# 纳豆激酶
# NATTOKINASE

EsseZyme™

中国纳豆激酶原料制造商
Nattokinase Manufacturer in China

中国纳豆激酶产品方案提供商
Nattokinase Product Solution Provider in China

口服乳剂及制备方法已获中国专利（专利号: ZL 201410198490.0）
Method of Nattokinase Oral Emulsion Preparation Has Obtained
A Chinese Patent（Patent No. ZL 201410198490.0）

纳豆激酶（nattokinase，简称NK）是在纳豆发酵过程中由纳豆枯草芽孢杆菌所产生的一种丝氨酸蛋白酶，具有直接水解交联纤维蛋白的作用，是纳豆中溶解血栓的最主要物质。是由日本心脑血管专家——须见洋行博士于1980年著名的“下午两点半实验”中提取出的天然溶栓物质。

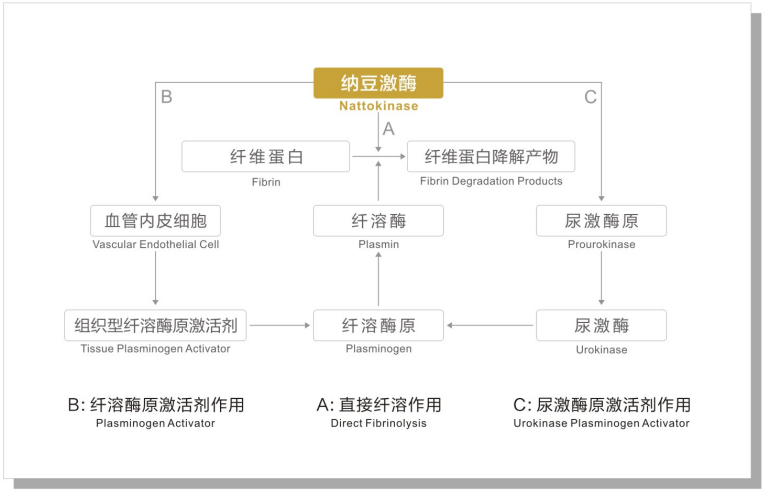
Nattokinase(NK),an important ingredient for dissolving thrombus in natto, is a serine proteinase from Bacillus subtilis which has the function of direct hydrolysis crosslinking.It is a natural thrombolytic substance extracted by Dr.Hiroyuki Sumi.



近年来，各国研究机构对纳豆激酶的基因序列和生理生化特性进行一系列研究，表明纳豆激酶的生物活性、安全性和溶栓效率均高于链激酶、尿激酶等常见溶栓物质，可作为一种新型的溶栓产品被开发并加以应用，就在2016年，欧盟食品安全局正式肯定纳豆激酶作为新资源食品的安全性，并将认证结果予以公布。

In recent years,the physiological and biochemical characteristics of nattokinase were investigated by many research institutions. The results indicated that the biological activity, safety and thrombolytic activity of nattokinase is stronger than streptokinase and urokinase. Nattokinase has been approved as a Novel Food Ingredient by EFSA in 2016.

## 纳豆激酶溶栓机制[1]
## THROMBOLYTIC EFFECT OF NATTOKINASE[1]



# 健康作用
# HEALTH EFFECTS

## 溶血栓（特别在针对陈旧性血栓尤为有效）

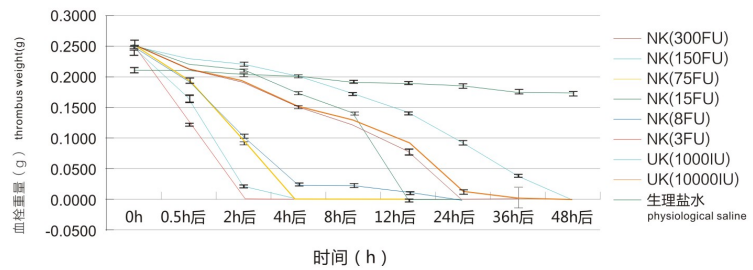
**Dissolve Thrombus(Especially for Obsolete Thrombosis)**

- 双骏生物“纳豆激酶与尿激酶的对比性研究”[2]：
  结论：在48小时溶栓实验中，在超过56小时的陈旧性血栓中应用300FU的纳豆激酶，显示血栓在2小时内被完全溶解；而应用150FU的纳豆激酶的溶栓速度明显高于相同当量的尿激酶 。

  A study on comparison of nattokinase and urokinase by SungenBio: Patients with obsolete thrombosis were treated with 300FU nattokinase in 48h experiment. The results indicated that the thrombus for over 56 hours had completely Dissolved within 2 hours. Thrombolysis rate of anothers who were treated with 150FU nattokinase is much higher than the same amount of urokinase[2].

