Treasures of the Sea and Land

By Hiroshi Ito, Ph.D.

- Fucoidan
- Agaricus Blazei Murrill

Contents

Fucoidan

What is Fucoidan?
The island of Okinawa, in Japan, is the best place on earth for healthy aging.
The Okinawans have:

•more people over 100 years old per 100,000 population than anywhere else in the world

•the lowest death rates from cancer, heart disease and stroke (the top three killers in the US)

•the highest life expectancy for both males and females over 65

•females in Okinawa have the highest life expectancy in all age groups

Added to their healthy diet, Okinawans have the highest per capita consumption of sea vegetables as mozuku, kombu, wakame etc.

What is Mekabu?

Wakame is a variety of seaweed that has been consumed in Japanese homes since ancient times in soups as miso soup, salads and stews.

Immunity related studies found that regions in Japan where highest amount of wakame are consumed had the lowest stroke rate in the population.

Mekabu is the flowering part of wakame seaweed. The ruffled, flowering sprout of wakame just above the root It has a sticky feel to it and has a mellow sweet flavor.

For the longest time, this part of Wakame seaweed was ignored as a less favored food ingredient but eventually, it was found that Mekabu is indeed a treasure chest of nutrients, extremely rich in a functional compound called Fucoidan.

Fucoidan is a sulfated polysaccharide found mainly in various species of brown algae and brown seaweed such as wakame, mozuku and kombu amongst other varieties of sea vegetables. In the seaweed, Fucoidan is the slimy substance that serves to restore and protect the plant from unwanted microorganisms as well as preventing moisture loss to the elements.

With over 900 studies found on Pub Med and interest from the pharmaceutical industry, Fucoidan is one of the most intriguing and powerful supplements on the market.

Fucoidan Benefits

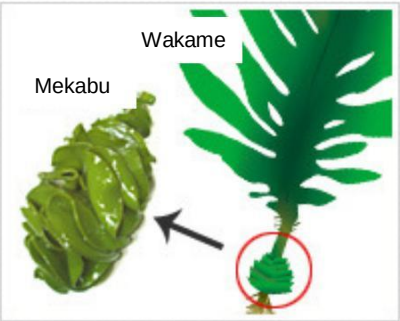
Scientific studies have shown that the continuous Fucoidan ingestion supports the increase in number of our NK cells (natural killer cells) and Killer T-cells which are some of the most important defense cells against cancer and various infectious diseases.

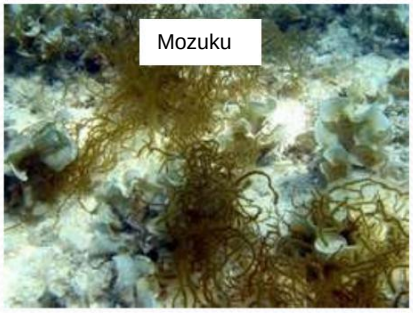
Added to this, Fucoidan also plays an important part in supporting the activity of macrophages and preventing the spread and development of cancer cells.

Another important benefit of Fucoidan is the suppression of allergic reactions.

Asthma, pollen and dust allergies, atopic dermatitis and food allergies basically occur as an excessive reaction to substances. Fucoidan, in these cases work as an immune modulator harmonizing and normalizing the responses of our immune system.

Studies also show that Fucoidan have antiviral and UV protecting properties as shown throughout the following notes.





Fucoidan from Mekabu and Fucoidan from Mozuku

Different kinds of Fucoidan vary in its polysaccharide structure composition and have different kinds of functionality.

