

## Aloe Vera Overview

There are two very different health benefits from Aloe vera. Gel from the Aloe leaf has been used for centuries as a topical remedy for minor burns, cuts, and other skin irritations. The second benefit is its laxative effects from internal use of Aloe juice or encapsulated powder.

The active constituents for aloe's laxative effect are known as anthraquinone glycosides, which are converted by intestinal bacteria into aglycones. The active compounds responsible for aloe's wound healing properties are likely a combination of several saccharide molecules. Other beneficial effects, especially from high fiber content of the plant, are on cardiac disease risk factors by reducing blood levels of cholesterol, triglycerides and glucose.

**Dosage:** Laxative - 50-200 mg per day or about 1-3 ounces of aloe gel can be taken by mouth for constipation relief. Aloe juice can also be used as part of a detoxification or cleansing protocol. As topical relief for minor skin irritations, aloe gel can be applied as needed throughout the day.

**Side Effects:** There are no significant side effects noted with aloe vera as an internal or topical agent, except in rare cases of aloe-latex allergy. Pregnant women, however, should avoid aloe-derived laxatives during pregnancy. However, excess consumption of oral aloe juice products (12-16 ounces per day) may lead to nausea, vomiting, and diarrhea.

(Source: [www.supplementwatch.com](http://www.supplementwatch.com))

## Research Overview

1. Aloesin and aloemmannan constituents in Aloe species are anti-inflammatory. (ANIMAL)
  - a. Aloesin prevents UVB-induced immune suppression.
  - b. The neutral polysaccharides, aloemmannan and acemannan show antitumor, antiinflammatory and immunosuppressive activities.
  - c. Glycoprotein fractions have bradykinin degrading and cell proliferation stimulating activities.
  - d. Aloesin, aloemmannan and verectin may act in concert to exert therapeutic properties for wounds, burns and inflammation.
  - e. Aloemmannan, together with acemannan are expected to participate in biological activity following oral administration.
2. The glycoprotein fraction of aloe showed a radical scavenging activity against superoxide anion as well as inhibition of cyclooxygenase2 and reduction of thromboxane A 2 synthase level in vitro. (BASIC RESEARCH)
3. Aloins bind and to inhibit Clostridium histolyticum collagenase reversibly and noncompetitively. Aloe gel and aloins also inhibit stimulated granulocyte matrix metalloproteinases (MMPs). (BASIC RESEARCH)
4. Local aloe vera treatment was a selective and nontraumatic method to treat the allergic rhinitis. (ANIMAL)
5. Aqueous cream was useful in reducing dry desquamation and pain related to radiation therapy. (HUMAN)
6. Lifelong Aloe vera ingestion had no deleterious side effects, and could also be beneficial for the prevention of age-related pathology. (ANIMAL)
7. Isorabaichromone, feruloylaloesin, and pcoumaroylaloesin fractions of aloe showed potent free radical and superoxide anion scavenging activities. (BASIC RESEARCH)
8. Aloeemodin may be useful in liver cancer prevention. (ANIMAL)
9. Chemical toxicity in rat hepatocytes was inhibited by aloe extract. (ANIMAL)
10. An aloe product significantly reduces the incidence of alveolar osteitis (after dental extraction) compared with a clindamycin product.
11. Aloe prevents pancreatic neoplasia in hamsters. (ANIMAL)
12. Aloe secundiflora could be a potential candidate on the management of Newcastle disease in chickens. (ANIMAL)
13. Aloe emodin, a natural constituent of aloe vera leaves, significantly inhibited the growth of Merkel cell carcinoma. (BASIC RESEARCH)
14. An aloe glycoprotein fraction is involved in the wound healing effect of aloe vera via cell proliferation and migration.
15. Oral administration of aloe vera might be a useful adjunct for lowering blood glucose in diabetic patients and for reducing blood lipid levels in patients with hyperlipidaemia. (REVIEW HUMAN)
16. Aloe vera could exhibit the actions of both antiinflammation and wound healing promotion when applied on a second-degree burn wound. (ANIMAL)
17. Aloe vera influences the wound healing process by enhancing collagen turnover in the wound tissue.
18. Wounds were treated either by topical application or oral administration of Aloe vera to rats and both treatments were found to result in similar effects. (ANIMAL)
19. Aloe vera treatment of wounds in diabetic rats may influence inflammation, fibroplasia, collagen synthesis and maturation, and wound contraction. These effects may be due to the reported hypoglycemic effects of the aloe gel. (ANIMAL)
20. Both topical and oral treatments with Aloe vera were found to have a positive influence on the synthesis of glycosaminoglycans (GAGs) and thereby beneficially modulate wound healing.

21. A component of aloe, acemannan, can stimulate macrophage cytokine production, nitric oxide release, surface molecule expression, and cell morphologic changes. (BASIC RESEARCH)
22. Aloe gel extracts permit a faster healing of burn wounds. (ANIMAL)
23. Aloe prevents progressive dermal ischaemia caused by burns, frostbite, electrical injury, distal dying flap and intraarterial drug abuse. (HUMAN)
24. Studies and case reports provide support for the use of aloe vera in the treatment of radiation ulcers and stasis ulcers in man, and burn and frostbite injuries in animals. (REVIEW)
25. Intraperitoneal acemannan in feline leukemia cats improved both the quality of life and the survival rate.
26. Acemannan has shown variable degrees of promise as a possible therapy for Irritable Bowel Disease. (HUMAN) for IBD.
27. Acemannan from aloe vera may provide functional food and potential drug source with antiviral and immunomodulating properties.
28. Acemannan enhances the respiratory burst (RE), phagocytosis, and killing of *Candida albicans* by mouse peritoneal macrophages. (ANIMAL)
29. Acemannan may function, at least in part, through macrophage activation.
30. Acemannan may cause the activation of macrophages by increasing the level of NO synthase at the level of transcription. (BASIC RESEARCH)
31. An acemannan product may be an effective adjunct to surgery and radiation therapy in the treatment of canine and feline fibrosarcomas. (ANIMAL)
32. Acemannan increased killing by T-lymphocytes by almost 50%. (BASIC RESEARCH)
33. Acemannan increases lymphocyte response by enhancement of monocyte release of Interleukin I. (BASIC RESEARCH)
34. 5,000 patients on dietary aloe reduced total cholesterol, triglycerides, and blood sugar level in diabetic patients, total lipids and also increased HDL. Clinically there was reduction in the frequency of anginal attacks and gradually, drugs, like verapamil, nifedipine, betablockers and nitrates, were tapered.
35. CARN 750, a polydispersed beta(1,4)linked acetylated mannan isolated from the Aloe vera plant increased hematopoietic activity in mice.
36. Aloe may increase tensile strength by increasing crosslinking in collagen and interactions with the ground substance.
37. Extracts of Aloe vera possess activities that reverse the degenerative skin changes seen with aging by stimulating the synthesis of collagen and elastin fibers.
38. In facial dermabrasion, wound healing was approximately 72 hours faster at the aloe site compared to polyethylene oxide gel wound dressings.
39. A particular fraction of aloe leaves prevented the growth of *Bacillus subtilis* by inhibiting primarily nucleic acid synthesis, after which protein synthesis is also inhibited.

Aloe Vera Abstracts (64)

Aloe Vera Citations (86)

1\_ Yakugaku Zasshi. 2003 Jul;123(7):51732.

[Antiinflammatory constituents, aloesin and aloemannan in Aloe species and effects of tanshinon VI in *Salvia miltiorrhiza* on heart]  
[Article in Japanese]

Yagi A, Takeo S.

Faculty of Pharmacy and Pharmaceutical Sciences, Fukuyama University, 985 Gakuencho, Fukuyama 7290292, Japan.

yagi@fupharm.fukuyamau.ac.jp

Cinnamoyl, pcoumaroyl, feruloyl, caffeoyl aloesin, and related compounds were isolated from Aloe species. The antiinflammatory and antioxidative activities of these compounds were examined based on the structureactivity relationship. It was suggested that the bioactivities may link to acyl ester groups in aloesin, together with those of aloesinrelated compounds. However, investigations using the contact hypersensitivity response indicated a preventive effect of aloesin on the UVB-induced immune suppression. Furthermore, aloesin inhibited tyrosine hydroxylase and dihydroxyphenylalanine (DOPA) oxidase activities of tyrosinase from normal human melanocyte cell lysates. These results show that aloesin prevents not only UVB-induced immune suppression, but also could be a positive pigmentaltering agent for cosmetic application. In preclinical study, aloe extract was investigated using phagocytosis and nitroblue tetrazolium chloride (NBT) reduction in adult bronchial asthma, and high molecularweight materials, such as polysaccharide and glycoprotein fractions, were identified as active ingredients. The neutral polysaccharides, aloemannan and acemannan showed antitumor, antiinflammatory and immunosuppressive activities, and glycoprotein fractions with bradykinin-degrading and cell proliferation-stimulating activities were identified from the nondialysate fraction of the gel part of Aloe species. Verectin fractionated from Aloe vera gel was examined biochemically and immunochemically, and verectin antibody was used in the appraisal of commercial Aloe vera gel products. It was reported that aloesin stimulates the proliferation of cultured human hepatoma SKHep 1 cells. Thus aloesin, related compounds, and high molecularweight materials, such as aloemannan and verectin, may act in concert to exert therapeutic properties for wounds, burns and inflammation. The biodisposition of fluoresceinylisothiocyanate (FITC)-labeled aloemannan (FITCAM) with the homogenate from some organs in mice was demonstrated, and FITCAM was metabolized to a smaller molecule (MW 3000) by the large intestinal microflora in feces. The modified aloe polysaccharide (MW: 80000) with cellulase under restricted conditions, immunologically stimulated the recovery of UVB-induced tissue injury. Thus the modified polysaccharides of aloemannan, together with acemannan (MW: about 600000), are expected to participate in biological activity following oral administration. The effects of tanshinone VI, a diterpenoid isolated from *Salvia miltiorrhiza*, on the heart are reviewed. First, the effects on the posthypoxic recovery of contractile function of perfused rat hearts were examined. Hypoxia/reoxygenation induced a release of purine nucleosides and bases (ATP metabolites) and resulted in little recovery of contractile force of reoxygenated hearts. Pretreatment of the perfused heart with 42 nM tanshinone VI under hypoxic conditions attenuated the release of ATP metabolites during hypoxia/reoxygenation. Treatment with tanshinone VI enhanced the posthypoxic recovery of myocardial contractility. These results show that tanshinone VI may protect the heart against hypoxia/reoxygenation injury and improve the posthypoxic cardiac function. Second, the effects of tanshinone VI on in vitro myocardial remodeling were examined. Cardiomyocytes and cardiac fibroblasts were isolated from neonatal rat hearts, and simultaneously prepared insulinlike growth factor1 (IGF1) induced the hypertrophy of cardiomyocytes. IGF1 increased the collagen synthesis of cardiac fibroblasts, that is, in vitro fibrosis. The hypertrophy of cardiomyocytes was attenuated in the presence of tanshinone VI in the culture medium. The fibrosis of cardiac fibroblasts was decreased by treatment with tanshinone VI. When tanshinone VI was added to cardiac fibroblast-conditioned medium, the medium-mediated hypertrophy of cardiomyocytes was also attenuated. These results show that tanshinone VI may attenuate in vitro cardiac remodeling. The series of studies has shown that tanshinone VI protects the myocardium against hypoxia/reoxygenation injury and attenuates progression of in vitro myocardial remodeling, suggesting that tanshinone VI is a possible agent for the treatment of cardiac disease with contractile failure.

2\_ Acta Pol Pharm. 2003 JanFeb;60(1):319.

Technology of eye drops containing aloe (*Aloe arborescens* Mill. Liliaceae) and eye drops containing both aloe and neomycin sulphate.

Kodym A, Marcinkowski A, Kukula H.

Department of Drug Form Technology, Ludwik Rydygier Medical University in Bydgoszcz.

Eye drops made of aloe are a sterile, aqueous extract of fresh leaves of *Aloe arborescens* Mill., containing necessary additives and neomycin sulphate. The aim of the studies was to establish the technology of eye drops containing biologically active aloe substances and those containing both chemical constituents of aloe and neomycin sulphate. Within the studies, the formulary content and the way of preparing eye drops were determined, criteria were defined and methods of qualitative assessment of drops were proposed. On the basis of the proposed analytical methods, the physicochemical and microbiological stability of the eye drops stored at a temperature of 20±5 degrees C was studied. As the criteria of qualitative assessment of the eye drops, the following analyses were considered: sterility, appearance of the eye drops (clarity), pH, osmotic pressure, density, viscosity, TLC analysis, content of aloenin and aloin, studies of antimicrobial activity of neomycin in the drops, and preservative efficiency of thiomersal in the eye drops. The studies showed that the additives such as: sodium chloride, benzalkonium chloride, chlorhexidine diacetate and digluconate, phenylmercuric borate and Nipagins M and P could not be used to prepare the eye drops because they were involved in pharmaceutical interactions with chemical constituents of aloe in the eye drops. The eye drops containing: aqueous extract of fresh leaves of aloe, boric acid, thiomersal, sodium pyrosulphite, disodium EDTA, betaphenylethyl alcohol and neomycin sulphate, both freshly prepared and after two years of storage, met the requirements of the Polish Pharmacopoeia (PPH

V) mentioned in the monograph *Guttate ophthalmicae*. They were sterile, clear, their osmotic pressure approximated the osmotic pressure of lacrimal fluid and they were characterized by appropriate pH. Aloenin in the drops was much more stable than aloin. Neomycin after two years of storage retained almost 98% of its starting antimicrobial activity which allows the conclusion that the biologically active aloe substances did not decrease the stability of neomycin in the drops. The preservation assay showed that thiomersal, both in the freshly prepared drops and after two years of storage, maintained antimicrobial activity, which was in accordance with PPh V.

