

nattokinase

Table of Contents

summary

Biological Properties

- Fibrinolytic Activity

- Mechanisms of Action

- Structural Characteristics

- Clinical Implications

Health Benefits

- Cardiovascular Health

- Blood Pressure Regulation

- Gastrointestinal Health

- Potential Neuroprotective Effects

- Safety and Considerations

Research and Clinical Studies

- Nattokinase Atherothrombotic Prevention Study (NAPS)

- Other Clinical Studies

- Funding and Ethical Considerations

Dietary Sources and Supplements

- Sources of Nattokinase

- Nattokinase Supplements

 - Considerations for Supplement Use

Regulatory Status

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summary

Nattokinase is a serine protease enzyme derived from natto, a traditional Japanese food made from fermented soybeans, which has gained recognition for its significant

fibrinolytic activity. It is known for its ability to break down fibrin, a key protein involved in blood clot formation, thus promoting healthier blood circulation and potentially lowering the risk of thrombotic disorders such as ischemic stroke and venous thromboembolism.[\[1\]\[2\]](#) This enzyme has been extensively studied for its cardiovascular benefits, leading to increased interest in its application as a dietary supplement aimed at enhancing heart health and regulating blood pressure.[\[3\]\[4\]](#)

The enzyme's mechanism of action involves the activation of plasminogen, which leads to the formation of plasmin—an important factor in the degradation of fibrin clots.[\[5\]](#) Furthermore, nattokinase has been shown to inhibit certain protease inhibitors, thereby enhancing its fibrinolytic efficacy. In addition to its cardiovascular effects, emerging research suggests potential neuroprotective properties, although these findings require further investigation to confirm their relevance in human health.[\[6\]\[7\]](#)

Despite the promising benefits, the safety and regulatory status of nattokinase remain subjects of scrutiny. The enzyme is not classified as Generally Recognized as Safe (GRAS) by the U.S. Food and Drug Administration (FDA), indicating that its safety in marketed forms has not been universally accepted, and concerns about potential side effects, particularly in individuals on anticoagulant therapy, exist.[\[8\]\[9\]](#) Consumers are urged to consult healthcare professionals prior to starting supplementation due to these considerations and the varying quality of commercially available nattokinase products.[\[10\]\[11\]](#)

Overall, nattokinase represents a noteworthy intersection of traditional dietary practices and modern health science, with its therapeutic potential warranting further exploration amidst ongoing discussions about its safety and effectiveness in clinical settings.[\[1\]\[3\]\[4\]](#)

Biological Properties

Nattokinase (NK) is a serine protease enzyme extracted from the traditional Japanese food natto, which is fermented soybeans. It exhibits a variety of biological properties that have garnered attention in both clinical and research settings.

Fibrinolytic Activity

Nattokinase is primarily recognized for its potent fibrinolytic activity, which refers to its ability to break down fibrin, a protein involved in blood clotting. Studies have shown that NK significantly enhances the degradation of fibrin by acting on plasminogen, leading to increased plasmin formation, which subsequently dissolves fibrin clots.[\[1\]\[2\]](#) The enzyme's effectiveness in promoting fibrinolysis has been established through various assays, demonstrating its therapeutic potential in treating thrombotic disorders[\[3\]\[4\]](#).

Mechanisms of Action

The mechanism by which nattokinase exerts its fibrinolytic effects involves its interaction with the fibrinolytic system, including the plasminogen/plasmin pathway. Nattokinase not only activates plasminogen but also inhibits several plasma protease inhibitors that would normally prevent fibrinolysis, thereby enhancing its own efficacy[1][5]. Moreover, in vitro studies indicate that nattokinase can inhibit angiotensin-converting enzyme (ACE), contributing to its cardiovascular benefits by promoting vasodilation and reducing blood pressure[6].

Structural Characteristics

The three-dimensional structure of nattokinase has been analyzed using homology modeling, revealing its close similarity to other subtilisin-like proteases. High-resolution X-ray crystallography has provided insights into its molecular architecture, aiding in the understanding of its functional properties and enzymatic mechanisms[12][13]. This structural knowledge is vital for potential modifications and enhancements of NK's activity and stability for therapeutic applications.

