



# Curcumin C3 Complex® 姜黄素



## 配方建议

By Sabinsa China





# 配方推荐

抗过敏，缓解哮喘，鼻炎等

保护关节

保护肝脏

调节肠胃道健康

调节血脂，抑制肥胖

脑部健康& 情绪调节

运动营养，运动后恢复



# 抗过敏，特别是季节性过敏，哮喘等 配方推荐

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Curcumin C3 Complex<sup>®</sup> 500mg 姜黄素

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BioPerine<sup>®</sup> 5mg 胡椒素

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Nigellin<sup>®</sup> 100mg 黑种草籽油

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以上为推荐剂量，每天**3**次



# 配方功效机理

01

姜黄素抑制环氧合酶炎症通路

02

黑种草籽油具有抗炎功效，增强免疫反应

03

黑种草籽油抗过敏，有效缓解过敏引起的鼻炎，哮喘等状况

04

胡椒素提高配方营养成分生物利用度

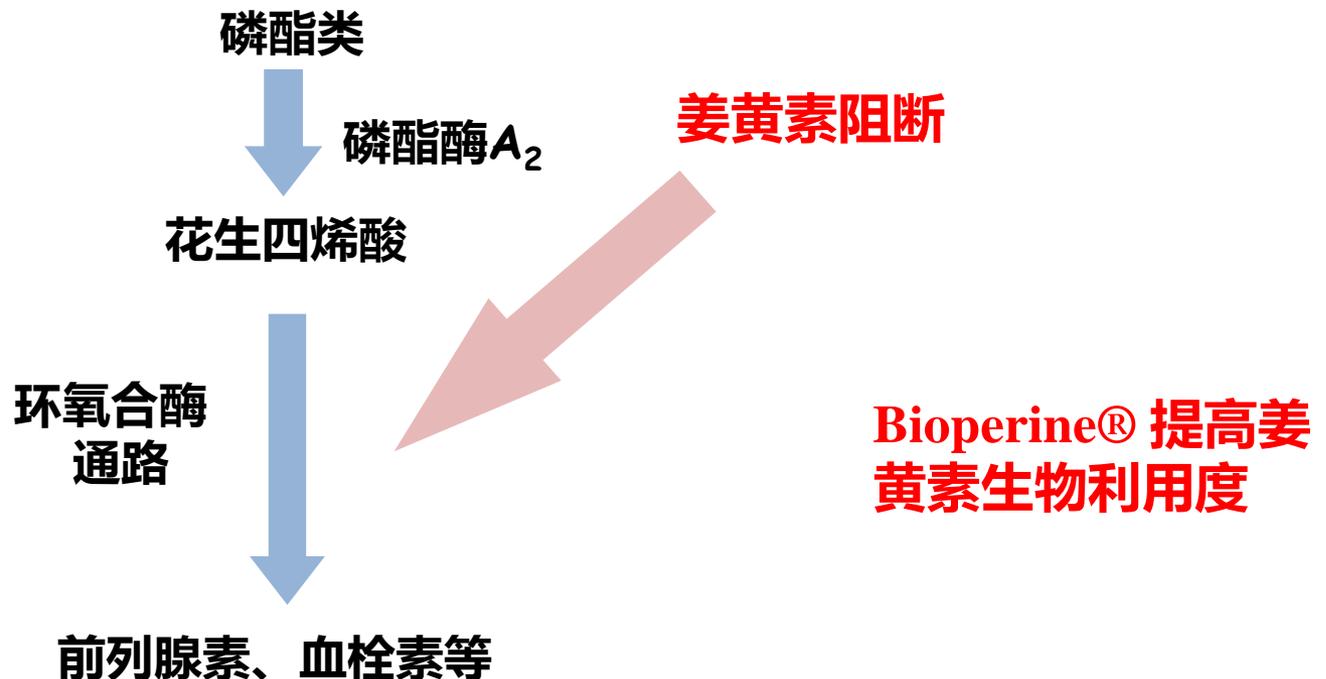
05

每天2次



# Curcumin C3 Complex® 姜黄素

## 姜黄素抑制花生四烯酸的级联炎症反应





# Nigellin® 黑种草籽油

Blessed Black Seed

源自中东阿拉伯和印度的药用植物，有数百年维持人整体健康的应用历史

**Nigellin™ BCS**

**CHEMICAL CONSTITUENTS**

One of the reasons for considering black seeds as the main sources of nutrition and healthcare might be due to the complex chemical structure of the seeds. These little seeds contain more than 100 different chemical constituents, including carbohydrates, proteins, volatile and fixed oils, and are also an abundant source of all the essential fatty acids. Thymoquinone is proved to be the main active constituent of the volatile oil of the black seed and is known to have several medicinal properties.

**A TIME-HONORED REMEDY**

Though black seed has been recognized as one of the most popular herbs in many parts of the world for centuries, extensive research during last 40 years has further validated its potential health benefits, viz. maintain healthy inflammatory response (Mahdavi *et al.*, 2016), asthma control support (Koshak *et al.*, 2017), improved glycemc control in diabetic patients (Bamosa *et al.*, 2010), protective role in diabetic nephropathy (Ansari *et al.*, 2017), healthy blood pressure (Dehkordi and Kamkaha, 2008) and lipid profile management (Sabzghabae *et al.*, 2012), helps boost male fertility (Marbat *et al.*, 2013; Kolahdooz *et al.*, 2014).

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

OUR INNOVATION IS YOUR ANSWER®  
www.sabinsa.com  
info@sabinsa.com

黑种草籽油富含100多种成分，包括碳水化合物，蛋白质，挥发性和非挥发性油脂，人体必须脂肪酸其中百里醌其具有多种医药用途的主要功效成分

缓解哮喘

抑制过敏反应

抗炎功效

调节血压和血脂

控制糖尿病人血糖

提高男性生育能力

加拿大功效宣称许可：

- 缓解过敏性鼻炎症状
- 减少过敏性鼻炎症状



# 护肝 推荐配方

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Curcumin C3 Complex® 500mg 姜黄素

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Milk Thistle Extract 250mg 水飞蓟提取物

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Saberry™ 200mg 印度醋栗

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Bioperine® 5mg 胡椒素

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以上为推荐剂量，每天2次





# 护肝 配方功效机理说明

01

姜黄素抗氧化、抗炎保护肝脏细胞

02

水飞蓟促进肝脏细胞新生，修复损伤

03

印度醋栗抗氧化，帮助肝脏解毒

04

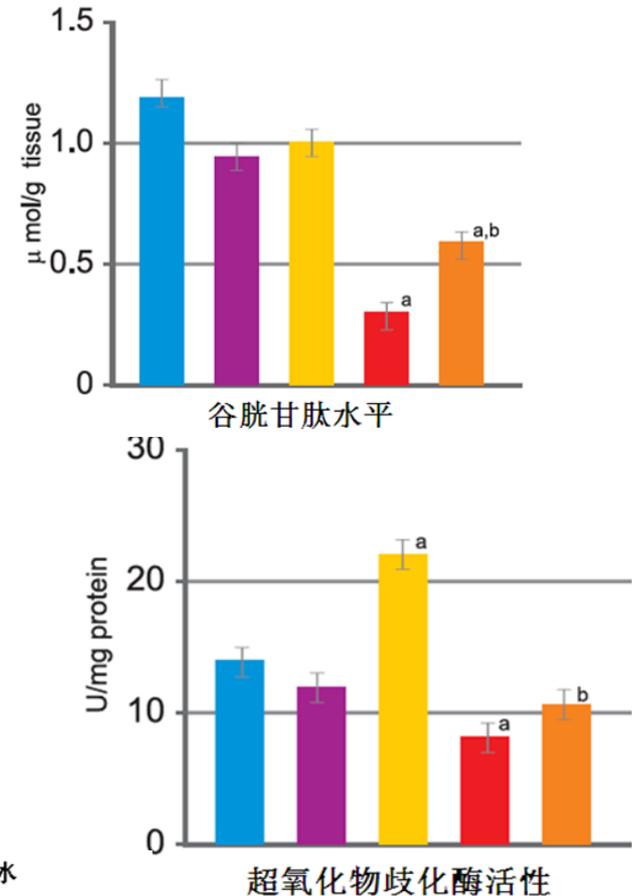
每天2次



# Curcumin C3 Complex® 姜黄素

## 姜黄素减少酒精对肝脏的损伤

- 姜黄素具有抗氧化功效，保护肝脏
- 姜黄素具有抗炎功效，通过抑制转录因子NFkB的激活
  - 抑制促炎细胞因子的分泌
  - 抑制环氧合酶 - 2 (COX-2)
  - 抑制诱导型一氧化氮合酶 (iNOS)
- 肝脏通过胆汁消除其毒性，姜黄可以提高胆汁流量，净化肝脏，修复肝脏细胞，重新赋予其解毒能力