3\_ *Planta Med.* 2003 Mar;69(3):26971.

Radical scavenging glycoprotein inhibiting cyclooxygenase2 and thromboxane A2 synthase from aloe vera gel.

Yagi A, Kabash A, Mizuno K, Moustafa SM, Khalifa TI, Tsuji H.

Faculty of Pharmacy and Pharmaceutical Sciences, Fukuyama University, GakuenCho, Fukuyama, Hiroshima, Japan.

yagi@fupharm.fukuyamau.ac.jp

An active glycoprotein fraction containing 58 % protein was isolated from Aloe vera gel by precipitation with 55 % ammonium sulfate followed by gel permeation using DEAE Sphacel A25, Sepharose 6B and Sephadex G50 columns in a yield of  $3 \times 10^3$  %. The glycoprotein fraction showed a single band corresponding to a subunit of verectin at the same position when stained with both Coomassie brilliant blue and periodic acidSchiff reagents on 18 % SDS PAGE. The molecular weight (14 kDa) was confirmed by Sephadex G50 column chromatography. The glycoprotein fraction showed a radical scavenging activity against superoxide anion generated by the xanthinexanthine oxidase system as well as inhibition of cyclooxygenase2 and reduction of thromboxane A 2 synthase level in vitro.

4\_ *J Wound Ostomy Continence Nurs.* 2003 Mar;30(2):6871.

Is aloe vera effective for healing chronic wounds?

Gallagher J, Gray M.

Massachusetts General Hospital, 32 Fruit Street, Boston, MA 02114, USA. jgallagher1@partners.org

Antimicrob Agents Chemother. 2003 Mar;47(3):11379. In vitro susceptibilities of *Shigella flexneri* and *Streptococcus pyogenes* to inner gel of *Aloe barbadensis* Miller. Ferro VA, Bradbury F, Cameron P, Shakir E, Rahman SR, Stimson WH. Department of Immunology, University of Strathclyde, Glasgow G4 ONR, United Kingdom. v.a.ferro@strath.ac.uk

*Aloe barbadensis* Miller (or Aloe vera) has widespread use in health products, and despite numerous reports on the whole plant, little work has been performed on the inner gel, which has been used extensively in these products. This report describes the in vitro susceptibilities of two bacteria to this component.

5\_ *Life Sci.* 2003 Jan 3;72(7):84350.

Inhibition of collagenase and metalloproteinases by aloins and aloe gel.

Barrantes E, Guinea M.

Department of Pharmacology, School of Pharmacy, University of Alcala, Ctra. MadridBarcelona Km 33.6, 28871 Alcala de Henares, Spain.

The effects of *Aloe barbadensis* gel and aloe gel constituents on the activity of microbial and human metalloproteinases have been investigated. *Clostridium histolyticum* collagenase (ChC) results dosedependently inhibited by aloe gel and the activityguided fractionation led to an active fraction enriched in phenolics and aloins. Aloins have been shown to be able to bind and to inhibit ChC reversibly and noncompetitively. Aloe gel and aloins are also effective inhibitors of stimulated granulocyte matrix metalloproteinases (MMPs). The remarkable structural resemblances between aloins and the pharmacophore structure of inhibitory tetracyclines, suggest that the inhibitory effects of aloins are via an interaction between the carbonyl group at C(9) and an adjacent hydroxyl group of anthrone (C(1) or C(8)) at the secondary binding site of enzyme, destabilizing the structure of granulocyte MMPs.

6\_ *Lin Chuang Er Bi Yan Hou Ke Za Zhi.* 2002 May;16(5):22931.

[Molecular biological study of aloe vera in the treatment of experimental allergic rhinitis in rat] [Article in Chinese]

Yu H, Dong Z, Yang Z.

Department of OtolaryngologyHead and Neck Surgery, ChinaJapan Union Hospital, Jilin University, Changchun 130031.

**OBJECTIVE:** To study the therapeutic mechanism of aloe vera in allergic rhinitis (AR). **METHOD:** Ovalbumin sensitized white rat used as animal models of AR were treated intranasally with aloe vera. At the end of treatment, the differences in the behavior science were observed; the changes in the nasal mucosa were studied by pathological; IL2, IL4 mRNA in the nasal mucosa and spleen were used to do reverse transcriptive polymerase chain reaction (RT-PCR). **RESULT:** The behavior science score of positive controls (8.42 +/- 1.06) was higher than the experimental group (2.02 +/- 0.42) and normal controls (0); inflammatory reactions in the experimental group nasal mucosa were remarkably relieved; the mean expression level of IL2 mRNA in the experimental group was higher significantly than positive controls ( $P < 0.01$ ); but that of IL4 mRNA was lower evidently ( $P < 0.01$ ). **CONCLUSION:** The aloe vera are suggested to be involved in the differentiation of CD4+ lymphocytes, by means of regulating the expression of Th1 and Th2 cytokines. The results suggests that local aloe vera treatment was a selective and nontraumatic method to treat the allergic rhinitis.

7\_ Pharmazie. 2002 Dec;57(12):8347.

Physicochemical and microbiological properties as well as stability of ointments containing aloe extract (*Aloe arborescens* Mill.) or aloe extract associated to neomycin sulphate.

Kodym A, Bujak T.

Department of Drug Form Technology, Karol Marcinkowski Medical Academy, Poznan.

The aim of the study was to work out methods of quality assessment of ointments containing dry extract from fresh leaves of *Aloe arborescens* Mill. (Liliaceae) and also of ointments containing both of dry extract and neomycin sulphate. The stability of the ointments, stored at 20 degrees C, was studied and the following criteria were considered: chromatographic analysis (TLC), pH of the ointments, the content of the substances in the dry extract converted to aloenin, the content of aloenin and aloin, antimicrobial activity of neomycin in the ointments, the size of the particles of the dry extract and of neomycin sulphate in the ointment suspension and the sterility of the ointments. After two years of storage at 20 degrees C, the ointments prepared with the anhydrous lipophilic base, did not change their physicochemical characteristics and neomycin in those ointments retained almost 100% of starting antimicrobial activity. Water or propylene glycol significantly decreased the stability of the biologically active substances of the dry extract in the ointments. Besides, in the ointments containing the dry extract and neomycin sulphate, the presence of water or propylene glycol induced degradation of the biologically active substances of the dry extract and a decrease in the antimicrobial activity of neomycin in the ointments. Considering the physicochemical and microbiological stability, the most advisable base for the ointments with aloe and neomycin sulphate was composed of white vaseline, liquid paraffin, solid paraffin, cholesterol.

8\_ Cancer Nurs. 2002 Dec;25(6):44251.

A Phase III study on the efficacy of topical aloe vera gel on irradiated breast tissue.

Heggie S, Bryant GP, Tripcony L, Keller J, Rose P, Glendenning M, Heath J.

Queensland Radium Institute, Division of Oncology, Royal Brisbane Hospital, Australia. Pauline\_Rose@health.qld.gov.au

The aim of the study was to see if topical aloe vera gel would be beneficial in reducing the identified skin sideeffects of radiation therapy, including erythema, pain, itching, dry desquamation, and moist desquamation, when compared with aqueous cream. The secondary aim was to assess the effect of other factors known to predict severity of radiation skin reaction, ie, breast size, smoking habit, and one or more drainages of lymphocele after surgery, on other skin side effects. A Phase III study was conducted involving 225 patients with breast cancer after lumpectomy or partial mastectomy, who required a course of radiation therapy using tangential fields. Patients were randomized to either topical aloe vera gel or topical aqueous cream to be applied 3 times per day throughout and for 2 weeks after completion of radiation treatment. Weekly skin assessments were performed by nursing staff. Aqueous cream was significantly better than aloe vera gel in reducing dry desquamation and pain related to treatment. Subjects with D cup or larger size breasts experienced significantly more erythema, regardless of treatment arm. For subjects who had undergone lymphocele drainage, the aloe vera group experienced significantly more pain than the aqueous cream group. Within the aqueous cream arm, smokers were significantly more likely to experience itching within the treatment field than were nonsmokers. Within the aloe vera arm, subjects who had undergone one or more lymphocele drainages after surgery were significantly more likely to experience erythema and itching within the treatment field than those who did not have drainage. In this study, aloe vera gel did not significantly reduce radiationinduced skin side effects. Aqueous cream was useful in reducing dry desquamation and pain related to radiation therapy.

9\_ Phytother Res. 2002 Dec;16(8):7128.

The influence of longterm Aloe vera ingestion on agerelated disease in male Fischer 344 rats.

Ikeno Y, Hubbard GB, Lee S, Yu BP, Herlihy JT.

Department of Physiology, University of Texas Health Science Center, San Antonio, Texas 782293900, USA.

The effects of longterm Aloe vera ingestion on agerelated diseases were investigated using male specific pathogenfree (SPF) Fischer 344 rats. Experimental animals were divided into four groups: Group A, the control rats fed a semisynthetic diet without Aloe vera; Group B, rats fed a diet containing 1% freeze-dried Aloe vera file; Group C, rats fed a diet containing 1% charcoalprocessed, freeze-dried Aloe vera file; and Group D, rats fed the control diet and given whole leaf charcoalprocessed Aloe vera (0.02%) in the drinking water. This study demonstrates that lifelong Aloe vera ingestion produced neither harmful effects nor deleterious changes. In addition, Aloe vera ingestion appeared to be associated with some beneficial effects on agerelated diseases. Groups B exhibited significantly less occurrence of multiple causes of death, and a slightly lower incidence of fatal chronic nephropathy compared with Group A rats. Groups B and C rats showed the trend, slightly lower incidences of thrombosis in the cardiac atrium than Group A rats. Therefore, these findings suggest that lifelong Aloe vera ingestion does not cause any obvious harmful and deleterious side effects, and could also be beneficial for the prevention of agerelated pathology. Copyright 2002 John Wiley & Sons, Ltd.

10\_ Planta Med. 2002 Nov;68(11):95760.

Antioxidant, free radical scavenging and antiinflammatory effects of aloesin derivatives in Aloe vera.

Yagi A, Kabash A, Okamura N, Haraguchi H, Moustafa SM, Khalifa TI.

Faculty of Pharmacy and Pharmaceutical Sciences, Fukuyama University, Gakuencho, Fukuyama, Japan.

Antioxidant components in Aloe vera were examined for lipid peroxidation using rat liver microsomal and mitochondrial enzymes. Among the aloesin derivatives examined, isorabaichromone showed a potent antioxidative activity. The DPPH radical and superoxide anion scavenging activities were determined. As one of the most potent components, isorabaichromone together with feruloylaloetin and p-coumaroylaloetin showed potent DPPH radical and superoxide anion scavenging activities. Electron spin resonance (ESR) using the spin trapping method suggested that the potent superoxide anion scavenging activity of isorabaichromone may have been due to its caffeoyl group. As *A. vera* has long been used to promote wound healing, the inhibitory effects of aloesin derivatives for cyclooxygenase (Cox)2 and thromboxane (Tx) A<sub>2</sub> synthase were examined and the participation of p-coumaroyl and feruloyl ester groups in the aloesin skeleton was demonstrated. These findings may explain, at least in part, the wound healing effects of *A. vera*. Abbreviations. ADP:adenosine diphosphate ASA:ascorbic acid BHT:butylated hydroxytoluene BSA:bovine serum albumin DMPO:5,5-dimethyl-1-pyrroline N-oxide DPPH:1,1-diphenylpicrylhydrazyl EDTA:edetic acid HEPES: N-(2-hydroxyethyl)piperazine N<sup>2</sup>-ethanesulfonic acid NADH:reduced nicotinamide adenine dinucleotide NADPH:reduced nicotinamide adenine dinucleotide phosphate NBT:nitroblue tetrazolium Pg:prostaglandin SOD:superoxide dismutase TBA:thiobarbituric acid TCA:trichloroacetic acid XOD:xanthine oxidase

11\_ Acta Pol Pharm. 2002 MayJun;59(3):1816.

Biopharmaceutical assessment of eye drops containing aloe (*Aloe arborescens* Mill.) and neomycin sulphate.

Kodym A, Grzeskowiak E, Partyka D, Marcinkowski A, Kaczynska-Dyba E.

Department of Drug Form Technology, Karol Marcinkowski Medical Academy in Poznan.

