

Clinical abstracts

Immunological benefits

An Anti-Complementary Polysaccharide With Immunological Adjuvant Activity From The Leaf Parenchyma Gel Of Aloe Vera

t' Hart LA; van den Berg AJ; Kuis L; van Dijk H; Labadie RP

Planta Med 55(6):509-12 1989 Dec

The aim of the study is to develop new substances with immunomodulatory activity. To this end, extracts from plants used in traditional medicine are used as starting material. This study deals with the mucilagenous leaf-gel of Aloe vera which is well reputed for its therapeutical effect on inflammatory-based disorders. The purification of an aqueous gel-extract guided by inhibition of complement activity in HPS is described. Using anion-exchange and gel permeation chromatography a highly active polysaccharide fraction was isolated, that is present in the gel in various chain lengths. The polysaccharides consist of several monosaccharides of which mannose is dominant. The inhibition is based on alternative pathway activation, resulting in consumption of C3. With respect to their biological activity the polysaccharides inhibit the opsonization of zymosan in HPS and display adjuvant activity on specific antibody production and the induction of delayed type hypersensitivity in mice.

Mechanisms Of Ultraviolet Induced Immune Suppression

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RPROJ/CRISP Epicutaneous exposure to ultraviolet (UV) radiation suppresses T cell-mediated immune responses to antigens encountered in the skin and permits the growth of highly immunogenic skin cancers in laboratory animals. Immune suppression by UV radiation is mediated by multiple, complex, and interacting mechanisms. Recent studies indicate the suppression is triggered by DNA damage followed by production of immunosuppressive cytokines, loss of antigen presenting cells (APC) from the skin, alteration of the functions of remaining APC, and induction of antigen-specific suppressor T cells. However, the regulation and interaction of these APC, and induction of antigen-specific suppressor T cells. However, the regulation and interaction of these APC and cytokine pathways are unclear and appears to be different for contact hypersensitivity (CHS) reactions to allergens in skin and delayed type hypersensitivity (DTH) reactions to micro-organisms. We have recently shown that crude extracts of Aloe barbadensis gel protects CHS and DTH responses against suppression by UV

radiation. Because Aloe extract provides broad protection for immune responses that are abrogated by UV by different mechanisms, it may act as a central controlling point in suppression. Alternatively Aloe may contain several agents that act on CHS and DTH separately. Furthermore, Aloe is chemically distinct from antibodies, cytokines, or other agents that have been used to probe suppression pathway induced by UV radiation, and it may be acting by a novel mechanism(s). We will test these hypotheses by exposing mice to UV radiation and examining the effect of Aloe treatment on the production of the regulatory cytokines TNF-alpha, IL-10, and IL-12 in cultured keratinocyte cell lines and in skin. We will investigate whether protection of CHS and DTH responses is mediated separately by different components in Aloe. We will also examine the effect of Aloe on the function of APC from the draining lymph nodes using the murine model of CHS response to the hapten fluorescein isothiocyanate, and the DTH response to *Candida albicans*. In addition, we propose to investigate the ability of Aloe to preserve immunity to UV-induced skin cancers. Clarification of the relationship of the CHS and DTH models to cutaneous tumor immunity may permit the design of therapeutic agents that are more effective in protecting humans against the development of skin cancer.

Aloctin A, An Active Substance Of Aloe Arborescens Miller As An Immunomodulator

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Phytotherapy Research (1993) Vol 7, No. Special issue, pp. S20-S22. 15 ref.

Aloctin A (Alo A), an active substance isolated from the leaves of *A. arborescens*, has many biological and pharmacological activities, such as mitogenic activity for lymphocytes, binding of human alpha 2-macroglobulin, complement activation via the alternative pathway, anti-inflammatory activity, anti-ulcer activity and antineoplastic activity. Alo A exhibited immunomodulatory activities on the immune responses of murine and human lymphoid cells *in vivo* and *in vitro*.

