



# **Osteoartitte; nutrasötikler, fonksiyonel besinler, besin takviyeleri**

Prof. Dr. Osman Tuğrul Eren  
SBU Şişli Hamidiye Etfal Eğitim ve Araştırma Hastanesi  
Ortopedi ve Travmatoloji Kliniği

- Complement Ther Med. 2016 Dec
- **Dietary supplementation is more prevalent among adults with arthritis in the United States population**
- **%62 Osteoartrit**
- **%50**

# Besin takviyesi harcaması

- 2015 21 milyar dolar Amerika
- Türkiye savunma sanayi 19 milyar dolar  
15. sıra 2018
- 2024 57 milyar dolar
- Kaliteli besinler ulaşması zor pahalı

# Nutrasötik

- 1989 yılı Dr Stephen DeFelice tarafından tanımlanmış,
- İngilizcedeki nutrition (besin) ve Farmasötik (tıbbi amaçlı olarak kullanılan ilaç)



# Nutrasötik ürün nedir?

- Bir hastalığın önlenmesi ve tedavisi de dahil olmak üzere, tıbbi yarar sağlayan, bitki, hayvan veya deniz kaynağından ekstrakte edilmiş, bir farmasötik hale getirilmiş, besin ürünleridir.
- Nutrasötik günlük kullandığımız gıda maddelerindeki bileşikleri (**esansiyel aminoasitleri, esansiyel yağ asitleri, vitaminler vs.**) içermektedir.
- Besin takviyesi, fonksiyonel besinler, vbs...
- FDA tanımıyor

# Nasıl elde ediliyor.!



- J Pharm Biomed Anal. 2019 Aug
- Toxicological screening and DNA sequencing detects contamination and adulteration in regulated herbal medicines and supplements for diet, weight loss and cardiovascular health.
- Crighton E ve ark, 2019
- %50 Kimyasal ve DNA bozulması
- İlaç eklemeleri ; parasetamol
- Kafein
- Kuş kıkırdağı,hind leylağı (neem)

# Dejeneratif Eklem Artriti

Genetik  
Faktörler

Çevresel  
Faktörler

T Lenfosit Aktivasyonu ve  
Proliferasyonu

B Lenfosit ve Makrofaj  
Aktivasyonu

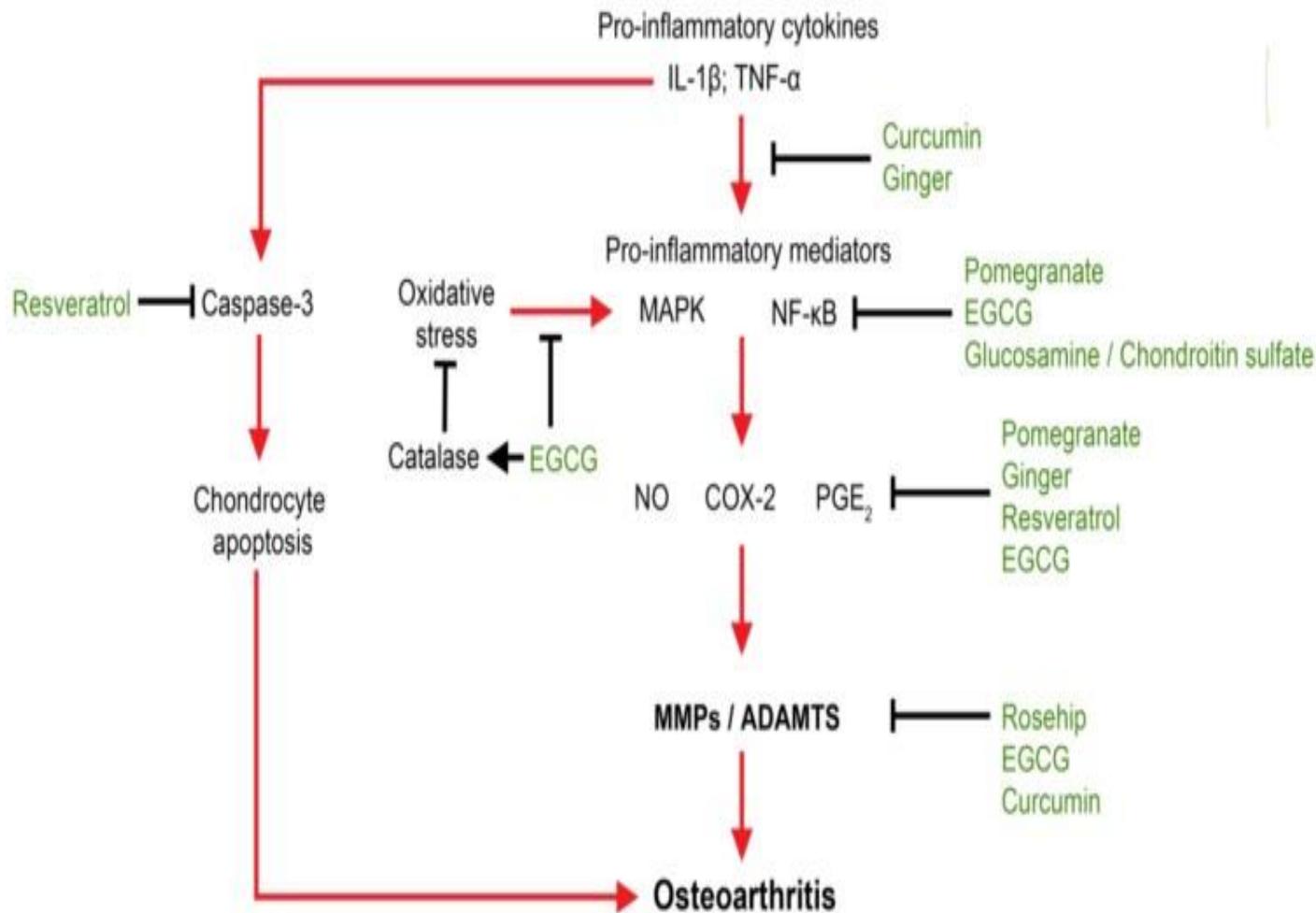
Proinflamatuvar  
Sitokinler (TNF, IL -1, 6,  
I2 vs)

