

## SUMMARY OF DATA FOR CHEMICAL SELECTION

Aloe Vera Gel  
8001-97-6

### BASIS OF NOMINATION TO THE NTP

Aloe vera is presented to the CSWG as a widely used cosmetic, food additive, and dietary supplement that results in exposure to adults, children, and the elderly. Naturally occurring aloe contains 1,8-dihydroxyanthracene derivatives that are known mutagens and that cause a laxative effect when aloe products are consumed orally. However, most aloe products sold for oral consumption in the over-the-counter dietary supplement market have reduced quantities of 1,8-dihydroxyanthracenes. Because of the part of the aloe plant used, aloe vera gel has an especially low concentration of 1,8-dihydroxyanthracenes.

The wound healing properties of aloe have been considered "common knowledge" for thousands of years. However, it is only with recent techniques that these properties have been shown scientifically. These recent studies also raise questions about the ability of aloe products to cause a proliferative effect on the cell, a process associated with a greater risk for carcinogenicity. Thus, aloe vera gel is recommended for a specialized dermal study to clarify if aloe products may be promoters if administered after initiation with a carcinogen.

### SELECTION STATUS

ACTION BY CSWG: 12/14/98

#### Studies requested:

- Cell transformation assay
- Mechanistic studies of cancer promotion using TGAC mouse model
- Use TPA and aloin as positive controls

Priority: High

#### Rationale/Remarks:

- Widespread oral and dermal exposure to humans
- Suspicion of carcinogenicity based on cell proliferation similar to that observed for croton oil

- Lack of information on toxicity
- Reconsider for traditional dermal initiation/promotion study after results of short-term studies are available

## CHEMICAL IDENTIFICATION

### CAS Registry No.:

Aloe, pharmaceutical grade                      8001-97-6

*Aloe barbadensis* Miller, extract              94349-62-9

### Synonyms:

Aloe, *Aloe vera* Tournefort ex Linne, *Aloe vulgaris*  
Lamark (Hecht, 1981; NLM, 1998)

### Botanical Names:

*Aloe barbadensis* Miller

Description: Although its lance-like spiny leaves give it the appearance of a cactus, the genus *Aloe* belongs to the lily family. Of the hundreds of species of aloe, only a few have commercial use. The aloe gel most often used in cosmetics and dietary supplements is taken from the species *Aloe barbadensis* Miller. This gel is a water-thin, almost colorless liquid extracted from the peeled, spineless leaves of the plant (Hecht, 1981).

Technical Products and Impurities: Aloe gel, aloe gel concentrate, and aloe gel powder are available from the following companies: Aloe Hi-Tech, Inc. and Florida Food Products, Inc. Aloe gel concentrate is also available from International Sourcing, Inc. Aloe vera gel is available from Active Organics, Inc.; Aloe Hi-Tech, Inc.; Bio-Botanica Inc.; Frutarom Meer Corporation; Har-Met International Inc.; International Sourcing Inc.; Lanaetex Products, Inc.; Madis Botanicals, Inc.; Natural Oils International; R.I.T.A. Corp.; and Stauber Performance Ingredients, Inc. Aloe vera gel, dried, is available from Aloe Hi-Tech, Inc. and Ashland Chemical Company (McCoy, 1998).

Aloe vera gel and other products containing aloe are sold in health food stores and vitamin shops. Some aloe products being advertised on the Internet are listed below in Table 1. In addition, personal grooming products containing aloe include lipstick, toothpaste, soap, bath gel, shampoo, conditioning rinse, and deodorant. Beauty products include exfoliating cleanser, facial mask powder, creams, and lotions (Westbury, 1998).

Table 1. Some aloe products sold to consumers

Product Name	Company	Description
Aloegold	Alternative Health Therapies	Bottles; whole aloe leaf, cold processed
Aloe Natural	Alternative Health Therapies	Bottles; aloe gel, cold processed
Aloe Fresh Moisturizing Liniment	Alternative Health Therapies	Skin cream; aloe solids, wintergreen, menthol & eucalyptus; vitamins A, C, E, D & B5
Aloe Fresh Bee Propolis Lotion	Alternative Health Therapies	Skin cream; aloe solids, bee products, vitamins A, C, E, D & B5
Aloe Fresh Aqua Gel	Alternative Health Therapies	Skin cream; aloe solids, bee products, vitamins A, C, E, D & B5
Emaloe	Agricultural Systems International	Hand and body lotion, face cream, and foot balm containing aloe vera and emu oil
Manapol	Caraloe, a subsidiary of Carrington Laboratories, Inc.	Various products produced from patented process using aloe vera gel
Sacred Mountain Aloe Concentrate	Sacred Mountain	Bottled drink; whole leaf aloe, citric acid, sodium benzoate, potassium sorbate

