# Fucoidan

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## • What is Fucoidan?

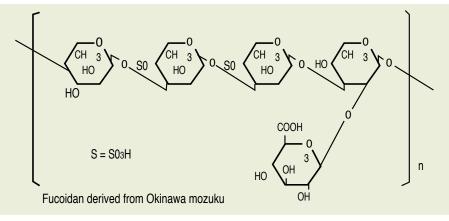
### I. What is Fucoidan?

Seaweeds have been known to have pharmacological benefits since ancient times and "Shen Nong Ben Cao Jing (The Divine Farmer's Herb-Root Classic)," believed to be the oldest book on medicinal substances in China, mentions the ability of a seaweed, probably brown alga hondawara, to heal tumor.

Fucoidan, present in brown algae just like hondawara, was discovered in 1913 by Professor Kylin of Uppsala University in Sweden as a source of sliminess of Kombu. Initially named "Fucoidin," the substance subsequently became known as "Fucoidan" based on the IUPAC rules (international naming rules for sugars).

Fucoidan is a specific source of sliminess only found in brown algae such as Kombu, Wakame (Mekabu) and Mozuku, and a type of water-soluble dietary fiber. Chemically, Fucoidan is a high-molecular polysaccharide whose main constituent is sulfated fucose. In addition to fucose, the saccharide chain that constitutes Fucoidan also includes galactose, mannose, xylose and uronic acid. The name "Fucoidan" does not represent substances of a given structure, but it is a general term that refers to high-molecular polysaccharides whose main constituent is fucose.

Today, active research is conducted on Fucoidan and various bioactive functions of Fucoidan, such as "anti-cancer action," "cholesterol-lowering action," "blood-pressure lowering action" and "anti-virus action," have been revealed.



## • What is Fucoidan?



Various brown seaweeds and Mozuku Farm

### II. Types of Fucoidan

Fucoidan refers to a type of polysaccharide which contains substantial percentages of L-fucose and sulfate groups, mainly derived from brown seaweeds. During the past decade, fucoidan has been extensively studied due to its numerous interesting biological activities. Recently the search for new alternative ways to treat cancer has raised the interest in the study of fucoidan. Several species of brown seaweeds have been used to extract fucoidan, for example, Mozuku, Mekabu (Wakame) and Kombu.

Mozuku (Cladosiphon okamuranus) is from the genus Cladosiphon, which is naturally found in Okinawa, Japan. Mozuku is rich in Fucoidan and it is the species with the highest amounts of sulfated polysaccharides. Fucoidan from Cladosiphon okamuranus is safe and it has a very strong potential for gastric protection and Angiogenesis inhibition. It has also been studied for its antiulcer and adhesion inhibitor activity for Helicobacter pylori. The Fucoidan obtained from Cladosiphon okamuranus has been studied extensively for its ability to inhibit stomach cancer cells.

Mekabu (Wakame – Undaria pinnatifida) has been grown for hundreds of years in Japan, Korea, Argentina and it has been found in Tasmania, Australia. Fucoidan from Undaria pinnatifida has been studied for its positive effects on inhibition of Herpes. Undaria is the most commonly eaten seaweed in Japan, and contains sulfated polysaccharides and other components with anti-tumor and antiviral activity. The brown alga, Undaria pinnatifida, is nutritious, having abundant protein, polysaccharide, and minerals. Besides being widely utilized as food, it has been used as alternative medicine.

Kombu (Laminaria japonica) has demonstrated to have antioxidant activities. Fucoidan of Laminaria japonica has also been reported to have antitumor activity and antivirus effect. Many studies show that Fucoidan from this species presents significant antioxidant activity and it is an excellent natural antioxidant and has a great potential for preventing free radical-mediated diseases.



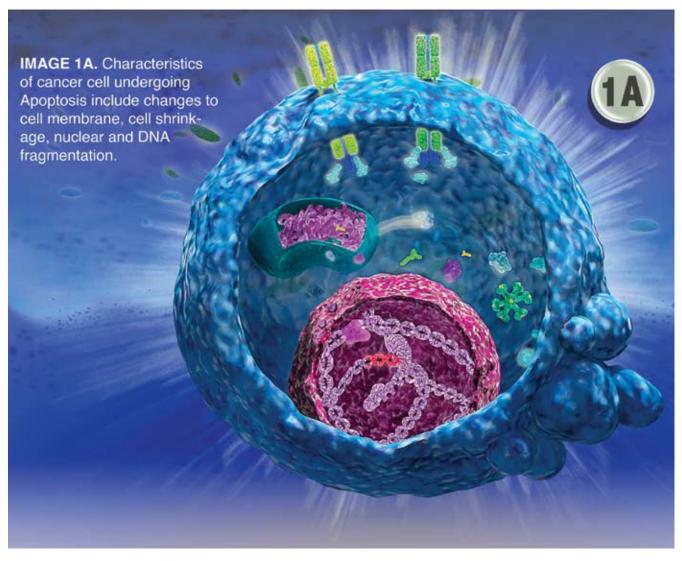
**I Apoptosis** is a genetically programmed mechanism of cell death. When certain stimulation is applied to a cell, its gene triggers the self-destruction device and the cell dies.

