hypersensitivity.<u>14</u>
- 3. *Anti-inflammatory action:* Aloe vera inhibits the cyclooxygenase pathway and reduces prostaglandin E2 production from arachidonic acid. Recently, the novel anti-inflammatory compound called C-glucosyl chromone was isolated from gel extracts.<u>8</u>
- 4. *Effects on the immune system:* Alprogen inhibit calcium influx into mast cells, thereby inhibiting the antigen-antibody-mediated release of histamine and leukotriene from mast cells.⁷ In a study on mice that had previously been implanted with murine sarcoma cells, acemannan stimulates the synthesis and release of interleukin-1 (IL-1) and tumor necrosis factor from macrophages in mice, which in turn initiated an

immune attack that resulted in necrosis and regression of the cancerous cells.<u>15</u> Several low-molecular-weight compounds are also capable of inhibiting the release of reactive oxygen free radicals from activated human neutrophils.<u>16</u>

- 5. *Laxative effects:* Anthraquinones present in latex are a potent laxative. It increases intestinal water content, stimulates mucus secretion and increases intestinal peristalsis.<u>17</u>
- 6. *Antiviral and antitumor activity:* These actions may be due to indirect or direct effects. Indirect effect is due to stimulation of the immune system and direct effect is due to anthraquinones. The anthraquinone Aloin inactivates various enveloped viruses such as herpes simplex, varicella zoster and influenza.¹⁸ In recent studies, a polysaccharide fraction has shown to inhibit the binding of benzopyrene to primary rat hepatocytes, thereby preventing the formation of potentially cancer-initiating benzopyrene-DNA adducts. An induction of glutathione S-transferase and an inhibition of the tumor-promoting effects of phorbol myristic acetate has also been reported which suggest a possible benefit of using aloe gel in cancer chemoprevention.<u>19,20</u>
- 7. *Moisturizing and anti-aging effect:* Mucopolysaccharides help in binding moisture into the skin. Aloe stimulates fibroblast which produces the collagen and elastin fibers making the skin more elastic and less wrinkled. It also has cohesive effects on the superficial flaking epidermal cells by sticking them together, which softens the skin. The amino acids also soften hardened skin cells and zinc acts as an astringent to tighten pores. Its moisturizing effects has also been studied in treatment of dry skin associated with occupational exposure where Aloe Vera gel gloves improved the skin integrity, decreases appearance of fine wrinkle and decreases erythema.<u>21</u> It also has anti-acne effect.
- 8. *Antiseptic effect:* Aloe Vera contains 6 antiseptic agents: Lupeol, salicylic acid, urea nitrogen, Cinnamonic acid, phenols and sulfur. They all have inhibitory action on fungi, bacteria and viruses.

Clinical uses: The clinical use of aloe vera is supported mostly by anecdotal data. Though most of these uses are interesting, controlled trials are essential to determine its effectiveness in all the following diseases. <u>22.23</u>

Uses based on scientific evidence: These uses have been tested in humans or animals. Safety and effectiveness have not always been proven.

Conditions: Seborrheic dermatitis,<u>24</u> psoriasis vulgaris,<u>25,26</u> genital herpes,<u>27,28</u> skin burns,<u>5,29</u> diabetes (type 2),<u>30</u> HIV infection,<u>31</u> cancer prevention,<u>32,33</u> ulcerative colitis<u>34</u> wound healing (results of aloe on wound healing are mixed with some studies reporting positive results<u>35</u> and others showing no benefit<u>36</u> or potential worsening<u>37,38</u>), pressure ulcers,<u>36</u> mucositis,<u>39</u> radiation dermatitis,<u>40</u> acne vulgaris,<u>41</u> lichen planus,<u>42</u> frostbite,<u>43</u> aphthous stomatitis,<u>44</u> and constipation.<u>17</u>

Uses based on tradition or theory: The below uses are based on tradition or scientific theories. They often have not been thoroughly tested in humans, and safety and effectiveness have not always been proven.

Conditions: Alopecia, bacterial and fungal skin infections, chronic leg wounds, parasitic infections, systemic lupus erythematosus, arthritis and tic douloureux.

Side effects

Topical: It may cause redness, burning, stinging sensation and rarely generalized dermatitis in sensitive individuals. Allergic reactions are mostly due to anthraquinones, such as aloin and barbaloin. It is best to apply it to a small area first to test for possible allergic reaction. *Oral:* Abdominal cramps, diarrhea, red urine, hepatitis, dependency or worsening of constipation. Prolonged use has been reported to increase the risk of colorectal cancer. Laxative effect may cause electrolyte imbalances (low potassium levels).

Contraindication: Contraindicated in cases of known allergy to plants in the Liliaceae family. **Pregnancy and breastfeeding:** Oral aloe is not recommended during pregnancy due to theoretical stimulation of uterine contractions, and in breastfeeding mothers, it may sometime causes gastrointestinal distress in the nursing infant.