Matriks Bozucu  
Enzimler  
(Metalloproteinazlar)

Oksidatif Stress  
(ROS, RSN)



Kartilaj ve Ekstrasellüler Kollajende  
Bozulma



# Placebo etkisi

- Fonksiyonel beyin MR
- Frontal lob aktivasyonu izleniyor
- Merkezi ağrı inhibisyonu
- Negatif etkiside olabilir
- Uyku yapabilir denirse

# OMEGALAR SAVASI



OMEGA 6

Doymuş  
Oksidan  
Enflamasyon

OMEGA 3

Doymamış  
Antioksidan  
Antienflamatuar

# Omega-3

- Temel Omega-3 yağ asitleri ;  
alfa-linolenik asit (**F vitaminini**)  
eikosapentaenoik asit (**EPA**)  
dokosaheksaenoik asit  
**(DHA)** dir.
- Alfa-linoleik yağ asidi bitkisel kaynaklı olup keten tohumu, dereotu, semizotu, tere gibi sebzelerde bulunur.
- Hayvansal kaynaklı olan EPA ve DHA sadece derin deniz balıkları, bazı algler ve balık yumurtasında bulunmaktadır.



# Omega-3

OSTEOARTHRITIS

## **Omega-3 fatty acids and synovitis in osteoarthritic knees**

*Leslie G. Cleland and Michael J. James*

Recently reported associations between synovitis, cartilage damage and plasma levels of omega-3 and omega-6 fatty acids in patients with osteoarthritis suggest that fish oil supplements might be beneficial additions to the therapeutic regime in this disease; however, questions remain regarding the details of this approach, and controlled trials are required.

Cleland, L. G. & James, M. J. *Nat. Rev. Rheumatol.* 8, 314–315 (2012); published online 17 April 2012;  
[doi:10.1038/nrrheum.2012.60](https://doi.org/10.1038/nrrheum.2012.60)

**Nat. Rev. Rheumatol  
2012**

Osteoartritik dizde tedaviye yardımcıdır. Ancak kontrollü klinik çalışmalar gereklidir.

# Omega-3

Osteoporos Int  
DOI 10.1007/s00198-015-3438-x



ORIGINAL ARTICLE

Supplementation with omega-3 fish oil has no effect on bone mineral density in adults with knee osteoarthritis: a 2-year randomized controlled trial

J. S. Chen<sup>1</sup> · C. L. Hui<sup>2</sup> · S. Lester<sup>3</sup> · C. D. Ruediger<sup>2</sup> · R. Battersby<sup>4</sup> · G. Jones<sup>5</sup> ·  
L. G. Cleland<sup>6</sup> · L. M. March<sup>1</sup>