- **II** Angiogenesis Inhibition Activity is blocking the generation of new blood vessels of cancer cells. Cancer cells grow at a constant speed at first and when cancer cell reached the size of 2 mm diameter, their growth speed accelerates. Cancer cells need nutrients and oxygen to metastasize, so they send signals to generate new blood vessels. Once cancer cells' new blood vessels are generated around them, they metastasize to other places. Therefore when the creation of new blood vessels is prevented, cancer cells cannot get nutrients and oxygen and cannot metastasize as well.
- Immunity-Enhancing Activity refers to an increase in the immunity. A leukocyte has monocyte, polymorph and lymphocyte, and they work effectively to support immune system. A polysaccharide stimulates intestinal immunity and activates its immune system; this Toll-Like Receptor promotes the process of signal transmission to T cells to cause them to attack other pathogens, which will consequently increase the immunity effectively. There are various cells that control our immunity. Representatives of such cells include granulocytes, macrophages, NK cells and lymphocytes, which all work together to enhance our immunity and attack and repel cancer cells. Among these cells, macrophages, NK cells and "T cells," which are types of lymphocyte, are particularly important to prevent the growth of cancer cells.

### I. Apoptosis What is Apoptosis?

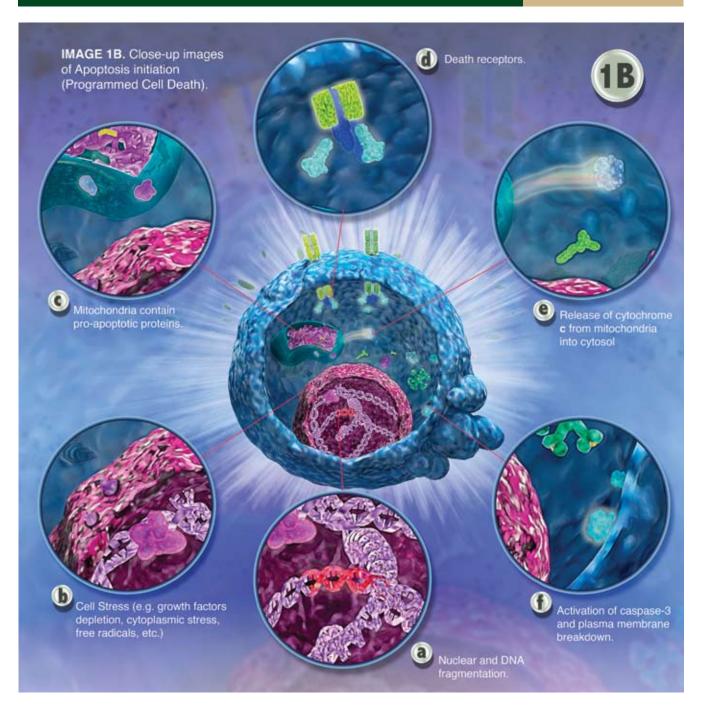
**"Apoptosis"** is a generally programmed mechanism of cell death. When certain stimulation is applied to a cell, its gene triggers the self-destruction device and the cell dies. Once apoptosis occurs to a cell, DNA of cancer cells will be fragmented and they will disappear.

### A tumor undergoing Apoptosis



## I. Apoptosis

### A tumor undergoing Apoptosis



### I. Apoptosis

A tumor undergoing Apoptosis

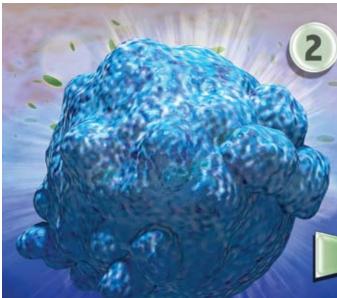


IMAGE 2. The breakdown of chromatin in the nucleus of cancer cell leads to nuclear condensation.

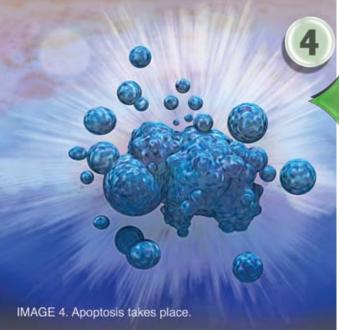




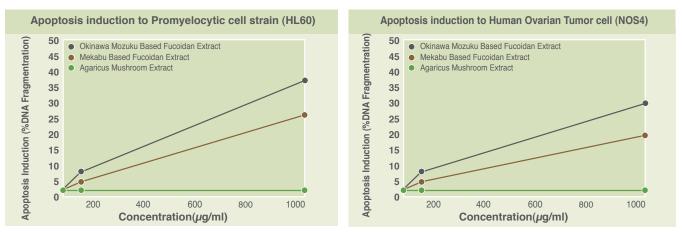
IMAGE 3. Cells continue to shrink.

## I. Apoptosis Proof of Apoptosis-Inducing Activity

A study on the influence of Mozuku (Cladosiphon okamuranus) derived Fucoidan, Mekabu (Undaria pinnatifida) derived Fucoidan, and Agaricus mycelium extract powder on apoptosis of promyelocytic leukemia cell strains (HL60) and cultured human ovarian tumor cell strains (NOS4) has been carried out. Apoptosis was determined.

