

Physician-requested Product Sheet



Product: Boluoke® Lumbrokinase

Category: Blood Viscosity

Product No.: BD202 - 60 capsules; BD260 - 120 capsules

Special Dietary Usefulness

Boluoke® (lumbrokinase) has been available to the North American health care professionals since November of 2001. It is a revolutionary product, and shows great promise in optimizing the fibrinolytic activity of the body with little side effects.

Lumbrokinase is also referred to as earthworm fibrinolytic enzymes (EFE), earthworm powder enzymes (EPE), or e-PA. For many centuries earthworm has been used in the Far East traditional medicine practice, and it was recorded in the "Ben Cao Gang Mu", the traditional Eastern world's pharmacopoeia, as a potent medicine for "Liver Wind uprising and Channel blockage" conditions.

In the 1980's, Japanese scholars like Dr. Hisashi Mihara and others succeeded in extracting a fibrin-dissolving enzyme from *Lumbricus rubellus* and found that this enzyme consists of a few proteolytic sub-enzymes, which are collectively named lumbrokinase.

Since then many Korean and Chinese researchers have compiled extensive scientific and clinical data on lumbrokinase extracted from *Lumbricus rubellus* and *Eisenia fetida*. In Japan and Korea lumbrokinase has been the main ingredient in "Dragon Heart", a popular health supplement for supporting circulatory health. In China, lumbrokinase has been studied thoroughly and has been used clinically for clot-induced hypoperfusion conditions since early 1990s.

Boluoke® (lumbrokinase) is the only fully researched oral fibrinolytic supplement on the market. Besides having in vitro studies, animal studies, toxicity studies, and pharmacokinetic studies done, Boluoke® has also been put through all phases of clinical trials (including randomized double blind controlled studies) in China.

Lumbrokinase has been studied as a treatment for various clinical conditions, including acute, sub-acute, and chronic conditions that are associated with the presence of hypercoagulation and hypoperfusion.

Lumbrokinase is a more potent enzyme preparation than nattokinase. One of the advantages of Boluoke® (lumbrokinase) is that it does not interfere with the clotting cascade, but instead, works by reducing fibrinogen and fibrin. Boluoke® does not affect INR or aPTT, thus is compatible with Coumadin® or heparin.

Boluoke® vs. Other Lumbrokinase Products

Comparing other lumbrokinase products to Boluoke® is like comparing apples and oranges. Boluoke®'s enzymatic strength is standardized against urokinase and t-PA. The imitation products are likely just earthworm protein extract containing little pure lumbrokinase or lumbrokinase of low enzymatic strength. Some companies are making products with 230mg to 250mg of lumbrokinase per capsule and trying to quote Boluoke®'s research as their own.



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Boluoke®'s capsules are of 200mg in size, and contain 20mg of lumbrokinase inside each capsule. Most of these other lumbrokinase are unable to distinguish between the weight of the capsule (i.e. 250 mg) and the active lumbrokinase per capsule (Boluoke® is 20 mg).

Boluoke® is the only fully researched oral fibrinolytic supplement on the market. Besides having in vitro studies, animal studies, toxicity studies, and pharmacokinetic studies done, Boluoke® has also been put through all phases of clinical trials (including randomized double blind controlled studies) in China. Boluoke® is the only Lumbrokinase that is backed by Phase I – III clinical trials in China, the one that is first used in hospitals in China, and covered by the Chinese National Fundamental Health Insurance.

A common question we receive is about potential side effects of Boluoke®. The earthworm has been used in Traditional Chinese Medicine for a few thousand years, and is considered to be one of the safest medicines in the traditional pharmacopoeias. In one of the largest clinic trials of Boluoke® involving 16 hospitals and 1560 patients in China, the overall adverse reaction rate was 1.92% (30 cases). 0.58% had skin itching, 0.19% had skin rash, and 1.15% had nausea or diarrhea; no hemorrhage or major side effect was reported. *Again, this research pertains only to Boluoke®.*

Many other lumbrokinase products cite the clinical results achieved with only Boluoke®, confusing the reader into assuming that the research was done on their formulations. However, their products may be very different, and your patients may have very different results.