- 生理盐水
- 二甲基亚砜
- 姜黄素
- 甲氨蝶呤
- 甲氨蝶呤+姜黄素

Hemeida et al. J Egypt Natl Canc Inst. 2008;20(2):141-8



# Saberry™ 印度醋栗



➤ 又名余甘子，天然生长于印度北部高山环境中，鲜果提取

➤ 阿育吠陀体系流传千年被应用最广泛的草药之一，被誉为“最好的返老还童草药”

➤ 功效：抗氧化，护肝，口服美容

适用产品：胶囊，片剂，或饮料中



抗氧化

护肝

水溶性

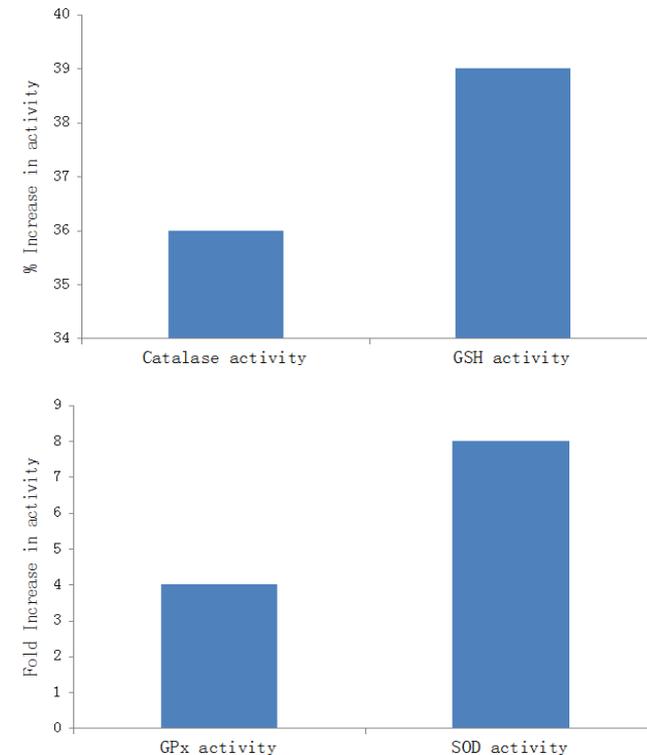


# Saberry® 印度醋栗

在CCL<sub>4</sub> 诱导大鼠肝脏毒性的实验中，研究人员发现 Saberry® 具有强大的抗氧化能力，能有效保护肝脏。研究显示，Saberry® 可以使体内的肝酶（转氨酶）趋于正常化。

服用Saberry®：

- ✓ 肝脏中的过氧化氢酶增加14 - 36%
- ✓ 肝脏中谷胱甘肽水平提高29 - 39%。
- ✓ 肝脏中谷胱甘肽过氧化物酶活性增加3 - 4倍。
- ✓ 肝脏中超氧化物歧化酶活性增加了5 - 8倍。





# 保护关节 推荐配方#1

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Curcumin C3 Complex<sup>®</sup> 500mg 姜黄素

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Bioperine<sup>®</sup> 5mg 胡椒素

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以上为推荐剂量，每天**3**次





# 保护关节 推荐配方#1

- ✓ 姜黄素500mg，复配5mg胡椒素，每天3次，
- ✓ 缓解关节僵硬，关节疼痛，提高关节活动性
- ✓ WOMAC，VAS和LPFI评分显示明显改善功效
- ✓ 利用胡椒素提高生物利用度
- ✓ 无副作用，不含氨糖或其他过敏原

Phys Ther. Res. (2014)  
 Published online in Wiley Online Library  
 (wileyonlinelibrary.com) DOI: 10.1002/pt.1174

## Curcuminoid Treatment for Knee Osteoarthritis: A Randomized Double-Blind Placebo-Controlled Trial

Yunes Panahi,<sup>1</sup> Ali-Reza Rahimiia,<sup>2,3\*</sup> Mojtaba Sharafi,<sup>2,3</sup> Gholamhossein Alekhiri,<sup>4</sup> Amin Sabahi<sup>5</sup> and Amirhossein Sahebkar<sup>2,6\*</sup>

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<sup>4</sup>Internal Medicine Department, Faculty of Medicine, Baqiyatallah University of Medical Sciences, Tehran, Iran  
<sup>5</sup>Biotechnology Research Center, Mashhad University of Medical Sciences, Mashhad, Iran  
<sup>6</sup>Neurogenic Inflammation Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

Treatment of osteoarthritis (OA) is challenging owing to the inefficacy and long-term adverse events of currently available medications including non-steroidal anti-inflammatory drugs. Curcuminoids are polyphenolic phytochemicals with established anti-inflammatory properties and protective effects on chondrocytes. The aim of this study is to investigate the clinical efficacy of curcuminoids in patients suffering from knee OA. A pilot randomized double-blind placebo-control parallel-group clinical trial was conducted among patients with mild-to-moderate knee OA. Patients were assigned to curcuminoids (1500mg/day in 3 divided doses; n = 19) or matched placebo (n = 21) for 6 weeks. Efficacy measures were changes in Western Ontario and MacMaster Universities Osteoarthritis Index (WOMAC), Visual analogue scale (VAS) and Lequesne's pain functional index (LPFI) scores during the study. There was no significant difference in age, gender, body mass index, and VAS, WOMAC and LPFI scores between the study groups at baseline ( $p > 0.05$ ). Treatment with curcuminoids was associated with significantly greater reductions in WOMAC ( $p = 0.001$ ), VAS ( $p < 0.001$ ) and LPFI ( $p = 0.013$ ) scores compared with placebo. With respect to WOMAC subscales, there were significant improvements in the pain and physical function scores ( $p < 0.001$ ) but not stiffness scores ( $p > 0.05$ ). There was no considerable adverse effect in both groups. To conclude, curcuminoids represent an effective and safe alternative treatment for OA. Copyright © 2014 John Wiley & Sons, Ltd.

Keywords: curcumin; herbal medicine; arthritis; pain

### INTRODUCTION

Osteoarthritis (OA) is the most common disease of joints in adults, and its prevalence is predicted to rise owing to the increasing pattern in risk factors such as sedentary life style and obesity (Neogi, 2013; Suri *et al.*, 2012). The most common symptoms of OA are pain, stiffness of the joint, crepitation on motion and limitation of joint motion (Neogi, 2013). Current standard of care for patients with OA mainly relies on the use of analgesics and non-steroidal anti-inflammatory drugs (NSAIDs). These treatments have partial efficacy in controlling disease symptoms, and their long-term use has been reported to cause several gastrointestinal, renal and cardiovascular side effects (Banfi *et al.*, 2007; Towheed *et al.*, 2003). These limitations necessitate further research to find more efficacious treatments that can be used safely in patients with OA.

