

The Longwood Herbal Task Force  
(<http://www.mcp.edu/herbal/default.htm>) and  
The Center for Holistic Pediatric Education and Research  
(<http://www.childrenshospital.org/holistic/>)

## ***Aloe vera (Aloe vera)***

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<p><b>Principal Proposed Uses:</b> Topical treatment of burns, abrasions, and canker sores; laxative</p> <p><b>Other Proposed Uses:</b> Experimental treatment of ulcers and HIV; immunostimulant</p>
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### ***Overview***

Numerous aloe species around the world are used for conditions ranging from dermatitis to cancer. Aloe gel's greatest use is as a skin salve and vulnerary for minor burns, abrasions, canker sores and other epithelial injuries. There is growing experimental evidence for its use as an antiviral, an ulcer remedy and an adjuvant cancer treatment due to its immune modulating effects. Aloe latex is a potent laxative that can cause severe cramping and diarrhea; it should not be used during pregnancy, lactation or by children less than 12 years old. Allergic reactions to aloe have been reported. Long-term use of anthraquinone laxatives may result in laxative dependence, pseudomelanosis coli, dehydration, potassium depletion, weakness, and arrhythmias. Aloe should not be used as a laxative by persons with undiagnosed abdominal pain, appendicitis, or intestinal obstruction.

### ***Historical and Popular Uses***

Ancient Egyptian papyrus and Mesopotamian clay tablets describe aloe as useful in curing infections, treating skin problems and as a laxative<sup>1</sup>. Cleopatra was said to include aloe cream in her beauty regimen<sup>2</sup>. Aloe was used by Hippocrates and Arab physicians, and was carried to the Western Hemisphere by Spanish explorers. Legend has it that Alexander the Great captured the island of Socotra in the Indian Ocean to secure its aloe supplies to treat his wounded soldiers<sup>3</sup>.

Aloe is also popular in both traditional Chinese and Ayurvedic medicine. The Chinese describe aloe's skin and the inner lining of its leaves as a cold, bitter remedy which is downward draining and used to clear constipation due to accumulation of heat (fire)<sup>4</sup>; the gel is considered cool and moist. In Ayurvedic medicine, the traditional medicine of India, aloe is used internally as a laxative, antihelminthic, hemorrhoid remedy, and uterine stimulant (menstrual regulator); it is used topically, often in combination with licorice root, to treat eczema or psoriasis. In Arabian medicine, the fresh gel is rubbed on the forehead as a headache remedy or rubbed on the body to cool it in case of fever, as well as being used for wound healing, conjunctivitis, and as a disinfectant and laxative<sup>5</sup>.

Today aloe vera gel is an active ingredient in hundreds of skin lotions, sun blocks and cosmetics<sup>6</sup>. The gel's use in cosmetics has been boosted by claims that it has similar anti-aging effects to vitamin A derivatives<sup>7</sup>. Aloe first gained popularity in the United States in the 1930's with reports of its success in treating X-ray burns<sup>8,9,10</sup>. Recently, aloe extracts have been used to treat canker sores, stomach ulcers and even AIDS. Some natural health enthusiasts promote aloe gel as a cleansing juice<sup>11</sup>. Some naturopaths promote aloe juice as a way to prevent and treat renal stones<sup>12</sup>. Many mothers keep a plant handy in the kitchen where it readily thrives in bright sunlight with little care<sup>13</sup>. When faced with a minor burn, a fresh leaf can be cut and the gel of the inner leaf applied directly to the burn immediately after the injury<sup>14</sup>. The inner leaf lining of the plant is used as a potent natural laxative. In a 1990 survey of members of a health maintenance organization, aloe vera was used by 64%; of these, 91% believed it had been helpful<sup>15</sup>. Aloe is also an ingredient in Compound Benzoin tincture<sup>16</sup>.

## **Botany**

*Medicinal species:* *Aloe vera*, *A. barbadensis* (Curacao or Barbados aloe), *A. vulgaris*, *A. arborescens*, *A. ferox* (Cape aloe), *A. perryi* (Socotrine or Zanzibar aloe). There are over 300 species of aloe, most of which are native to South Africa, Madagascar and Arabia<sup>5</sup>. The different species have somewhat different concentrations of active ingredients<sup>17,18</sup>.

*Common names:* Aloe, aloe capensis, aloe spicata, aloe vera, Barbados aloe, Cape aloe, chirukattali (India), Curacao aloe, Ghai kunwar (India), Ghikumar (India), Indian aloes, kumari (Sanskrit), laloi (Haiti), lohoi (Vietnam), luhui (Chinese), nohwa (Korean), rokai (Japanese), sabilla (Cuba), Socotrine aloe, subr (Arabic), Zanzibar aloe<sup>5,19,20</sup>. The name aloe is derived from the Arabic word alloeh meaning a shining bitter substance<sup>16</sup>. NOTE: “aloes” refers to the latex leaf lining used as a laxative; aloe wood (mentioned in the Bible) is an entirely different plant.

*Botanical family:* Liliaceae

*Plant description:* The aloe plant has long (up to 20 inches long and 5 inches wide), triangular, fleshy leaves that have spikes along the edges. The fresh parenchymal *gel* from the center of the leaf is clear; this part is sometimes dried to form aloe vera *concentrate* or diluted with water to create aloe *juice* products. The sticky *latex* liquid is derived from the yellowish green pericyclic tubules that line the leaf (rind); this is the part that yields laxative anthraquinones<sup>21,22</sup>. The flowers (not used medicinally) are yellow.

*Where it's grown:* Aloes are indigenous to South Africa and South America, but are now cultivated worldwide except in tundra, deserts and rain forests. In the US aloe is commercially cultivated in southern Texas<sup>23</sup>. It takes approximately four years to reach maturity and has a lifespan of about 12 years.

## Biochemistry

### AloeVera: Potentially Active Chemical Constituents

From the gel:

- Polysaccharides: glucomannan and acemannan
- Other: carboxypeptidase, magnesium, zinc, calcium, glucose, cholesterol, salicylic acid, prostaglandin precursors (gamma-linolenic acid [GLA]), vitamins A, C, E, lignins, saponins, plant sterols and amino acids<sup>3,24</sup>

From the latex leaf lining:

- Anthraquinone glycosides: aloin, aloe-emodin, barbaloin (15% -30%)<sup>25</sup>

The *gel* or *mucilage* obtained from the flesh of the leaf contains quite different compounds from the bitter *latex* extracted from the leaf lining<sup>26</sup>. Aloe gel is 99% water with a pH of 4.5 and is a common ingredient in many non-prescription skin salves. The gel contains an emollient polysaccharide, *glucomannan*. It is a good moisturizer, which accounts for its use in many cosmetics<sup>27</sup>. *Acemannan*, the major carbohydrate fraction in the gel, is a water-soluble long chain mannose polymer which accelerates wound healing, modulates immune function (particularly macrophage activation and production of cytokines) and demonstrates antineoplastic and antiviral effects<sup>28,29,30</sup>. The gel also contains *bradykininase*, an anti-inflammatory<sup>31</sup>, *magnesium lactate*, which helps prevent itching, and salicylic acid and other *antiprostaglandin* compounds which relieve inflammation.