#### Method of experiment

Applied Mozuku (Cladosiphon okamuranus) derived Fucoidan, Mekabu (Undaria pinnatifida) derived Fucoidan, and Agaricus mycelium extract powder onto each promyelocytic leukemia cell strain (HL60) and cultured human ovarian tumor cell strains (NOS4) and cultured them.



EFFECTS OF EACH TYPE OF FUCOIDAN AND AGARICUS INDUCING APOPTOSIS When Agaricus was applied to the cancer cell, there was no apoptosis effect. The results did reveal that Mozuku derived Fucoidan and Mekabu derived Fucoidan exhibited a high ability to induce apoptosis.

Mie University professor, Taguchi: Fucoidan Apoptosis Test



Added Fucoidan into Cancer cells and checked the result after 24 hours



Before: Cancer Cells exist



After: Cancer Cells disappeared after 24 hours

### I. Apoptosis Proof of Apoptosis-Inducing Activity

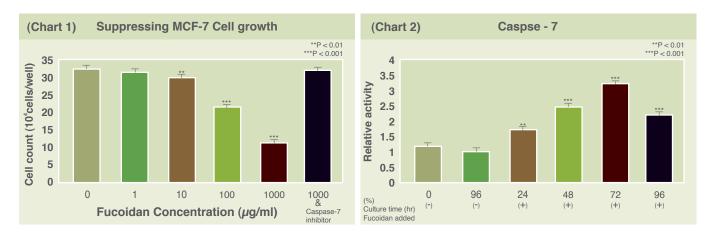
We examined how Mozuku derived Fucoidan would affect apoptosis induction on the growth of human breast cancer cell strains (MCF-7).

#### Method of experiment

Mozuku derived Fucoidan and Mozuku derived Fucoidan prepared with caspase-7 inhibitors were added to human breast cancer cell strains (MCF-7), and the cells were cultured. As a control, nothing was added to the culture. (Chart 1)

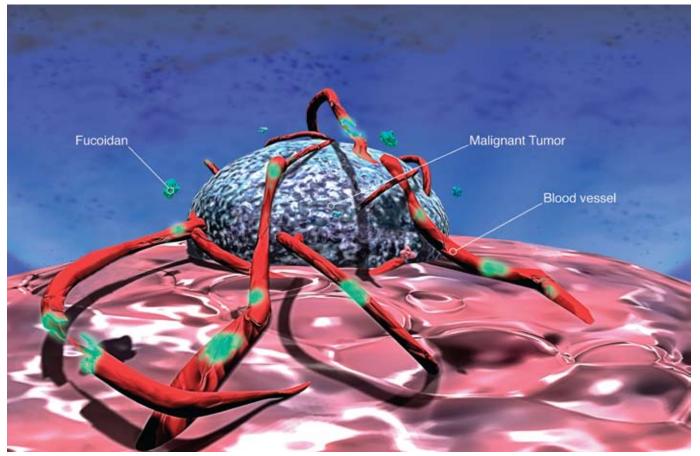
We examined the activation of caspase-7 after Fucoidan was added to the cultured cells. (Chart 2)

**Caspase:** Caspase-7, apoptosis-related cysteine peptidase. Caspase-7 is a member of the caspase (cysteine aspartate protease) family of proteins, and has been shown to be an executioner protein of apoptosis. Sequential activation of caspases plays a central role in the execution-phase of cell apoptosis. Caspases exist as inactive proenzymes which undergo proteolytic processing by upstream caspases (caspase-8, -9) at conserved aspartic residues to produce two subunits, large and small, that dimerize to form the active enzyme in the form of a heterotetramer.



EFFECTS OF MOZUKU DERIVED FUCOIDAN INDUCING APOPTOSIS Once Fucoidan was presented to the cancer cells; human breast cancer cells had a decrease of density dependence. When Fucoidan 1000μg was presented to human breast cancer cells, cancer cells were decreased, however breast cancer cells did not change when Fucoidan 1000μg with caspase-7 inhibitor was presented. (Chart 1) Therefore we thought that Mozuku derived Fucoidan induced apoptosis activating caspase-7. So, then we measured caspase-7, caspase-7 was activated by Fucoidan.(Chart 2)

### II. Angiogenesis Inhibition Activity



(Angiogenesis inhibition image: Formation of new blood vessel is inhibited by Fucoidan to prevent metastasis of cancer cells)

### How does Angiogenesis inhibition help us?

Angiogenesis means formation of new blood vessels from existing blood vessels. When we are injured, angiogenesis occurs to heal the wound. However, angiogenesis is also occurring in the process of growth of cancer cells. Cancer cells try to form blood vessels to obtain oxygen and nutrients they need to grow. If angiogenesis is inhibited, cancer cells cannot form new vessels and thus cannot grow. Also, it has been shown that cancer cells metastasize by utilizing new blood cells. Therefore, inhibiting angiogenesis prevents metastasis of cancer cells.