Substance	Functionality Report
Mekabu	Immune modulation Macrophage function activation NK cells activation IFN-γ, IL-12 creation Killer T cell activation Anti allergic function IgE production control IL-4, IL-5, IL-13 production control Eosinophil control Pollen allergy relief Anti-tumor function Anti-virus Anti body production support Virus multiplication control Protozoan infection prevention Suppression of Angiogenesis
Okinawa Mozuku	Anti-tumor function Anti allergic function Helicobacter Pylori control Anti ulcer function Apoptosis

Apoptosis

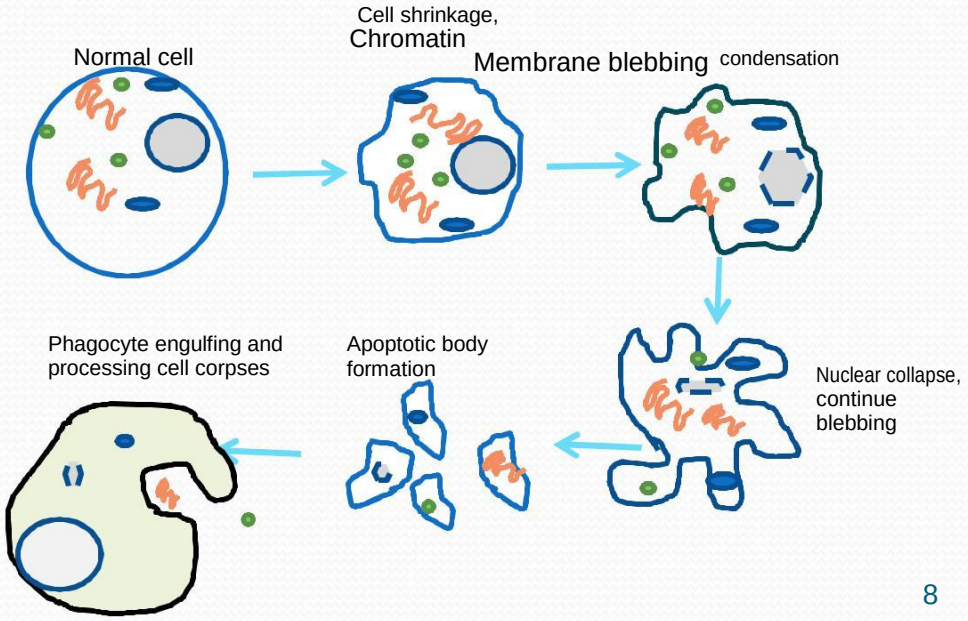
Leading Universities in Japan as Keio and Fukuoka Universities as well as the National Cancer Center amongst other study centers have researched and found that Fucoidan showed unique functionality in cancer cases.

It was found that Fucoidan , a polysaccharide rich in monosaccharide βGlucan, contains a high percentage of sulfates in its constitution compared to other brown algae. Innumerous studies showed that Fucoidan in fact, induces apoptosis , supports the immune system and suppresses angiogenesis of cancer cells.

Apoptosis is a pattern of cell death affecting single cells, marked by shrinkage of the cell, condensation of chromatin, and fragmentation of the cell into membrane-bound bodies that are eliminated by phagocytosis. Often used synonymously with programmed cell death. It is a natural trait carried by all living cells and necessary for the cycle of life. However in cancer cells, apoptosis does not occur naturally. Cancerous cells continue on multiplying indefinitely. That's what makes cancer cells so harmful and difficult to treat.

Fucoidan activates an apoptosis inducing enzyme in the cancerous cell, starting the self destruction process.

Apoptosis Illustration



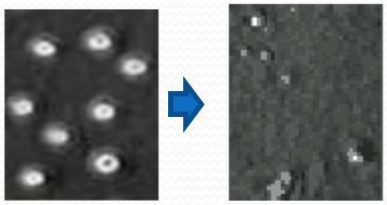
Apoptosis Research

Dr. Nobuo Fujii (specialist in food functionality science) from the University of Kagoshima conducted the following experiment to identify the effect of Fucoidan on apoptosis in cancer cells.

2 types of cancer cells were utilized: HL60 (Human promyelocytic leukemia cells) and NOS4 (cultured human ovarian tumor cell). Mekabu Fucoidan and Mozuku Fucoidan were added to Culture plates and Apoptosis effect were observed. When apoptosis occur, there is DNA fragmentation. Using Electrophoresis method, the percentage of DNA fragmentation was determined proving the efficacy of Fucoidan in inducing apoptosis in cancerous cells.