NK体外溶栓作用曲线

Thrombolytic Action Curve of NK(In Vitro)




- 2015年上海市心血管病研究所关于“血栓弹力图体外评估纳豆激酶对人体凝血系统的影响研究”[3]：
  结论：比较不同剂量纳豆激酶溶血栓效果，纳豆激酶对于血栓的溶解效果十分明显，血栓的溶解时间随计量的提升明显减少。

  A Study"Thromboelastic diagram of the effect of natto kinase on human coagulation system in vitro evaluation" from Shanghai Institute of Cardiovascular Diseases in 2015:The study compared different doses of nattokinase and reported that dissolution time decreases with the increase of dose[3].

不同剂量NK对血栓弹力图测量值的影响

Effects of Different Doses of NK on Thrombelastogram Measurements

（n=20，$\bar{x}\pm s$）

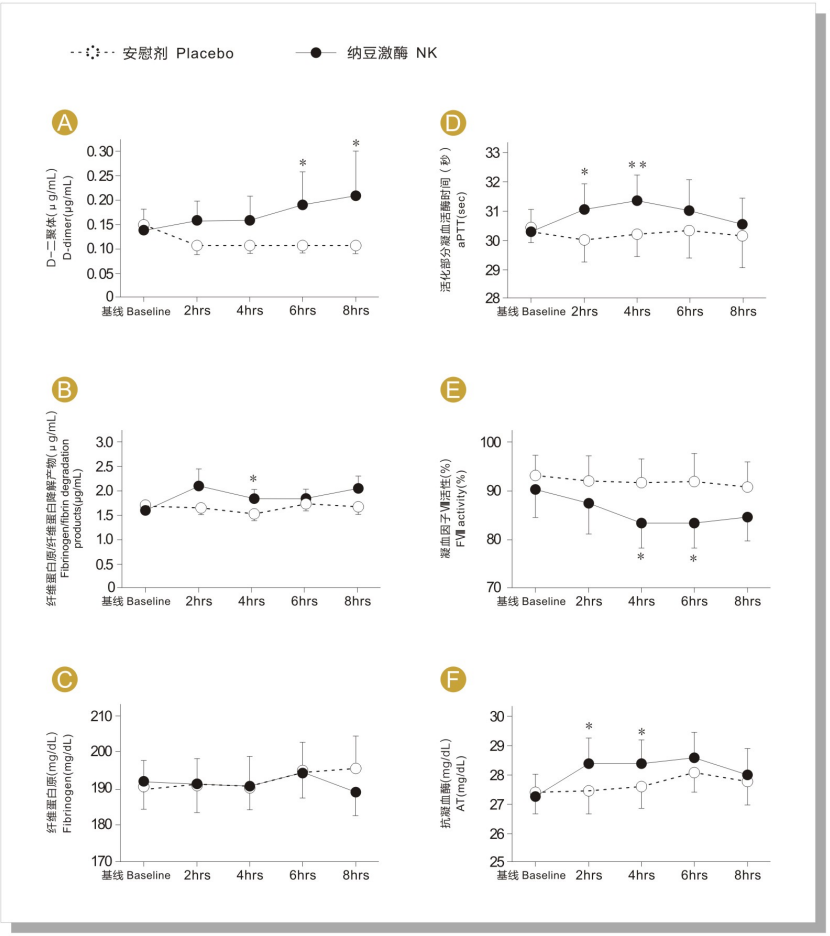
| 组别/group | R时间/min | α角/° | MA值/mm | Ly30/% |
|---|---|---|---|---|
| 对照组 control group | 1.49±0.55 | 74.99±5.83 | 76.21±5.26 | 0.61±0.42 |
| 低剂量NK组 low dose NK group | 1.68±0.53 | 73.39±7.25 | 74.29±6.03 | 0.51±0.39 |
| 中剂量NK组 medium dose NK group | 1.45±0.42 | 72.65±7.67 | 46.83±7.23**▲▲ | 13.52±13.16**▲▲ |
| 高剂量NK组 high dose NK group | 1.61±0.53 | 48.76±10.57**▲▲ | 6.54±1.43**▲▲ | 40.98±10.47**▲▲ |