The leaf lining (latex, resin or sap) contains *anthraquinone glycosides* (aloin, aloe-emodin and barbaloin) that are potent stimulant laxatives. These water soluble glycosides are split by intestinal bacteria into aglycones which effect the laxative action. The laxative effect from aloe is stronger than from any other herb, including senna, cascara or rhubarb root; it also has more severe side effects such as cramping, diarrhea, and nausea<sup>32</sup>. For medicinal use, the leaf lining is dried and the residue is used as an herbal laxative. The products are usually taken at bedtime. They are poorly absorbed after oral administration, but moderately well absorbed after bacterial

hydrolysis. They are eliminated in the urine, bile, feces and breast milk. They turn alkaline urine red<sup>33</sup>. Most herbalists recommend that they be avoided during pregnancy due to the risk of stimulating uterine contractions and also avoided during lactation due to the risk of excretion in breast milk<sup>34</sup>. Aloe is seldom recommended as a first choice among laxative preparations due to the severe cramping and nausea associated with its use.

### *Experimental Studies*

#### **Aloe Vera: Potential Clinical Benefits**

1. Cardiovascular: none
2. Pulmonary: none
3. Renal and electrolyte balance: none
4. Gastrointestinal/hepatic: Stimulant laxative (leaf lining); gastric and duodenal ulcers (gel); inflammatory bowel disease (gel, experimental use)
5. Neuropsychiatric: none
6. Endocrine: Hypoglycemic (gel)
7. Hematologic: none
8. Rheumatologic: none
9. Reproductive: Emmenagogue (leaf lining, traditional use)
10. Immune modulation: Immunostimulant, anti-inflammatory (gel)
11. Antimicrobial: Antibacterial, antiviral, antifungal (gel)
12. Antineoplastic: Antitumor, attenuation of adverse effects of cancer therapies (gel)
13. Antioxidant: none
14. Skin and mucus membranes: Vulnerary (wound healing), psoriasis remedy (gel)
15. Other/miscellaneous: none

1. **Cardiovascular:** none
2. **Pulmonary:** none
3. **Renal and electrolyte balance:** none

- 4. Gastrointestinal/hepatic:** Stimulant laxative (leaf lining), gastric and duodenal ulcers (gel), inflammatory bowel disease (gel, experimental use)
- a. Laxative (leaf lining): *Barbaloin*, or *aloin*, derived from the inner sheath cells of the leaves, is a bitter, yellow laxative.
    - i. *In vitro data*: Aloe affects the sodium/potassium pump and chloride channels at the colonic membrane<sup>37,38</sup>.
    - ii. *Animal data*: Aloe's anthraquinones enhance intestinal propulsion and water secretion in mice<sup>39</sup>.
    - iii. *Humans data*: The anthraquinones found in the latex stimulate chloride and water secretion into the large intestine, inhibit its reabsorption and stimulate peristalsis<sup>33,40</sup>. Typical onset of action is 6–12 hours after a single oral dose; this can be accompanied by severe cramping, bloody diarrhea and nausea. Randomized controlled trials have documented its potency as a cathartic in chronically constipated adults<sup>41</sup>.
  - b. Gastric and duodenal ulcers (gel)<sup>42</sup>.
    - i. *In vitro data*: Aloe-emodin inhibits growth of *Helicobacter pylori* in a dose-dependent fashion<sup>43</sup>.
    - ii. *Animal data*: Aloe vera inhibits gastric acid secretion in mice and rats and has protective effects against gastric mucosal damage in rats<sup>44</sup>. Pretreatment with aloe vera extract reduced aspirin-induced gastric mucosal injury by 70% in experimental rats<sup>45</sup>. Aloe extracts also suppressed the ulcerogenic effects of stress in experimental rats<sup>46</sup>.
    - iii. *Human data*: A 1960's pilot study of 18 adults indicated that aloe vera gel might be helpful in treating patients with duodenal ulcers. However, there was not a comparison group of untreated patients, nor were details given on other remedies the patients might have been using<sup>47</sup>.
  - c. Inflammatory bowel disease (gel). Acemannan is under consideration as an experimental remedy for inflammatory bowel disease<sup>35,36</sup>; no experimental data.

**5. Neuropsychiatric:** none

6. **Endocrine:** Hypoglycemic (gel)
- i. *In vitro data:* none
  - ii. *Animal data:* Aloe gel caused low blood sugar in diabetic laboratory mice in some studies<sup>48,49</sup>. It lowered blood sugar in both diabetic and normal mice in another study<sup>50</sup>, but had no impact on blood sugar levels in diabetic or normal animals in other studies<sup>51,52</sup>.
  - iii. *Human data:* Nearly half of diabetic patients surveyed in Texas reported using aloe vera or other herbal remedies as complementary therapies for their diabetes<sup>53</sup>. Aloe gel appeared to enhance the hypoglycemic effect of glibenclamide when given orally to diabetic patients in doses of 1 – 2 tablespoons twice daily<sup>54,55</sup>. There are no reported randomized controlled trials comparing aloe to any oral hypoglycemic agent or insulin in treating human diabetics. There are no studies evaluating the potential toxicity of taking aloe products orally by patients requiring medical therapy for glycemic control.
7. **Hematologic:** none
8. **Rheumatologic:** none
9. **Reproductive:** Emmenagogue (leaf lining; traditional use)
- i. *In vitro data:* none
  - ii. *Animal data:* Aloe extracts at doses of 100 – 150 mg/kg had no abortifacient effects in pregnant rats<sup>20</sup>.
  - iii. *Human data:* none
10. **Immune modulation:** Immunostimulant and anti-inflammatory (gel)<sup>56,57</sup>
- i. *In vitro data:* Acemannan increases monocyte and macrophage activity and cytotoxicity, stimulates killer T-cells and enhances macrophage candidacidal activity *in vitro*<sup>29,58,59,60,61,62</sup>. Acemannan enhances macrophage release of interleukin-1 (LI-1), interleukin-6 (IL-6), tumor necrosis factor alpha (TNF- $\alpha$ ), and interferon gamma (INF- $\gamma$ ) in a dose-dependent fashion<sup>29,63</sup>.
- On the other hand, aloe extracts block prostaglandin and thromboxane production from arachidonic acid, reducing inflammation<sup>64,65,66</sup>.

- ii. *Animal data:* Acetylated mannans from aloe injected subcutaneously into myelosuppressed mice stimulated an increase in white blood cell counts, splenic cellularity, and absolute numbers of neutrophils, lymphocytes and monocytes<sup>67,68,69,70,71,72</sup>. Aloe extracts reduced the production of interleukin-10 following exposure to ultraviolet radiation, reducing the suppression of delayed type hypersensitivity<sup>73,74,75</sup>.

Aloe enhanced the anti-inflammatory activity of hydrocortisone while blocking its wound healing inhibition when applied topically to mice<sup>76,77</sup>. Aloe extracts had anti-inflammatory effects equivalent to hydrocortisone in the mouse ear model; although hydrocortisone administration was associated with a decrease in thymus weight, the aloe extracts had no such effect<sup>78</sup>. In rat paw models, fresh aloe gel showed significant anti-inflammatory activity and increased wound strength<sup>79,80</sup>. Rats with adjuvant-induced arthritis exhibited fewer symptoms when treated with a topical preparation containing aloe<sup>81</sup>. Aloe extracts also blocked mast cell inflammatory responses to antigen-antibody complexes<sup>82,83</sup>.