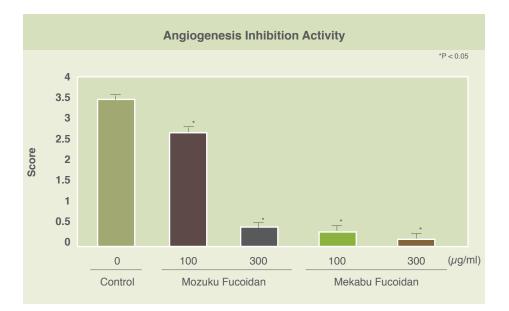
### II. Angiogenesis Inhibition Activity

### Proof of Angiogenesis Inhibition

We verified the Angiogenesis-inhibiting activity of Mozuku-derived Fucoidan and Mekabu-derived Fucoidan using Human Umbilical Vein Endothelial Cells (HUVECs).

#### Method of experiment

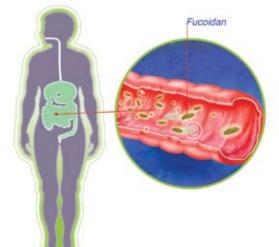
Samples of Mozuku-derived Fucoidan and Mekabu-derived Fucoidan prepared to different concentrations were added to Human Umbilical Vein Endothelial Cells (HUVECs) and the cells were cultured. As a control, Phosphate Buffered Saline (PBS) was added to HUVECs and they were cultured.



EFFECTS OF VARIOUS TYPES OF FUCOIDAN ON ANGIOGENESIS INHIBITION

Both Mozuku-derived Fucoidan and Mekabu-derived Fucoidan inhibited Angiogenesis to different degrees according to their concentration. Also, the Angiogenesis-inhibiting activity of Mekabu-derived Fucoidan was greater than that of Mozuku-derived Fucoidan.

### III. Immunity-Enhancing Activity

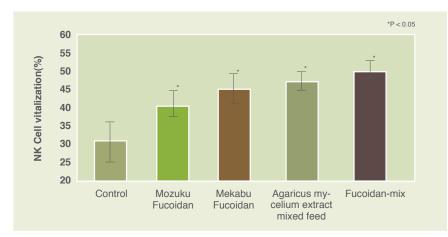


### **Immune Stimulation**

Immune stimulation refers to the stimulation of the immune system by an external source. By increasing the immunity, every living organism can be protected from virus and invasion of foreign particles; therefore they can keep themselves healthy.

### Proof of NK (Natural Killer)-Cell Activation

The NK cell activation triggered by Fucoidan was studied through comparing growth of sarcoma 180 (mouse ascites tumor cells) in BALB/C mice. This test was conducted with five groups of mice, which had been respectively fed, for 23 days, on "control feed", "Mozuku (Cladosiphon okamuranus) Fucoidan mixed feed", "Mekabu (Foot Stem of kelp (Laminaria japonica)) Fucoidan mixed feed", "Agaricus mycelium extract mixed feed", and "Fucoidan-mix feed".



#### EFFFECTIVENESS OF FUCOIDAN-MIX FEED The highest increase in the activity was observed with the Fucoidan-mix fed mice.

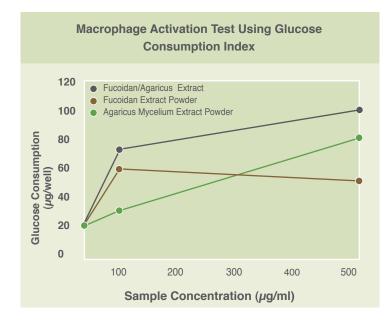
## III. Immunity-Enhancing Activity

### Proof of Macrophage Activation

Macrophage is a phagocyte cell, which has many important immunological functions such as digestion of foreign bodies in the system, meditation and control of immune reactions (e.g. antigen presentation), release of cytokines and oxygen radicals, and inhibition and elimination of tumor cells. Activation of macrophage releases oxygen radicals, and glucose metabolizing system is known to be involved in it. Thus, glucose consumption can be treated as a reasonable index for activation of immune system.

From the result, an increase in glucose consumption by macrophage was obtained; therefore, activation of immune system by Fucoidan was confirmed.

Examination method: We examined the macrophage collected from the abdominal cavity of mice was added to Mozuku and measured quantity of the glucose in the nutrient medium that cultured for four hours.



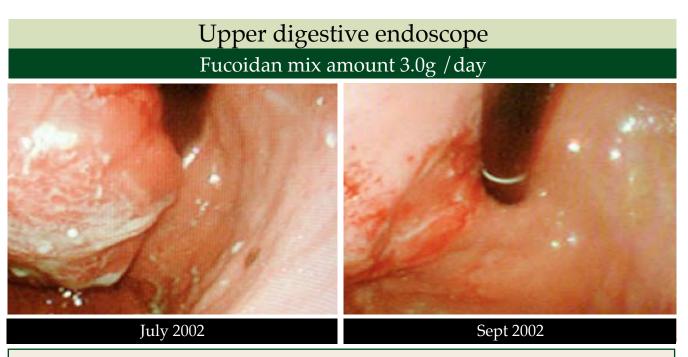
EFFECTIVENESS OF MOZUKU FUCOIDAN AND AGARICUS MYCELIUM POWDER

A mixture of Fucoidan (Fucoidan extracted Mozuku, and Agaricus mycelium) gives higher glucose consumption than when they are taken individually. Therefore, the mixture of Fucoidan and Agaricus has a better ability to activate immune system.

