Alzheimer's disease

☐ **1:** Neuron. 1996 Sep;17(3):553-65.

Microglial cells internalize aggregates of the Alzheimer's disease amyloid beta-protein via a scavenger receptor.

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Microglia are immune system cells associated with Alzheimer's disease plaques containing beta-amyloid (A beta). Murine microglia internalize microaggregates of fluorescently labeled or radioiodinated A beta peptide 1-42. Uptake was confirmed using aggregates of unlabeled A beta detected by immunofluorescence. Uptake of A beta was reduced by coincubation with excess acetyl-low density lipoprotein (Ac-LDL) or other scavenger receptor (SR) ligands, and DiI-labeled Ac-LDL uptake by microglia was blocked by excess A beta. CHO cells transfected with class A or B SRs showed significantly enhanced uptake of A beta. These results show that microglia express SRs that may play a significant role in the clearance of A beta plaques. Binding to SRs could activate inflammation responses that contribute to the pathology of Alzheimer's disease.

PMID: 8816718 [PubMed - indexed for MEDLINE]

BREAST CANCER

1: Anticancer Res. 2000 Sep-Oct;20(5A):3265-71.

Analysis of the in vitro inhibition of mammary adenocarcinoma cell adhesion by sulphated polysaccharides.

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Evidence is mounting that changes in the ability of cancer cells to adhere to extracellular matrices (ECM) play a decisive role in metastasis spread. We have investigated the effect of different sulphated polysaccharides on the adhesion of MCF7 and MDA-MB231 adenocarcinoma breast cells to different substrata: a reconstituted basement membrane (Matrigel) and various adhesion-mediating proteins (fibronectin, laminin, type IV collagen). Most of them inhibited cell adhesion and the most active component is a galactose rich units polysaccharide, carrageenan iota. Taken together, the results suggest that this inhibitory activity depends on the charge density related to sulphate groups, the molecular weight and also the carbohydrate structure. These products very likely unstabilize the interaction between the glucosaminoglycan portion of proteoglycans and the ECM proteins and then block the ability of these adhesive proteins to bind to cells.

PMID: 11062752 [PubMed - indexed for MEDLINE]

CHOLESTEROL

1: Biol Pharm Bull. 1994 Jun;17(6):784-8.

Preparation of aminated fucoidan and its evaluation as an antithrombotic and antilipemic agent.

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Fucoidan, a sulfated poly(L-fucopyranose), is an effective anticoagulant in vitro and in vivo. In the present study, an aminated derivative of fucoidan was prepared and examined for its fibrinolytic and anticoagulant activities. The aminated derivative was more potent than native fucoidan as a stimulator of tissue plasminogen activator-induced plasma clot lysis, and its effectiveness was comparable to that of oversulfated fucoidan reported previously. Furthermore, the ability of aminated fucoidan to accelerate heparin cofactor II-mediated thrombin inhibition was 2.3 times more potent than that of native fucoidan. Aminated fucoidan effectively prevented endotoxin-induced hepatic vein thrombosis in hyperlipemic rats and decreased the elevated levels of serum cholesterol and triglyceride. The present results that the anticoagulant and antilipemic potency of fucoidan can be improved by charge modification may provide useful clues for the development of an ideal anticoagulant and antilipemic drug.

PMID: 7951138 [PubMed - indexed for MEDLINE]

1: Microcirculation. 2004 Dec;11(8):645-54.

Inhibition of leukocyte adherence enables venular control of capillary perfusion in streptozotocin-induced diabetic rats.