- iii. *Human data:* In a case series of 14 HIV-1+ patients who were prescribed 800 mg/day of acemannan, there was a significant increase in the number of circulating monocyte and macrophages which mirrored clinical improvements<sup>84</sup>. In a pilot study in HIV-infected persons acemannan increased the number of white blood cells and improved symptoms<sup>85</sup>. Aloe extracts also increased phagocytosis in asthmatic adults<sup>86</sup>.

There are no reported trials evaluating the effectiveness of aloe as a systemic anti-inflammatory agent in humans.

## 11. **Antimicrobial:** Antibacterial, antiviral, antifungal (gel)

### a. Antibacterial

- i. *In vitro data:* Aloe gel is bacteriostatic or bactericidal against a variety of common wound-infecting bacteria in vitro: *Staphylococcus aureus*, *Streptococcus pyogenes*, *Serratia marcescens*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *E. coli*, *Salmonella typhosa* and *Mycobacterium tuberculosis*<sup>64,87</sup>. Aloe-emodin also inhibits the growth of *Helicobacter pylori* in a dose-dependent fashion<sup>43</sup>.



ii. *Animal data:* none

iii. *Human data:* none

b. Antiviral

i. *In vitro data:* Acemannan acts alone and synergistically with azidothymidine (AZT) and acyclovir to block reproduction of Herpes and the AIDS virus<sup>88,89,90</sup>.

ii. *Animal data:* none

iii. *Human data:* Acemannan hydrogel (trade name is Carrisyn) is currently under investigation as a treatment for persons infected with HIV; doses are up to 250 milligrams QID (about one quart of raw aloe gel daily)<sup>13,85</sup>. In pilot randomized controlled trials of HIV+ adults with low CD4 counts, aloe did not contribute significantly to therapy with ZDV or ddI in terms of effects on CD4 counts, p24 antigen levels or viral load<sup>91,92</sup>.

In a randomized, controlled double blind clinical trial of 60 men suffering from an initial episode of Herpes simplex infection, those assigned to treatment with an aloe vera extract (0.5%) in a hydrophilic cream had a significantly faster healing time and a higher number of healed lesions than the placebo comparison group<sup>93</sup>.

c. Antifungal

i. *In vitro data:* none

ii. *Animal data:* Aloe extract treatment of guinea pig feet that had been infected with *Trichophyton mentagrophytes* resulted in a 70% growth inhibition compared with untreated animals<sup>94</sup>.

iii. *Human data:* none

12. **Antineoplastic:** Antitumor, attenuation of adverse effects of cancer therapies (gel)

a. Antitumor

i. *In vitro data:* Aloin A and B, aloesin and aloeresin were devoid of antitumor activity, but aloe emodin caused cytostatic and necrotic effects on human K562 leukemia cell lines<sup>95</sup>.

- ii. *Animal data:* Acemannan has demonstrated activity against feline leukemia virus and solid tumors<sup>28,96,97,98,99,100,101</sup>. For example, among cats with feline leukemia, a virally-induced disease with a mortality rate of 70% - 100%, a six-week treatment series with acemannan injections (2 mg/kg per weekly dose) resulted in a 71% survival rate<sup>98</sup>.

In a group of laboratory mice implanted with malignant sarcoma cells who were treated with intraperitoneal injections of acemannan, all the mice in the control group developed malignant tumors and died within seven weeks, but 40% of the treated mice survived and showed signs of tumor necrosis and regression<sup>28</sup>. In rats, concurrent treatment with aloe extracts inhibited hepatic tumor induction<sup>102,103</sup>. In a study of dogs and cats with fibrosarcomas treated with daily injections of acemannan in combination with surgery and radiation therapy, significant shrinkage of tumors and increase in necrosis and inflammation were observed<sup>99</sup>. In another study of 46 dogs and cats with spontaneous tumors who were treated with acemannan injections, 26 had histopathologic evidence of tumor necrosis and 12 exhibited significant clinical improvement; soft tissue sarcomas appeared to be particularly susceptible to treatment<sup>97</sup>.

- iii. *Human data:* Based on findings from animal studies, aloe research in human cancer patients is currently in progress. At the University of Texas-Houston Medical School and Herman Hospital, a Phase I study with injectable aloe for cancer patients is being conducted. In a preliminary study of 50 patients suffering from lung cancer, gastrointestinal tract tumors, brain stem gliomas or breast cancer who were treated with melatonin alone or melatonin plus aloe, those in the combination therapy group had significantly better one-year survival<sup>104</sup>

- b. Attenuation of adverse effects from cancer therapies (gel). Aloe vera gel has been recommended to treat radiation-induced dermatitis and mucositis.

- i. *In vitro data:* See Immune modulation and Skin and mucus membranes: vulnerary.
- ii. *Animal data:* See Immune modulation and Skin and mucus membranes: vulnerary.

- iii. *Human data:* In two phase III pilot studies of patients with radiation-induced dermatitis treated with either 98% pure aloe vera gel administered twice daily beginning within three days of radiation treatment for ten weeks, placebo or no treatment, dermatitis scores were nearly identical in all treatment groups<sup>105</sup>; there was no apparent benefit from aloe treatment. There are no studies of aloe's use to treat mucositis.

13. **Antioxidant:** none

14. **Skin and mucus membranes:** Vulnerary (wound healing), psoriasis remedy (gel)

a. Vulnerary (wound healing)

- i. *In vitro data:* See Immune modulation. Fresh aloe gel promotes attachment and growth of normal human cells grown in monolayer cultures; however, commercially prepared products do not have similar effects, and actually appear to be toxic to cell cultures<sup>106</sup>. Aloe gel appears to increase blood flow to injured cells<sup>107</sup>. Aloe extracts demonstrate dose-dependent angiogenic activity in the chick embryo and calf pulmonary models<sup>108,109</sup>.
- ii. *Animal data:* Aloe treatment enhanced collagen deposition and cross-linking in granulation tissue in rat wounds<sup>110</sup>. In other animal studies, aloe sped wound healing from burns, frostbite, electrical injuries, caustic chemicals and surgery and improved scar strength compared with topical antibiotic medication<sup>111,112,113</sup>. Aloe has proven an effective healing agent for dairy cattle suffering from cracked teats<sup>114</sup>.

In experimentally-induced deep burns in guinea pigs and mice, aloe vera killed bacteria and promoted epithelialization significantly better than placebo, and in some cases as well as silver sulfadiazine ointment<sup>115,116</sup>. Acemannan-containing skin dressings reduced radiation-induced dermatitis in experimental mice<sup>117</sup>. In rat paw models, fresh aloe gel significantly increased wound strength and had anti-inflammatory activities<sup>79</sup>.

Both normal and diabetic mice who received aloe injections healed skin wounds more quickly and had better blood circulation around the wound, less

inflammation and a higher pain threshold than comparison mice<sup>118, 119, 120, 121, 122, 123</sup>. Aloe-containing cream also reduced experimentally induced frostbite in white rabbits<sup>124</sup>.

