革命性的维生素K2 REVOLUTIONARY VITAMIN K2



中国天然维生素K2原料制造商

Natural Vitamin K2 Manufacturer in China

中国天然维生素K2产品方案提供商

Natural Vitamin K2 Product Solution Provider in China

提纯技术已获国家发明专利(专利号: ZL 201410564384.X)

Purification Technology Has Obtained A National Invention Patent (Patent No. ZL 201410564384.X)

维生素K2,也称甲基萘醌(Menaquinone),通常用MK来表示。它由一组化合物组成,共有14种形式,差别在于侧链的长短不一,代表性的分子是MK-4和MK-7。其中MK-7具备功能广泛、活性强大、半衰期长、安全等特点。美国国立卫生研究院(National Institutes of Health,NIH)膳食补充剂办公室(Office of Dietary Supplements,ODS)评价维生素K2为革命性和多能性的维生素,具有健康保健的广阔应用前景。

Vitamin K2, also known as Menaquinone (MK), consists of 14 compounds. The difference is the length of the side chains. The representative molecules are MK-4 and MK-7.MK-7 is characterized by extensive functions, strong activity, long half-life and safety of vitamin K2. NIH and ODS evaluated vitamin K2 as a revolutionary and multipotent vitamin for the application prospect of health care.

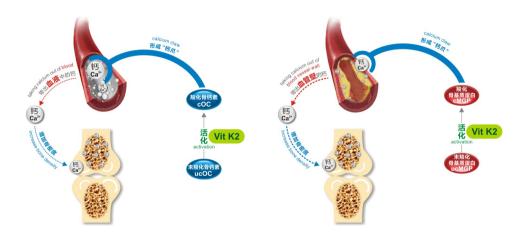
骨骼健康程度取决于成骨细胞的形成与钙对骨骼的补充。研究证实,维生素 K2(MK-7)可以清理游离在血管中并发生错误沉淀的钙离子,重新聚合并正确 运输到骨骼中,是保障骨骼和心血管健康极其重要的天然维生素。

Good bone health depends on bone formation carried out by osteoblasts and calcium supplement. New research reveals that Vitamin K2(MK-7) moves calcium deposits from blood vessels and correctly deposited into the bones. It is of great importance to bone and cardiovascular health,

维生素K2——领钙入骨 VITAMIN K2——GET CALCIUM INTO YOUR BONE

成骨机制中存在名为"y羧化酶"的转化酶原,其可羧化一组特定蛋白,提升钙在骨骼的沉积。作为y羧化酶重要的辅助因子,维生素K2(MK-7)是羧化过程与钙吸收中不可或缺的重要维生素。

 γ –glutamyl carboxylase is an enzyme that carboxylates a specific set of proteins and promotes bone deposition. Vitamin K2(MK-7) plays an essential role as cofactor for the enzyme γ –glutamyl carboxylase, which is involved in carboxylation and calcium absorption,



钙吸收过剩会对骨骼、心血管、大脑及肾脏肝脏等细胞组织、器官有非常严重的致病风险。钙游离在血管中会造成严重的钙沉积问题,不仅损伤血管发生钙化,还影响到心脏等器官和大脑神经中枢的健康。

Excessive calcium absorption can pose a very serious risk to the bone, cardiovascular, brain, kidney, liver and other cell tissues and organs. These imbalances also can cause calcium to deposit in the blood vessels and contribute to vascular calcification or heart disease.

维生素K2(MK-7)通过羧化成骨机制中的骨钙素和骨基质蛋白,抓取游离在血液与沉积在血管中的钙, 防止钙化风险的发生,降低了心血管及大脑发生疾病的风险。

Vitamin K2 (MK-7) is essential for trapping and binding calcium into bone. It can reduce the risk of cardiovascular and heart disease through the carboxylated osteocalcin and bone matrix protein.