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OBJECTIVE: Vasoactive molecules can diffuse from venules to dilate closely paired arterioles and enhance capillary perfusion. Venular control of capillary flow has been found to be dependent on nitric oxide (NO), which might be scavenged rapidly in diabetic microvasculature due to the presence of activated leukocytes. This study attempts to improve venular control of capillary flow using fucoidan, which inhibits venular leukocyte adhesion. METHODS: Microvascular red blood cell velocity was measured in the mesentery of streptozotocin-induced diabetic rats, with and without fucoidan treatment, and in normal rats. Arteriolar pathways leading to branching capillaries were videotaped to measure the percent of the surrounding area occupied by a venule (% pairing). Microvascular wall NO was measured using fluorescent diaminofluorescein-2-diacetate in diabetic rats, with and without fucoidan treatment. RESULTS: In normal rats, close pairing of venules to arterioles resulted in faster capillary flow. However, after 4-5 weeks of diabetes, the correlation between capillary velocity and % pairing was no longer significant. Capillary velocity and % pairing decreased approximately 50% in comparison to normal rats. Treatment of diabetic rats with fucoidan restored venular control of capillary flow and increased NO levels. CONCLUSION: Leukocyte-derived mediators that scavenge NO may lead to inadequate venular control of capillary flow in diabetes.

PMID: 15726832 [PubMed - indexed for MEDLINE]

☐ **1:** Helicobacter. 2003 Feb;8(1):59-65.

Preventive effects of Cladosiphon fucoidan against Helicobacter pylori infection in Mongolian gerbils.

Shibata H, **Iimuro M**, **Uchiya N**, **Kawamori T**, **Nagaoka M**, **Ueyama S**, **Hashimoto S**, **Yokokura T**, **Sugimura T**, **Wakabayashi K**.

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BACKGROUND: Recently, the acquisition by Helicobacter pylori of resistance to antibiotics has become a serious problem. Therefore, nonantibiotic substances are required to diminish H. pylori-induced gastric lesions. In the present study, the effects of Cladosiphon fucoidan were examined in terms of H. pylori attachment to porcine gastric mucin in vitro and Helicobacter pylori-induced gastritis in vivo. METHODS: The inhibitory effect of Cladosiphon fucoidan and other polysaccharides on H. pylori attachment to porcine gastric mucin was assayed in vitro with mucin-coated microtiter plates. The effect of Cladosiphon fucoidan on H. pylori-induced gastritis was examined in vivo using Mongolian gerbils. H. pylori-inoculated gerbils were given fucoidan in drinking water. Six weeks after H. pylori-inoculation, gerbils were sacrificed for macroscopic and microscopic examination of gastric lesions and counting of viable H. pylori in the gastric mucosa. RESULTS: Cladosiphon fucoidan inhibited the H. pylori attachment to porcine gastric mucin at pH 2.0 and 4.0. Two other sulfated polysaccharides, Fucus fucoidan and dextran sulfate sodium, also inhibited the attachment but only at pH 2.0. Inhibitory effects of these three sulfated polysaccharides were not observed at pH 7.2 and nonsulfated polysaccharides, such as mannan and dextran, exerted no influence at any pH. In the in vivo experiment, the H. pylori-induced gastritis and the prevalence of H. pylori infected animals were markedly reduced by fucoidan in a dose-dependent manner, at doses of 0.05 and 0.5% in the drinking water. CONCLUSION: Cladosiphon fucoidan may deserve particular attention as a safe agent that can prevent H. pylori infection and reduce the risk of associated gastric cancer.

PMID: 12603617 [PubMed - indexed for MEDLINE]

HIV

1: Experientia. 1989 Oct 15;45(10):996-8.

Further characterization of sulfated homopolysaccharides as anti-HIV agents.

Sugawara I, **Itoh W**, **Kimura S**, **Mori S**, **Shimada K**.

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Fucoidan and dextran sulfate showed anti-HIV activities against mononuclear cells from AIDS patients, and they abrogated HIV reverse transcriptase (RT) activity by interacting with the HIV envelope in the membranes of target cells. Furthermore, they showed a synergistic effect with azidothymidine (AZT).

PMID: 2478388 [PubMed - indexed for MEDLINE]

HIV

☐ **1:** Biochim Biophys Acta. 1992 Dec 10;1180(2):180-6.

Maleylated human serum albumin inhibits HIV-1 infection in vitro.