注：与对照组相比，**P<0.01；与低剂量NK组相比，▲▲ P<0.01

**note:** compared with the control group, **P<0.01; compared with low dose NK group, ▲▲P<0.01

- 2015年《科学报告》刊载的“单剂口服纳豆激酶可增强溶栓和抗凝血性能研究”[4]：
  结论：通过增加纳豆激酶在血清中的含量与活性，证实在2-8小时后，血管中血栓的纤维蛋白及血凝现象均被纤溶酶有效裂解，并激活多个抗血栓和纤溶途径，以消除血栓形成的可能。

  A Study “A single-dose of oral nattokinase potentiates thrombolysis and anti-coagulation profiles”published in ***Scientific Reports*** in 2015 reported that increasing the content and activity of nattokinase in serum,fibrin of thrombus in the blood vessels and hemagglutination were cleavaged by plasmin after 2-8h.Antithrombotic and fibrinolytic pathways were activated to prevent thrombosis[4].

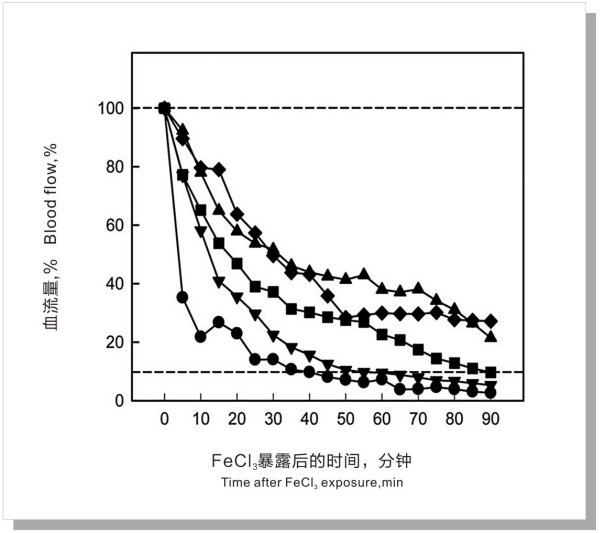


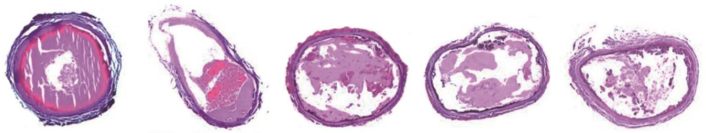
## 抗血凝

**Anticoagulant**

2013年 “纳豆激酶通过抑制血小板聚集和血栓形成来改善血液流动研究”[5]：
结论：纳豆激酶能明显抑制胶原蛋白和凝血酶诱导的血小板聚集，通过摄入纳豆激酶，因血凝造成的血管阻塞完全打开，并阻断了因血凝造成的血栓及血管壁损伤的发生风险。

A study “Nattokinase improves blood flow by inhibiting platelet aggregation and thrombus formation” in 2013 reported that Nattokinase significantly inhibited both the collagen- and thrombin-induced platelet aggregations,and fully prevented the occlusion.It also inhibited platelet aggregation by blocking thromboxane formation, and thereby delay thrombosis following oxidative arterial wall injury[5].



赋形剂 Vehicle | 纳豆(50mg/kg) Natto(50 mg/kg) | 纳豆(160mg/kg) Natto(160 mg/kg) | 纳豆(500mg/kg) Natto(500 mg/kg) | 阿司匹林(30mg/kg) Aspirin(30 mg/kg)

