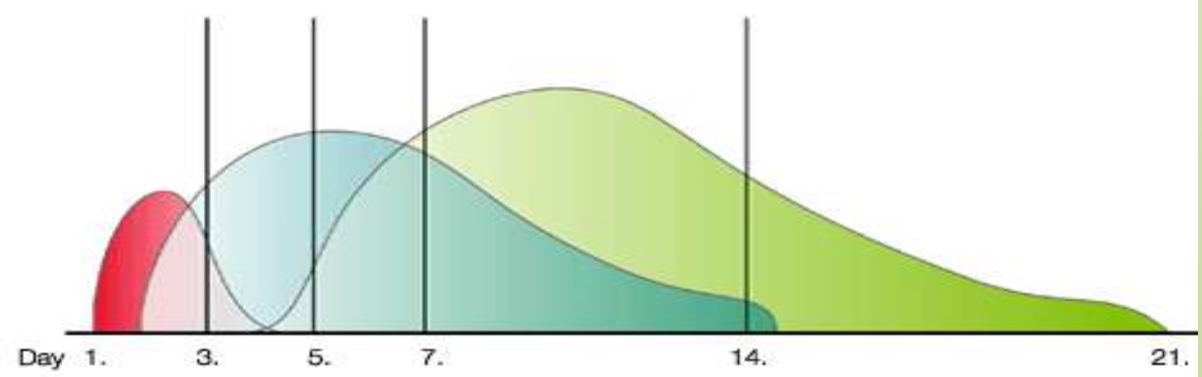
Nutrizione e supplementazione nell'atleta infortunato

Carmine Orlandi
Consigliere nazionale SINSeB

Nutraceutici in medicina dello sport

Processo di guarigione delle lesioni



Fase Infiammatoria

Fase Proliferativa

Fase di Rimodellamento

Modulare la risposta infiammatoria

- L'inattività è uno stato infiammatorio low-grade
- La risposta infiammatoria è necessaria nel processo di guarigione

Evitare una risposta infiammatoria eccessiva
Evitare uno stato infiammatorio prolungato

Bosutti A et al. **Calorie restriction modulates inactivity-induced changes in the inflammatory markers C-reactive protein and pentraxin-3**. J Clin Endocrinol Metab 2008; 93:3226-3229.

Tipton KD. **Nutrition for Acute Exercise-Induced Injuries**. Ann Nutr Metab 2010;57 (Suppl. 2):43-53

Characterization of inflammatory responses to eccentric exercise in humans

Running title: Inflammation and eccentric exercise

Jonathan Peake[1], Kazunori Nosaka[2], Katsuhiko Suzuki[1]