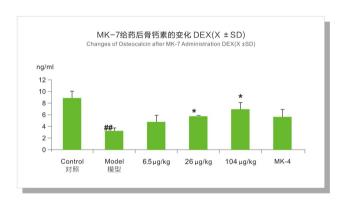
维生素K2的健康作用

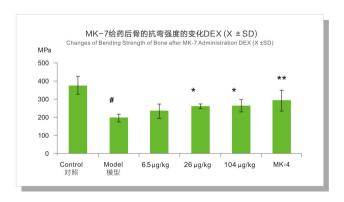
THE HEALTH EFFECTS OF VITAMIN K2

骨骼健康

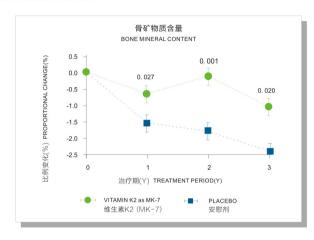
Bone Health

- 双骏生物联合沈阳药科大学开展"维生素K2治疗骨质疏松研究":
 结论:维生素K2可转化骨钙素,提升钙在骨骼的沉积,达到改善骨质疏松的作用。
- A study "The relationship between vitamin K2 intake and Osteoporosis" has been investigated by SungenBio & Shenyang Pharmaceutical University. The research indicated that vitamin K2 enhances osteocalcin transformation and improves the deposition of calcium into the bones. Vitamin K2 has also been proven effective for the prevention and treatment of osteoporosis.

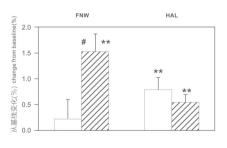




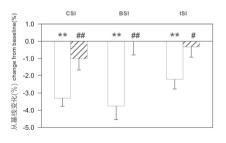
- 2013年一项"3年低剂量的维生素K2-7补充有助于减少绝经后妇女的骨质流失研究"^[1]: 结论:补充维生素K2能羧化骨钙素,减少未羧化骨钙素含量;与钙质转化为骨骼吸收的骨钙蛋白, 提升骨骼钙水平,降低骨质丢失造成的骨密度下降。
- A study "Three-year low-dose menaquinone-7 supplementation helps decrease bone loss in healthy postmenopausal
 women"in 2013 confirmed that osteocalcin is carboxylated by vitamin K2. Vitamin K2 supplemention reduces serum
 concentrations of under--carboxylated osteocalcin and helps decrease bone loss. It is necessary in the process for
 absorption of osteocalcin into the bone".



- 2007年一项"补充维生素K2可以改善绝经后妇女髋部骨几何结构与骨强度指数研究"^[2]:
 结论:摄入维生素K2对于骨强度指数有明显改善,主要变化在骨矿含量及股骨颈宽度增加,且骨骼抗压抗冲击强度有显著的加强。
- A study "Vitamin K2 supplementation improves hip bone geometry and bone strength indices in postmenopausal
 women"demonstrated that Vitamin K2 is essential for maintaining bone strength in postmenopausal women, and
 also improved bone mineral content and femoral neck width".



股骨颈宽度(FNW)和髋轴长度(HAL) Femoral Neck Width (FNW) and Hip Axis Length (HAL)



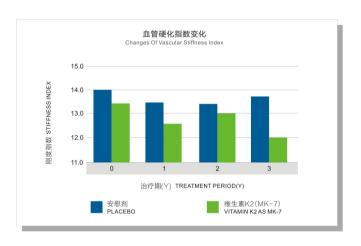
抗压强度指数(CSI)抗弯强度(BSI)和冲击强度(ISI) Compressive Strength Index (CSI) Bending Strength Index(BSI) Impact strength Index(ISI)

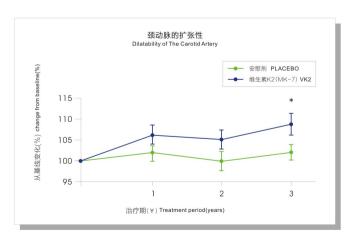
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心血管健康

