

Fucoidan Tsushin News Letter

vol.4 Dec. 2010

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

Antitumor (Anticancer) effect of fucoidan

Tottori University Faculty of Agriculture publicized
an achievement of joint research with
Marine Products Kimuraya Co., Ltd.
in a symposium.

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

Sunao ABE

Joined our company in 2007.
Started joint research with Tottori University
Faculty of Medicine in 2008.
The research theme is "Various health
enhancement actions of fucoidan" .
Also, in addition to fucoidan, he is
researching various possibilities of sea algae.
His hobby is cooking and exploring new
recipes on holidays.
He is "a researcher by nature" .



Fucoidan was clarified in the experiment to exert antitumor effects by oral administration

This time we will explain to you about the antitumor effects by oral administration of fucoidan.

Reports on “antitumor effect by oral administration” are rare; therefore this might be a meaningful report.

Examined various effects by oral administration of fucoidan on cancer bearing mice.

Marine Products Kimuraya has produced mozuku fucoidan and carried out various research assignments on fucoidan since the outbreak of mass food-poisoning of E. coli O-157 in Osaka.

On the occasion of our participation application of “City Area Industry, Academia, Government Cooperation Program”, sponsored by “Ministry of Education, Culture, Sports, Science and Technology” in 2004, our research activity took a significant step forward.

We also started interaction with Tottori University Faculty of Agriculture Dept. of Veterinary Medicine, and with Faculty of Medicine.

Through various research groups, we progressed from the basic research level using the culture cell in test tubes, to animal clinical tests, activity tests on healthy persons and clinical tests on patients.

This time we introduce our joint research achievement of antitumor effect by oral administration of fucoidan with a research group led by Prof. Yoshiharu OKAMOTO, of Tottori University Faculty of Agriculture Dept. of Veterinary Medicine.

“Oral administration” means literally “take-in by mouth”.

This is a beneficial method of administration for patients because it is not necessary to use special instruments to administer directly into blood by “injection” or “intravenous drip”.

In the experiment, we divided cancer bearing mice into two groups.

One group was administered fucoidan, the other group was not, and we then compared and analyzed the results as part of a long-term by observational study.

The experiment by oral administration was a research to confirm the results of the test tube level research, by living body actually, and further because reports of antitumor effect by oral administration are rare.



Prof. Yoshiharu OKAMOTO of Tottori University
Faculty of Agriculture
Dept. of Veterinary Medicine. (Right side)

This report, therefore, became quite meaningful.

Survival days of the administration of fucoidan group were prolonged about 2 times.

Particular note is “influence on survival days”.

As you can see in the figure, the group which was given the mixed feeding stuff with fucoidan survived about 2 times longer, compared with the group which was given normal feeding stuff.

We can't simply compare mice with humans.

However it became a significant achievement for people who desire progress of cancer treatment, because we can now report a new possibility of fucoidan, as well as “Suppressant function of side-effect caused by anticancer agents ” that was introduced in “Fucoidan Tsushin News Letter Vol. 2”.

The discovery in this research was applied for the International Patent (PCT).

We continue to pursue further possibility of fucoidan and challenge for clarification of them.

We work on various research assignment of fucoidan, other than “Antitumor effect” which was introduced in this volume, such as “Antibacterial action (Antibacterial action of E. coli. O-157)”, “Preventive action of thrombosis”, “Improving action of acidic urine”, “Improving action of environment inside intestines” “Reducing effect of a hangover and a sick from drinking”, and “Acceleration effect of fucoidan for regeneration of cartilage” and etc.

Through these research activities, we pursue further possibility of fucoidan and challenge for clarification of them.

Antitumor effect by oral administration of fucoidan

July, 2010, at the 24th “Chitin, Chitosan Symposium” held in Tokyo, a research team from Tottori University Faculty of Agriculture, Veterinary Department released a study on the antitumor effect by oral administration in the animal clinical tests.

Following is the outline of the contents.

Much research on the antitumor effects by fucoidan is in vitro ①, and as for research in vivo ②, there are reports about local administration to the abdominal cavity ③ or to veins or to tumor tissues.

Actually there are few research studies on the antitumor effects by oral administration. Next, we conducted joint research together with Tottori University Dept. of Veterinary,

by oral administration of fucoidan to cancer bearing mouse ④, and we examined the influence on tumor growth, immune cells, production of cytokine ⑤, and survival days of the cancer bearing mice.

