

Fucoidan Tsushin News Letter vol.2 Jun. 2010

The pioneer of mozuku sea algae foods Marine Products Kimuraya Co., Ltd.



Suppressant function of fucoidan of side-effects caused by anticancer agents

Publicized the result of the clinical test of joint research
with Tottori University Faculty of Medicine

Marine Products Kimuraya Co., Ltd.
Director, Head of R&D Division

Yasunari MIKI

Involved in joint research of functional assessment
of fucoidan with Shimane University Faculty of
Agriculture (Now, Faculty of Life and Environmental
Science), since 1993, And with Tottori University
Faculty of Medicine, since 2005.

His extensive research is guided by his great
fascination of the beneficial effect of fucoidan
already discovered and still to be discovered in the
futureHis is enjoying Imagined-picture and Flower
arrangement in his private life.

Confirmed first time in the world that mozuku fucoidan suppressed side-effects of cancer-inhibiting agents^① at clinical tests.

Marine Products Kimuraya Co., Ltd. is pursuing joint research to conduct experiments and clinical tests to evaluate the beneficial effects of fucoidan.
Now we introduce you the contents.

Incident of E. coli O-157 was a trigger to start joint research on fucoidan with Shimane University and acquire a patent

The mass food-poisoning outbreak of E. coli O-157, which occurred in Osaka, in 1996, was a trigger for Marine Products Kimuraya Co., Ltd. to start production and research on fucoidan.

At that time, we conducted joint research with Shimane University on microbiological controls in to provide thorough scientific hygiene management of our products.

Then to confirm the safety of our seasoned mozuku pack against E. coli O-157, we added experimentally O-157 to seasoned mozuku pack and researched the effect this had on our products.

Generally, antibiotics as one of antimicrobials can kill E. coli O-157, at the same time verotoxin^② is produced, and it increases severity of patients.

However, as a result of our research, we clarified that E. coli O-157 were killed without production of verotoxin in the seasoned mozuku products.

In further research, it was clarified that high polymer fraction^③ of hydrothermally extracted substance from mozuku without vinegar had an antibacterial activity.



Human stomach cancer cell



Human stomach cancer cell added fucoidan (became circular stopping its action due to activation of fucoidan)

Later it was clarified that the high polymer fraction of hydrothermally extracted substance from mozuku had the same constituents as fucoidan. This became a trigger for us to start researching fucoidan.

Later we developed our own technology to produce refined fucoidan from mozuku.

We have continued to conduct joint research with Shimane University to clarify the physiological activity of fucoidan.

Then Nov. 2, 2007 we acquired the patent for suppression effect of side-effects of anticancer agents by fucoidan derived from mozuku. (Title: Suppressant agent of side-effects of medical agents)



Marine Products Kimuraya Co., Ltd. acquired the following patent certificate: (Title of the Invention: Suppressant agent of side-effects of medical agents. Patent No. 4034146)

To clinical tests from the level of cell research. Started joint research with Tottori University Faculty of Medicine in 2005.

Our treatment for various research assignments started jointly with Shimane University in 1996. In those days, our research was limited to basic test tube level studies of cultured cells.

Gradually, we extended the scope of our research to animal tests, action test on healthy persons, and clinical tests on patients.

Our commencement of collaboration with Tottori University Faculty of Medicine was an epoch-making milestone in our research. In 2004, we jointly applied to participate in “The City Area Industry, Academia, Government Cooperation Program” sponsored by “Ministry of Education, Culture, Sports, Science and Technology”.

The next year, we started the first joint, basic, clinical research with Tottori University Faculty of Medicine on the prevention and therapy for life-style related diseases by sea algae and fucoidan derived from sea algae.

Through our joint research with Tottori University Faculty of Medicine, we have conducted activity tests and clinical tests on mozuku fucoidan and could achieve the various results as the “Improvement effect of acidic urine by fucoidan” and the “Effect to lead to prevent thrombosis by fucoidan”.

When we participated in “The City Area Industry, Academia, Government Cooperation Program” between Jun. 2006 and Mar. 2009, we supplied our mozuku fucoidan as research materials to expand our joint research with Tottori University.



Tottori University Faculty of Medicine

At “Japan Surgical Association”, the result of the clinical test in joint research with Tottori University Faculty of Medicine was publicized.