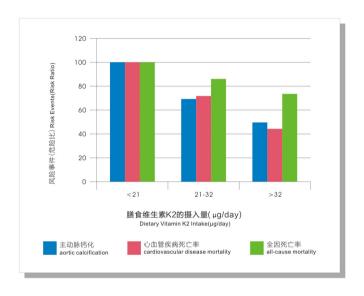
Cardiovascular Health

- 2015年《Thrombosis and Haemostasis》刊载关于"改善绝经妇女血管硬化和增强张性研究"^③: 结论:研究证实,羧化增加骨基质蛋白,使其聚集在动脉内层的弹性纤维周围,剥离抓取沉积在 动脉管壁上的钙,达到保护血管,避免发生钙化风险。
- Thrombosis and Haemostasis published a research about "Enhance vascular reactivity and reduce vascular sclerosis in
 postmenopausal women" no 2015. The research indicated that carboxylation of bone matrix protein influences the risk of
 calcification. MGP keeps calcium out of arteries and potect the blood vesselsⁱⁿ.





- 荷兰鹿特丹一项长达10年,超过4800人的研究"饮食摄入的维生素K2与降低患冠心病的风险有关: 鹿特丹的研究"^[4]:
- 结论:证实补充维生素K2,主动脉钙化的危险降低50%;心血管疾病死亡危险降低50%;各种原因导致的死亡率降低25%。
- The Rotterdam study "Dietary intake of menaquinone is associated with a reduced risk of coronary heart disease "had
 followed more than 4800 initially healthy persons for over a 10 year period. The study shows that people who consumed most
 vitamin K2, had a 50% reduced risk of arterial calcification and also a 50% risk reduction for cardiovascular, and 25%
 reduction of all-cause mortality".



肾脏健康

Kidney Health

- 2014年一项"在血液透析患者中补充维生素K2:一项随机的剂量测定研究"^[6]:
 结论:通过给予200名需长期血液透析的肾病患者分别摄入不同剂量的维生素K2共8周,结果发现患者血液中Gas6水平随着维生素K2摄入剂量的增高,呈现逐渐下降趋势,具有显著相关性(r=-0.24,P<0.01)。维生素K2的摄入可有效降低需进行血液透析的肾病患者的血管钙化风险。
- A study "Vitamin K2 supplementation in haemodialysis patients: a randomized dose-finding study ":200 patients with long-term
 hemodialysis were randomly allocated to supplementation of vitamin K2 for 8 weeks. The research have observed a downward
 trend in Gas6 with increasing dose of vitamin K2, showed a signifficant positive correlation (r=-0.24, P<0.01). Vitamin K2
 supplementation may reduce the risk of vascular calcification in Hemodialysis patients with kidney disease[®].

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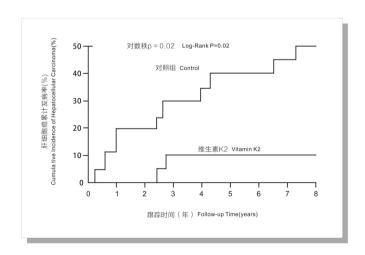
肝脏健康

Liver Health

- 双骏生物联合美国堪萨斯大学肿瘤研究中心在《Current Molecular Medicine》杂志发表了研究论文"维生素K2增强肝再生与卵形细胞扩张和2-AAF/PH大鼠模型中Matrilin-2的表达上调有关"^[6]:结论:从器官、细胞、蛋白、mRNA四个维度都证明,维生素K2能促进肝细胞再生,其机理为:维生素K2诱导Matrilin-2 mRNA增殖,增加Matrilin-2蛋白表达水平,激活肝干细胞促进肝再生。
- SungenBio and University of Kansas Center for Cancer Research published "Vitamin K2-Enhanced Liver Regeneration is Associated with Oval Cell Expansion and Up-Regulation of Matrilin-2 Expression in 2-AAF/PH Rat Model" in Current Molecular Medicine

Conclusion:Organ, cell, protein and mRNA proved that Vitamin K2 can promote liver cell regeneration. Vitamin K2 treatment enhances liver regeneration, which is associated with expansion and matrilin-2 up-regulation.