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In recent years, there has been a surge of interest to find herbal remedies for OA owing to the strong ethnobotanical evidence and identified analgesic, anti-inflammatory and muscle relaxant properties for such therapies (Chopra *et al.*, 2013; Fehri *et al.*, 2011; Lee *et al.*, 2013; Yu *et al.*, 2013). Turmeric is a widely used spice with numerous applications in the Asian traditional medicine, including treatment of joint pain and inflammation. Curcuminoids are coloring and bioactive constituents of turmeric that, despite their low occurrence of about 2–5%, are responsible for most of the biological and pharmacological properties of turmeric. Curcuminoids are among the most extensively studied natural products with a plethora of known biological actions important for the treatment of different diseases (Balecaro *et al.*, 2014; Gupta *et al.*, 2013a; Gupta *et al.*, 2013b; Kim *et al.*, 2012; Mohammadi *et al.*, 2013; Na *et al.*, 2013; Panahi *et al.*, 2014a, b; Sahebkar, 2010; Sahebkar *et al.*, 2013; Sahebkar, 2014a, b; Shehzad *et al.*, 2013a). Among the biological effects of curcuminoids important for joint health are anti-inflammatory (Buhmann *et al.*, 2011; Buhmann *et al.*, 2010; Oaki *et al.*, 2009; Madhy-Hartert *et al.*, 2009), anti-oxidative (Buhmann *et al.*, 2011; Buhmann *et al.*, 2010; Oaki *et al.*, 2009) and antioxidant effects (Panahi *et al.*, 2012a; Sahebkar *et al.*, 2013). However, clinical studies investigating the therapeutic efficacy of curcuminoids in patients with OA

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## 保护关节 推荐配方#2

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Curcumin C3 Complex® 500mg 姜黄素

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Ginger Extract SCFE 544mg 生姜提取物

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Boswellin Super 200mg 乳香提取物

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以上为推荐剂量，每天2次



# 保护健康 配方#2功效机理

01

姜黄素抑制环  
氧合酶炎症通  
路

02

乳香提取物抑  
制5-脂氧合酶  
炎症通路

03

生姜提取物具  
有抗炎和镇痛  
作用

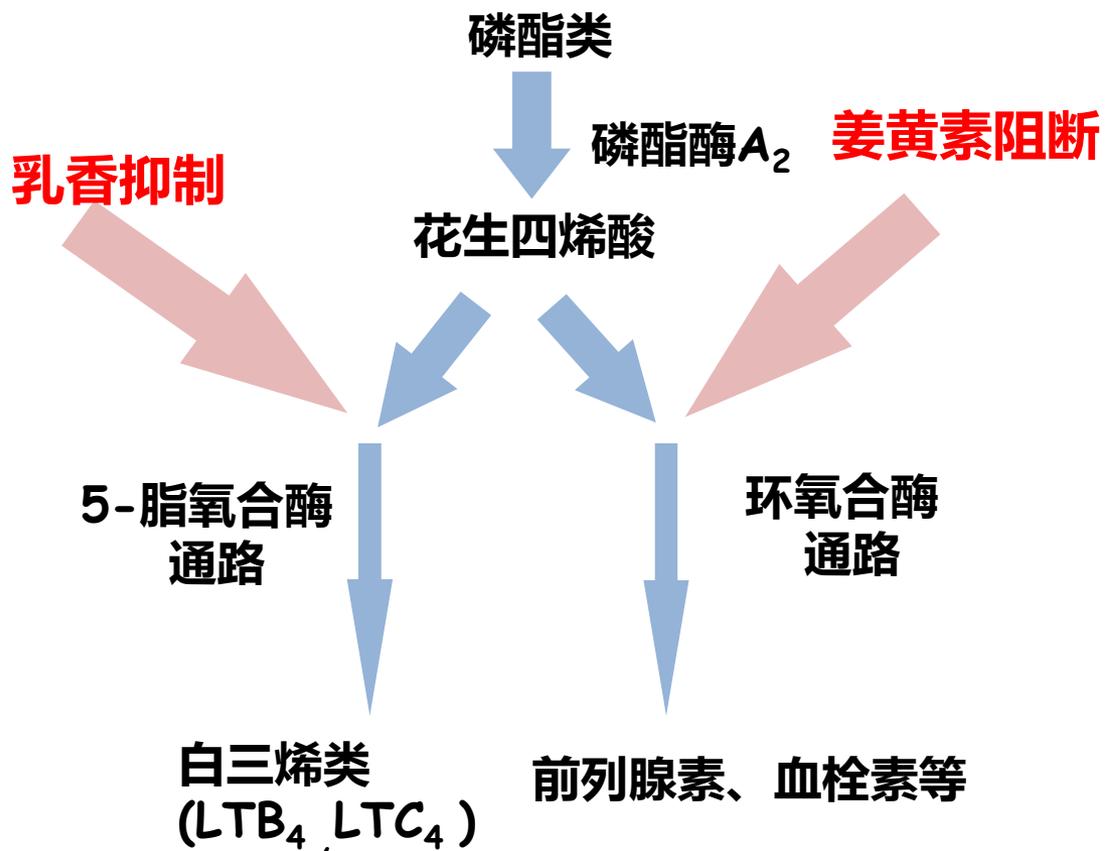
04

每天2次



# 姜黄素，乳香协同增效

## 花生四烯酸的级联炎症反应



姜黄素和乳香提取物  
双重抗炎功效



# 保护关节 推荐配方#2

## Boswellin Super 乳香



- 齿叶乳香, 树脂分泌物
- 有效成分: 乳香酸及其衍生物
- 在传统的阿育吠陀医学中治疗炎症反应

## Ginger Extract SCFE 生姜

◆ 超临界萃取

◆ 油状提取物: 20% 姜辣素 /  
35% 姜辣素





# 保护关节 推荐配方#2

Research Article

[Natrojan & Majeed 3(2): Feb., 2012]  
ISSN: 0976-7126



INTERNATIONAL JOURNAL OF PHARMACY & LIFE SCIENCES

To assess the efficacy & safety of NILIN™ SR tablets in the management of osteoarthritis of knee

Shankaran Natarajan<sup>1\*</sup> and Muhammed Majeed<sup>2</sup>  
Advisor / Sr. Vice President - R & D, Sami Labs, Bangalore, Karnataka - India  
Founder & Managing Director, Sami Labs, Bangalore, Karnataka - India

### Abstract

To assess the efficacy & safety of Nilin™ SR tablets in the management of osteoarthritis of knee. 32 subjects from the age group 40-65 years having osteoarthritis of the knee, with no other rheumatologic condition were enrolled. Subjects were judged to have osteoarthritis with clinical diagnostic features; Knee pain for most days of the month, Morning stiffness of less than 30 minute duration, stiffness while resting the affected joint and age over 40 years. The primary outcome was self-reported pain, stiffness and physical function scores as measured with the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), 6-minute walk distance and VAS scale measured at 0hr and 1, 2 and 4hrs respectively. Secondary outcomes included laboratory investigations and serological biomarker, i.e. Hs-CRP. A significant improvement in the clinical and biochemical endpoints along with excellent tolerability indicates that Nilin™ SR can be used for the long term management of Osteoarthritis. Of the 32 subjects 30 subjects completed the study. Wilcoxon paired sample test indicated WOMAC Score significantly reduced from baseline to final visit for all the three parameters; Pain (P<0.0001) Stiffness (P<0.0001) and Physical disability (P<0.0001). A significant reduction was also noted in the visual analogue scale over the course of 4 hours after ingestion of medication. A significant improvement in the 6-minute walk distance (P < 0.05) and decrease in Hs-CRP levels was observed. No adverse events were reported in the trial.