**Osteoporosis International  
2016**

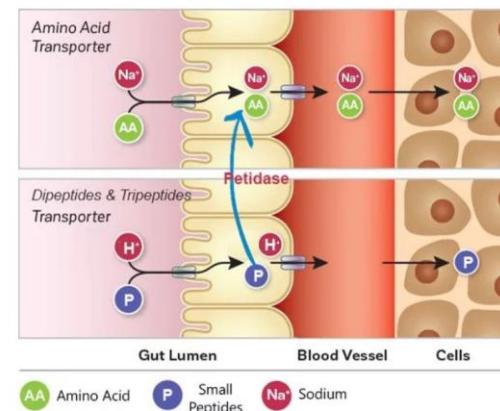
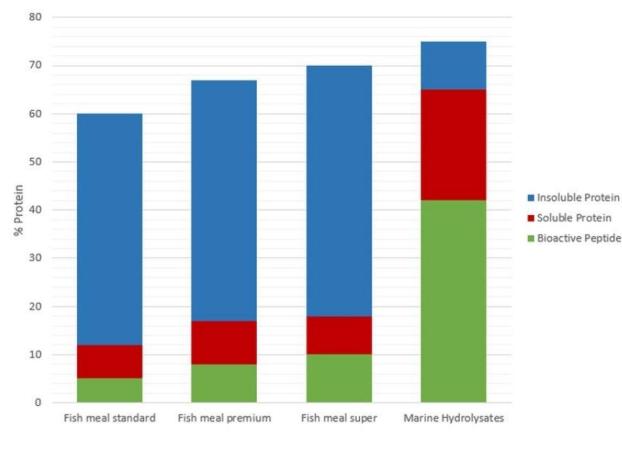
Osteoartritik dizde kemik mineral dansitesine ektisi bulunamamıştır.

**Omega 3 yağ asidinin en çok zararı, kan sulandırıcı ilaçlarla beraber alındığında ortaya çıkmıştır. Antikoagülanlar ile vücutta tepkiye yol açan omega 3, beyin kanamasına ve hatta felçlere neden olabilir.**

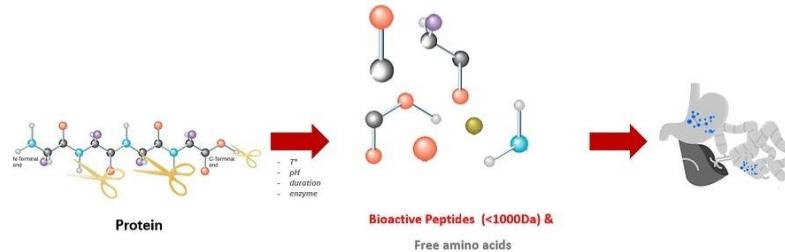
Hayvansal veya Bitkisel protein

Enzimatik hidroliz  
Fermentasyon  
Kimyasal hidroliz

Biyoaktif  
Protein  
Peptitler



# Hidrolize Kollajen ; Tip II yapımını uyarır



Osteoarthritis Cartilage. 2012 Aug  
**Symptomatic and chondroprotective treatment with collagen derivatives in osteoarthritis: a systematic review**

8 çalışma bulunabilmiş  
sonuçlar belirsiz

# **A double-blind, placebo-controlled, randomised, clinical study on the effectiveness of collagen peptide on**

- 2014  
**osteoarthritis**
- 30 hasta

Suresh Kumar ve ark  
**J Sci Food**

- Kondrosit diferansiyasyonu
- Proteoglikan sentezi

## An Observational 1-Month Trial on the Efficacy and Safety of Promerim for Improving Knee Joint

Bekir Eray Kilinc<sup>1</sup>, Yunus Oc<sup>2</sup>, Gungor Alibakan<sup>2</sup>, Emre Bilgin<sup>3</sup>  
Muharrem Kanar<sup>2</sup> and Osman Tugrul Eren<sup>2</sup>

<sup>1</sup>Golhisar State Hospital, Orthopedics Department, Burdur, Turkey. <sup>2</sup>Şişli Hamidiye Etfal Training and Research Hospital, Orthopedics, Istanbul, Turkey. <sup>3</sup>Tepecik Training and Research Hospital, Orthopedics, Izmir, Turkey.

Clinical Medicine Insights: Arthritis and Musculoskeletal Disorders  
Volume 11: 1–4  
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[sagepub.co.uk/journalsPermissions.nav](http://sagepub.co.uk/journalsPermissions.nav)  
DOI: 10.1177/1179544118757496  


### ABSTRACT

**OBJECTIVE:** This study was conducted to evaluate the efficacy and tolerability of the oral intake of promerim in the elimination of acute pain and discomfort associated with knee osteoarthritis (OA).

**METHODS:** Single-center, 1-month, prospective, observational clinical trial. A total of 92 patients not older than 70 years were included. Patients were offered to use 720-mg promerim for the first 15 days after admission after breakfast and then 360mg for the second 15 days. All patients were analyzed with the visual analog scale (VAS) for pain, which ranges from 0 to 10, and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score before the start of treatment and 1 month after the start. Statistical analysis was performed by SPSS 15.0 software. An  $\alpha$  level of  $P < .05$  was assumed to be statistically significant.