Immunomodulating Properties Of An Extract Isolated & Partially Purified From Aloe Vahombe Study Of Antitumoral Properties & Contribution To The Chemical Nature & Active Principle

Ralamboranto L; Rakotovao LH; Le Deaut JY; Chaussoux D; Salomon JC; Fournet B; Montreuil J; Rakotonirina-Randriambeloma PJ; Dulat C; Coulanges P
Arch Inst Pasteur Madagascar 50(1):227-56 1982

An immuno-modulator 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 tumor of the immunostimulant fraction. We have observed cures, only in the case of the McC3-1 tumor but it is encouraging to note that under different experimental conditions the rate of growth of tumors 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.

Two Functionally & Chemically Distinct Immunomodulatory Compounds In The Gel Of Aloe

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J Ethnopharmacol May-Jun 1988, 23 (1) p61-71

An aqueous extract of Aloe vera gel was analyzed guided by modulatory activity with regard to the in vitro activation of human complement and of human polymorphnuclear leucocytes (PMN). Upon ultrafiltration a high (h-Mr) and a low (l-Mr) molecular mass fraction were obtained. Pre-incubation of human pooled serum with the h-Mr fraction resulted in a depletion of classical and alternative pathway complement activity. In contrast, only the l-Mr fraction could inhibit the production of free oxygen rad-icals by activated PMNs. The latter activity cannot be attributed to non-specific effects like toxicity, interference with stimulant binding or scavenger activity.

Studies On Optimal Dose & Administration Schedule Of A Hematopoietic Stimulatory Beta-(1,4)-Linked Mannan

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Int J Immunopharmacol 18(2):113-26 1996 Feb

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 irradiation-induced 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 (G-CSF). Hematopoietic progenitors, measured as interleukin-3-supported colony forming units-culture (CFU-C) and high proliferative potential colony-forming cells (HPP-CFC) assays, were similarly increased by CARN 750 in the spleen but not in the bone marrow. The frequency of splenic HPP-CFCs and absolute number of splenic HPP-CFCs and CFU-Cs were optimally increased by 1 mg/animal of CARN 750. In contrast, bone marrow cellularity, frequency and absolute number of HPP-CFCs and CFU-Cs had as a dosage optimum 2 mg/animal of CARN 750. These parameters were similarly increased by G-CSF. 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 G-CSF.

**Purification & Characterization Of Two Lectins From Aloe Arborescens Mill.
Suzuki I; Saito H; Inoue S; Migita S; Takahashi T**

J Biochem (Tokyo) 85(1):163-71 1979 Jan

Two lectins have been isolated from leaves of *Aloe arborescens* Mill by salt precipitation, pH-dependent fractionation and gel filtration. One lectin (P-2) has a molecular weight of approximately 18,000, consists of two subunits (alphabeta) and contains more than 18% by weight of neutral carbohydrate. The smaller subunit (alpha) has a molecular weight of approximately 7,500 and the larger subunit (beta) a molecular weight of approximately 10,500. The other lectin (S-1) has a molecular weight of approximately 24,000, consists of two subunits (gamma2) with a molecular weight of approximately 12,000 and contains more than 50% by weight of neutral carbohydrate. An interesting feature of the amino acid compositions of these lectins is the high proportion of acidic amino acids, such as aspartic acid and glutamic acid, and the low proportion of methionine and histidine. S-1 has a strong hemagglutinating activity. On the other hand, P-2 has not only hemagglutinating activity but also mitogenic activity on lymphocytes, precipitate-forming reactivity with serum proteins, one of which is alpha2-macroglobulin, and complement C3 activating activity via the alternate pathway.

