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REVIEW ARTICLE

REVIEW ON ALOE VERA

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Abstract

The Aloe vera plant has been known and used for centuries for its health, beauty, medicinal and skin care properties. There are over300 species of aloe, which grows mainly in the dry regions of Africa, Asia, Europe and America. 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. The plant has triangular, fleshy leaves with serrated edges, yellow tubular flowers and fruits that contain numerous seeds. Aloe vera contains 75 potentially active constituents: vitamins, enzymes, minerals, sugars, lignin, saponins, salicylic acids and amino acids. Several studies was done on aloe vera for evaluating different properties namely Antiulcer activity, Antidiabetic, Antihypercholestermic, Antioxidative Effect, Antibacterial activity, Antiviral activity, Antifungal activity, Antiacne, Cardiac stimulant, Nutraceutical, Moisturizer, Immunomodulator, Protection of skin from UV-A & UV-B rays and Wound healing property. Aloe vera could be used in various conditions like Mild to moderate burns**,** Erythema**,** Genital herpes**,** Seborrheic dermatitis**,** Psoriasis vulgaris**,** Skin moisturizer**,** Type 2 diabetes**,** Oral lichen planus infections**,** Angina pectoris**,** Ulcerative colitis**,** UV-induced erythema**,** Kidney stones and Alveolar osteitis. In general, topical application of aloe vera preparations has been regarded as safe as assessed by the Cosmetic Ingredient Review Expert Panel. However, several case reports of the development of hypersensitivity reactions and contact dermatitis in response to topically applied aloe gel preparations have been published.

REVIEW OF ALOE VERA

In recent times, focus on plant research has increased all over the world and a large body of evidence has collected to show immense potential of medicinal plants used in various traditional systems.[1]In future more coordinated multidimensional research aimed at correlating botanical and phytochemical properties to specific pharmacological activities is expected.

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."

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 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]

Vernacular names

Sanskrit	:	Kumari
Hindi	:	Giloya
English	:	Aloe
Kannada	:	Lolesara
Malayalam	:	Kattarvazha
Tamil	:	Soththu Kathalai

Medicinal species [3]

There are over 300 species of aloe, most of which are native to South Africa, Madagascar and Arabia.The different species have somewhat different concentrations of active ingredients. Examples of different species are Aloe vera, A. vulgaris, A.arborescens, A.ferox (Cape aloe), A. perryi (Socotrine or Zanzibar aloe). 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.

Habitat

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.[3]

Plant description

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. [2]

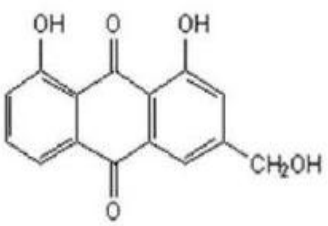
1) An inner clear gel that contains 99% water and rest is made of glucomannans, amino acids, lipids, sterols and vitamins.
2) The middle layer of latex which is the bitter yellow sap and contains anthraquinones and glycosides.
3) The outer thick layer of 15-20 cells called as rind which has protective function and synthesizes carbohydrates and proteins. Inside the rind are vascular bundles responsible for transportation of substances such as water (xylem) and starch (phloem).[4]

Constituents of aloe vera [5]

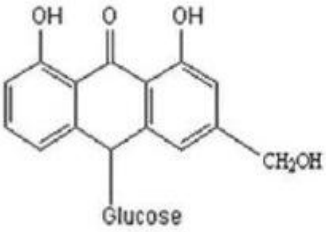
Anthraquinones	Saccharides	Vitamins	Inorganic Compounds
Aloin / Barbaloin	Cellulose	B1	Calcium
Isobarbaloin	Glucose	B2	Sodium
Aloe-emodin	Mannose	B6	Chlorine
Emodin	L-Rhamnose	Choline	Manganese
Aloetic Acid	Aldopentose	Folic Acid	Zinc
Ester of Cinnamic Acid		Ascorbic Acid	Chromium
Anthranol		α-Tocopherol	Copper
Chrysophanic Acid		β –Carotene	Magnesium
Resistannol Anthracene			Iron
Ethereal oil			