**Key-Words:** Nilin SR, Osteoarthritis, WOMAC, VAS scale

### Introduction

Arthritis is a common condition affecting millions of people all over the world. Osteoarthritis is one of the conditions commonly encountered among people. Osteoarthritis (OA) or degenerative joint disease is one of the oldest and most common type of arthritis. It is characterized by the breakdown of the joint's cartilage. Cartilage is the part of the joint that cushions the ends of bones. Its breakdown causes bones to rub against each other, causing pain and loss of movement. Most commonly affecting middle-aged and older people, OA can range from very mild to very severe. It affects hands and weight-bearing joints such as knees, hips, feet and the back. There are many factors that can cause OA. Although age is a risk factor, research has shown that OA is not an inevitable part of aging. Obesity may lead to OA of the knees. In addition, people with joint injuries due to sports, work related activity or accidents may be at an increased risk of developing OA. Women are more commonly affected than men.

Genetics has a role in the development of OA, particularly in the hands. Some people may be born with defective cartilage or defects in the way that joints fit together. As a person ages, this can cause early cartilage breakdown in the joint and there may be some inflammation, with enzymes released and more cartilage damaged.

NILIN™ SR is an original research with selected ingredients proven to restore joint health and revive joint mobility. NILIN™ SR aims to regenerate cartilage, reduce inflammation, and exert an antioxidant action. It retards the progression of Osteoarthritis, alleviates the signs and symptoms of arthritis and significantly improves quality of life.

The formulation NILIN™ SR contains the following components:

Boswellia acid (Boswellin®) is a well-tolerated, safe and effective anti-inflammatory agent without any associated untoward side effects. Boswellin® inhibits leukotriene synthesis and the enzyme HLE (Human Leukocyte Elastase). Boswellin® reduces joint discomfort, morning joint stiffness, improves grip strength and joint performance. Studies in India showed ingestion of an alcoholic extract of Boswellia

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Int. J. of Pharm. & Life Sci. (IJPLS), Vol. 3, Issue 2: Feb.: 2012, 1413-1423

• 单中心，公开标签临床测试，32名40-65岁膝盖关节炎受试者，周期56天

• 姜黄素250mg,乳香272mg,生姜100mg,每次2片，每天2次

• 双层片剂，缓释药效

• WOMAC评分（骨关节炎指数评分）显示骨关节炎患者的疼痛程度，僵硬程度和关节功能有显著改善

• VAS评分（视觉模拟评分）显示服用4小时疼痛值明显改善

• 6分钟步行距离明显提高



# 肠胃道健康 推荐配方#1

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Curcumin C3 Complex<sup>®</sup> 500mg 姜黄素

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LactoSpore<sup>®</sup> 2B cfu 凝结芽孢杆菌

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**以上为推荐剂量，每天3次**



# 肠胃道健康 配方#1作用机理

01

姜黄素抗炎  
保护肠粘膜  
完整性

02

姜黄素调节  
肠道菌落多  
样性

03

凝结芽孢杆  
菌—益生菌，  
平衡肠道菌  
群

04

每天3次



# 肠胃道健康 推荐配方#1

## Curcumin C3 Complex® 姜黄素

抗炎，保护  
肠粘膜

调节肠道菌  
群多样性

双盲单中心，受试者30人，8周  
剂量：姜黄素3g 复配 胡椒素3.75mg，每  
天2次

机理：调节肠道功能，减少脂多糖诱导的  
促炎症细胞因子的分泌，保护紧密连接蛋白  
不降解

结果：姜黄素提升65%菌落多样性

Brief Communication

### Effects of Turmeric and Curcumin Dietary Supplementation on Human Gut Microbiota: A Double-Blind, Randomized, Placebo-Controlled Pilot Study

Christine T. Peterson, PhD<sup>1</sup>, Alexandra R. Vaughn, PhD<sup>2,3</sup>, Vandana Sharma, PhD<sup>4</sup>, Deepak Chopra, MD<sup>5,6</sup>, Paul J. Mills, PhD<sup>1</sup>, Scott N. Peterson, PhD<sup>7</sup>, and Raja K. Sivarami, MD<sup>8,9,10</sup>

#### Abstract

**Background:** *Curcuma longa* (common name: turmeric) and one of its biologically active constituents, curcumin, have received increased clinical attention. Insufficient data exist on the effects of curcumin and turmeric on the gut microbiota and such studies in humans are lacking. **Methods:** Turmeric tablets with extract of piperine (Biperpine) (n = 6), curcumin with Biperpine tablets (n = 5), or placebo tablets (n = 3) were provided to healthy human subjects and subsequent changes in the gut microbiota were determined by 16S rDNA sequencing. **Results:** The number of taxa detected ranged from 172 to 325 bacterial species. The placebo group displayed an overall reduction in species by 15%, whereas turmeric-treated subjects displayed a modest 7% increase in observed species posttreatment. Subjects taking curcumin displayed an average increase of 69% in detected species. The gut microbiota response to treatment was highly personalized, thus leading to responders and nonresponders displaying response concordance. These "responsive" subjects defined a signature involving uniform increases in most *Clostridium* spp., *Bacteroides* spp., *Citrobacter* spp., *Corynebacter* spp., *Enterobacter* spp., *Enterococcus* spp., *Klebsiella* spp., *Proteobacteria* spp., and *Pseudomonas* spp. Common to these subjects was the reduced relative abundance of several *Bifidob* spp. and most *Ruminococcus* spp. *Candidatus* All participants' microbiota displayed significant variation over time and individualized response to treatment. Among the responsive participants, both turmeric and curcumin altered the gut microbiota in a highly similar manner, suggesting that curcumin may drive the majority of observed changes observed in turmeric-treated subjects.

#### Keywords

microbiota, gastrointestinal, turmeric, curcumin, antioxidant

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*Curcuma longa* (common name: turmeric) and one of its biologically active constituents, curcumin, are receiving increased clinical attention globally due to mounting evidence demonstrating therapeutic potential derived from outcomes that include anti-inflammatory, antioxidant, and neurotrophic effects.<sup>1</sup> Ayurveda and other traditional systems of medicine commonly use turmeric as a medicinal herb, culinary spice, and digestive.<sup>2</sup> Integrative health practitioners from allopathic fields have adopted turmeric and curcumin for a variety of applications in clinical practice,<sup>3</sup> and a burgeoning interest among dietary public drives the growing global curcumin market.

Human clinical trial interventions have been heterogeneous in that various forms of curcumin, mixtures of curcuminoids,

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<sup>4</sup> Sanford Burnham Preybe Medical Discovery Institute, La Jolla, CA, USA  
<sup>5</sup> Chopra Foundation, Carlsbad, CA, USA  
<sup>6</sup> California State University, Sacramento, CA, USA  
<sup>7</sup> Pacific Skin Institute, Sacramento, CA, USA  
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# 肠胃道健康 推荐配方#1

## LactoSpore® 凝结芽孢杆菌

稳定，耐高温，  
耐受胃酸

产乳酸，抑制有  
害菌过度增殖

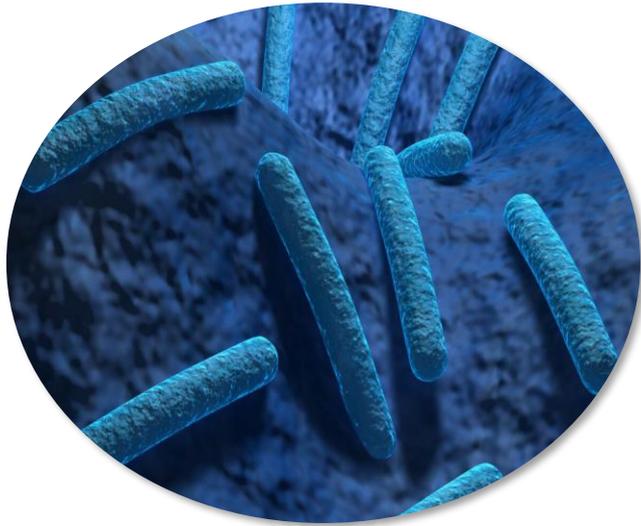
“活”的益生菌

平衡肠道菌落

加拿大IBS宣称



# LactoSpore® 活的益生菌



- 杆状，革兰氏阳性，芽孢杆菌纲（芽孢在细胞内形成）菌
- 兼性厌氧菌
- 萌发条件，37°C，pH < 3，水活度 > 0.8
- 在37°C，pH值在5.5到6.2的范围对其生长最有益