Interactions: Application of aloe to skin may increase the absorption of steroid creams such as hydrocortisone. It reduces the effectiveness and may increases the adverse effects of digoxin and digitoxin, due to its potassium lowering effect. Combined use of Aloe vera and furosemide may increase the risk of potassium depletion. It decreases the blood sugar levels and thus may interact with oral hypoglycemic drugs and insulin.

Thus, though Aloe vera has wide spectrum of the properties and uses, some of them could be myths and some of them could be real magic. In future, controlled studies are required to prove the effectiveness of Aloe vera under various conditions.

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Organic St. John's Wort Oil- Calendula Extract

European Union herbal monograph on *Calendula officinalis* L., flos EMA/437450/2017 European Union herbal monograph on Hyperici herba EMEA/HMPC/745582/2009

1. *officinalis* Linn. (Pot marigold) has been traditionally used in the treatment of inflammations of internal organs, gastrointestinal ulcers and dysmenorrhea and as a diuretic and diaphoretic in convulsions. It is also used for inflammations of the oral and pharyngeal mucosa, wounds and burns. *Calendula* is a cleansing and detoxifying herb and the infusion treat chronic infections. The dried flower heads have been used for their antipyretic, anti-tumor and cicatrizing effects. Topical application of infusion of flowers is used as antifungal and antiseptic in wounds, marks, freckles, sprain and conjunctivitis. *Calendula* tea is used as eyewashes, gargles, diaper rashes and other inflammatory conditions of the skin and mucous membranes. Mother tincture of *C. officinalis* is

used in homoeopathy for the treatment of mental tension and insomnia. Medicinal properties of *C. officinalis* have been mentioned in Ayurvedic and Unani system of medicine indicating that leaves and flowers are antipyretic, anti-inflammatory, antiepileptic and antimicrobial. In traditional and homoeopathic medicine, *C. officinalis* has been used for poor eyesight, menstrual irregularities, varicose veins, hemorrhoids and duodenal ulcers. In the middle ages, *Calendula* flowers were used for liver obstructions, snake bites and to strengthen the heart. It was used in the 18th century as a remedy for headache, jaundice and red eyes. The plant was employed in the civil war to treat wounds and as a remedy for measles, smallpox and jaundice.

Decoction and infusion of *Calendula persica* C.A. Mey aerial parts are employed for the treatment of kidney stones.

In a randomized, open controlled study, the effects of three ointments were compared after topical treatment of patients with 2 nd or 3 rd degree burns for 17 days: *Calendula* flower ointment (prepared by digestion in vaseline) (n = 53) or vaseline only (n = 50) or a proteolytic ointment (n = 53). The success rates were considered to be 37/53 for *Calendula* flower ointment, 27/50 for vaseline and 35/53 for the proteolytic ointment. [78] In an open uncontrolled pilot study, 30 patients with burns or scalds were treated 3 times/day for up to 14 days with a hydrogel containing 10% of a hydro-ethanol extract. The symptoms reddening, swelling, blistering, pain, soreness and heat sensitivity were scored before, during and at the end of treatment.

Total score and individual scores for each symptom improved. In women with surgical wounds, local application of a mixture containing 70% oily extract of *Hypericum perforatum* and 30% oily extract of Phase III randomized single blinded trial of *C. officinalis* compared with trolamine for the prevention of acute dermatitis during irradiation for breast cancer was conducted. Patients who had been operated on for breast cancer and who were to receive post-operative radiation therapy were randomly allocated to application of

either *Calendula* ointment containing 20% of fresh *Calendula* aerial parts in petroleum jelly (126 patients) or trolamine (128 patients) on the irradiated fields after each session.

The primary end point was the occurrence of acute dermatitis of grade 2 or higher. Secondary end points were the occurrence of pain, the quantity of the topical agent used and the patient satisfaction. The occurrence of acute dermatitis of grade 2 or higher was significantly lower

(41% vs. 63%; P < 0.001) with the use of *Calendula* than with trolamine. Moreover, patients receiving *Calendula* had less frequent interruption of radiotherapy and significantly reduced radiation-induced pain. Clinical examination of an ointment with *C. officinalis* extract was carried out in 34 patients with venous leg ulcer. A total of 21 patients with 33 venous ulcers were treated with ointment, applied twice a day for 3 weeks.

This review includes 84 references on The genus Calendula (Asteraceae) and comprises ethnopharmacology, morphology and microscopy, phytoconstituents, pharmacological reports, clinical studies and Toxicology of The prominent species of Calendula. Triterpene alcohols, Triterpene saponins, flavonoids, carotenoids and polysaccharides constitute major classes of phytoconstituents of The genus. A few species of This genus have medicinal value, among These Calendula officinalis Linn., has been Traditionally used in The Treatment of various skin Tumors, dermatological lesions, ulcers, swellings and nervous disorders as well as almost 200 cosmetic formulations, i.e., creams, lotions, shampoos. Despite a long Tradition of use of some species, The genus has not been explored properly. In The concluding part, The future scope of Calendula species has been emphasized with a view To establish Their multifarious biological activities and mode of action

St. John's Wort (SJW) is an herbaceous medical plant. Since ancient times, SJW has been used to treat different kinds of mental and physical diseases and, for its antiseptic, anti-inflammatory and antibacterial properties.