The subject of the studies was eye drops made of aloe, containing the group of aloe chemical substances of anti-inflammatory use and neomycin sulphate. The aim of the studies was to evaluate the permeability of biologically active aloe substances, determined as aloenin, through synthetic lipophilic and hydrophilic membranes in a standard perfusion apparatus and in vitro verification of the transport possibilities of these substances through the isolated cornea of pig's eye. The permeability process of biologically active aloe substances determined as aloenin, through synthetic lipophilic and hydrophilic membranes, was analyzed using the first-order kinetics. Estimated quotas of permeability rate constant show that the investigated chemical compounds of aloe, included in the eye drops, diffused through the applied membranes. The studies of permeability through isolated pig's cornea proved that biologically active aloe substances could not overcome this biological barrier. On the basis of biopharmaceutical studies it can be concluded that the eye drops containing aloe and neomycin sulphate, due to the lack of permeating abilities through the eye cornea, should be particularly useful in the treatment of inflammations and infections of external parts of the eye, such as conjunctiva, eyelid edges, lacrimal sac and cornea.

12\_ Life Sci. 2002 Sep 6;71(16):187992.

The antiproliferative activity of aloemodin is through p53-dependent and p21-dependent apoptotic pathway in human hepatoma cell lines.

Kuo PL, Lin TC, Lin CC.

Graduate Institute of Natural Products, College of Pharmacy, Kaohsiung Medical University, Kaohsiung 807, Taiwan, ROC.

The aim of this study is to investigate the anticancer effect of aloemodin in two human liver cancer cell lines, Hep G2 and Hep 3B. We observed that aloemodin inhibited cell proliferation and induced apoptosis in both examined cell lines, but with different antiproliferative mechanisms. In Hep G2 cells, aloemodin induced p53 expression and was accompanied by induction of p21 expression that was associated with a cell cycle arrest in G1 phase. In addition, aloemodin had a marked increase in Fas/APO1 receptor and Bax expression. In contrast, with p53-deficient Hep 3B cells, the inhibition of cell proliferation of aloemodin was mediated through a p21-dependent manner that did not cause cell cycle arrest or increase the level of Fas/APO1 receptor, but rather promoted aloemodin-induced apoptosis by enhancing expression of Bax. These findings suggest that aloemodin may be useful in liver cancer prevention.

13\_ Pharmacol Toxicol. 2002 May;90(5):27884.

Protective effect of aloe extract against the cytotoxicity of 1,4-naphthoquinone in isolated rat hepatocytes involves modulations in cellular thiol levels.

Norikura T, Kennedy DO, Nyarko AK, Kojima A, Matsui Yuasa I.

Department of Food and Human Health Sciences, Graduate School of Human Life Science, Osaka City University, Osaka, Japan.

Aloe is a familiar ingredient in a wide range of health care and cosmetic products and has been reported to possess various physiological effects, antioxidative, anticarcinogenic, anti-inflammatory and laxative. Aloe has also been reported to have an effect on liver function. The cytoprotective effect of aloe extract against 1,4-naphthoquinone-induced hepatotoxicity was evaluated in primary cultured rat hepatocytes. After exposure to 1,4-naphthoquinone (100 µM), a decrease in cell viability measured as >60% lactate dehydrogenase depletion was induced. Cellular glutathione (GSH) and protein SH levels were also significantly decreased in a time-dependent manner. However, addition of aloe extract resulted in a dose-dependent improvement of these effects. This cytoprotective effect of aloe could be attributed to its inhibition of GSH and protein SH depletions. The effect of the aloe extracts was also dose-dependent. Addition of diethyl maleate (1 mM), a cellular glutathione-depleting agent, to hepatocytes treated with both 1,4-naphthoquinone and aloe extract, induced depletion of GSH, but did not affect protein SH or lactate dehydrogenase. These

results suggest that the 1,4-naphthoquinone-induced toxicity in rat hepatocytes was inhibited by aloe extract, and that this protective effect was due to the maintenance of cellular thiols, especially proteinSH.

14\_ J Oral Maxillofac Surg. 2002 Apr;60(4):3749; discussion 379.

Reduction in the incidence of alveolar osteitis in patients treated with the SaliCept patch, containing Acemannan hydrogel.

Poor MR, Hall JE, Poor AS.

University of Texas Southwestern Medical School, Dallas, TX, USA. Txpoors@aol.com

**PURPOSE:** In the present study, we compared the incidence of alveolar osteitis (AO) in patients treated with either clindamycinsoaked Gelfoam (Pharmacia and Upjohn Co, Kalamazoo, MI) or SaliCept Patches (Carrington Laboratories, Inc, Irving, TX). The SaliCept Patch is a freeze-dried pledget that contains Acemannan Hydrogel (Carrington Laboratories) obtained from the clear inner gel of Aloe vera L. **PATIENTS AND METHODS:** A retrospective evaluation was performed of the records of 587 patients (1,031 sockets) whose extraction sites had been treated with clindamycinsoaked Gelfoam. A prospective trial was conducted in which 607 patients (1,064 sockets) had 2 SaliCept Patches placed immediately after extraction. The same surgeon treated all patients. **RESULTS:** Analysis restricted to mandibular third molar sites showed that 78 of 975 sites (8.0%) in the Gelfoam group developed AO, whereas only 11 of 958 sites (1.1%) in the SaliCept group developed AO ( $P < .0001$ ). Further analysis of all extraction sites revealed that the incidence of AO in the Gelfoam group was 7.6% compared with 1.1% in the SaliCept-treated group ( $P < .0001$ ). **CONCLUSIONS:** The study results suggest that the SaliCept Patch significantly reduces the incidence of AO compared with clindamycinsoaked Gelfoam. Copyright 2002 American Association of Oral and Maxillofacial Surgeons

15\_ J Okla Dent Assoc. 2002 Winter;92(3):403.

The clinical effects of saline and aloe vera rinses on periodontal surgical sites.

Rieger L, Carson RE.

Department of Dental Hygiene, University of Oklahoma, College of Dentistry, USA.

16\_ Cancer Lett. 2002 Apr 25;178(2):11722.

Chemopreventive effects of Aloe arborescens on N-nitrosobis(2-oxopropyl)amine-induced pancreatic carcinogenesis in hamsters.

Furukawa F, Nishikawa A, Chihara T, Shimpo K, Beppu H, Kuzuya H, Lee IS, Hirose M.

Division of Pathology, Biological Safety Research Center, National Institute of Health Sciences, 1181 Kamiyoga, Setagayaku, Tokyo 1588501, Japan.

The modification effects of freeze-dried aloe (*Aloe arborescens*) whole leaf powder during the initiation phase of carcinogenesis were investigated in hamsters treated with N-nitrosobis(2-oxopropyl)amine (BOP). Female Syrian hamsters were given four weekly subcutaneous injections of BOP at a dose of 10mg/kg and then given 0, 1 or 5% aloe in their diet for 5 weeks. At week 54 of the experiment, all surviving animals were sacrificed and development of neoplastic and preneoplastic lesions was assessed histopathologically. The incidences of pancreatic adenocarcinomas, atypical hyperplasias or total atypical hyperplasias plus adenocarcinomas were significantly ( $P < 0.05$ ) decreased with BOP+5% aloe, and that of adenocarcinomas were also significantly ( $P < 0.05$ ) reduced in the BOP+1% aloe as compared to the BOP alone group. Multiplicities of pancreatic adenocarcinomas, atypical hyperplasias or total lesions were also significantly ( $P < 0.01$  or  $P < 0.05$ ) lower in the BOP+5% aloe group than with the BOP alone. Quantitative data for neoplastic lesions in the lung, liver, gall bladder, kidney and urinary bladder of hamsters were not significantly different among the three groups. In a satellite experiment, pretreatment with aloe significantly ( $P < 0.01$ ) reduced the formation of O<sup>6</sup>-methyldeoxyguanosine in epithelial cells of pancreatic ducts as compared to the BOP alone value. Our results thus indicate that aloe prevents BOP-induced pancreatic neoplasia in hamsters in relation to decreased DNA adduct formation in the target tissue.

17\_ J Ethnopharmacol. 2002 Mar;79(3):299-304.

Evaluation of the efficacy of the crude extract of *Aloe secundiflora* in chickens experimentally infected with Newcastle disease virus.

Waihenya RK, Mtambo MM, Nkwengulila G.

Department of Zoology and Marine Biology, University of Dar es Salaam, PO Box 35064, Dar es Salaam, Tanzania.

Two replicate experiments were carried out to verify the efficacy of Aloe species (*Aloaceae*) as used for the control of Newcastle disease (ND) in rural poultry in free-range systems among several communities in Tanzania. Four months old local chickens free of Newcastle disease antibodies were used. Following inoculation with ND virus, body weights, clinical signs, antibody levels and mortality were monitored. Results showed that there was reduced mortality rate and the severity of clinical signs during the acute phase of the infection in Aloe treated chickens compared with the nontreated ones. However, there was no significant effect of the Aloe on the antibody levels that were attributed to the recovery of the surviving chickens. The findings of this study suggest that *Aloe secundiflora* could be a potential candidate on the management of Newcastle disease in chickens. Further studies are in progress to identify the active ingredients of *A. secundiflora* against Newcastle disease virus.

18\_ Am J Dermatopathol. 2002 Feb;24(1):1722.

The effect of aloe emodin on the proliferation of a new Merkel carcinoma cell line.

Wasserman L, Avigad S, Beery E, Nordenberg J, Fenig E.

Felsenstein Medical Research Center, Sackler Faculty of Medicine, Tel Aviv University, Rabin Medical Center Beilinson Campus, Petah Tikva 49100, Israel. yardenam@clalit.org.il

A freefloating cell line has been established from a metastatic lesion of a Merkel cell carcinoma (MCC) patient. The cell line was characterized by immunocytochemical reactions with antibodies against the epithelial and neuroendocrine antigens: cytokeratin 20, neuronspecific enolase, chromogranin A, neurofilament protein, synaptophysin, and calcitonin. Karyotype analysis of the MCC cells showed deletion in chromosomes 3 and 7, loss of chromosome 10, and several translocations in other chromosomes. No mutation was detected in the TP53 gene, after analyzing the complete coding region. Growth factors such as basic fibroblast growth factor, transforming growth factorbeta, and nerve and epidermal growth factors had no effect on the proliferation of the cells. The differentiationinducing agents sodium butyrate and dimethyl sulfoxide, especially the former, markedly inhibited the proliferation of the MCC cells. Aloe emodin, a natural constituent of aloe vera leaves, significantly inhibited the growth of MCC cells. Aloe emodin has been reported to be nontoxic for normal cells but to possess specific toxicity for neuroectodermal tumor cells. Differentiationinducing agents, and aloe emodin, merit further investigation as potential agents for treating MCC.

19\_ Br J Dermatol 2001 Oct;145(4):53545

The woundhealing effect of a glycoprotein fraction isolated from aloe vera.

Choi SW, Son BW, Son YS, Park YI, Lee SK, Chung MH.

Department of Pharmacology, Seoul National University College of Medicine, Seoul 110799, Korea.

**BACKGROUND:** Aloe vera has been used as a family medicine for promoting wound healing, but it is not known which component of the plant is effective for this purpose. **OBJECTIVES:** To isolate and characterize the component effective in wound healing. **METHODS:** Chromatography, electrophoresis and spectroscopic methods were used. The cellproliferation activity of each component isolated was measured by a [3H]thymidine uptake assay. The cellproliferation activity of the effective component was tested on a threedimensional raft culture (cell culture technique by which artificial epidermis is made from keratinocytes). The effect of the active component on cell migration and wound healing was observed on a monolayer of human keratinocytes and in hairless mice. **RESULTS:** A glycoprotein fraction was isolated and named G1G1M1DI2. It showed a single band on sodium dodecyl sulphatepolyacrylamide gel electrophoresis, with an apparent molecular weight of about 5.5 kDa. It exhibited significant [3H] thymidine uptake in squamous cell carcinoma cells. The effect of G1G1M1DI2 on cell migration was confirmed by accelerated wound healing on a monolayer of human keratinocytes. When this fraction was tested on a raft culture, it stimulated the formation of epidermal tissue. Furthermore, proliferation markers (epidermal growth factor receptor, fibronectin receptor, fibronectin, keratin 5/14 and keratin 1/10) were markedly expressed at the immunohistochemical level. The glycoprotein fraction enhanced wound healing in hairless mice by day 8 after injury, with significant cell proliferation. **CONCLUSIONS:** It is considered that this glycoprotein fraction is involved in the woundhealing effect of aloe vera via cell proliferation and migration.

20\_ Br J Gen Pract 1999 Oct;49(447):8238

Aloe vera: a systematic review of its clinical effectiveness.

Vogler BK, Ernst E.

Department of Complementary Medicine, School of Postgraduate Medicine and Health Sciences, University of Exeter.

**BACKGROUND:** The use of aloe vera is being promoted for a large variety of conditions. Often general practitioners seem to know less than their patients about its alleged benefits. **AIM:** To define the clinical effectiveness of aloe vera, a popular herbal remedy in the United Kingdom. **METHOD:** Four independent literature searches were conducted in MEDLINE, EMBASE, Biosis, and the Cochrane Library. Only controlled clinical trials (on any indication) were included. There were no restrictions on the language of publication. All trials were read by both authors and data were extracted in a standardized, predefined manner. **RESULTS:** Ten studies were located. They suggest that oral administration of aloe vera might be a useful adjunct for lowering blood glucose in diabetic patients as well as for reducing blood lipid levels in patients with hyperlipidaemia. Topical application of aloe vera is not an effective preventative for radiationinduced injuries. It might be effective for genital herpes and psoriasis. Whether it promotes wound healing is unclear. There are major caveats associated with all of these statements. **CONCLUSION:** Even though there are some promising results, clinical effectiveness of oral or topical aloe vera is not sufficiently defined at present.