Sources: Agricultural Systems International, 1998; Alternative Health Therapies, 1998; Caraloe, 1998; Sacred Mountain, 1998

The International Aloe Science Council (IASC) conducts a certification program to assure customers of the authenticity of aloe products. All members of the IASC are required to disclose the origin of their product and the identity and concentration of any non-aloe constituents in their products. These disclosures include genus and species of aloe, nature of starting material, *i.e.*, whole leaf or gel, and the name of all non-aloe constituents, their concentration as a percentage of total product weight, and the purity of the constituent if less than 98 percent (IASC, 1998a).

Chemical Composition: An HPLC profile that identifies freshly prepared aloe extract or frozen extract is available (Wang & Strong, 1996). The plant is 96 percent water; the rest is essential oils, amino acids, minerals, vitamins, enzymes, and glycoprotein (Anon., 1996).

According to the certification program established by the IASC, whole leaf aloe vera gel has the following standards: pH 3.5 to 4.7; solids 0.46 to 1.31 percent; calcium 98.2 to 448 mg/l; magnesium 23.4 to 118 mg/l; and malic acid 817.8 to 3427.8 mg/l (IASC, 1998b). To date, the IASC has certified, or has under certification, 16 raw materials produced from *Aloe vera* L. Additionally, the IASC has granted certification to 54 companies manufacturing 250 products being sold in 52 countries (IASC, 1997).

Polymerase chain reaction has also been used as a technique for the detection of aloe and identification of its plant origin. Three different DNA markers were developed that are specific for aloe and are reproducible at low concentrations without spurious artifacts. The yield of DNA from extraction of aloe leaves and from processed aloe, using guanidine thiocyanate followed by isopropanol precipitation, varied from 10  $\mu\text{g/g}$  of fresh leaf tissue to as low as 1 pg/ml from 10 ml of 1:1 decolorized gel or retail drink products (Orndorff, 1996).

Aloe polysaccharides consist of linear chains of  $\beta$ -1-4-linked glucose and mannose molecules: owing to the presence of these two simple hexose sugars, they are also called glucomannans, and because there is much more mannose than glucose present, they are also called polymannans. These linear chains range in size from a few molecules to several thousand molecules. By convention the lower limit is usually taken as a molecular weight of about 1,000 daltons to qualify as a polysaccharide. Different molecular-sized fractions may possess different physical characteristics and widely differing potential biological activities. Whatever the length of the chain or the physical characteristics, they are all properly designated aloe polysaccharides (Danhof, 1998).

The simplest assay of polysaccharides for aloe is the alcohol precipitable hexose test. Using this test, it is possible to establish a normal range for polysaccharides in reference to *Aloe barbadensis* gel Standard Sample and to determine the range for polysaccharide content in authentic commercial aloe powder materials. The test, with the IASC certification tests, will detect adulteration with maltodextrin (Pelley, 1996).

## EXPOSURE INFORMATION

Production and Producers: Aloe vera products are produced by cold extraction of the leaf, which is called a filet. Either the whole leaf or the soft, gelatinous filling may be used. The outer skin contains more aloin, which is responsible for the laxative effect of aloe. Dietary supplement producers often remove the outer skin from products intended for ingestion (Alternative Health Therapies, 1998).

Aloe vera should be processed within hours after being harvested to prevent oxidation. Also aloe vera should be cold processed, not heated or treated with chemicals. Cold processing ensures that the gel product is essentially the same as the freshly cut leaf (Anon, 1996).

Aloe products were in use at the time of Cleopatra and Alexander the Great (Anon, 1998), and they are now popular food and cosmetic additives and dietary supplements. With a 4.3 percent market share, aloe gel was the seventh largest selling herbal product in health food stores in 1995 (Rawls, 1996). Aloe was ranked number six in herbal supplement sales in natural food stores in the US based on sales for 1996 and the first two months of 1997 as reported in survey questionnaires from 100 of 9,000 stores in the industry (Blumenthal, 1998).