**gras**  
Generally Recognized As Safe

**6B cfu/g**

**15B cfu/g**

**100B cfu/g**



## 肠胃道健康 推荐配方#2

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Curcumin C3 Complex<sup>®</sup> 100mg 姜黄素

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Digezyme 50mg 消化酶

---

LactoSpore<sup>®</sup> 250million cfu 凝结芽孢杆菌

---

Ginger SCFE 50mg 生姜提取物

---

以上为推荐剂量，每天3次



## 肠胃道健康 配方#2机理

01 姜黄素在结肠内具有广谱抗炎功效

02 凝结芽孢杆菌维持肠道菌群平衡

03 消化酶帮助消化微营养素

04 生姜提取物提供生热作用

05 摄入的姜黄可以降低结肠癌风险



# Digezyme® 消化酶



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Health Plus  
Digezyme



# 血脂调节，抑制肥胖 推荐配方

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Curcumin C3 Complex<sup>®</sup> 500mg 姜黄素

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Fabenol<sup>®</sup> Max 400mg 白芸豆

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Bioperine<sup>®</sup> 5mg 胡椒素

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以上为推荐剂量，每天**2-3**次



# 血脂调节，抑制肥胖 配方功效机理

01

姜黄素减少  
系统性炎症，  
降低氧化应  
激反应

02

白芸豆提取  
物， $\alpha$ -淀  
粉酶抑制剂，  
减少淀粉吸  
收

03

胡椒素提高  
生物利用度

04

每天2-3次



# Curcumin C3 Complex® 姜黄素

## 随机双盲交叉试验, 30名受试者, 持续1个月

## 姜黄素500mg,胡椒素5mg, 每天2次

## 机理: 减少系统性炎症反应

## 结果: 降低炎症标志物水平

Hindawi Publishing Corporation  
The Scientific World Journal  
Volume 2014, Article ID 808164, 10 pages  
http://dx.doi.org/10.1155/2014/808164

**Clinical Study**  
**Investigation of the Effects of Curcumin on Serum Cytokines in Obese Individuals: A Randomized Controlled Trial**

Shiva Ganjal,<sup>1,2</sup> Amirhossein Sahebkar,<sup>3,4</sup> Elzhe Mahdipour,<sup>5</sup> Khadijeh Jamialahmadi,<sup>5,6</sup> Sepideh Torabi,<sup>7</sup> Saeed Akhlaghi,<sup>8</sup> Gordon Ferns,<sup>9</sup> Seyed Mohammad Reza Partzadeh,<sup>7</sup> and Majid Ghayour-Mobarhan<sup>10</sup>

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**Background:** Obesity is a disorder often accompanied by a heightened state of systemic inflammation and immunoreactivity. The present randomized, crossover trial aimed to investigate the efficacy of curcumin, a bioactive polyphenol with established anti-inflammatory and immunomodulatory effects, on the serum levels of a panel of cytokines and mediators in obese individuals. **Methods:** Thirty obese individuals were randomized to receive curcumin at a daily dose of 1g or a matched placebo for 4 weeks. Following a 2-week wash-out period, each group was assigned to the alternate treatment regimen for another 4 weeks. Serum samples were collected at the start and end of each study period. Serum levels of IL-1 $\beta$ , IL-1 $\alpha$ , IL-2, IL-4, IL-6, IL-8, IL-10, VEGF, TNF $\alpha$ , ICAM-1, and TNFSF were measured using a multiplex flowcytometry-based method. **Results:** Mean serum IL-1 $\beta$  ( $P = 0.042$ ), IL-4 ( $P = 0.006$ ), and VEGF ( $P = 0.01$ ) were found to be significantly reduced by curcumin therapy. In contrast, no significant difference was observed in the concentrations of IL-2, IL-6, IL-8, IL-10, TNF $\alpha$ , ICAM-1, and MCP-1. **Conclusions:** The findings of the present trial suggested that curcumin may exert immunomodulatory effects via altering the circulating concentrations of IL-1 $\beta$ , IL-4, and VEGF.

### 1. Introduction

Obesity is a global health problem and is increasing in prevalence (~60%) over the past 20 years. According to the World Health Organization (WHO) statistics, there were ~1.6 billion overweight adults globally, of whom about 400 millions were obese in 2005 [1]. The list of comorbidities associated with obesity is extensive, among which is cardiovascular disease [2]. A plethora of scientific evidence has confirmed the predisposing effects of obesity on the

development and progression of atherosclerosis as well as the risk of other coronary risk factors including hypertension, type 2 diabetes, and dyslipidemia. Obesity is associated with a strong inflammatory response and is often accompanied by increased levels of proinflammatory cytokines and impaired antioxidant status [3], the most important source of proinflammatory cytokines in obesity is macrophages that infiltrate adipose tissue as a response to the adipocyte growth, decreased blood supply, hypoxia, and tissue necrosis. These events collectively predispose to a systemic inflammation

## 随机双盲交叉试验, 30名受试者, 持续1个月

## 姜黄素500mg,胡椒素5mg, 每天2次

## 肥胖受试者中的氧化应激反应明显降低

### Curcuminoids Modulate Pro-Oxidant–Antioxidant Balance but not the Immune Response to Heat Shock Protein 27 and Oxidized LDL in Obese Individuals

Anirudhchris Sah-Char,<sup>1,2</sup> Akram Mohammadi,<sup>2</sup> Ali Akbari,<sup>3</sup> Shamin Rahimi,<sup>3</sup> Shima Tavallaei,<sup>4</sup> Mehdiad Iranzadeh,<sup>5</sup> Saeed Akhlaghi,<sup>6</sup> Gordon AA Ferns,<sup>7</sup> and Majid Ghayour-Mobarhan<sup>10\*</sup>

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<sup>3</sup>Department of Medicine, Islamic Azad University, Mashhad, Iran  
<sup>4</sup>Deputy of Research, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran  
<sup>5</sup>Neiguan & Sunan Medical School, Division of Medical Education, Mayfield House, University of Brighton, BN1 9PX, UK  
<sup>6</sup>Medical Education Research Department, AC/2346-Abdolk, Mashhad, Iran

Curcuminoids have potentially important functional qualities including anti-inflammatory and antioxidant properties. In this randomized, double-blind, placebo-controlled, cross-over trial, the effects of a curcuminoid supplement on serum pro-oxidant–antioxidant balance (PAB) and antibody stress to Hsp27 (anti-Hsp27) and oxidized LDL (anti-oxLDL) were investigated. Thirty obese individuals were randomized to receive either curcuminoids (1 g/day) or placebo for a period of 30 days. After a wash-out period of 2 weeks, subjects were crossed over to the alternate regimen for another 30 days. Serum PAB along with anti-Hsp27 and anti-oxLDL were measured at the beginning and at the end of each study period. There was no significant crossover effect for any of the assessed parameters. Curcuminoid supplementation was associated with a significant decrease in PAB ( $P = 0.004$ ). However, no significant change was observed in serum concentrations of anti-Hsp27 or anti-oxLDL ( $P > 0.05$ ). These findings suggest that oral curcuminoids supplementation (1 g/day) is effective in reducing oxidative stress burden, though this work is to be validated in larger study populations. Copyright © 2013 John Wiley & Sons, Ltd.