There are several negative studies of aloe's effectiveness as a vulnerary. In one study of rabbits with corneal epithelial lesions, aloe vera gel exhibited no healing advantage over Ringer's solution treatment<sup>125</sup>. In a study of experimentally-induced burns in guinea pigs, aloe vera gel was less effective than silver sulfadiazine<sup>126</sup>.

iii. *Human data:* In humans, aloe has been reported to accelerate healing from deep scrapes, frostbite, flash burns of the conjunctiva, and even canker sores<sup>26, 111, 127, 128, 127, 129, 130, 131, 132, 133</sup>. Only one study has had an opposite effect; that is, aloe-treated surgical wounds healing by secondary intention took longer to heal than comparison wounds<sup>134</sup>. Despite the conflicting research, some dentists and otolaryngologists use aloe gel to promote healing in injured tissues in the mouth, nose, sinuses and ear<sup>135</sup>.

Aloe gel has most often been used as a topical treatment for burn wounds<sup>136</sup>. In a study of 27 adults with partial thickness burns, those treated with aloe healed an average of six days faster than those treated with Vaseline gauze<sup>137</sup>.

b. Psoriasis remedy

i. *In vitro data:* See Immune modulation

ii. *Animal data:* See Immune modulation

iii. *Human data:* In a 1995 double-blind, placebo controlled study of aloe's effect on 60 patients with psoriasis vulgaris, an aloe vera extract (0.5%) in a hydrophilic cream resulted in a significant clearing of the psoriatic plaques in 83.3% of the aloe-treated patients versus 6.6% of the placebo group<sup>138</sup>. The aloe treatment was well tolerated with no adverse drug-related side effects.

15. **Other/miscellaneous:** none

## ***Toxicity and Contraindications***

*All herbal products carry the potential for contamination with other herbal products, pesticides, herbicides, heavy metals and pharmaceuticals.*

*Allergic reactions can occur to any natural product in sensitive persons.*

*Allergic reactions:* Contact dermatitis has been reported<sup>105, 139, 140, 141</sup>.

*Potentially toxic compounds in aloe:* Anthraquinone glycosides

*Acute toxicity:* Occasionally the gel stings a bit when it is first applied and, in rare cases, can aggravate irritated or surgically abraded skin<sup>142</sup>. Stinging can be reduced by keeping the gel in the refrigerator so it is cold when applied. Toxicity studies in mice, rats and dogs revealed no acute toxicity with acemannan given orally or injected<sup>143</sup>. A Virginia physician lost his license to practice after an investigation into three deaths caused by injecting aloe vera into patients as a cancer remedy<sup>144</sup>.

Acute toxicity associated with the leaf lining is largely gastrointestinal: severe cramping, diarrhea, and nausea. Discoloration of the urine may occur. Severe overdoses have also been associated with nephritis, gastrointestinal hemorrhage, dyspnea, palpitations and fluid depletion. Due to its side effects, aloe latex has largely been superseded by gentler laxatives.

*Chronic toxicity:* Long-term ingestion of aloe leaf lining (laxative use) can lead to potassium deficiency, muscle weakness and cardiac arrhythmias. Long-term use (greater than four months) of anthraquinones is also associated with development of pseudomelanosis coli, which is reversible when use of the agent is discontinued<sup>40</sup>. Long-term use may also result in dependence on laxatives for normal colonic function. Aloe gel does not cause mutagenesis, embryogenesis, fetotoxic or teratogenic effects<sup>145</sup>; there are no data on carcinogenicity<sup>40</sup>. The anthraquinones may cause genotoxicity<sup>146</sup>.

*Limitations during other illnesses or in patients with specific organ dysfunction:*

Anthraquinone laxatives are typically contraindicated in patients with acute surgical abdomen, bowel obstruction, fecal impaction, hypersensitivity to anthraquinones, and

symptoms of appendicitis or undiagnosed abdominal pain. Due to possible hypoglycemic effects, caution should be used by diabetic patients taking aloe orally<sup>147</sup>.

*Interactions with other herbs or pharmaceuticals:* Low levels of potassium (due to laxative overuse) could interfere with cardiac glycosides as well as affect other antiarrhythmic agents. Potassium deficiency can be exacerbated by simultaneous applications of thiazide diuretics, cortico-adrenal steroids or licorice root. Due to the potential enhancement of oral hypoglycemic agents, caution should be used by diabetic patients taking aloe laxatives concurrently with hypoglycemic agents<sup>147</sup>. Topical use may enhance absorption of hydrocortisone<sup>76</sup>. The high mucilage content in aloe gel may interfere with absorption of other oral administered medications if taken concurrently<sup>147</sup>.

*Safety during pregnancy, lactation and/or childhood:* Aloe and aloin toxicology has been insufficiently investigated, therefore aloe should be avoided during pregnancy. In addition, anthraquinone glycoside constituents of the leaf juice may be secreted into breast milk, so aloe and aloin should be avoided during lactation<sup>147</sup>. Rats fed dried aloe leaves during pregnancy had offspring with an increased rate of embryonic death and skeletal abnormalities<sup>148</sup>; in another study in rats and mice, aloe did not increase fetal mortality, though they did lead to substantial maternal toxicity<sup>149</sup>. There are no data on safety during childhood, but most herbalists recommend avoiding its oral use in children less than twelve years old.

## ***Typical Dosages***

*Provision of dosage information does NOT constitute a recommendation or endorsement, but rather indicates the range of doses commonly used in herbal practice.*

*Doses are given for single herb use and must be adjusted when using herbs in combinations.*

*Doses may also vary according to the type and severity of the condition treated and individual patient conditions.*

*Aloe gel* is applied topically three to four times daily as needed for cosmetic or vulnerary purposes

*Aloe leaf lining* comes in a powder, or in aqueous and aqueous-alcoholic extracts in powder or

liquid form. Unless otherwise prescribed, the individually correct dosage is the minimal

amount to maintain a soft stool (typically 50 –300 milligrams in a single dose)<sup>11</sup>. This

usually arrives at 10-30 mg hydroxyanthracene derivatives per day taken before bedtime,

calculated as anhydrous aloin<sup>145,150</sup>. The typical dose of aloes tincture (1:40 in 45%

ethanol) is 2-8 ml po in the evening<sup>25</sup>. Aloe should not be taken for more than ten

consecutive days<sup>145</sup>

*Overdose* (of the leaf lining laxative) is considered 1 gram daily for more than 1 –2 days; this can cause colonic perforation, bloody diarrhea, and nephritis<sup>11</sup>

*Pediatric dosages*: Unknown. The gel appears to be safe for external use. The latex leaf lining is not typically recommended for children less than 12 years old due to its harsh effects<sup>11</sup>.