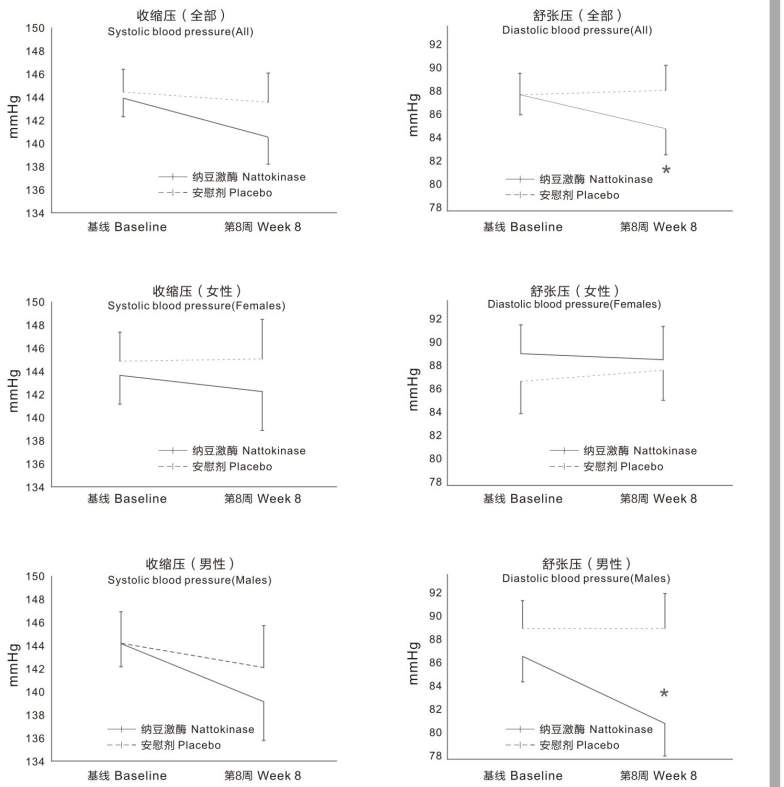


## 降血压

**Reduce Blood Press**

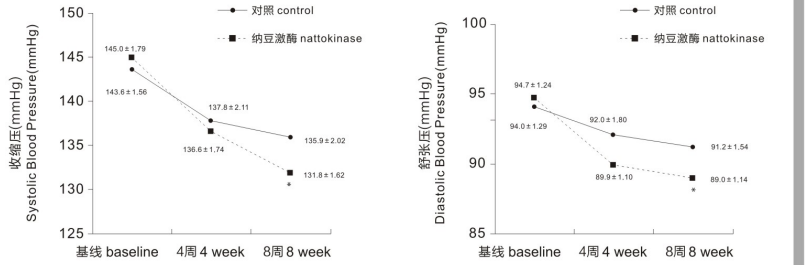
- 2016年一篇评估北美人群的“纳豆激酶的消耗与血压的降低和血管性风险标记有关研究”[6]：
结论：纳豆激酶在溶解血栓的同时改善血管的弹性，调节血管的收缩压和舒张压，防止因血栓造成血压上升，效果对比一般安慰剂更加显著。

A study"Consumption of nattokinase is associated with reduced blood pressure and von Willebrand factor, a cardiovascular risk marker: results from a randomized, double-blind, placebo-controlled, multicenter North American clinical trial" in 2016 is to evaluate the effects of consumption of nattokinase on hypertension in a North American hypertensive population,and reported that nattokinase promoted blood vessel elasticity and dissolved thrombus or blood clots. Consumption of nattokinase was associated with a reduction in both systolic and diastolic BP, the effect was much more effective than the placebo[6].



- 2008年的“纳豆激酶对血压的影响：随机对照试验性高血压研究”[7]：
  结论：通过为期8周的血压干预测试，表明摄入纳豆激酶可减少血管收缩压（SBP）和舒张压(DBP)，这一结果证实纳豆激酶可用以预防和改善高血压症状。

The study “Effects of Nattokinase on Blood Pressure: A Randomized, Controlled Trial” in 2008 reported that nattokinase supplementation resulted in a reduction in SBP and DBP. These findings suggest that increased intake of nattokinase may play an important role in preventing and treating hypertension[7].




## 抗动脉粥样硬化

**Anti-atherosclerosis**

2003年一项“用发酵大豆进行膳食补充可抑制内膜增厚研究”[8]：
结论：纳豆激酶可有效溶解造成动脉粥样硬化发生的血栓、胆固醇等物质，这一方式使得血管内膜增厚减少，降低了动脉粥样硬化发生风险。

A study “Dietary supplementation with fermented soybeans suppresses intimal thickening”in 2003 confirmed that natto extracts, because of their thrombolytic activity, suppress intimal thickening after vascular injury as a result of the inhibition of mural thrombi formation[8].