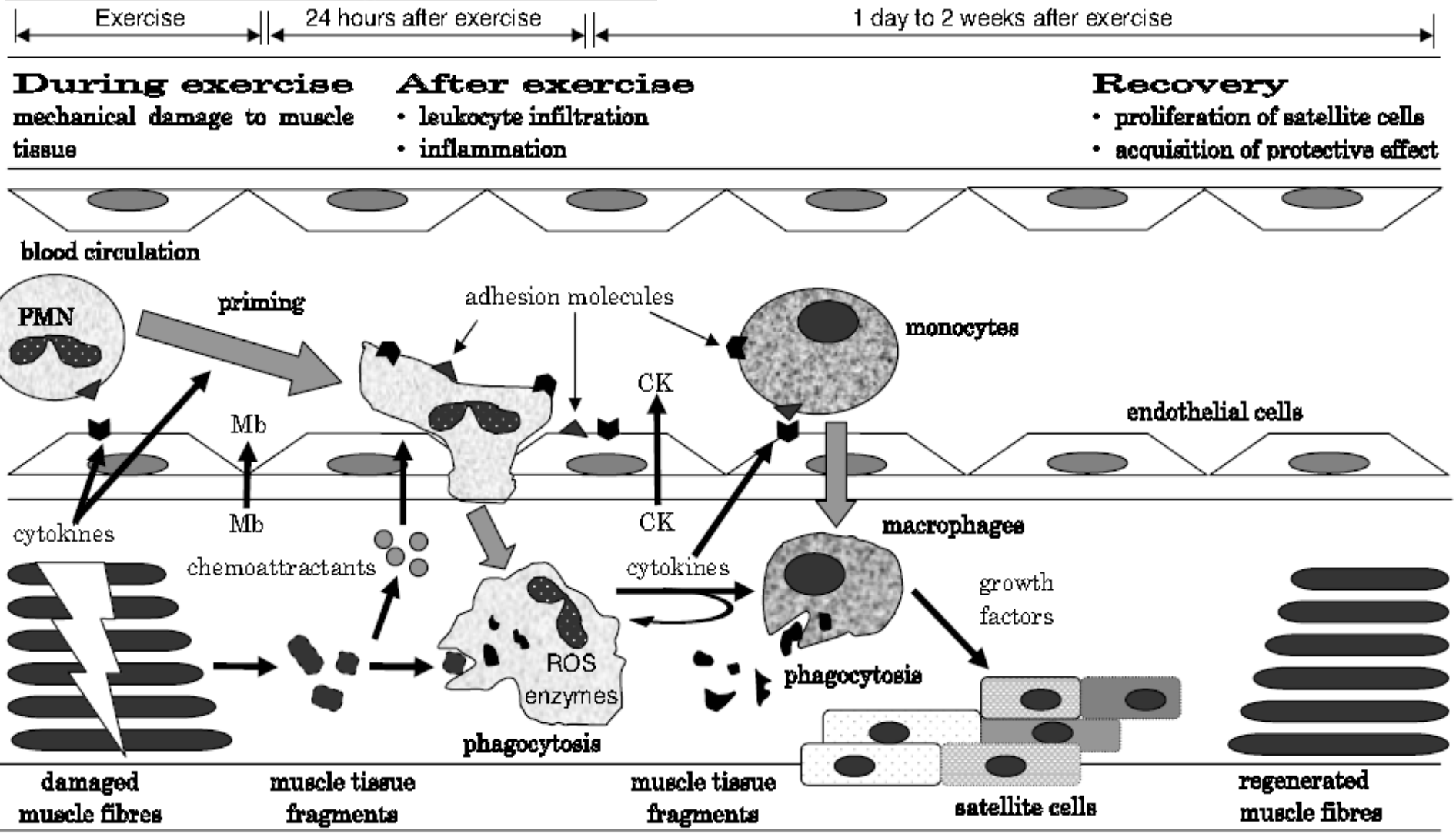
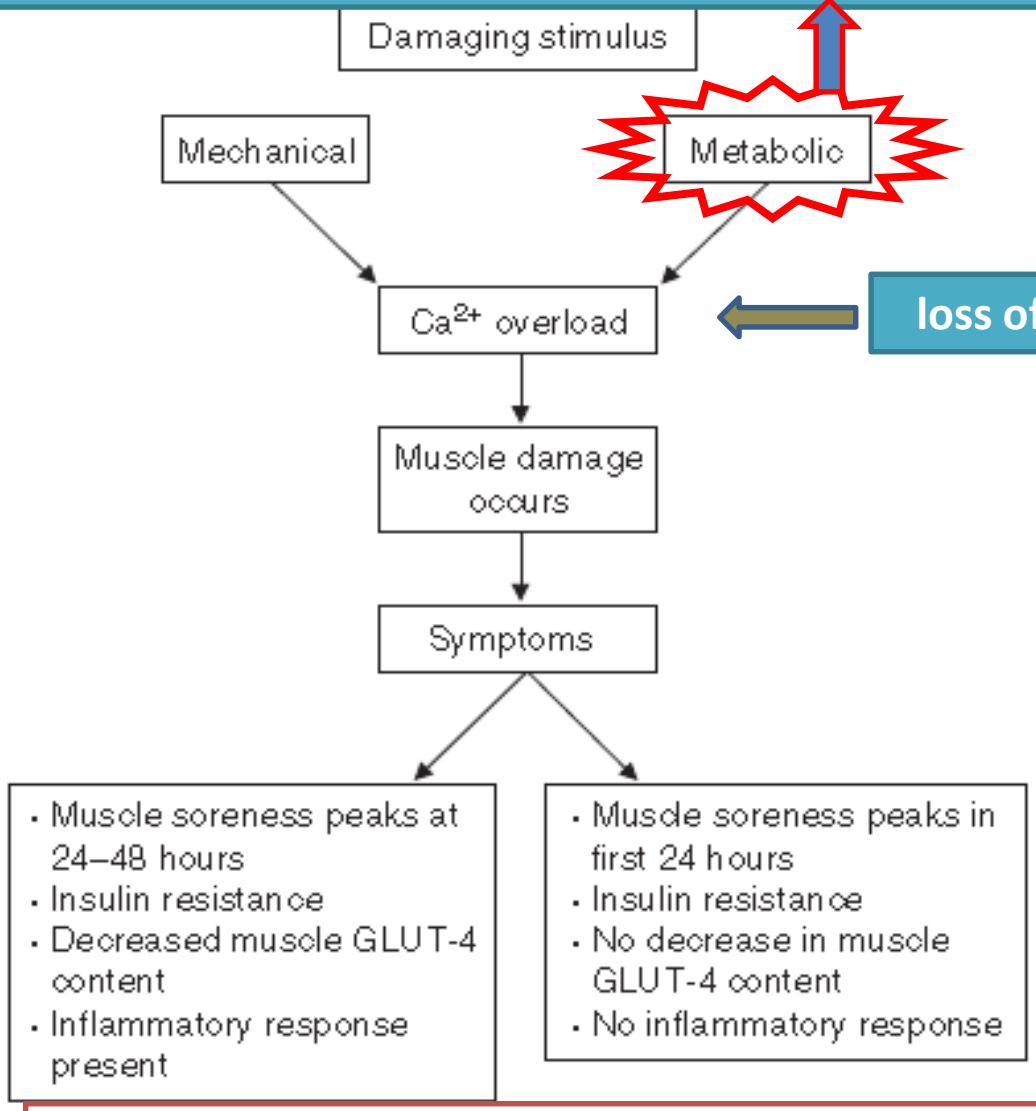