Enzymes	Nonessential Amino Acids	Essential Amino Acids	Miscellaneous
Cyclooxygenase	Histidine	Lysine	Cholesterol
Oxidase	Arginine	Threonine	Triglycerides
Amylase	Hydroxyproline	Valine	Steroids
Catalase	Aspartic Acid	Leucine	β-Sitosterol
Lipase	Glutamic Acid	Isoleucine	Lignins
Alkaline phospahatase	Proline	Phenylalanine	Uric Acid
Carboxypeptidase	Glycine	Methionine	Gibberellin
	Alanine		Lectin like substances
			Salicylic Acid
			Arachidonic Acid

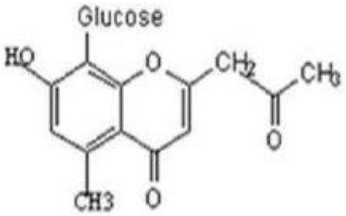
Structures of main anthraquinone compounds of aloe vera[6]



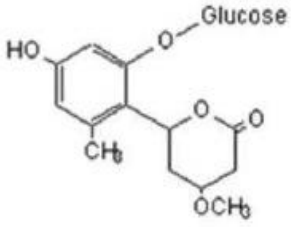
Aloe-emodin



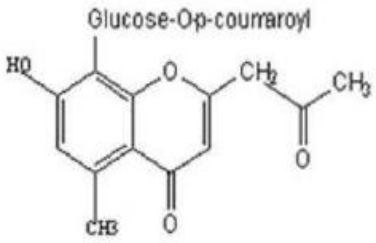
Aloin/Barbaloin



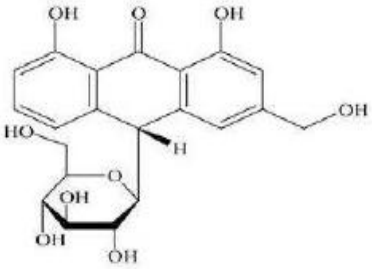
Aloesin/Aloeresin



Aloenin



Aloeresin A



Isobarbaloin

PLATE 1: Aloe vera plant

Active components with its properties: [2]

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

- **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.
- **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.
- **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.

- **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].Recently, a glycoprotein with antiallergic properties, called alprogen and novel anti-inflammatory compound, C-glucosyl chromone, has been isolated from Aloe vera gel.
- **Anthraquinones:** It provides 12 anthraquinones, which are phenolic compounds traditionally known as laxatives. Aloin and emodin act as analgesics, antibacterials and antivirals.
- **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.
- **Hormones:** Auxins and gibberellins that help in wound healing and have anti-inflammatory action.
- **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 anti-inflammatory 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.

Studies on aloe vera to evaluate different properties

1. Antiulcer activity [7]

A. vera extract inhibits acid secretion which may be due to the presence of lectins in the plant. It has been shown that lectins inhibit aminopyrine uptake by parietal cells, thus the ability of the extract to inhibit gastric acid output may be as a result of direct action on the acid producing cells.

2. Antidiabetic, Antihypercholestermic and Antioxidative Effect [8]

The results of the study showed that the hypoglycemic effect of aloe vera gel extract might be due to the presence of hypoglycemic trace elements as Cr, Zn and Mn which potentiate insulin action. Also, the glucose lowering effect could be explained by the antioxidant activity of aloe vera gel extract because it attenuated oxidative damage in the serum of alloxan induced diabetic rats.

3. Antibacterial activity [9]

A polyherbal formulation called BASANT had been constituted with curcumin, purified extracts of Emblica officinalis (Amla), purified saponins from Sapindus mukorossi, Aloe vera and rose water. It was shown to be effective in inhibiting Neisseria gonorrhoeae, Candida glabrata, Candida albicans and Candida tropicalis.

4. Antiviral activity [10]

The study showed A.barbadensis extracts inhibited viral growth in human cell lines. The MS2 plaque reduction assay was used to detect antiviral activity.

5. Antifungal activity [11]

The study showed antifungal property as they progressively inhibited the growth of *M.* furfur on Sabouraud's dextrose agar medium. Aloe vera was found more effective than other species tested.

6. Antiacne [12]

It was concluded from the study that aqueous extract of *Garcinia mangostana* and *Aloe vera* can be formulated in an aqueous based gel system for topical therapy of mild acne vulgaris.

7. Cardiac stimulant [13]

It was observed from the study that the active ingredient present in aloe vera may be acting either on the β-receptors or any other receptors that are blocked by propranolol, but was not able to identify the ingredients which is responsible for the positive inotropic and chronotropic effect on isolated heart.