The Port Import/Export Reporting Service (PIERS) reported aloe vera gel imports of 10.8 million pounds over the 14.5 month period from June 27, 1997 to September 16, 1998 (Dialog Information Services, 1998). Nearly all imports were from the Dominican Republic. PIERS also reports figures for aloe vera, aloe vera salve base, aloe powder, concentrated aloe vera, aloe vera concentrate, concentrated aloe, patch aloe vera gel, dry aloe bark, refrigerated aloe vera softgel, aloe leaves, aloe bar soap, fresh and mashed aloe pulp, aloe medicinal cream, aloe tablets, and aloe incense.

Aloe vera gel is not listed in EPA's Toxic Substances Control Act (TSCA) Inventory (NLM, 1998).

Use Pattern: The gelatinous extract of aloe has been used therapeutically for centuries. It has been used to promote rapid healing of burns and to impede surface bacterial growth in burned tissues and to promote healing of dermal ulcers, wounds, and frostbite (Peng *et al.*, 1991). Aloe vera has also been used for many years as an ingredient in cosmetics such as face and hand creams, lotions, and skin moisturizers (Hecht, 1981). Recent applications include diapers, baby wipes, tissues, and bandages.

The German Commission E permits the use of aloe for treatment of constipation. This use is based on the presence of 1,8-dihydroxyanthracene derivatives which have a laxative effect. The monograph indicated side effects of cramp-like discomfort of the gastrointestinal tract and recommends a dose of 20-30 mg hydroxyanthracene derivatives/day, calculated as anhydrous aloin. The monograph warns against chronic use or abuse due to loss in potassium, an increase in effectiveness of cardiac glycosides, and an effect on antiarrhythmic agents (Blumenthal, 1998).

Human Exposure: There is a potential for widespread exposure of men, women, and children to aloe vera gel because of its widespread use in herbal remedies, in "health" oriented drinks, and in cosmetics and personal care products.

Starting over 50 years ago, aloe gel was being processed and marketed as a drink product. Today the industry is flourishing and the gel is being used in many products such as fresh gel, juice, and other formulations for health, medical, and cosmetic purposes. As aloe marketing increases, many more people are purchasing creams, ointments, juices, and even facial tissue and shampoo containing aloe gel. Of the many aloe-based products on the market, some contain the concentration of aloe claimed; others have lesser amounts of aloe than claimed on the labels, and some may contain no aloe at all (Wang & Strong, 1996).

Because of aloe gel's reputation as a folk remedy for burns and wounds, some people keep one or more plants readily available at home (Wang & Strong, 1996).

The National Occupational Exposure Survey (NOES), which was conducted by the National Institute for Occupational Safety and Health (NIOSH) between 1981 and 1983, estimated that 30,874 workers, including 23,491 female workers, were potentially exposed to aloe vera in the workplace. The NOES database does not contain information on the frequency, level, or duration of exposure to workers of any chemicals listed therein (NLM, 1998). Since the early 1980s, the use of aloe products has increased dramatically, suggesting that more workers probably have potential exposure to aloe products than recorded in NOES.

Environmental Occurrence: There are over 500 species of aloe growing in climates worldwide.

It grows mainly in dry regions of Africa, Asia, Europe, and America. Aloe plants range in height from a few inches to 30 feet or more. The leaves of many species can become quite large and are lance shaped with jagged edges (Anon, 1996).

No information on environmental contamination with aloe vera gel from its manufacture or from the manufacture of products containing aloe vera gel was identified in the available literature.

Regulatory Status: No standards or guidelines have been set by NIOSH or the Occupational Safety and Health Administration (OSHA) for occupational exposure to or workplace maximum allowable levels of aloe vera gel. Aloe vera gel was not on the American Conference of Governmental Industrial Hygienists (ACGIH) list of compounds for which recommendations for a Threshold Limit Value (TLV) or Biological Exposure Index (BEI) are made.

Aloe has been regulated by the Food and Drug Administration (FDA) for many years. The drug aloe is a powerful cathartic, used at one time in laxatives for humans and for horses.



Aloe was also approved by FDA as a natural flavoring substance in food. Aloe vera in cosmetics comes under a different set of rules. FDA does not have the authority to require that manufacturers test cosmetic products for safety before they go on the market. The Agency can take action against an adulterated or misbranded product (Hecht, 1981).