Clinical Implications

Clinical studies have demonstrated that nattokinase supplementation can effectively improve thrombolytic activity, suggesting a role in managing conditions such as ischemic stroke and venous thromboembolism. For instance, NK has been shown to significantly reduce the incidence of blood clots in various animal models and pilot studies in humans[5][14]. Furthermore, its safety profile and efficacy have made it an attractive candidate for further investigation in thrombotic disease management.

Health Benefits

Nattokinase is a fibrinolytic enzyme derived from natto, a traditional Japanese food made from fermented soybeans. This supplement has gained popularity due to its potential cardiovascular health benefits, which include promoting healthy blood flow and maintaining clear arteries.

Cardiovascular Health

Nattokinase is primarily recognized for its ability to break down fibrin, a protein involved in blood clotting, which can significantly lower the risk of blood clots[15]. Regular intake of nattokinase has been linked to improved blood circulation and reduced arterial stiffness, contributing to overall heart health[16][7]. Research has demonstrated that consuming a minimum of 2000 fibrin units (FU) of nattokinase per day for eight weeks can lead to significant reductions in both systolic and diastolic blood pressure compared to placebo groups[15].

Blood Pressure Regulation

One of the prominent benefits of nattokinase is its role in regulating blood pressure. By reducing the stickiness of arterial plaque, nattokinase promotes easier blood

flow through the arteries, which can help manage hypertension and lower the risk of related health complications[7]. Studies have shown that daily administration of nattokinase can lead to notable decreases in diastolic blood pressure, especially among individuals with "high-normal" blood pressure[6].

Gastrointestinal Health

Nattokinase also supports gastrointestinal health by stabilizing and normalizing digestive processes. This enzyme can help alleviate symptoms such as diarrhea, bloating, and cramping, thereby contributing to a more comfortable digestive experience[7].

Potential Neuroprotective Effects

Emerging research suggests that nattokinase may have neuroprotective properties. An animal study indicated that it could potentially lower the levels of amyloid plaques in the brain, which are associated with neurodegenerative diseases, though further studies are necessary to confirm these effects in humans[7].

Safety and Considerations

While nattokinase offers several health benefits, it is essential to consult a healthcare provider before starting supplementation, especially for individuals with underlying health conditions or those taking anticoagulant medications. Potential side effects may include allergic reactions in individuals with soy allergies, increased risk of bleeding, and complications during surgery or pregnancy[16][17]. Overall, nattokinase is a well-researched supplement that provides a promising natural approach to enhancing cardiovascular health and overall well-being.

Research and Clinical Studies

Nattokinase, an enzyme derived from fermented soybeans, has gained attention in recent years for its potential cardiovascular benefits, particularly in the prevention and management of atherosclerosis and hyperlipidemia. Various clinical studies have been conducted to evaluate the efficacy, safety, and pharmacodynamics of nattokinase.

Nattokinase Atherothrombotic Prevention Study (NAPS)

One notable clinical trial is the Nattokinase Atherothrombotic Prevention Study (NAPS), which was a randomized controlled trial aimed at assessing the effectiveness of nattokinase in preventing cardiovascular events. The principal investigator of the study was Howard N. Hodis, M.D., from the Atherosclerosis Research Unit at the University of Southern California[18]. The study had a primary purpose focused on prevention and utilized a randomized, quadruple-masked design with parallel assignment of interventions. Participants were selected based on specific criteria, including clinical signs of cardiovascular disease, diabetes, and other conditions that

could confound the results, such as uncontrolled hypertension and current use of anticoagulants[18][19].

The primary outcome measures of the study included the impact of nattokinase on thrombus formation and cardiovascular risk factors, while secondary outcome measures assessed broader health implications[18].

Other Clinical Studies

Several other studies have explored the pharmacokinetics and safety of nattokinase. For example, a study conducted in the United Kingdom by GlaxoSmithKline focused on the safety and tolerability of the ELLIPTA® dry powder inhaler in chronic obstructive pulmonary disease (COPD) patients, providing insights into comparative inhalation therapies[19]. Additionally, a large clinical study involving 1,062 participants investigated the effective management of atherosclerosis and hyperlipidemia with nattokinase. This study, published in , emphasized the enzyme's role as a potential lipid-lowering agent, contributing to the management of cardiovascular health[20][1].