*Trade names*: Acibar, Dermaide, Herbal Harvest Aloe Extract, Hepatica, Laxatan, Lucida, Naturade Stomach Formula Aloe Vera Gel, Nature's Bounty Herbal Sure Aloe Vera, Nature's Herbs Aloe Vera Vel, Standardized Aloes Extract<sup>22</sup>

*Multi-ingredient preparations containing aloe*: Aristochol, Blistex Aloe and Vitamin E, Cleansing Herb Tablets, Diaparene Corn Starch, Hawaiian Tropic Cool Aloe with I.C.E., Hemorid for Women, Nasal Moist Gel, Natures Remedy, Vitaglow Herbal Laxative, Vagisil

*Availability of standardized preparations*: Yes, in Britain and Europe

*Dosages used in herbal combinations*: Variable

## REFERENCES

1. Shelton RM. Aloe vera. Its chemical and therapeutic properties. *Int J Dermatol* 1991; 30:679-83.
2. Haller J. A drug for all seasons: medical and pharmacological history of aloe. *Bull NY Acad Sci* 1990; 66.
3. Atherton P. Aloe vera: magic or medicine? *Nurs Stand* 1998; 12:49-52, 54.
4. Bensky D, Gamble A, Kaptchuk TJ. *Chinese herbal medicine : materia medica*. Seattle, Wash.: Eastland Press, 1993:xxv, 556.
5. Ghazanfar SA. *Handbook of Arabian medicinal plants*. Boca Rato: CRC Press, 1994.
6. Grindlay D, Reynolds T. The Aloe vera phenomenon: a review of the properties and modern uses of the leaf parenchyma gel. *J Ethnopharmacol* 1986; 16:117-51.
7. Danhof I. Potential reversal of chronological and photo-aging of the skin by topical application of natural substances. *Phytotherapy Research* 1993; 7:S53-S56.
8. Rowe T. Effect of fresh Aloe vera in the treatment of third degree roentgen reactions on white rats. *J Am Pharm Assoc* 1940; 29:348.
9. Rowe T. Further observations on the use of *aloe vera* leaf in the treatment of third degree x-ray reactions. *J Am Pharm Assn* 1941; 30:266.
10. Lewis WH. *Medical botany : plants affecting man's health*. New York: Wiley, 1977.
11. McGuffin M, Hobbs C, Upton R, Goldberg A. *American Herbal Products Association's Botanical Safety Handbook*. Boca Raton. New York: CRC Press, 1997:231.
12. Murray MT, Pizzorno JE. *An Encyclopedia of Natural Medicine*. Rocklin, CA: Prima Publishing, 1991.
13. Duke JA. *Green Pharmacy*. Emmaus, PA: Rodale Press, 1997:507.
14. Ship A. Is topical aloe vera plant mucus shelpful in burn treatment? *JAMA* 1977; 238:1770.
15. Brown JS, Marcy SA. The use of botanicals for health purposes by members of a prepaid health plan. *Res Nurs Health* 1991; 14:339-50.
16. Robbers JE, Speedie MK, Tyler VE. *Pharmacognosy and pharmacobiotechnology*. Baltimore: Williams & Wilkins, 1996:ix, 337.
17. Yagi A, Tsunoda M, Egusa T, Akasaki K, Tsuji H. Immunochemical distinction of Aloe vera, *A. arborescens*, and *A. chinensis* gels [letter]. *Planta Med* 1998; 64:277-8.
18. van Wyk BE, van Rheede van Oudtshoorn MC, Smith GF. Geographical variation in the major compounds of Aloe ferox leaf exudate. *Planta Med* 1995; 61:250-3.
19. Kapoor LD. *CRC handbook of ayurvedic medicinal plants*. Boca Raton: CRC Press, 1990.
20. Ross IA. *Medicinal plants of the world : chemical constituents, traditional, and modern medicinal uses*. Totowa, N.J.: Humana Press, 1999:xi, 415.
21. Murray MT. *The healing power of herbs : the enlightened person's guide to the wonders of medicinal plants*. Rocklin, CA: Prima Pub., 1995:xiv, 410.



22. Schulz V, Hansel R, Tyler VE. Rational Phytotherapy: A Physicians' Guide to Herbal Medicine. Berlin: Springer, 1997:306.
23. Foster S. Aloe. Herbs for Health 1999:59-60.
24. Afzal M, Ali M. Identification of some prostanoids in Aloe vera extracts. Planta Medica 1991; 57:38-40.
25. Bradley PR. British herbal compendium : a handbook of scientific information on widely used plant drugs / published by the British Herbal Medicine Association and produced by its Scientific Committee. Bournemouth, Dorset: The Association, 1992.
26. Klein AD, Penneys NS. Aloe vera. J Am Acad Dermatol 1988; 18:714-20.
27. Henry R. An updated review of aloe vera. Cosmetics and toiletries 1979; 94:42-50.
28. Peng SY, Norman J, Curtin G, Corrier D, McDaniel HR, Busbee D. Decreased mortality of Norman murine sarcoma in mice treated with the immunomodulator, Acemannan. Mol Biother 1991; 3:79-87.
29. Zhang L, Tizard IR. Activation of a mouse macrophage cell line by acemannan: the major carbohydrate fraction from Aloe vera gel. Immunopharmacology 1996; 35:119-28.
30. Ramamoorthy L, Kemp MC, Tizard IR. Acemannan, a beta-(1,4)-acetylated mannan, induces nitric oxide production in macrophage cell line RAW 264.7. Mol Pharmacol 1996; 50:878-84.
31. Yagi A, Harada N, Yamada H, Iwadare S, I. N. Antibradykinin active material in *Aloe saponaria*. J Pharmaceut Sci 1982; 71:1172-74.
32. Schilcher H. Phytotherapy in paediatrics : handbook for physicians and pharmacists : with reference to commission E monographs of the Federal Department of Health in Germany : includes 100 commission E monographs and and 15 ESCOP monographs. Stuttgart: medpharm Scientific Publishers, 1997:181.
33. Bissett NG. Herbal drugs and phytopharmaceuticals. Stuttgart: MedPharm CRC Press, 1994:566.
34. Hoffman D. The complete illustrated holistic herbal. Rockport, MA: Element Books Inc., 1996.
35. Robinson M. Optimizing therapy for inflammatory bowel disease. Am J Gastroenterol 1997; 92:12S-17S.
36. Robinson M. Medical therapy of inflammatory bowel disease for the 21st century. Eur J Surg Suppl 1998; 582:90-8.
37. Ishii Y, Tanizawa H, Takino Y. Studies of Aloe. III. Mechanism of cathartic effect (2). Chem Pharm Bull (Tokyo) 1990; 38:197-200.
38. Honig J, Geck P, Rauwald H. Inhibition of Cl<sup>-</sup> channels as a possible base of laxative action of certain anthraquinones and anthrones. Planta Medica 1992; 58:586-7.
39. Yagi T. The synergistic purgative action of aloe-emodin anthrone and rhein anthrone in mice: Synergism in large intestinal propulsion and water secretion. J Pharm Pharmacol 1997; 49:22-25.
40. Blumenthal M. The complete German Commission E monographs : therapeutic guide to herbal medicines. Austin: American Botanical Council, 1998.
41. Odes H, Madar Z. A double-blind trial of a celandin, aloevera, and psyllium laxative preparation in adult patients with constipation. Digestion 1991; 49:65-71.