**RESULTS:** This study comprised 92 patients (69 women and 23 men) with a mean age of 51.5 (range: 40–69) years. Before treatment, the mean VAS score was  $5.6 \pm 1.1$ , and after treatment, the mean VAS score was  $2.6 \pm 1.7$ . Treatment with promerim consistently showed a significant decrease in the VAS score ( $P < .001$ ). The mean WOMAC score of the patients was  $46.4 \pm 8.2$  before treatment. After treatment, the mean WOMAC score was  $72.1 \pm 14.4$ . Treatment with promerim consistently showed a significant increase in the WOMAC score ( $P < .001$ ).

**CONCLUSIONS:** The results of this single-center, open-label clinical study demonstrate that promerim is a viable natural treatment option for treating knee OA. We recommend that 720-mg promerim taken once daily for the first 15 days after admission and 360mg taken once daily for the next 15 days significantly and rapidly reduced composite pain and stiffness in the knee OA within 1 month.

- J Med Food. 2019 Aug 5.
- A Randomized, Double-Blind, Placebo-Controlled, Prospective Clinical Trial Evaluating Water-Soluble Chicken Eggshell Membrane for Improvement in Joint Health in Adults with Knee Osteoarthritis.
- Hewlings S, Kalman D, Schneider LV
- 88 hasta
- 12 hafta iyileşme

# Bitkisel Nutrasöтикler

## Akgünlük (*Boswellia serrata*)

- Hindistan, Afrika'nın kuzeyi ve Asya'nın ortasında yetişen bir ağaçtır.
- Kabuğunun soyulması ile elde edilen reçine kullanılmaktadır.



# Akgünlük (*Boswellia serrata*)

## Inhibition of Leukotriene B<sub>4</sub> Formation in Rat Peritoneal Neutrophils by an Ethanolic Extract of the Gum Resin Exudate of *Boswellia serrata*

H. P. T. Ammon<sup>1,3</sup>, T. Mack<sup>1</sup>, G. B. Singh<sup>2</sup>, and H. Safayhi<sup>1</sup>

<sup>1</sup> Department of Pharmacology, Pharmaceutical Institute, University of Tübingen, Auf der Morgenstelle 8, D-7400 Tübingen, Federal Republic of Germany

<sup>2</sup> Pharmacology Department, Regional Research Laboratory, Jammu-Tawi, India

<sup>3</sup> Address for correspondence

Received: July 31, 1990

**Int J 1990**

invitro ve hayvan model çalışmalarında boswellic asid anti-inflamatuvar etkisini **5-LO (5-lipoxygenase )**, **5-HETE (5-hydroxyeicosatetraenoic acid )**, **LTB-4 (leukotriene B4 )** sentezi inhibisyonu ile yapar.

**Ciddi kabızlık ve alerjik yan etkileri mevcut**

Clin Rheumatol. 2016 Oct;35.

Improved WOMAC score following 16-week treatment with bromelain for knee osteoarthritis.

Kasemsuk T ve ark.

- Bromelain (Ananas)
- Caessalpinia sappan (Güneydogu asyada ağaç, brazilin )





# Capsaicin; ağrı reseptör blokajı



Arthritis Rheumatol. 2019 Sep;71(9):

Randomized, Double-Blind, Placebo-Controlled Trial of Intraarticular Trans-Capsaicin for Pain Associated With Osteoarthritis of the Knee.

Stevens RM ve ark.,

Diallyl sulphide (sarımsak ekstresi)

# **Kedi Pençesi (Cat's Claw) *Uncaria Tomentosa***

yağmur  
ormanlarında yetişen  
tropik bir asma  
çeşididir.

**“Yağmur  
Ormanlarının  
Kutsal Çiçeği”**



# Kedi Pençesi (Cat's Claw) *Uncaria Tomentosa*

Inflamm. res. 50 (2001) 442–448  
1023-3830/01/090442-07 \$ 1.50+0.20/0

© Birkhäuser Verlag, Basel, 2001

Inflammation Research

Efficacy and safety of freeze-dried cat's claw in osteoarthritis of the knee: mechanisms of action of the species *Uncaria guianensis*

J. Piscoya<sup>1</sup>, Z. Rodriguez<sup>1</sup>, S.A. Bustamante<sup>2</sup>, N.N. Okuhama<sup>3</sup>, M.J.S. Miller<sup>3</sup> and M. Sandoval<sup>3</sup>

Inflamm. Res. 2001

Glikosid-7 adlı maddenin doğal anti-inflamatuar olduğu belirtilmiştir.