Funding and Ethical Considerations

Research involving nattokinase has been supported by various funding sources, including key research and development programs in China and other institutions aimed at advancing the understanding of this enzyme's clinical applications[21]. All studies have adhered to international ethical guidelines, ensuring proper consent and ethical treatment of participants, including approval from institutional review boards[21].

Through these studies, nattokinase has emerged as a promising alternative in the prevention and treatment of cardiovascular diseases, with ongoing research needed to fully elucidate its mechanisms and long-term effects[3][1].

Dietary Sources and Supplements

Nattokinase is an enzyme derived from natto, a traditional Japanese food made from fermented soybeans. This food has been consumed for over 1,000 years and is known for its unique texture and distinctive flavor, often compared to strong cheeses due to its pungent aroma[22][23]. The fermentation process involves the addition of the bacterium *Bacillus subtilis* var. natto, which produces the enzyme nattokinase as it acts on the soybeans[6][5].

Sources of Nattokinase

The primary dietary source of nattokinase is natto itself, which is commonly consumed in Japan. Natto is typically served with rice and can also be enjoyed on toast or as a sushi ingredient[6][5]. Despite the growing popularity of nattokinase, it is important to note that this enzyme is not found in other soy-based foods, as its production is specific to the fermentation process of natto[23][5].

Nattokinase Supplements

In addition to dietary sources, nattokinase is available as a dietary supplement. These supplements are marketed for their potential cardiovascular benefits, including the improvement of blood circulation, lowering blood pressure, and supporting heart health[10][16][11]. As with any supplement, it is recommended to choose products that are third-party tested and to consult with a healthcare provider or a registered dietitian before starting supplementation[1][10].

Considerations for Supplement Use

While nattokinase supplements may offer advantages, they are not without risks. Individuals who are allergic to soy, those taking blood-thinning medications, or individuals with specific health conditions should exercise caution and seek medical advice before using these supplements[16][11][5]. Side effects, although rare, can include severe allergic reactions, excessively low blood pressure, and increased bleeding risk[10][16]. Therefore, personalized consultation is crucial to ensure safe and effective use.

Regulatory Status

Nattokinase, a fibrinolytic enzyme derived from the traditional Japanese food natto, is subject to specific regulatory considerations in various jurisdictions. In the United States, the Food and Drug Administration (FDA) regulates dietary supplements, including nattokinase, under a different framework than foods and pharmaceuticals. This means that manufacturers are responsible for ensuring the safety and accurate labeling of nattokinase products, rather than the FDA pre-approving them for safety or efficacy before they are marketed[8][6].

Currently, nattokinase does not have Generally Recognized as Safe (GRAS) status with the FDA, indicating that it has not been universally accepted as safe for consumption in its marketed forms[6]. Consequently, claims made by manufacturers regarding the safety and efficacy of nattokinase products may not be substantiated by rigorous scientific review[6][9].

Additionally, in Canada, Health Canada has received applications for the approval of nattokinase as a novel food, reflecting a growing interest in its potential health benefits, particularly concerning cardiovascular health[6]. However, caution is warranted as some studies examining the benefits of nattokinase are often funded by manufacturers, which may lead to potential biases in research outcomes[24].

While research suggests that nattokinase can be effective for cardiovascular health, its safety profile, especially concerning genotoxicity and interactions with other medications, is still under investigation. For instance, studies have shown that acute administration of nattokinase in mice did not result in any toxicological signs, indicating a high maximum daily tolerated dose[25]. Nevertheless, its use is advised to be approached with caution, particularly in individuals with certain health conditions or

those who are pregnant or breastfeeding, as safety data in these populations are limited[10][3].

As the body of research continues to evolve, it remains critical for consumers to consult healthcare professionals before using nattokinase or any supplement for health purposes, especially given the lack of comprehensive FDA oversight[9].

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