8. In Polycystic ovarian syndrome [14]

Data from an "in vitro" study indicated that AVG acts directly on key enzymes like 3β HSD, decreasing enzyme activity and modulating the flux toward estradiol formation. However, the specific phyto--component acting on the enzyme system needs to be identified. In conclusion, the present study indicated that AVG had potential efficacy in the prevention and maintenance of PCOS.

9. A Potent Nutraceutical [15]

The Aloe vera gel showed a significant increase in body weight and hematological parameter, which confirmed its nutraceutical property. The investigation clearly indicated that Aloe vera gel has a powerful antioxidant activity against various oxidative systems and hematological activity. (It is also a bone marrow stimulant).

10. Moisturizer [16]

Aloe vera extract produced skin hydration. The mechanism predicted was humectants mechanism along with the occlusive layer formation on the skin by the formulations.

11. Immunomodulator [17]

The study showed that the higher dose of Aloe vera gel extract stimulated the proliferation of stem cells, as seen from an increase in total white blood cells. Hence it was concluded that the Aloe vera gel extract may be a potential candidate in several immune-suppressed clinical conditions.

12. Protection of skin from UV-A & UV-B rays [18]

Most commonly used herbs were aloe vera, basil, green tea, almond, olive, jojoba, and cucumber etc, incorporated in herbal sunscreens.

13. Wound healing [19]

The study reported to promote gain in tensile strength in the incision wound model, but they donot modify the granulation phase of healing. These herbs have also been reported to promote epithelization and wound contraction in cases of excision wound models. This property may be due to the effect of these herbs on migration and mitosis of epithelial cells, and promotion of contraction of myo-fibroblasts is responsible for wound contraction.

Various clinical studies on aloe vera (aloe barbadensis mill.) Inner gel[20]

Number	Author/Year	Subject	Design	Duration	Dosage	Preparation	Results
1)	**Agarwal, 1985**	Angina pectoris and diabetes	IC, R, N=5,000	5 years	100mg fresh inner gel in combination with bread containing seeds from Plantago ovata	Fresh flesh gelatin from Aloe vera, not chemically defined	Improvement after 2 weeks persisted for whole observation period with diabetic patients benefiting most from the Aloe and Plantago treatment, clinical parameters including cholesterol, triglycerides, and blood glucose levels normalized over time.
2)	**Schmidt et al, 1991**	Surgical wounds	R, SC, N=21	Time to Complete healing	Initially change of wound dressing every 8 hours until granulation tissue established, thereafter every 12 hours	Carrington Dermal wound gel®, standard treatment as control	Significant delay in wound healing for aloe gel group compared to standard treatment (P=0.003).

3)	**Montaner e t al, 1996**	HIV infection	R, DB, PC, MC, N=63	48 weeks	4x/day capsules	100 mg acemannanin capsules or equivalent placebo	Acemannan or placebo in addition to standard treatment showed no differences in CD4 count or survival after 48 weeks.
4)	**Syed et al, 1996**	Genital herpes	R, DB, PC, PG, N=120	2 weeks	3x/day to herpetic lesions, max. 30 applications	Aloe extract 0.5% in hydrophilic cream or gel	Both aloe cream & gel were effective in reducing healing time compared to placebo (4.8 vs. 7.0 vs. 14.0 days, respectively), aloe cream was more efficacious in number of cured patients compared to gel (70% vs. 45% vs. 7%, respectively, no side effects observed.
5)	**Syed et al, 1996**	Psoriasis vulgaris	R, PC, PG, N=60	4 weeks	3x/day to lesions, max. 15 applications per week	Aloe extract 0.5% in hydrophilic cream	Aloe hydrophilic cream cured 83.3% of patients treated vs. 6.6% in the control group. Psoriatic plaques were significantly (P<0.001) reduced and biopsies presented with reduced inflammation and parakeratosis.