This experiment results were reconfirmed by the Bio-oriented Technology Research Advancement Institution, a Ministry of Agriculture, Forestry, and Fisheries and Ministry of Finance authorized juridical institution and the Glico engineering research institute of Aomori prefecture in 1996.

Dr. Amano research analyst of Sea greens from Mie University together with Dr. Taguchi, a molecular cell biologist professor conducted an experiment using human cancerous cell in culture solution. To this, Fucoidan extract in a physiological solution was added and studied. This mixture was observed in a controlled temperature of 37 C for 24 hours. A surprising result was found. Most cancer cells in this solution showed the outline of the cell had collapsed after a few hours. After 24 hours, almost all the cancer cell had died and in the following hours, dead cancer cells have even faded in the solution.



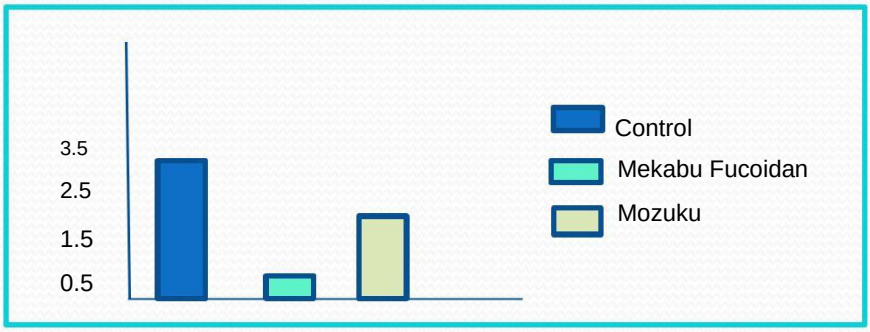
48 hours later

Angiogenesis

In the tumor growth process, cancer cells need more and more nutrients. This is where angiogenesis comes into play. Tumor angiogenesis is the proliferation of a network of blood vessels that penetrates into cancerous growths, supplying nutrients and oxygen and removing waste products. Tumor angiogenesis actually starts with cancerous tumor cells releasing molecules that send signals to surrounding normal host tissue. This signaling activates certain genes in the host tissue that, in turn, make proteins to encourage growth of new blood vessels. With new blood vessels in place, it becomes easy for cancer to grow and spread or metastasize to other parts of the body.

Studies throughout the international medical community and specifically by Riken labs in Japan have shown that in in vivo experiments, patients who were administered Fucoidan have a slower rate of cancer advancement which shows that angiogenesis is suppressed with the use of Fucoidan

In vitro angiogenesis test using endothelial cells. The higher the score, the higher is the rate of new vessels formation.

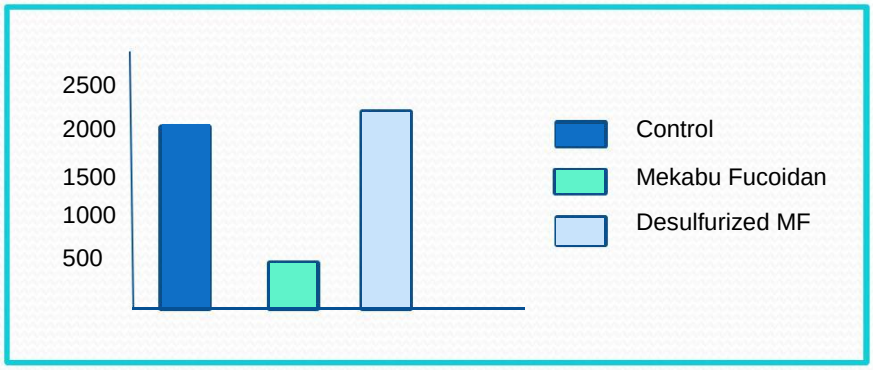


Immune support

At the same time, it was also found that Fucoidan boost immune response of NK (natural killer) cells and T cells. Activated, all immune cells including macrophages and lymphocytes work together attacking foreign microorganisms and tumor cells which are unnatural to the body.