A 35 kDa Mannose-Binding Lectin With Hemagglutinating & Mitogenic Activities From "Kidachi Aloe" (*Aloe Arborescens* Miller Var. *Natalensis* Berger)

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J Biochem (Tokyo) 118(6):1205-10 1995 Dec

A novel lectin was isolated from the leaf skin of "Kidachi Aloe" (*Aloe arborescens* Miller var. *natalensis* Berger) by sequential chromatographies on Sephadex G-25 gel filtration, DEAE ion exchange, and Superdex 75 gel filtration columns. The native lectin exhibited a molecular mass of about 35 kDa on both gel filtration on a Superdex 75 column and native-PAGE under nonreducing conditions. SDS-PAGE in the presence or absence of beta-mercaptoethanol revealed two distinct peptides with molecular masses of about 5.5 and 2.3 kDa, respectively, in addition to a major 9.2 kDa subunit, indicating the presence of a partially processed subunit. The N-terminal amino acid sequence of the intact subunit showed homology with that of snowdrop lectin. The native lectin showed hemagglutinating activity toward rabbit but not human and sheep erythrocytes, and specifically bound to mannose like snowdrop lectin did, indicating that the Aloe and snowdrop lectins are structurally and functionally similar proteins. In addition, the native lectin showed strong mitogenic activity toward mouse lymphocytes.

Aloesin Up-Regulates Cyclin E/CDK2 Kinase Activity Via Inducing The Protein Levels Of Cyclin E, CDK2 & CDC25A In SK-HEP-1 Cells

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Biochem Mol Biol Int 41(2):285-92 1997 Feb

In the present study, we show that aloesin, which is a low molecular weight ingredients present in Aloe vera, stimulates the proliferation of cultured human hepatoma SK-HEP-1 cells. The incorporation of [3H] thymidine into DNA in the cell cultures was significantly increased at a dose of 10 microM aloesin. The aloesin-induced DNA synthesis appears to require newly synthesized proteins because cycloheximide treatment blocked the DNA synthesis evoked by this compound. We then examined whether this compound increases the intracellular levels of cell cycle regulators by immunoblotting. The data showed that aloesin increased the levels of cyclin E, CDK2, and CDC25A in SK-HEP-1 cells. In addition, immuno-complex kinase assays showed that aloesin up-regulated the enzyme activity of cyclin E/CDK2 kinase in a dose-dependent manner. Collectively, these results suggest that aloesin stimulates the proliferation of SK-HEP-1 cells by inducing the intracellular levels of cyclin E/CDK2 kinase complex and CDC25A, which, together, result in the up-regulation of cyclin E-dependent kinase activity.

Effect Of Chemotherapy Combined With The Use Of Tissue Preparations On Nonspecific Immunity In Patients With Pulmonary Tuberculosis

Nersesian ON; Bogatyreva EV

Probl Tuberk ISS 1, 1990, P28-31

General and local nonspecific immunity was studied in 143 new cases of pulmonary tuberculosis (71 and 72 persons, respectively). The results showed that combination of chemotherapy using desensitizing agents and tissue preparations according to V. P. Filatov (a suspension of placenta tissue and Aloe) had an immunomodulating effect. The efficacy of the combined chemotherapy amounted to 87 per cent with an account of the general immunity status.

Immunostimulant Properties Of An Extract Isolated & Partially Purified From Aloe Vahombe

Solar S; Zeller H; Rasolofonirina N; Coulanges P; Ralamboranto L;

Andriatsimahavandy AA; Rakotovao LH; Le Deaut JY

Arch Inst Pasteur Madagascar 47(1):9-39 1980

When the mice are given a hypodermic infection of unrefined Vahombe extract, the Aloe called Vahombe is a liliaceous plant growing in the South of Madagascar, they are protected against the infection caused by the Klebsiella, a pneumonia vector to man, giving rise to an experimental septicaemia in the mouse. Neither bactericide nor bacteriostatic activity has been detected yet about Aloe extract. The anti-infectious activity is proportional to the dose of extract injected, the protecting power is the greatest when the mice have been treated with Aloe, two or three days previously to the infection due to Klebsiella pneumoniae. We have

determined the LD50 (Lethal dose 50) for the check batches (non-treated mice) and for the batches of protected mice. We were able to show that the previous injection developed the resistance to infection, multiplied from thirtyfold to a hundredfold. We have tackled the purification of the substance—made soluble after lyophilisation of the crude extract—by means of filtration with Sephadex G50. It would be the first time, for all we know, that a substance endowed with organism. At present we are proceeding with the purification of the active principle and contemplating trying the protective power upon virus infections as well as upon cancerous or parasitic ones.