On the raw material market, the price of lumbrokinase can vary by up to 15 fold, and the enzymatic strengths of various Lumbrokinase also differ greatly. In addition, lumbrokinase is a preparation containing multiple enzyme fractions, and the extraction and purification method determines the composition of the various enzyme fractions. Thus different extraction methods will produce different sub-fractions of lumbrokinase. This is the reason why Boluoke® does not significantly change prothrombin time (PT) or activated partial thromboplastin time (aPTT), while other lumbrokinase sources may significantly alter PT or aPTT as shown in studies. No other lumbrokinase product can provide you with this assurance.

Boluoke® seems to be beneficial for any illness that has an accompanying hypercoagulable blood state, which has been shown to be present in many chronic illnesses. Some practitioners are also recommending Boluoke® for those who choose to be on hormone replacement therapy or birth control pills, and for those who could not tolerate standard preventative pharmaceutical drugs.

more →

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Features & Benefits

Boluoke® (lumbrokinase) is the only fully researched oral fibrinolytic supplement on the market, and it is the number one choice among health care professionals for their patients.

Features	Benefits
Clinically studied in double blind controlled studies	<ul style="list-style-type: none"> the only lumbrokinase product with the research to prove efficacy
Maximum 20mg of actual Lumbrokinase per capsule	<ul style="list-style-type: none"> highest level of pure Lumbrokinase (active ingredient) on the market
Lumbrokinase had been safely used together with Heparin or Coumadin in various clinical studies	<ul style="list-style-type: none"> does not have adverse drug interactions nor increase the chance of bleeding other than what is inherent to other blood thinners

Supplement Facts

Serving Size: 1 capsule
 Servings per Container: 60

Amount Per Serving		% Daily Value
Lumbrokinase	20mg	*

*Daily Value is not established.

Other Ingredients: gelatin, polysaccharide

Suggested Use

As a dietary supplement, if Boluoke® is to be taken for chronic conditions it should be taken at the dose of 1 capsule one to three times daily 30 minutes before the meal. However, the practitioner may recommend 2 capsules three times daily for 3 to 6 weeks in conditions with severe hypoperfusion.

Cautions

The patient should stop Boluoke® 1 week prior to surgery, and should be able to resume taking Boluoke® 15 days after surgery or at the physician's discretion. Lumbrokinase is not known to interact with any other medications at this point. However, the latest research shows that lumbrokinase strongly inhibits adhesion molecules on platelets. Thus it is advised that lumbrokinase not be taken concurrently with other strong anti-platelet medications like Plavix, Ticlid, etc. Pregnant patients should only use Boluoke® under physician's approval and guidance. Those with allergy to lumbrokinase or earthworm; or with recent surgery, lumbar puncture, or arterial puncture; trauma; aneurysm; active internal bleeding or GI ulceration; or any other bleeding disorders should not use lumbrokinase.

Research Papers

1. Fan Q, Wu C, et al. Some features of intestinal absorption of intact fibrinolytic enzyme III-1 from Lumbricus rubellus. Biochem Biophys Acta, 2001; 1526(3): 286-92
2. Gao Y, Qin MZ. Lumbrokinase in treatment of patients with hyperfibrinogenemia of coronary atherogenesis disease. Journal of Capital University of Medical Sciences, 1999; 4(20)
3. Gong B, Wu XY. Observation of using Baiao lumbrokinase capsules to treat ischemic cerebrovascular accident with hyperlipidemia. Capital Medicine, 2000; 7(12): 39
4. Guo ZF, Liu XX. Observation of treating ischemic cerebrovascular accident with Baiao lumbrokinase capsules. Capital Medicine, 2000; 7(11): 45
5. Huang ZD, Li ZW, Zhang WX. Lumbrokinase in treating cerebral infarction. Chinese Journal of New Drugs and Clinical Remedies, 2000; 6(19): 453-455

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Boluoke® FAQ

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1. How do you pronounce “Boluoke®”?

Boluoke should be pronounced: [bo-lo'-k]

2. How long before surgery should the patient stop taking Boluoke®? The patient should stop Boluoke® 1 week prior to surgery, and should be able to resume taking Boluoke® 15 days after surgery or at the physician’s discretion.

3. Can lumbrokinase be safely used together with other blood thinners?

Lumbrokinase had been safely used together with blood thinners like Aspirin, Heparin or Coumadin in various clinical studies, and does not have adverse drug-drug interactions nor increase the chance of bleeding other than what is inherent to the blood thinners. In a 1989 study Park et al. gave lumbrokinase to 10 normal volunteers, 10 DVT patients on warfarin, and 5 patients with essential hypertension. No change in PT, APTT was observed during the course of treatment, and there was no hemorrhagic complication.