Since 1994, dietary supplements, including some aloe products, have been regulated under the Dietary Supplement Health and Education Act (DSHEA). The DSHEA requires no proof of safety for dietary supplements on the market before October 15, 1994. Labeling requirements for such supplements allow warnings and dosage recommendations as well as substantiated “structure or function” claims. All claims must prominently note that they have not been evaluated by the FDA, and they must bear the statement “This product is not intended to diagnose, treat, cure, or prevent any disease” (Croom & Walker, 1995).

## EVIDENCE FOR POSSIBLE CARCINOGENIC ACTIVITY

Human Data: No epidemiological studies or case reports investigating the association of exposure to aloe vera gel and cancer risk in humans were identified in the available literature.

Although aloe vera has been used for centuries to stimulate wound healing, scientific documentation of its benefits has been difficult. In a relatively recent study, 18 patients with facial scarring from acne vulgaris underwent bilateral full-face dermabrasion. Following the abrasion, one side of the face was covered with polyethylene oxide dressings presoaked with aloe vera gel. Polyethylene oxide dressings alone were used on the other side. Dressings were changed every 12 hours for four or five days. At five days, the dressings were changed to Polysporin ointment applications. The aloe site healed more rapidly in every case. Intense vasoconstriction and a reduction in edema were obvious on the aloe gel-treated side at 24-48 hours. By the third to fourth day, there was less crusting on the aloe gel side. By the fifth to sixth day, the new epidermis often covered 90 percent of the aloe gel-treated side, but only 40-50 percent of the other side. By the tenth day, the healing on both sides appeared equal (Fulton, 1990).

As of October 20, 1998, the FDA Special Nutritionals Adverse Event Monitoring System listed 30 matches for aloe in 27 adverse event reports. In 7 of the 30 events, the only ingredient listed was aloe vera. Adverse events reported included stomach problems; nausea, dizziness and tiredness; buzzing and tingling in ears, pressure in head, dizziness, increased blood pressure, panic attacks, teeth chattering, insomnia, inability to concentrate, and memory problems; paroxysmal atrial fibrillation with rapid ventricular response with symptomatic lightheadedness and palpitations; red, itchy rash; shakiness, no strength, dizzy spells, blood pressure varies from 100/56 to 140/100; and aseptic meningitis and stroke (FDA, 1998).

Animal Data: *Acute Studies.* The major carbohydrate fraction obtained from the gel of the aloe vera leaf is often called acemannan. Acemannan is predominantly a  $\beta$ -(1,4)-linked

galactomannan with acetylated mannose residues (Reynolds, 1985). The acute oral toxicity of acemannan in rats and mice is >5 g/kg (Fogleman *et al.*, 1992). For pharmaceutical aloe, corresponding figures were >5 g/kg in rats and >10 g/kg in mice (NLM, 1998).

*Subacute/Subchronic Studies.* In preliminary oral repeat-dose studies, acemannan was given daily by gavage for 14 days to 5 groups of 5 male and 5 female rats at doses ranging from 1,000 to 5,000 mg/kg/day. Abnormal respiration, distended abdomens, and decreased defecation were observed in all dose groups. One female receiving 1,000, 1 male receiving 2,000, and 2 female rats receiving 5,000 mg/kg/day died. Deaths were considered due to the physical mixture which prevented stomach emptying. Dogs accepted up to 1,500 mg acemannan/kg/day po without apparent effect (Fogleman *et al.*, 1992).

Acemannan was administered po to groups of 40 male and 40 female Sprague-Dawley rats at 0, 200, 650, or 2,000 mg/kg/day for 6 months. Hematology and serum chemistry determinations and urinalyses conducted at 1, 3, and 6 months all showed values within the normal range. Necropsy examinations were conducted on all animals that died while on test, on 10 rats/sex/group at 90 days, and on all survivors at 6 months. Organ weights and gross and microscopic pathology from the treated rats were normal and similar to corresponding controls (Fogleman *et al.*, 1992).

Acemannan was also administered po to 4 groups of 4 male and 4 female beagle dogs from 7 months until 10 months of age. Doses were 0, 100, 400, or 1,500 mg/kg/day for 90 days. Serum chemistry, hematologic, and urinalysis data collected before initiation of exposure, at 45 days, and at termination were within normal limits. No significant gross or microscopic lesions associated with ingestion of acemannan were noted at necropsy (Fogelman *et al.*, 1992).

