

# New Effects of NKCP for the Prevention of Thrombosis

## Interview with Masahito Hitosugi

(Assistant Professor, Department of Legal Medicine, Dokkyo University School of Medicine)



**Thrombosis, including pulmonary thromboembolism (PTE), is one cause of sudden death. It is possible for PTE to occur in anyone, and its occurrence is not easily predicted by tests or by any other measures. However, studies conducted by Masahito Hitosugi, Assistant Professor of the Department of Legal Medicine, Dokkyo University School of Medicine and colleagues, have found that NKCP—a functional food made from *Bacillus subtilis natto*—has a preventive effect against thrombosis. So far, three functions of NKCP have been shown: a thrombolytic action, an anticoagulant effect, and a blood viscosity-reducing effect. In a clinical study conducted in human subjects, effects such as an improvement in shoulder stiffness have been found to occur after intake of NKCP. For this report, we asked Assistant Professor Hitosugi about the characteristics and effects of NKCP, as well as the findings of his studies.**

### Towards the prevention of unpredictable sudden death

—Can you tell us the characteristics of NKCP?

**Hitosugi:** A major characteristic of NKCP is that it is made from *Bacillus subtilis natto*. NKCP is a fragment of Bacillopeptidase F, one of the proteins produced during the growth of *Bacillus subtilis natto*. It is a substance that is completely different from nattokinase, although both substances are produced from *Bacillus subtilis natto*. Nattokinase consists primarily of the protein subtilisin. More specifically, NKCP and nattokinase differ in protein conformation, amino acid sequence, and molecular weight.

—Why did you focus your attention on NKCP?

**Hitosugi:** I previously worked as a hospital physician. In this job, I had a patient who experienced sudden death. He collapsed suddenly, and I rushed up to him, calling his name, but he was in cardiorespiratory arrest by the time I reached him. This event led me to begin studying the area of sudden death.

The definition of sudden death is an unexpected intrinsic death that occurs within 24 hours of the onset of sudden collapse. The predominant causes of sudden death are cardiac diseases. The so-called “economy-class syndrome” (ECS), which includes pulmonary thromboembolism (PTE), is one of the causes of sudden death.

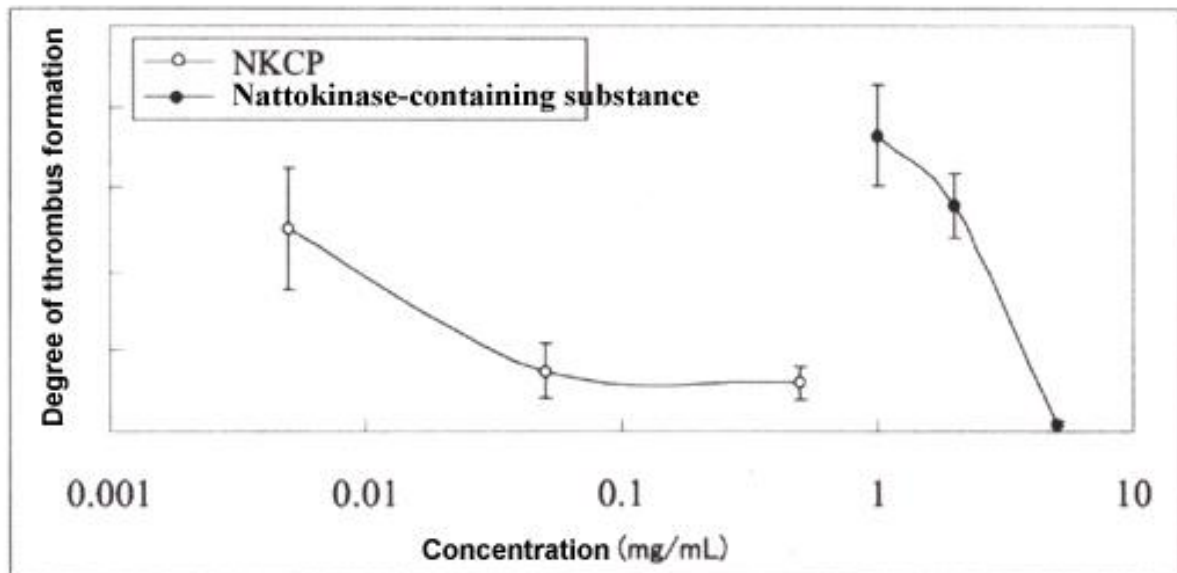
Passengers in business or first class, and those traveling by automobile or train are also at risk of developing ECS, and thus it is now called traveler's thrombosis. The disease is caused by the formation of blood clots in a leg vein, which then enter the bloodstream and travel to the heart. The clot eventually blocks the pulmonary artery, which can result in death. If you have a chance to see a picture of a PTE taken on dissection, you can see the pulmonary artery is completely blocked with rubber-like blood clots.

Death does not always occur following the development of PTE, but sudden death is unpredictable. Thus, it is important to prevent thrombosis in order to prevent sudden death. Through studying sudden death, I have come to recognize the importance of thrombosis prevention. It has been found that 20 to 30% of causes of deaths are due to thrombotic events, including PTE, coronary thrombosis, which can result in myocardial infarction or angina, and cerebral thrombosis, which can result in stroke. This figure suggests that the prevention of thrombosis is highly important, not only for the prevention of PTE, but also for the prevention of other cardiac and cerebrovascular diseases.

