

# Nattokinase in the Prevention and Treatment of Atherosclerotic Cardiovascular Disease

Human Data Promising as Supplement Widely Used in Post COVID-19 and Vaccine Injury Syndromes



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Approximately 15% of Americans who took a COVID-19 vaccine have some new medical illness and regret the shot. Many are looking to nattokinase in formulations of Spike protein support supplements asking is it safe, and what is the track record for this Asian discovery?

Chen et al reviewed human studies before the pandemic on the use of nattokinase with this introduction: “Natto, a cheese-like food made of soybeans fermented with *Bacillus subtilis*, has been consumed as a traditional food in Asian countries for more than 2000 years. Natto consumption is believed to be a significant contributor to the longevity of the Japanese population. Recent studies demonstrated that a high natto intake was associated with decreased risk of total CVD mortality and, in particular, a decreased risk of mortality from ischaemic heart diseases. Before the 1980s, very little was known about the mechanism by which natto consumption led to overall cardiovascular health. In 1987, Sumi et al discovered that natto contained a potent fibrinolytic enzyme called nattokinase (NK). Since then, a considerable amount of NK research has been performed on NK in Japan, Korea, China, and the United States, and these studies confirmed that NK, an alkaline protease of 275 amino acid residues with a molecular weight of approximately 28 kDa, is the most active ingredient of natto and is responsible for many favourable effects on cardiovascular health. First, NK has potent fibrinolytic/antithrombotic activity. In addition, in both animal and human studies, NK also has an antihypertensive, anti-atherosclerotic, lipid-lowering, antiplatelet/anticoagulant, and neuroprotective actions...The most unique feature of NK is that, as a single compound, it possesses multiple CVD preventative and alleviating pharmacologic effects (namely, antithrombotic, antihypertensive, anticoagulant, anti-atherosclerotic, and neuroprotective effects). There are no other drugs or drug candidates

with multiple pharmacologic properties similar to NK. In addition, NK is a natural product that can be administered orally, has a proven safety profile, is economical to use, and provides distinct advantages over other pharmaceutical products.”

In drug development, the most important early observations are on safety. There are two units used in nattokinase dosing, e.g. 100 mg=2000 fibrinolytic units (FU). In the table, Lampe et al in 2016 tested nattokinase up to 10 mg/kg/day (~160,000 FU for an 80 kg person). That means in doses of 100 mg or 2000 FU twice a day are well within a safety range to avoid significant toxicities.

## Nattokinase: A Promising Alternative in Prevention and Treatment of Cardiovascular Diseases

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**ABSTRACT:** Cardiovascular disease (CVD) is the leading cause of death in the world and our approach to the control and management of CVD mortality is limited. Nattokinase (NK), the most active ingredient of natto, possesses a variety of favourable cardiovascular effects and the consumption of Natto has been linked to a reduction in CVD mortality. Recent research has demonstrated that NK has potent fibrinolytic activity, antihypertensive, anti-atherosclerotic, and lipid-lowering, antiplatelet, and neuroprotective effects. This review covers the major pharmacologic effects of NK with a focus on its clinical relevance to CVD. It outlines the advantages of NK and the outstanding issues pertaining to NK pharmacokinetics. Available evidence suggests that NK is a unique natural compound that possesses several key cardiovascular beneficial effects for patients with CVD and is therefore an ideal drug candidate for the prevention and treatment of CVD. Nattokinase is a promising alternative in the management of CVD.

**KEYWORDS:** Nattokinase, natto, cardiovascular disease, antithrombotic agents, antihypertensive drugs, atherosclerosis

Table 1.