#### Clinical Data Provided by Dr. Daisuke Tachikawa Medical Doctor, Oncologist

### Gastric Cardia Cancer

- Age: 80-year old
- Gender: Male
- Main claim: Hematemesis
- An anamnesis: Cerebral infarction/angina
- Existing medical history: He visited our clinic due to hematemesis in July 2002. The results showed that he had Cardia cancer. He and his family refused to undergo any surgery due to his age and also because he had cerebral infraction and angina. I decided not to use any chemotherapy. Under sufficient concept informed, I performed only Fucoidan mix treatment.



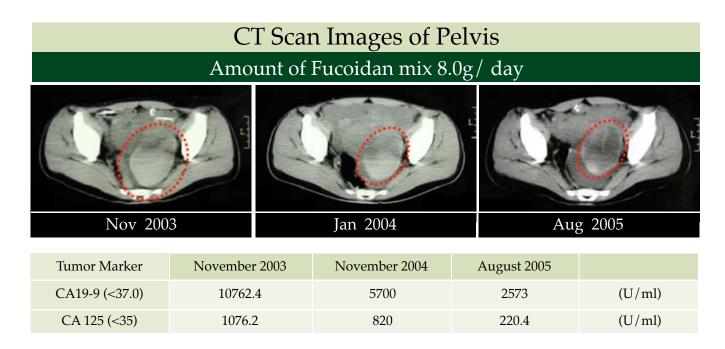
#### **Result:**

After taking Fucoidan mix for 3.0 g per day, his tumor almost disappeared in two months.

Clinical Data
Provided by Dr. Daisuke Tachikawa Medical Doctor, Oncologist

#### Ovarian cancer, cancerous peritonitis, cancerous ascites

- Age: 30-year old
- Gender: Female
- Main claim: Abdominal bloating
- An anamnesis: There is no notice
- Existing medical history: She felt abdominal expansion in October, 2003 and she had a medical examination at a university hospital. She had surgery due to the ovarian cancer, cancerous peritonitis and cancerous ascites. After the surgery, her doctors recommended performing the chemotherapy and radiation therapy, but she refused to do them. Under my sufficient informed concept, I started performing the Fucoidan therapy.



#### **Result**:

Her tumor marker decreased, and tumor size decreased 11cm ~6cm as well.

#### Clinical Data Pro Med

Provided by Dr. Daisuke Tachikawa Medical Doctor, Oncologist

#### Prostate cancer

- Age: 70-year old
- Gender: Male
- Main claim: Total lassitude
- An anamnesis: There is no notice
- Existing medical history: His family doctor diagnosed as the prostate cancer in 2003. His doctor recommended the surgery, but his inflammation was serious, so his doctor postponed his surgery and performed the hormone therapy instead. However his tumor maker was not stabilized and he had very strong side effects due to the hormone therapy. Therefore, his Dr. decided to stop the hormone therapy. He came to my clinic and requested in February, 2004 that he preferred to have the alternative medicine treatment instead of chemotherapy and surgery. Because he wanted to support his male sex organs I performed a treatment with the Mix Fucoidan and Didzen rich isoflavon agrycon.

Pelvis CT									
Amount of Fucoidan mix 8.0g/day									
July 2004				Sept 2004					
Tumor Marker	February 2004	April 2004	August 2004		Immune function test	April 2004	August 2004		
PSA (<4.0)	10.0	0.96	3.62	(ng/ml)	IL-2R (220~530)	338	356	(U/ml)	

**RESULT:** His PSA decreased from 10.0 to 0.96 and his tumor got smaller on the CT scan. His quality of life was kept without losing the function of his male sex organs.

Clinical Data

Provided by Dr. Daisuke Tachikawa Medical Doctor, Oncologist

### Liver cancer / Hepatitis C

- Age: 70-year old
- Gender: Male
- Main claim: Total lassitude
- An anamnesis: There is no notice
- Existing medical history: He claimed total lassitude and visited his family doctor. His doctor diagnosed as the liver cancer and C-typed hepatitis in March, 2004. He refused his doctor suggestion that he undergo surgery or transarterial embolization (TEA) and hepatic arterial infusion. He visited my clinic as a second opinion and I gave the same suggestion that his doctor did, but he and his family refused it and I started performing the Fucoidan therapy under my sufficient informed concept.

Abdomen CT										
Fucoidan 2.5g/day			Fucoidan 2.5g/day			I	Fucoidan 4.0g/day			
June 2004			Jan 2005			July 2005				
Tumor Marker	April 2004	June 2004	July 2005		Lab Test	April	2004	June 2004	July 2005	
AFP(<10.0)	20.3		44.6	(ng/ml)	GOT/GPT (10~40/5~40)	135,	/214	49/68	35/57	(IU/ml)
PIVKA_II (<35)	8430	1600	119	(mAU/ml)	γ-GTP (<70)	1	12	77	78	(IU/ml)

**RESULT:** His GOT/GPT. PIVKA-II dropped sharply with one month intake of Fucoidan, and January 2005 after 10 months have passed, the tumor size had not changed on CT scan and the liver function level was normal as well. In May 2005, his tumor got larger, so I decided to increase Fucoidan mixed amount as 4 g per day, after that his tumor shrunk dramatically and became the condition of PR (partial response).