21\_ J Med Assoc Thai 2000 Apr;83(4):41725

Therapeutic effects of Aloe vera on cutaneous microcirculation and wound healing in second degree burn model in rats.

Somboonwong J, Thanamitramanee S, Jariyapongskul A, Patumraj S.

Department of Physiology, Faculty of Medicine, Chulalongkorn University Hospital, Bangkok, Thailand.

**OBJECTIVE:** To demonstrate the microcirculatory and wound healing effects of Aloe vera on induced second degree burn wounds in rats. **METHOD:** A total of 48 male Wistar rats were equally divided into 4 groups as follows: sham controls, untreated burnwound rats, those treated with oncedaily application of normal saline (NSS) and those treated with oncedaily application of lyophilized Aloe vera gel. The animals in each group were equally subdivided into 2 subgroups for the study of cutaneous microcirculation and wound healing on day 7 and 14 after burn. Dorsal skinfold chamber preparation and intravital fluorescence microscopic technique were performed to examine dermal microvascular changes, including arteriolar diameter, postcapillary venular permeability and leukocyte adhesion on postcapillary venules. **RESULTS:** On day 7, the vasodilation and increased postcapillary venular

permeability as encountered in the untreated burn were found to be reduced significantly ( $p < 0.05$ ) in both the NSS and Aloe veratreated groups, but to a greater extent in the latter. Leukocyte adhesion was not different among the untreated, NSS and Aloe veratreated groups. On day 14, vasoconstriction occurred after the wound had been left untreated. Only in the Aloe veratreated groups, was arteriolar diameter increased up to normal condition and postcapillary venular permeability was not different from the sham controls. The amount of leukocyte adhesion was also less observed compared to the untreated and NSS treated groups. Besides, the healing area of the Aloe veratreated wound was better than that of the untreated and NSS treated groups during 7 and 14 days after burn. CONCLUSION: Aloe vera could exhibit the actions of both antiinflammation and wound healing promotion when applied on a second degree burn wound.

1 Indian J Exp Biol 1998 Sep;36(9):896901

Influence of Aloe vera on collagen turnover in healing of dermal wounds in rats.

Chithra P, Sajithlal GB, Chandrakasan G.

Department of Biochemistry, Central Leather Research Institute, Adyar, Chennai, India.

Treatment of fullthickness wounds with A. vera, on rats resulted in increased biosynthesis of collagen and its degradation. A corresponding increase in the urinary excretion of hydroxyproline was also observed. Elevated levels of lysyl oxidase also indicated increased crosslinking of newly synthesised collagen. The results suggest that A. vera influences the wound healing process by enhancing collagen turnover in the wound tissue.

22\_ Mol Cell Biochem 1998 Apr;181(12):716

Influence of Aloe vera on collagen characteristics in healing dermal wounds in rats.

Chithra P, Sajithlal GB, Chandrakasan G.

Department of Biochemistry, Central Leather Research Institute, Adyar, Madras, India.

Wound healing is a fundamental response to tissue injury that results in restoration of tissue integrity. This end is achieved mainly by the synthesis of the connective tissue matrix. Collagen is the major protein of the extracellular matrix, and is the component which ultimately contributes to wound strength. In this work, we report the influence of Aloe vera on the collagen content and its characteristics in a healing wound. It was observed that Aloe vera increased the collagen content of the granulation tissue as well as its degree of crosslinking as seen by increased aldehyde content and decreased acid solubility. The type I/type III collagen ratio of treated groups were lower than that of the untreated controls, indicating enhanced levels of type III collagen. Wounds were treated either by topical application or oral administration of Aloe vera to rats and both treatments were found to result in similar effects.

23\_ J Ethnopharmacol 1998 Jan;59(3):195201

Influence of aloe vera on the healing of dermal wounds in diabetic rats.

Chithra P, Sajithlal GB, Chandrakasan G.

Department of Biochemistry, Central Leather Research Institute, Adyar, Chennai, India.

The positive influence of Aloe vera, a tropical cactus, on the healing of fullthickness wounds in diabetic rats is reported. Fullthickness excision/incision wounds were created on the back of rats, and treated either by topical application on the wound surface or by oral administration of the Aloe vera gel to the rat. Wound granulation tissues were removed on various days and the collagen, hexosamine, total protein and DNA contents were determined, in addition to the rates of wound contraction and period of epithelialization. Measurements of tensile strength were made on treated/untreated incision wounds. The results indicated that Aloe vera treatment of wounds in diabetic rats may enhance the process of wound healing by influencing phases such as inflammation, fibroplasia, collagen synthesis and maturation, and wound contraction. These effects may be due to the reported hypoglycemic effects of the aloe gel.

24\_ J Ethnopharmacol 1998 Jan;59(3):17986

Influence of Aloe vera on the glycosaminoglycans in the matrix of healing dermal wounds in rats.

Chithra P, Sajithlal GB, Chandrakasan G.

Department of Biochemistry, Central Leather Research Institute, Madras, India.

The influence of Aloe vera (L.) Burman f. on the glycosaminoglycan (GAG) components of the matrix in a healing wound was studied. Wound healing is a dynamic and complex sequence of events of which the major one is the synthesis of extracellular matrix components. The early stage of wound healing is characterized by the laying down of a provisional matrix, which is then followed by the formation of granulation tissue and synthesis of collagen and elastin. The provisional matrix or the ground substance consists of GAGs and proteoglycans (PGs), which are protein GAG conjugates. In the present work, we have studied the influence of Aloe vera on the content of GAG and its types in the granulation tissue of healing wounds. We have also reported the levels of a few enzymes involved in matrix metabolism. The amount of ground substance synthesized was found to be higher in the treated wounds, and in particular, hyaluronic acid and dermatan sulphate levels were increased. The levels of the reported glycohydrolases were elevated on treatment with Aloe vera, indicating increased turnover of the matrix. Both topical and oral treatments with Aloe vera were found to have a positive influence on the synthesis of GAGs and thereby beneficially modulate wound healing.

## 25\_ Immunopharmacology 1996 Nov;35(2):11928

Activation of a mouse macrophage cell line by acemannan: the major carbohydrate fraction from Aloe vera gel.

Zhang L, Tizard IR.

Department of Veterinary Pathobiology, Texas A & M University College Station 77843, USA.

Acemannan is the name given to the major carbohydrate fraction obtained from the gel of the Aloe vera leaf. It has been claimed to have several important therapeutic properties including acceleration of wound healing, immune stimulation, anticancer and antiviral effects. However, the biological mechanisms of these activities are unclear. Because of this wide diversity of effects, it is believed that they may be exerted through pluripotent effector cells such as macrophages. The effects of acemannan on the mouse macrophage cell line, RAW 264.7 cells were therefore investigated. It was found that acemannan could stimulate macrophage cytokine production, nitric oxide release, surface molecule expression, and cell morphologic changes. The production of the cytokines IL6 and TNFalpha were 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 IFNgamma. These results suggest that acemannan may function, at least in part, through macrophage activation.

## 26\_ Comparative evaluation of aloe vera in the management of burn wounds in guinea pigs

RodriguezBigas M.; Cruz N.I.; Suarez A.

Division of Plastic Surgery, University of Puerto Rico School of Medicine, San Juan 00936 Puerto Rico

PLAST. RECONSTR. SURG. (USA) , 1988, 81/3 (386389)

An experimental study was designed using Hartley guinea pigs, who received fullthickness burns covering 3 percent of their body surface area by direct contact with a hot plate. A total of 40 animals were equally divided among four modalities of closed burn wound management as follows: group I: silver sulfadiazine (Silvadine); group II: aloe vera gel extract (Carrington Dermal Wound Gel); group III: salicylic acid cream (aspirin); and group IV: plain gauze occlusive dressing only. The dressings were changed daily, and the size and appearance of each burn wound were recorded until complete healing. On the sixth postburn day, quantitative burn wound cultures were made. The average time to complete healing in the control group was 50 days, and the only significant difference was found in the aloe veratreated animals, which healed on an average of 30 days ( $p < 0.02$ ). Wound bacterial counts were effectively decreased by silver sulfadiazine ( $p = 0.015$ ) and by aloe vera extract ( $p = 0.015$ ). From our data it appears that aloe gel extracts permit a faster healing of burn wounds.

## 27\_ Beneficial effects of Aloe in wound healing

Heggens J.P.; Pelley R.P.; Robson M.C.

Department of Surgery, University of Texas Medical Branch, Galveston, TX 77550 USA

PHYTOTHER. RES. (United Kingdom) , 1993, 7/SPEC. ISS. (S48S52)

The therapeutic effects of Aloe vera have been examined in preventing progressive dermal ischaemia caused by burns, frostbite, electrical injury, distal dying flap and intraarterial drug abuse. In vivo analysis of these injuries showed that the mediator of progressive tissue damage was thromboxane A<sub>2</sub> (TxA<sub>2</sub>). Experimentally Aloe was compared to a variety of antithromboxane agents to include U38450, a lodoxamide, a lazaroid and Carrington wound gel. In the burn injury Aloe was comparable to the lodoxamide and lazaroid with an 82% to 85% tissue survival when compared with the control and the Carrington wound gel ( $p = 0.05$ ). Tissue survival in the experimental frostbite injury was 28.2% when compared with the control ( $p = 0.05$ ). Similar results were obtained for the electrical injury, and intra arterial drug abuse. Clinically burn patients treated with Aloe healed without tissue loss as did those with frostbite ( $p = 0.001$ ). In the intraarterial drug abuse patients Aloe reversed the tissue necrosis. This therapeutic approach was used to prevent progressive tissue loss in each injury by actively inhibiting the localized production of TxA<sub>2</sub>. Aloe not only acts as a TxA<sub>2</sub> inhibitor but maintains a homeostasis within the vascular endothelium as well as the surrounding tissue.

## 28\_ Aloe vera

Klein A.D.; Penneys N.S.

Department of Dermatology, University of Miami School of Medicine, Miami, FL USA

J. AM. ACAD. DERMATOL. (USA) , 1988, 18/4 I (714720)

We review the scientific literature regarding the aloe vera plant and its products. Aloe vera is known to contain several pharmacologically active ingredients, including a carboxypeptidase that inactivates bradykinin in vitro, salicylates, and a substance (s) that inhibits thromboxane formation in vivo. Scientific studies exist that support an antibacterial and antifungal effect for substance(s) in aloe vera. Studies and case reports provide support for the use of aloe vera in the treatment of radiation ulcers and stasis ulcers in man and burn and frostbite injuries in animals. The evidence for a potential beneficial effect associated with the use of aloe vera is sufficient to warrant the design and implementation of well controlled clinical trials.

## 29\_ Studies of the effect of acemannan on retrovirus infections: clinical stabilization of feline leukemia virusinfected cats.

Sheets MA; Unger BA; Giggelman GF Jr; Tizard

IR Animal Medical and Surgical Hospital, Irving, TX.

Mol Biother (UNITED STATES) Mar 1991, 3 (1) p415

Feline leukemia is a disease induced by an oncornavirus infection that inevitably causes clinically affected cats to die. It has been estimated that 40% of cats are dead within 4 weeks and 70% within 8 weeks of the onset of clinical symptoms. Acemannan is a complex carbohydrate with both immunostimulatory and direct antiviral properties. Administration of acemannan for 6 weeks intraperitoneally to clinically symptomatic cats significantly improved both the quality of life and the survival rate. Twelve weeks after initiation of treatment, 71% of treated cats were alive and in good health.

### 30\_ Biological activity of Aloe vera

Davis R.H.; Leitner M.G.; Russo J.M.; Maro N.P.

Pennsylvania College of Podiatric Medicine, Department of Physiological Sciences, Philadelphia, PA 19107 USA  
MED. SCI. RES. (UK) , 1987, 15/5 (235)

In this study, the authors attempted to show the comparative biological activity of Aloe vera as measured by standard antiinflammatory tests. Wound healing was improved 24% in mice by a 100 mg/kg Aloe vera dose whereas 10 mg/kg improved healing 31% in rats. A slightly greater response of 44% was obtained on inhibiting mustard induced edema by 10 mg/kg Aloe vera. A marked inhibition of 58% PMN infiltration into an inflamed area by 2 mg/kg aloe was noted. No reduction of granuloma tissue formation around a cotton pellet under the skin was shown at doses up to 400 mg/kg. These data suggest that Aloe vera inhibits inflammation and improves wound healing. Aloe vera probably does not act like a steroid since it was most effective on acute inflammation and had no effect on granuloma tissue formation.

### 31\_ Pharmacological studies on a plant lectin Aloctin A. II. Inhibitory effect of Aloctin A on experimental models of inflammation in rats

Saito H.; Ishiguro T.; Imanishi K.; Suzuki I.