4. Is there any known drug interaction with lumbrokinase?

Lumbrokinase is not known to interact with any other medications at this point. However, the latest research shows that lumbrokinase strongly inhibits adhesion molecules on platelets. Thus it is advised that lumbrokinase not be taken concurrently with other strong anti-platelet medications like Plavix, Ticlid, etc.

5. Has there been any study comparing lumbrokinase with other anti-platelet medicine?

Lumbrokinase has been put head-to-head with ticlopidine (Ticlid) in a clinical trial and the results showed that lumbrokinase is as effective as ticlopidine in reducing symptoms and improving EKG readings (Zheng HJ, 2000)

6. Can Boluoke® be used on pregnant women?

There is currently no clinical study using lumbrokinase on pregnant women, even though teratogenicity studies on animals showed no effect on pregnancy weight, fetal growth, abortion rate, still birth rate, and fetal resorption rate in mice compared to the placebo group. There was also no birth defect detected. However, pregnant patients should only use Boluoke® under physician’s approval and guidance.

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Boluoke® FAQ (continued)

7. How fast and how much can Boluoke® lower the patient's plasma fibrinogen level?

The rate would vary depending on the condition being treated and the starting fibrinogen level.

Some studies showed a reduction of 21% in 12 weeks, and some showed a reduction rate of 33% in 21 days. Most trials showed a reduction rate that is in between. On average, a reduction rate of 10-20% (or more) in 4 weeks can be expected when patients are on the full dosage of 2 capsules three times daily. Boluoke® will not reduce plasma fibrinogen level to below normal.

8. What is lumbrokinase's effect on FDP (Fibrin Degradation Product) or D-Dimer?

FDP and D-Dimer levels have been shown to increase sharply within three days of lumbrokinase administration in healthy and hyperfibrinosis individuals. Elevated FDP and D-Dimer levels indicate an increased fibrinolysis activity.

9. Does Boluoke® affect ESR or C-RP?

There are studies showing that lumbrokinase can significantly decrease ESR, C-RP, and TXB2.

10. What are the contra-indications for taking Boluoke®?

Contra-indications for Boluoke® are: allergy to lumbrokinase or earthworm; recent surgery, lumbar puncture, or arterial puncture; trauma; aneurysm; active internal bleeding or GI ulceration; or any other bleeding disorders.

11. Is Boluoke® effective in treating atherosclerosis?

There is currently no data on Boluoke®'s effect on atherosclerotic plaques. Because arterial plaques consist of cholesterol, minerals, cells and other substances beside fibrin, and Boluoke® may not be able to reduce them on its own. Boluoke® is more likely to prevent plaque formation or re-formation in combination with chelation treatment. There is, however, evidence showing that lumbrokinase has a synergistic effect when combined with antibiotics in the killing of bacteria with a protective bio-film (e.g. nanobacteria, pseudomonas). Even though it is still controversial, some researchers believe that nanobacteria play a central role in the atherosclerotic process

12. Can Boluoke® be combined with other enzyme products?

There is a theoretical possibility that Boluoke® may be cleaved and rendered ineffective by other enzymes, so we currently do not recommend dosing Boluoke® with another enzyme product. If you do have to take other enzyme products while on Boluoke®, try to space more time between the dosing of the two enzyme products (i.e. at least 2 hours).

13. How is Boluoke® different from other products that contain lumbrokinase?

Boluoke® has been through all phases of clinical trials in China. All other lumbrokinase products currently on the market often are citing Boluoke's® credential and research, and are not disclosing the enzymatic strength of their lumbrokinase (Boluoke's® enzymatic strength is standardized against Urokinase and t-PA activities). So be careful not to fall for second grade imitation products!

14. What is the suggested protocol for taking Boluoke®?"

If Boluoke® is to be taken for chronic conditions, it should be taken at the dose of 1 capsule one to three times daily 30 minutes before the meal. However, the practitioner may recommend 2 capsules three times daily for 3 to 6 weeks in conditions with severe hypoperfusion."