The use of topical formulations of SJW (*H. perforatum*) for wound healing, alone or in combination with other herbaceous medical remedy, has been widely described in rats, golden hamsters, humans, in vitro, on cultured NIH3T3 fibroblasts. To the authors knowledge, few scientific works have been carried out on the use of *H. perfoliatum* in any species;, and no scientific evidences exist on the use of SJW as an antibacterial remedy and for wound healing in horses.

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<u>Arora, D.; Rani, A.; Sharma, A.</u> A review on phytochemistry and ethnopharmacological aspects of genus *Calendula* (Review) <u>Pharmacognosy Reviews</u> 7 (13), 2013, 179-187

Panthenol

Vitamin B5 and its derivatives are well known in personal care applications and are often used in wound healing and soothing compositions. However, little is known about the biochemical pathways involved. A better knowledge of these pathways would help to understand some of the mechanisms of action and suggest further applications. We have investigated the transformation of D-panthenyl triacetate (PTA) into D-panthenol (PAN) and its skin diffusion on human volunteers by Raman spectroscopy. Additionally, we have utilized human skin biopsies and guantitative RT-PCR to demonstrate the effect of PTA compared to PAN on 27 metabolic markers when introduced at 2% in a cosmetic emulsion. Then we conducted a double-blind clinical study to measure the effect of PTA compared to PAN on wound healing, measured by transepidermal water loss (TEWL), when incorporated at 3% in a cosmetic emulsion. Results show de-acetylation of PTA into PAN and an increased activity of PTA compared to PNA over time in the skin. Metabolic marker analysis demonstrates stimulation of energetic pathways such as glycolysis and the citric acid cycle, but also of synthesis pathways such as isoprenoids and lipid synthesis, by PTA and PAN. Finally, the clinical study demonstrates a statistically significant effect by PTA on wound healing after 72 hours when compared to a saline treatment. Statistical significance was not achieved by PAN or a placebo treatment. Due to the differences between PTA and PAN action, different applications in personal care products can be suggested. Moreover, PTA seems more effective than PAN for a long-lasting wound healing action.

<u>Dell'Acqua, G.,Schweikert, K.P</u>anthenyl triacetate transformation, stimulation of metabolic pathways, and wound-healing properties in the human skin <u>Journal of cosmetic science</u> 63(1), 2012, 1-13

In this study, 5% barbatiman and 5% chitosan creams were evaluated as adjuvants in the tissue repair process by secondary intention of rabbit's skin wounds. Four equidistant wounds were induced in the dorsal skin of 20 adult male rabbits, which were submitted to healing by secondary intention and treated with 5% chitosan cream (QC, n=5), 5% barbatiman cream (BC, n=5), 2% allantoin cream (n=5), and base cream (n=5). The creams were applied with the aid of disposable spatulas after washing the wounds. The wounds were daily analyzed by clinical examination for 21 days and histological analyses were performed on the 3 rd , 14 th , and 21 st day after induction.

The microscopic evaluation of the wounds of all groups showed macroscopic features of the healing process at different time intervals. The QC and BC treatments helped in the skin repair process in rabbits when compared to the other two treatments. They induced fibroblast activation and early collagen deposition, and modulated re-epithelialization and neovascularization. Thus, it was concluded that BC and QC are efficient and economically feasible as adjuvants in the healing process of skin wounds in rabbits.

Allantoin

Allantoin is found in many vegetal and animal sources. Allantoin is the final product of purines metabolism in mammals but in primates. Currently, allantoin is synthetically produced and has demonstrated healing properties, promoting dead skin cells detachment and healthy tissue growth; it is safely used in 0.5-2.0% concentration; however, its mechanism of action remains unknown. Hypertrophic scars are an important Aesthetic and sometimes functional problem and for this reason, allantoin has been tested in this pathology. In **rats**, local allantoin improves experimental healing, which is evidenced by a lesser healing tissue growth,

congestion and inflammation, and also by the stimulation of collagen skin deposition. In cesarean section surgical wound, topical allantoin improves skin colour and decreases stiffness and roughness of the healing area. Efficacy and safety of allantoin was demonstrated in patients with radiotherapy skin lesions and in patients with hypertrophic scars, in comparison to locally applied corticosteroids. Allantoin produces less adverse events, telangiectasia and skin atrophy than steroidal agents, both within the scar and its surrounding tissues

<u>Natera, Y.M., Saenz, A.M.</u> Allantoin in the healing of surgical and radiotherapy skin lesions <u>Informe Medico</u> 17(4), 2015, 132-137