**Keywords:** curcumin; heat shock protein 27; oxidized low-density lipoprotein; oxidative stress

### INTRODUCTION

Curcumin (diferuloyl methane; C<sub>21</sub>H<sub>20</sub>O<sub>6</sub>) is a hydrophobic polyphenol that may be extracted from dried rhizomes of the herb *Curcuma longa* L. (turmeric). Turmeric is widely used as a spice in Indian, Middle Eastern and South Eastern Asian cooking, and its diverse medical properties have been applied in several traditional systems of medicine (Lao et al., 2006; Anand et al., 2008). Recent studies have shown that curcumin has potentially important biological activities including anti-inflammatory, antioxidant, immunomodulatory, neuro- and cardioprotective properties. It has therefore been proposed for the treatment of various types of cancer, arthritis, cardiometabolic, cystic fibrosis and pulmonary disorders (Lu et al., 1997; Bhatt et al., 2003; Devrot et al., 2004; Uddin et al., 2005; Ak and Ghosh, 2008; Goel et al., 2008; Akab and Vaini, 2010; Ma et al., 2010; Mahouza et al., 2010; Chandran and Goel, 2012; Panahi et al., 2012a, 2012b; Tu et al., 2012; Sahebkar, 2012).

Oxidative stress is a condition arising from a physiological imbalance between pro-oxidant and biological antioxidant species (Choi and Robinson, 1990). Oxidative stress plays a significant role in the pathogenesis of various disorders including atherosclerosis and subsequent cardiovascular disease (Ashok and Ali, 1999). One of the principal mechanisms for the involvement of oxidative stress in the pathogenesis of atherosclerosis is oxidation of LDL and formation of oxidized LDL (oxLDL) particles. Upon oxidation, the affinity of LDL for its receptor decreases whilst it becomes more prone to interact with scavenger receptors of macrophages and promote foam cell formation (Steinberg, 1997). OxLDL has well-known immunogenic properties and induces an immune response that is related to the severity of atherosclerosis (Shoenfeld et al., 2004). OxLDL is toxic for many of cells such as endothelial cells and impairs the integrity of such cells (Heiser et al., 1983). OxLDL also triggers chemotaxis of circulating monocytes which is regarded as an important step in the progression and exacerbation of atherosclerosis (Quinn et al., 1987).

Another important consequence of oxidative stress is inducing the expression and release of heat shock proteins (Hsps). Hsps are abundant intracellular proteins that protect cell in under stress. The upregulation of these proteins during stressful conditions activate the cell protective mechanisms (Pouggaldamyan et al., 2013).

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# Curcumin C3 Complex® 姜黄素—血脂调节，促进代谢



**Lipid-modifying effects of adjunctive therapy with curcuminoids—piperine combination in patients with metabolic syndrome: Results of a randomized controlled trial**

Yunes Panahi<sup>a</sup>, Nahid Khalili<sup>b</sup>, Mahboobeh Sadat Hosseini<sup>b</sup>, Mohammad Abbasnazari<sup>c</sup>, Amirhossein Sahebkar<sup>d,e,\*</sup>

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<sup>e</sup> Metabolic Research Centre, Royal Perth Hospital, School of Medicine and Pharmacology, University of Western Australia, Perth, Australia

#### KEYWORDS

Cardiometabolic syndrome;  
Curcuma longa;  
Hypercholesterolemia;  
Randomized controlled trial;  
Turmeric

#### Summary

**Background:** Dyslipidemia is an established feature of metabolic syndrome (MS) that is associated with an increased risk of atherosclerotic cardiovascular disease. Curcuminoids are natural products with anti-atherosclerotic and lipid-modifying effects but their efficacy in patients with MS has not yet been tested.

**Objectives:** To investigate the effects of bioavailability-enhanced curcuminoids, as adjunctive to standard of care, on serum lipid concentrations in patients with MS.

**Methods:** Patients diagnosed with MS according to the NCEP-ATPIII criteria who were receiving standard of care were assigned to either curcuminoids (C3 complex®; 1000 mg/day; n=50) or placebo (n=50; matched with drug capsules in shape and color) for 8 weeks. In order to improve the oral bioavailability, curcuminoids were co-administered with piperine (bioferine®) in a ratio of 100:1. Serum concentrations of total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides, small dense LDL (sdLDL), lipoprotein(a) [Lp(a)], and non-HDL-C were determined at baseline and at the end of 8-week treatment period.

## 随机双盲平行试验，受试者117，周期2个月

## 姜黄素500mg，胡椒素5mg，每天2次

## 降低低密度胆固醇，总胆固醇和甘油三脂水平降低，提高高密度胆固醇水平

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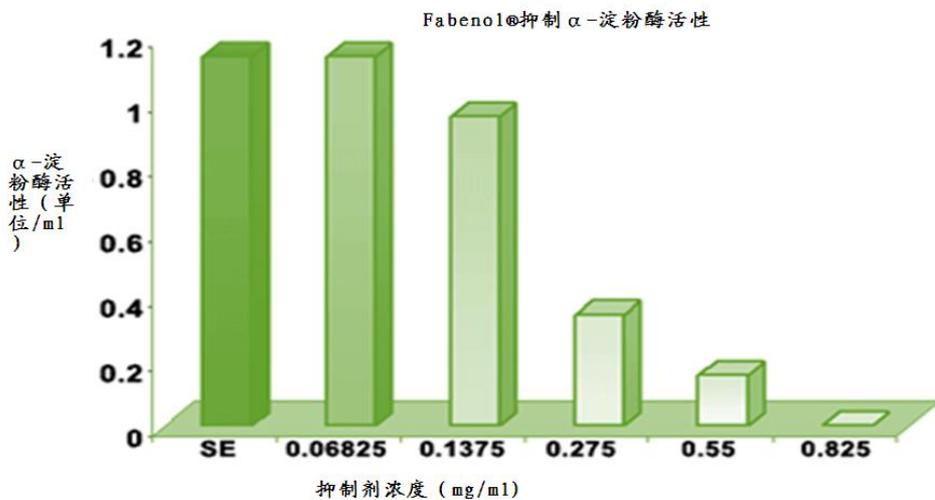


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•有效，安全





# 脑部健康 推荐配方

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Curcumin C3 Complex<sup>®</sup> 100mg 姜黄素

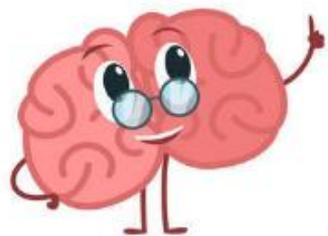
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Fish Omega Oil 100mg 鱼油

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Bioperine<sup>®</sup> 5mg 胡椒素

---



以上为推荐剂量，每天 1次



# 脑部健康 配方功效机理

01

**姜黄素具有  
保护神经功  
效，抗抑郁  
功效**

02

**鱼油抗抑郁，  
健康脑部功  
能和提高记  
忆力**

03

**胡椒素提高  
姜黄素和鱼  
油的生物利  
用度**

04

**姜黄素和鱼  
油具有协同  
增效作用，  
适用于年轻  
和年老群体**



# 情绪管理，抗MDD配方推荐

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Curcumin C3 Complex<sup>®</sup> 250mg 姜黄素

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LactoSpore<sup>®</sup> 1B cfu 凝结芽孢杆菌

---

以上为推荐剂量，每天 2次



# 情绪调节 功效机理

01

最新研究显示，姜黄素具有保护神经作用

02

姜黄素减少氧化应激反应

03

肠道黏膜完整性影响到大脑健康

04

凝结芽孢杆菌缓解可以抑郁程度，频率和时长



# 情绪管理，抗MDD配方推荐

PHYTOTHERAPY RESEARCH  
Phytother Res (2014)  
Published online in Wiley Online Library  
(wileyonlinelibrary.com) DOI: 10.1002/ptr.2211

## Investigation of the Efficacy of Adjunctive Therapy with Bioavailability-Boosted Curcuminoids in Major Depressive Disorder

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<sup>5</sup>Metabolic Research Center, Royal Perth Hospital, School of Medicine and Pharmacology, University of Western Australia, Perth, Australia