We transplanted a cultured tumor part derived from colon cancer to the mice which were given feeding stuff adding 5 % of fucoidan for four weeks.

Even after the transplant, we gave continuously the feeding stuff including 5 % fucoidan.

On the date of two weeks after we transplanted, we measured the weight of the tumor and observed tumor tissues histologically.

Compared with the group which was given normal feeding stuff without the addition of fucoidan, in the group which was given fucoidan, both the growth rate of tumor and the tumor weight were suppressed.

Also, we orally administered fucoidan to mice for 10 weeks and obtained the blood and the spleen.

We measured cytokine density from the blood serum, and the immune cell ratio from the spleen cells.

The cytokine density (IL-2) ⑥ of the group which were given fucoidan increased.

In the analysis of spleen cells, it was confirmed that the ratio of NK-cell ⑦ increased and the positive rate CD4 ⑧ decreased.

Further we continued to give the feeding stuff adding 5 % fucoidan to the cancer bearing mice and checked the survival days.

The group which was orally administered fucoidan prolonged the survival days about 2 times longer than the group which weren't given fucoidan.

From the experiment, we clarified that fucoidan showed antitumor effects.

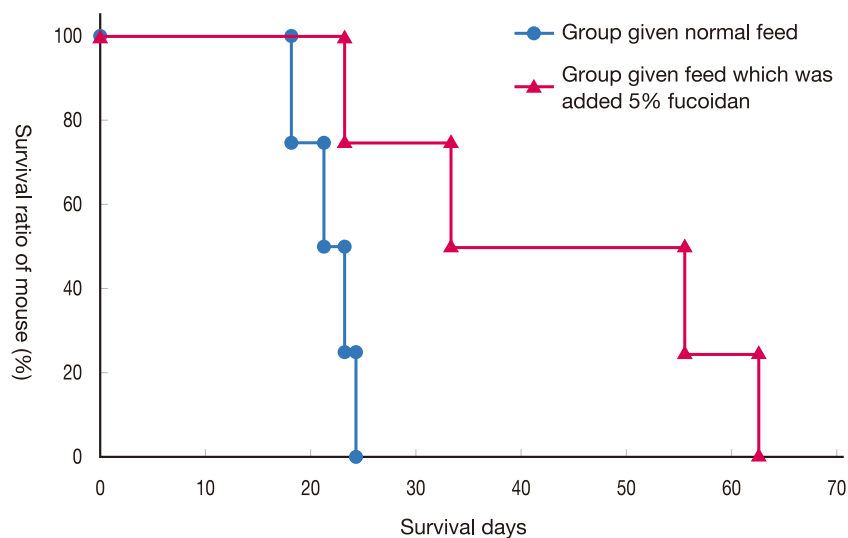
This suggests the possibility that fucoidan works well due to multiple effects on the suppression of cell division, apoptosis ⑨ induction effect, immune activation effect.

Also by oral administration of fucoidan, we clarified that cancer bearing mice prolonged their survival days.

[Reference]

1) Research on Chitin, Chitosan Vol. 16 No. 2, p150-151 (2010)

2) Patent Publication (PCT) WO 2010/110223



Glossary

① **in vitro** : Artificially constituting experimental environment like experiment in the test tube. Depending of each field though, “experiment of culture cell in vessel” meets its definition.

② **in vivo** : It means to “within an organism”, contrasts with “in vitro”.

Contrasting with culture cell, it means to animal tests.

③ **Abdominal cavity** : The space where such organs fit in the lower part of the diaphragm as stomach and intestines.

④ **Cancer bearing** : It means “having cancer in the body”.

⑤ **Cytokine** : Protein which is secreted from the immune system. It holds a roll to deliver information to the specific cells.

There are many species, and some are related to inflammation and proliferation of cells.

⑥ **IL-2** : Abbreviation of Interleukin-2.

One of the Cytokines.

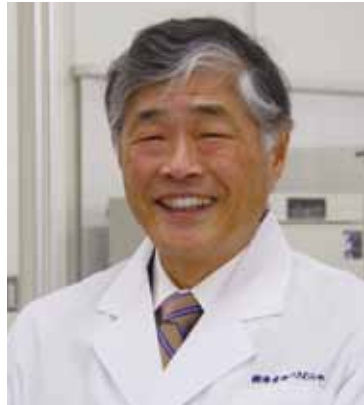
It activates cells which remove foreign materials and cells which make antibody.

⑦ **NK cell** : A kind of lymphocytes. It has a roll to attack especially tumor cells and cells infected by virus.