Through our joint research with Tottori University Faculty of Medicine, we have conducted activity tests and clinical tests on mozuku fucoidan to confirm that “Mozuku fucoidan is useful for countermeasure of side-effects of chemotherapy

against advancing recurrent colorectal cancer”.

This achievement was publicized by a research group of Tottori University Faculty of Medicine at the “Japan Surgical Association”. This landmark research, the first of its kind in the world, confirmed that mozuku fucoidan suppressed side-effects of cancer-inhibiting agents in the clinical tests.

This confirmation that mozuku fucoidan helps patients who are suffering from side-effects of cancer-inhibiting agents is a significant achievement.

We continue to challenge as an innovator of fucoidan research.

Examination of effectiveness of fucoidan derived from sea algae as a countermeasure of side-effects of chemotherapy against advancing recurrent colorectal cancer

A research group of Tottori University Faculty of Medicine publicized that “mozuku (one type of sea algae) fucoidan is useful as a countermeasure of side-effects of chemotherapy against advancing recurrent colorectal cancer” at “Japan Surgical Association”, held at “Kyoto International Conference Center” Nov. 19~21, 2009. Following is the summary of this research.

For advancing recurrent colorectal cancer, chemotherapy using anticancer agent is useful, however, due to severe side-effects of anticancer agents, there are patients to whom chemotherapy can hardly be treated.

Therefore, Tottori University and Marine Products Kimuraya Co., Ltd. conducted joint research to examine the suppression effects of mozuku fucoidan against side-effects of cancer-inhibiting agents.

In the clinical tests, we divided 17 patients who would receive systemic chemotherapy into a group of 9 patients who would be administered fucoidan and 8 patients who wouldn't be administered fucoidan.

The administered group ingested fucoidan for 6 months from the first day of therapy. As chemotherapy FOLFOX^④, or FOLFIRI^⑤ were applied and they made assessment using adverse event CTCAE-v3.0^⑥.

As for immunity function, they made assessment by index of NKG2D^⑧ which were expressed at lymphocyte CD8T^⑦.

As the result, among the group of non-administration of fucoidan showed side-effects as grade 3^⑨ such as fatigue for 5 persons, nausea for 3 persons, vomiting for 1 person, loss of appetite for 3 persons.

While among the group of administration of fucoidan, only 1 person complained about loss of appetite.

As for this result, a patent was applied as a suppressant agent of side-effects of cancer-inhibiting agents.

New result was publicized at “Japan Surgical Association” .

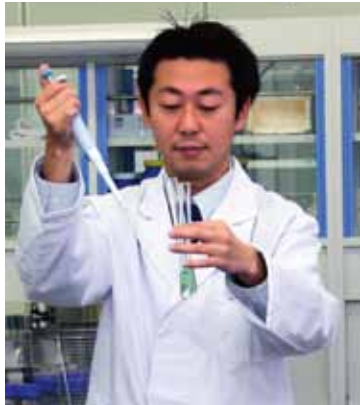
Confirmed also in clinical tests suppressant effect of side-effects.

	Non administration of fucoidan (8 persons)	Administration of fucoidan (9 persons)
Fatigue	5 persons	0 person
Nausea	3 persons	0 person
Vomiting	1 person	0 person
Loss of appetite	2 persons	1 person

*71st General assembly of Japan Surgical Association
From the explaining “Examination of usefulness of fucoidan derived from sea algae as a countermeasure of side-effects of chemotherapy against advancing recurrent colorectal cancer”

