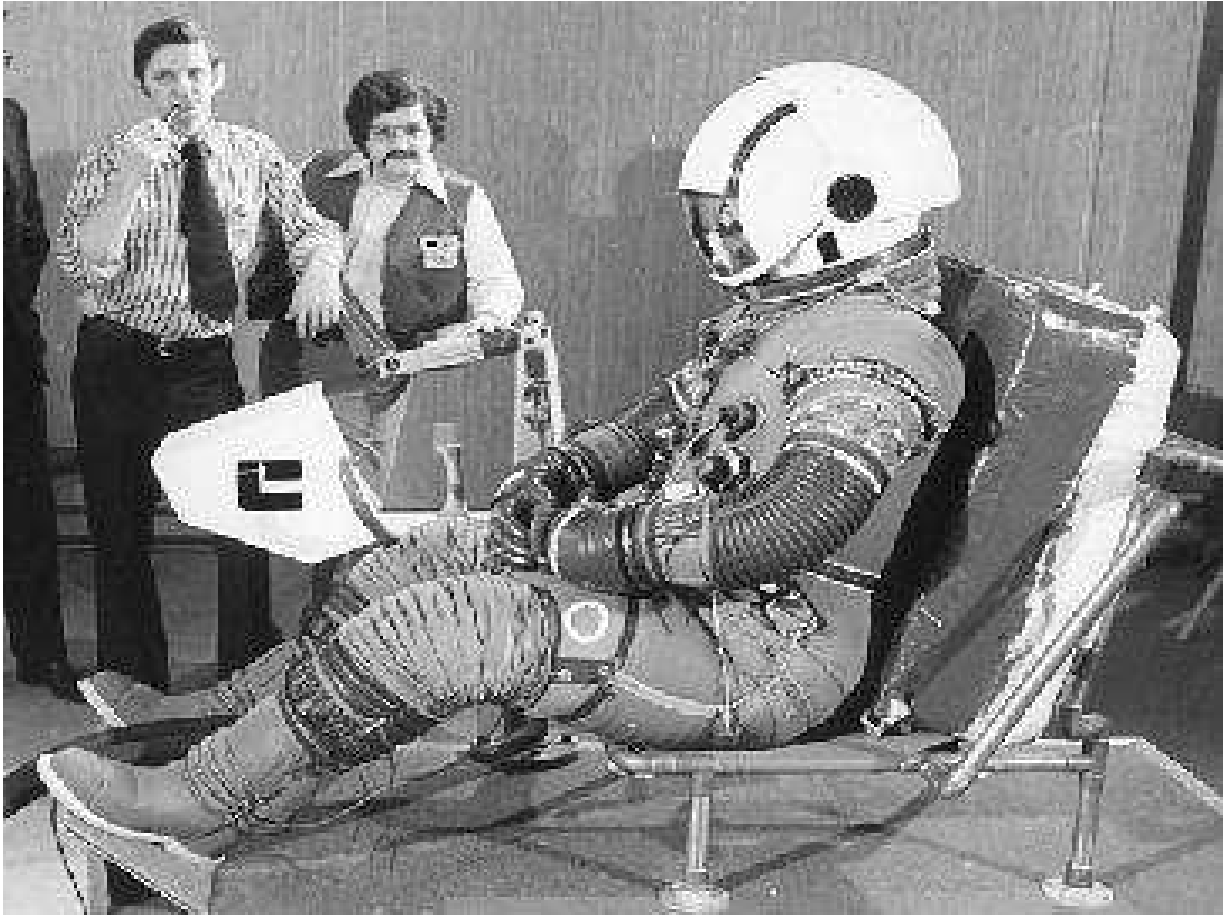


OSTEOARTHRITIS:

GLUCOSAMINE AND BEYOND



PRESENTED BY DANIEL A. WASSERMAN, DOM

BROWARD SPINE INSTITUTE

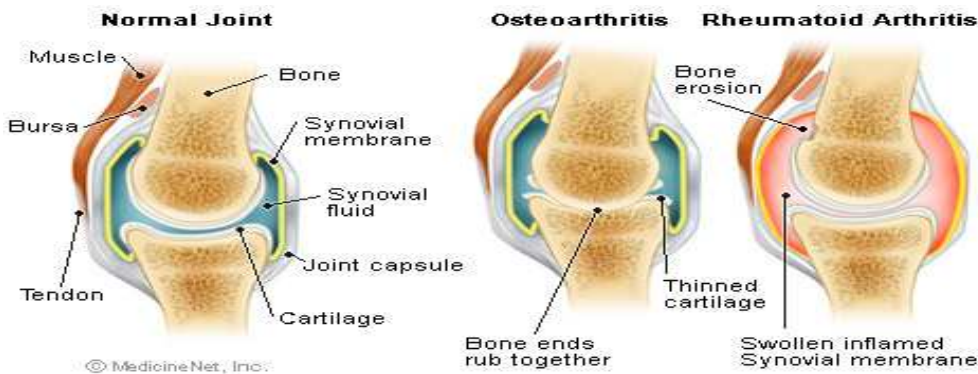
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STATISTICS

Over 40 Millions Americans have Osteoarthritis
Annual costs more than \$82 billion
Up to 80% of people over 50 years of age

DEFINITION

Osteoarthritis is characterized by progressive degeneration of the joint cartilage, joint pain and reduced mobility. This form of arthritis most often affects those of the hands, knees, hips, and spine, although any joint can be affected.



Normal and Arthritic Joints

SYMPTOMS

Early morning stiffness
Stiffness following periods of rest
Pain that worsens on joint use
Loss of joint function

DEFINITIONS

Chondrocytes = cells that produce cartilage
NSAID = non-steroidal anti-inflammatory drug (Motrin, Naprosyn, Alleve, Advil)
Proteoglycan = proteins in cartilage that hold on to water

JOINT MATRIX

Normal cartilage is a complex material consisting of a solid matrix composed primarily of collagen and proteoglycan, which is saturated with water. The interaction of the physical and biochemical structures of cartilage is necessary to allow the normal function of providing nearly frictionless motion, wear resistance, joint congruence, and transmission of load to subchondral bone. Chondrocytes are responsible for synthesizing and maintaining this material. Osteoarthritis occurs when there is disruption of normal cartilage structure and homeostasis.

WESTERN MEDICAL APPROACH

- Pain Medicine
- Injections
- Surgery

[Am J Med.](#) 1987 Nov 20;83(5A):29-34.