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Maleylated-human serum albumin (Mal-HSA) inhibited human immunodeficiency virus type-1 (HIV-1) infection of MT-4 cells in vitro. It was also found to inhibit the fusion between uninfected CD4+ cells (Molt-4 clone 8 cells) and HIV-1 infected cells (Molt-4/HIV-1) to form syncytia. To investigate the mechanism of the inhibition, a study was designed to determine whether Mal-HSA could bind to CD4+ cells. Mal-HSA could bind to both MT-4 cells and Molt-4 clone 8 cells with high affinity, Kd = 2.0 nM and Kd = 5.8 nM, respectively. However, Mal-HSA could neither inhibit anti CD4 antibody Leu 3a binding to Molt-4 clone 8 cells nor modulate the expression of CD4 molecules on the surface of the cells. Mal-HSA binding to Molt-4 clone 8 cells was completely inhibited by sulfated polysaccharides bearing anti-HIV activity, such as dextran sulfate, fucoidan and carrageenan. Other HIV-1 susceptible human T-cell lines, such as Molt-4, CEM-5, H-9 and HuT-78 cells, also have Mal-HSA binding sites showing a high affinity, Kd = 0.9 +/- 0.4 nM. Mal-HSA binding proteins of Molt-4 clone 8 cells were identified by ligand blotting as 155 and 220 kDa proteins. Unlike dextran sulfate, Mal-HSA could not inhibit reverse transcriptase activity of HIV-1. These results indicate that Mal-HSA inhibits HIV-1 infection and syncytia formation, and suggest that 155 and/or 220 kDa proteins of target cells are involved in HIV-1 adsorption and/or the membrane fusion between HIV-1 and target cells.

PMID: 1281431 [PubMed - indexed for MEDLINE]

KIDNEY CANCER

1: J Biol Chem. 1994 Apr 1;269(13):9817-21.

Hepatocyte growth factor specifically binds to sulfoglycolipids.

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Hepatocyte growth factor (HGF) is a heparin-binding pleiotropic factor that acts on a variety of epithelial cells. The interaction of human HGF with glycolipids was studied by overlaying them with 125I-HGF on thin layer chromatograms and by a solid-phase assay using lipids adsorbed on microtiter plates. Among various glycolipids tested, HGF was found to bind to sulfoglycolipids, including galactosylceramide sulfate (SM4), lactosylceramide sulfate (SM3), and gangliotriaosylceramide bis-sulfate. In contrast, HGF failed to bind to gangliosides or neutral glycolipids. HGF binding to SM4 was strongly inhibited by dextran sulfate, heparin, and fucoidan, whereas neither keratan sulfate nor hyaluronic acid had any inhibitory activity. When glycolipids from a renal cancer cell line, SMKT-R3, which overexpresses sulfoglycolipids, were developed on a thin layer chromatogram, SM4 and SM3 were the only glycolipids that bound HGF. We further examined the effect of the incorporation of glycolipids into SMKT-R3 cells on HGF binding to the cells. The incorporation of SM4 into the cells enhanced HGF binding to SMKT-R3 cells, while that of galactosylceramide, a precursor of SM4, had no effect. These observations indicated that SM4 exogenously incorporated into the cell membranes could react with HGF and suggested that endogenous sulfoglycolipids on SMKT-R3 cells might function as reservoirs for HGF.

PMID: 8144574 [PubMed - indexed for MEDLINE]

LEUKEMIA

☐ **1:** Nutr Cancer. 2005;52(2):189-201.

Fucoidan extracted from Cladosiphon okamuranus Tokida induces apoptosis of human T-cell leukemia virus type 1-infected T-cell lines and primary adult T-cell leukemia cells.

Haneji K, **Matsuda T**, **Tomita M**, **Kawakami H**, **Ohshiro K**, **Uchihara JN**, **Masuda M**, **Takasu N**, **Tanaka Y**, **Ohta T**, **Mori N**.