# Kedi Pençesi (Cat's Claw) *Uncaria Tomentosa*



Contents lists available at SciVerse ScienceDirect

Neurochemistry International

journal homepage: [www.elsevier.com/locate/nci](http://www.elsevier.com/locate/nci)



Neuroprotective effects of aqueous extracts of *Uncaria tomentosa*: Insights from 6-OHDA induced cell damage and transgenic *Caenorhabditis elegans* model

Zhenhua Shi<sup>a,1</sup>, Zhongbing Lu<sup>b,1</sup>, Yashuo Zhao<sup>a</sup>, Yueqi Wang<sup>a</sup>, Xi Zhao-Wilson<sup>c</sup>, Peng Guan<sup>a</sup>, Xianglin Duan<sup>a</sup>, Yan-Zhong Chang<sup>d,\*</sup>, Baolu Zhao<sup>d,e,\*</sup>

<sup>a</sup>The Institute of Molecular Neurobiology and Neuropharmacology, Hebei Normal University, Shijiazhuang 050016, China

<sup>b</sup>College of Life Sciences, University of Chinese Academy of Science, Beijing 100049, China

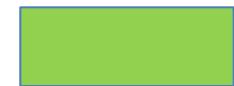
<sup>c</sup>BioMarker Pharmaceuticals, Inc., 5941 Optical Court, San Jose, CA 95138, USA

<sup>d</sup>Pony Testing International Group Co. Ltd, Beijing 100080, China

<sup>e</sup>State Key Laboratory of Brain and Cognitive Science, Institute of Biophysics, Chinese Academy of Science, Beijing 100101, China

**Neurochem. Int 2013**

**AC-II; Cat's Claw bitkisinin alkaloid içermeyen, %8 karboksi alkil ester (CAE) içeren özel bir ekstresidir. DNA onarıcı ve anti-inflamatuvar**



**Cat's Claw bitkisinin Baş ağrısı, baş dönmesi ve kusma görülebilir. Kan basıncı düşük olanlarda kullanımı tehlikelidir.**

# Devil's claw

## Şeytan pençesi (*Harpagophytum procumbens*)

- Kökü yüksek konsantrasyonlarda, aktif bileşigi olan harpagosid içerir
- Harpagosid, anti-inflamatuar ve antioksidan etkiler üreten bir glukozid'dir



# Devil's claw

## Şeytan pençesi (*Harpagophytum procumbens*)

THE JOURNAL OF ALTERNATIVE AND COMPLEMENTARY MEDICINE  
Volume 12, Number 10, 2006, pp. 981–993  
© Mary Ann Liebert, Inc.

### Devil's Claw (*Harpagophytum procumbens*) as a Treatment for Osteoarthritis: A Review of Efficacy and Safety

SARAH BRIEN, Ph.D.,<sup>1</sup> GEORGE T. LEWITH, M.A., D.M., F.R.C.P., M.R.G.C.P.,<sup>1</sup>  
and GERRY McGREGOR, Ph.D.<sup>2</sup>

## The J of Alter and Comp. Med2006

- Hayvan çalışmalarında, anti-inflamatuar ve analjezik etkileri saptanmıştır.
- Cox-2 anti-inflamatuar ilaçlar ile aynı şekilde çalıştığı görülmüştür.
- Aynı zamanda, inflamasyonda rol alan lökotrienler de değişikliklere sebep olmaktadır.
- *duedoneal ülser ve hamilelikte kontraendike*



# Beyaz Hindiba

- BMC Musculoskelet Disord. 2010 Jul 9;11:156.
- Phase I, placebo-controlled, dose escalation trial of chicory root extract in patients with osteoarthritis of the hip or knee.
- Olsen NJ ve ark.
- 40 hasta
- Sonuçlar iyi

# Yeşil Çay



Vitamin C ve E den  
50-100 kat daha fazla  
antioksidan



Antioksidan  
Antiinflamatuar

Aloe vera

# S-adenosyl Methionine (SAM-e)

## Safety and efficacy of S-adenosylmethionine (SAMe) for osteoarthritis

### A meta-analysis

KAREN L. SOEKEN, PhD; WEN-LIN LEE, RN, PhD; R. BARKER BAUSELL, PhD;  
MARIA AGELLI, MD, MS; AND BRIAN M. BERMAN, MD

Baltimore, Maryland

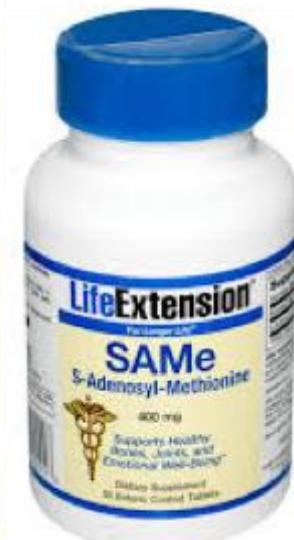
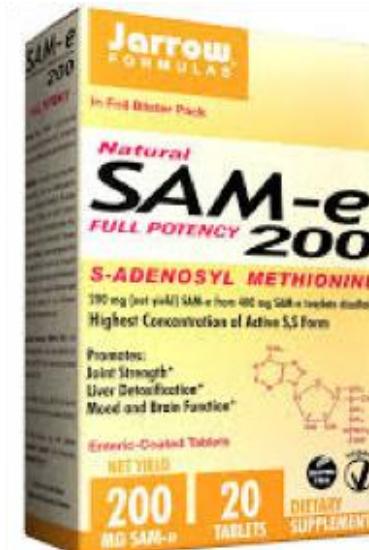
The Journal of Family Practice • MAY 2002 • VOL. 51, NO. 5 ■ 425

