

# Possibility of Preventing Arteriosclerosis by Reducing Thrombosis Risk

## NKCP, a purified filtrate of *Bacillus subtilis natto* culture

Cardiac and cerebrovascular diseases are the second and third leading causes of death after cancer, and thrombosis is deeply involved in the development of cardiac and cerebrovascular diseases. While better lifestyles are the basis for preventing thrombosis, use of functional food has gained attention as a dietary approach to reducing the risk of thrombosis.

NKCP, produced and distributed by Daiwa Pharmaceutical Co., Ltd, is a protease prepared from *Bacillus subtilis natto* culture, which has been confirmed to exert a thrombolytic action and inhibit coagulation. Recently, the efficacy and safety of the long-term intake of NKCP has been reported, and the possibility of preventing thrombosis and arteriosclerosis has become more real.

Dr. Masahito Hitosugi of Dokkyo University School of Medicine, who conducted the study, gives an outline of the study results and actions of NKCP.



### Dr Masahito Hitosugi

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Graduated from the Jikei University School of Medicine in 1994. Worked at Kawasaki Municipal Hospital. Graduated from Jikei University Postgraduate School in 2000. He was a lecturer at that university, and has held his current position since 2002. Director of Japanese Society of Biorheology. Member of the committee of the Japanese Society of Legal Medicine, physician authorized by the Japanese Society of Legal Medicine. Medical examiner for the Tochigi Police Force.

## **Efficacy of NKCP in preventing thrombosis because of its actions on the coagulation-fibrinolysis system.**

**First of all, would you please explain the relationship between thrombosis and arteriosclerosis?**

Dr. Hitosugi: In Japan, cardiac and cerebrovascular diseases account for about 30 percent of deaths, the main causes after cancer. It is known that most of these cases occur because of the formation of thrombi resulting from the rupture of unstable plaque.

**What approaches are possible for preventing thrombosis?**

Dr. Hitosugi: Reduced blood fluidity, vascular endothelial damage, and abnormal blood components are considered to be involved in the mechanism of developing thrombosis. Therefore, preventing these three conditions is considered to be the basic concept of preventing thrombosis.

Reduced blood fluidity causes higher blood viscosity and contributes towards thrombus formation. The vascular endothelium functions as a barrier between the vascular lumen and the vessel wall and exerts an antithrombotic action. And when the endothelium is damaged, as a matter of course, thrombi can form more easily. Abnormal blood components are related to lower blood fluidity because of reduced water content and abnormalities in factors that inhibit thrombus formation.

**And how about the relationship between thrombosis and lifestyle-related diseases?**

Dr. Hitosugi: Diabetes and an abnormal lipid profile cause changes in blood components such as increased blood glucose and cholesterol levels, thus leading to increased blood viscosity, reduced fluidity, and vascular endothelial damage. And in subjects with metabolic syndrome, some adipocytokines released from the visceral fat cause abnormality in blood components and promote thrombus formation.

**What is the role expected from NKCP with regard to preventing thrombosis?**

Dr. Hitosugi: The active ingredient of NKCP is a protein called bacillopeptidase F. So far, *in vitro* studies, animal experiments, and clinical studies in humans have confirmed three actions of NKCP on the coagulation-fibrinolysis system; these are a thrombolytic action, an

inhibitory action on blood coagulation, and an improvement of blood fluidity. And they suggest the usefulness of NKCP for preventing thrombosis.

### **Significant improvement achieved in subjective symptoms of headaches, neck stiffness, and cold extremities**

**You have studied the effects of a long-term intake of NKCP. Please give us an overview of that study.**

Dr. Hitosugi: Subjects with a mean age of 35.5, who gave their consent to the investigation, were asked to take NKCP for a certain period and were examined for changes in subjective symptoms. The male to female ratio was 2 to 3, and a relatively young age group was selected to exclude the influence of old age. The mean BMI was 22.1 to exclude the influence of obesity. The mean period of intake of NKCP was 21 months, and the mean daily dose was 1,300 mg.