Current medications have limited efficacy in controlling the symptoms of major depressive disorder (MDD), and are associated with several adverse events on long-term use. Curcuminoids are extremely safe and multifunctional phytopharmaceuticals that have been shown to alleviate depressive symptoms in a variety of experimental models. The present study aimed to investigate the efficacy of curcuminoids as an add-on to standard antidepressants in patients with MDD. One hundred and eleven subjects were assigned to standard antidepressive therapy plus curcuminoids–piperine combination (1000–10 mg/day; n=61) or standard antidepressive therapy alone (n=50) for a period of 6 weeks. Efficacy measures were changes in the psychological status on the basis of the Hospital Anxiety and Depression Scale (HADS) and Beck Depression Inventory II (BDI-II). The HADS total and subscale scores were reduced by the end of trial in both study groups. There were significantly greater reductions in total HADS score and subscales of anxiety and depression in the curcuminoids versus control group (p < 0.001). Likewise, reductions in BDI-II total score and scores of somatic and cognitive subscales were found to be greater in the curcuminoids compared with control group (p < 0.001). Co-administration of curcuminoids with piperine may be used as a safe and effective add-on to standard antidepressants in patients with MDD. Copyright © 2014 John Wiley & Sons, Ltd.

Keywords: curcumin; piperine; depression; anxiety; clinical trial.

### INTRODUCTION

Major depressive disorder (MDD) is the most common psychological disorders (World Health Organization, 2008) and is associated with a significant impairment of individual quality of life because of the symptoms such as irritable mood, disrupted sleep, loss of motivation, anhedonia, fatigue, decreased concentrating power, and even suicidal ideation. Currently available pharmacotherapies for MDD mainly act through modulation of serotonergic and noradrenergic neurotransmission and have been found to be clinically effective. Nevertheless, a considerable proportion of MDD patients do not respond to routine antidepressant medications (Nemeroff, 2007). Moreover, existing antidepressant medications usually cause several adverse events. Because MDD is a chronic and recurrent condition, such adverse events can result in treatment intolerance and low compliance of the patient. Hence, there is an ongoing attempt to develop new antidepressants with improved efficacy and

greater tolerability. For this purpose, natural products are of particular interest given their safety, multifunctional effects, and ethnopharmacological and traditional uses.

Curcuminoids are polyphenolic natural products that are responsible for the yellow color and most of the pharmacological activities of the famous spice, turmeric. Curcuminoids have been the subject of extensive scientific research during the past two decades, making them the most widely studied phytochemicals. Curcuminoids constitute about 5% of turmeric composition and comprise curcumin (65–80%; also referred to as curcumin I), demethoxycurcumin (15–25%; curcumin II), and bisdemethoxycurcumin (5–15%; curcumin III). Curcuminoids possess several medicinal properties, and their efficacy has been confirmed against a wide array of diseases (Ganjali *et al.*, 2014; Gupta *et al.*, 2013a, 2013b; Iranshahi *et al.*, 2010; Panahi *et al.*, 2014a; Sahebkar, 2010, 2013, 2014a, 2014b, 2014c; Shehzad *et al.*, 2013a, 2013b). Most of the pharmacological properties of curcuminoids are due to their potent anti-inflammatory (Panahi *et al.*, 2014b; Shehzad *et al.*, 2013b) and antioxidant (Ak and Gulcin, 2008; Panahi *et al.*, 2014c; Sahebkar *et al.*, 2013) effects. Notably, the beneficial effects of curcuminoids have been shown in different experimental models of depression and anxiety (Kulkarni *et al.*, 2008; Wang *et al.*, 2008; Xia *et al.*, 2007; Xu *et al.*, 2008b, 2007; Yu *et al.*, 2002). Several mechanisms may account for the antidepressant and

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Accepted 7 July 2014

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## Curcumin C3 Complex® 姜黄素

### 抗焦虑

### 随机双盲交叉实验，受试者111人，6周

### 剂量：姜黄素500mg+胡椒素5mg，2次/天

### 机理：姜黄素具有减少氧化应激反应，保护神经作用，同时回复5-羟色胺，多巴胺和去甲肾上腺素的水平

### 结果：姜黄素能降低医院焦虑和抑郁量表(HADS)以及贝克抑郁量表II (BI-II)。



# 情绪管理，抗MDD配方推荐

## LactoSpore® 凝结芽孢杆菌

随机双盲交叉实验，受试者40人，90天

剂量：凝结芽孢杆菌 2B cfu /天

机理：肠道黏膜和肠道壁的完整性影响到大脑

结果：IBS，抑郁前后症状，频率、和时长均有改善

food & nutrition  
research

ORIGINAL ARTICLE

*Bacillus coagulans* MTCC 5856 for the management of major depression with irritable bowel syndrome: a randomised, double-blind, placebo controlled, multi-centre, pilot clinical study

Muhammed Majeed<sup>1,2,3\*</sup>, Kalyanam Nagabhushanam<sup>2</sup>, Sivakumar Arumugam<sup>1</sup>, Shaheen Majeed<sup>2,3</sup> and Furqan Ali<sup>4</sup>

<sup>1</sup>Sarini Labs Limited, Bangalore, Karnataka, India; <sup>2</sup>Sabinsa Corporation, East Windsor, NJ, USA; <sup>3</sup>Sabinsa Corporation, Payson, UT, USA; <sup>4</sup>ClinWorld Private Limited, Bangalore, Karnataka, India

Abstract

**Background:** The modification of microbial ecology in human gut by supplementing probiotics may be an alternative strategy to ameliorate or prevent depression.

**Objective:** The current study was conducted to assess the safety and efficacy of the probiotic strain *Bacillus coagulans* MTCC 5856 for major depressive disorder (MDD) in IBS patients.

**Method:** Patients ( $n = 40$ ) diagnosed for MDD with IBS were randomised (1:1) to receive placebo or *B. coagulans* MTCC 5856 at a daily dose of  $2 \times 10^9$  cfu (2 billion spores) and were maintained to the end of double-blind treatment (90 days). Changes from baseline in clinical symptoms of MDD and IBS were evaluated through questionnaires.

**Results:** Significant change ( $p = 0.01$ ) in favour of the *B. coagulans* MTCC 5856 was observed for the primary efficacy measure Hamilton Rating Scale for Depression (HAM-D), Montgomery-Asberg Depression Rating Scale (MADRS), Center for Epidemiological Studies Depression Scale (CES-D) and Irritable bowel syndrome quality of life questionnaire (IBS-QOL). Secondary efficacy measures i.e. Clinical Global Impression-Improvement rating Scale (CGI-I), Clinical Global Impression Severity rating Scale (CGI-S), Gastrointestinal Discomfort Questionnaire (GI-DQ) and Modified Epworth Sleepiness Scale (mESS) also showed significant results ( $p = 0.01$ ) in *B. coagulans* MTCC 5856 group compared to placebo group except dementia total reaction scoring. Serum myeloperoxidase, an inflammatory biomarker was also significantly reduced ( $p < 0.01$ ) when compared with the baseline and end of the study. All the safety parameters remained well within the normal clinical range and had no clinically significant difference between the screening and at the end of the study. **Conclusion:** *B. coagulans* MTCC 5856 showed robust efficacy for the treatment of patients experiencing IBS symptoms with major depressive disorder. The improvement in depression and IBS symptoms was statistically significant and clinically meaningful. These findings support *B. coagulans* MTCC 5856 as an important new treatment option for major depressive disorder in IBS patients.