6)	**Williams et al, 1996**	Radiation-induced dermatitis	R, DB, PC, N=191	Duration of radiation treatment	2x/day to irradiated area	98% pure, fresh aloe gel with added inert gel, patients could use hydrocortisone cream	No significant improvement in all parameters evaluated for aloe gel vs. placebo inert gel.
7)	**Heggie et al, 1998**	Radiation-Induced dermatitis	R, DB, PC, MC, N=208	Duration Of radiation treatment & 2 weeks post-treatment	3x/day to affected area	98% aloe gel & aqueous cream as placebo	No differences between aloe & placebo in severity of itching, erythema, or moist desquamation, but aqueous cream was significantly better in reducing moderate pain and dry desquamation.
8)	**Vardy et al, 1999**	Seborrheic dermatitis	DB, R, PC, N=44	4-6 weeks	2x/day to affected areas	Aloe emulsion (30%crude extract) in defined base, different base as placebo	Responder percentage higher in aloe group vs. placebo (58 vs. 15% assessed by physician), significant decrease in scaliness ($P<0.008$) and pruritus ($P<0.046$) in aloe group
9)	**Olsen et al, 2001**	Radiation-induced dermatitis	R, SB, SC, N=70	Duration of radiation treatment	6-8x/day to irradiated area	100% pure aloe gel (Fruit of the Earth) in addition to mild soap or mild soap alone, patients could use prescribed skin care products	Delayed onset of skin changes in aloe gel group ($P=0.013$), no placebo gel used, so effect not clearly associated with aloe.

10)	**Poor et al, 2002**	Alveolar osteitis	R, N=1,194	7 days post-surgery	SaliCept Patch® applied to surgery site	SaliCept patch contained acemannan hydrogel, compared to clindamycin Gelfoam, concurrent pain & antibiotic medication was identical	Significantly lower incident of alveolar osteitis & symptoms in SaliCept patch group compared to clindamycin Gelfoam group. Parameters used were based on physician evaluation & patient survey.
11)	**West et al, 2003**	Xerosis	PB, SC, N=29	30 days, 30 days rest, 10 days	Wearing glove with aloe gel for 8h/day	Aloetouch®, glove with dried, pure freeze-dried aloe gel which converts to a gel upon contact with skin moisture, no placebo	One hand covered in Aloetouch glove for 8h while other hand served as control—no placebo, baseline evaluation unblinded, outcome evaluation by photography and blinded, significant improvement for Aloetouch hand vs. uncovered hand ($P<0.0001$), but questionable since no placebo for general moisturizing effect used.

12)	**Langmead et al, 2004**	Ulcerative colitis	R, DB, PC, N=44	1 month	2x/day 100 ml	Aloe gel Natural Living Products ® formulation	2:1 aloe gel & placebo ratio in study, improvements in clinical response (P=0.048), but not for histological or sigmoidoscopic evaluations
13)	**Su et al, 2004**	Radiation-induced mucositis	R, DB, SC, PC, N=58	Duration of radiation treatment & 6 weeks	4x/day 20 ml p.o.	Lily of the Desert® 94.5% aloe vera	No significant differences in mucositis parameters between aloe
14)	**Paulsen et al, 2005**	Psoriasis vulgaris	DB, R, PC, SC, IC, N=40	4 weeks	2x/day to left or right arm, treatment with emollients and Vaseline allowed	ACTIV aloe® (Aloe vera Group ApS, Søborg, Denmark) with 98% aloe leaf gel	Placebo was more effective than aloe gel (P<0.0197) at first follow up visit (week 8), but not different at later time point (week12).
15)	**Dal'Belo et al, 2006**	Moisturizer	R, SB, PC, N=20	Short-term (0-3h) & long-term (2 weeks)	Single application & 2x/day for 2 weeks	0.1%, 0.25%, or 0.5% of freeze-dried 200:1 concentrAte ACTIValoe® aloe GEL FD200 in hydrophilic cream	Short-term significant increase in water content of the stratum corneum for 0.25 and 0.5% of aloe at 1, 2, and 3h after application (at leastP<0.01), long-term increase in water content for all 3 Aloe vera creams after 1 and 2 weeks (atleast P<0.01) compared to placebo, no changes in transepidermal water loss during entire trial

16)	**Davis et al, 2006**	Irritable Bowel Syndrome	R, DB, PC, N=41	1 month	4x/day 50 ml	Aloe gel Natural Living Products ® formulation	Patients recruited from refractory pool, no significant changes in IBS or pain scores (P=0.46 & P=0.12 respectively) between aloe & placebo group at 3 months after treatment
17)	**Choonhakarn et al, 2008**	Oral lichen planus infections	R, DB, PC, N=54	8 weeks	2x/day to affected area	70% aloe mucilage in hydrophi lic gel base, gel base as placebo control	81% of aloe patients showed good response to treatment vs. 4% in placebo group (P<0.001) with no side effects.
18)	**Reuter et al, 2008**	UV-induced erythema	R, DB, PC, SC, N=40	2 days	Occlusive bandage for 2 days	97.5% aloe gel compared to 0.25% prednicarbate, 1% hydrocortisone in placebo gel, 1% hydrocortisone cream, & placebo gel	Significant reduction of erythema by aloe gel compared to 1% hydrocortison e in placebo gel after 2 days, 1% hydrocortison e cream was more effective.
19)	**Rajar et al, 2008**	Lichen planus	R, DB, PC, SC, N=34	8 weeks	2x/day to erosive and ulcerative lesions	Aloe vera gel, not further specified	Lesions were significantly reduced in Aloe vera gel group compared to placebo with good response (at least 50% improvement) in 82% of patients compared to 5% in placebo group

