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

Acceleration effect of regeneration of cartilage by fucoidan

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

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

Hitoshi KAWAMOTO

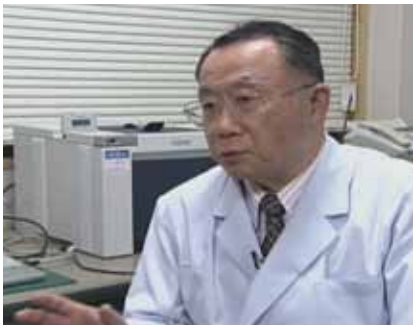
Obtained Doctorate of Agriculture in 1996, Shimane University United Graduate School of Agricultural Science.
Started joint research with Tottori University Faculty of Medicine in 2006.
Researching functional assessment of fucoidan for regeneration of cartilage at laboratory of Prof. Saburo Minami, of the Faculty of Agriculture, Dept. of Veterinary Medicine.
Enjoys fishing in the rich Japan Sea in his private life.

Epoch-making effect which nobody anticipated. Even possible linkage to clarify the mechanism of physiological activity effect

Marine Products Kimuraya Co., Ltd. advances research of fucoidan from various angles.
This time we introduce you to our epoch-making research achievement in the new field as “Acceleration effect of fucoidan for regeneration of cartilage”.

Confirmed acceleration of regeneration of cartilage of rabbits which were administered fucoidan.

Marine Products Kimuraya has produced mozuku fucoidan and carried out various research studies on fucoidan since outbreak of mass food-poisoning of E. coli O-157 in Osaka.
This time we introduce you the promotion effect of fucoidan for regeneration of cartilage as a singular research work.
This is an achievement of joint research with Tottori University Faculty of Agriculture Dept. of Veterinary Medicine, who is conducting the latest research on cartilage regeneration.



Prof. Saburo Minami
Tottori University Faculty of Agriculture
Dept. of Veterinary Medicine

In the experiment, we divided 24 rabbits with damaged cartilage into two groups. One group was administered fucoidan and the other was not.
Next we compared the degree of cartilage recovery between the two groups.
This study found that the group that was administered fucoidan experienced roughly 6 times more cartilage regeneration than the non-administered group.

Nobody expected such fucoidan effect. Professors specializing in the field were very surprised.

We encountered Prof. Saburo MINAMI, who led the research group, 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 with each other and started joint research since Sep. 2009, independently.

Prof. Minami confessed that he hadn't expected that fucoidan would have such a dramatic effect on the acceleration of cartilage regeneration.
Generally animal skins, animal cartilage and materials contained in crustaceans are used as materials for regeneration, therefore those materials are expected to accelerate cartilage regeneration.
That's why the experiment result has such a big impact that he commented as follows:
"Fucoidan is a high molecular substance which has sulfated polysaccharide.
Sulfated polysaccharide is a very important substance for cartilage.
I have researched about regeneration of cartilage by various materials for 10 years and fucoidan was comparable to those materials.
I'm very surprised by the fact that cartilage is regenerated by high molecule polysaccharide."

Fucoidan is a polysaccharide included in viscous constituent of sea algae. Mozuku is guarded by this viscous constituent.

We have great hopes in the future progress of research aimed at discovering the possible secrets of fucoidan.

The reason why fucoidan showed "acceleration effect of fucoidan for regeneration of cartilage" should be clarified.
Fucoidan is not a direct material of cartilage, therefore if we can clarify the mechanism of the acceleration effect of fucoidan on cartilage regeneration, this would help to clarify the mechanism of general physiological activity of fucoidan, although we are doing animal clinical tests.
Please pay attention to our future progress.
We work on various fucoidan research studies, such as "Antibacterial action (antibacterial action of E. coli. O-157)", "Inhibiting action of proliferation of cancer cell", "Preventive action of thrombosis", "Improving action of acidic urine", "Improving action of environment inside intestines" and etc.
Through these research activities, we pursue further possibilities of fucoidan and the challenge of clarifying them.