Lab. Ultrastruct. Res., Aichi Cancer Cent. Res. Inst., Nagoya 464 JAPAN  
JPN. J. PHARMACOL. (JAPAN) , 1982, 32/1 (139142)

A glycoprotein, Aloctin A, which was isolated from Aloe arborescens Mill, markedly inhibits adjuvant arthritis in rats and carrageenininduced edema in rats.

### 32\_ Induction of apoptosis in a macrophage cell line RAW 264.7 by acemannan, a beta(1,4) acetylated mannan

Ramamoorthy L.; Tizard I.R. L. Ramamoorthy,

Dept. of Veterinary Pathobiology, Texas A and M University, College Station, TX 77843 United States  
Molecular Pharmacology (United States) , 1998, 53/3 (415421)

Acemannan is a polydispersed beta(1,4)linked acetylated mannan with antiviral properties. It is an immunomodulator, and studies in our laboratory have shown that it causes activation of macrophages. In the presence of IFN $\gamma$ , acemannan induced apoptosis in RAW 264.7 cells. These cells exhibited chromatin condensation, DNA fragmentation, and laddering characteristic of apoptosis. The induction of apoptosis by acemannan and IFN $\gamma$  does not seem to be mediated by nitric oxide, since NnitroL arginine methyl ester, the nitric oxide inhibitor, had no effect. Acemannan in the presence of IFN $\gamma$  also inhibited the expression of bcl2. These results suggest that acemannan in the presence of IFN $\gamma$  induces apoptosis in RAW 264.7 cells through a mechanism involving the inhibition of bcl2 expression.

### 33\_ Optimizing therapy for inflammatory bowel disease

Robinson M. Dr. M.

Robinson, Oklahoma Found. for Digestive Res., Oklahoma City, OK United States  
American Journal of Gastroenterology (United States) , 1997, 92/12 SUPPL. (12S17S)

This review focuses on current developments in the major categories of therapy used in the management of inflammatory bowel disease (IBD). Conventional corticosteroids, although a mainstay of the acute treatment of IBD for many years, have many drawbacks, including a variety of side effects particularly with chronic use. Budesonide appears to be relatively safe and at least moderately effective in inducing remission in active distal ulcerative colitis (UC) and Crohn's disease. Aminosalicylates, both oral and topical, have proven useful in managing mild to moderate active UC and mild active Crohn's disease, as well as in maintaining remission. Data from recent trials suggest that higher doses of mesalamine are generally more efficacious than lower doses. In addition, a combination of oral and rectal formulations may succeed when one route, alone, is not successful. The immunomodulatory agents azathioprine, 6 mercaptopurine, and methotrexate have been shown to be effective in the treatment of IBD and are now widely accepted as valuable parts of the therapeutic armamentarium. Cyclosporine, although effective, is associated with many toxicities, and patients must be monitored closely in centers experienced with this agent. Clinical trials of IL10, IL11, and antiTNF $\alpha$  have also shown promise. Antibiotics have been used empirically for many years in the treatment of IBD. Larger clinical trials are warranted to explore the potential efficacy of antibiotic therapy. This has been accomplished with metronidazole in Crohn's disease, and other antibiotic trials are underway at this time. The investigational agents acemannan, heparin, and transdermal nicotine have also shown variable degrees of promise as possible therapies for IBD. Despite the variety of agents available for the treatment of IBD, none is ideal or universally accepted. Ongoing research into the well established

therapeutic agents, as well as novel drugs with more precise targets, may contribute to the design of a more nearly optimal regimen for IBD in the nottoo distant future.

#### 34\_ Purification and characterization of bioactivity compound acemannan from Aloe vera

So Young Lee; Il Whan Ryu; Chang Sub Shim S.Y. Lee, R and D  
Center, Kim Jeong Moon Aloe Co., LTD, Cheonan 330880 South Korea  
Korean Journal of Pharmacognosy (South Korea) , 1997, 28/2 (6571)

This study was carried out to purify and to characterize various bioactive material acemannan from Aloe vera. Purified acemannan was mannose (67%) and acetyl group (23%), and the rest of glucose was galactose that consists of long chain polydispersed beta(1,4) linked mannan polymers. The sugar and acetyl group in the molecule were linked by molar ratio of 3:1. This polysaccharide from Aloe vera may provide functional food and potential drug source with antiviral and immunomodulating properties.

#### 35\_ Upregulation of phagocytosis and candidicidal activity of macrophages exposed to the immunostimulant, acemannan

Stuart R.W.; Lefkowitz D.L.; Lincoln J.A.; Howard K.; Gelderman M.P.; Lefkowitz S.S.  
S.S. Lefkowitz, Department Biological Sciences, Texas Tech University, Lubbock, TX 79409 USA  
International Journal of Immunopharmacology (United Kingdom) , 1997, 19/2 (7582)

Previous studies by these investigators have shown that mannosylated bovine serum albumin (mBSA) enhances the respiratory burst (RE), phagocytosis, and killing of *Candida albicans* by resident murine peritoneal macrophages (Mphi). Upregulation of the above Mphi functions was associated with binding of mBSA to the Mphi mannose receptor. The present study was done to determine if the immunostimulant, acemannan prepared from aloe vera, could stimulate Mphi in a similar manner. Resident peritoneal Mphi collected from C57BL/6 mice were exposed to acemannan for 10 min. The RE was measured using chemiluminescence and demonstrated approximately a twofold increase above the media controls. In studies involving phagocytosis, Mphi were exposed to acemannan, washed and exposed to *Candida* at a ratio of 1:5. The percent phagocytosis and *Candida* killing were determined using fluorescence microscopy. There was a marked increase in phagocytosis in the treated cultures (45%) compared to controls (25%). Macrophages exposed to acemannan for 10 min resulted in ca 38% killing of *Candida albicans* compared with 05% killing in controls. If Mphi were incubated with acemannan for 60 min, 98% of the yeast were killed compared to 05% in the controls. The results of the present study indicate that short term exposure of Mphi to acemannan upregulates the RE, phagocytosis and candidicidal activity. Further studies are needed to clarify the potential use of this immunostimulant as an antifungal agent.

#### 36\_ Activation of a mouse macrophage cell line by acemannan: The major carbohydrate fraction from Aloe vera gel

Zhang L.; Tizard I.R.  
Dept. of Veterinary Pathobiology, Texas A and M University, College Station, TX 77843 USA  
Immunopharmacology (Netherlands) , 1996, 35/2 (119128)

Acemannan is the name given to the major carbohydrate fraction obtained from the gel of the Aloe vera leaf. It has been claimed to have several important therapeutic properties including acceleration of wound healing, immune stimulation, anticancer and antiviral effects. However, the biological mechanisms of these activities are unclear. Because of this wide diversity of effects, it is believed that they may be exerted through pluripotent effector cells such as macrophages. The effects of acemannan on the mouse macrophage cell line, RAW 264.7 cells were therefore investigated. It was found that acemannan could stimulate macrophage cytokine production, nitric oxide release, surface molecule expression, and cell morphologic changes. The production of the cytokines IL6 and TNFalpha were 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 IFNgamma. These results suggest that acemannan may function, at least in part, through macrophage activation.

#### 37\_ Acemannan, a beta(1,4)acetylated mannan, induces nitric oxide production in macrophage cell line RAW 264.7

Ramamoorthy L.; Kemp M.C.; Tizard I.R.  
Dept. of Veterinary Pathobiology, Texas A and M University, College Station, TX 77843 USA  
Molecular Pharmacology (USA) , 1996, 50/4 (878884)

Acemannan is a polydispersed beta(1,4)linked acetylated mannan with antiviral properties. It is an immunomodulator, and studies in our laboratory have shown that it causes activation of macrophages. Inducible NO synthase is generally expressed after transcriptional induction and is known to mediate some of the cytotoxic action of activated macrophages. Acemannan, in the presence of interferongamma, greatly increased the synthesis of NO in RAW 264.7 cells. This increase was preceded by increased expression of mRNA for the inducible form of macrophage NO synthase. Preincubation with pyrrolidine dithiocarbamate inhibited the induction, indicating the involvement of nuclear factor kappaB. These results suggest that acemannan causes the activation of macrophages by increasing the level of NO synthase at the level of transcription.

#### 38\_ The effect of Acemannan Immunostimulant in combination with surgery and radiation therapy on spontaneous canine and feline fibrosarcomas

King G.K.; Yates K.M.; Greenlee P.G.; Pierce K.R.; Ford C.R.; McAnalley B.H.; Tizard I.R.  
Carrington Laboratories, Inc., 1300 E. Rochelle Boulevard, Irving, TX 75235 USA  
Journal of the American Animal Hospital Association (USA) , 1995, 31/5 (439447)

Eight dogs and five cats with histopathologically confirmed fibrosarcomas were treated with Acemannan Immunostimulant in combination with surgery and radiation therapy. These animals had recurring disease that had failed previous treatment, a poor prognosis for survival, or both. Following four to seven weekly acemannan treatments, tumor shrinkage occurred in four (greater than 50%; n = 2) of 12 animals, with tumors accessible to measurement. A notable increase in necrosis and inflammation was observed. Complete surgical excision was performed on all animals between the fourth and seventh week following initiation of acemannan therapy. Radiation therapy was instituted immediately after surgery. Acemannan treatments were continued monthly for one year. Seven of the 13 animals remain alive and tumorfree (range 440+ to 603+ days) with a median survival time of 372 days. The data suggests that Acemannan Immunostimulant may be an effective adjunct to surgery and radiation therapy in the treatment of canine and feline fibrosarcomas.

#### 39\_ Acemannan containing wound dressing gel reduces radiation induced skin reactions in C3H mice

Roberts D.B.; Travis E.L. Texas Univ. M. D. Anderson  
Can. Ctr., Box 66, 1515 Holcombe Blvd., Houston, TX 770304095 USA  
International Journal of Radiation Oncology Biology Physics (USA) , 1995 , 32/4 (10471052)

Purpose: To determine (a) whether a wound dressing gel that contains acemannan extracted from aloe leaves affects the severity of radiation induced acute skin reactions in C3H mice; (b) if so, whether other commercially available gels such as a personal lubricating jelly and a healing ointment have similar effects; and (c) when the wound dressing gel should be applied for maximum effect. Methods and Materials: Male C3H mice received graded single doses of gamma radiation ranging from 30 to 47.5 Gy to the right leg. In most experiments, the gel was applied daily beginning immediately after irradiation. To determine timing of application for best effect, gel was applied beginning on day 7, 0, or +7 relative to the day of irradiation (day 0) and continuing for 1, 2, 3, 4, or 5 weeks. The right inner thigh of each mouse was scored on a scale of 0 to 3.5 for severity of radiation reaction from the seventh to the 35th day after irradiation. Dose response curves were obtained by plotting the percentage of mice that reached or exceeded a given peak skin reaction as a function of dose. Curves were fitted by logit analysis and ED50 values, and 95% confidence limits were obtained. Results: The average peak skin reactions of the wound dressing gel treated mice were lower than those of the untreated mice at all radiation doses tested. The ED50 values for skin reactions of 2.02.75 were approximately 7 Gy higher in the wound dressing geltreated mice. The average peak skin reactions and the ED50 values for mice treated with personal lubricating jelly or healing ointment were similar to irradiated control values. Reduction in the percentage of mice with skin reactions of 2.5 or more was greatest in the groups that received wound dressing gel for at least 2 weeks beginning immediately after irradiation. There was no effect if gel was applied only before irradiation or beginning 1 week after irradiation. Conclusion: Wound dressing gel, but not personal lubricating jelly or healing ointment, reduces acute radiationinduced skin reactions in C3H mice if applied daily for at least 2 weeks beginning immediately after irradiation.

#### 40\_ Nitric oxide production by chicken macrophages activated by Acemannan, a complex carbohydrate extracted from Aloe vera

Karaca K.; Sharma J.M.; Nordgren R.  
University of Minnesota, College of Veterinary Medicine, Department of Pathobiology, St Paul, MN 55108 USA  
International Journal of Immunopharmacology (United Kingdom) , 1995, 17/3 (183188)

Cultures of normal chicken spleen cells and HD11 line cells produce nitric oxide (NO) in response to Acemannan, a complex carbohydrate derived from the Aloe vera plant. Neither cell type produced detectable amounts of NO in response to similar concentrations of yeast mannan, another complex carbohydrate. Nitric oxide production was dose dependent and inhibitable by the nitric oxide synthase inhibitor N(G)methylLarginine. In addition, the production of NO was inhibited by preincubation of ACM with concanavalin A in a dosedependent manner. These results suggest that ACMinduced NO synthesis may be mediated through macrophage mannose receptors, and macrophage activation may be accountable for some of the immunomodulatory effects of ACM in chickens.

