What Is Nattokinase?

Nattokinase is a potent fibrinolytic enzyme extracted and highly purified from a traditional Japanese food called Natto. Natto is a fermented cheese-like food that has been used in Japan for over 1000 years for its popular taste and as a folk remedy for heart and vascular diseases. Natto is produced by a fermentation process by adding Bacillus natto, a beneficial bacteria, to boiled soybeans. The resulting nattokinase enzyme, is produced when Bacillus natto acts on the soybeans. While other soy foods contain enzymes, it is only the natto preparation that contains the specific nattokinase enzyme.

The Discovery of Nattokinase

Doctor Hiroyuki Sumi had long researched thrombolytic enzymes searching for a natural agent that could successfully dissolve thrombus associated with cardiac and cerebral infarction (blood clots associated with heart attacks and stroke). Sumi discovered nattokinase in 1980 while working as a researcher and majoring in physiological chemistry at Chicago University Medical School. After testing over 173 natural foods as potential thrombolytic agents, Sumi found what he was looking for when Natto was dropped onto artificial thrombus (fibrin) in a Petri dish and allowed it to stand at 37 C (approximately body temperature). The thrombus around the natto dissolved gradually and had completely dissolved within 18 hours. Sumi named the newly discovered enzyme "nattokinase", which means "enzyme in natto". Sumi commented that nattokinase showed "a potency matched by no other enzyme." 1,7

Potent Thrombolytic Activity

The human body produces several types of enzymes for making thrombus, but only one main enzyme for breaking it down and dissolving it - plasmin. The properties of nattokinase closely resemble plasmin. According to Dr. Martin Milner, from the Center for Natural Medicine in Portland, Oregon, what makes nattokinase a particularly potent treatment, is that it enhances the body's natural ability to fight blood clots in several different ways; Because it so closely resembles plasmin, it dissolves fibrin directly. In addition, it also enhances the body's production of both plasmin and other clot-dissolving agents, including urokinase (endogenous). "In some ways, Milner says, nattokinase is actually superior to conventional clot-dissolving drugs. T-PAs (tissue plasminogen activators) like urokinase (the drug), are only effective when taken intravenously and often fail simply because a stroke or heart attack victim's arteries have hardened beyond the point where they can be treated by any other clot-dissolving agent. Nattokinase, however, can help prevent that hardening with an oral dose of as little as 100 mg a day." 1,7

The Prolonged Action of Nattokinase

Provided by participant (and user of Nattokinase) in Lynn Koiner’s Medical Astrology Workshop (Oct. 10, 2009)
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Nattokinase produces a prolonged action (unlike antithrombin drugs that wear off shortly after IV treatment is discontinued) in two ways: it prevents coagulation of blood and it dissolves existing thrombus. Both the efficacy and the prolonged action of NK can be determined by measuring levels of EFA (euglobulin fibrinolytic activity) and FDP (fibrin degradation products), which both become elevated as fibrin is being dissolved. By measuring EFA & FDP levels, activity of NK has been determined to last from 8 to 12 hours. An additional parameter for confirming the action of NK following oral administration is a rise in blood levels of TPA antigen (tissue plasminogen activator), which indicates a release of TPA from the endothelial cells and/or the liver.6,7

The Mechanism Behind Thrombus

Blood clots (or thrombi) form when strands of protein called fibrin accumulate in a blood vessel. In the heart, blood clots cause blockage of blood flow to muscle tissue. If blood flow is blocked, the oxygen supply to that tissue is cut off and it eventually dies. This can result in angina and heart attacks. Clots in chambers of the heart can mobilize to the brain. In the brain, blood clots also block blood and oxygen from reaching necessary areas, which can result in senility and/or stroke.1

Thrombolytic enzymes are normally generated in the endothelial cells of the blood vessels. As the body ages, production of these enzymes begins to decline, making blood more prone to coagulation. This mechanism can lead to cardiac or cerebral infarction, as well as other conditions. Since endothelial cells exist throughout the body, such as in the arteries, veins and lymphatic system, poor production of thrombolytic enzymes can lead to the development of thrombotic conditions virtually anywhere in the body.7