Figure 1. Exercise-induced muscle damage and subsequent muscle inflammation and regeneration process (PMN, polymorphonuclear leucocyte; Mb, myoglobin; CK, creatine kinase; ROS, reactive oxygen species)

level of ATP could decrease to concentrations sufficiently low to induce muscle damage, particularly in the presence of severe glycogen depletion.

the activation of number of Ca2+ dependant proteolytic and phospholipolytic pathways, which degrade structural and contractile myofibre proteins as well as the myofibre membrane.



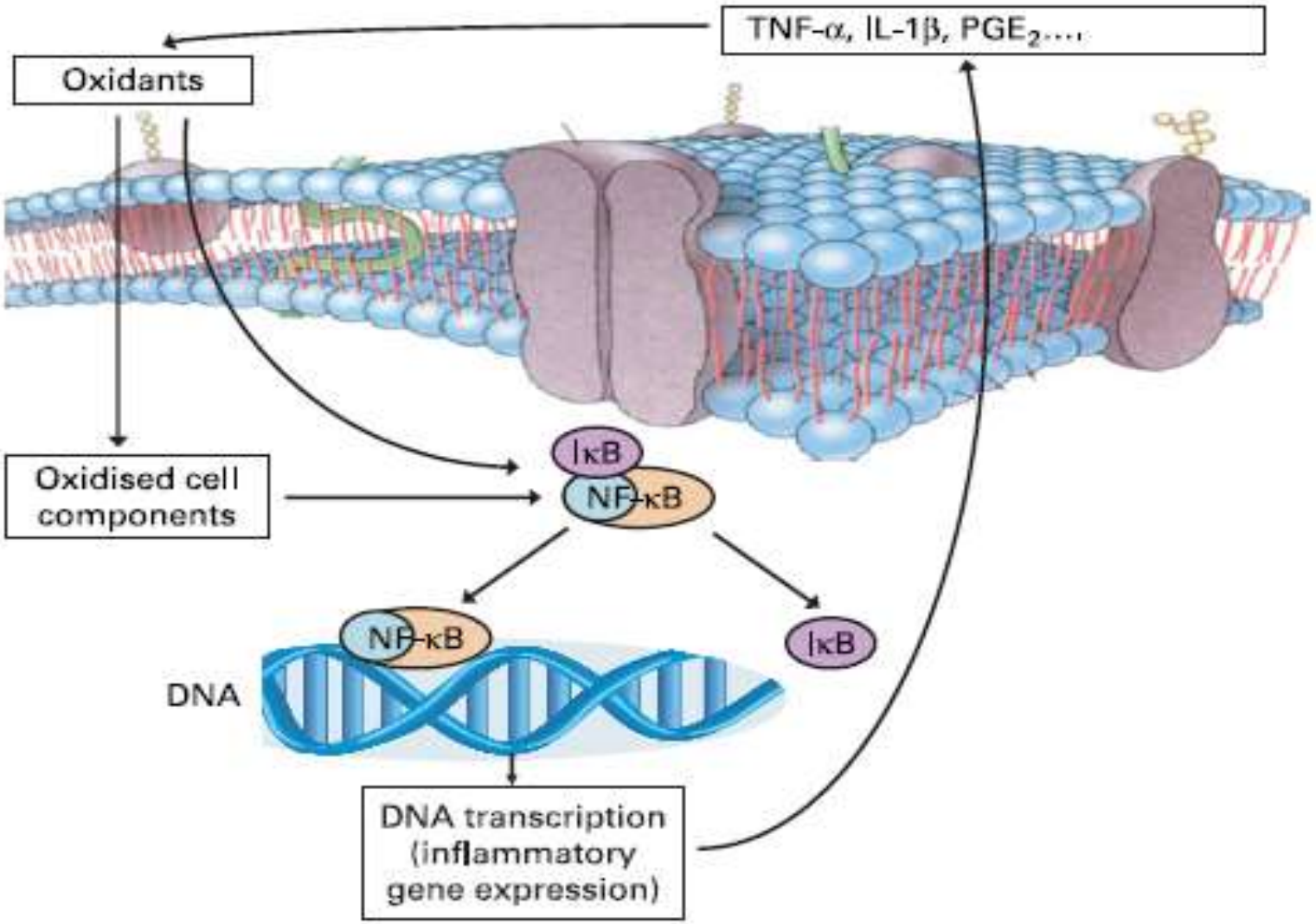
loss of Ca^{2+} homeostasis in SERCA

Phagocytic phase during which the inflammatory response allows the removal of damaged tissue, and the regenerative phase, during which the damaged muscle fibres rapair

Metabolic Stress Model

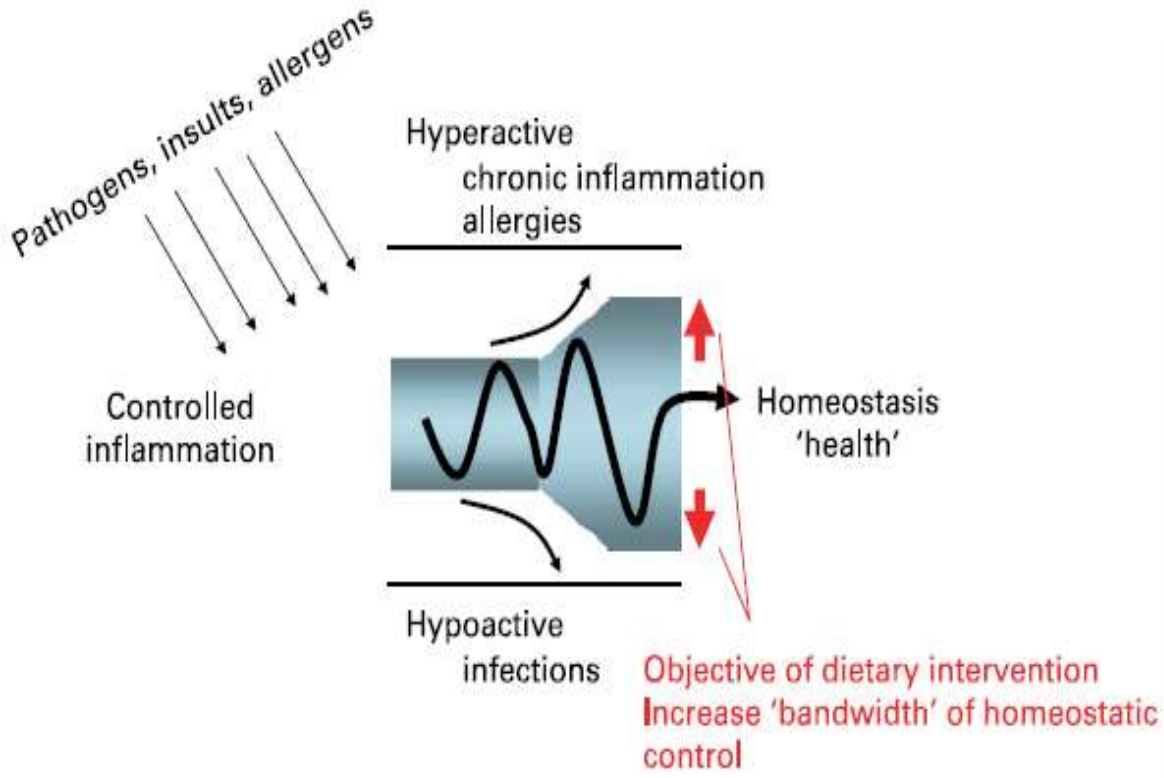
Sports Med. 2007;37(10):827-36.
Metabolic consequences of exercise-induced muscle damage.
Tee JC, Bosch AN, Lambert MI.