| YEAR | LOCATION OF STUDY | SIZE OF STUDY | CLINICAL CONDITION OBSERVED      | SUMMARY OF FINDINGS  | REFERENCES                   |
|------|-------------------|---------------|----------------------------------|--|------------------------------|
| 1990 | Japan             | 12            | Fibrinolytic activity            | 3x NK daily oral administration resulted in enhanced fibrinolytic activity in the plasma and production of tissue plasminogen activator  | Sumi et al <sup>6</sup>      |
| 2004 | Japan             | 24            | Ischaemic stroke                 | NK demonstrated a clear neuroprotective effect in patients with acute ischaemic stroke   | Shah et al <sup>56</sup>     |
| 2008 | Korea             | 86            | Hypertension                     | NK supplementation resulted in a reduction in both systolic and diastolic BP ( $P < .05$ )   | Kim et al <sup>8</sup>       |
| 2009 | Taiwan            | 45            | Blood coagulation factors        | 2 mo of NK treatment significantly decreased fibrinogen, factor VII, and factor confirming a promising cardiovascular benefit  | Hsia et al <sup>17</sup>     |
| 2009 | Taiwan            | 30            | Hyperglycaemia                   | A decrease in serum cholesterol, LDL-C, and HDL-C in the NK group was observed following 8 wk of treatment (4000 FU), but the difference was not statistically significant   | Wu et al <sup>42</sup>       |
| 2013 | USA               | 11            | Pharmacokinetics                 | NK can be measured directly in the human blood after single dosing. Serum levels of NK peaked at approximately 13.3h±2.5h  | Ero et al <sup>60</sup>      |
| 2015 | Japan             | 12            | Thrombolysis and anticoagulation | Blood fibrin/fibrinogen degradation products (thrombolysis and anticoagulation profile) were significantly increased 4h after NK administration following a single dose of 2000 FU ( $P < .05$ ), supporting NK as a useful fibrinolytic/anticoagulant agent to reduce the | Kurosawa et al <sup>16</sup> |

| risk of thrombosis and CVDs in humans |       |    |  |  |                                 |
|---------------------------------------|-------|----|--|--|---------------------------------|
| 2016                                  | USA   | 79 | Hypertension and von Willebrand factor | NK consumption for 8 wk led to beneficial changes to BP in hypertensive patients. A decrease in vWF was seen in the female population consuming NK   | Jensen et al <sup>15</sup>      |
| 2016                                  | USA   | 11 | Toxicology/toxicity                    | NK consumption of 10 mg/kg/day for 4 wk was well tolerated in healthy human volunteers suggesting that the oral consumption of NK is of low toxicological concern  | Lampe and English <sup>61</sup> |
| 2017                                  | China | 76 | Atherosclerosis and hyperglycaemia     | Daily NK treatment (6500 FU for 26 wk) effectively suppressed the progression of atherosclerosis in patients with atherosclerotic plaques by reducing CCA-IMT and carotid plaque size significantly. NK treatment reduced total cholesterol, LDL-C, and triglyceride and increased HDL-C in hyperlipidaemic patients | Ren et al <sup>9</sup>          |

Abbreviations: BP, blood pressure; CCA-IMT, common carotid artery; CVD, cardiovascular disease; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; NK, nattokinase.

In summary this review is reassuring that the ever increasing use of nattokinase in post-COVID-19 and after COVID-19 vaccine injuries is safe and reasonably well tolerated. There may be additional benefits on the cardiovascular system. There is a pressing need for continued clinical development for the COVID-19 and cardiovascular indications. Patients wanting to use the supplement ahead of the emerging science should discuss with a knowledgeable healthcare professional and be on alert for intolerances, allergic reactions, or bleeding complications.

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Chen H, McGowan EM, Ren N, Lal S, Nassif N, Shad-Kaneez F, Qu X, Lin Y. Nattokinase: A Promising Alternative in Prevention and Treatment of Cardiovascular Diseases. *Biomark Insights*. 2018 Jul 5;13:1177271918785130. doi: 10.1177/1177271918785130. PMID: 30013308; PMCID: PMC6043915.

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## 15 Comments





**Scott Bailey** Mar 19

I'm vaccine injured and have been taking it for 18 months. For me it had a very dramatic effect. I'm convinced I wasn't yet another Died Suddenly story because of it. I now have normal d-dimer, crp results. Although my EKG is still significantly different than it was pre-vaccination. I'm guessing that will never go back to normal.

LIKE (32) REPLY ...



**Old Guy** Mar 19

Natto contains vitamin K2. Vitamins D3, K2 and magnesium are a big deal in atherosclerosis prevention. As I understand it, K2 activates osteocalcin helping calcium deposition in bone and acts on matrix GLP to prevent deposition of calcium in arteries. (or something very much like that- if memory serves). I'm not quite sure how to put this together with the nattokinase, but these all seem to me to be important parts to consider in this important matter.

LIKE (30) REPLY ...

3 replies

13 more comments...