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Adult T-cell leukemia (ATL) is caused by human T-cell leukemia virus type 1 (HTLV-1) and remains incurable. The highest endemic area of HTLV-1 carriers in Japan is located in Okinawa, and novel treatments are urgently needed in this area. We extracted fucoidan, a sulfated polysaccharide, from the brown seaweed Cladosiphon okamuranus Tokida cultivated in Okinawa, Japan and examined its tumor-suppression activity against ATL. Fucoidan significantly inhibited the growth of peripheral blood mononuclear cells of ATL patients and HTLV-1-infected T-cell lines but not that of normal peripheral blood mononuclear cells. Fucoidan induced apoptosis of HTLV-1-infected T-cell lines mediated through downregulation of cellular inhibitor of apoptosis protein-2 and survivin and G1 phase accumulation through the downregulation of cyclin D2, c-myc, and hyperphosphorylated form of the retinoblastoma tumor suppressor protein. Further analysis showed that fucoidan inactivated NF-kappaB and activator protein-1 and inhibited NF-kappaB-inducible chemokine, C-C chemokine ligand 5 (regulated on activation, normal T expressed and secreted) production, and homotypic cell-cell adhesion of HTLV-1-infected T-cell lines. In vivo use of fucoidan resulted in partial inhibition of growth of tumors of an HTLV-1-infected T-cell line transplanted subcutaneously in severe combined immune deficient mice. Our results indicate that fucoidan is a potentially useful therapeutic agent for patients with ATL.

PMID: 16201850 [PubMed - indexed for MEDLINE]

1: Am J Hematol. 2005 Jan;78(1):7-14.

Fucoidan induces apoptosis of human HS-sultan cells accompanied by activation of caspase-3 and down-regulation of ERK pathways.

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Fucoidan, a sulfated polysaccharide in brown seaweed, was found to inhibit proliferation and induce apoptosis in human lymphoma HS-Sultan cell lines. Fucoidan-induced apoptosis was accompanied by the activation of caspase-3 and was partially prevented by pretreatment with a pan-caspase inhibitor, z-VAD-FMK. The mitochondrial potential in HS-Sultan cells was decreased 24 hr after treatment with fucoidan, indicating that fucoidan induced apoptosis through a mitochondrial pathway. When HS-Sultan was treated with 100 microg/mL fucoidan for 24 hr, phosphorylation of ERK and GSK markedly decreased. In contrast, phosphorylation of p38 and Akt was not altered by treatment with fucoidan. L-selectin and P-selectin are known to be receptors of fucoidan; however, as HS-Sultan does not express either of these selectins, it is unlikely that fucoidan induced apoptosis through them in HS-Sultan. The neutralizing antibody, Dreg56, against human L-selectin did not prevent the inhibitory effect of fucoidan on the proliferation of IM9 and MOLT4 cells, both of which express L-selectin; thus it is possible fucoidan induced apoptosis though different receptors These results demonstrate that fucoidan has direct anti-cancer effects on human HS-Sultan cells through caspase and ERK pathways.

PMID: 15609279 [PubMed - indexed for MEDLINE]

LIVER CANCER

☐ **1:** Hepatol Res. 2006 Jul;35(3):190-8. Epub 2006 May 4.

Fucoidan prevents concanavalin A-induced liver injury through induction of endogenous IL-10 in mice.

Saito A, **Yoneda M**, **Yokohama S**, **Okada M**, **Haneda M**, **Nakamura K**.

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Fucoidan is a complex of sulfated polysaccharides derived from non-mammalian origin such as marine brown algae and induces cytokine expression. We investigated the effect of fucoidan on concanavalin A (Con A)-induced liver injury in mice. Liver injury was induced by an intravenous injection of Con A (18.5mg/kg). Various doses of fucoidan (1-30mg/kg) were intravenously administered 30min before Con A injection. The plasma alanine aminotransferase (ALT) and several cytokines levels were determined, and hepatic histological changes were also assessed. The effect of fucoidan administration by itself on induction of interleukin (IL)-10 in plasma and liver tissue was investigated. Con A administration induced an elevation of plasma ALT level, and fucoidan administration dose-dependently prevented the Con A-induced elevation of plasma ALT. Con A administration increased plasma TNF-alpha and IFN-gamma levels, and fucoidan pretreatment significantly inhibited these alterations and increased plasma IL-10 level. The inhibitory effect of fucoidan on Con A-induced liver injury and production of proinflammatory cytokines were reversed by anti-mouse IL-10 antibody pretreatment. Fucoidan induced the IL-10 production in plasma and liver tissue. These findings suggest that fucoidan prevents Con A-induced liver injury by mediating the endogenous IL-10 production and the inhibition of proinflammatory cytokine in mice.