## Clinical Data Provided by Dr. Daisuke Tachikawa Medical Doctor, Oncologist

### Left side Breast Cancer/Metastasized to Lung /Cancerous Peritonitis

- Age: 60-year old
- Gender: Female
- Main claim: There is no notice
- An anamnesis: Heterologous mastectomy Stage IV (in 2001)
- Existing medical history: Performed the left side heterologous mastectomy to the left side of her breast where she had the cancer. She was then followed by 6 crews of chemotherapy (CMF) and her doctors noticed that her progress was not good. Later I not only found her cancer was metastasized to lung in April 2002, but also examined the complication of pleuritis due to hydrothorax. At that time, her hydrothorax cytodiagnosis was class V. I changed the chemo-medication to Taxol starting in June, but she started losing her appetite. Therefore, I decided to start the Fucoidan treatment under her and her family's authorization.

Chest X-ray								
Fucoidan mix amount 4.0g/day								
	June 2002 C	Class V	Aug 2002	Class I				
Tumor Marker	July 2002	August 2002	September 2002					
CEA (<5.0)	264	235	187	(ng/ml)				
NCC-ST-439(<7.0)	110	120	79	(U/ml)				
CA15-3 (<25.0)	110	130	97	(U/ml)				
<b>RESULT:</b> Once she started the Fucoidan treatment, we noticed an increased in her								

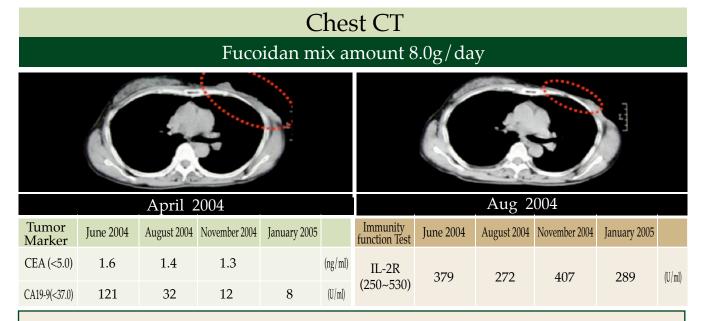
**RESULT:** Once she started the Fucoidan treatment, we noticed an increased in her appetite after 2 crews of chemotherapy. There was a decrease in her hydrothorax and her hydrothorax cytodiagnosis became class I.

Clinical Data

Provided by Dr. Daisuke Tachikawa Medical Doctor, Oncologist

#### Left Breast Cancer / Metastasis Breast cancer (right)/Both side neck/ Under Clavicle/metastasized to Axillary lymph nods

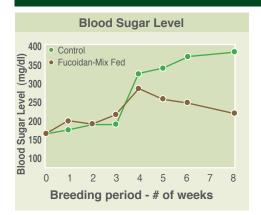
- Age: 40-year old
- Gender: Female
- Main claim: Left side breast had a bump
- An anamnesis: There is no notice
- Existing medical history: She noticed a bump on her breast and she had a mammography at the hospital. She visited my clinic before knowing the results because she wanted to know about Fucoidan. I examined her and her results showed that she had cancer on her left breast. The cancer had already metastasized to her right breast, both side necks, under clavicle and axillary lymph nodes. She requested to be treated by only Fucoidan mix treatment, but I performed her treatment with Fucoidan and chemotherapy (Taxol) because it could be more effective when treating her cancer. Also, I performed hyperbaric oxygen therapy to her to get better results.



**RESULT:** After 6 cycles of chemotherapy, I noticed a change in the tumor marker and no metastasis in tumor to any other organs. We also recognized shrinking of the original tumor in the breast and in the metastasized lymph nodes, as well as disappearance of right and left sides of lymph edema.

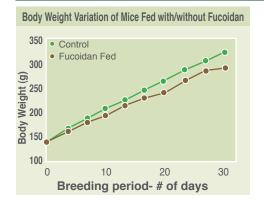
## Other Fucoidan Benefits

### Fucoidan Suppressing Blood-Sugar Level



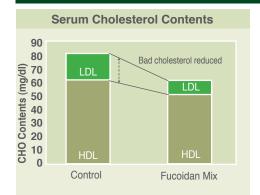
Influences of Fucoidan on blood-sugar level were investigated by use of enzyme electrode method. Two groups of KK-Ay mice (model mice for high blood-sugar/diabetes) were bred on an ordinary feed and a Fucoidan-mix feed, respectively. Blood-sugar level was substantially suppressed in the Fucoidan-mix fed mice. (Collaboration of Kagoshima University and NPO Fucoidan Research Center)

### Fucoidan Weight Control Effectiveness



In order to investigate influences of Fucoidan on fats, two groups of Wister/ST mice were bred on an ordinary feed and a Fucoidan-mix feed, respectively for 1 month. Their body weights, fat tissue contents were compared. A significant reduction of body weight can be seen in Fucoidan fed mice. (Collaboration of Kagoshima University and NPO Fucoidan Research Center)