Fucoidan was also shown to be effective in controlling and suppressing the growth of various strands of viruses as influenza, avian influenza and herpes simplex at Kobe International Immunology symposium in Japan in 2010.

Virus concentration in Bronchoalveolar lavage (BAL) 3 days after infection with influenza virus in mice.



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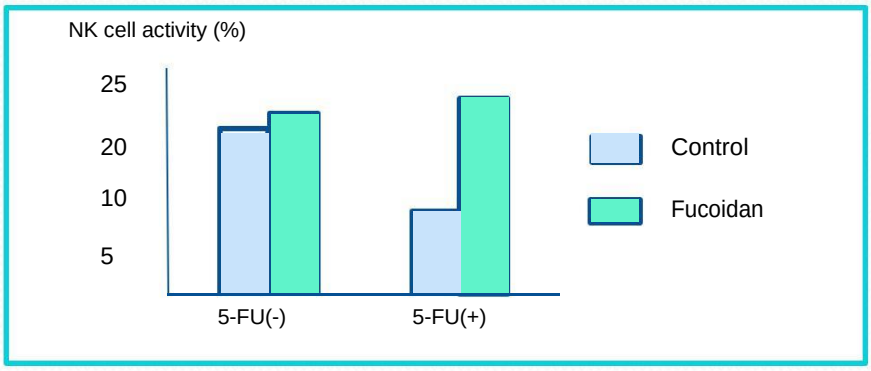
Immune protection against side effects of chemo

5FU also known as Fluorouracil is a chemotherapy drug for some types of cancer such as bowel, breast, stomach, pancreas and gullet (esophagus) cancer. One of the side effects of administering this drug is the lowering of immunity with decrease in the number of NK cells. Riken experimented the effects on NK cells in mice which were fed Fucoidan in a 7 days research. The results as seen below, showed that NK cell activity rate in the group fed with Fucoidan actually increased in the presence of 5-FU. In the stage where the immune system is working normally (5FU-), Fucoidan shows no notable activity but when 5FU lowers the immune system (5FU+), Fucoidan fed group show active NK cell preservation and enhancement.

Immune support

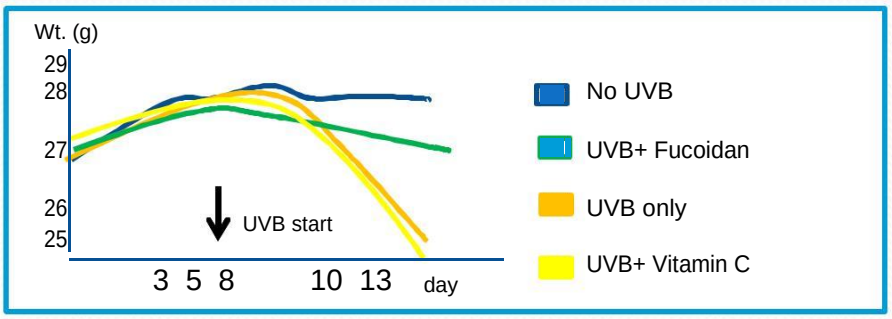


UVB protection

Riken Labs in Japan realized an extensive experiment aiming to reveal the benefits of Fucoidan in protecting the skin and immune system against harmful UVB rays.

UV rays cause well known skin damage and when this damage is repeated, skin DNA is injured resulting in skin cancer. It is also known that UV rays also lower the immune system and affect the vision.

In a experiment using BALB/c mice, it was proven that the exposure to UVB weakens the immune system, causing considerable weight loss. Mice that were exposed to UVB but were fed Fucoidan, showed minimal weight loss proving Fucoidan effectiveness against immune depression.