I have been looking for a simple and feasible prophylactic approach, focusing on Japanese foods, with the thinking that it would be great to be able to prevent thrombosis simply by consuming our daily meals. I subsequently discovered NKCP produced from *Bacillus subtilis natto*. At that time, the effects of NKCP had not been identified clearly, but it had been reported that shoulder stiffness improved in normal people consuming NKCP. When I performed my study, NKCP was shown to have a greater effect than that of a substance containing nattokinase (Figure). These findings led me to appreciate the effects of NKCP from a scientific viewpoint.

—Didn't you think about prophylaxis using antithrombotic drugs?

**Hitosugi:** A drug is prescribed when a person has a disorder, after a diagnosis by a physician at a hospital or clinic. However, it is not possible to tell who is at risk of sudden death at any particular time or place, so the best prevention methods are those that can be easily adopted by a large number of people. In this sense, if the benefit of a functional food can be demonstrated scientifically, then consuming this food prophylactically has to be the best approach, with such foods readily available from pharmacies or other shops.



**Figure. Anticoagulant effects of a nattokinase-containing substance and NKCP**  
(Modified from page 365 of the Abstracts of 54th Symposium on Rheology.)

### Three functions of NKCP identified by basic researches

—Could you please tell us specifically about the effects of NKCP identified so far?

**Hitosugi:** The safety of NKCP has already been established in a number of basic studies and animal tests, so we asked healthy volunteers to take NKCP. After taking NKCP, many of the volunteers reported that their blood circulation had improved. These were only the impressions of individuals, so of course the effects still need to be demonstrated scientifically.

Our group previously developed a proprietary blood viscometer to evaluate the effects of pharmaceuticals. When we examined the effect of NKCP using this device, it indicated that

NKCP significantly reduced blood viscosity, with an effect comparable to that of the anticoagulant heparin.

We continued to use NKCP and conducted a wide range of studies, including animal experiments, in vitro tests, and a study of the effects on artificial thrombi. As a result of these studies, we found NKCP to have three major effects: the reduction in blood viscosity and anticoagulant effects, which were shown using our blood viscometer, and a thrombolytic action, which led to the dissolution of thrombi. All of these effects have been demonstrated objectively, and many of the study results have been published as research papers.

A beneficial effect of NKCP was actually previously shown in human subjects, with an improvement in shoulder stiffness after one month of intake. In addition, a study using human blood demonstrated that the blood viscosity decreased within several hours after intake. However, many issues remain unclear, including how NKCP is absorbed and taken into the bloodstream. We will continue to study NKCP further.

—How can these findings be applied for the prevention of thrombosis?

**Hitosugi:** The major causes of the onset of thrombosis include abnormalities in the vessel wall, in blood flow, and in the blood constituents. An abnormality in any of these can lead to the induction of thrombus formation. Elderly people often have weak vessel walls, and diabetic or hyperlipidemic patients have abnormal blood constituents.

In people who are seated for long periods of time or who are confined to bed, blood flow tends to decrease. Many people have these risk factors, but these cannot always be avoided. Therefore, we expect that prophylactic intake of NKCP has potential in reducing the incidence of thrombosis in such people.

—You said that anyone can develop PTE but that it is difficult to predict the onset. What types of people should take NKCP?

**Hitosugi:** Although anyone has the potential to develop thrombosis, those who have any risk factors are more susceptible to the disease. We think that those who have risk factors should be the targets of dietary therapy using functional foods.

For example, an obese person with high blood sugar and cholesterol levels who does not exercise much should be involved in some form of thromboprophylaxis, such as taking NKCP, to reduce their risk as much as possible.

—A person having many risk factors can be taking many types of drugs. Does concomitant use of NKCP cause any problems?

**Hitosugi:** NKCP is not a chemical product, rather it is a product extracted from natural *Bacillus subtilis natto*. Thus, it is a very safe substance. With regard to drug interactions in general, many studies have reported that natto reduced the effects of warfarin because it contains vitamin K. In contrast, NKCP contains a very limited amount of vitamin K. Our study demonstrated that the intake of NKCP was not associated with a reduced effect of warfarin. Needless to say, warfarin has an anticoagulant effect and people should be careful, as it is possible that this anticoagulant effect is increased with the concomitant intake of NKCP.

### **Intake of functional foods should be based on scientifically demonstrated effects.**

—What do you think are the advantages in preventing thrombosis with functional foods?

**Hitosugi:** Recently, the prevention of lifestyle-related diseases has been widely called for. Prevention of lifestyle-related diseases ultimately leads to the prevention of thrombosis. NKCP is a functional food with the potential to help in the prevention of thrombosis.

In Japan, functional foods are attracting increasing attention, and a substantial number of people now take supplements. An Internet survey revealed that 76% of respondents had used some form of supplement food, suggesting that more than half of the Japanese population use supplement foods.

Some people under-use supplement foods and functional foods on account that many of their effects are unclear. In my opinion, if their effects were established scientifically, it would be better to take these products proactively. In general, people aged 40 years or older are reported to be at a greater risk of thrombosis. A person aged 40 years or older with any risk factors, such as obesity, should take NKCP.

—Could you please talk about the future challenges of your researches?

**Hitosugi:** Currently, not all the mechanisms of NKCP intake have been determined, including its absorption and its actions. We need to elucidate these, in animal tests and in clinical trials, while identifying the groups of people likely to benefit most from its intake.

Meanwhile, we face a systematic challenge in Japan because, in many cases, the cause of sudden death is not fully examined. Only a limited number of areas have a system for

determining the cause of sudden death by autopsy. Thus, for the analysis of statistics on death due to thrombosis, we have to overcome the great challenge posed by the lack of reliable data on such cases.