20)	**Choonhakarn et al, 2009**	Lichen planus	R, DB, PC, SC, N=54	8 weeks	2x/day to erosive and ulcerative lesions	Aloe vera gel (containing 70% of aloe mucilage)	Lesions were significantly reduced in Aloe vera gel group compared to placebo with complete remission or good response in 88% of patients compared to 4% in placebo group
21)	**Choonhakarn et al, 2010**	Psoriasis vulgaris	DB, R, SC, N=80	8 weeks	2x/day to affected area, no other treatment allowed	Aloe vera cream (containing 70% of aloe mucilage) compared to 0.1% triamcinolone acetonide cream	Aloe vera cream was atleast as effective in reducing psoriatic plaque in patients as triamcinolone acetonide cream with significant more reduction in psoriasis area severity index and equal reduction in dermatology life quality index

Abbreviation key: IC- Interpatient control, PB-Partially blinded, SC- Single centre, MC- Multicentre, R-Randomized, DB- Double blinded, PC- Placebo controlled, SB- Single blinded, PG- Parallel group.

USES

- Mild to moderate burns[21–23]
- Erythema[24]
- Genital herpes[25,26]
- Seborrheic dermatitis[27]
- Psoriasis vulgaris[28]
- Skin moisturizer[29]
- Type 2 diabetes[30-32]
- Oral lichen planus infections[33,34]
- Angina pectoris[32]
- Ulcerative colitis[35-39]
- UV-induced erythema[24]
- Kidney stones[40,41]
- Alveolar osteitis[42]

Dosage

- For seborrheic dermatitis: 30% aloe vera in a hydrophilic emulsion twice daily to affected area[27]
- For psoriasis and genital herpes: Hydrophilic cream containing 0.5% aloe gel 3 times daily to affected area[26,28]

- Treatment of diabetes and angina pectoris: recommended in humans, 100 mg of fresh inner gel each day or 1 tablespoon twice daily.[32,43]
- For ulcerative colitis and irritable bowel syndrome: a dose of 25–50 ml of 95% aloe inner gel is recommended 3 times daily.[35]
- Adjuvant therapy in feline and canine malignancies: Acemannan Immunostimulant®, a special preparation of the clear mucilaginous gel specifically for injection, for intraperitoneal injection in cats and dogs following chemotherapy. Weekly injections over at least 6 weeks; recommended dose is 1 mg/kg body weight of animal.[44,45]

Duration of Administration

External administration 3–4 times daily to affected area until improvement is seen.[25,27,28] No information for duration after oral application in humans is available, but generally the gel is taken as long as the symptoms persist.[32]

Contraindications

Known allergy against aloe vera; discontinue use if skin irritation develops or worsens[46].

Pregnancy and Lactation

It is not recommended to use aloe vera gel during pregnancy or while breastfeeding.[47] There is, however, no evidence that suggests a reproductive or genotoxic effect of topical aloe vera inner gel preparations. Internal use in combination with digoxin is contraindicated due to possible acceleration of potassium depletion.[48]

Adverse Effects

In general, topical application of aloe vera preparations has been regarded as safe as assessed by the Cosmetic Ingredient Review Expert Panel.[47] However, several case reports of the development of hypersensitivity reactions and contact dermatitis in response to topically applied aloe gel preparations have been published.[49–53] This allergic reaction has been attributed in most cases to anthraquinone contaminations in the gel.[46] Macrophage infiltration and emesis has been observed in dogs treated intravenously with acemannan.[54] Oral application of aloe vera gel may lower blood glucose levels and enhance the activity of antidiabetic treatments.[32]No genotoxic effects have been observed following oral administration of an aloe vera inner leaf gel (Qmatrix® by Aloecorp, Inc., which is a standardized inner gel extract that has not been heated after extraction from the leaf) to rats after 90 days.[55] An important factor for adverse effects is the purity of the aloe vera gel used, since anthraquinones like aloin might be related to the development of hypersensitivity reactions.[49,56]