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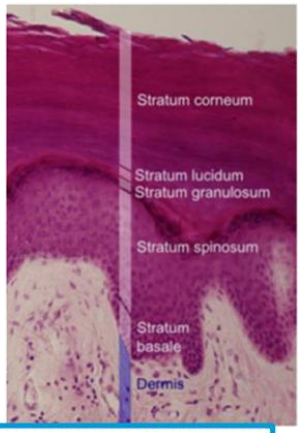
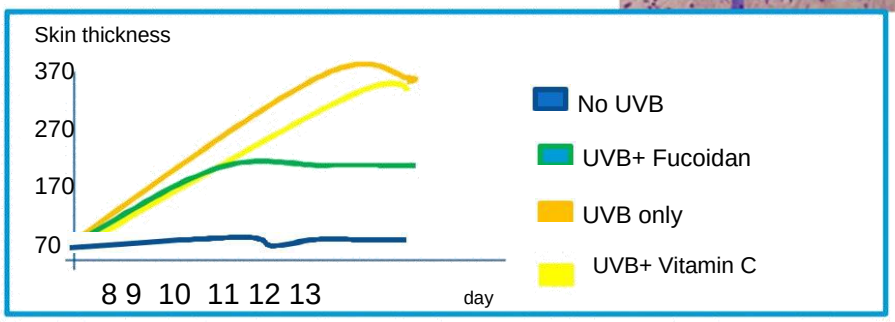
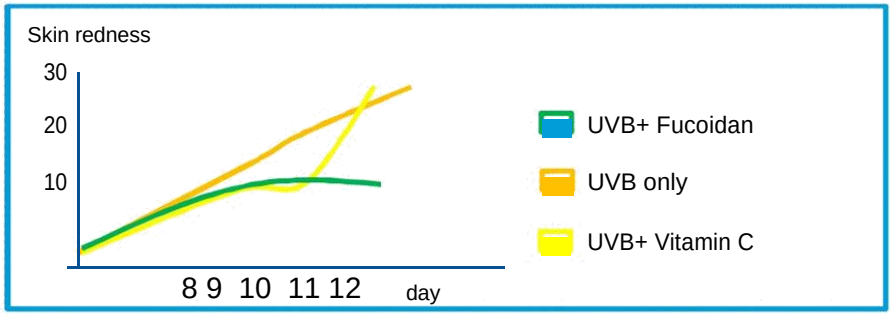


In the same research, it was found that Fucoidan also plays a role in preventing skin redness and thickening (stratum spinosum) due to UV exposure. BALB/c mice were exposed to UVB for 5 days .

As seen in the results below, Mice fed with Fucoidan showed better results than those without any dietary addition and even those which were fed vitamin C.





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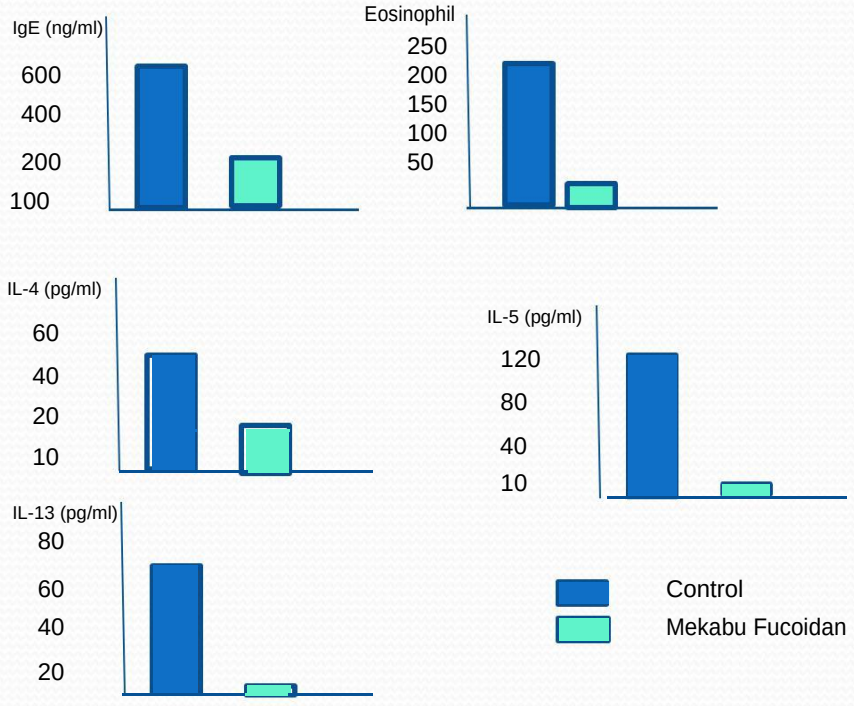
Anti Allergic