#### 41\_ A betalinked mannan inhibits adherence of Pseudomonas aeruginosa to human lung epithelial cells

Azghani A.O.; Williams I.; Holiday D.B.; Johnson A.R.  
Department of Biochemistry, Univ. of Texas Health Science Center, Tyler, TX 75710 USA  
Glycobiology (United Kingdom) , 1995, 5/1 (3944)

Adherence through carbohydratebinding adhesins is an early step in colonization of the lung by gram negative organisms, and because published data indicate that binding involves mannose groups, we tested the ability of a betalinked acetylmannan (acemannan) to inhibit adherence of Pseudomonas aeruginosa to cultures of human lung epithelial cells. Adherence of radiolabelled P.aeruginosa to A549 cells (a type II like pneumocyte line) increased linearly with the duration of the incubation. Acemannan inhibited adherence of bacteria, and the extent of inhibition was related to the concentration of the mannan. Inhibition required continued contact between acemannan and the target epithelial cells; cells washed free of acemannan no longer discouraged bacterial binding. Comparison of binding between seven different strains of P.aeruginosa indicated that fewer mucoid than nonmucoid bacteria adhered, but binding of either phenotype was inhibited by acemannan. Mannose, methyl

alphaDmannopyranoside, methyl betaD mannopyranoside and dextran did not affect adherence of any of the nonmucoic strains. Mannose inhibited adherence by one mucoic strain, but not the other, indicating differences between strains of the same phenotype. Since prior treatment of epithelial cells with concanavalin A did not affect acemannan induced inhibition of bacterial adherence, we concluded that the inhibitory effect of acemannan probably does not involve mannosecontaining receptors.

42\_ Complex carbohydrates in development as human pharmaceuticals  
Simon P.M.  
Neose Pharmaceuticals Inc., 102 Witmer Rd, Horsham, PA 19044 USA  
EXPERT OPIN. INVEST. DRUGS (United Kingdom) , 1994, 3/3 (223239)

There are many actual and potential pharmaceutical uses of complex carbohydrates. These include: direct uses as therapeutic pharmaceutical agents; indirect use as pharmaceutical excipients and carriers; use as diagnostic agents, whether for ex vivo testing or in vivo imaging; oligosaccharides as vaccines; and nutritional. In addition, complex carbohydrates may be employed in medical devices and other medical products. This overview will focus attention on antiadhesive oligosaccharides under investigation in the therapy of inflammatory and infectious diseases as well as cancer, glycan immune adjuvants, heparin derived agents for cardiovascular indications, cyclic oligosaccharides as amphiphilic carrier agents and immunogenic oligosaccharides as cancer vaccine components. In addition to reviewing pertinent preclinical research that points toward potential novel therapeutic agents, emphasis will be placed on compounds currently in clinical development. Chemical issues that affect the manufacture of therapeutic complex carbohydrates will also be considered.

43\_ Pilot study of the effect of acemannan in cats infected with feline immunodeficiency virus  
Yates K.M.; Rosenberg L.J.; Harris C.K.; Bronstad D.C.; King G.K.; Biehle G.A.; Walker B.; Ford C.R.; Hall J.E.; Tizard I.R.  
Carrington Laboratories, Irving, TX 75062 USA  
VET. IMMUNOL. IMMUNOPATHOL. (Netherlands) , 1992, 35/12 (177189)

Acemannan, a complex carbohydrate shown to stimulate interleukin1, tumor necrosis factor alpha and prostaglandin E2 production by macrophages, has also demonstrated antiviral activity in vitro against human immunodeficiency virus, Newcastle disease virus and influenza virus. A pilot study was undertaken to determine acemannan's effect in 49 feline immunodeficiency virus (FIV) infected cats with clinical signs of disease (Stage 3, 4 or 5), 23 of which had severe lymphopenia. Cats received acemannan either by intravenous (Group 1) or subcutaneous (Group 2) injection once weekly for 12 weeks, or by daily oral (Group 3) administration for 12 weeks. Upon entry into the study, cats were randomly assigned to one of the three groups. Laboratory analyses were performed at the beginning of the study and at Weeks 6 and 12. Cats were allowed to continue with a predetermined maintenance regimen of acemannan after completing the 12week study. Thirteen cats died during the course of treatment. Upon necropsy, the most frequent histopathologic findings were neoplastic, kidney and pancreatic disease. Friedman's twoway ANOVA test showed no significant differences in efficacy among groups administered acemannan by the different routes. Therefore, groups were combined and a signedranks test was used to determine changes over time. A significant increase was seen in lymphocyte counts ( $P < 0.001$ ). Neutrophil counts decreased significantly ( $P = 0.007$ ), as did incidence of sepsis ( $P = 0.008$ ). When cats entering with lymphopenia were analyzed separately, a much greater increase in lymphocyte counts was noted (235%) compared with nonlymphopenic cats (42%). A survival rate of 75% was found for all three groups. Thirtysix of 49 animals are alive 519 months postentry. These results suggest that acemannan therapy may be of significant benefit in FIVinfected cats exhibiting clinical signs of disease.

44\_ Antigen dependent adjuvant activity of a polydispersed beta(1,4)linked acetylated mannan (acemannan)  
Chinnah A.D.; Baig M.A.; Tizard I.R.; Kemp M.C.  
Department of Veterinary Pathology, College of Veterinary Medicine, Texas A and M University, College Station, TX 778434467  
USA  
VACCINE (United Kingdom) , 1992, 10/8 (551557)

The adjuvant properties of a polydispersed beta(1,4)linked acetylated mannan, acemannan (ACEM), were evaluated. Dayold broiler chicks were randomly selected and allocated to four flocks (Vac 14). The Vac 1 flock was sham vaccinated with saline. The Vac 2 flock was vaccinated with an oilbased vaccine (Breedervac III; Newcastle disease virus (NDV), infectious bursal disease virus (IBDV) and infectious bronchitis virus). The Vac 3 flock was vaccinated with a vaccineACEM mixture, and the Vac 4 flock was vaccinated with vaccine and ACEM at separate anatomical sites. ELISA titres to NDV and IBDV were determined. The immune response to NDV at 21 days postvaccination (PV) was significantly enhanced ( $P$  less than or equal to 0.05) by the addition of ACEM to the vaccine, compared with vaccination without ACEM. Subsequently, the vaccineACEM mixture appeared to suppress the immune response to NDV. However, at day 35 PV, 95% of the Vac 3 chicks compared with 90% of the Vac 2 and 89% of the Vac 4 chicks exhibited protective titres. The response to IBDV differed from that to NDV. At day 21 PV the immune response to IBDV was essentially the same for all flocks that received vaccine, i.e. addition of ACEM to the vaccine did not significantly enhance the immune response; however, it did significantly ( $P$  less than or equal to 0.05) sustain the immune response at days 28 and 35. In addition to the observed effect on titres to NDV and IBDV, ACEM also had an effect on flock immunity. ACEM administration at a separate site resulted in higher protective titres and a narrower titre group distribution. Overall, this study clearly showed that ACEM exhibits adjuvant properties and that the adjuvant effect is antigen dependent. It enhanced the immune response to both NDV and IBDV.

#### 45\_ The impact of acemannan on the generation and function of cytotoxic T lymphocytes

Womble D.; Helderman J.H.

Department of Internal Medicine, Division of Nephrology, Vanderbilt University, S3223 Medical Center North, Nashville, TN 37232372 USA

IMMUNOPHARMACOL. IMMUNOTOXICOL. (USA) , 1992, 14/12 (6377)

Acemannan, an antiviral agent with immune enhancement capabilities, was studied for its impact on cytotoxic T lymphocyte (Tc) function generated in response to alloantigen. To investigate whether acemannan directly stimulated the generation of Tc from primary mixed lymphocyte cultures (MLC), the drug was added at the initiation of the MLC. There was a dose-related, statistical increase in killer T cell generation produced by acemannan in the clinically relevant dose range. The lowest test dose of the drug ( $2.6 \times 10^9$  M) increased chromium release near twofold; the  $2.6 \times 10^8$  M dose gave a maximal 3.5 fold increase in cytotoxic T cells. To study whether acemannan enhanced the capacity of Tc once generated to alloantigen to destroy targets bearing the sensitizing antigens, MLR were established in the absence of any drug. Acemannan at the two highest doses increased the functional capacity of Tc to destroy target cells to which they had been sensitized in the MLR. To control for the possibility that acemannan was directly cytotoxic to target cells, targets were incubated alone with drug and without sensitized killer T cells. No dose of acemannan was found to be cytotoxic to these cells. In conclusion, acemannan did enhance the generation of cytotoxic T cells when added at the initiation of the MLR. When acemannan was added at the completion of allostimulation, an increase of almost 50% killing by Tc was also observed. These effects can not be explained by direct drug related toxicity and suggest a functional correlate to the previously described immune enhancing properties of the agent. As this drug is being tested for the treatment of HIV infections, these data provide at least one immunologic mechanism by which acemannan may be clinically salutary.

#### Enhancement of alloresponsiveness of human lymphocytes by acemannan (Carrisyn(TM))

Womble D.; Helderman J.H.

Renal Immunology Laboratory, The University of Texas Southwestern Medical Center at Dallas, Dallas, TX USA

INT. J. IMMUNOPHARM. (United Kingdom) , 1988, 10/8 (967974)

Healing powers have been imputed as being a feature of the gel from the aloe vera plant for centuries. The recent isolation of the active ingredient, acemannan, has made testing of this drug important. Since the drug appears to enhance monocyte function in other experiments, these studies were designed to test the capacity of acemannan to enhance immune response to alloantigen and to test whether the potential enhancement is a monocyte driven phenomenon. Acemannan did not enhance lymphocyte response to syngeneic antigens in the mixed lymphocyte culture (MLC) but importantly increased alloantigenic response in a dose-response fashion ( $2.6 \times 10^7$  to  $2.6 \times 10^9$  M). This effect of acemannan was shown to be a specific response and to concur with concentrations of in vitro acemannan achievable in vivo. A separate series of mixing experiments demonstrated that acemannan incubation with monocytes permitted monocyte driven signals to enhance T cell response to lectin. It is concluded that acemannan, the active ingredient of the aloe vera plant, is an important immunoenhancer in that it increases lymphocyte response to alloantigen. It is suggested that the mechanism involves enhancement of monocyte release of IL1 under the aegis of alloantigen. This mechanism may explain in part the recently observed capacity of acemannan to abrogate viral infections in animal and man.

#### 46\_ Prevention of atheromatous heart disease

Agarwal O.P.

482, Sahukara, Bareilly 243 001 UP INDIA

ANGIOLOGY (USA) , 1985, 36/8 (485492)

Five thousand patients of atheromatous heart disease, presented as angina pectoris, were studied over a period of five years. After adding the 'Husk of Isabgol' and 'aloe vera' (an indigenous plant known as gheeguarkapaththa) to the diet, a marked reduction in total serum cholesterol, serum triglycerides, fasting and post prandial blood sugar level in diabetic patients, total lipids and also increase in HDL were noted. Simultaneously the clinical profile of these patients showed reduction in the frequency of anginal attacks and gradually, the drugs, like verapamil, nifedipine, betablockers and nitrates, were tapered. The patients most benefited, were diabetics (without adding any antidiabetic drug). The exact mechanism of the action of the above two substances is not known, but it appears, that probably they act by their high fibre contents. Both these substances need further evaluation. The most interesting aspect of the study was that no untoward side effect was noted and all the five thousand patients are surviving till date.

#### 47\_ [Effects of aloe extracts, aloctin A, on gastric secretion and on experimental gastric lesions in rats]

Saito H; Imanishi K; Okabe S

Yakugaku Zasshi (JAPAN) May 1989, 109 (5) p3359

Effect of aloctin A, glycoprotein isolated from leaves of *Aloe arborescens* MILL, on gastric secretion and on acute gastric lesions in rats were examined. Aloctin A given intravenously dose dependently inhibited the volume of gastric juice, acid and pepsin output in pylorus ligated rats. Aloctin A given intravenously significantly inhibited the development of Shay ulcers and indomethacin induced gastric lesions in rats. It also inhibited water immersion stress lesions induced in pylorus ligated rats.

#### 48\_ Lectins modulate prostaglandin Esub 2 production by rat peritoneal macrophages

Ohuchi K.; Watanabe M.; Takahashi E.; et al.

Department of Biochemistry, Faculty of Pharmaceutical Sciences, Tohoku University, Aoba, Aramaki, Sendai 980 JAPAN  
AGENTS ACTIONS (SWITZERLAND) , 1984, 15/34 (419423)

The effect of Alectin A (Alo A), a lectin having antiinflammatory activities, on prostaglandin (PG) Esub 2 production by activated rat peritoneal macrophages was compared with that of concanavalin A (Con A), wheat germ agglutinin (WGA), pisum sativum agglutinin (PSA) and soybean agglutinin (SBA). Alo A, WGA, Con A and PSA at 10 mug per ml inhibited PG Esub 2 production. But SBA, even at a dose of 1 mug per ml, stimulated PG Esub 2 production. The inhibition by Alo A treatment of the release of radioactivity from (sup 3H)arachidonic acidlabeled macrophages and the stimulation of this release by SBA treatment were observed. The uptake of (sup 5sup 1Cr)labeled sheep red blood cells by the macrophage was inhibited by Alo A, Con A, and PSA, all at 10 mug per ml and SBA at 1 mug per ml, however, WGA at 10 mug per ml stimulated the uptake of the sheep red blood cells. The mechanism of the antiinflammatory properties of Alo A was discussed.

#### 49\_ Studies on optimal dose and administration schedule of a hematopoietic stimulatory beta(1,4) linked mannan

Egger S.F.; Brown G.S.; Kelsey L.S.; Yates K.M.; Rosenberg L.J.; Talmadge J.E.