# The J of Fam Pract. 2002

- SAM-e NSAID kadar efektif
- Tolerabilite NSAID'dan iyi

Hücrenin ürettiği doğal bir maddedir.  
adenosin trifosfat (ATP) ve metionin

*Anti-depresanlarla etkileşim, bipolar  
rahatsızlığı ve monoamin oksidaz inhibitörü  
(MAOI) kullananlara tavsiye edilmez.*



# Zerdeçal (Turmeric, Curcumin Longa)



NIH Public Access

Author Manuscript

*Int J Biochem Cell Biol.* Author manuscript; available in PMC 2010 January 1.

Published in final edited form as:  
*Int J Biochem Cell Biol.* 2009 ; 41(1): 40–59. doi:10.1016/j.biocel.2008.06.010.

## Potential Therapeutic Effects of Curcumin, the Anti-inflammatory Agent, Against Neurodegenerative, Cardiovascular, Pulmonary, Metabolic, Autoimmune and Neoplastic Diseases

Bharat B. Aggarwal<sup>1</sup> and Kuzhuvvelil B. Harikumar

Cytokine Research Laboratory, Department of Experimental Therapeutics, The University of Texas M. D. Anderson Cancer Center, Houston, Texas



**Int J Biochem Cell Biol.**  
**2009**

- Fosfolipaz, lipooksigenaz, sikloooksigenaz 2, lökotrienes, tromboksan, prostaglandinler, nitrik oksit, kollajenaz, elastaz, hiyalüronidaz, monosit kemoatraktan protein-I (MCP-I) COX-2, TNF- $\alpha$ , , 5-LOX, IL-1, IL-6, IL-8 zerdeçal ekstiresi ( curcumin) ile inhibe olur.

# Zerdeçal (Turmeric, Curcumin Longa)



NIH Public Access

Author Manuscript

*Int J Biochem Cell Biol.* Author manuscript; available in PMC 2010 January 1.

Published in final edited form as:

*Int J Biochem Cell Biol.* 2009 ; 41(1): 40–59. doi:10.1016/j.biocel.2008.06.010.

**Potential Therapeutic Effects of Curcumin, the Anti-inflammatory Agent, Against Neurodegenerative, Cardiovascular, Pulmonary, Metabolic, Autoimmune and Neoplastic Diseases**

Bharat B. Aggarwal<sup>1</sup> and Kuzhuvvelil B. Harikumar

Cytokine Research Laboratory, Department of Experimental Therapeutics, The University of Texas M. D. Anderson Cancer Center, Houston, Texas

- Antioksidant
- Anti-inflamatuar
- Antikarsinojenik
- Antimikrobial Efekt
- İmmuniteti Güçlendirme

**Int J Biochem Cell Biol.  
2009**

**Anafilaksi ve platelet fonksiyon bozukluğu gelişebilir.**

Arthritis Res Ther. 2019 Jul 27;

Bio-optimized Curcuma longa extract is efficient on knee osteoarthritis pain: a double-blind multicenter randomized placebo controlled three-arm study.