An allergy is a hypersensitivity disorder of the immune system. Allergic reactions occur when a person's immune system reacts to normally harmless substances in the environment. A substance that causes a reaction is called an allergen. Allergic reactions are distinctive because of excessive activation of certain white blood cells called mast cells and basophils by a type of antibody called Immunoglobulin E (IgE). This reaction results in an inflammatory response which can range from uncomfortable to dangerous.

In various studies on allergen response with mice after 4 days feeding them Fucoidan, it was detected much lower IgE, Eosinophil granulocyte, IL-4, IL-5, IL-13 levels when allergens were introduced showing its efficacy in suppressing allergic reaction in cases of hay fever, atopic dermatitis and asthma.



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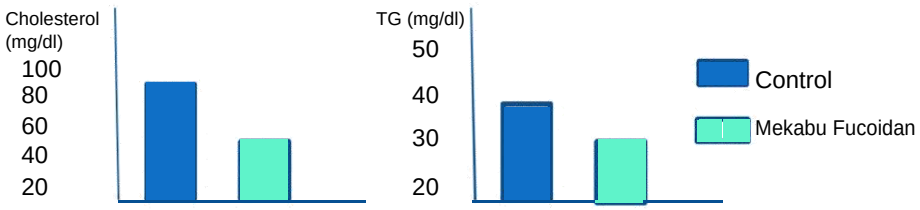
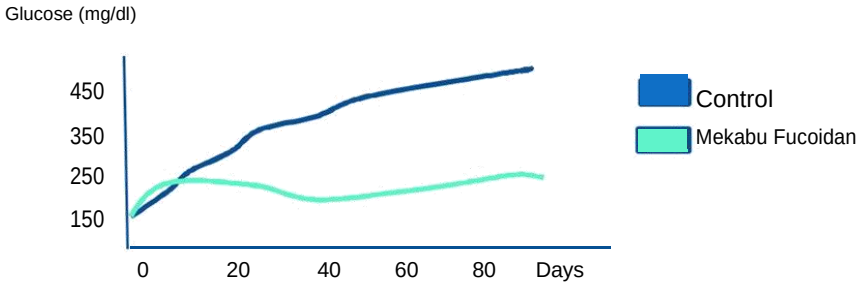
Controlling Cholesterol and Diabetes

Dr. Fujii from the University of Kagoshima confirmed in his animal research that Fucoidan is effective in curbing cholesterol and triglycerides levels. One group of rats were fed Fucoidan added to the regular diet for 1 month while the second only received regular diet. Fucoidan absorbs fats that are ingredients for cholesterol and triglycerides in intestines and carry them out as feces. Cholesterol is made from bile acid recollected from the intestines. Fucoidan also absorbs this bile acid further preventing the production of cholesterol in the liver. Also, Fucoidan was found to reduce the formation of thrombus thus supporting healthy blood flow.



In another study, regarding diabetes and blood sugar levels, Dr. Fujii found that Fucoidan actually slowed the speed of food transported in the intestines also slowing the absorption rate of glucose and controlling the spike in blood sugar level after meals. Less insulin is needed giving time for the pancreas to recuperate.



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AGARICUS BLAZEI

Agaricus Blazei Murill (Hime-matsutake) is a fairly new species of mushroom that has attracted the attention of many scientists in the world.

It grows spontaneously in Piedade highlands of southeastern Brazil, where it is known as "Cogumelo de Deus" or Mushroom of Gods. Due to the special conditions of air, soil, moisture and high temperature, its cultivation has only been possible a few decades ago and is now practiced in Japan and some parts of South America and China. Conditions for growth of this mushroom are high temperature, much humidity, purified air, soil containing wild horse droppings, little rain in the evenings.