**What parameters were evaluated to study the changes in subjective symptoms?**

Dr. Hitosugi: The parameters were headaches, dizziness/giddy feeling, neck stiffness, malaise, and cold extremities. They were evaluated on a scale of four levels — no symptoms, mild, moderate, and severe. In addition, the time from the start of intake to the onset of the change was recorded.

**And what were the results?**

Dr. Hitosugi: The most significant change was observed with regard to headaches. A significant improvement was found at 2.5 months on average. Neck stiffness was improved at 1.4 months on average, and cold extremities at 4.5 months on average. No significant improvement was found with regard to malaise and dizziness/giddy feeling (Table 1).

**Table 1** Changes in subjective symptoms after intake of NKCP

|                             | Symptoms before intake of NKCP | Improvement of symptoms after intake of NKCP | Mean intake period to onset of the change (months) |
|-----------------------------|--------------------------------|--|--|
| Headaches                   | 8                              | 8  | 2.5  |
|                             | * P<0.01                       |  |  |
| Neck stiffness              | 17                             | 16   | 1.4  |
|                             | * P<0.001                      |  |  |
| Cold extremities            | 12                             | 8  | 4.5  |
|                             | * P<0.01                       |  |  |
| Malaise                     | 4                              | 3  | 0.8  |
|                             | N.S.                           |  |  |
| Dizziness/<br>giddy feeling | 6                              | 5  | 2.6  |
|                             | N.S.                           |  |  |

(Modified from Food Function 2008, Vol. 4 No. 2)

**NKCP is recommended to people in a state of *mibyō* (pre-symptom) without medical abnormalities and people with borderline conditions.**

**From these results, how do you rate the usefulness of NKCP?**

Dr. Hitosugi: I think that the subjective symptoms were obviously improved through increased blood fluidity and improved local circulation. The results are considered to support the already-known modulating action of NKCP to maintain the balance of the coagulation- fibrinolysis system from the aspect of improvements in clinical symptoms.

What should be emphasized in the present study is that the subjects were from a group which did not have any disease at the time and had no history of lifestyle-related diseases. There are people who have subjective symptoms, even if no abnormality is recognized objectively. I think this suggests that there is a state of *mibyō* (pre-symptom) that cannot be confirmed through laboratory test values and diagnostic imaging.

**The reduction of thrombosis suggests that NKCP is useful for treating arteriosclerosis and metabolic syndrome.**

Dr. Hitosugi: Naturally, because thrombosis is associated with arteriosclerosis, NKCP is expected to be useful for preventing arteriosclerosis. The prevention of arteriosclerosis and

metabolic syndrome both aim eventually to prevent cardiovascular events. While dietary habits and lifestyles have to be improved, NKCP can be considered also a useful tool to achieve changes in people's behavior.

**How should we use NKCP to prevent thrombosis and arteriosclerosis?**

Dr. Hitosugi: Patients who have already been diagnosed as having thrombosis or a lifestyle-related disease need to be examined and treated regularly in medical institutions. But there are subjects who complain of various subjective symptoms even though they are found to be all right in health checkups. And in addition to these subjects, the intake of NKCP is recommended to subjects with borderline conditions.

Particularly, more than 70 percent of people in Japan are said to have taken functional foods or supplements at some time. Safety requirements are placed on functional foods besides efficacy, and the safety of NKCP as a food-derived component has been fully demonstrated.

**Is there any part of the study that needs to be investigated thoroughly in the future?**

Dr. Hitosugi: In a questionnaire survey, most people name "improvement of subjective symptoms" and "prevention of diseases" as the leading reasons why they continue taking NKCP. As functional foods are expected to relieve symptoms too, it was important that the effects of a long-term intake of NKCP were evaluated in the present study.

In future, I envisage there will be prospective studies related to preventing thrombosis, and these will provide more strong evidence on NKCP's usefulness for preventing thrombosis.

**Thank you very much.**

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