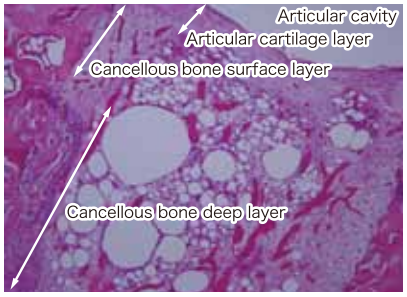
Effect of mozuku fucoidan for experimentally damaged articular cartilage

The Research group of Tottori University Faculty of Agriculture Dept. of Veterinary Medicine, publicized that fucoidan derived from mozuku sea algae is useful for acceleration-effect of healing the damaged joint cartilage, in the academic booklet "Glucosamine ① Research Vol. 6" 2010, issued by "Association for Glucosamine Research".
Following is the outline of the contents:
It is known that human osteoarthritis (OA) develops by age-related decline of synthesis capability of cartilage tissues or by the result of mechanical wear due to over exercise.
Present treatment of disorders involving damage of the joint cartilage include: non-steroid anti-inflammatory drug ②, medical therapy by steroid, surgery treatment ③, administration of supplement.
Among the results of research on glucosamine chondroitin sulfate ①, the possibility of involving substance which have sulfate group was considered for prevention and therapy.
Then Tottori University Faculty of Agriculture Dept. of Veterinary Medicine and Marine Products Kimuraya Co., Ltd. jointly examined the healing acceleration effects on cartilage damage by fucoidan derived from mozuku, which is a sulfated polysaccharide.

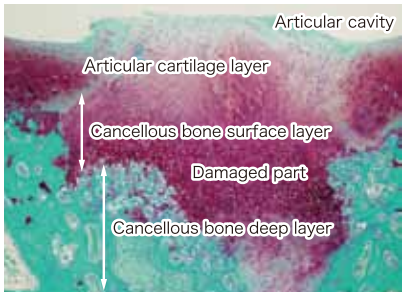
To examine the healing acceleration effects on cartilage damage, we divided 24 rabbits which were damaged by drill at 3 places of the femur, ④ into two groups arbitrarily.
The group of administered fucoidan had oral administration of fucoidan dissolved in water for 3 weeks. The group not administered fucoidan had tap water freely. After experiment, we quantified the level of repair level of damaged part by megascopic observation, comparing with the beginning of experiment. We also conducted image analysis ⑤ of the sliced section which was treated by hematoxylin-eosin stain, safranine stain-O (SO), alcian blue (AB).
The repair level of the group of non-administered fucoidan was 1.1 points, the fucoidan-administered group was 1.78 points.
Histologically the damaged part of the Control was filled up with collagen fiber ⑥ and fibroblast ⑦ and etc., while the damaged part of the group of administrated fucoidan was constituted of chondroblast and chondrocyte.
In image analysis of sliced section of AB stain, SO stain, the group of non-administration was 5989 pixels, 2018 pixels, the group administrated fucoidan was 27,175 pixels, 29,474 pixels.
In the group administered fucoidan, the healing acceleration effects on cartilage accompanied with regeneration of glycosaminoglycan ⑧, and proteoglycan ⑨ were clearly shown.

[Reference]

Glucosamine research 6 (2010) “New development”

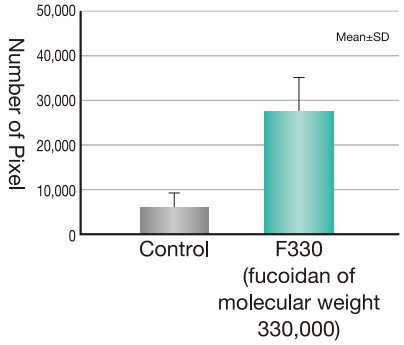


Tissue image (hematoxylin-eosin stain specimen) of damage part of the Control.
Neither at articular cartilage layer at damage part nor at surface layer of cancellous bone nor at deep layer, regeneration image of cartilage and cancellous bone weren’ t seen.

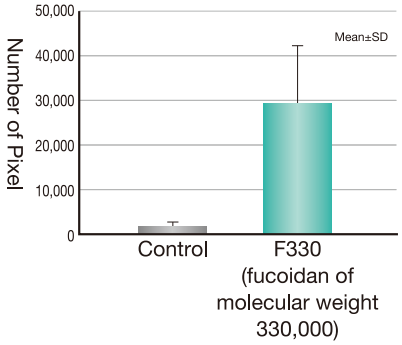


Tissue image (safranine stain-O (SO) specimen) at the damaged parts of F330 (fucoidan of molecular weight 330,000).
Reconstruction image was seen at the articular cartilage layer, at the surface layer and at the deep layer of cancellous bone, and trabeculae weren’ t seen.

Comparison of Glycosaminoglycan amount (alcian blue stain) of the damaged hole.