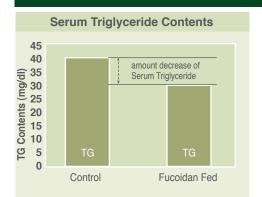
#### Fucoidan Serum Cholesterol Effectiveness



In order to investigate influences of Fucoidan on serum cholesterol, two groups of Wister/ST mice were bred on an ordinary feed and a Fucoidan-mix feed, respectively. Their serum cholesterol contents were compared. We found Fucoidan fed mice had reductions in both LDL (Lower Density Lipoprotein-cholesterol). Comparing with HDL cholesterol and LDL cholesterol, reduction of LDL cholesterol became larger than HDL. (Collaboration of Kagoshima University and NPO Fucoidan Research Center)

## Other Fucoidan Benefits

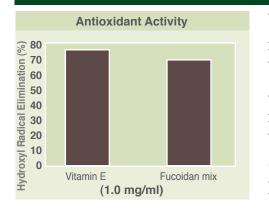
### Fucoidan Influence to Serum Triglyceride



In order to investigate influences of Fucoidan on serum Triglyceride, two groups of Wister/ST mice were bred on an ordinary feed and a Fucoidan-mix feed, respectively. Their serum triglyceride contents were compared. Reductions TG (TriGlyceride) were observed in Fucoidan fed mice.

(Collaboration of Kagoshima University and NPO Fucoidan Research Center)

### Fucoidan Antioxidant Effect



When we evaluated the comparison of hydroxyl radical elimination activity between Fucoidan mix and Vitamin E which is known as an anti-oxidizer generally by Hyaluronic acid Oxidation Method, Fucoidan mix showed almost the same antioxidant effect with Vitamin E.

(Collaboration of Kagoshima University and NPO Fucoidan Research Center)

### Other Benefits

- Anti- Coagulation
- Skin moisturizing Effect
- Prevention of Rise in Blood Pressure
- Improvement in Intestinal Environment
- Anti-Helicobacter Pylori Activity
- Anti-Ulcer Activity
- Enhancement of Hepatic Functions
- Relieving Effect on Allergic Activities (Hay Fever, Atrophy, etc.)

- Anti-HIV Activity
- Hair-Growth Effect
- Anti-Viral, Anti-Bacterial Activity

### I. Apoptosis-Inducing Activity

## **1** Bao S, Li Y, Lei X, Wohltmann M, Jin W, Bohrer A, Semenkovich CF, Ramanadham S, Tabas I, Turk J.

Attenuated Free Cholesterol Loading-induced Apoptosis but Preserved Phospholipid Composition of Peritoneal Macrophages from Mice That Do Not Express Group VIA Phospholipase A2. J Biol Chem. 2007 Sep 14;282(37):27100-14. Epub 2007 Jul 12. PMID: 17627946 [PubMed - in process]

#### **2** Maruyama H, Tamauchi H, Iizuka M, Nakano T.

The role of NK cells in antitumor activity of dietary Fucoidan from Undaria pinnatifida sporophylls (Mekabu). Planta Med. 2006 Dec;72(15):1415-7. Epub 2006 Oct 20. PMID: 17054048 [PubMed - indexed for MEDLINE]

#### **3** Johnson JD, Hess KL, Cook-Mills JM.

CD44, alpha(4) integrin, and fucoidin receptor-mediated phagocytosis of apoptotic leukocytes. J Leukoc Biol. 2003 Nov;74(5):810-20. Epub 2003 Aug 11. PMID: 12960273 [PubMed - indexed for MEDLINE]

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Apoptotic neutrophils are phagocytosed by fibroblasts with participation of the fibroblast vitronectin receptor and involvement of a mannose/fucose-specific lectin. J Immunol. 1994 Oct 1;153(7):3218-27. PMID: 7522254 [PubMed - indexed for MEDLINE]

### II. Angiogenesis Inhibition Activity

#### **1** Boisson-Vidal C, Zemani F, Caligiuri G, Galy-Fauroux I, Colliec-Jouault S, Helley D, Fischer AM.

Neoangiogenesis induced by progenitor endothelial cells: effect of Fucoidan from marine algae. Cardiovasc Hematol Agents Med Chem. 2007 Jan;5(1):67-77. Review. PMID: 17266549 [PubMed - indexed for MEDLINE]

#### **2** Matsubara K, Xue C, Zhao X, Mori M, Sugawara T, Hirata T.

Effects of middle molecular weight Fucoidans on in vitro and ex vivo angiogenesis of endothelial cells. Int J Mol Med. 2005 Apr;15(4):695-9. PMID: 15754034 [PubMed - indexed for MEDLINE]

## **3** Eichhorn ME, Strieth S, Krasnici S, Sauer B, Teifel M, Michaelis U, Naujoks K, Dellian M.

Protamine enhances uptake of cationic liposomes in angiogenic microvessels. Angiogenesis. 2004;7(2):133-41. PMID: 15516834 [PubMed - indexed for MEDLINE]