42. Parmar N. Evaluation of Aloe vera leaf exudate and gel for gastric and duodenal anti-ulcer activity. *Fitoterapia* 1986; 57.
43. Wang H, Chung J, Ho C, Wu L, Chang S. Aloe-emodin effects on arylamin N-acetyltransferase activity in the bacterium *Helicobacter pylori*. *Planta Medica* 1998; 64:176-8.
44. Suvitayay W, Bunyaphatsara N, Thirawarapan S, Watanabe K. Gastric acid secretion in inhibitory and gastric lesion protective effects of aloe preparation. *Thai Journal of Phytopharmacy* 1997; 4:1-11.
45. Maze G, Terpolilli R, Lee M. Aloe vera extract prevents aspirin-induced gastric mucosal injury in rats. *Medical Science Research* 1997; 25:765-66.
46. Teradaira R, Singzato M, Beppu H, Fujita K. Antigastric ulcer effects in rats of *Aloe arborescens* Miller var. *natalensis* Berger. *Phytotherapy Research* 1993; 7.
47. Blitz J, Smith J, Gerard J. Aloe vera gel in peptic ulcer therapy: preliminary report. *J American Osteopathic Association* 1963; 62:731-35.
48. Ajabnoor M. Effect of aloes on blood glucose levels in normal and alloxan diabetic mice. *J Ethnopharmacology* 1990; 28:215-20.
49. Ghannam N. The antidiabetic activity of aloes: preliminary clinical and experimental observations. *Hormone Res* 1986; 24:288-94.
50. Beppu H, Nagamura Y, Fujita K. Hypoglycemic and antidiabetic effects in mice of *Aloe arborescens* Miller var. *natalensis* Berger. *Phytotherapy Research* 1993; 7:S37-S42.
51. Bwititi P, Musabayane C. The effects of plant extracts on plasma glucose levels in rats. *Acta Medica et Biologica* 1997; 45:167-9.
52. Koo M. Aloe vera: antiulcer and antidiabetic effects. *Phytotherapy Research* 1994; 8:461-4.
53. Noel P, Pugh J, Larme A, Marsh G. The use of traditional plant medicines for non-insulin dependent diabetes mellitus in South Texas. *Phytotherapy Research* 1997; 11:512-17.
54. Bunyaphatsara N, Yongchaiyudha S, Rungpitarangsi V. Antidiabetic activity of Aloe vera L juice II. Clinical trial in diabetes mellitus patients in combination with glibenclamide. *Phytomed* 1996; 3:245-8.
55. Yongchaiyudha S, Rungpitarangsi V, Bunyaphatsara N, Chokechaijaroenporn O. Antidiabetic activity of Aloe vera L juice. I. Clinical trial in new cases of diabetes mellitus. *Phytomed* 1996; 3:241-3.
56. t Hart LA, van Enckevort PH, van Dijk H, Zaat R, de Silva KT, Labadie RP. Two functionally and chemically distinct immunomodulatory compounds in the gel of Aloe vera. *J Ethnopharmacol* 1988; 23:61-71.
57. t'Hart LA, van den Berg AJ, Kuis L, van Dijk H, Labadie RP. An anti-complementary polysaccharide with immunological adjuvant activity from the leaf parenchyma gel of Aloe vera. *Planta Med* 1989; 55:509-12.
58. Womble D, Helderma JH. Enhancement of allo-responsiveness of human lymphocytes by acemannan (Carrisyn). *Int J Immunopharmacol* 1988; 10:967-74.

59. Womble D, Helderman JH. The impact of acemannan on the generation and function of cytotoxic T-lymphocytes. *Immunopharmacol Immunotoxicol* 1992; 14:63-77.
60. Marshall G, Druck J. In vitro stimulation of NK activity by acemannan (ACM). *J Immunol* 1993; 150:1381.
61. Messel J, Denham D. The effect of Carrisyn on the immune system. *Am Soc Exp Biol J 2: Abstracts* 1988:2239.
62. Stuart RW, Lefkowitz DL, Lincoln JA, Howard K, Gelderman MP, Lefkowitz SS. Upregulation of phagocytosis and candidicidal activity of macrophages exposed to the immunostimulant acemannan. *Int J Immunopharmacol* 1997; 19:75-82.
63. Marshall G, Gibbons A, Parnell L. Human cytokines induced by acemannan. *J Allergy Clin Immunol* 1993; 91:295.
64. Robson M, Hegggers J, Hagstrom W. Myth, magic, witchcraft, or fact? *Aloe vera* revisited. *J Burn Care Rehab* 1982; 3:157-62.
65. Cera L, Hegggers J, Robson M. The therapeutic effect of Aloe vera cream (Dermaid aloe) in thermal injuries: two case reports. *J Am Animal Hosp Assoc* 1980; 16:768.
66. Vazquez B, Avila G, Segura D, Escalante B. Antiinflammatory activity of extracts from Aloe vera gel. *J Ethnopharmacol* 1996; 55:69-75.
67. Egger SF, Brown GS, Kelsey LS, Yates KM, Rosenberg LJ, Talmadge JE. Hematopoietic augmentation by a beta-(1,4)-linked mannan. *Cancer Immunol Immunother* 1996; 43:195-205.
68. Egger SF, Brown GS, Kelsey LS, Yates KM, Rosenberg LJ, Talmadge JE. Studies on optimal dose and administration schedule of a hematopoietic stimulatory beta-(1,4)-linked mannan. *Int J Immunopharmacol* 1996; 18:113-26.
69. Davis RH, Leitner MG, Russo JM. Topical anti-inflammatory activity of Aloe vera as measured by ear swelling. *J Am Podiatr Med Assoc* 1987; 77:610-2.
70. Davis RH, Rosenthal KY, Cesario LR, Rouw GA. Processed Aloe vera administered topically inhibits inflammation. *J Am Podiatr Med Assoc* 1989; 79:395-7.
71. Davis RH, Leitner MG, Russo JM, Byrne ME. Anti-inflammatory activity of Aloe vera against a spectrum of irritants. *J Am Podiatr Med Assoc* 1989; 79:263-76.
72. Davis RH, Stewart GJ, Bregman PJ. Aloe vera and the inflamed synovial pouch model. *J Am Podiatr Med Assoc* 1992; 82:140-8.
73. Byeon S, Pelley R, Ullrich S, Waller T, Bucana C, Strickland R. Aloe barbadensis extracts reduce the production of interleukin-10 after exposure to ultraviolet radiation. *J Invest Dermatol* 1998; 110:811-17.
74. Chong K, SEong S, Young K, Ro S, Myung H. Prevention of ultraviolet radiation-induced suppression of accessory cell function of Langerhans cells by Aloe vera. *Immunopharmacology* 1997; 37:153-62.