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Comparison Of Boluoke® (lumbrokinase) With Other Enzymes

Product Name	Boluoke®	Nattokinase	Boluoke® Imitators	Serrapepti- dase	Bromelain
Packaging	60 capsule	90 capsules mostly	30 to 36 capsules	60-90 tablets	quite variable
Main Ingredient(s)	20mg lumbrokinase per cap	38mg nattokinase per cap mostly	200mg to 250mg of lumbrokinase or lumbrokinase/ herbs mixture per cap	5 or 10mg of serrapepti- dase per cap usually	500mg of bromelain per cap, but varies greatly between companies
Enteric coated	Yes	Yes	Yes	Yes	No
Dosage	1 cap one to three times daily for prevention; 2 caps three times daily for active treatment	2 caps three times daily	4 capsules daily; or 6 to 9 capsules daily	10mg three times daily	750-2000mg per day usually, or higher
Source of enzymes	Earthworms	Natto cheese	Earthworm	Silkworm	Pineapple & its stems
Historical usage of enzyme source with a safe record	Yes, in Traditional Chinese Medicine for a few thousand years	Yes, in traditional Japanese diet as Natto for over a thousand years	Yes, in Traditional Chinese Medicine for a few thousand years	No	Yes
History of large clinical use with a safe record	Yes, in China hospitals since 1995 with excellent safety record	No	No	No	Yes

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pH and temperature stability	Stable up to 65°C in the pH range of 2-12. Optimal pH is between 4-10	Stable up to 60°C in the pH range of 6-12	Unknown	Unknown	Active mainly between pH 4.5-9.8 range. Heat sensitive
Fibrinolytic strength in plasmin unit (CU)	~100 CU/g wet weight	~40 CU/g wet weight	Unknown	Technically not a true fibrinolytic enzyme	Technically not a true fibrinolytic enzyme
Enzyme in product is standardized against Urokinase & t-PA	Yes. Each mg of lumbrokinase in Boluoke contains no less than 120,000u of tPA activity, and no less than 100u of Urokinase activity	No. But 1mg of nattokinase (95% pure from cDNA source) contains ~12,000u of tPA activity (commercial nattokinase is much weaker); and that 1mg wet weight Natto contains ~1.6u of Urokinase activity	No. The ingredients in the imitation products is likely just earthworm protein extract, or lumbrokinase of lower enzymatic strength	No. Technically not a true fibrinolytic enzyme	No. Usually standardized to milk clotting unit (MCU), or gelatin digestive unit (GDU). Products on the market have quite variable enzymatic activities, from 1000 to 500,000 MCU per gm
Dissolves fibrin directly	Yes	Yes	Yes	No evidence yet, only anecdotal	No, but indirectly by activating fibrinolysis
Activates T-PA	Yes	Yes	Yes	No evidence yet	Yes
Decreases platelet aggregation	Yes	No evidence yet	No evidence yet, but likely	No evidence yet	Yes