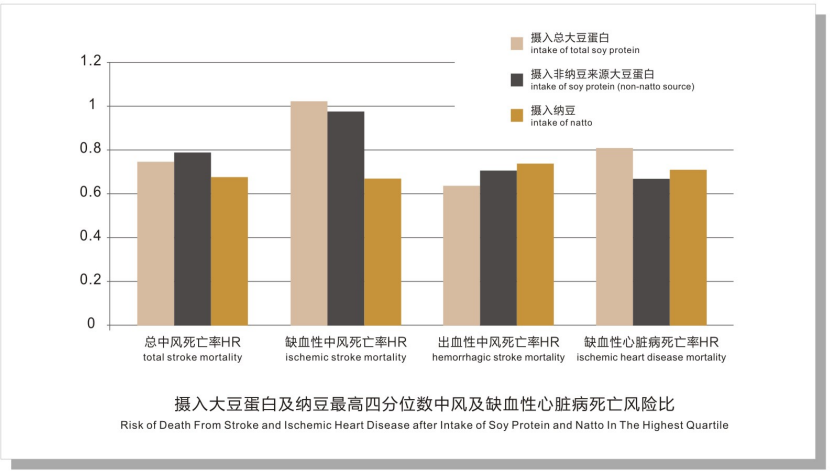


## 降低中风风险

**Reduce The Risk of Stroke**

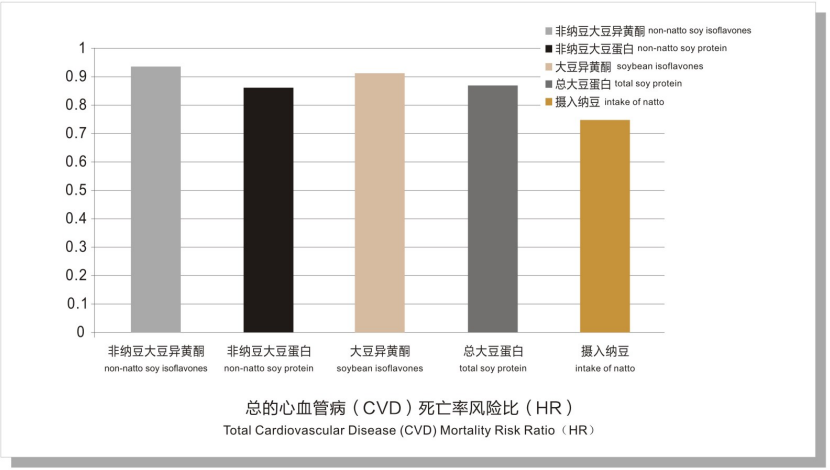
2017年 日本高山研究所一项“日本成人食用大豆、纳豆和心血管疾病死亡率研究”[9]：
结论：在降低中风及缺血性心脏病的死亡率方面，通过摄入纳豆可显著降低这两者造成的死亡风险。实验数据表明，相较于大豆，纳豆降低心血管疾病（CVD）死亡率风险的效果更加优秀。

the Takayama study of “Dietary soy and natto intake and cardiovascular disease mortality in Japanese adults” in 2017 reported that natto intake may contribute to the reduction of stroke and ischemic heart disease mortality. Data suggest that the effect of natto on the risk of reducing Cardiovascular disease（CVD） mortality is more excellent than soybeans[9].




摄入大豆蛋白及纳豆最高四分位数中风及缺血性心脏病死亡风险比

Risk of Death From Stroke and Ischemic Heart Disease after Intake of Soy Protein and Natto In The Highest Quartile




总的心血管病（CVD）死亡率风险比（HR）

Total Cardiovascular Disease (CVD) Mortality Risk Ratio（HR）

## 保护心肌缺血

**Protect Myocardial Ischemia**

2006年 一项“重组纳豆激酶对小型猪冠状动脉血栓的溶解作用研究”[10]
结论：证实纳豆激酶可有效缩小血栓面积，减轻心肌缺血，降低了心肌梗死发生风险。

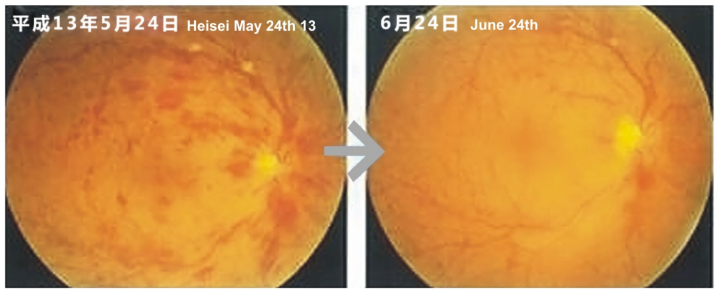
“Recombinant nattokinase for the dissolution of coronary thrombosis in small pigs” in 2016 confirmed that nattokinase can reduce the risk of myocardial infarction and effectively decrease thrombus formation[10].