Henrotin Y ve ark Belçika

- 150 hasta
- 90 gün takip
- Sonuçlar iyi

# Glukozamin Sulfat

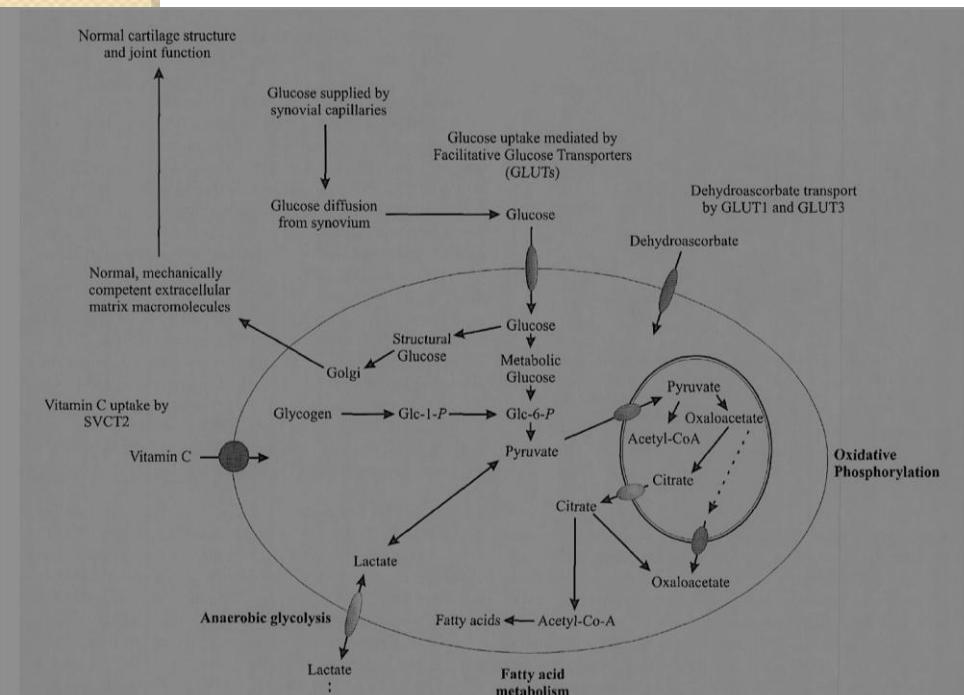
Kondrositleri aktive ederek proteoglikan sentezini uyarırlar.  
karın ağrısı, mide yanması,  
bulantı ve ishaldır.

## Glucosamine Sulfate for Osteoarthritis

Carlos C da Camara and Gregory V Dowless

*Ann Pharmacother* 1998;32:580-7.

## Ann Pharmacother 1998





**REVIEW ARTICLE**

## What about supplements for osteoarthritis? A critical and evidenced-based review

Evan S. VISTA<sup>1</sup> and Chak S. LAU<sup>2</sup>

<sup>1</sup>Joint & Bone Center, University of Santo Tomas Hospital, España, Manila, Philippines, and <sup>2</sup>Division of Rheumatology and Clinical Immunology, Department of Medicine, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong, China

**Int. J. of Rheumatic Diseases 2011**

- Cochrane incelemesi
- Osteoartrit için glukozamin tedavisi içeren 25 çalışma (4963 hasta)
- Glukozamin kullanımının yararını göstermeye başarısız olmuştur.

# Kondroitin Sulfat

Therapeutic Advances in Musculoskeletal Disease

Review

## Chondroitin sulfate in the treatment of osteoarthritis: from *in vitro* studies to clinical recommendations

Yves Henrotin, Mariane Mathy, Christelle Sanchez and Cecile Lambert

Ther Adv Musculoskel Dis

[2010] 2(6) 335–348

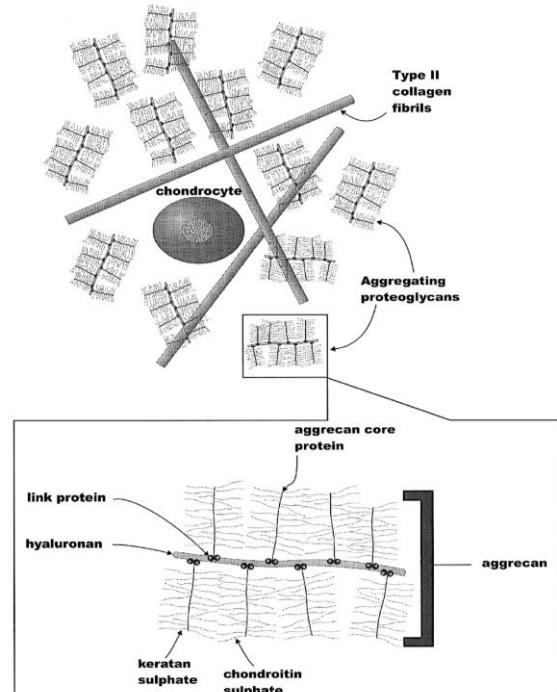
DOI: 10.1177/  
1759720X10383076

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<http://www.sagepub.co.uk/journalsPermissions.nav>

## Ther. Adv. Musculoskeletal Dis.

- Anabolik 2010
- Anti-katabolik
- Anti-apoptotik Efektı

Diyabetik ve hemofilik hastalarda dikkat edilmeli



# **2013 AAOS Kılavuzu**

- Glukozamin ve Kondrotin sülfat  
Kuvvetli dercede önerilmemektedir.

## **2014 OARSI**

**Kullanılması belirsiz**

Bor

[Environ Health Perspect.](#) 1994 Nov; 102(Suppl 7): 83–85.