Effects of nonsteroidal anti-inflammatory drugs on chondrocyte metabolism in vitro and in vivo.

[Brandt KD.](#)

Department of Medicine, Indiana University School of Medicine, Indianapolis 46223.

Salicylates and several other nonsteroidal anti-inflammatory drugs (NSAIDs) that are commonly employed in the treatment of osteoarthritis effectively decrease joint pain and increase mobility. Data from in vivo studies suggest that salicylate administration may accelerate articular cartilage damage in several animal models of osteoarthritis. At in vitro concentrations comparable to those that are achieved in the synovial fluid of patients treated with the drug, several NSAIDs suppress proteoglycan synthesis by the chondrocyte. These NSAID-related effects on chondrocyte metabolism appear unrelated to inhibition of prostaglandin synthetase, and are much more profound in osteoarthritic cartilage than in normal cartilage, due to enhanced uptake of NSAIDs by the osteoarthritic cartilage. Depletion of matrix proteoglycans appears to be a major factor in the increased vulnerability of chondrocytes in degenerating cartilage to effects of NSAIDs. If similar changes occur in the cartilage of patients with arthritis treated with NSAIDs, despite the symptomatic improvement that these drugs produce, cartilage degeneration could be accelerated.

[Eur J Rheumatol Inflamm.](#) 1993;13(1):7-16.

Anti-inflammatory drugs and their effects on cartilage synthesis and renal function.

[Shield MJ.](#)

Department of Medical and Clinical Research, Searle, Bucks, United Kingdom.

Growing evidence suggests that nonsteroidal anti-inflammatory drugs (NSAIDs), while able to alleviate inflammation, may damage articular cartilage, though both chondrodestructive and chondroprotective

activities have been observed with different NSAIDs. Experiments have shown that certain NSAIDs at pharmacologic concentrations achievable in man consistently inhibit glycosaminoglycan (GAG) synthesis. With regard to renal aspects, the effects of NSAIDs...upsets the balance that maintains renal function. In situations in which there is reduced renal reserve, reduction of renal PG synthesis by NSAIDs will adversely affect maintenance of renal blood flow and glomerular filtration rate and excretion of sodium, potassium, and water.

"Each year, use of NSAIDs (Non-Steroidal Anti-Inflammatory Drugs) accounts for an estimated 7,600 deaths and 76,000 hospitalizations in the United States."

(NSAIDs include aspirin, ibuprofen, naproxen, diclofenac, ketoprofen, and tiaprofenic acid.)

Source: "Unnecessary Prescribing of NSAIDs and the Management of NSAID-Related Gastropathy in Medical Practice," Annals of Internal Medicine, September 15, 1997, 127:429-438

Approximately 32,000 hospitalized patients (and possibly as many as 106,000) in the USA die each year because of adverse reactions to their prescribed medications.

Source: Lazarou, J, Pomeranz, BH, Corey, PN, "Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies," Journal of the American Medical Association (Chicago, IL: American Medical Association, 1998)

[Scand J Gastroenterol.](#) 1979;14(5):605-7.

Effect of deglycyrrhizinated liquorice on gastric mucosal damage by aspirin.

[Rees WD](#), [Rhodes J](#), [Wright JE](#), [Stamford LF](#), [Bennett A](#).

Gastric mucosal damage induced by giving 60 mg aspirin orally to rats was reduced by simultaneous administration of 100-500 mg deglycyrrhizinated liquorice. Human faecal blood loss induced by 975 mg aspirin orally three times a day was less when 350 mg deglycyrrhizinated liquorice was given with each dose of aspirin.

[Am J Gastroenterol.](#) 1999 Jul;94(7):1818-22.

Phospholipid association reduces the gastric mucosal toxicity of aspirin in human subjects.

[Anand BS](#), [Romero JJ](#), [Sanduja SK](#), [Lichtenberger LM](#).

Department of Medicine, Baylor College of Medicine and Houston VA Medical Center, Texas, USA.

OBJECTIVE: In previous studies on rats, we have shown that aspirin-induced injury to the gastric mucosa is markedly reduced or completely abolished if Aspirin is chemically associated with the phospholipid, phosphatidylcholine (PC). The present study shows that acute aspirin-induced damage to the gastric mucosa can be reduced by chemically associating Aspirin with PC. The mechanism of

mucosal protection provided by this compound is not related to any alteration in the ability of Aspirin to inhibit mucosal COX activity. We believe this protection is attributable to the maintenance of the defensive hydrophobic barrier of the gastric mucosa.

X-RAYS

[Arthritis Rheum.](#) 1988 Feb;31(2):204-9.

Radiographic assessment and psychologic variables as predictors of pain and functional impairment in osteoarthritis of the knee or hip.

[Summers MN](#), [Haley WE](#), [Reveille JD](#), [Alarcon GS](#).

Department of Psychology, School of Medicine, University of Alabama, Birmingham.

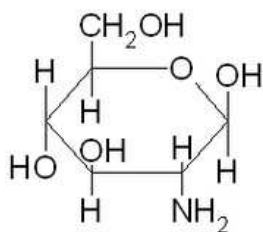
Sixty-five outpatients with osteoarthritis of the knee and/or hip were assessed using radiographic ratings [X-ray] of disease severity, measures of psychologic coping, and multidimensional clinical outcomes of degree of pain and functional impairment. [X-ray of] disease severity accounted for little of the individual variability in clinical outcomes. Even after controlling for disease severity, psychologic variables remained strong predictors of individual differences in functional impairment and pain. Psychologic processes deserve greater clinical and research attention as potential mediators between disease severity and clinical outcome.

FORMAT

Six categories of Supplementation:

- Glucosamine/Chondroitin/MSM
- Vitamin/minerals
- Essential Fatty Acids
- Hormones
- Herbal supplements
- Dietary strategies

Glucosamine



Glucosamine is the most fundamental building block required for the all of the primary components of cartilage. These include glycosaminoglycans, collagen, hyaluronic acid, proteoglycans, as well as other joint lubricants and protectants.

[Osteoarthritis Cartilage.](#) 1994 Mar;2(1):61-9.

Glucosamine sulfate compared to ibuprofen in osteoarthritis of the knee.

[Muller-Fassbender H](#), [Bach GL](#), [Haase W](#), [Rovati LC](#), [Setnikar I](#).

Rheumazentrum, Bad Abbach, Germany.