PMID: 16678479 [PubMed - in process]

LIVER CANCER

1: Eur J Pharmacol. 2008 Feb 12;580(3):380-4. Epub 2007 Nov 17.

Fucoidan partly prevents CCl(4)-induced liver fibrosis.

Hayashi S, **Itoh A**, **Isoda K**, **Kondoh M**, **Kawase M**, **Yagi K**.

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Fucoidan, a sulfated polysaccharide extracted from brown algae, has a wide range of biological activities, including anti-inflammatory, anti-viral, and anti-tumor activities. In the present study, we investigated the effects of fucoidan on CCl(4)-induced liver fibrosis. Administration of fucoidan reduced CCl(4)-induced acute and chronic liver failure. Hepatic fibrosis induced by CCl(4) was also attenuated by injection of fucoidan. Damage to hepatocytes and activation of hepatic stellate cells are key events in liver fibrosis, and, interestingly, treatment of hepatocytes with fucoidan prevented CCl(4)-induced cell death and inhibited the proliferation hepatic stellate cells. These results indicate that fucoidan might be a promising anti-fibrotic agent possessing dual functions, namely, protection of hepatocytes and inhibition of hepatic stellate cell proliferation.

PMID: 18068155 [PubMed - in process]

LUNG CANCER

1: Experientia. 1989 Jun 15;45(6):584-8.

Blocking of lectin-like adhesion molecules on pulmonary cells inhibits lung sarcoma L-1 colonization in BALB/c-mice.

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Adhesion and inhibition experiments with pulmonary cells of BALB/c-mouse origin and syngeneic sarcoma L-1 cells indicated that L-fucose specific lectin-like adhesion molecules, presumably situated on pulmonary cell surfaces are (at least partly) responsible for the specificity of this cell-cell interaction. Addition of specific sugars and glycoconjugates (L-fucose and fucoidan, respectively) to the incubation medium evidently inhibited the adhesion process as quantified using radiolabelled tumor cells. Unspecific carbohydrates (e.g. D-galactose) did not affect the cellular interaction. In vivo, repeated administration of fucoidan (but not of unspecific glycoconjugates) significantly inhibited the settling of metastatic sarcoma L-1 cells in the lungs of BALB/c-mice. Therefore, when lectin-like adhesion molecules on pulmonary cells were blocked with competitive glycoconjugates, tumor cell colonization of the lung could be significantly inhibited.

PMID: 2737266 [PubMed - indexed for MEDLINE]

LUNG CANCER

1: Anticancer Res. 1996 May-Jun;16(3A):1213-8.

Antitumor and antiproliferative effects of a fucan extracted from ascophyllum nodosum against a non-small-cell bronchopulmonary carcinoma line.

Riou D, **Colliec-Jouault S**, **Pinczon du Sel D**, **Bosch S**, **Siavoshian S**, **Le Bert V**, **Tomasoni C**, **Sinquin C**, **Durand P**, **Roussakis C**.

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Fucans, sulfated polysaccharides extracted from brown seaweeds, have been shown to be endowed with inhibitory effects cell growth in various experimental models. We studied both the antiproliferative and antitumor properties of a fucoidan extract (HF) obtained from the brown seaweed Ascophyllum nodosum on a cell line derived from a non-small-cell human bronchopulmonary carcinoma (NSCLC-N6), this type of carcinoma is particularly chemo-resistant. HF exerts in vitro a reversible antiproliferative activity with a block observed in the G1 phase the cell cycle. Studies performed with the NSCLC-bearing nude mice show antitumor activity at subtoxic doses. These preliminary results indicate that HF exhibits inhibitory effect both in vitro and in vivo and is very potent antitumor agent in cancer therapy.