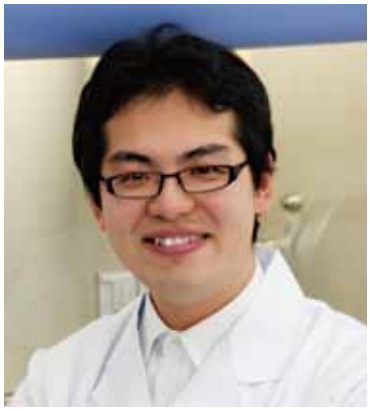
Comparison of proteoglycan amount (safranine stain-O) of the hole of damage



Glossary

①Glucosamine･Chondroitin sulfate：Substances much included in crab shell and shrimp shell.
②Non-steroid anti-inflammatory drug：Anti-inflammatory drug like aspirin which is not steroid.
Used for treatment of pain, fever, inflammation.
③Surgery treatment：Surgery to remove part of the joint which is deformed or cut and replacement surgery to artificial joint.
④Femur: Mammal's longest and largest volume of bone which constitutes between crotch and knee.
⑤Image analysis：From the tissue pictures magnified 200 times of damage hole, being selected within 20,000 pixels at random and numbers of pixels of cartilage matrix in its range are measured by image analysis soft.
⑥Collagen fiber： Fiber which is formed by collagen got together. Can be observed by an optical microscope
⑦Fibroblast：One of the cells constituting connective tissue which fill the gaps of tissues and organs in the body. In case that tissues are damaged, it makes collagen to assist repair.
⑧Glycosaminoglycan：Muco-polysaccharide existing in the all tissues of connective tissues of animals. It is stained indigo blue by AB stain.
⑨Proteoglycan：A kind of glycoprotein which many sugar chains combine.
It forms a complex with such fibered protein as collagen. It is stained purplish red color by SO stain.

Supporting people of fucoidan research ③



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

Sunao ABE

In order to accumulate new evidence (Scientific knowledge) of fucoidan, one by one.

In Tottori University days, I researched the life-span of nematode which is a 1mm long tinny bug.
In those days, because the research budget was quite limited, I couldn't do latest research using such cutting-edge methods, such as HPLC (High performance liquid chromatography) and MALDI/TOF-MS (Micro mass spectrometric analysis).
Then I moved to the Graduate School of Agricultural and Life Sciences in the University of Tokyo. At Prof. Keiko Abe's Biochemistry laboratory, I did basic research on the sense of taste experimenting Japanese killifish, and completed my master's degree.
Since Prof. Abe and Prof. Matsuda, of Shimane University Faculty of Life and Environmental Science, are friends through their joint research, I had a opportunity to meet Prof. Matsuda.
Because I wished to work at a local food company, Prof. Abe introduced me to Marine Products Kimuraya Co., LTD. and joined the company in 2007.
Thus my social life started in the new environment, where the new factory of fucoidan was built.
First I was assigned to the Production Dept., where I have learned the necessary manners and rules as a member of society.
As an on-the-job training, I visited Iheya island, in Okinawa, where our contracted fishermen are working to culture mozuku and I enjoyed the mother sea which

produces fucoidan.
After I was assigned to the R&D Division, to learn the production line operation and the process of extracting and refining fucoidan, I used to rotate back and forth between the factory and the R&D Division.
During my university days, spent in a crowded laboratory, I was embarrassed to now be able to research in wide-open space, handling the most advanced equipment.
The machines in the factory and the laboratory instruments are unlike the equipment I used in my university days, but senior R&D Division managers provided me great assistance to understand how to work in my new environment.
When I was assigned to the R&D Division, I was assigned to work on experiments intended for humans, together with our technical advisor, Prof.
Emeritus Dr. Kasagi, who retired from Tottori University Faculty of Medicine in 2007.
Since I was unfamiliar with this research field, I learned from Dr. Kasagi everything, from how-to-plan, to how to manage experiment results.
Because there wasn't enough evidence about fucoidan's effects on humans, I started new research focusing on the acquisition of "Food for Specified Healthy Use" for fucoidan.
According to Dr. Kasagi's advice, taking notice of the function of dietary fiber of fucoidan, I was to research the regulating functions of intestines by fucoidan.
In order to examine the regulating functions of intestines by fucoidan, I did internal tests of people in our company, and collected basic data.
Now I am carrying out research on various actions to be induced by improvement of the environment of intestines.
I would like to accumulate new evidence (Scientific knowledge) of fucoidan one by one, doing clinical tests for healthy persons and patients as well, in reference to results of basic experiment such as the cell test and the animal clinical test.

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