Glucosamine sulfate is able to stimulate proteoglycan synthesis by chondrocytes and has mild anti-inflammatory properties. We conducted a randomized, double-blind, parallel-group study of glucosamine sulfate 500 mg t.i.d. vs ibuprofen 400 mg t.i.d., orally for 4 weeks. The study included 200 hospitalized patients with active OA of the knee, symptoms for at least 3 months and a Lequesne's index of at least 7 points. Patients were evaluated weekly. Response was defined as a reduction in the Lequesne's index by at least 2 points if the enrollment value was higher than 12 points, or by at least 1 point if the enrollment value was 12 or less points, together with a positive overall assessment by the investigator. The improvement tended to be sooner under ibuprofen; but there was no difference from the 2nd week onward, with a success rate of 52% in the ibuprofen group and of 48% in the glucosamine group ($P = 0.67$) at the end of treatment. The average Lequesne's index at enrollment was around 16 points and decreased by over 6 points in both groups, again with the above described trend. On the other hand, 35% of patients on ibuprofen reported adverse events, mainly of gastrointestinal origin, vs 6% adverse events with glucosamine ($P < 0.001$, Fisher's Exact test). The number of adverse event related drop-outs was different between the two groups (7% vs 1%). Glucosamine sulfate was therefore as effective as ibuprofen on symptoms of knee OA. These data confirm glucosamine sulfate as a safe symptomatic Slow Acting Drug for OA.

[Curr Med Res Opin.](#) 1982;8(3):145-9.

Double-blind clinical evaluation of the relative efficacy of ibuprofen and glucosamine sulphate in the management of osteoarthrosis of the knee in out-patients.

[Lopes Vaz A](#).

A double-blind trial was carried out in 40 out-patients with unilateral osteoarthrosis of the knee to compare the efficacy and tolerance of oral treatment with 1.5 g glucosamine sulphate or 1.2 g ibuprofen daily over a period of 8 weeks. Pain scores decreased faster during the first 2 weeks in the ibuprofen than in the glucosamine treatment group. Although the rate of decrease was slower, the reduction in pain scores was continued throughout the trial period in patients on glucosamine and the difference between the two groups turned significantly in favour of glucosamine at Week 8. No significant differences were observed in swelling or any of the other parameters monitored. Tolerance was satisfactory with both treatments, with only minor complaints being reported by 2 patients on glucosamine compared with 5 patients on ibuprofen.

[Lancet.](#) 2001 Jan 27;357(9252):251-6.

Long-term effects of glucosamine sulphate on osteoarthritis progression: a randomised, placebo-controlled clinical trial.

Bone and Cartilage Metabolism Research Unit (WHO Collaborating Center for Public Aspects of Osteoarticular Disorders), University of Liege,

We did a randomised, double-blind placebo controlled trial, in which 212 patients with knee osteoarthritis were randomly assigned 1500 mg sulphate oral glucosamine or placebo once daily for 3 years. The 106 patients on placebo had a progressive joint-space narrowing. There was no significant joint-space loss in the 106 patients on glucosamine sulphate: -0.06 mm (-0.22 to 0.09). Similar results were reported with minimum joint-space narrowing. As assessed by WOMAC scores, symptoms worsened slightly in patients on placebo compared with the improvement observed after treatment with glucosamine sulphate. There were no differences in safety or reasons for early withdrawal between the treatment and placebo groups.

[Pharmatherapeutica](#). 1982;3(3):157-68.

Oral glucosamine sulphate in the management of arthrosis: report on a multi-centre open investigation in Portugal.

[Tapadinhas MJ](#), [Rivera IC](#), [Bignamini AA](#).

Patients received 1.5 g daily in 3 divided doses over a mean period of 50 +/- 14 days. The results from 1208 patients were analyzed and showed that the symptoms of pain at rest, on standing and on exercise and limited active and passive movements improved steadily through the treatment period. The improvement obtained lasted for a period of 6 to 12 weeks after the end of treatment. Objective therapeutic efficacy was rated by the doctors as 'good' in 59% of patients, and 'sufficient' in a further 36%.

[Dtsch Med J](#). 1965 Jul 5;16(13):446-9.

[Glucosamine in the therapy of degenerative rheumatism]

Substance: Glucosamine

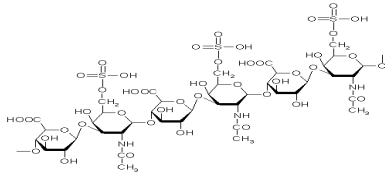
Prime Action: Rebuilding cartilage, while reducing pain

Dosage: 1500mg per day in divided doses, use pure Glucosamine Sulfate

Other Uses: migraines,

Warnings: Allergies to shellfish (although vegetarian sources are available)

CHONDROITIN (shark cartilage, sea cucumber)



A natural component of the cartilage that cushions joints, chondroitin sulfate is a compound that appears to block the enzymes that can destroy crucial cartilage tissue. It is also believed to promote water retention and elasticity in joint cartilage.

[J Rheumatol.](#) 1996 Aug;23(8):1385-91.

Comparison of the antiinflammatory efficacy of chondroitin sulfate and diclofenac sodium in patients with knee osteoarthritis.

[Morreale P](#), [Manopulo R](#), [Galati M](#), [Boccanera L](#), [Saponati G](#), [Bocchi L](#).

Clinical Institute of Orthopaedics and Traumatology, University of Siena, Italy.

146 patients with knee OA were recruited into 2 groups. RESULTS: Patients treated with the NSAID showed prompt and plain reduction of clinical symptoms, which, however, reappeared after the end of treatment; in the CS group, the therapeutic response appeared later in time but lasted for up to 3 months after the end of treatment. CONCLUSION: CS seems to have slow but gradually increasing clinical activity in OA; these benefits last for a long period after the end of treatment.

[J Rheumatol.](#) 2001 Jan;28(1):173-81.

Chondroitin sulfate in osteoarthritis of the knee: a prospective, double blind, placebo controlled multicenter clinical study.

[Mazieres B](#), [Combe B](#), [Phan Van A](#), [Tondut J](#), [Grynfeldt M](#).

Service de Rhumatologie, CHU Rangueil, Toulouse, France. mazieres@cict.fr

OBJECTIVE: To assess the efficacy and safety of chondroitin sulfate (CS) 1 g/day per os compared to placebo, in a double blind, randomized, parallel group study patients (63 in CS group and 67 in placebo group), with 3 months treatment followed by a 3 month posttreatment period, in patients with femorotibial osteoarthritis (OA). At treatment endpoint, the AFI showed greater but nonsignificant improvement in the CS than in the placebo group. Adverse event rates did not differ significantly.