75. Strickland F, Pelley R, Kripke M. Prevention of ultraviolet radiation-induced suppression of contact and delayed hypersensitivity by Aloe barbadensis gel extract. *Journal of Investigative Dermatology* 1994; 102:197-204.
76. Davis RH, Parker WL, Murdoch DP. Aloe vera as a biologically active vehicle for hydrocortisone acetate. *J Am Podiatr Med Assoc* 1991; 81:1-9.
77. Davis RH, DiDonato JJ, Johnson RW, Stewart CB. Aloe vera, hydrocortisone, and sterol influence on wound tensile strength and anti-inflammation. *J Am Podiatr Med Assoc* 1994; 84:614-21.
78. Hutter J, Salman M, Stavinoha W, et al. Antiinflammatory C-glucosyl chromone from Aloe barbadensis. *Journal of Natural Products* 1996; 59:541-43.
79. Udupa S, Udupa A, Kulkarni D. Anti-inflammatory and wound healing properties of Aloe vera. *Fitoterapia* 1994; 65:141-45.
80. Chauhan O, Godhwani JL, Khanna NK, Pendse VK. Antiinflammatory activity of Muktaashukti bhasma. *Indian J Exp Biol* 1998; 36:985-9.
81. Davis R. Topical effect of aloe with ribonucleic acid and vitamin C on adjuvant arthritis. *J Am Pod Med Assoc* 1985; 76:61-66.
82. Ro J, Lee B, Chung M, et al. The inhibitory mechanism of aloe glycoprotein (NY945) on the mediator release in the guinea pig lung mast cell activated with antigen-antibody complexes. *Korean J Physiol Pharmacol* 1998; 2:119-31.
83. Yamamoto M, Sugiyama K, Yokota M, Maeda Y. Inhibitory effects of aloe extracts on antigen- and compound 48/80 induced histamine release from rat peritoneal mast cells. *Japanese Journal of Toxicology and Environmental Health* 1993; 39:395-400.
84. McDaniel H, Combs C, HR M, Carpenter R, Kemp M, McAnalley B. An increase in circulating monocyte/macrophages (M/M) is induced by oral acemannan in HIV-1 patients. *Am J Clin Pathol* 1990; 94:516-7.
85. McDaniel H, Carpenter R, Kemp M, Kahlon J, McAnalley B. Extended survival and prognostic criteria for Acemannan (ACE-M) treated HIV Patients. *Antiviral Res Suppl* 1990; 1:117.
86. Shida T. Effect of aloe extract on peripheral phagocytosis in adult bronchial asthma. *Planta Medica* 1985; 51:273-5.
87. Lorenzetti L, Salisbury R, Beal J, Baldwin J. Bacteriostatic property of Aloe vera. *J Pharmacol Sci* 1964; 53:1287.
88. Kemp M, Kahlon J, Chinnah A, et al. *In vitro* evaluation of the antiviral effects of acemannan on the replication and pathogenesis of HIV-1 and other enveloped viruses: modification of the processing of glycoprotein precursors. *Antiviral Res Suppl* 1990; 1:83.

89. Kahlon JB, Kemp MC, Yawei N, Carpenter RH, Shannon WM, McAnalley BH. In vitro evaluation of the synergistic antiviral effects of acemannan in combination with azidothymidine and acyclovir. *Mol Biother* 1991; 3:214-23.
90. Kahlon JB, Kemp MC, Carpenter RH, McAnalley BH, McDaniel HR, Shannon WM. Inhibition of AIDS virus replication by acemannan in vitro. *Mol Biother* 1991; 3:127-35.
91. Montaner JS, Gill J, Singer J, et al. Double-blind placebo-controlled pilot trial of acemannan in advanced human immunodeficiency virus disease. *J Acquir Immune Defic Syndr Hum Retrovirol* 1996; 12:153-7.
92. Singer J, Gill J, Arseneau R, McLean B. A randomized, placebo-controlled trial of oral acemannan as an adjunctive to antiretroviral therapy in advanced disease. *Int Conf AIDS* 1993; 9:494.
93. Syed T, Afzal M, Ashfax A, Holt A, Ali A, Ahmad S. Management of genital herpes in men with 0.5% Aloe vera extract in a hydrophilic cream: a placebo-controlled double blind study. *Journal of Dermatological Treatment* 1997; 8:99-102.
94. Kawai K, Beppu H, Shimpo K, et al. In vivo effects of Aloe arborescens Miller var. natalensis Berger on experimental tinea pedis in guinea pig feet. *Phytotherapy Research* 1998; 12:178-82.
95. Grimaudo S, Tolomeo M, Gancitano R, D'Alessandro N, Aiello E. Effects of highly purified anthraquinoid compounds from Aloe vera on sensitive and multidrug resistant leukemia cells. *Oncology Reports* 1997; 4:341-43.
96. Corsi MM, Bertelli AA, Gaja G, Fulgenzi A, Ferrero ME. The therapeutic potential of Aloe Vera in tumor-bearing rats. *Int J Tissue React* 1998; 20:115-8.
97. 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; 3:207-13.
98. Sheets MA, Unger BA, Giggelman GF, Jr., Tizard IR. Studies of the effect of acemannan on retrovirus infections: clinical stabilization of feline leukemia virus-infected cats. *Mol Biother* 1991; 3:41-5.
99. 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; 31:439-47.
100. Yates KM, Rosenberg LJ, Harris CK, et al. Pilot study of the effect of acemannan in cats infected with feline immunodeficiency virus. *Vet Immunol Immunopathol* 1992; 35:177-89.
101. Desai KN, Wei H, Lamartiniere CA. The preventive and therapeutic potential of the squalene-containing compound, Roindex, on tumor promotion and regression. *Cancer Lett* 1996; 101:93-6.
102. Tsuda H, Matsumoto K, Ito M, Hirano I, Kawai K, Beppu H. Inhibitory effect of Aloe arborescense Miller var. natalensis Berger (Kidachi aloe) on induction of preneoplastic focal lesions in the rat liver. *Phytotherapy Research* 1993; 7:S43-S47.
103. Shamaan NA, Kadir KA, Rahmat A, Ngah WZ. Vitamin C and aloe vera supplementation protects from chemical hepatocarcinogenesis in the rat. *Nutrition* 1998; 14:846-52.