Glossary

- ①**Cancer-inhibiting agent**: Same as anticancer agent. Softly expressed wording at clinical test.
- ②**Verotoxin**: Toxin which a part of pathogenic fungus as pathogenic e. coli bacteria and a part of dysentery bacillus secretes
- ③**Fraction**: Constituent separated from mixture of multiple substances.
- ④**FOLFOX**: A standard chemotherapy for large intestine cancer, which is combination use of 5-FU (anticancer agent), I-Leucovorin (a kind of vitamins which activates 5-FU action) and oxaliplatin (anticancer agent).
- ⑤**FOLFIRI**: A standard chemotherapy for large intestine cancer, which is combination use of 5-FU (anticancer agent), I-Leucovorin (a kind of vitamins which activates 5-FU action) and CPT11 (irinotecan: an anticancer agent derived from a Chinese plant)
- ⑥**Adverse event CTCAE-v3.0**: Worldwide definition and standard about adverse event such as side-effect and toxicity, which was made by National Cancer Institute USA. Also showing definition of terms and disease severity.
- ⑦**Lymphocyte CD8T**: Lymphocyte, one of white blood cells, which has function to destroy cells infected with viruses and cancer cells.
Cells which attack foreign substances and unnecessary cells.
- ⑧**NKG2D**: A molecule existing at the cell surface of CD8T lymphocyte and NK cell (natural killer cell).
Natural killer cell is one of cells to attack cancer cell and the like, same as CD8T lymphocyte.
While NKG2D reacts with substances at the surface of cancer cell, CD8T lymphocyte and NK cell become active and attack cancer cells.
- ⑨**Grade 3**: The grade of disease severity due to adverse event CTCAE-v3.0 such as side-effect and toxicity. There are defined 5 grades from 0 to 4. Grade 0 means normal, grade 1: mild, grade 2: moderate, grade 3: advanced, grade 4: serious.



Marine Products Kimuraya Co., Ltd.
Senior researcher of R&D Division
Dr. of Agriculture Hitoshi Kawamoto

Hitoshi KAWAMOTO

I would like to continue to clarify the power of high polymer mozuku fucoidan scientifically

In the Spring of 1996, when I joined Marine Products Kimuraya Co., LTD., the company was producing and selling seasoned mozuku products.

First, I was assigned to the production department and experienced various tasks including: production operation and improvement of production line, which are critical to the success of a food company.

When I joined the company, we had already started joint research with Shimane University Faculty of Life and Environmental Science.

Around that time, the mass food-poisoning outbreak of E. coli O-157 occurred. This outbreak led to unprecedented demand for high quality food industry hygiene management, to safeguard the food supply.

Since our company and Shimane University jointly started research to confirm the safety our mozuku products, I have been engaged in this research work.

Since I studied chemistry in my university days, this was my first experience to conduct research treating organisms and pathogenic microorganism.

I remember that I worked on this biological experiment all night, which was difficult because biology was a new field of study for me.

After days of trial and error, we successfully confirmed the safety of our products and discovered fucoidan, which was a useful and versatile constituent of mozuku.

I was able to advance this research during my Masters and Doctoral courses at Shimane University, while retaining my job at our company.

In 2001 using culture cells, we made the epoch-making discovery that fucoidan has a suppressant effect of side-effects of anticancer agents.

Further we confirmed the inhibiting effect of proliferation of cancer cells and studied research methods of gene and protein, and acquired technology to further extend our fucoidan research.

To complete my doctor's course and qualify for my doctorate degree, I was obliged to prepare an academic article detailing my research achievements.

The article had to pass through an examination process and be approved for publication in a research journal.

Actually I hadn't made considerable academic achievements worthy of endorsement of examination, and I faced a further challenge writing this article in English, because I was not particularly proficient in English.

Those experiences, leading up to my eventual doctorate degree award, taught me that many of the food materials commonly used in traditional Japanese diets and are associated with good health maintenance and health promotion, but those beneficial effect had not been scientifically verified.

Among such food materials, sea algae and viscous food have long been considered "good for health", but this fact had not been sufficiently verified.

Although fucoidan is an extracted material from mozuku, which is associated with good health, I noticed fucoidan had also not been adequately verified through scientific research...

Then Marine Products Kimuraya Co., LTD. determined to research fucoidan with full force and started joint research on functional assessment of fucoidan for health action of human and animal, primarily in collaboration with Tottori University Faculty of Medicine, Faculty of Agriculture Dept. of Veterinary Medicine.

In this joint research with Tottori University Faculty of Medicine, we started research of culture cell level and mouse level and now we are doing research of human action-tests and human clinical test.

In the joint research with Tottori University Faculty of Agriculture, Faculty of Technology, we are doing research on fucoidan production methods and in our joint research with the Department. of Veterinary Medicine, we are doing research on animal action-test and animal clinical test, such as rabbits, mice, etc.

These research projects have been conducted and are ongoing in connection with "The City Area Industry, Academia, Government Cooperation Program", by joint research with Tottori University, with Tottori Prefecture and with the Tottori Institute of Industrial Technology.

I would like to clarify "fucoidan power" which is extracted from the traditional Japanese food material, mozuku, and which has a number of beneficial effects on human health.

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