## 改善眼部微循环，保护视力

**Improve Eye Microcirculation and Protect Eyesight**

2001年，日本研究机构证实纳豆激酶可消除视网膜静脉血管的栓塞现象，这一效果揭示纳豆激酶在改善眼部微循环及提升并保护视力方面有显著效果。

In 2001, Japanese research institutions confirmed that nattokinase can eliminate the risk of retinal venous thrombosis. These findings suggest that nattokinase has a significant effect on improvement of eye microcirculation and eyesight.




网膜中心静脉塞栓症的治疗病例
Treatment of Central Retinal Vein Plugs

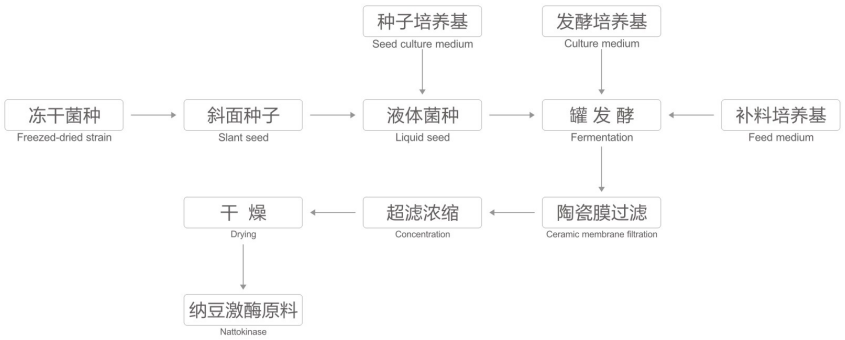
## 双骏生物自主创新第四代生产技术

UTILIZES FOURTH GENERATION NATTOKINASE PRODUCTION TECHNOLOGY BY SUNGENBIO

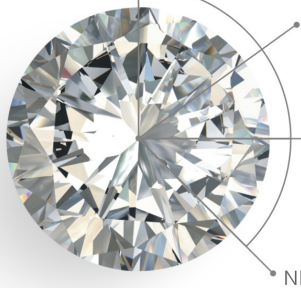
| 技术 Technology | 工艺 Process | 成分 Component | 最高活性 The Highest Activity |
|---|---|---|---|
| 第一代 The First Generation | 手工 Handcraft | 纳豆激酶、纳豆菌、嘌呤 Nattokinase, Bacillus subtilis natto,Purine | 1,000FU/g |
| 第二代 The Second Generation | 固体发酵 Solid Fermentation | 纳豆激酶、纳豆菌、嘌呤 Nattokinase, Bacillus subtilis natto,Purine | 3,500FU/g |
| 第三代 The Third Generation | 液体发酵 Liquid Fermentation | 纳豆激酶、嘌呤 Nattokinase,Purine | 20,000FU/g |
| 第四代 The Fourth Generation | 深层液体发酵、膜集成 Submerged Liquid Fermentation, Membrane integration | 高活性纳豆激酶 High-activity Nattokinase | 750,000FU/g |

## 高活性绿色生产流程

## HIGH-ACTIVITY GREEN PRODUCTION PROCESS



# 纳豆激酶活性检测
# NATTOKINASE ACTIVITY DETECTION



纤维蛋白平板法 (国际通用)
Fibrin Plate Method(International General Method)

分光光度法 (国际通用)
Spectrophotometry (International General Method)

高效液相色谱法(HPLC法) (双骏研发独有，快速判断)
HPLC (Sungenbio Proprietary Technology,Quick Detection)

NKIU法（以纳豆激酶纯品作为对照）(双骏未来研发方向，精准检测)
NKIU(Using Pure Nattokinase as Reference)
(Future Research Direction by Sungenbio,Accurate Detection)