104. Lissoni P, Giani L, Zerbini S, Trabattoni P, Rovelli F. Biotherapy with the pineal immunomodulating hormone melatonin versus melatonin plus aloe vera in untreatable advanced solid neoplasms. *Nat Immun* 1998; 16:27-33.
105. Williams MS, Burk M, Loprinzi CL, et al. Phase III double-blind evaluation of an aloe vera gel as a prophylactic agent for radiation-induced skin toxicity. *Int J Radiat Oncol Biol Phys* 1996; 36:345-9.
106. Tyler VE. *The honest herbal : a sensible guide to the use of herbs and related remedies*. New York: Pharmaceutical Products Press, 1992:xviii, 375.
107. Brasher WJ, Zimmermann ER, Collings CK. The effects of prednisolone, indomethacin, and Aloe vera gel on tissue culture cells. *Oral Surg Oral Med Oral Pathol* 1969; 27:122-8.
108. Lee M, Yoon S, Lee S, Chung M, Park Y. In vivo angiogenic activity of dichloromethane extracts of Aloe vera gel. *Archives of Pharmacal Research* 1995; 18:332-35.
109. Lee MJ, Lee OH, Yoon SH, et al. In vitro angiogenic activity of Aloe vera gel on calf pulmonary artery endothelial (CPAE) cells. *Arch Pharm Res* 1998; 21:260-5.
110. Chithra P, Sajithlal GB, Chandrakasan G. Influence of Aloe vera on collagen turnover in healing of dermal wounds in rats. *Indian J Exp Biol* 1998; 36:896-901.
111. Hegggers J, Pelley R, Robson M. Beneficial effects of Aloe in wound healing. *Phytotherapy Research* 1993; 7:S48-S52.
112. Hegggers J, Kucukcelebi A, Stabenau C, Ko F, Broemeling L, Robson M. Wound healing effects of aloe gel and other topical antibacterial agents on rat skin. *Phytotherapy Research* 1995; 9:455-57.
113. Hegggers JP, Elzaim H, Garfield R, et al. Effect of the combination of Aloe vera, nitroglycerin, and L-NAME on wound healing in the rat excisional model. *J Altern Complement Med* 1997; 3:149-53.
114. Jimenez-Magallanes L, Sumano-Lopez H. The use of aloe vera for the treatment of teat cracks and lacerations in dairy cattle. *Veterinaria Mexico* 1995; 26:271-2.
115. Rodriguez-Bigas M, Cruz NI, Suarez A. Comparative evaluation of aloe vera in the management of burn wounds in guinea pigs. *Plast Reconstr Surg* 1988; 81:386-9.
116. Bunyaphatsara N, Jirakulchaiwong S, Thirawarapan S, Manonukul J. The efficacy of aloe vera cream in the treatment of first, second and third degree burns in mice. *Phytomedicine* 1996; 2:247-51.
117. Roberts DB, Travis EL. Acemannan-containing wound dressing gel reduces radiation-induced skin reactions in C3H mice. *Int J Radiat Oncol Biol Phys* 1995; 32:1047-52.
118. Davis RH, Kabbani JM, Maro NP. Aloe vera and wound healing. *J Am Podiatr Med Assoc* 1987; 77:165-9.
119. Davis RH, Leitner MG, Russo JM. Aloe vera. A natural approach for treating wounds, edema, and pain in diabetes. *J Am Podiatr Med Assoc* 1988; 78:60-8.
120. Davis RH, Leitner MG, Russo JM, Byrne ME. Wound healing. Oral and topical activity of Aloe vera. *J Am Podiatr Med Assoc* 1989; 79:559-62.

121. Davis RH, Donato JJ, Hartman GM, Haas RC. Anti-inflammatory and wound healing activity of a growth substance in Aloe vera. *J Am Podiatr Med Assoc* 1994; 84:77-81.
122. Chithra P, Sajithlal GB, Chandrakasan G. Influence of aloe vera on the healing of dermal wounds in diabetic rats. *J Ethnopharmacol* 1998; 59:195-201.
123. Chithra P, Sajithlal GB, Chandrakasan G. Influence of Aloe vera on collagen characteristics in healing dermal wounds in rats. *Mol Cell Biochem* 1998; 181:71-6.
124. Miller MB, Koltai PJ. Treatment of experimental frostbite with pentoxifylline and aloe vera cream. *Arch Otolaryngol Head Neck Surg* 1995; 121:678-80.
125. Green K, Tasi J, Luxenberg M. Effect of aloe vera on corneal epithelial wound healing. *Journal of Toxicology-Cutaneous and Ocular Toxicology* 1996; 15:301-4.
126. Kaufman T, Kalderon N, Ullmann Y, Berger J. Aloe vera gel hindered wound healing of experimental second-degree burns: a quantitative controlled study. *J Burn Care Rehabil* 1988; 9:156-9.
127. McCauley RL, Heggors JP, Robson MC. Frostbite. Methods to minimize tissue loss. *Postgrad Med* 1990; 88:67-8, 73-7.
128. Fulton JE, Jr. The stimulation of postdermabrasion wound healing with stabilized aloe vera gel-polyethylene oxide dressing. *J Dermatol Surg Oncol* 1990; 16:460-7.
129. Plemons J, Rees T, Binnie W, Wright J, Guo I, Hall J. Evaluation of acemannan in the treatment of recurrent aphthous stomatitis. *Wounds: a compendium of clinical research and practice* 1994; 6:40-45.
130. Heggors JP, Robson MC, Manavalen K, et al. Experimental and clinical observations on frostbite. *Ann Emerg Med* 1987; 16:1056-62.
131. Lawrence D. Treatment for flash burns on the conjunctiva. *N Engl J Med* 1984; 311:413.
132. Garnick JJ, Singh B, Winkley G. Effectiveness of a medicament containing silicon dioxide, aloe, and allantoin on aphthous stomatitis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1998; 86:550-6.
133. Anonymous. Aloe vera product achieves a label claim for the relief of pain associated with canker sores. *Holistic Health News* 1995; 8:8.
134. Schmidt JM, Greenspoon JS. Aloe vera dermal wound gel is associated with a delay in wound healing. *Obstet Gynecol* 1991; 78:115-7.
135. Thompson JE. Topical use of aloe vera derived allantoin gel in otolaryngology. *Ear Nose Throat J* 1991; 70:119.
136. Heck E, Head M. Aloe vera gel cream as a topical treatment for outpatient burns. *Burns* 1981; 7:291-4.
137. 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* 1995; 78:403-9.
138. Syed TA, Ahmad SA, Holt AH, 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; 1:505-9.
139. Shoji A. Contact Dermatitis. Contact dermatitis to Aloe arborescens. 1982; 8:164-7.

140. Morrow D, Rapaport M, Strick R. Hypersensitivity to aloe. *Arch Dermatology* 1980; 116:1064-65.
141. Hogan D. Widespread dermatitis after topical treatment of chronic leg ulcers and stasis dermatitis. *Can Med Assoc J* 1988; 138:336-8.
142. Hunter D, Frumkin A. Adverse reactions to vitamin E and aloe vera preparations after dermabrasion and chemical peel. *Cutis* 1991; 47:193-6.
143. Fogleman RW, Chapdelaine JM, Carpenter RH, McAnalley BH. Toxicologic evaluation of injectable acemannan in the mouse, rat and dog. *Vet Hum Toxicol* 1992; 34:201-5.
144. Anonymous. MD Loses license after injecting aloe kills 3. *National Council Against Health Fraud* 1997; 20:4.
145. Anonymous. *Monographs on the medicinal uses of plants*. Exeter: European Scientific Cooperative on Phytotherapy, 1997.
146. Muller S. Genotoxicity of the laxative drug components emodin, aloe-emodin, and danthron in mammalian cells: topoisomerase II mediated? *Mutat Res* 1996; 371:165-73.
147. Brinker FJ. *Herb contraindications and drug interactions : with appendices addressing specific conditions and medicines*. Sandy, Or.: Eclectic Institute, 1997:146.
148. Nath D, Sethi N, Singh R, Jain A. Commonly used Indian abortifacient plants with special reference to their teratologic effects in rats. *J Ethnopharmacology* 1992; 36:147-54.
149. Parry O, Matambo C. Some pharmacological actions of aloe extracts and *Cassia abbreviata* on rats and mice. *Cent Afr J Med* 1992; 38:409-14.
150. Fleming T. *PDR for herbal medicines*. Montvale, NJ: Medical Economics Company, Inc., 1998.