PMID: 8702239 [PubMed - indexed for MEDLINE]

LUNG CANCER

1: Anticancer Res. 1995 Sep-Oct;15(5B):1937-47.

Immunological analysis of inhibition of lung metastases by fucoidan (GIV-A) prepared from brown seaweed Sargassum thunbergii.

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The antimetastatic effect of GIV-A (fucoidan) and/or 5-FU was examined in an experimental model of lung metastases induced by Lewis lung carcinoma in mice. Injection of GIV-A i.p. after removal of the implanted primary tumor inhibited the development of lung metastases. Combination treatment with GIV-A and 5-FU inhibited significantly the lung metastases. The number of peritoneal macrophages, total cells and macrophages in the lung increased in mice treated with GIV-A. Binding of the third component of complement (C3) cleavage products (C3b) to the C3 receptor on peritoneal macrophages after i.v. injection of GIV-A was enhanced, as shown by the fluorescent antibody technique. Lung metastases were inhibited by i.v. injection of peritoneal macrophages activated with GIV-A. GIV-A depressed aniline hydroxylase and aminopyrine demethylase activities of the hepatic microsomal drug-metabolizing system in tumor-bearing mice. Moreover, the concentration of 5-FU in the tissues (lung, liver, kidney, spleen and blood) was increased significantly by coadministration of GIV-A. The picryl chloride-induced delayed type hypersensitivity (PC-DTH) response in mice was depressed after the implantation of tumor and treatment with 5-FU. GIV-A restored the suppression of PC-DTH by 5-FU, but did not increase the PC-DTH of normal mice. GIV-A not only enhanced the degree of spleen cell-mediated sheep red blood cell (SRBC) hemolysis (quantitative hemolysis of SRBC), the indexes of the spleen and thymus and the number of spleen cells, but also restored the suppressive effect of 5-FU. In the group receiving GIV-A, the percentages of splenic Thy1.2-, L3T4- and asialo GM1-positive cells were significantly increased as compared with the tumor-bearing mice treated with saline. Furthermore, the L3T4+/Lyt2+ ratio showed a tendency to increase, and the Lyt2+/Thy1.2+ ratio was decreased. These results suggest that the antitumor effect of GIV-A may be correlated with the changing pattern of the Thy1.2-, L3T4- and asialo GM1-positive cells, C3 activation, macrophage activation and depression of the hepatic microsomal drug-metabolizing system. These findings raise the possibility that GIV-A may have clinical value in the prevention of cancer metastasis.

PMID: 8572581 [PubMed - indexed for MEDLINE]

STOMACH CANCER

☐ **1:** J Nutr Sci Vitaminol (Tokyo). 1999 Jun;45(3):325-36.

Inhibitory effect of Cladosiphon fucoidan on the adhesion of Helicobacter pylori to human gastric cells.

Shibata H, KimuraTakagi I, Nagaoka M, Hashimoto S, Sawada H, Ueyama S, Yokokura T.

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We studied the inhibitory effect of Cladosiphon fucoidan on the attachment of Helicobacter pylori (H. pylori), a gastroduodenal pathogen, to human gastric cell lines. The bacterial binding in these cell lines was inhibited more by Cladosiphon fucoidan (IC50 = 16-30 mg/mL), than by the fucoidan from Fucus (IC50 > 30 mg/mL). Dextran sulfate, another sulfated polysaccharide, did not inhibit the binding at all. Pre-incubating the bacterial suspension with fucoidans reinforced the inhibitory ability of these components, and reduced the IC50 value of Cladosiphon fucoidan to approximately 1 mg/mL. However, the binding was not inhibited by pre-treatment of gastric cells with these components. It was also shown that this fucoidan blocks both Leb- and sulfatide-mediated attachment of H. pylori to gastric cells. Furthermore, fucoidan-binding proteins were found on the H. pylori cell surface by Western blot analysis. Thus, the inhibitory effect exerted by Cladosiphon fucoidan on binding between H. pylori and gastric cells might result from the coating with this component of the bacterial surface.

