

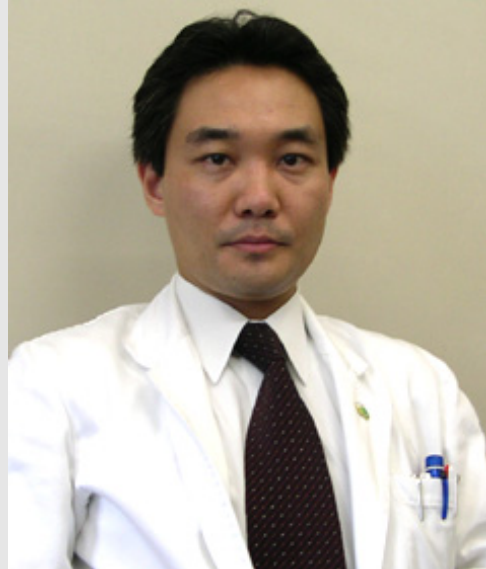
Preventing Thrombosis: A Scientifically Demonstrated Effect on Coagulation and Fibrinolysis

"NKCP" Purified Natto Culture Filtrate

The westernisation of the Japanese diet has increased the level of risk of thrombosis and its complications, myocardial and cerebral infarction and pulmonary thromboembolism, which have attracted notice as a cause of sudden death. A preventative approach is required to decrease the risk of thrombosis.

The "NKCP" Purified Natto Culture Filtrate, an original development of Daiwa Pharmaceutical, has already been shown to be useful in treating thrombolysis and inhibiting thrombus formation. Recent studies have also shown that it decreases the viscosity of blood and improves its fluidity.

In this issue, Dr Hitosugi explains the action of "NKCP," based on the results of his studies up to the present, and comments on its place in daily clinical practice, focusing on the prevention of thrombosis.



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 the current position since 2002.

In 2001, he became a member of the "Study Committee for Economy Class Syndrome" in Japanese Society of Aerospace and Environmental Medicine. His roles also include acting as a medical examiner for the Tochigi Police Force, and he is a physician authorized by the Japanese Society of Legal Medicine and a member of the committee of the Japanese Society of Legal Medicine.

The dietary approach to prevention of sudden death due to thrombosis

First of all, can you tell me about the stance you take in your research?

Hitosugi: I specialise in legal medicine, much of which is concerned with diagnosing sudden or traumatic death.

Myocardial and cerebral infarctions due to thrombosis are well known to be diseases responsible for sudden death. Pulmonary thromboembolisms have also attracted attention in this area. Keeping one's body in the same position, for example sitting down for a long time, a common event in daily life, causes thrombi to form.

Why did you begin to focus on "NKCP"?

Hitosugi: Improvements in lifestyle, including food and exercise, are important for preventing thrombosis. Prevention is crucial in the case of sudden death, because there is no possible treatment. The most convenient and useful prevention method is improving one's lifestyle.

"NKCP" is a food-derived functional food. I began to approach the idea prevention from the angle of food, and this led me to study "NKCP."

Confirmed decreases in blood viscosity and improvements in blood fluidity

Can you summarise the findings of your studies up to the present?

Hitosugi: The main ingredient of "NKCP" is a protein called bacillopeptidase F, which has been shown to be one of several proteases secreted externally by natto bacteria.

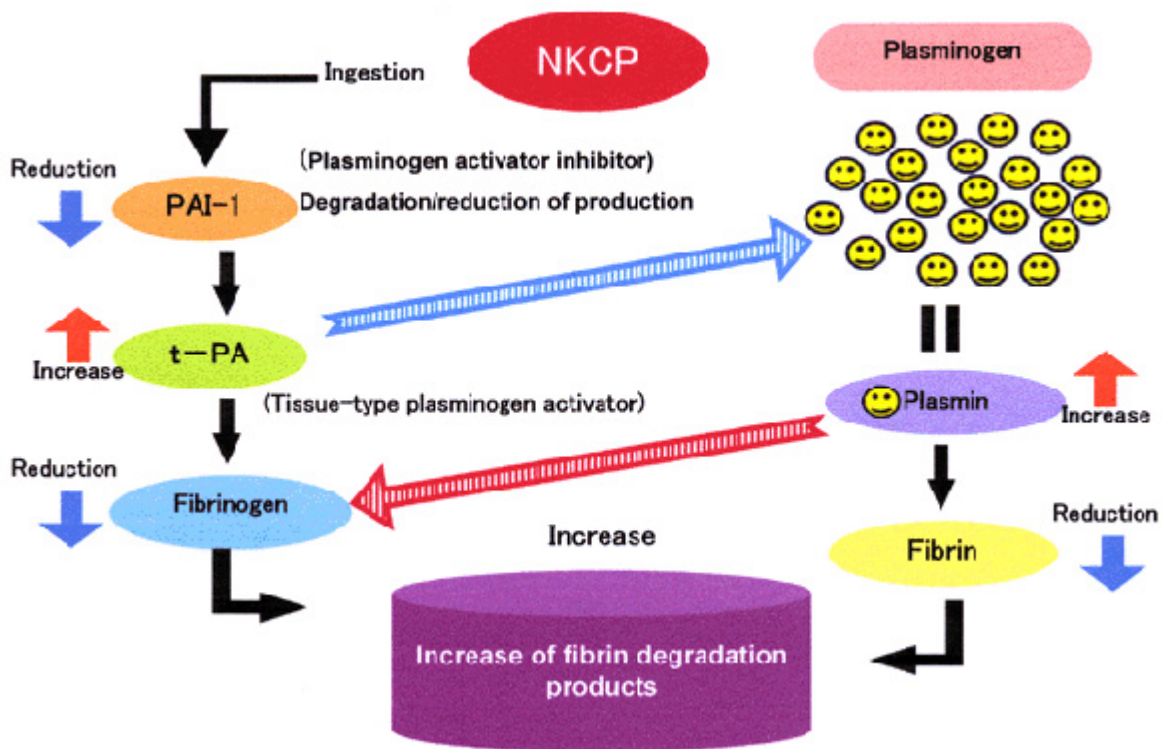
We studied "NKCP" using animals, using in vitro human blood and then finally by administering it to humans. The studies showed that "NKCP" exhibits physiological activity which affects blood coagulation and fibrinolysis (Figure 1).