- "维生素K2在肝硬化患者肝细胞癌发展中的作用研究" ^[7]: 结论:针对肝癌转化风险研究中,维生素K2通过诱导Matrilin-2 mRNA增殖,增加Matrilin-2蛋白表达水平, 促进肝细胞再生。这一调节机制能有效抑制肝癌细胞生长,对肝癌转化达到了20%的明显抑制效果。
- A study "Role of Vitamin K2 in the Development of Hepatocellular Carcinoma in Women With Viral Cirrhosis of the Liver "shows that
 Vitamin K2 treatment enhances liver regeneration, which is associated with martin-2 mRNA expression and matrilin-2 up-regulation.
 The vitamin K2 actions can effectively inhibit the growth of liver cancer cells and decrease the risk of liver cancer by 20%".



辅助治疗帕金森氏症

Adjuvant Treatment of Parkinson's Disease

2012年《SCIENCE》刊载的一篇"维生素K2是一种线粒体电子载体,可以挽救pink1缺乏研究"^[8]:结论:维生素K2可以改善线粒体内的电子运输,因此可以使细胞中受损线粒体恢复正常,解决了导致帕金森氏症PINK1基因缺陷问题。

A study "Vitamin K2 is a mitochondrial electron carrier that rescues pink1 deficiency" published in **SCIENCE**(2012), shows that vitamin k2 can improve electron transport in the mitochondria and cures mitochondrial dysfunction to solve the defect of PINK1 gene in Parkinson's disease. "I.

改善糖尿病并发症

Improve Diabetes Complications

2009年关于"骨钙素的非羧化形式与改良的葡萄糖耐受性有关,并增强了中年男性受试者的细胞功能研究"^[0] 结论:糖尿病很大程度是因胰脏局部血管钙化造成胰岛素分泌功能降低,研究者认为维生素K2在消除钙化问题的同时,可提升胰岛素分泌反应,降低糖尿病发生风险。

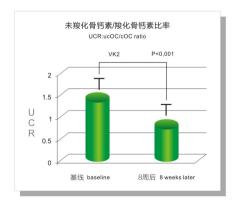
A study "The uncarboxylated form of osteocalcin is associated with improved glucose tolerance and enhanced beta-cell function in middle-aged male subjects" indicated that diabetes is associated with reduced insulin secretion caused by pancreatic calcification. Vitamin K2 increases insulin sensitivity, thereby helping to reduce the risk of diabetes!".

改善儿童生长痛

Improve Growing Pains in Children

"维生素对健康儿童骨钙素羧化作用的影响研究"^[10]:结论:儿童发育期常出现骨骼关节疼痛问题,研究认为这与维生素K2存量不足存在关系,补充维生素K2可增加骨骼骨质的积蓄,降低未羧化骨钙素,减少儿童发育过程中骨骼疼痛问题。

A study "The effect of menaquinone-7 (vitamin K2) supplementation on osteocalcin carboxylation in healthy prepubertal children" indicated that one of the most common causes of joint pain in childhood is Vitamin K2 deficiency. Vitamin K2 supplements enhance osteocalcin accumulation and reduces serum concentrations of undercarboxylated osteocalcin".



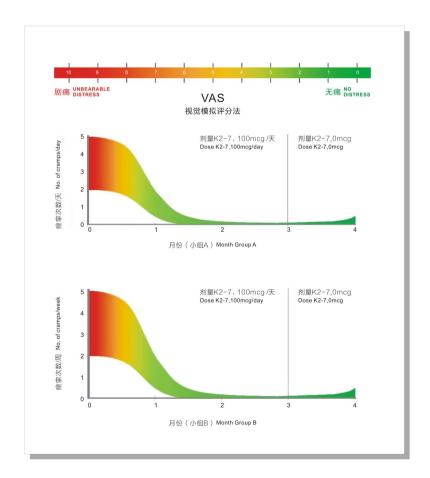
改善肌肉痉挛

Improve Muscle Spasms

2015年《Thrombosis and Haemostasis》刊载的一篇"维生素K2(MK-7)补充剂改善绝经后妇女的动脉硬化:双盲随机临床试验研究" $^{[1]}$:

结论:维生素K2(MK-7)可加速手臂与大腿的血液流速,减轻因血管钙化引起肌肉痉挛所带来的不适感。

A study "Vitamin K2 (MK-7) supplementation improves arterial stiffness in healthy postmenopausal women: a double-blind randomised clinical tria" published in *Thrombosis* and *Haemostasis* in 2015 indicated that Vitamin K2 (MK-7) can accelerate blood flow in arm and thigh and reduce muscle spasms and pain caused by vascular calcification".



维生素K2活化靶点

Active Target for Vitamin K2

已知的人体维生素K2活化靶点拥有17种蛋白,维生素K2作为人体细胞生长代谢的重要辅助因子,将会有更多未知的维生素K2依赖性蛋白等待被发掘,从而展现出维生素K2越来越广泛的生理活性功能。

There are currently 17 different vitamin K-dependent proteins known, which means that vitamin K2 will be one of the most important cofactor for growth and metabolism of human cells. In the future, there will be more unknown vitamin K2 dependent proteins waiting to be discovered, thus demonstrating the increasingly extensive physiological activity of vitamin K2.

17种维生素K依赖性蛋白[12]

17 Vitamin K-dependent (VKD) Proteins

蛋白名称	位置	功能
Vitamin K dependent Gla protein	Location	Function
凝血因子II、VII、IX、X	肝脏	促凝活性
Clotting factors II,VII,IX and X	Liver	Haemostasis(procoagulant activity)
蛋白C、S、Z	肝脏	抗凝血活性
Protein C. S and Z	Liver	Haemostasi(anticoagulant activity)
骨钙素	骨	钙和骨代谢
OC(Osteocalcin)	Bone	Calcium and Bone metabolism
骨基质蛋白	软骨、血管	抑制血管钙化
MGP (Matrix-Gla-Protein)	Cartilage、blood vessels	Inhibitor of vascular calcification
Gas6	血管、心脏 blood vessels、heart	细胞生长、凋亡、吞噬作用 Cell growth (endothellum, smooth muscle cells involved in cell signaling, in the regulation of a protease cascade relevant in growth regulation.), apoptosis,phagocytosis
GRP	软骨 Cartilage	与异位钙化相关,存在于皮肤 基底细胞和乳腺癌 Associated with ectopic calcifications, in skin basal cell and breast carcinomas
TMG3,TMG4	各种组织 Various Tissues	信号转导至磷脂酰丝氨酸 Signal transduction to phosphatidylserine
Tgfbi	各种组织 Various Tissues	含有CRS和C-谷氨酸残基。Tgfbl的已知功能取决于C-羧化的程度尚不清楚 Contains CRS and c-glutamic acid residues. The extent to which known functions of Tgfbi depend on c-carboxylation is not yet known.
骨膜素	各种组织	骨代谢,细胞迁移,血管生成
Periostin	Various Tissues	Bone metabolism, cell migration, Angiogenesis
PRGP1, PRGP2	各种组织 Various Tissues	到目前为止的功能主要是未知的 Function to date mainly unknown

"双骏生物维生素K2科研基金" & "维生素K2研究中心"

"SUNGENBIO VITAMIN K2 RESEARCH FUND" & "VITAMIN K2 RESEARCH CENTER"

"双骏生物维生素K2科研基金"于2017年5月在中国科学营养大会上正式成立,面向全球公开招标具有重要科学意义、应用价值和可行性的维生素K2相关研究课题,为国际维生素K2研究领域带来新的发展与突破; "维生素K2研究中心"于2017年11月由沈阳药科大学与双骏生物联合成立,为国际第一家维生素K2专项研究中心,将建设成为世界先进的维生素K2专项科技研发中心、科研人才培养中心和国际合作交流中心。

SungenBio Vitamin K2 Research Fund was formally established at the China Scientific Nutrition Conference in May 2017. It collects vitamin K2 related research projects that have important scientific significance, application value, and feasibility through global open tendering process, bringing new development and breakthrough for international vitamin K2 research field. Vitamin K2 Research Center was jointly established by Shenyang Pharmaceutical University and SungenBio in November 2017. It is the first international research center of vitamin K2, which will be built into the world's advanced vitamin K2 special scientific and technological research center, scientific research personnel training center and international cooperation and exchange center.