*Chronic Studies:* No 2-year carcinogenicity studies of aloe vera gel in animals were identified in the available literature.

Short-Term Tests: A water extract of a crude preparation of *Aloe ferox* Mill., a product similar to *Aloe barbadensis* Mill., was positive in the *Bacillus subtilis* spore rec-assay carried out in strains H17 and M45; a corresponding test on a methanol extract was negative. These assays were conducted without S-9. Neither the water extract nor the methanol extract produced mutations in *Salmonella typhimurium* strains TA98 or TA100 with or without S-9. Cell killing was noted in half the assays (Morimoto *et al.*, 1982). Acemannan was negative in the standard Ames test against *S. typhimurium*, with and without S-9, at dosages as high as 800  $\mu\text{L}/\text{plate}$  (Fogleman *et al.*, 1992).

Metabolism: No studies evaluating the metabolism of aloe vera gel were found in the available literature. Pharmacokinetic studies with 20 mg/kg acemannan po in beagle dogs showed the polysaccharide was absorbed from the gut and reached peak blood levels within 4-6 hours. The half life was >48 hours (Fogleman *et al.*, 1992).

Other Biological Effects: Antigenotoxic and Chemopreventive Effects. The antigenotoxic and chemopreventive effects of aloe vera have been examined. *Aloe barbadensis* Miller (polysaccharide fraction) caused a time-course and dose-dependent inhibition of [ $^3\text{H}$ ]benzo[a]pyrene (B[a]P)-DNA adduct formation in primary rat hepatocytes ( $1 \times 10^6$  cells/ml) treated with [ $^3\text{H}$ ]B[a]P (4 nmol/ml). At concentrations of 0.4-250  $\mu\text{g}/\text{ml}$  aloe, the binding of [ $^3\text{H}$ ]B[a]P metabolites to rat hepatocyte DNA was inhibited by 9.1-47.9 percent. Also in rat hepatocytes cultured for 3-48 hours with aloe (250  $\mu\text{g}/\text{ml}$ ) and [ $^3\text{H}$ ]B[a]P (4 nmol/ml), [ $^3\text{H}$ ]B[a]P-DNA adducts were significantly reduced by 36 percent compared with [ $^3\text{H}$ ]B[a]P alone. Aloe also inhibited cellular uptake of [ $^3\text{H}$ ]B[a]P in a dose-dependent manner at a concentration of 0.4-250  $\mu\text{g}/\text{ml}$  by 6.3-34.1 percent. After a single oral administration of B[a]P to male ICR mice (10 mg/mouse), benzo[a]pyrene diol epoxide I (BPDE-I)-DNA adduct formation and persistence for 16 days following daily treatment with aloe (50 mg/mouse) were quantified by an enzyme-linked

immunosorbent assay using monoclonal antibody 8E11. In this animal model, BPDE-I-DNA adduct formation was significantly inhibited in various organs (liver, kidney, forestomach, and lung) ( $P < 0.001$ ). When mice were pretreated with aloe for 16 days before B[a]P treatment, inhibition of BPDE-I-DNA adduct formation and persistence was enhanced. Glutathione S-transferase activity was slightly increased in the liver but cytochrome P450 content was not affected by aloe. These results suggested to the authors that the inhibitory effect of aloe on BPDE-I-DNA adduct formation might have a chemopreventive effect by inhibition of B[a]P absorption (Kim & Lee, 1997).

The carbohydrate fraction of aloe gel, acemannan has been reported to promote healing in humans, and has been employed for the treatment of fibrosarcomas in dogs and cats. Zhang and Tizard (1996) reported that acemannan could stimulate macrophage cytokine production, nitric oxide release, surface molecule expression, and morphologic changes in a mouse macrophage cell line. The production of the cytokines IL-6 and TNF- $\alpha$  was dependent on the dose of acemannan provided. Nitric oxide production, cell morphologic changes and surface antigen expression were increased in response to stimulation by a mixture of acemannan and Interferon- $\gamma$ . These results suggested to the authors that acemannan may function, at least in part, through macrophage activation.