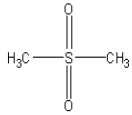
Substance: Chondroitin

Prime Action: rebuilding cartilage, while reducing pain

Dosage: 400-600mg, three times per day

Warnings: Allergies to shellfish (although vegetarian sources are available), possible interaction with blood-thinners

MSM (methylsulfonylmethane)



Methylsulfonylmethane

Source of organic sulfur, a necessary building block for proteins, especially those found in the hair, muscles, and connective tissue of the joints and skin.

[Osteoarthritis Cartilage](#). 2005 Nov 22

Efficacy of methylsulfonylmethane (MSM) in osteoarthritis pain of the knee: a pilot clinical trial.

[Kim LS](#), [Axelrod LJ](#), [Howard P](#), [Buratovich N](#), [Waters RF](#).

Southwest College Research Institute, Southwest College of Naturopathic Medicine & Health Sciences, Tempe, AZ, USA.

A randomized, double-blind, placebo-controlled trial was conducted. Fifty men and women, 40-76 years of age with knee OA pain were enrolled in an outpatient medical center. Intervention was MSM 3g or placebo twice a day for 12 weeks (6g/day total). Compared to placebo, MSM produced significant decreases in pain and physical function impairment. No notable changes were found in stiffness and aggregated total symptoms scores. MSM also produced improvement in performing activities of daily living when compared to placebo on the SF-36 evaluation ($P < 0.05$). CONCLUSION: MSM (3g twice a day) improved symptoms of pain and physical function during the short intervention without major adverse events.

Randomised, Double-Blind, Parallel, Placebo-Controlled Study of Oral Glucosamine, Methylsulfonylmethane and their Combination in Osteoarthritis

Usha P.R.¹; Naidu M.U.R.¹

The aim of this study was to compare the efficacy and safety of oral glucosamine (Glu), methylsulfonylmethane (MSM), their combination and placebo in osteoarthritis of the knee. **Patients and design:** A total of 118 patients of either sex with mild to moderate osteoarthritis were included in the study and randomised to receive either Glu 500mg, MSM 500mg, Glu and MSM or placebo capsules three times daily for 12 weeks. The combination produced a statistically significant decrease in the Lequesne index. All treatments were well tolerated. Glu, MSM and their combination produced an analgesic and anti-inflammatory effect in osteoarthritis. Combination therapy showed better efficacy in reducing pain and swelling and in improving the functional ability of joints than the individual agents. All the treatments were well tolerated. The onset of analgesic and anti-inflammatory activity was found to be more rapid with the combination than with Glu. It can be concluded that the combination of MSM with Glu provides better and more rapid improvement in patients with osteoarthritis.

Substance: MSM (methylsulfonylmethane)

Prime Action: reducing pain and inflammation, contributing necessary sulfur to cartilage

Dosage: 500-6000mg per day

Other Uses: Cancer, allergies <<<<2600mgperday>>>>, autoimmune diseases

Warnings: Appears very safe, naturally-occurring in body

Vitamins/ Minerals/ Amino Acids

Niacinamide (Vitamin B3)



One of the two forms of Vitamin B3 (niacin). The body uses the water-soluble vitamin B3 in the process of releasing energy from carbohydrates. It is needed to form fat from carbohydrates and to process alcohol.

[Inflamm Res.](#) 1996 Jul;45(7):330-4.

The effect of niacinamide on osteoarthritis: a pilot study.

[Jonas WB](#), [Rapoza CP](#), [Blair WF](#).

Office of Alternative Medicine, [National Institute of Health](#), Bethesda, MD 20892, USA.

OBJECTIVE: To evaluate the effect of niacinamide, on selected parameters of osteoarthritis using a double-blind, placebo controlled study design. **METHODS:** Seventy two patients with osteoarthritis were randomized for treatment with niacinamide (3000mg/day) or an identical placebo for 12 weeks. Outcome measures included global arthritis impact and pain, joint range of motion and flexibility, erythrocyte sedimentation rate, complete blood count, liver function tests, cholesterol, uric acid, and fasting blood sugar. Compliance was monitored with a pill record sheet and interview. **RESULTS:** Global arthritis impact improved by 29% in subjects on niacinamide and worsened by 10% in placebo subjects (p = 0.04). Pain levels did not change but those on niacinamide reduced their anti-inflammatory medications by 13% (95% CI 9, 94; p = 0.01). Niacinamide reduced erythrocyte sedimentation rate by 22% (95% CI 6, 51; p < 0.005) and increased joint mobility by 4.5 degrees over controls (8 degrees vs 3.5 degrees; p = 0.04). Side effects were mild but higher in the niacinamide group (40% vs 27%, p = 0.003). **CONCLUSION:** This study indicates that niacinamide may have a role in the treatment of osteoarthritis. Niacinamide improved the global impact of osteoarthritis, improved joint flexibility, reduced inflammation, and allowed for reduction in standard anti-inflammatory medications when compared to placebo.

Substance: Niacinamide

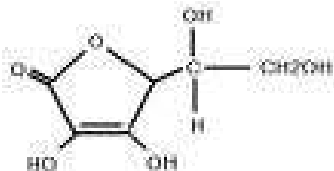
Prime Action: Anti-inflammatory action

Dosage: 1000-3000mg per day, take in 250-500mg doses spread out in the day

Other Uses: Acne (Topical), anxiety, schizophrenia, Type I Diabetes

Warnings: The 'niacinamide' form of Niacin is quite safe, rare liver problems have been seen. Have your doctor check liver enzyme levels every three months. Don't use with epilepsy medication. Occasional Nausea.

Vitamin C (Ascorbic Acid)



Among other functions, vitamin C stimulates collagen function and proteoglycan synthesis. Highly effective antioxidant completely protecting lipids from peroxidative damage.

[Arthritis Rheum.](#) 1996 Apr;39(4):648-56.

Do antioxidant micronutrients protect against the development and progression of knee osteoarthritis?

[McAlindon TE](#), [Jacques P](#), [Zhang Y](#), [Hannan MT](#), [Aliabadi P](#), [Weissman B](#), [Rush D](#), [Levy D](#), [Felson DT](#).

Arthritis Center, Boston University Medical Center, Massachusetts, 02118, USA.