⑧ **CD4** : One of the white blood cells. It has a function to destroy infected cells by virus at lymphocytes and to destroy cancer cells.

This cell attacks foreign materials and unnecessary cells by immune activity.

⑨ **Apoptosis** : It means programmed-in death of cell namely “managed and adjusted suicide of cells” in order to keep good situation of an Individual.



Marine Products Kimuraya Co., Ltd.
Technical advisor
Prof. Emeritus of Shimane University

Hideyuki MATSUDA

About “Wonderful achievement which was confirmed in the joint research by Marine Products Kimuraya and Prof. Yoshiharu OKAMOTO”

My research area is mainly “applied microbiology”, and I am a professional of extraction, refinement, functional assessment of material of health food which is applied micro-bioscience and micro-biotechnology, gene engineering.

I carried out research on the decomposer-organism of chitin • chitosan as my lifework. I successfully isolated and identified more than 20 kinds of dominant microorganisms, including new genus and new species bacterial strains which produce chitosan oligosaccharide.

I not only analyzed the genes of these new microorganisms chitinase and Chitosanase, but also researched on antibacterial activity of microbe-treated chitosan against microbial plant diseases.

This is applied as the technology broadly for biological production with less use of agricultural chemicals as well as in good yield.

In the research with microbial functional engineering and science, on the useful material having medicinal action, I have analyzed and applied gene as well as functional regulation factor of quinones and enzyme represented by CoQ10.

Also, I did joint research on the development and breeding of a new useful enzyme for brewing, on breeding of a good yeast for brewing which is isolated from the nature of Shimane and improving brewing technology.

I have also strived to properly train our young engineers.

On the occasion of research of microbiological control, about 20 years ago, I engaged with Marine Products Kimuraya Co., Ltd., with whom I had done joint research such as “Experiment of activity against O-157”, “Effect against stomach cancer in the culture cell”.

In the experiment of culture cell we discovered the “Suppression effect of fucoidan for side-effects of anticancer agents”, and “Inhibition effect of proliferation of cancer cell”. This News Letter is introducing the joint research achievement of antitumor effect by oral administration of fucoidan with Tottori University Faculty of Agriculture Department of Veterinary Medicine.

This is the research achievement of activity of fucoidan on mice, developing our research result which was used on culture cells.

In the experiment, we transplanted cultured cancer cells to mice and checked survival days and immune activity as well, comparing mice given the feed stuff added fucoidan for 4 weeks before the start of experiment, with the case given normal feed.

As the result, comparing the case preliminarily administered fucoidan, with the case non-administered, the life-prolonging effect surprisingly showed the survival days prolonged 2 times more.

Our encounter with Prof. Yoshiharu OKAMOTO, who led the research group, was at the time of our application for “City Area Industry, Academia, Government Cooperation Program”, sponsored by “Ministry of Education, Culture, Sports, Science and Technology”.

On the occasion of our participation in the Program during Jun. 2006 to Mar. 2009, we interacted each other and started joint research independently.

As far as we heard, while we started the research, Prof. Okamoto was not sure of antitumor efficacy in case of actual intake at an individual level.

We also thought we would like to study the activity at the animal level, to confirm the results of inhibiting effect of proliferation of cancer cell at culture cell level.

In the experiment using culture cell, fucoidan can touch directly culture cells, but in case of animal test, it was a question if or not fucoidan would activate against cancer cells because fucoidan was only ingested and couldn't touch cancer cell directly.

Because fucoidan is high polymer, being different from the case of culture cells, and it wasn't clear how it activated the cells which fucoidan couldn't touch directly and by what kind of mechanism it would activate.

Thanks to the research achievement by Prof. Okamoto, it was clarified that immune activity was enhanced while fucoidan was ingested, and that cancer cell-division was inhibited, as the result, survival dates of the mice which were transplanted cancer were prolonged.

The mechanism of antitumor effect by oral administration of fucoidan should be clarified by further research.

However I consider that not only immunity is highly concerned but also various activities such as inhibition of proliferation of cancer cells and apoptosis induction and the like intricately got involved in.

It is delightful that although I discovered suppressant effect of side-effects of anticancer agents as well as inhibition effect of proliferation of cancer in the culture cell level, Prof. Okamoto further achieved in the animal clinical tests such wonderful results as an activating action of immunity and as a life prolongation activation. I really hope we can make the next leap forward with our ongoing research.

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