Female CFW mice that received acemannan intraperitoneally following subcutaneous transplants of murine sarcoma cells showed an increased survival rate. The sarcomas in animals treated with acemannan at the time of tumor cell implantation were infiltrated by immune system cells, became necrotic, and regressed. The authors postulated that acemannan-stimulated synthesis of monokines resulted in the initiation of immune attack, necrosis, and regression of the implanted sarcomas (Peng *et al.*, 1991).

*Cell Proliferation.* Several *in vitro* studies have shown that aloe substances can stimulate fibroblast and epithelial cell growth and induce lectin-like responses in immune cells involved in skin wound repair processes. Aloe treatment of skin cell cultures has been shown to stimulate *in vitro* cell growth and to cause more rapid wound healing of skin

cells *in vivo*. In addition, studies of aloe treatment of cells of the immune system, *e.g.*, lymphocytes, have shown that aloe substances can stimulate lymphocyte blastogenesis and can induce agglutination of human and canine peripheral blood erythrocytes. In a recent effort to extend these studies, Bouthet and coworkers (1995) measured the comparative effects of aloe substances on proliferation in human embryonic lung cells (HEL) and cultured rat adrenal pheochromocytoma (PC12) cells. Replicate cultures of cells in suspension were prepared and serial 2-fold dilutions from a stock aloe solution ( $2.5\mu\text{g}$  protein/ml) were added. The plates were visually checked each day during a 12-day period. The growth of PC12 cells treated in suspension with 0.162 to  $0.625\mu\text{g/ml}$  of aloe gel was significantly stimulated after 2 days, whereas the growth of suspension treated HEL cells was not markedly stimulated. Noting that aloe also improved cell attachment to the extracellular matrix, the authors suggested that the response seen could have represented more than cell proliferation, possibly an increased viability of the PC12 cells.

Yagi and coworkers (1996) isolated and characterized the fraction of aloe gel that causes cell proliferation. Fractions of aloe gel were prepared using diethylaminoethyl (DEAE) Sephadex A-25, Sepharose 6B, and Sephadex G-50 columns. These fractions were tested for proliferation of human dermal and baby hamster kidney cells in an *in vitro* assay. The glycoprotein fraction promoted cell growth, while the neutral polysaccharide fraction did not show growth stimulation. An active glycoprotein fraction showed a single band upon electrophoresis; its molecular weight was 29 kD and its isoelectric point was pH 6.8.

Samples of food grade aloe and decolorized processed aloe vera gel were also tested in an innovative *in vitro* system designed to be virtually identical to human skin. Both substances induced an increase in basal keratinocyte proliferation in a dose-dependent manner (Bowles, 1994).

Fractions of extracts from fresh aloe leaves markedly promoted attachment of normal human fetal lung cells in tissue cultural tubes, their growth in cultures. The fresh aloe extracts also enhanced healing of wounded cell monolayers. Human cervical carcinoma

cells were unresponsive to the fresh aloe. In contrast, fractions of aloe gel commercially stabilized to prolong shelf life were equally cytotoxic to human normal and tumor cells *in vitro*. These results suggested to the authors that the commercial preparations may contain substances introduced during commercial processing that can markedly disrupt the *in vitro* attachment and growth of human cells (Winters *et al.*, 1981).

Structure-Activity Relationships: Aloe vera gel is a complex biological product. It has been suggested that the toxic effects observed are from anthraquinones formed by oxidation of low molecular weight components such as aloin. Aloin is a glycoside derivative of aloe-emodin which is present in the outer skin of the plant. Some support for this conclusion is given by the study of Avila and coworkers (1997) who tested the cytotoxicity of a low-molecular weight (<10,000) fraction (LMWF) of aloe vera gel. The LMWF induced disruption of intercellular junctions and detachment of individual chicken fibroblast cells from the bottom of the flask, with formation of cell-free gaps in the monolayer. The LMWF also inhibited the production of reactive oxygen species by human polymorphonuclear leukocytes stimulated by zymosan. The toxic activity of LMWF was comparable to that of aloe-emodin and aloin.

In this situation, a functional comparison between aloe vera gel and croton oil may be a more appropriate comparison. The growth-promoting activity of croton oil led to the finding that tetradecanoylphorbol-13-acetate (TPA), a component of croton oil, is a tumor promoting agent. Although the individual compounds in aloe vera gel responsible for cell proliferation and wound healing have not been identified, attention needs to be given to the possibility that compounds functionally similar to TPA might be present in aloe.

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