It has recently been revealed that thrombotic clogging of the cerebral blood vessels may be a cause of dementia. It has been estimated that sixty percent of senile dementia patients in Japan is caused by thrombus. Thrombotic diseases typically include cerebral hemorrhage, cerebral infarction, cardiac infarction and angina pectoris, and also include diseases caused by blood vessels with lowered flexibility, including senile dementia and diabetes (caused by pancreatic dysfunction). Hemorrhoids are considered a local thrombotic condition. If chronic diseases of the capillaries are also considered, then the number of thrombus related conditions may be much higher. Cardiac infarction patients may have an inherent imbalance in that their thrombolytic enzymes are weaker than their coagulant enzymes. Nattokinase holds great promise to support patients with such inherent weaknesses in a convenient and consistent manner, without side effects.1,6,7

Nattokinase is capable of directly and potently decomposing fibrin as well as activating pro-urokinase (endogenous).
Research In The United States

Dr. Martin Milner of the Center for Natural Medicine in Portland, Oregon and Dr. Kouhei Makise of the Imadeqawa Makise Clinica in Kyoto, Japan were able to launch a joint research project on nattokinase and write an extensive paper on their findings. "In all my years of research as a professor of cardiovascular and pulmonary medicine, natto and nattokinase represents the most exciting new development in the prevention and treatment of cardiovascular related diseases," Dr. Milner said. "We have finally found a potent natural agent that can thin and dissolve clots effectively, with relative safety and without side effects." 1

Animal & Human Studies

Nattokinase has been the subject of 17 studies, including two small human trials.

Dr. Sumi and his colleagues induced blood clots in male dogs, then orally administered either four capsules of nattokinase (250 mg per capsule) or four placebo capsules to each dog. Angiograms (X-rays of blood vessels) revealed that the dogs who received nattokinase regained normal blood circulation (free of the clot) within five hours of treatment. Blood clots in the dogs who received only placebo showed no sign of dissolving in the 18 hours following treatment.1,3

Researchers from Biotechnology Research Laboratories and JCR Pharmaceuticals Co. of Kobe, Japan, tested nattokinase's ability to dissolve a thrombus in the carotid arteries of rats. Animals treated with nattokinase regained 62 percent of blood flow, whereas those treated with plasmin regained just 15.8 percent of blood flow.1

Researchers from JCR Pharmaceuticals, Oklahoma State University, and Miyazaki Medical College tested nattokinase on 12 healthy Japanese volunteers (6 men and 6 women, between the ages of 21 and 55). They gave the volunteers 200 grams of natto (the food) before breakfast, then tracked fibrinolytic activity through a series of blood plasma tests. The tests indicated that the natto generated a heightened ability to dissolve blood clots: On average, the volunteers' ELT (a measure of how long it takes to dissolve a blood clot) dropped by 48 percent within two hours of treatment, and volunteers retained an enhanced ability to dissolve blood clots for 2 to 8 hours. As a control, researchers later fed the same amount of boiled soybeans to the same volunteers and tracked their fibrinolytic activity. The tests showed no significant change.1,3,6

The Benefits of Nattokinase on Blood Pressure

Traditionally in Japan, Natto has been consumed not only for cardiovascular support, but also to lower blood pressure. In recent years, this traditional belief has been confirmed by several clinical trials. In 1995, researchers from Miyazaki Medical College and Kurashiki University of Science and Arts in Japan studied the effects of nattokinase on blood pressure in both animal and...
human subjects (see below). In addition, the researchers confirmed the presence of inhibitors of angiotensin converting enzyme (ACE), which converts angiotensin I to its active form angiotensin II within the test extract, which consisted of 80% ethanol extract of lyophilized viscous materials of natto. ACE causes blood vessels to narrow and blood pressure to rise - by inhibiting ACE, nattokinase has a lowering effect on blood pressure.1,2

Animal Study

After a single intraperitoneal administration of 400-450 grams of the test extract (equivalent to 25 mg of natto food) into male Wister rats, systolic blood pressure (SBP) significantly decreased from 166 + mmHg to 145 + 24 mmHg in just two hours (p<0.05), and decreased further to 144 + 27 mmHg in 3 hours (p<0.05). On average, this data represents a 12.7 percent drop in SBP within two hours.1,2