## 高效液相色谱法
## HPLC

双骏生物率先将HPLC法应用在纳豆激酶的检测上，不但能快速检测纳豆激酶含量，而且为纳豆激酶成药性研究提供定量方法。

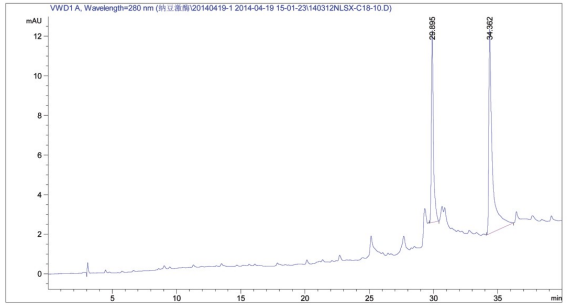
Nattokinase activity was determined by HPLC.It not only can quickly detect nattokinase content, but also provide a quantitative method for the study of nattokinase drug properties.

检测方法：
1）检测器要求：HPLC-UV
2）流动相：乙腈：0.1%TFA（0min-2min：乙腈：0.1%TFA=7%：93%；2min-30min：乙腈：0.1%TFA=61%：39%）
3）检测波长：UV280nm
4）色谱柱：4.6mm*25cm；5μm；Zorbax 300SB C3
5）柱温：25℃
6）流速：1.0ml/min

Detection method:
1) Detector Requirements: HPLC-UV
2) mobile phase: acetonitrile：0.1%TFA（0min-2min：acetonitrile：0.1%TFA=7%：93%；2min-30min：acetonitrile：0.1%TFA=61%：39%）
3) Detection wavelength: UV280nm
4) Column: 4.6mm*25cm; 5 μm; Zorbax 300SB C3
5) Column temperature: 25° C
6) Flow rate: 1.0ml/min



双骏生物纳豆激酶HPLC-UV法检测图谱
The HPLC-UV Spectrogram of Nattokinase Products by Sungenbio

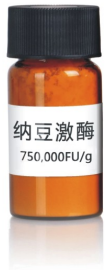



## NKIU法
## NKIU

双骏生物通过蛋白纯化工艺，获得纳豆激酶纯品，活性单位为750,000FU/g，双骏生物将推动NKIU作为纳豆激酶活性测定单位。

Nattokinase pure products (Activity 750,000FU/g )were purified by protein purification process. Nattokinase activity unit was defined as NKIU by SungenBio.

蛋白质纯化设备
protein purification equipment




双骏生物纳豆激酶纯品
nattokinase pure products from Sungen

# 产品特点
# CHARACTERISTIC

纯正纳豆菌发酵
Fermented from bacillus subtilis

活性高达65000FU/g（分子量27728D）
Activity 65000 FU/g (Molecular weight :27728D)

无防腐剂、无添加剂、无化学物质、无溶剂
No preservatives, No additives, No chemical substances, Solvent-free

品质稳定
Stable quality

加工性能良好
Outstanding processing performance

# 产品应用
# APPLICATION

保健食品（辅助防治动脉硬化、降血压、保护心脑血管等）
Health food (For preventing arteriosclerosis, lowering blood pressure, protecting cardiovascular and cerebrovascular diseases, etc.)

营养补充剂、食品（辅助改善眼部微循环，保护视力等）
Nutritional supplements, foods (helping to improve eye microcirculation, protecting eyesight, etc.)

| 产品规格 Product Specification | | 包装规格 Package Specification |
|---|---|---|
| 65000FU/g<br>40000FU/g<br>20000FU/g<br>10000FU/g | 5kg×3袋/桶<br>5kg×3 foil bags/fifer drum | LDPE（低密度聚乙烯）袋<br>密封真空铝箔袋<br>密封纸板桶<br>LDPE (low density polyethylene)bag<br>Sealed vacuum aluminum<br>Foil bag sealed carton |
| 5000FU/g<br>2000FU/g | 10kg×2袋/桶<br>10kg×2 foil bags/fifer drum | LDPE（低密度聚乙烯）袋<br>密封真空铝箔袋<br>密封纸板桶<br>LDPE (low density polyethylene)bag<br>Sealed vacuum aluminum<br>Foil bag sealed carton |



# 参考文献
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