Drug Interactions

When aloe vera gel is administered topical, it is generally regarded as safe.[47] Aloe gel might enhance the ability of hydrocortisone to reduce swelling if applied topically.[57] If ingested, it might lead to increased hypoglycemia in conjunction with oral antidiabetics or insulin.[46]The American Pharmaceutical Association rates aloe vera gel for external use in category 2, meaning that "according to a number of well-designed studies and common use, this substance appears to be relatively effective and safe when used in recommended amounts."[58] Aloe vera inner gel may significantly increase the absorption of vitamins C and E after oral application.[59] Aloe vera gel for systemic application is not recommended in combination with antidiabetic, diuretic, or laxative drugs; sevoflurane; or digoxin.[57] In general, a 2-hour time period is recommended between oral drug application and aloe vera ingestion due to increased intestinal motility and reduced drug absorption.[48] If aloe vera gel is used with any other prescription drug, the patient should inform the physician and/or pharmacist.

REFERENCES

1. S.A. Dahanukar, R.A. Kulkarni, N.N. Rege. Pharmacology of medicinal plants and natural products. Indian Journal of Pharmacology 2000; 32: S81-S118.
2. Surjushe A, Vasani R, Saple DG. Aloe vera: A short review. Indian J Dermatol 2008;53:163-6
3. Sharrif Moghaddasi M, Sandeep Kumar Verma. Aloe vera their chemical composition and applications: A review. Int J Biol Med Res. 2011; 2 (1) 466-471.

4. Tyler V. The honest herbal: A sensible guide to the use of herbs and related remedies. 3rd ed. Binghamton, New York: Pharmaceutical Products Press; 1993.
5. B.K Vogler, E Ernst. Aloe vera : a systemic review of its clinical effectiveness. British Journal of General Practice, 1999;49: 823-828.
6. Suga, T. and Hirata, T. (1983) The efficacy of the Aloe plant chemical constituents and biological activities. Cosmetics and Toiletries 98, 105-108.
7. Sai Krishna Borra , Radha Krishna Lagisetty and Gowrinath Reddy Mallela.Anti-ulcer effect of Aloe vera in non-steroidal anti-inflammatory drug induced peptic ulcers in rats. African Journal of Pharmacy and Pharmacology Vol. 5(16), pp. 1867-1871, 29 October, 2011
8. Enas Ali Kamel Mohamed, Antidiabetic, Antihypercholestermic and Antioxidative Effect of Aloe Vera Gel Extract in Alloxan Induced Diabetic Rats; Australian Journal of Basic and Applied Sciences, 5(11): 1321-1327, 2011
9. Nandagopal B, Sankar S, Ramamurthy M, Sathish S, Sridharan G. Could the products of Indian medicinal plants be the next alternative for the treatment of infections?. Indian J Med Microbiol 2011;29:93-101
10. Cock I, Kalt FR. A modified MS2 bacteriophage plaque reduction assay for the rapid screening of antiviral plant extracts. Phcog Res 2010;2:221-8
11. Vijayakumar R, Muthukumar C, Kumar T, Saravanamuthu R. Characterization of *Malassezia Furfur* and its control by using plant extracts. Indian J Dermatol 2006;51:145-8