Human Study

The same natto extract was then tested on human volunteers with high blood pressure. Blood pressure levels were measured after 30 grams of lyophilized extract (equivalent to 200 grams of natto food) was administered orally for 4 consecutive days. In 4 out of 5 volunteers, the systolic blood pressure (SBP) decreased on average from 173.8 + 20.5 mmHg to 154.8 + 12.6 mmHg. Diastolic blood pressure (DBP) decreased on average from 101.0 + 11.4 mmHg to 91.2 + 6.6 mmHg. On average, this data represents a 10.9 percent drop in SBP and a 9.7 percent drop in DBP.1,2,6

Conclusion

The traditional Japanese food Natto has been used safely for over 1000 years. The potent fibrinolytic enzyme nattokinase appears to be safe based upon the long-term traditional use of this food. Nattokinase has many benefits including convenience of oral administration, confirmed efficacy, prolonged effects, cost effectiveness, and can be used preventatively. It is a naturally occurring, food based dietary supplement that has demonstrated stability in the gastrointestinal tract, as well as to changes in pH and temperature.

Glossary of Terms:

Cardiac Infarction: Heart attack.
Cerebral Infarction: Stroke.
Fibrin: A whitish, filamentous protein formed by the action of thrombin on fibrinogen and makes up part of coagulum or blood clots.
Fibrinolytic: Pertaining to or causing the breaking up of blood clots.
Infarction: Cardiac or cerebral tissue death due to failure of blood supply to the area usually caused by a blood clot.

Plasmin: An endogenously produced fibrinolytic enzyme.

Plasminogen: A precursor to plasmin. A protein found in many tissues and body fluids.

Thrombus: A blood clot that obstructs a blood vessel or a cavity of the heart.

Thrombolytic: Pertaining to or causing the breaking up of a thrombus.

TPA: Tissue plasminogen activator.

t-PAs: The most commonly used thrombolytic drugs including activase, urokinase, and streptokinase.

Urokinase: An endogenously produced thrombolytic enzyme & also a commonly used thrombolytic drug given intravenously to cardiac and cerebral infarction patients.

References

Selected Abstracts:

Potent fibrinolytic enzyme from a mutant of Bacillus subtilis IMR-NK1.

Chang CT, Fan MH, Kuo FC, Sung HY.
Department of Food and Nutrition, Providence University, Shalu, Taiwan, Republic of China.

A mutant of Bacillus subtilis IMR-NK1, which is used for the production of domestic "natto" in Taiwan, produced high fibrinolytic enzyme activity by solid-state fermentation using wheat bran as medium.

Provided by participant (and user of Nattokinase) in Lynn Koiner’s Medical Astrology Workshop (Oct. 10, 2009)
See www.lynnkoiner.com for more on Medical Astrology and a Medical Sharing section.
Purification and characterization of a fibrinolytic enzyme produced from Bacillus sp. strain CK 11-4 screened from Chungkook-Jang.

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Bacillus sp. strain CK 11-4, which produces a strongly fibrinolytic enzyme, was screened from Chungkook-Jang, a traditional Korean fermented-soybean sauce. The fibrinolytic enzyme (CK) was purified from supernatant of Bacillus sp. strain CK 11-4 culture broth and showed thermophilic, hydrophilic, and strong fibrinolytic activity.

Thrombolytic effect of nattokinase on a chemically induced thrombosis model in rat.

Fujita M, Hong K, Ito Y, Fujii R, Kariya K, Nishimuro S.
Biotechnology Research Laboratories, JCR Pharmaceuticals Co., Ltd., Kobe, Japan.