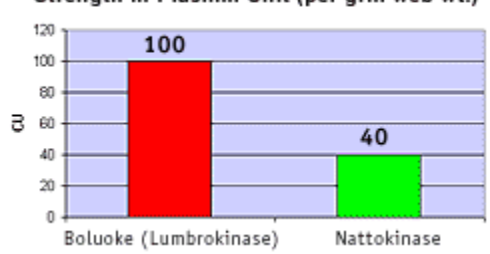
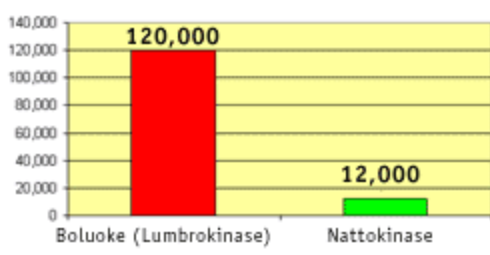
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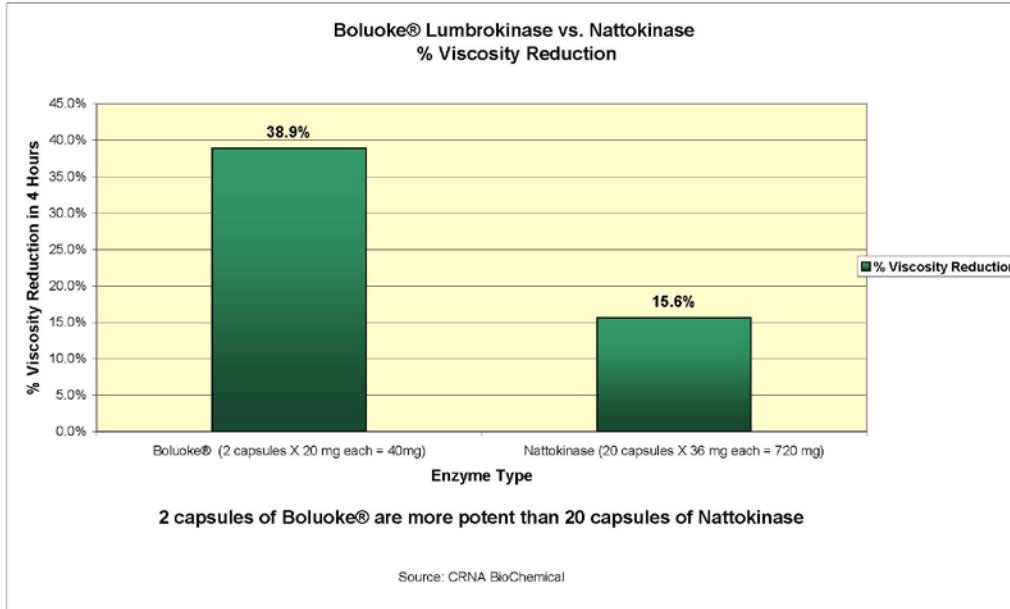
Lower blood and plasma viscosity	Yes	Yes	Yes	No evidence yet	No evidence yet, but likely
Decreases plasma fibrinogen level	Yes	No evidence yet, but likely	No evidence yet, but likely	No evidence yet	Yes, in animal studies
Reduces ESR & C-RP	Yes	No evidence yet	No evidence yet	No evidence yet, but likely	No direct evidence, but likely
Reduces cholesterol and triglycerides	Yes, mildly	No evidence yet	No evidence yet	No evidence yet	No evidence yet
Reduces Thromboxane B2	Yes	No evidence yet	No evidence yet	No evidence yet, but likely	No direct evidence, but likely
Effects on PT or APTT	Boluoke has been shown to not affect PT or APTT significantly	Possible, especially when combined with Coumadin. Natto cheese has high content of Vit. K	Unknown. However, some lumbrokinase preparations has been shown to affect aPTT in the past	Unknown	Markedly prolong PT and APTT
Human clinical trials done	Yes. Phase I to III clinical trials completed on Boluoke specifically	Only 2 small human trials	Unknown	Yes, mainly on tissue swelling, inflammation, & chronic respiratory diseases	Yes
Double-Blind study done	Yes	No	N/A	Yes	Yes

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LD50	Known. Human clinical dose is about 1/2000 to 1/4000 of the LD50 dose in mice	Undetermined, but greater than 5000mg/kg	Unknown	Unknown	Greater than 10g/Kg
Toxicity Studies	No toxicity seen on the nervous, cardiovascular, respiratory systems, nor on kidney/liver functions and hematology.	No toxicity seen in rodents given 700 times the physiological dose for humans	One product shows that doses up to 200 times of human dose did not produce toxicity in mice	Unknown	No toxicity seen at doses up to 750mg/Kg daily for 6 months in dogs. However, there are reports of palpitation by patients at doses above 700mg/d.
Mutagenicity	Negative Ames, lymphocyte DNA mutation tests	Unknown	Unknown	Unknown	No effects at 1.5g/Kg/day to rats
Teratogenicity	No effect on pregnancy weight, fetal growth, abortion rate, still birth rate, and fetal resorption rate in mice. No birth defect observed.	Unknown	Unknown	Unknown	No effects at 1.5g/Kg/day to rats

Fibrinolytic Strength Comparison Chart

Fibrinolytic Strength	Boluoke® (Lumbrokinase)	Nattokinase	Chart
Plasmin Unit (CU/g wet wt.)	100	40	<p>Strength in Plasmin Unit (per grm wet wt.)</p>  <p>Boluoke® Nattokinase 1,2</p>
t-PA Unit (u/mg)**	120,000	12,000	<p>Strength in t-PA Unit (per mg)</p>  <p>Boluoke (Lumbrokinase) Nattokinase</p>



1. Sumi H, Hamada H, Tsushima H, et al. *Experientia* 1987; 43(10): 1110-1
2. Liu BY, Song HY. *Sheng Wu Hua Xue Yu Sheng Wu Wu Li Xue Bao (Shanghai)* 2002; 34 (3) 338-40

* * The nattokinase used in measuring the t-PA activity is from research cDNA source, a much stronger enzyme than the commercially available source from natto extract.

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