Oxidant stress and inflammation



Representation of the interaction between oxidant stress and inflammation. IkB, inhibitory subunit of NF-kB; IL, interleukin; NF-kB, nuclear factor k B; PG, prostaglandin; TNF, tumor necrosis factor.

Various dietary components including long chain v-3 fatty acids, antioxidant vitamins, plant flavonoids, prebiotics and probiotics have the potential to modulate predisposition to chronic inflammatory conditions and may have a role in their therapy.



Concept of how nutrients might act in an anti-inflammatory manner.

mechanisms including decreasing inflammatory mediator production through effects on cell signaling and gene expression (ω–3 fatty acids, vitamin E, plant flavonoids), reducing the production of damaging oxidants (vitamin E and other antioxidants), and promoting gut barrier function and anti inflammatory responses (prebiotics and probiotics).

Vol. 101 Supplement No. S1 May 2009 British Journal of Nutrition

J Hum Nutr Diet. 2003 Apr;16(2):97-109.
Nutritional management of rheumatoid arthritis: a review of the evidence.
Rennie KL1, Hughes J, Lang R, Jebb SA.

Supplementation with long-chain n-3 polyunsaturated fatty acids (PUFA) consistently demonstrates an improvement in symptoms and a reduction in NSAID usage. Evidence relating to other fatty acids, antioxidants, zinc, iron, folate, other B vitamins, calcium, vitamin D and fluoride are also considered. The present evidence suggests that RA patients should consume a balanced diet rich in long-chain n-3 PUFA and antioxidants.

Version 3. F1000Res. 2014 May 23 [revised 2016 Jan 6];3:116.
Post-operative rehabilitation and nutrition in osteoarthritis.
Musumeci G1, Mobasheri A2, Trovato FM3, Szychlinska MA1, Imbesi R1, Castrogiovanni P1

GINGER
Rich in gingerols, reduces inflammation and muscle and joint pain

PINEAPPLE
Contains Bromelain which is an effective anti-inflammatory

THYME
It has the same effectiveness of dexamethasone in reducing pain

TART CHERRIES
Rich in antioxidants, act as pain relievers

NATURAL PAINKILLERS

OLIVE OIL
Contains compounds similar to ibuprofen

SALMON
Rich in Omega-3 fatty acids, reduces joint pain and inflammation

RED GRAPES
Contain resveratrol which contains anti-inflammatory properties

FISH OIL
Contains decosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA)with anti-inflammatory properties