### III. Immunity-Enhancing Activity

#### **1** Pierini LM.

Uptake of serum-opsonized Francisella tularensis by macrophages can be mediated by class A scavenger receptors. Cell Microbiol. 2006 Aug;8(8):1361-70. PMID: 16882038 [PubMed - indexed for MEDLINE]

#### **2** Hirayasu H, Yoshikawa Y, Tsuzuki S, Fushiki T.

Sulfated polysaccharides derived from dietary seaweeds increase the esterase activity of a lymphocyte tryptase, granzyme A. J Nutr Sci Vitaminol (Tokyo). 2005 Dec;51(6):475-7. PMID: 16521710 [PubMed - indexed for MEDLINE]

#### **3** Choi EM, Kim AJ, Kim YO, Hwang JK.

Immunomodulating activity of arabinogalactan and Fucoidan in vitro. J Med Food. 2005 Winter;8(4):446-53. PMID: 16379554 [PubMed - indexed for MEDLINE]

#### 4 Zhang Z, Guo K, Schluesener HJ.

The immunostimulatory activity of CpG oligonucleotides on microglial N9 cells is affected by a polyguanosine motif. J Neuroimmunol. 2005 Apr;161(1-2):68-77. PMID: 15748945 [PubMed - indexed for MEDLINE]

### IV. Anti-Cancer Activity by Fucoidan

#### Colon cancer

Stimulation of macrophages by mucins through a macrophage scavenger receptor. Inoue M, Fujii H, Kaseyama H, Yamashina I, Nakada H. PMID: 10527877 [PubMed - indexed for MEDLINE]

#### 2 Breast cancer

Fucoidan induces apoptosis through activation of caspase-8 on human breast cancer MCF-7 cells. Yamasaki-Miyamoto Y, Yamasaki M, Tachibana H, Yamada K. PMID: 19754176 [PubMed - indexed for MEDLINE]

#### Lung cancer

Blocking of lectin-like adhesion molecules on pulmonary cells inhibits lung sarcoma L-1 colonization in BALB/c-mice. Roszkowski W, Beuth J, Ko HL, Uhlenbruck G, Pulverer G. PMID: 2737266 [PubMed - indexed for MEDLINE]

#### 4 Lymphoma

Sulfated polysaccharides inhibit lymphocyte-to-epithelial transmission of human immunodeficiency virus-1. Pearce-Pratt R, Phillips DM. PMID: 8838015 [PubMed - indexed for MEDLINE]

#### 5 Leukemia

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.

PMID: 16201850 [PubMed - indexed for MEDLINE]

#### 6 Melanoma

Laminin-dependent and laminin-independent adhesion of human melanoma cells to sulfatides. Roberts DD, Wewer UM, Liotta LA, Ginsburg V. PMID: 2967105 [PubMed - indexed for MEDLINE]

## Frequently Asked Questions

### Q1 How much Fucoidan should I take each day?

▲ To maintain health on a daily basis, it is generally recommended to take at least one gram per day. If you have "lifestyle-related" health concerns such as diabetes or high blood pressure and want to improve the conditions related to that ailment, take at least two or three grams a day. If you have cancer or other serious diseases, it is recommended that your daily dose be a minimum of 2-8 grams.

## Q2 What is the best way to maximize the fighting action of Fucoidan?

To maximize the fighting action of Fucoidan, it is recommended to take the product four times a day: in the morning, at noon, in the evening, and before sleep. The body's natural immunity is greatest during the daytime when we are active but it decreases when the body is at rest (while we sleep). Contrastingly, malignant cells are most active when the body is at rest. So, it's very important to take Fucoidan before going to bed. Don't worry about consuming too much Fucoidan as it is essentially the same as eating seaweed.

### Q3 Are there any side effects when taking Fucoidan?

Fucoidan, unlike chemically synthesized drugs, consists of natural ingredients such as Mozuku and Mekabu. So you can take as much as you want without worry. Over 10 years have passed since the product was introduced to the market, but no major side effects have been reported.

Of course, Fucoidan contains seaweed, which is a rich source of fiber, so taking it in excessive amounts may make your stool softer than usual. However, this is only a temporary condition, and after a while you will return to normal regularity.

## Frequently Asked Questions

### Q4 Can I take other drugs while I take Fucoidan?

Remember, Fucoidan is not a drug. It is a natural ingredient found in Mozuku (Cladosiphon okamuranus) and Mekabu (the pleated section of Wakame – Undaria pinnatifida). There should be no harmful effect when taking prescribed drugs together with Fucoidan, since it would be the same as taking those drugs after eating seaweed.



If you have any questions about Fucoidan,

please send an e-mail to info@k-fucoidan.com or call us at

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Most of the information in this catalog is provided by \*NPO Research Institute of Fucoidan in Japan.

Effectiveness and benefits of Fucoidan described in this cataglog doesn't prove the effectiveness and benefits of Umino Shizuku Fucoidan. \*NPO Fucoidan Research Lab is a Japanese nonprofit organization that has studied and researched Fucoidan on the possibility of self-healing power of Fucoidan. Their study has mainly focused on using Fucoidan to reinforcement of the self-healing (immunity power) that a human being basically has.



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