"维生素K2科研基金"研究课题

Vitamin K2 Research Fund Projects

单位 Units	课题 Projects
川北医学院 North Sichuan Medical College	维生素K2对维持性血液透析患者血管钙化的预防作用 The Preventive Effect of Vitamin K2 on Vascular Calcification in Maintenance Hemodialysis Patients
哈尔滨医科大学 Harbin Medical University	关于维生素K2与骨和骨骼肌健康效应关系的研究 Study on The Relationship between Vitamin K2 and Health Effects of Bone and Skeletal Muscles
哈尔滨医科大学 Harbin Medical University	关于维生素K2与眼底病变、糖尿病及心血管疾病关系的研究 Study on The Relationship between Vitamin K2 and Fundus Disease, Diabetes and Cardiovascular Diseases
中国营养学会营养与 保健食品分会 China Nutrition and Health Food Association	食品中维生素K2的测定 Determination of Vitamin K2 in Foods
沈阳药科大学 Shenyang Pharmaceutical University	维生素K2(MK7)对肿瘤的影响 The Effect of Vitamin K2 (MK7) on Tumor
大连医科大学 Dalian Medical University	维生素K2对冠状动脉粥样硬化心脏作用研究 Research on The Effect of Vitamin K2 on Coronary Atherosclerosis

100%全反式维生素K2(MK-7) 100% ALL-TRANS VITAMIN K2 (MK-7)

双骏生物运用独有提纯技术所获得的天然维生素K2,对人体具有非常高的亲和度,是具有最高活性的 100%全反式维生素K2(MK-7),内控指标比美国药典USP39-NF34标准(维生素K2(MK-7)反式 占比\$98%)更高。

Natural vitamin K2 produced by SungenBio is 100% all trans Vitamin K2(MK-7) with the highest activity and a very high affinity for the human body. The internal control index is higher than USP39-NF34 standard (The ratio of trans vitamin K2(MK-7) is \geq 98%).

检测方法:

- 1) 检测器要求·HPI C-UV
- 2) 流动相: 水:无水乙醇:甲醇:四氢呋喃=1:15:80:10
- 3)检测波长: UV268nm
- 4) 色谱柱: 4.6mm*25cm; 5 µm; packing L62
- 5)柱温:25℃
- 6) 流速: 0.8ml/min

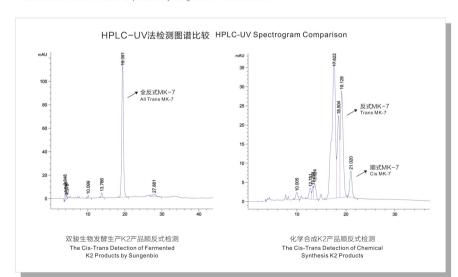
注:方法来源USP39-NF34(反式与顺式的保留时间比例为1.0:1.1)

结论:双骏生物提供的维生素K2(MK-7)为100%全反式结构。

Detection method:

- 1) Detector requirements: HPLC-UV
- 2) Mobile phase: water: absolute ethanol: methanol: tetrahydrofuran = 1:15:80:10
- 3) Detection wavelength: UV268nm
- 4) Column: 4.6mm*25cm; 5μm; packing L62
- 5) Column temperature: 25°C
- Flow rate: 0.8ml/min

Note: Method Source: USP39-NF34 (trans and cis retention time ratio is 1.0:1.1) Conclusion: Vitamin K2 (MK-7) provided by SungenBio is 100% all-trans.



产品特点 **CHARACTERISTIC**

纯种纳豆菌, 天然绿色安全 Fermented from bacillus subtilis, green and safe.