Immunostimulating Properties Of An Extract Isolated From Aloe Vahombe.

2. Protection In Mice By Fraction F1 Against Infections By Listeria Monocytogenes, Yersinia Pestis, Candida Albicans & Plasmodium Berghei **Brossat JY; Ledaut JY; Ralamboranto L; Rakotovao LH; Solar S; Gueguen A; Coulanges P**

Arch Inst Pasteur Madagascar 48(1):11-34 1981

A partially purified extract of leaves of Aloe vahombe, a plant endemic in the south of Madagascar, administered intravenously to mice, protects them against infection of bacteria (*Listeria monocytogenes*, *Yersinia pestis*), parasites (*Plasmodium berghei*) and fungus (*Candida albicans*). The protective fraction must be administered two days before inoculation of the pathogenic agent. These results significantly confirm those we obtained in earlier study on mice infection by *Klebsiella pneumoniae*. Currently we are testing the protective action of the purified extract on the experimental development of sarcomas, and we are in the process of analyzing the mode of action of this non specific immunostimulant.

Aloemannan, Significant Antitumor Efficacy

Winters, WD

Health Science Center, University Of Texas

In 1977 while conducting a series of animal experiments using aloemannan a mucopolysaccharide of *Aloe arborescens*, detected aloemannan a significant antitumor efficacy. Unlike usual anticancer drugs killing cancer cells directly, it acts as a stimulus for the body's defense mechanism, or immunity to suppress tumor. In other words, it prohibits multiplication of cancer cells while it is coexistent with them. Prof. Winters and his group of the Health Science Center at the University of Texas verified their test-tube experiments using human cervical cancer cells that Aloe vera extract prohibits the growth of cancer cells.

Plant Lectin, ATF1011, On The Tumor Cell Surface Augments Tumor-Specific Immunity Through Activation Of T Cells Specific For The Lectin

Yoshimoto R; Kondoh N; Isawa M; Hamuro J

Cancer Immunol Immunother 25(1):25-30 1987

The possibility that a plant lectin as a carrier protein would specifically activate T cells, resulting in the augmentation of anti-tumor immunity was investigated. ATF1011, a nonmitogenic lectin for T cells purified from *Aloe arborescens* Mill, bound equally to normal and tumor cells. ATF1011 binding on the MM102 tumor cell surfaces augmented anti-trinitrophenyl (TNP) antibody production of murine splenocytes when the mice were primarily immunized with TNP-conjugated MM102 tumor cells. The alloreactive cytotoxic T cell response was also augmented by allostimulator cells binding ATF1011 on the cell surfaces. These augmented responses may be assumed to be mediated by the activation of helper T cells recognizing ATF1011 as a carrier protein. Killer T cells were induced against ATF1011 antigen in the H-2 restricted manner using syngeneic stimulator cells bearing ATF1011 on the cell surfaces. When this lectin was administered intralesionally into the tumors, induction of cytotoxic effector cells was demonstrated. These results suggest that intralesionally administered ATF1011 binds to the tumor cell membrane and activates T cells specific for this carrier lectin in situ, which results in the augmented induction of systemic anti-tumor immunity.

Aloe Vera & AIDS Research

Various AIDS studies were completed by researchers such as Dr. Terry Pulse, M.D., Dr. Reg McDaniel, M.D., Dr. Terry Watson, D.O., Dr. Clumeck, M.D. (of Belgium) and others throughout the 1980's using oral mucopolysaccharides. The results were impressive, demonstrating in many of the studies an average of 70% improvement in symptoms and laboratory criteria within 3 to 4 months. Many patients stated that opportunistic infections had stopped and they were able to return to normal activity. In one dramatic case, a man with advanced AIDS had 17 liver tumors and after one and a half years on oral Aloe mucopolysaccharides, his T-Cell count was normal and all the tumors had dissolved (confirmed by x-ray films).