Can you tell me about the activity of "NKCP" in more detail?

Hitosugi: We studied its effects in an animal experiment using a rat thrombus formation model. A solution of "NKCP" in physiological saline was infused intestinally, and at the same time thrombus was induced. The APTT (activated partial thromboplastin time) and PT (prothrombin time) were measured after 6 hours.

The APTT prolonged in a dose-dependent manner, compared with the control group, showing a significant difference. Almost the same tendency was observed for PT, although the change was smaller (Table 1).

Figure 1 Fibrinolytic cascade activated by "NKCP"



What were the results of the study using human blood?

Hitosugi: Our study centred on the effects on blood coagulation and fibrinolysis. The study showed that there was a reaction inhibiting coagulation and a plasmin-independent fibrinolytic effect. This effect was shown to be dependent on the concentration of "NKCP."

What about the study involving oral administration to humans?

Hitosugi: We measured several blood parameters, and confirmed that the ELT (euglobulinlysis time) shortened, and that the t-PA (tissue plasminogen activator) level increased significantly.

As coagulation was suppressed, the viscosity of the blood decreased and its fluidity improved. This suggested that "NKCP" was capable of preventing thrombosis, by acting on both coagulation and fibrinolysis.

Were there any other characteristic changes?

Hitosugi: We studied the subjective symptoms before and after oral administration. Shoulder stiffness, in particular, improved significantly, suggesting improved local circulation due to increased fibrinolytic activity (Table 2).

To what extent were you able to clarify the mechanism of the action of "NKCP" on blood?

Hitosugi: Several enzymatic reactions are involved in blood coagulation and fibrinolysis, and "NKCP" may inhibit some of these. Further study will be needed to understand this fully.

Oral administration recommended for people with a high risk of thrombosis

What kind of people should take "NKCP"?

Hitosugi: "NKCP" may be useful for decreasing the risk of thrombosis due to its action.

The risk factors for thrombosis are known; people with lifestyle-related diseases, people who have just had surgery, and people who stay in a sitting position for a long time have a higher level of risk. I strongly recommend "NKCP" to these people.

How safe is it?

Hitosugi: "NKCP" originates from a food ingredient. Large-dose toxicity studies have confirmed that it has a high level of safety.

What do you think the role for functional foods is?

Hitosugi: Nowadays, many patients use functional foods and supplements in addition to medicine. Given this, it is important to put their use on a scientific basis and establish criteria for selecting them.

What approach will you take in future studies of "NKCP"?

Hitosugi: The pharmacokinetic nature of "NKCP" is almost completely unknown. As its basic structure, including its amino acid sequence, has been clarified, we plan to study how it works in the living body.

Thank you very much.

Table 1 Thrombus formation inhibited by the administration of "NKCP" in rats

NKCP(mg/kg)	Groups(n=6)				
	Cont.	5	15	100	250
APTT(s)	33	37	46	52	63
PT(s)	16	17	19	21	21

Adapted from a presentation at the 51st Rheology Symposium

Table 2 Changes in subjective symptoms after the oral administration of "NKCP" (n=23)

Symptom	Severity	Prior to administration	1 Month	2 Months
Headache	Severe	1	1	1
	Moderate	7	3	4
	No symptom (including mild headache)	15	16	16
	Remarkable improvement	—	3	2
	Shirley-Williams multiple test	—	N.S.	N.S.
Shoulder stiffness	Severe	5	1	1
	Moderate	10	9	10
	No symptom (including mild shoulder stiffness)	8	9	11
	Remarkable improvement	—	4	1
	Shirley-Williams multiple test	—	P<0.05	P<0.05
Dizziness	Severe	0	0	0
	Moderate	6	4	4
	No symptom (including mild dizziness)	17	18	18
	Remarkable improvement	—	1	1
	Shirley-Williams multiple test	—	N.S.	N.S.

Data is expressed as a number of patients. Significant differences were tested using multiple comparison. N.S. means no significant difference. p<0.05 means a significant difference at a significance level of 5%. Journal of Japanese Society of Rheology, 18, No. 1, 2004

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