OBJECTIVE: Cumulative damage to tissues, mediated by reactive oxygen species, has been implicated as a pathway that leads to many of the degenerative changes associated with aging. Six hundred forty participants received complete assessments. Incident and progressive OA occurred in 81 and 68 knees, respectively. We found no significant association of incident OA with any nutrient. A 3-fold reduction in risk of OA progression was found for vitamin C intake. This related predominantly to a reduced risk of cartilage loss. Those with high vitamin C intake also had a reduced risk of developing knee pain. A reduction in risk of OA progression was seen for beta carotene and vitamin E intake.

Substance: Vitamin C

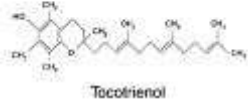
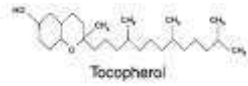
Prime Action: Stimulates collagen production, antioxidant

Dosage: 500-1000mg per day

Other Uses: Fragile Capillaries, bruising, gingivitis, glaucoma, bronchitis, wound healing, gastritis, gout, autism.....

Warnings: No Toxicities at 1000mg

Vitamin E



[Z Rheumatol.](#) 1990 Nov-Dec;49(6):369-73.

[High dosage vitamin E therapy in patients with activated arthrosis]

[Scherak O](#), [Kolarz G](#), [Schodl C](#), [Blankenhorn G](#).

Ludwig-Boltzmann-Institut für Rheumatologie und Fokalgeschehen, Baden, Österreich.

The known antiphlogistic in vitro effect of vitamin E was tested in a double-blind randomized study in patients with osteoarthritis. Fifty-three in-patients with osteoarthritis of the hip (n = 34) or the knee (n = 19) were treated for 3 weeks with 400 mg vitamin E (d-alpha-tocopherolacetate, V, n = 26) or 50 mg Diclofenac (D, n = 27) three times daily. A standardized therapeutic exercise program was performed; local therapy was not permitted. There were no significant differences in the efficacy of the two drugs, although one patient of the V-group refused further treatment after 8 days because of inefficacy. V reduced or abolished the pain at rest in 77% (D in 85%), the pain on pressure in 67% (D in 50%), and the pain on movement in 62% (D in 63%). Both treatments appeared to be equally effective in reducing the circumference of the knee joints (p = 0.001) and the walking time (p less than 0.001) and in increasing the joint mobility (p less than 0.002). Patients (n = 11) with a plasma-alpha-tocopherol increase higher than two standard deviations of the mean value at onset (greater than 25.2 mg/l) seemed to have a more pronounced reduction of pain (eight out of 11 patients) compared with four out of 11 patients with a moderate increase of vitamin E. Side effects occurred in two out of 26 patients with V (7.7%), and in 25.9% during D-treatment. One patient with D therefore stopped the therapy after 9 days.

[Z Orthop Ihre Grenzgeb.](#) 1986 May-Jun;124(3):340-3.

[Clinical effectiveness of Spondyvit (vitamin E) in activated arthroses. A multicenter placebo-controlled double-blind study]

[Blankenhorn G](#).

50 patients with osteoarthritis were randomly assigned to two groups and treated over a period of 6 weeks with vitamin E-capsules (daily dose 400 I.E. d-alpha-tocopherylacetate) or an identical placebo preparation. The results of this double-blind controlled clinical trial showed that vitamin E was superior to placebo with respect to the relief of pain (pain at rest, pain during movement, pressure-induced pain) and the necessity of additional analgetic treatment (p less than 0.05 to p less than 0.01). Improvement of mobility was better in the group treated with vitamin E. However, this result was not statistically significant. The profile and the intensity of adverse reactions in both the vitamin E and placebo group was practically identical. This clinical

study shows antiphlogistic efficacy of vitamin E in patients with osteoarthritis. In view of the possibility to reduce standard antiphlogistic, analgetic therapy together with the very good tolerance this result may be very important for the treatment of chronic rheumatic inflammatory disease.

Vitamin E is ineffective for symptomatic relief of knee osteoarthritis: a six month double blind, randomised, placebo controlled study.

Brand C, Snaddon J, Bailey M, Cicuttini F.

Vitamin E supplements may not be effective in treating osteoarthritis (OA) of the knee, according to research published in the October edition of *Annals of the Rheumatic Diseases*. The new study, the largest to date of vitamin E as a treatment of osteoarthritis, contradicts the findings of previous clinical trials. It is not known why the new research conflicts with the results of previous clinical trials. The study's authors suggest that insufficient numbers of participants, short duration, and inferior evaluation techniques in the previous trials may have produced less valid results. In previous trials, participants had an intake of 400 to 1,600 IU of vitamin E per day . Those in the new study took 500 IU per day for six months. In successful trials of vitamin E supplementation, clinical effects were obtained within several weeks.

Substance: Vitamin E

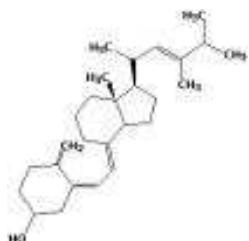
Prime Action: Fat-soluble Antioxidant, slows breakdown of cartilage, anti-inflammatory

Dosage: 400-1200IU per day

Other Uses: Immune function, Intermittent claudication, Rheumatoid arthritis, Alzheimer's, wound healing

Warnings: Toxic in high doses above 1200IU/day, interacts with some Medication

Vitamin D



The fat-soluble vitamin D's most important role is maintaining blood levels of calcium, which it accomplishes by increasing absorption of calcium from food and reducing urinary calcium loss. Both effects keep calcium in the body and therefore spare the calcium that is stored in bones. When necessary, vitamin D transfers calcium from the bone into the bloodstream, which does not benefit bones. Vitamin D has a direct affect on the synthesis of cartilage.

Vitamin D plays a role in immunity and blood cell formation and also helps cells "differentiate"—a process that may reduce the risk of cancer. From animal and human studies, researchers have

hypothesized that vitamin D may protect people from multiple sclerosis, autoimmune arthritis, and juvenile diabetes.

[Arthritis Rheum.](#) 1999 May;42(5):854-60.

Serum vitamin D levels and incident changes of radiographic hip osteoarthritis: a longitudinal study. Study of Osteoporotic Fractures Research Group.

[Lane NE](#), [Gore LR](#), [Cummings SR](#), [Hochberg MC](#), [Scott JC](#), [Williams EN](#), [Nevitt MC](#).