12. Bhaskar G, Arshia S, Priyadarshini S. Formulation and evaluation of topical polyherbal antiacne gels containing Garcinia mangostana and Aloe vera. Phcog Mag 2009;5:939
13. Kumar P, Goyal M, Tewari S. Positive inotropic and chronotropic effect of aloe gel on isolated rat heart. Indian J Pharmacol 2007;39:249-50
14. Maharjan R, Nagar PS, Nampoothiri L. Effect of *Aloe barbadensis* Mill. formulation on Letrozole induced polycystic ovarian syndrome rat model. J Ayurveda Integr Med 2010;1:273-9
15. Ojha S, Sonker K, Pandey M, Saraf SA. Aloe vera gel: A potent nutraceutical. J Nat Pharm 2011;2:36-9
16. Saraf S, Sahu S, Kaur C, Saraf S. Comparative measurement of hydration effects of herbal moisturizers. Phcog Res 2010;2:146-51
17. Madan J, Sharma AK, Inamdar N, Rao HS, Singh R. Immunomodulatory properties of aloe vera gel in mice. Int J Green Pharm 2008; 2:152-4.
18. Kapoor S, Saraf S. Efficacy Study of Sunscreens Containing Various Herbs for Protecting Skin from UVA and UVB Sunrays. Phcog Mag 2009;5:238-48
19. Gupta N, Jain UK. Prominent wound healing properties of indigenous medicines. J Nat Pharm 2010;1:2-13
20. Oliver Grundmann. Aloe vera Gel Research Review. Natural Medicine Journal 2012; 4 (9)
21. Thamlikitkul V, Bunyapraphatsara N, Riewpaiboon W, Theerapong S, Chantrakul C, Thanaveerasuwan T. Clinical trial of aloe vera Linn. for treatment of minor burns. *Siriraj Hosp Gaz.*1991;43(5):313-316.
22. Visuthikosol V, Chowchuen B, Sukwanarat Y, Sriurairatana S, Boonpucknavig V. Effect of aloe vera gel to healing of burn wound a clinical and histologic study. *J Med Assoc Thai.* Aug 1995;78(8):403-09.
23. Akhtar MA, Hatwar SK. Efficacy of aloe vera extract cream in management of burn wound. *J Clin Epidemiol.* 1996;49:24.
24. Reuter J, Jocher A, Stump J, Grossjohann B, Franke G, Schempp CM. Investigation of the anti-inflammatory potential of Aloe vera gel (97.5%) in the ultraviolet erythema test. *Skin Pharmacol Physiol.*2008;21(2):106-10.
25. Syed TA, Afzal M, Ashfaq AS. Management of genital herpes in men with 0.5% Aloe vera extract in a hydrophilic cream. A placebo-controlled double-blind study. *J Derm Treatment.* 1997;8(2):99-102.
26. Syed TA, Cheeman KM, Ahmad SA, Holt AH. Aloe vera extract 0.5% in hydrophilic cream versus Aloe vera gel for the management of genital herpes in males. A placebo-controlled, doubleblind, comparative study. *J Eur Acad Dermatol Venereol.* 1996;7:294-95.
27. Vardy AD, Cohen AD, Tchetov T. A double-blind, placebo-controlled trial of Aloe vera (A. barbadensis) emulsion in the treatment of seborrheic dermatitis. *J Derm Treatment.* 1999;10(1):7-11.
28. Syed TA, Ahmad SA, Holt AH, Ahmad SA, Ahmad SH, Afzal M. Management of psoriasis with Aloe vera extract in a hydrophilic cream: a placebo-controlled, double-blind study. *Trop Med Int Health.*1996;1(4):505-09.