Department of Pathology/Microbiology, University of Nebraska, Medical Center, South 42nd Street, Omaha, NE 68198 USA  
International Journal of Immunopharmacology (United Kingdom) , 1996, 18/2 (113126)

Several complex carbohydrates have been found to significantly stimulate hematopoiesis. CARN 750, a polydispersed beta(1,4) linked acetylated mannan isolated from the Aloe vera plant, has been shown to have activity in wound repair, to function as a antineoplastic, and to activate macrophages. We report, herein, the hematoaugmenting properties of CARN 750 and its optimal dose and timing of administration in an animal model of irradiationinduced myelosuppression. We observed that subcutaneous injections of 1 mg/animal of CARN 750 had equal or greater stimulatory activity for white blood cell (WBC) counts and spleen cellularity as well as on the absolute numbers of neutrophils, lymphocytes, monocytes and platelets than did higher or lower doses of CARN 750 or an optimal dose of granulocyte colony stimulating factor (GCSF). Hematopoietic progenitors; measured as interleukin3 supported colony forming unitsculture (CFUC) and high proliferative potential colonyforming cells (HPP CFC) assays, were similarly increased by CARN 750 in the spleen but not in the bone marrow. The frequency of splenic HPPCFCs and absolute number of splenic HPPCFCs and CFUCs were optimally increased by 1 mg/animal of CARN 750. In contrast, bone marrow cellularity, frequency and absolute number of HPPCFCs and CFUCs had as a dosage optimum 2 mg/animal of CARN 750. These parameters were similarly increased by GCSF. In studies to determine the optimal protocol for the administration of CARN 750 we found that the hematopoietic activity of CARN 750 increased with the frequency of administration. The greatest activity in myelosuppressed mice was observed for all hematopoietic parameters except the platelet number in mice receiving daily administration of 1 mg/animal of CARN 750 with activity equal to or greater than GCSF.

#### Influence of aloe vera on the healing of dermal wounds in diabetic rats

Chithra P.; Sajithlal G.B.; Chandrakasan G. G.

Chandrakasan, Department of Biochemistry, Central Leather Research Institute, Adyar, Chennai 600 020 India  
Journal of Ethnopharmacology (Ireland) , 1998, 59/3 (195201)

The positive influence of Aloe vera, a tropical cactus, on the healing of fullthickness wounds in diabetic rats is reported. Fullthickness excision/incision wounds were created on the back of rats, and treated either by topical application on the wound surface or by oral administration of the Aloe vera gel to the rat. Wound granulation tissues were removed on various days and the collagen, hexosamine, total protein and DNA contents were determined, in addition to the rates of wound contraction and period of epithelialization. Measurements of tensile strength were made on treated/untreated incision wounds. The results indicated that Aloe vera treatment of wounds in diabetic rats may enhance the process of wound healing by influencing phases such as inflammation, fibroplasia, collagen synthesis and maturation, and wound contraction. These effects may be due to the reported hypoglycemic effects of the aloe gel.

#### 50\_ Influence of Aloe vera on the glycosaminoglycans in the matrix of healing dermal wounds in rats

Chithra P.; Sajithlal G.B.; Chandrakasan G. G.

Chandrakasan, Department of Biochemistry, Central Leather Research Institute, Madras 600 020 India  
Journal of Ethnopharmacology (Ireland) , 1998, 59/3 (179186)

The influence of Aloe vera (L.) Burman f. on the glycosaminoglycan (GAG) components of the matrix in a healing wound was studied. Wound healing is a dynamic and complex sequence of events of which the major one is the synthesis of extracellular matrix components. The early stage of wound healing is characterized by the laying down of a provisional matrix, which is then followed by the formation of granulation tissue and synthesis of collagen and elastin. The provisional matrix or the ground substance consists of GAGs and proteoglycans (PGs), which are proteinGAG conjugates. In the present work, we have studied the influence of Aloe vera on the content of GAG and its types in the granulation tissue of healing wounds. We have also reported the levels of a few enzymes involved in matrix metabolism. The amount of ground substance synthesized was found to be higher in the treated wounds, and in particular, hyaluronic acid and dermatan sulphate levels were increased. The levels of the reported glycohydrolases were elevated on treatment with Aloe vera, indicating increased turnover of the matrix. Both topical and oral treatments with Aloe

vera were found to have a positive influence on the synthesis of GAGs and thereby beneficially modulate wound healing.

#### 51\_ Prevention of ultraviolet radiation induced suppression of accessory cell function of Langerhans cells by Aloe vera gel components

Chong Kil Lee; Seong Sun Han; Young Keun Mo; Ro Sa Kim; Myung Hee Chung; Young In Park; Seung Ki Lee; Yeong Shik Kim C.K. Lee,

College of Pharmacy, Chungbuk National University, Cheongju 360765 South Korea  
Immunopharmacology (Netherlands) , 1997, 37/23 (153162)

The active components of Aloe vera gel that can prevent ultraviolet B (UVB) induced suppression of accessory cell function of Langerhans cells (LC) were purified by activity guided sequential fractionation followed by in vitro functional assay. The functional assay was based on the fact that exposure of freshly isolated murine epidermal cells (EC) to UVB radiation resulted in impairment of accessory cell function of LC, as measured by their ability to support antiCD3 monoclonal antibody (mAb) primed T cell mitogenesis. This UVB suppressed LC accessory cell function was prevented by addition of partially purified Aloe gel components to cultures of UVB irradiated EC. The Aloe gel components appeared to prevent events occurring within the first 24 h after UVB irradiation that lead to the impairment of accessory cell function. The Aloe gel components did not cause proliferation of anti CD3 mAb primed T cells, nor did induce proliferation of normal EC. The activity guided final purification of Aloe gel components resulted in the isolation of two components. Both of the components were small molecular weight (MW) substances with an apparent MW of less than 1,000 Da but different from each other in net charge characteristics at pH 7.4. These results suggest that Aloe vera gel contains at least two small molecular weight immunomodulators that may prevent UVB induced immune suppression in the skin.

#### 52\_ Isolation and characterization of the glycoprotein fraction with a proliferation promoting activity on human and hamster cells in vitro from Aloe vera gel

Yagi A.; Egusa T.; Arase M.; Tanabe M.; Tsuji H.

Japan Planta Medica (Germany) , 1997, 63/1 (1821)

Fractions of leaf gel from Aloe barbadensis Mill. were prepared by gel permeation using DEAE Sephadex A25, Sepharose 6B, and Sephadex G50 columns. These were then tested by in vitro assays for proliferation of human normal dermal and baby hamster kidney cells. The glycoprotein fraction promoted cell growth, while the neutral polysaccharide fraction did not show any growth stimulation. Moreover, the polar colored glycoprotein fraction strongly inhibited the in vitro assays. An active glycoprotein fraction (protein 82%, carbohydrate 11%) examined on polyacrylamide gel electrophoresis (PAGE) and SDS PAGE showed a single band. Its molecular weight was 29 kD on a Sephadex G50 column and its isoelectric point was pH 6.8. Immunoblotting after SDS PAGE showed that the glycoprotein was composed of two subunits (14 kD). Deglycosylation of glycoprotein (Pg212b fraction) by trifluoromethanesulphonic acid provided a protein band with a molecular weight of 13 kD on SDS PAGE. The colored glycoprotein fraction was shown on SDS PAGE to be a mixture with a molecular weight of 18 kD 15 kD. It was later hydrolyzed with 10% H<sub>2</sub>SO<sub>4</sub> to produce phenolic substances.

#### 53\_ The preventive and therapeutic potential of the squalene containing compound, Roindex, on tumor promotion and regression

Desai K.N.; Wei H.; Lamartiniere C.A.

Dept. Pharmacology and Toxicology, University of Alabama at Birmingham, University Station, Birmingham, AL 35294 USA  
Cancer Letters (Ireland) , 1996, 101/1 (9396)

Recent scientific evidence has shown free radicals or reactive oxygen species (ROS) to play an important role in the initiation and progression of cancer. Many radical scavengers have also been found to help reduce the attacks by these ROS. Interestingly, the ROS scavengers that have been investigated are naturally occurring compounds such as vitamins C and E. Roindex is a formulation of squalene, vitamin A, vitamin E, and aloe vera. It was our goal to investigate whether Roindex was able to prevent the development of chemically induced cancer and to cause regression of any tumors already formed in a mouse skin model. In the prevention study, skin tumors were initiated in 50 female CD1 mice with 7,12 dimethylbenz(a)anthracene (DMBA) and promoted with 12-O-tetradecanoylphorbol-13-acetate (TPA). The mice were treated with either mineral oil, 5% squalene, or Roindex. At the end of the prevention study, there was a 33.34% incidence of tumors (multiplicity of 1.40) in the mineral oil treatment group, 26.67% (multiplicity of 1.46) and 20.00% (multiplicity of 0.467) in the 5% squalene and Roindex groups, respectively. The tumor regression study involved the selection of mice with tumors and possible regression of these tumors with Roindex treatment. There was a regression of 33.34% of the tumors in the Roindex treated group (39 tumors to 26 tumors) compared to the nontreated group whose tumors regressed only 3.44% (29 tumors to 28 tumors).

#### 54\_ Wound healing effects of aloe gel and other topical antibacterial agents on rat skin

Heggers J.P.; Kucukcelebi A.; Stabenau C.J.; Ko F.; Broemeling L.D.; Robson M.C.

Dept Surg Plastic/Microbiol/Immunol., Univ. Texas Medical Branch/Shriners, Burns Institute, Galveston, TX 77550 USA  
Phytotherapy Research (United Kingdom) , 1995, 9/6 (455457)

The effects of topical antibacterials were studied in an acute wound healing model. Sprague-Dawley rats after appropriate anaesthesia received four 1.5 cm<sup>2</sup> dorsal defects through the skin and panniculus carnosus. Skin defects were treated for 14 days

with 2% mupirocin ointment, 1% clindamycin cream, 1% silver sulfadiazine cream+Aloe vera gel, and silver sulfadiazine combined with Aloe gel. An untreated group served as controls. Each group was comprised of 10 animals each to achieve statistical significance. Wound closure rate was assessed by serial planimetry. Following healing, the breaking strength of each resultant scar was determined. Wound half-lives and overall healing rates were calculated by regressing the log of the areas of all wounds over time. Overall healing rates of all the treated groups were significantly different compared with control group ( $p < 0.05$ ). The Aloe group had the shortest half-life and healed faster than the control group. All the other treated groups had no longer half-lives when compared with the control group. While silver sulfadiazine+Aloe increased the breaking strength of the healed wound, Aloe alone did not, but demonstrated an increase over the control. Topical Aloe significantly enhances the rate of wound healing and when combined with silver sulfadiazine reverses the wound retardant effect observed with silver sulfadiazine. Clindamycin and mupirocin significantly delay wound closure. However mupirocin enhanced the breaking strength of the wound.

#### 55\_ Antiinflammatory and wound healing properties of Aloe vera

Udupa S.L.; Udupa A.L.; Kulkarni D.R.

Department of Biochemistry, Kasturba Medical College, 576119 Manipal, Karnataka India

FITOTERAPIA (Italy) , 1994, 65/2 (141145)

The fresh juice of the indigenous drug *A. vera* (0.2 ml/100 g, i.p.) was studied for its antiinflammatory and wound healing properties in rats. Antiinflammatory action was studied by observing percent reduction in carrageenin-induced paw oedema at 3 h. Wound healing effects were studied on incision (skin breaking strength), excision (percent wound contraction and epithelisation time) and dead space (granuloma breaking strength and biochemical parameters) wound models. *A. vera* showed significant anti-inflammatory activity in acute inflammatory model without any significant effect on chronic inflammation. Significant increase in breaking strength (skin and granuloma tissue), enhanced wound contraction and decreased epithelisation period were observed. An increase in lysyl oxidase activity and mucopolysaccharide content were also seen. This drug could therefore increase tensile strength by increasing crosslinking in collagen and interactions with the ground substance.

#### 56\_ Potential reversal of chronological and photoaging of the skin by topical application of natural substances

Danhof I.E.

North Texas Research Laboratory, 222 SW 2nd St., Grand Prairie, TX 75051 USA

PHYTOTHER. RES. (United Kingdom) , 1993, 7/SPEC. ISS. (S53S56)

Aging changes in the skin, in which degenerative changes exceed regenerative changes, are characterized by thinning and wrinkling of the epidermis together with the appearance of lines, creases, crevices and furrows, especially accentuated in lines of facial expression. These changes are brought about both by chronological (genetically determined) and photo (solar radiation-determined) factors. The reason for the readily apparent surface morphological alterations is found in changes in the underlying dermis characterized by the loss of fascicular and soluble collagen and elastin fibres, with lessened support of epidermal layers, and lessened circulatory perfusion. Many so-called 'antiaging' actions of topically applied materials are nothing more than transient hydrational/moisturizing effects, which, while lessening the prominence of undesirable surface defects and blemishes, do nothing to change the dermal losses. True 'antiaging' actions would require evidence for the return toward normal of the regenerative/degenerative balance exemplified by increased collagen and elastin synthesis. Evidence is accruing that four groups of topically applied substances, namely, (a) nonsaponifiable fractions of avocado and soybean oils, (b) vitamin A derivatives, (c) alphahydroxy acids (AHAs), and (d) extracts of *Aloe vera*, possess activities which reverse the degenerative skin changes seen with aging by stimulating the synthesis of collagen and elastin fibres, thereby restoring toward normal the regenerative/degenerative equilibrium.