Division of Rheumatology, University of California, San Francisco 94143, USA.

OBJECTIVE: The purpose of this study was to determine the relationship of serum levels of 25-vitamin D and 1,25-vitamin D to incident changes of radiographic hip osteoarthritis (OA) among elderly white women. **METHODS:** Baseline and followup hip radiographs of 237 subjects were obtained an average of 8 years apart. Logistic and linear regression were used to examine the association of 25- and 1,25-vitamin D levels with radiographic changes, adjusting for age, health status, physical activity, weight, vitamin D supplement use, and calcaneal bone mineral density. **RESULTS:** The risk of incident hip OA defined as the development of definite joint space narrowing was increased for subjects who were in the middle and lowest tertiles for 25-vitamin D compared with subjects in the highest tertile.

Substance: Vitamin D

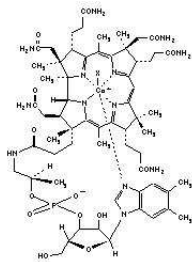
Prime Action: Vitamin D has a direct affect on the synthesis of cartilage.
Fat-soluble Antioxidant.

Dosage: 400-1000IU per day

Other Uses: Osteoporosis, cancer, autoimmune disorders

Warnings: Toxic in high doses, interacts with verapamil

Vitamin B12 (cobalamin)



Vitamin B12 is needed for normal nerve cell activity, DNA replication, and production of the mood-affecting substance [S-adenosyl-L-methionine](#) (SAME). Vitamin B12 acts with [folic acid](#) and [vitamin B6](#) to control homocysteine levels. Increases bone-production cells.

[J Am Coll Nutr.](#) 1994 Aug;13(4):351-6.

The effect of folate and cobalamin on osteoarthritic hands.

[Flynn MA](#), [Irvin W](#), [Krause G](#).

Department of Family and Community Medicine, University of Missouri-Columbia 65212.

This controlled, double-blinded, crossover study reports the effect of folate and cobalamin supplements in 26 humans diagnosed for an average 5.7 years with idiopathic osteoarthritis of the hands who had been medicated by prescribed nonsteroidal anti-inflammatory drugs (NSAID). METHODS: Subjects entered the study after a 10-day washout period from use of all anti-arthritis drugs, vitamins, and minerals. They were randomly allocated to consume daily 6400 micrograms folate or 6400 micrograms folate plus 20 micrograms cobalamin or lactose placebo each for 2 months. For all subjects mean right and left hand grip values were higher with combined cobalamin-folate ingestion than with other "vitamin" supplements and were equivalent to NSAID use. Number of tender hand joints were greater with use of NSAID than with use of cobalamin-folate. Side effects with the vitamin combination were none; side effects of NSAID are many, and the cost of vitamins and acetaminophen also is lower. CONCLUSION: The limited number of subjects in this study demonstrates that ingestion of a prescribed cobalamin-folate supplement and acetaminophen as needed resulted in positive outcomes.

Substance: Vitamin B12

Prime Action: Crucial in nerve cell regeneration. Affects bone production.

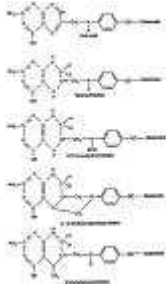
Dosage: 25-2000 mcg per day

Other Uses: Osteoporosis, anemia, depression, neuropathies...

Warnings: Extremely safe

Note: Choose methylcobalamin' form of vitamin b12

Folic Acid (Folate, vitamin B9)



Needed for cell replication and growth. Folic acid helps form building blocks of DNA, the body's genetic information, and building blocks of RNA, needed for protein synthesis in all cells. Therefore, rapidly growing tissues, such as those of a fetus, and rapidly regenerating cells, like red blood cells and immune cells, have a high need for folic acid.

Substance: Folic Acid

Prime Action: Nerve, Blood, DNA, Everything

Dosage: 400-5000mcg

Other Uses: High Homocysteine, Depression, Gingivitis, Osteoporosis, anemia, depression, neuropathies...

Warnings: Extremely safe, interacts with epilepsy medication

Note: Supplement with some vitamin b12

Boron

Boron appears to affect the metabolism of calcium, magnesium, copper, phosphorus, and vitamin D. Preliminary research suggests that boron might affect bone and joint health, but little specific information is known. The most promising research with boron has linked supplementation to reduced loss of calcium in urine. This effect might lead to a lower risk of osteoporosis.

[Environ Health Perspect.](#) 1994 Nov;102 Suppl 7:83-5.

Essentiality of boron for healthy bones and joints.

[Newnham RE.](#)

Rex Newnham and Associates, North Yorkshire, England.

Since 1963, evidence has accumulated that suggests boron is a safe and effective treatment for some forms of arthritis. Epidemiologic evidence that in areas of the world where boron intakes usually are 1.0 mg or less/day the estimated incidence of arthritis ranges from 20 to 70%, whereas in areas of the world where boron intakes are usually 3 to 10 mg, the estimated incidence of arthritis ranges from 0 to 10%.

The preceding data indicate that boron is an essential nutrient for healthy bones and joints, and that further research into the use of boron for the treatment or prevention of arthritis is warranted.

Area	Boron Intake (milligrams/day)	Arthritis (%)
Jamaica	less than 1	70
Brazil	1	30
United States	1-2	20
South Africa	3-5	4
Australia	4-6	1
Israel	8-10	Less than 1

In 1990, Richard Travers, M.D. completed a double-blind placebo study with osteoarthritic patients using doses of 6 milligrams per day. During the eight-week study 5 patients were given the boron and 5 patients were given a placebo. At the end of the study all five of the treated group had significantly improved while only one of the placebo group improved. There were no side effects^v.

Substance: Boron

Prime Action: Affects utilization of calcium, magnesium, copper. Increases estrogen and testosterone

Dosage: 1-6 mg per day

Other Uses: Osteoporosis, osteoarthritis, rheumatoid arthritis

Warnings: Potential interaction with hormone replacement therapy

Selenium

Selenium activates an antioxidant enzyme called glutathione peroxidase, which may help protect the body from cancer. Yeast-derived forms of selenium have induced "apoptosis" (programmed cell death) in cancer cells in test tubes and in animals. A double-blind trial that included over 1,300 people found those given 200 mcg of yeast-based selenium per day for 4.5 years had a 50% drop in the cancer death rate compared with the placebo group.⁴ In that same study, however, selenium supplementation was associated with a significant increase in the risk of developing one type of skin cancer (squamous cell carcinoma). Another study found that men consuming the most dietary selenium (assessed indirectly by measuring toenail selenium levels) developed 65% fewer cases of advanced prostate cancer than did men with the lowest levels of selenium intake.