Lab studies showed that helper lymphocytes (CD4) rose to three times the pre-treatment levels. HIV-1 virus could no longer be cultured. P-24 antigen levels for the virus dropped or became negative.

Researchers at Vanderbilt Medical Center in Nashville, Tennessee discovered that Aloe mucopolysaccharides alters synthesis and thus the structure of the AIDS virus envelope necessary for infecting lymphocytes. Further studies at The Southern Research Institute found that there is suppression of the viral messenger RNA in HIV-1 infected leukocytes. Therefore, the reproduction of HIV-1 is inhibited with a natural and non-toxic substance.

In studies completed at the Fort Worth Medical Center Complex it was demonstrated that a person's leukocytes were rendered resistant to HIV-1 virus in culture tests outside the body.

Effects Of Aloe Extracts On Human Normal & Tumor Cells In-Vitro

Winters WD; Benavides R; Clouse WJ

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Econ Bot 35 (1), 1981, 89-95

Fractions of leaf extracts from 2 local types, labeled Aloe vera (subsequently identified as *A. barbadensis* Mill., and *A. saponaria* Haw.), were prepared by differential centrifugation and tested by in vitro assays for the presence of lectin-like activities and for effects on the attachment and growth of human normal and tumor cells. Fractions of extracts of fresh leaves and commercially *A. vera* gel had high levels of lectin-like substances measured by immunodiffusion and nemagglutination assays. Substances in fluid fractions from both fresh leaf sources markedly promoted attachment and growth of human normal cells.

A Study By Dr. Terry Pulse, M.D. Of 29 AIDS Patients

Journal of Advancement in Medicine Winter 1990, Volume 3, No. 4

Patients took 1200 mg of the active ingredient in Aloe vera juice daily as well as nutrient supplements. We quote directly from Dr. Pulse's report of the results, which are fantastic: "No adverse effects attributable to the essential fatty acid capsules were observed nor any side effects of the nutritional supplementation powder nor of the Aloe vera juice. Most patients who were symptomatic reported that within three to five days their energy levels improved, fever disappeared, night sweats stopped, cough decreased or stopped altogether, shortness of breath decreased, lymph nodes decreased in size, diarrhea stopped, strength improved and the only measurable side effect of this particular study was weight gain, which is a desirable effect. There were no biochemical abnormalities noted on MAC in this particular study. AZT induced anemia improved on this particular regimen. Chest x-rays remained normal throughout the study. No changes in EKG from baseline were observed. There was great improvement in all patients to hypersensitivity skin testing at the end of 90 days... Not only did the patients improve clinically and functionally, but their Karnofsky scores improved in 93.1% of the patients at 90 days and in 100% at 180 days. 51.7% of the patient's T4 helper lymphocytes increased at 90 days and 32.2% at 180 days, with 25% reactive HIV P24 core antigen converted to negative at 90 days and 180 days."

Purification Of Active Substances Of Aloe Arborescens Miller & Their Biological & Pharmacological Activity

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Phytother Res. (1993) 7 (Spec. Issue, Proceedings of the International Congress of Phytotherapy, 1991), S14-S19

The authors purified Aloctin A from *Aloe arborescens* Miller and defined its chem., biol. and pharmacol. activities. Aloctin A consists of two discrete bands, a and b with a combined S-S bond. Its mol. wt. for a is 7500 and the mol. wt. for b is 10,500. Aloctin A has many biol. and pharmacol. activities as follows: 1. hemagglutinating activity; 2. cytoagglutinating activity; 3. mitogenic activity of lymphocytes; 4. ppt. - forming reactivity with $\alpha 2$ -macroglobulin; 5.

complement C3 activating activity; 6. inhibition of heat-induced hemolysis of rat erythrocytes; 7. anti-tumor effect; 8. anti-inflammatory effect; 9. inhibition of gastric secretion and gastric lesions.