29. Dal'Belo SE, Gaspar LR, Maia Campos PM. Moisturizing effect of cosmetic formulations containing Aloe vera extract in different concentrations assessed by skin bioengineering techniques. *Skin Res Technol.* 2006;12(4):241-46.
30. Tanaka M, Misawa E, Ito Y, et al. Identification of five phytosterols from Aloe vera gel as anti-diabetic compounds. *Biol Pharm Bull.* 2006;29(7):1418-22.
31. Yeh GY, Eisenberg DM, Kaptchuk TJ, Phillips RS. Systematic review of herbs and dietary supplements for glycemic control in diabetes. *Diabetes Care.* 2003;26(4):1277-94.
32. Agarwal OP. Prevention of atheromatous heart disease. *Angiology.* 1985;36(8):485-92.
33. Choonhakarn C, Busaracome P, Sripanidkulchai B, Sarakarn P. The efficacy of aloe vera gel in the treatment of oral lichen planus: a randomized controlled trial. *Br J Dermatol.* 2008;158(3):573-77.
34. Hayes SM. Lichen planus--report of successful treatment with aloe vera. *Gen Dent.* May-1999;47(3):268-72.
35. Langmead L, Feakins RM, Goldthorpe S, et al. Randomized, double-blind, placebo-controlled trial of oral aloe vera gel for active ulcerative colitis. *Aliment Pharmacol Ther.* 2004;19(7):739-47.
36. Blitz JJ, Smith JW, Gerard JR. Aloe vera gel in peptic ulcer therapy: preliminary report. *J Am Osteopath Assoc.* 1963;62:731-35.
37. Davis K, Philpott S, Kumar D, Mendall M. Randomised double-blind placebo-controlled trial of aloe vera for irritable bowel syndrome. *Int J Clin Pract.* 2006;60(9):1080-86.
38. Avijgan M. Phytotherapy: an alternative treatment for non-healing ulcers. *J Wound Care.*2004;13(4):157-58.
39. Kirdpon S, Kirdpon W, Airarat W, Thepsuthammarat K, Nanakorn S. Changes in urinary compositions among children after consuming prepared oral doses of aloe (Aloe vera Linn). *J Med Assoc Thai.* 2006;89(8):1199-205.
40. Kirdpon S, Kirdpon W, Airarat W, Trevanich A, Nanakorn S. Effect of aloe (Aloe vera Linn.) on healthy adult volunteers: changes in urinary composition. *J Med Assoc Thai.* 2006;89 Suppl 2:S9-14.
41. Poor MR, Hall JE, Poor AS. Reduction in the incidence of alveolar osteitis in patients treated with the SaliCept patch, containing Acemannan hydrogel. *J Oral Maxillofac Surg.* 2002;60(4):374-79.
42. King GK, Yates KM, Greenlee PG, et al. The effect of Acemannan Immunostimulant in combination with surgery and radiation therapy on spontaneous canine and feline fibrosarcomas. *J Am Anim Hosp Assoc.* 1995;31(5):439-47.
43. Harris C, Pierce K, King G, Yates KM, Hall J, Tizard I. Efficacy of acemannan in treatment of canine and feline spontaneous neoplasms. *Mol Biother.* 1991;3(4):207-13.
44. Elton B Stephens Company (EBSCO) Commodity Research Bureau (CRB). Aloe. 2008. Accessed 08/03/2008, 2008.
45. World Health Organization (WHO), ed *WHO Monographs on Selected Medical Plants, Vol 1.* 1 ed. Geneva, Switzerland: World Health Organization; 1999. Organization WH, ed. WHO Monographs on Selected Medical Plants; No. 1.
46. World Health Organization (WHO), ed *WHO Monographs on Selected Medical Plants, Vol 1.* 1 ed. Geneva, Switzerland: World Health Organization; 1999. Organization WH, ed. WHO Monographs on Selected Medical Plants; No. 1.
47. CIREP CIREP. Final Report on the Safety Assessment of Aloe Andongensis Extract, Aloe Andongensis Leaf Juice, Aloe Arborescens Leaf Extract, Aloe Arborescens Leaf Juice, Aloe Arborescens Leaf Protoplasts, Aloe Barbadensis Flower Extract, Aloe Barbadensis Leaf. *Int J Toxicol.* 2007;26 :1-50.
48. Jellin JM. Aloe. In: Database NMC, ed. Natural Medicines Comprehensive Database: Therapeutic Research Faculty; 2008.
49. Morrow DM, Rapaport MJ, Strick RA. Hypersensitivity to aloe. *Arch Dermatol.* 1980;116(9):1064-65.
50. Shoji A. Contact dermatitis to Aloe arborescens. *Contact Dermatitis.* 1982;8(3):164-67.
51. Nakamura T, Kotajima S. Contact dermatitis from aloe arborescens. *Contact Dermatitis.*1984;11(1):51.
52. Hunter D, Frumkin A. Adverse reactions to vitamin E and aloe vera preparations after dermabrasion and chemical peel. *Cutis.* 1991;47(3):193-96.
53. Ferreira M, Teixeira M, Silva E, Selores M. Allergic contact dermatitis to Aloe vera. *Contact Dermatitis.* 2007;57(4):278-79.
54. Fogleman RW, Chapdelaine JM, Carpenter RH, McAnalley BH. Toxicologic evaluation of injectable acemannan in the mouse, rat and dog. Vet Hum Toxicol. 1992;34(3):201-05.
55. Williams LD, Burdock GA, Shin E, et al. Safety studies conducted on a proprietary high-purity aloe vera inner leaf fillet preparation, Qmatrix. Regul Toxicol Pharmacol. 2010;57(1):90-8.

56. Fujii S. Evaluation of hypersensitivity to anthraquinone-related substances. *Toxicol.*2003;193(3):261-67.
57. Brinker F. Herb Contraindications and Drug Interactions. 2nd ed: Eclectic Medical Publications; 1998.
58. Peirce A. The American Pharmaceutical Association Practical Guide to Natural Medicines. Vol 1. First ed: William Morrow; 1999.
59. Vinson JA, Al Kharrat H, Andreoli L. Effect of Aloe vera preparations on the human bioavailability of vitamins C and E. Phytomedicine. 2005;12(10):760-65.