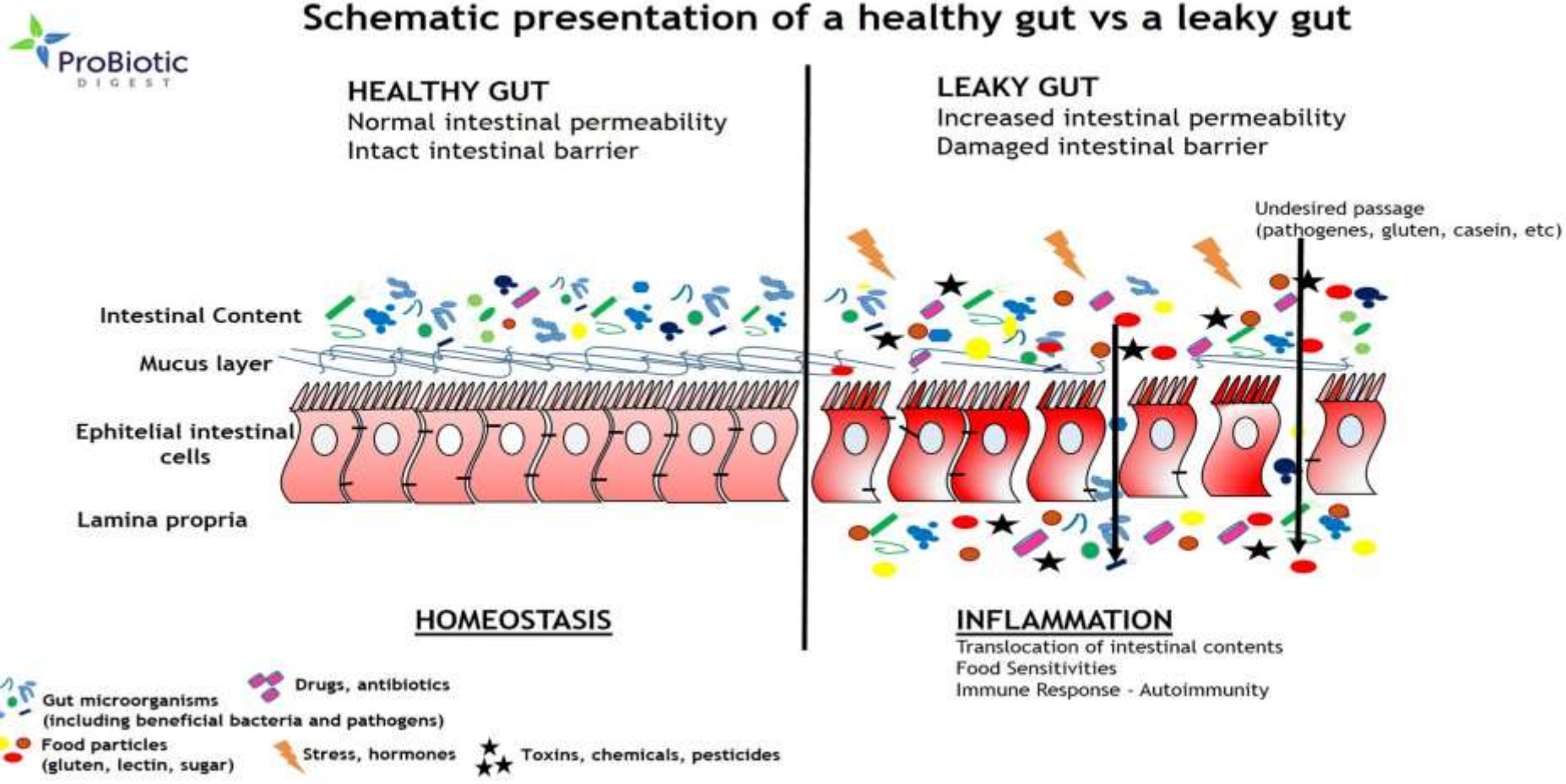
Foods containing compounds with anti-inflammatory and analgesic properties, that may help ease the symptoms of osteoarthritis as well as improve the overall health of patients.