Nattokinase is a new fibrinolytic enzyme which cleaves directly cross-linked fibrin in vitro. In this study, we investigated the thrombolytic effect of nattokinase on a thrombus in the common carotid artery of rat in which the endothelial cells of the vessel wall were injured by acetic acid. When a section of occluded vessel was stained for CD61 antigen by immunofluorescence utilizing a monoclonal antibody, the antigen was localized around the surface of the occluded blood vessels. This result suggests that the occlusive thrombosis was caused by platelet aggregation. In addition, thrombolysis with urokinase (UK; 50000 IU/kg, i.v.) or tissue plasminogen activator (tPA; 13300 IU/kg, i.v.) in our model was observed to restore the blood flow over a 60 min monitoring period. The results indicate that our chemically induced model is useful for screening and evaluating a thrombolytic agent. We evaluated the thrombolytic activity of nattokinase using this model and compared it with fibrino(geno)lytic enzyme, plasmin or elastase. On a molar basis, the recovery of the arterial blood flow with nattokinase, plasmin and elastase were 62.0 +/- 5.3%, 15.8 +/- 0.7% and 0%, respectively. The results indicate that the thrombolytic activity of nattokinase is stronger than that of plasmin or elastase in vivo.

Transport of nattokinase across the rat intestinal tract.

Fujita M, Hong K, Ito Y, Misawa S, Takeuchi N, Kariya K, Nishimuro S.
Biol Pharm Bull 1995 Sep;18(9):1194-6
Biotechnology Research Laboratories, JCR Pharmaceuticals Co., Ltd., Kobe, Japan.
Intraduodenal administration of nattokinase (NK) at a dose of 80 mg/kg, resulted in the degradation of fibrinogen in plasma suggesting transport of NK across the intestinal tract in normal rats. The action of NK on the cleavage of fibrinogen in the plasma from blood samples drawn at intervals after intraduodenal administration of the enzyme was investigated by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) and Western blotting analysis with an anti-fibrinogen gamma chain antibody. In parallel with the degradation process, plasma recalcification times were remarkably prolonged NK was also detected in the plasma from blood samples drawn 3 and 5 h after administration of the enzyme by SDS-PAGE and Western blotting analysis with an anti-NK antibody. The results indicate that NK is absorbed from the rat intestinal tract and that NK cleaves fibrinogen in plasma after intraduodenal administration of the enzyme.

Purification and characterization of a strong fibrinolytic enzyme (nattokinase) in the vegetable cheese natto, a popular soybean fermented food in Japan.


A strong fibrinolytic enzyme (nattokinase) was purified from the vegetable cheese natto. Nattokinase was extracted from natto with saline and isolated by sequential use of hydrophobic chromatography. The isolated protein gave a single sharp band on SDS-PAGE either before or after reduction. The sequence, as determined by automated Edman degradation of the uncleaved molecule and its enzymatically derived peptide, consisted of a total 275 amino acid residues (M.W = 27,728) and exhibited a high homology with the subtilisins.

Enhancement of the fibrinolytic activity in plasma by oral administration of nattokinase.


The existence of a potent fibrinolytic enzyme (nattokinase, NK) in the traditional fermented food called 'natto', was reported by us previously. It was confirmed that oral administration of NK (or natto) produced a mild and frequent enhancement of the fibrinolytic activity in the plasma, as indicated by the fibrinolytic parameters, and the production of tissue plasminogen activator. NK capsules were also administered orally to dogs with experimentally induced thrombosis, and lysis of the thrombi was observed by angiography. The results obtained suggest that NK represents a possible compound for use not only in the treatment of embolism but also in the prevention of the disease, since NK has a proven safety and can be mass produced.

Provided by participant (and user of Nattokinase) in Lynn Koiner’s Medical Astrology Workshop (Oct. 10, 2009)
See www.lynnkoiner.com for more on Medical Astrology and a Medical Sharing section.
A novel fibrinolytic enzyme (nattokinase) in the vegetable cheese Natto; a typical and popular soybean food in the Japanese diet.

Sumi H, Hamada H, Tsushima H, Mihara H, Muraki H.
Experientia 1987 Oct 15;43(10):1110-1
Department of Physiology, Miyazaki Medical College, Japan.

A strong fibrinolytic activity was demonstrated in the vegetable cheese Natto, which is a typical soybean food eaten in Japan. The average activity was calculated at about 40 CU (plasmin units)/g wet weight. This novel fibrinolytic enzyme, named nattokinase, was easily extracted with saline. Nattokinase not only digested fibrin but also the plasmin substrate H-D-Val-Leu-Lys-pNA (S-2251).