#### 57\_ The stimulation of postdermabrasion wound healing with stabilized aloe vera gel/polyethylene oxide dressing

Fulton J.E. Jr.

The Acne Research Institute, 1587 Monrovia Street, Newport Beach, CA 92663 USA

J. DERMATOL. SURG. ONCOL. (USA) , 1990, 16/5 (460467)

Fullface dermabrasion provided an ideal opportunity to document the effects of dressings on wound healing management. Following the procedure, the abraded face was divided in half. One side was treated with the standard polyethylene oxide gel wound dressings. The other side was treated with a polyethylene oxide gel dressing saturated with stabilized aloe vera. The polyethylene oxide dressing provided an excellent matrix for the release of aloe vera gel during the initial 5 days of wound healing. By 2448 hours there was dramatic vasoconstriction and accompanying reduction in edema on the aloe-treated side. By the third to fourth day there was less exudate and crusting at the aloe site, and by the fifth to sixth day the reepithelialization at the aloe site was complete. Overall, wound healing was approximately 72 hours faster at the aloe site. This acceleration in wound healing is important to reduce bacterial contamination, subsequent keloid formation, and/or pigmentary changes. The exact mechanism of acceleration of wound healing by aloe vera is unknown.

#### Partial purification and some properties of an antibacterial compound from Aloe vera

Levin H.; Hazenfratz R.; Friedman J.; Palevitch D.; Perl M.

Agricultural Research Organization, The Volcani Center, Bet Dagan 50 250 Israel

PHYTOTHER. RES. (United Kingdom) , 1988, 2/2 (6769)

Aqueous or ethanolic extracts of Aloe leaves were examined for antibacterial properties. The crude extracts strongly stimulated bacterial growth. Separation of various fractions by thin layer chromatography (TLC) resulted in a fraction which inhibited the growth of *Bacillus subtilis*. A concomitant examination of protein and nucleic acid synthesis in *B. subtilis* in the presence of the inhibitory compound indicated that the plant extract inhibits primarily nucleic acid synthesis, after which protein synthesis is also inhibited. The inhibitor seemed to be present in all examined Aloe species but at different concentrations. On a dry weight basis, the inhibitory effect was equally distributed between the skin and the gel fraction.

58\_ Cutaneous tissue repair: Practical implications of current knowledge.

II Reed B.R.; Clark R.A.F.

Department of Dermatology, University of Colorado Health Sciences Center, Denver, CO 80262 USA

J. AM. ACAD. DERMATOL. (USA) , 1985, 13/6 (919941)

This article reviews the scientific basis for the certain factors that delay wound repair in the clinical setting. A brief history of wound healing is given, followed by a discussion of endogenous local factors (bacterial infection, hypoxia, foreign body, and desiccation) and endogenous systemic factors (nutritional deficiencies, aging, coagulation disorders, and the EhlersDanlos syndromes) associated with poor wound repair. Also reviewed are the mechanisms by which exogenously administered agents (glucocorticoids, antineoplastic agents, and anticoagulants) may delay healing. Commonly used topical antimicrobials, their spectrum of activity, and evidence of effects on wound healing are examined. Finally, properties of commercially available wound coverings and wound care in the future are discussed.

59\_ Pathophysiology of inadvertent intraarterial drug injection injuries

Smith D.J. Jr.; Zachary L.S.; Hegggers J.P.; Robson M.C.

Division of Plastic and Reconstructive Surgery, Department of Surgery, Wayne State University School of Medicine, Detroit, MI 48201 USA

SURG. FORUM (USA) , 1985, VOL. 36 (578580)

Inadvertent injection of drugs intraarterially produces a welldefined clinical syndrome whose pathophysiology remains unclear. Distal necrosis, endarteritis, and an intense inflammatory reaction of surrounding tissues results in a progressive ischemic injury with eventual tissue loss. Although vasospasm and particulate embolization of end arteries are the two most commonly accepted theories, neither adequately explains the intense inflammatory reaction and swelling in the adjacent tissue. Numerous methods of treatment have been advocated based on these theories, and none have proven effective. The progressive nature of this injury is similar to the progressive injury seen in the burn wound, frostbite, and the distal dying flap. Thromboxane, a vasoconstrictor and platelet aggregator, has been found to be a central mediator in these injuries. Blockade of thromboxane production with specific or nonspecific antithromboxane agents had led to improved tissue survival in experimental and clinical studies. This study was designed to determine the role of thromboxane in intraarterial drug injections and to determine if blockade of thromboxane with specific or nonspecific blocking agents would result in increased tissue survival.

60\_ Thromboxane inhibitors for the prevention of progressive dermal ischemia due to the thermal injury

Hegggers J.P.; Robson M.C.; Zachary L.S.

Wayne State University School of Medicine, Detroit, MI USA

J. BURN CARE REHABIL. (USA) , 1985, 6/6 (466468)

Progressive dermal ischemia resulting from a burn injury can be prevented by topical application of antithromboxane compounds. Using the Zawacki burn model, two experimental thromboxane synthetase inhibitors, UK 38485 and U63557A, were each mixed in a pharmaceutical cream base and compared with a known phospholipase inhibitor, methylprednisolone acetate, and two known thromboxane synthetase inhibitors, imidazole and an Aloe vera preparation. Control animals received no treatment. Comparative biopsies were examined by the peroxidaseantiperoxidase procedure for the presence or absence of thromboxane. UK 38485 and U63557A as topical therapeutic creams inhibited thromboxane production in the burn and were equal to or better than the two known antithromboxane inhibitors. Longitudinal studies showed that both UK 38485 and U63557A reversed progressive dermal ischemia and that healing occurred within three weeks postburn, comparable to burns treated with imidazole and A. vera.

61\_ Frostbite injuries: A rational approach based on the pathophysiology

McCaughey R.L.; Hing D.N.; Robson M.C.; Hegggers J.P.

Sect. Plast. Reconstr. Surg., Univ. Chicago, Chicago, IL 60637 USA

J. TRAUMA (USA) , 1983, 23/2 (143147)

The breakdown products of arachidonic acid have been implicated as mediators of progressive dermal ischemia in both cold and thermal injuries. Increased tissue survival can be demonstrated experimentally with the preservation of the dermal microcirculation by using antiprostaglandin agents and thromboxane inhibitors. Thirtyeight consecutive patients (28 males and 10 females aged 2 mo to 46 yr) with frostbite injuries were treated at the University of Chicago's Burn Center in January 1982 with a protocol designed to decrease the production of thromboxane locally and prostaglandins systemically. All patients recovered without significant tissue

loss. The average hospital stay was 5.6 days for acute injuries and 6.9 days for subacute injuries.

62\_ Aloe vera (gel) cream as a topical treatment for outpatient burns

Heck E.; Head M.; Nowak D.; et al.

Dept. Surg., Univ. Texas Hlth Sci. Cent., Dallas, Tex. USA

BURNS (ENGLAND) , 1981, 7/4 (291294)

The objectives in the use of topical agents in burn therapy are bacterial control and relief of pain. In this study a commonly discussed 'home remedy' now commercially available is compared with a widely used prescription agent in the control of bacterial flora in outpatient burn wounds. Additionally, the study examines healing times in the two groups for any demonstrated effect.

63\_ Hematopoietic augmentation by a beta(1,4)linked mannan

Egger S.F.; Brown G.S.; Kelsey L.S.; Yates K.M.; Rosenberg L.J.; Talmadge J.E.

USA Cancer Immunology Immunotherapy (Germany) , 1996, 43/4 (195205)

CARN 750 (injectable acemannan) is a polydispersed beta(1,4)linked acetylated mannan isolated from the Aloe barbadensis plant. It has multiple therapeutic properties including activity in wound repair and as a biological agent for the treatment of neoplasia in animals as well as the ability to activate macrophages. We report herein that CARN 750 directly or indirectly has significant hematoaugmenting properties. We observed that the subcutaneous administration of CARN 750 significantly increases splenic and peripheral blood cellularity, as well as hematopoietic progenitors in the spleen and bone marrow as determined by the interleukin3responsive colonyforming unit culture assay and the highproliferativepotential colonyformingcell (HPPCFC) assay (a measure of primitive hematopoietic precursors) in myelosuppressed (7 Gy) C57BL/6 mice. The greatest hematopoietic effect was observed following sublethal irradiation in mice receiving 1 mg CARN 750/animal, with less activity observed at higher or lower doses. Further, CARN 750, following daily injection, has activity equal to or greater than the injection of an optimal dose of granulocytecolonystimulating factor (GCSF) in myelosuppressed mice. In this comparison, significantly greater activity was observed in the splenic and peripheral blood cellularity, and in the frequency and absolute number of splenic HPPCFC as compared to the mice receiving GCSF at 3 microg/animal. CARN 750, when administered to myelosuppressed animals, decreased the frequency of lymphocytes with a concomitant significant increase in the frequency of polymorphonuclear leukocytes (PMN). However, owing to the increased cellularity, a significant increase in the absolute number of PMN, lymphocytes, monocytes and platelets was observed, suggesting activity on multiple cell lineages. The latter is the primary difference in activity as compared to GCSF which has activity predominantly on PMN.

64\_ Arch Inst Pasteur Madagascar 1982;50(1):22756

[Immunomodulating properties of an extract isolated and partially purified from Aloe vahombe. 3.Study of antitumoral properties and contribution to the chemical nature and active principle]. [Article in French]

Ralamboranto L, Rakotovao LH, Le Deaut JY, Chaussoux D, Salomon JC, Fournet B, Montreuil J, RakotonirinaRandriambeloma PJ, Dulat C, Coulanges P.

An immunomodulator fraction (Alva) extracted from an endemic plant, in the south of Madagascar, the Aloe vahombe, significantly protects mice against bacterial, parasitic and fungal infections. Wishing to verify whether the fraction Alva was active in tumour reduction, we studied its effect on the development of experimental fibrosarcoma and melanoma in mice by intravenous and intracutaneous injections and injections directly into the tumour of the immunostimulant fraction. We have observed cures, only in the case of the McC31 tumour but it is encouraging to note that under different experimental conditions the rate of growth of tumours in animals which were treated is slower than in those not treated. The Alva fraction is a substance which is hydrosoluble, thermostabile, having a molecular weight exceeding 30 000 and is a polysaccharide. The predominant sugars are glucose and mannose in 3:1 ratio. Preliminary studies of its action seem to indicate that the Alva fraction acts upon nonspecific response and could possibly stimulate the phagocyte activity of the peritoneal macrophagus.

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Aloe vera fact or quackery

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Intermountain Reg. Poison Control Cent., Dept. Pharm. Pract., Univ. Utah Coll. Pharm., Salt Lake City, Ut. 84132 USA

VET. HUM. TOXICOL. (USA) , 1980, 22/6 (418424)

The therapeutic efficacy of Aloe vera cream (Dermaide Aloe(Reg.trademark)) in thermal injuries: Two case reports

Cera L.M.; Heggars J.P.; Robson M.C.; Hagstrom W.J.

Univ. Chicago Hosp. Clin., Chicago, Ill. 60637 USA

J. AM. ANIM. HOSP. ASSOC. (USA) , 1980, 16/5 (768772)

Aloe extract slows CD4 decrease

AIDS PATIENT CARE (USA) , 1993, 7/3 (176)

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Drug inhibits KS

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Parmar N.S.; Tariq M.; AlYahya M.A.; et al.

Research Centre, College of Pharmacy, King Saud University, Riyadh11451 SAUDI ARABIA

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Use of immunomodulators as an aid to clinical management of feline leukemia virus infected cats.

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Department of Veterinary Pathobiology, College of Veterinary Medicine, Texas A&M University, College Station 77843.

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Aloe vera does not affect cutaneous erythema and blood flow following ultraviolet B exposure

Crowell J.; Hilsenbeck S.; Penneys N.

Box 016940, Miami, FL 33101 USA

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An anticomplementary polysaccharide with immunological adjuvant activity from the leaf parenchyma gel of Aloe vera

'T Hart L.A.; Van den Berg A.J.J.; Kuis L.; Van Dijk H.; Labadie R.P.

Department of Pharmacognosy, Faculty of Pharmacy of the State University of Utrecht, Catharijnesingel 60, 3511 GH Utrecht Netherlands

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Determination of the position of the Oacetyl group in a beta(1 right arrow 4)mannan (acemannan) from Aloe barbardensis Miller

Manna S.; McAnalley B.H.

C. Pepper Inst. Aging/Therap. Res., Florida Institute of Technology, 150 West University Boulevard, Melbourne, FL 329016988 USA

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Fogleman R.W.; Chapdelaine J.M.; Carpenter R.H.; McAnalley B.H.

Upper Black Eddy, PA 18972 USA

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Aloe vera, fiction or fact

Natow A.J.

New York University Medical Center, Skin and Cancer Unit, New York, NY USA

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Heggens J.P.; Robson M.C.

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New York University Medical Center, Skin and Cancer Unit, New York, NY USA

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Leung A.

35 Cumberland Rd., Glen Rock, NJ 07452 USA

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