Substance: Selenium <<<<BRAZIL NUTS>>>>

Prime Action: Very intense antioxidant, aids in cartilage synthesis

Dosage: 200mcg per day

Other Uses: Immune support, Cancer, Liver Damage, hypothyroidism

Warnings: Very safe at recommended dose

ZINC

Zinc is an essential mineral that is a component of more than 300 enzymes needed to repair wounds, maintain fertility in adults and growth in children, synthesize protein, help cells reproduce, preserve vision, boost immunity, and protect against free radicals, among other functions.

Some anti-inflammatory and antioxidant activity.

Substance: Zinc

Prime Action: Very intense antioxidant, aids in cartilage synthesis

Dosage: 15-30 mg per day

Other Uses: Immune support, wound repair, Growth, acne, dermatitis

Warnings: Very safe at recommended dose. If using zinc long term, must take
With copper

Copper

It is needed to absorb and utilize iron. It is also part of the antioxidant enzyme, superoxide dismutase (SOD). Copper is needed to make adenosine triphosphate (ATP), the energy the body runs on. Synthesis of some hormones requires copper, as does the synthesis of collagen (the "glue" that holds connective tissue together).

[Agents Actions.](#) 1976 Jul;6(4):454-9.

An investigation of the therapeutic value of the 'copper bracelet'-dermal assimilation of copper in arthritic/rheumatoid conditions.

[Walker WR](#), [Keats DM](#).

From over 300 arthritis sufferers...This involved wearing 'copper bracelets' and placebo bracelets (amodised aluminum resembling copper) alternately. Preliminary results show that, to a significant number of subjects, the wearing of the 'copper bracelet' appeared to have some therapeutic value.

Substance: Copper

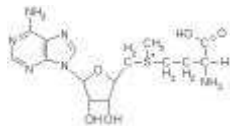
Prime Action: Energy and blood production, synthesis of collagen

Dosage: 1-3 mg per day

Other Uses: Anemia, osteoporosis

Warnings: Very safe at recommended dose. Don't use "Cupric Oxide" form.

SAM-e (S-Adenosylmethionine)



SAM-e is the most active methyl donor in your body. This natural occurring substance appears to promote production of cartilage proteoglycans, and is therapeutically beneficial in osteoarthritis in well-tolerated oral doses. In clinical trials involving over 22,000 patients, SAM-e was shown to be as effective as NSAIDs, but is better tolerated.

Used in Europe as a first line drug for depression, working as well as antidepressant drugs.

[Am J Med.](#) 1987 Nov 20;83(5A):66-71.

Italian double-blind multicenter study comparing S-adenosylmethionine, naproxen, and placebo in the treatment of degenerative joint disease.

[Caruso I](#), [Pietrogrande V](#).

Department of Rheumatology, L. Sacco Hospital, Milan, Italy.

In a double-blind study, the efficacy and tolerability of S-adenosylmethionine (SAMe) were evaluated in comparison with those of placebo and naproxen in the treatment of osteoarthritis of the hip, knee,

spine, and hand. Thirty-three centers, 18 rheumatologic and 15 orthopedic, participated in this study. A total of 734 subjects, including 582 with hip osteoarthritis or knee osteoarthritis, were enrolled. SAME administered orally at a dose of 1,200 mg daily was shown to exert the same analgesic activity as naproxen at a dose of 750 mg daily. Both drugs were more effective than placebo (p less than 0.01). Tolerability of SAME was significantly better than that of naproxen, both in terms of physicians' (p less than 0.025) and patients' (p less than 0.01) judgments and in terms of the number of patients with side effects (p less than 0.05). There was no difference between SAME and placebo in the number of side effects. Ten patients in the SAME group and 13 in the placebo group withdrew from the study because of intolerance to the drug.

[Am J Med.](#) 1987 Nov 20;83(5A):81-3.

Double-blind clinical trial of S-adenosylmethionine versus ibuprofen in the treatment of osteoarthritis.

[Muller-Fassbender H.](#)

[Am J Med.](#) 1987 Nov 20;83(5A):89-94.

A long-term (two years) clinical trial with S-adenosylmethionine for the treatment of osteoarthritis.

[Konig B.](#)

Institute of General Medicine, University of Mainz, Federal Republic of Germany.

In a long-term multicenter open trial involving 10 general practitioners, the efficacy and tolerance of S-adenosylmethionine (SAME) were studied for 24 months in 108 patients with osteoarthritis of the knee, hip, and spine. At the end of the 24-month observation period, 97 of the patients were still in the study. The patients received 600 mg of SAME daily (equivalent to three tablets of 200 mg each) for the first two weeks and thereafter 400 mg daily (equivalent to two tablets of 200 mg each) until the end of the 24th month of treatment. Separate evaluations were made for osteoarthritis of the knee, hip, cervical spine, and dorsal/lumbar spine. The severity of the clinical symptoms (morning stiffness, pain at rest, and pain on movement) was assessed using scoring before the start of the treatment, at the end of the first and second week of treatment, and then monthly until the end of the 24-month period. SAME administration showed good clinical effectiveness and was well tolerated. The improvement of the clinical symptoms during therapy with SAME was already evident after the first weeks of treatment and continued up to the end of the 24th month. Non-specific side effects occurred in 20 patients, but in no case did therapy have to be discontinued. Most side effects disappeared during the course of therapy. Moreover, during the last six months of treatment, no adverse effect was recorded. Detailed laboratory tests carried out at the start and after six, 12, 18, and 24 months of treatment showed no pathologic changes. SAME administration also improved the depressive feelings often associated with osteoarthritis.

Fish Oil

Crucial component of the central nervous system. Plays a key role in inflammation. Cardioprotective- lowers LDL cholesterol and triglycerides, inhibits atherosclerosis, prevents blood clots.

[Proc Nutr Soc.](#) 2002 Aug;61(3):381-9.

Effects of n-3 fatty acids on cartilage metabolism.

[Curtis CL](#), [Rees SG](#), [Cramp J](#), [Flannery CR](#), [Hughes CE](#), [Little CB](#), [Williams R](#), [Wilson C](#), [Dent CM](#), [Harwood JL](#), [Caterson B](#).