PMID: 10524351 [PubMed - indexed for MEDLINE]

TUMOR

1: Anticancer Res. 2005 May-Jun;25(3B):2129-33.

Inhibitory effect of fucoidan on the adhesion of adenocarcinoma cells to fibronectin.

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Fucoidans inhibit tumour cell adhesion to various substrata, but their mechanisms of action are not fully understood. Using 3H-fucoidan, we observed that fucoidan binds to fibronectin, this binding being saturable and sensitive to ionic strength and pH. The interaction occurred on at least four different sites along the polypeptide chain, two of them being the heparin-binding sequences. Moreover, when MDA-MB-231 tumour cells were exposed to DTAF-fucoidan, internalization occurred and punctuated vesicles were observed in the perinuclear region. The treated cells also showed a different morphology with a cytoskeleton devoid of vinculin and a reorganiztion of the repartition of the integrin-alpha5 subunit on the cell surface. Based on these data, we hypothesize that fucoidan inhibits the adhesion of MDA-MB-231 cells to fibronectin i) by blocking the protein's heparin- and cell-binding domains, ii) by modulating the reorganization of the integrin alpha5 subunit and iii) by down-regulating the expression of vinculin.

PMID: 16158954 [PubMed - indexed for MEDLINE]

TUMOR

1: Glycobiology. 2007 May;17(5):541-52. Epub 2007 Feb 12.

A comparative study of the anti-inflammatory, anticoagulant, antiangiogenic, and antiadhesive activities of nine different fucoidans from brown seaweeds.

Cumashi A, Ushakova NA, Preobrazhenskaya ME, D'Incecco A, Piccoli A, Totani L, Tinari N, Morozevich GE, Berman AE, Bilan MI, Usov AI, Ustyuzhanina NE, Grachev AA, Sanderson CJ, Kelly M, Rabinovich GA, Iacobelli S, Nifantiev NE; Consorzio Interuniversitario Nazionale per la Bio-Oncologia, Italy.

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The anti-inflammatory, antiangiogenic, anticoagulant, and antiadhesive properties of fucoidans obtained from nine species of brown algae were studied in order to examine the influence of fucoidan origin and composition on their biological activities. All fucoidans inhibited leucocyte recruitment in an inflammation model in rats, and neither the content of fucose and sulfate nor other structural features of their polysaccharide backbones significantly affected the efficacy of fucoidans in this model. In vitro evaluation of P-selectin-mediated neutrophil adhesion to platelets under flow conditions revealed that only polysaccharides from Laminaria saccharina, L. digitata, Fucus evanescens, F. serratus, F. distichus, F. spiralis, and Ascophyllum nodosum could serve as P-selectin inhibitors. All fucoidans, except that from Cladosiphon okamuranus carrying substantial levels of 2-O-alpha-D-glucuronopyranosyl branches in the linear (1-->3)-linked poly-alpha-fucopyranoside chain, exhibited anticoagulant activity as measured by activated partial thromboplastin time whereas only fucoidans from L. saccharina, L. digitata, F. serratus, F. distichus, and F. evanescens displayed strong antithrombin activity in a platelet aggregation test. The last fucoidans potently inhibited human umbilical vein endothelial cell (HUVEC) tubulogenesis in vitro and this property correlated with decreased levels of plasminogen-activator inhibitor-1 in HUVEC supernatants, suggesting a possible mechanism of fucoidan-induced inhibition of tubulogenesis. Finally, fucoidans from L. saccharina, L. digitata, F. serratus, F. distichus, and F. vesiculosus strongly blocked MDA-MB-231 breast carcinoma cell adhesion to platelets, an effect which might have critical implications in tumor metastasis. The data presented herein provide a new rationale for the development of potential drugs for thrombosis, inflammation, and tumor progression.

PMID: 17296677 [PubMed - indexed for MEDLINE]