现代生物技术诱导产出高活性菌种 High activity strains induced by modern biotechnology.

合理培养基配方设计, 多要素动态控制技术 Reasonable culture formula, Multi-factor dynamic control technology.

零有机溶剂提取,物理分离浓缩技术,无二次污染 Physical separation and concentration technology without organic solvents.

无防腐剂、无添加剂、无化学溶剂、无合成 No preservatives, No additives, No chemical substances, Solvent-free

活性稳定持久 Stable and durable bioactivity

生产工艺对比 PROCESS COMPARISON

双骏生物纳豆发酵物理提纯	化学合成
Fermentation of Natto & Physical Purification(Sungen)	Chemical synthesis
100%全反式	25%-95%反式
100% all trans	25%-95% trans
投料安全、天然可控	化工工艺,有化学溶剂残留
Natural and controllable	Chemical process with chemical solvent residue
物理多级膜浓缩工艺,零残留 Multi-stage membrane process,non-residue	分离过程复杂,杂质多 Complicated separation process with many impurities
零污染	化工、环境污染大
Environmentally friendly	Chemical and environmental pollution

高活性绿色生产流程 HIGH-ACTIVITY GREEN PRODUCTION PROCESS



*维生素K2(发酵法)国家标准制定者(卫计委2016年第8号公告) Vitamin K2 National Standards Developer (NHFPC Announcement No. 8 in 2016 of NHFPC)

*产品列入保健食品备案原料目录(卫计委2016年第205号公告)

ESSE K2[™] have been included in the Health Food Raw Materials Directory (Announcement No. 205 in 2016 of NHFPC)

*双骏生物维生素K2获得欧盟新资源食品认证 EU NOVEL FOODS approval

制定国家标准,实现微量定量

适用类型 Appropriate Type ————————————————————————————————————	分析方法 Analytical Method	检测精度 Detection Precision	相关依据 Decision Basis
原料 (油剂或粉剂)	HPI C-UV	纳克 ng	卫计委2016年第8号公告方法 Announcement No.8 in 2016 of NHFPC
Ingredient(Powder&Oil)	TIPEC-0V		USP39-NF-34中Menaquinone-7方法 USP39-NF-34
	HPLC-UV	纳克 ng	卫计委2016年第8号公告方法 (需根据具体配方做方法学验证)
膳食补充剂	HPLC-FLD	皮克 pg	Announcement No. 8 in 2016 of NHFPC (Methodological verification should be made according to the formula)
Dietary Supplements	LIBLO LIV	纳克	USP39-NF-34 中Menaquinone-7方法 (需根据具体配方做方法学验证)
	HPLC-UV	ng	USP39-NF-34(Methodological verification should be made according to the formula)

产品应用 APPLICATION

保健食品(辅助补钙、辅助防治骨质疏松症等)

Health food (For Calcium Supplementation, prevention of Osteoporosis, etc.)

营养补充剂、食品(辅助补钙等)

Nutrition supplements, foods (For calcium supplements, etc.)

饮料(运动饮料,辅助改善肌肉痉挛等)

Drinks (sports drinks, help improve muscle spasms, etc.)

产品规格 Product Specification		包装规格 Packing Specification
油剂 Oil	1500ppm 2000ppm 4500ppm 15000ppm 20000ppm	20公斤 密封铝罐 20kg Sealed aluminum cans
粉剂 Powder	1000ppm 2000ppm 4500ppm 15000ppm 20000ppm	1公斤×25袋/桶 5公斤×5袋/桶 LDFE(低密度聚乙烯)袋 密封真空铝箔袋
水溶性粉剂 Water-soluble Powder	1000ppm 2000ppm	密封纸板桶 1kg×25 foil bags/fifer drum 5kg×5 foil bags/fifer drum LDPE(low density polyethylene)bag Sealed vacuum aluminum foil bag Sealed carton
适应碱性粉剂 Powder suitable for alkaline	2000ppm	

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