Artificial cultivation of this Brazilian mushroom was achieved for the first time in the world by Iwade Fungology Institute (founder: Dr. Inosuke Iwade, a professor at Tokyo University and Mie University) after many trials and errors. This mushroom was presented by professors Hitoshi Ito, Keishiro Shimura and Sensuke Naruse of mushroom research group at Mie University medical school as a highlight at the "the 39th General Meeting of Japanese Cancer Academy" in 1980

Agaricus Blazei Murrill is a unique type of mushroom that has immunomodulation (adjustment of the immune response to a desired level, as in immunopotentiation, immunosuppression, or induction of immunological tolerance.) properties. Modulation is partly caused by a group of extremely efficient immune-stimulants: Beta-1,3-D-glucans and Beta-1,6-D-glucans which are very active constituents. There are also other immune-modulating substances such as proteo-glucans and estradiol. Agaricus Blazei Murill extracts, similar to glucans, enhance innate immunity by targeting immune cells such as macrophages, monocytes, dendritic cells, polymononuclear leukocytes and NK (natural killer) cells. The glucans in Agaricus are potent activators of these phagocytic cells.

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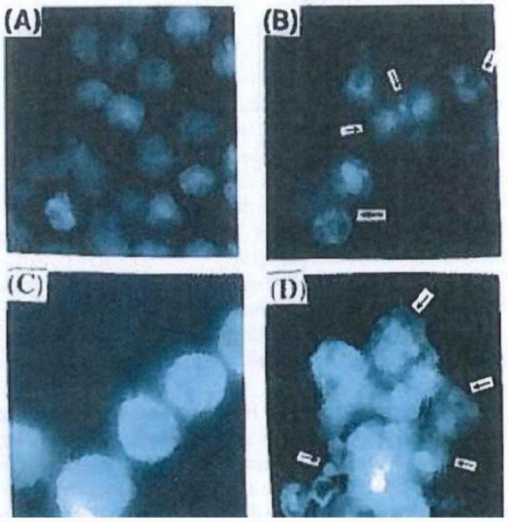
Studies by professor Hiroshi Itoh of Mie Medical University in Japan and Head of Pharmacological Fungi Research lab, showed the benefit of Agaricus Blazei Murrill in inducing apoptosis in Lung, Stomach and colon cancer cells, as well as in diminishing the side effects of chemotherapy

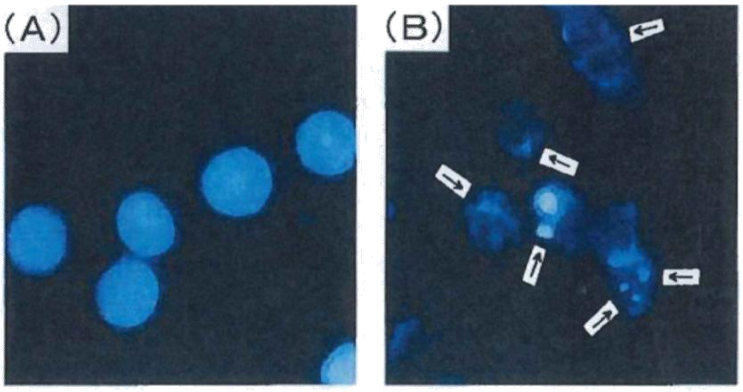
Blazein of a new steroid isolated from Agaricus Blazei Murrill (himematsutake) induces cell death and morphological change indicative of apoptotic chromatin condensation in human lung cancer LU99 and stomach cancer KATOIII cells: Hiroko Itoh, Hitoshi Ito and Hiroshige Hibasami (faculties of Bioresources and medicine, Mie University, Mie 514-0033, Japan, research Institute of Mycology and Pharmacology, Mie 514-0033, Japan



A) Non treated LU99 cells
B) LU99 cells treated with 200 µM Blazein
C) Non treated KATOIII cells
D) KATOIII cells treated with 300 µM Blazein

Apoptotic DNA fragmentation was observed in both cases. Arrows indicate apoptotic cells