Trial Registration: Clinical Trials Registry India Identifier: CTRI/2015/05/005754

**Keywords:** probiotic; *B. coagulans* MTCC 5856; LactoSpore®; major depression; irritable bowel syndrome

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Major depressive disorder (MDD) is characterised by an increased medical morbidity, mortality, feelings of guilt, low mood, reduced quality of life, disturbed sleep or appetite (1). MDD is one of the most common mental disorders worldwide, with a life time prevalence of 16.2% and a 12-month prevalence of 6.6% in developed countries (2, 3). Furthermore, between 30 and 40% of patients who suffer from MDD never achieve symptom resolution with standard antidepressant treatment (4). Alternative approaches such as cognitive behavioural therapy and lifestyle interventions need

highly trained therapists and several weeks to months to achieve effectiveness (5). Therefore, there is a need for new and additional treatment options for depression.

Irritable bowel syndrome (IBS) is characterised by the alterations in bowel function or discomfort, abdominal pain or bloating, and diarrhoea or constipation (6). The prevalence of IBS is estimated between 9 and 23% in the population across the world (6–8) and affects ~21% of the population in South America and ~7% of the population in Southeast Asia (9). Although IBS is classified as a functional gastrointestinal disorder which is a chronic

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# 运动营养 推荐配方

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Promond™ 杏仁蛋白

---

Cococin™ 椰胚乳精华

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以上为推荐剂量，运动前，后使用



# 运动营养 作用机理

01

杏仁蛋白，  
纯植物蛋白，  
乳糖不耐者  
友好

02

植物蛋白替  
代乳清蛋白

03

椰胚乳精华  
补充电解质  
和能量

04

运动前、后  
使用



# Promond™ 杏仁蛋白

## --纯植物蛋白



甜杏仁

100%纯天然

素食友好

口感好

水溶性

- 植物来源：杏仁蛋白，喜马拉雅山脉地区的甜杏仁
- 蛋白含量：不少于50%  
亮氨酸，异亮氨酸和缬氨酸1:1:1黄金配比
- 纯植物蛋白，对乳糖不耐者友好，不会导致腹胀和胃部不适





# Cococin™ 椰胚乳精华

## --提供电解质和能量

- 提供电解质，如钾，镁，钠等
- 提供能量，碳水化合物
- 提供身体必须的营养素，蛋白质、氨基酸、维生素等

电解质 K, Mg  
, Na

碳水化合物

氨基酸

维生素



Component	Sports drinks (mg/100 ml)	Coconut water (mg/100 ml)
Potassium	11.7	294
Sodium	41	25
Chloride	39	118
Magnesium	7	10
Sugars	6	5



# 运动健康，运动后恢复推荐配方

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Curcumin C3 Complex<sup>®</sup> 250mg 姜黄素

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Digezyme<sup>®</sup> 50mg 消化酶

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以上为推荐剂量，每天 **2-3**次

**姜黄素抑制受伤后炎症反应**

**消化酶具有抑制延迟性运动损伤DOMS功效**



# Digezyme® 消化酶

## --DOMS



Sports Nutrition and Therapy

Majeed et al., Sports Nutr Ther 2016, 1(3)  
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Research Article

OMICS International

### Multi-Enzyme Complex for the Management of Delayed Onset Muscle Soreness after Eccentric Exercise: A Randomized, Double Blind, Placebo Controlled Study

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#### Abstract

**Background:** Delayed onset muscle soreness (DOMS) results from muscle overload or strenuous exercise that goes beyond the intensity or duration for which the muscle is accustomed to perform. It is accompanied with the sensation of pain, tenderness, deep aches, and stiffness in muscles that usually begins several hours after the unaccustomed exercise. The aim of this study was to compare the efficacy of multi enzyme complex with a matching placebo in reducing pain associated with DOMS induced by standardized eccentric exercise.

**Methods:** Twenty healthy males (10 pairs) were randomized in this double blind, placebo controlled trial to receive a placebo or multi enzyme complex capsule (50 mg) thrice a day for a period of 3 days. Muscle differences within the group and between groups were assessed at each data collection time-point using Analysis of Covariance (ANCOVA) and Wilcoxon signed rank sum test for all outcome measures.

**Results:** In this controlled clinical study, intake of multi enzyme complex for 3 days resulted in no statistically significant changes in the descriptive statistics and efficacy analysis in muscle power and grip strength measured by hand held dynamometer. Algebraic readings of thigh muscle showed statistical significance (p<0.043). Outcomes were observed in McGill Pain Questionnaire showing high statistical significance. Reducing trend was observed in bio markers of muscle damage (creatinine kinase and lactate dehydrogenase) as well.

**Conclusion:** The study results suggest that compared to placebo, Multi enzyme complex supplementation improves the outcome measures related to DOMS induced by standardized eccentric exercise.

**Keywords:** Delayed onset muscle soreness (DOMS); Muscle soreness questionnaire (MSQ); Pressure pain threshold (PPT); Hand held dynamometer; Illinois agility run test; Multi-enzyme complex

#### Introduction

Delayed onset muscle soreness is related to muscle damage occurring several hours after unaccustomed exercise, particularly when eccentric muscle activity is involved [1-2]. Contracting muscles are flexibly lengthened with eccentric exercise like downhill running which limits physical function for several days [3,4]. This triggers an inflammatory response and the production of reactive oxygen species (ROS) that sustain inflammation and oxidative stress by promoting the activation of transcription factors like the nuclear factor- $\kappa$ B (NF- $\kappa$ B), a pro-inflammatory master switch that controls the production of inflammatory markers and mediators [5]. The inflammatory response ensures musculoskeletal injury; uncontrolled inflammation may prolong skeletal muscle recovery [4].

Delayed onset muscle soreness (DOMS) is a well-documented phenomenon, often occurring as the result of the unaccustomed or high intensity eccentric exercise. Associated symptoms include muscle shortening, increased passive stiffness, swelling, decreases in strength and power, localized soreness and disturbed proprioception. Symptoms will often occur within 24 h post-exercise and typically subside after 3-4 days. The severity of damage and soreness varies as a function of several factors [6].

Considerable amount of research on the treatment of DOMS has been carried out till date but no single treatment has been proven successful in consistently preventing or treating DOMS. Treatment strategies have often integrated multiple therapeutic approaches such as cryo therapy, ultrasound, compression therapy, stretching and deep

tissue massage [7-11]. There is some evidence that ibuprofen, naproxen, and massage may accelerate the resolution of DOMS [12]. In addition, several dietary supplements have been tested in the treatment of DOMS including protein, vitamin C, proteases (enzymes), phosphatidylserine, chondroitin sulphate, and fish oil, all with variable success [4,12-18].

Non-steroidal anti-inflammatory drugs (NSAIDs) like ibuprofen are used widely as anti-DOMS recourse. NSAIDs are known to interfere with chemo taxis of monocytes as well as inhibit neutrophil aggregation [19]. Monocytes produce cytokines, which are responsible for most of the physiological responses accompanying injury, and neutrophils produce elastase and collagenase, which increase vascular permeability via degradation of the vasculature and healthy tissue near the injury site [20]. It is possible that the use of NSAIDs may impair and lengthen the healing process.

In spite of inconsistencies, dose and timing of various NSAIDs also in different studies there are side effects such as gastrointestinal distress and hypertension. Hence NSAIDs are not an optimal choice for treating DOMS [12]. Using enzymes to combat DOMS is also well established.

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- 随机双盲对照试验，受试者20人，3天

- 口服剂量50mg，每天3次

- 机理：过量、超常规运动与炎症反应和ROS产生有关，引发氧化应激反应和炎症反应，而**蛋白酶具有抗炎功效**

- 结果：Digezyme®可以缓解肌肉疼痛和僵硬，改善DOMS症状



# 运动健康，抗肌肉萎缩推荐配方

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Curcumin C3 Complex<sup>®</sup> 250mg 姜黄素

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Bioperine 5mg 胡椒素

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以上为推荐剂量，每天 2-3次

**姜黄素具有抑制NF-kB 功效，NF-kB在肌肉萎缩中起主要作用**

**胡椒素提高姜黄素生物利用度达20倍**



Thank you

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