PMCID: PMC1566627

Research Article

## Essentiality of boron for healthy bones and joints.

[R E Newnham](#)

- Kemik yoğunluğuna katkıda bulunarak, osteoporozu önleyebilir.
- Artrit semptomlarını azaltır.
- Kas kütlesini iyileştirerek iskelet yapısının güçlü olmasına yardımcıdır.

**Biyolojide boratlar memelilere düşük düzeyde toksiktir**



**Manganez**

**Çinko**

**Krom**

**Demir**

**Bakır**

**Bull NY Acad Med. 1984**

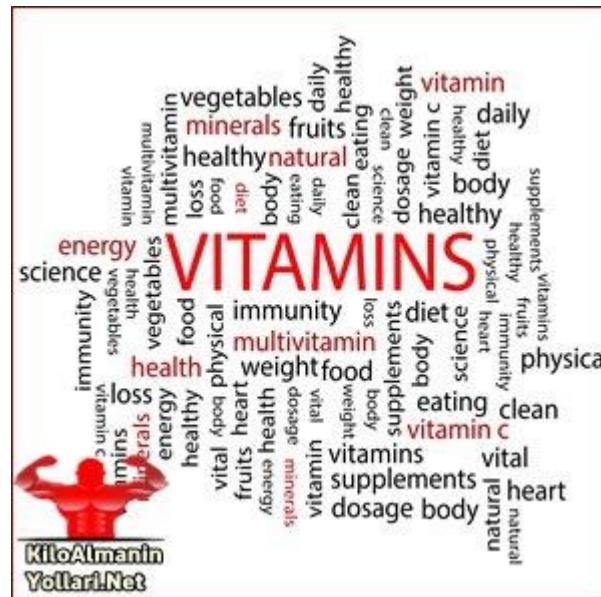
- Sağlıklı kemik yapısına, kemik metabolizmasına katkıda bulunur
- Kemik yapımı için gerekli koenzim
- Bağ dokularının oluşumu, kalsiyum metabozması , tiroid bezinin ve seks hormonlarının düzgün çalışması, kan şekeri seviyesinin düzenlenmesi

# Bamya tohumu (okra seed)

- Antioksidan, antiinflamatuar
- Solaline
- Oksalat
- Selenium antioksidan,

# Vitaminler

- A vitamini
  - C vitamini
  - D vitamini
  - E vitamini
  - K vitamini



Arthritis Care Res (Hoboken). 2019 Jul  
Associations between Vitamin C and D Intake and Cartilage  
Composition and Knee Joint Morphology over 4 years: Data from the  
Osteoarthritis Initiative.  
Joseph GB ve ark

- 1785 OA
- MR
- 4 yılda 400 U haftada D vitamini
- Kıkırdak hasarı daha az



## A Review of Nutraceuticals in Joint Arthritis

Loseli M<sup>1</sup>, Awwad GEH<sup>2</sup> and Bradshaw AR<sup>1</sup>

<sup>1</sup>Department of Orthopaedics, Wagga Wagga Base Hospital, NSW 2650, Australia

<sup>2</sup>Department of Orthopaedic Surgery, Royal Adelaide Hospital, NSW 2650, Australia

\*Corresponding author: Loseli M, Department of Orthopaedics, Wagga Wagga Base Hospital, NSW 2650, Australia, Tel: +61 2 6938 6666; Fax: +61 2 6938 6488; E-mail: [matakitau@hotmail.com](mailto:matakitau@hotmail.com)

Rec date: Feb 16, 2015, Acc date: Apr 20, 2015, Pub date: May 06, 2015,

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**J Pain Relief 2015**

Nutrasötik ajanlar ağrıyı azaltmakta ve bazı hastalarda eklem fonksiyonlarında iyileştirmelerine rağmen RA ve OA'in doğal progresyonunu durdurması veya gerilemesi ile ilgili güçlü bir kanıt bulunmamaktadır.

14-17 October 2014, Istanbul, Turkey



## 2014 Annual Conference & Exhibition

### Functional Foods, Nutraceuticals, Natural Health Products, and Dietary Supplements

14-17 October 2014, Istanbul - Turkey



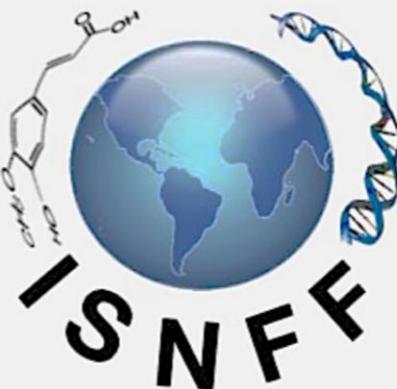
The 10th International Conference and Exhibition on Nutraceuticals & Functional Foods

"Platform for Foods, Nutrition and Medical Science"

October 22(Sun.) - 25(Wed.), 2017  
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(The 10th International Conference  
and Exhibition on Functional Foods,  
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