Cardiff School of Biosciences, Cardiff University, UK.

This study set out to investigate how n-3 PUFA and other classes of fatty acids affect both degradative and inflammatory aspects of metabolism of articular cartilage chondrocytes using an in vitro model of cartilage degradation. Using well-established culture models, cartilage explants from normal bovine and human osteoarthritic cartilage were supplemented with either n-3 or n-6 PUFA, and cultures were subsequently treated with interleukin 1 to initiate catabolic processes that mimic cartilage degradation in arthritis. Results show that supplementation specifically with n-3 PUFA, but not n-6 PUFA, causes a decrease in both degradative and inflammatory aspects of chondrocyte metabolism, whilst having no effect on the normal tissue homeostasis. Collectively, our data provide evidence supporting dietary supplementation of n-3 PUFA, which in turn may have a beneficial effect of slowing and reducing inflammation in the pathogenesis of degenerative joint diseases in man.

[Arthritis Rheum.](#) 2002 Jun;46(6):1544-53.

Pathologic indicators of degradation and inflammation in human osteoarthritic cartilage are abrogated by exposure to n-3 fatty acids.

[Curtis CL](#), [Rees SG](#), [Little CB](#), [Flannery CR](#), [Hughes CE](#), [Wilson C](#), [Dent CM](#), [Otterness IG](#), [Harwood JL](#), [Caterson B](#).

Connective Tissue Biology Laboratories, School of Biosciences, Cardiff University, Museum Avenue, Cardiff CF10 3US, Wales, UK.

OBJECTIVE: To determine if n-3 polyunsaturated fatty acid (PUFA) supplementation (versus treatment with n-6 polyunsaturated or other fatty acid supplements) affects the metabolism of osteoarthritic (OA) cartilage. **METHODS:** The metabolic profile of human OA cartilage was determined at the time of harvest and after 24-hour exposure to n-3 PUFAs or other classes of fatty acids, followed by explant culture for 4 days in the presence or absence of interleukin-1 (IL-1). Parameters measured were glycosaminoglycan release, aggrecanase and matrix metalloproteinase (MMP) activity, and the levels of expression of messenger RNA (mRNA) for mediators of inflammation, aggrecanases, MMPs, and their natural tissue inhibitors (tissue inhibitors of metalloproteinases [TIMPs]). **RESULTS:** Supplementation with n-3 PUFA (but not other fatty acids) reduced, in a dose-dependent manner, the endogenous and IL-1-induced release of proteoglycan metabolites from articular cartilage explants and specifically abolished endogenous aggrecanase and collagenase proteolytic activity. Similarly, expression of mRNA for ADAMTS-4, MMP-13, and MMP-3 (but not TIMP-1, -2, or -3) was also specifically abolished with n-3 PUFA supplementation. In addition, n-3 PUFA supplementation abolished the expression of mRNA for mediators of inflammation (cyclooxygenase 2, 5-lipoxygenase, 5-lipoxygenase-activating protein, tumor necrosis factor alpha, IL-1alpha, and IL-1beta) without affecting the expression of message for several other proteins involved in normal tissue homeostasis. **CONCLUSION:** These studies show that the pathologic indicators manifested in human OA cartilage can be significantly altered by exposure of the cartilage to n-3 PUFA, but not to other classes of fatty acids.

Avocado/Soya Unsaponifiables (ASU)

Complex mix of the unsaponifiable fractions of avocado and soy oil. Enhances cartilage synthesis, protects the joints from inflammation. Preserves joint space.

[Arthritis Rheum.](#) 1998 Jan;41(1):81-91.

Symptomatic efficacy of avocado/soybean unsaponifiables in the treatment of osteoarthritis of the knee and hip: a prospective, randomized, double-blind, placebo-controlled, multicenter clinical trial with a six-month treatment period and a two-month followup demonstrating a persistent effect.

[Maheu E](#), [Mazieres B](#), [Valat JP](#), [Loyau G](#), [Le Loet X](#), [Bourgeois P](#), [Grouin JM](#), [Rozenberg S](#).

Hopital Cochin, Paris, France.

OBJECTIVE. To assess the efficacy and safety of avocado/soybean unsaponifiables (ASU) in the treatment of patients with symptomatic osteoarthritis (OA) of the knee or hip, as well as the potential residual effects of ASU after stopping treatment, to determine whether ASU might be a symptomatic slow-acting drug for the treatment of OA. **METHODS.** One hundred sixty-four patients with regular, painful, primary OA of the knee (n = 114) or hip (n = 50) entered a prospective, randomized, double-blind, placebo-controlled, parallel-group, multicenter trial with a 6-month treatment period and a 2-month posttreatment followup. Overall functional disability was significantly reduced in the ASU group. Improvement appeared more marked in patients with hip OA. A residual effect was observed at month 8. Tolerance was good to excellent for most patients. **CONCLUSION.** ASU treatment showed significant symptomatic efficacy over placebo in the treatment of OA, acting from month 2 and showing a persistent effect after the end of treatment.

Other Non-Pharmaceutical Modalities

Herbal Medicine — Several herbal medicines may help control the symptoms of osteoarthritis in some people, but the benefits of these therapies are still uncertain. Boswellia serrata, Reumalex, ginger, tumeric, willow bark, stinging nettle, Articulon F, and devils claw.

Capsaicin cream — Some people experience relief of arthritis pain when they apply creams containing capsaicin, the active substance in hot chili pepper. Capsaicin depletes a pain-causing substance in nerve endings and lessens the pain of osteoarthritis by about 30 percent. Forty percent of people experience side effects when using capsaicin cream, including burning, stinging, and redness of the skin.

Acupuncture – 3000 years worth of experience

Magnets –

Kaprex – Special extract of rosemary, hops and olive that control inflammatory chemicals.

Saloxicin – white willow bark extract, original aspirin without the gastrointestinal side effects

Zeel – homeopathic medicine used throughout the world. Some studies indicate its safety and efficacy.

Diet

Decrease: red meats, organ meats, fried foods, egg yolks, white flour products, white rice, soft drinks, fruit juices, sugary treats, hydrogenated oils (margarine, processed foods)

Increase: fresh vegetables, fruits, salmon, tuna, anchovies, sardines, mackerel, kingfish, nuts , seeds, whole grains

Nightshades – Some people do very well by avoiding vegetables in this family (eggplant, potatoes, peppers, tomatoes, tobacco).