Induction of apoptosis by Blazein of a new steroid isolated from Agaricus Blazei Murrill (himematsutake) in human colon cancer COLO201 cells. Hiroko Itoh, Masaki Fujishima, Yukari Arakawa, Hiroshige Hibasami, Fukuyoshi Nakata, Hitoshi Itoh. Laboratory of marine Biochemistry, Faculty of Biosources, Mie University, Sun Chlorella Corp., research and development, Faculty of Medicine. School of Nursing, Mie University, Powerful Healthy Food Corp., Research Institute of Mycology and Pharmacology



A) Non treated COLO201 cells
B) COLO201 cells treated with 200 µM Blazein

Dr. Hiroshi Ito from Mie prefecture, Japan, together with many other scientists have already announced and published over 70 research results on Agaricus Blazei Murrill. Dr. Ito is the responsible scientist who developed Iwade strain 101 which contains the highest amounts of effective constituents.

Agaricus (Himematsutake) originally comes from the outskirts of Sao Paulo, Brazil. The Iwade 101 seed strain was brought to Japan in 1965 and required 10 years to be successfully developed and cultivated.

Agaricus fruiting bodies contain-(13)-D-glucan, -(16)-D-glucan protein complexes and RNA-protein complexes, which help maintain health, and mycelia section contain glucomannan. In addition to them, it is discovered to be rich in vitamins and minerals, which are necessary for health maintenance. Much research on Agaricus (Himematsutake) has been presented at meetings of the Japan Pharmacological Society and the Japanese Cancer Association.

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Immune Research Results

The polysaccharide-protein complexes called Beta-1,6-D-glucan and an almost identical chemical, Beta-1,3-D-glucan in the Agaricus Blazei Murrill have been found to be remarkable immune stimulants and macrophage as well as interferon, T cells, and natural killer cells activators. Macrophages are our first line of defense and play an important role in our immune response to any attack by any intruder. Macrophages are the immune cells that recognize and destroy any organisms, cells, and substances that don't belong in the body, as in the case of viruses, bacteria, fungi, yeast, heavy metals, pollutants, bits of dead tissue, mutated cells, tumor cells, etc.

Agaricus Blazei Iwade strain 101 has been tested in mice to show effectiveness in enhancing the effectiveness while curbing the side effects of chemotherapy using Endoxan, daunomycin, mitomycin C, Cytarabine and 5-FU.

A study of liver function and Agaricus Blazei Iwade strain 101 showed that rats suffering from viral hepatitis had lower levels of transamilases GOT and GPT (which indicates liver damage levels)

Agaricus was also found to control histamine release in atopic dermatitis cases ,asthma and allergy cases. Although its action is not as strong as regularly sold steroids anti-histamine preparations, Agaricus has no side effects as skin thinning, splitting or rebounds when treatment is interrupted. Through these researches, Agaricus Blazei Murrill was found to be not only enhance immunity but also modulate over active immune responses.

Iwade strain 101 Agaricus Blazei Murrill powder and mycelium powder patents:

1802776 Liver support MP

1802777 Liver support MP

1442648 Anti tumor polysaccharide manufacturing procedure for the fruiting body extract MP

1442647 Anti tumor polysaccharide manufacturing procedure for the mycelium extract MP

2526185 Broken cell wall manufacturing procedure
2814209 Anti cancer MP

3362984 Energy based cell wall breaking technology

6120772 Anti Aids, Aids symptom control (US) MP

EP1002541B1 Anti Aids, Aids symptom control (GB, FR, GER, SW, IT)

MP 3524145 Anti Aids, Aids symptom control (fruiting body extract) (JP)

MP 4010519 Anti Aids, Aids symptom control (Mycelium extract) (JP)

MP 4057107 Glucomannam anti tumor MP 3065590 Substance

activation method

3853724 Functional food

MP: Medical patent

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Hiroko Itoh, Masaki Fukushima, Yukari Arakawa, Hiroshige Hibasami, Fukuyoshi Nakata and Hiroshi Ito. Induction of apoptosis by Blazein of a new steroid isolated from Agaricus Blazei Murrill (himematsutake) in Human colon cancer COLO201 cells 2010

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