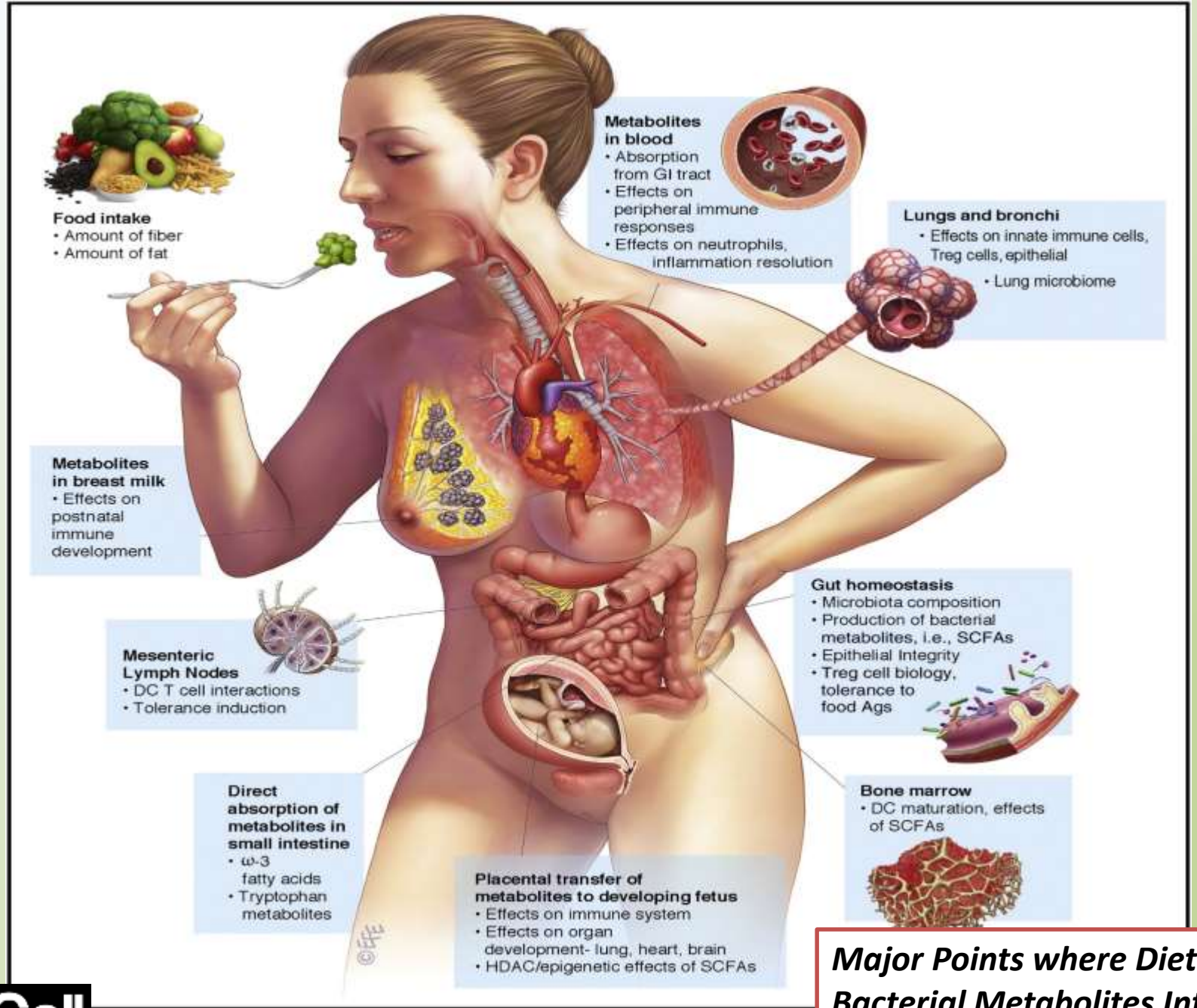
JPEN J Parenter Enteral Nutr. 2011 Sep;35(5 Suppl

Gut microbiota, intestinal permeability, obesity-induced inflammation, and liver injury.

Frazier TH1, DiBaise JK, McClain CJ.

alterations in gut microbiota, increased intestinal permeability, and metabolic endotoxemia likely play a role in the development of a chronic low-grade inflammatory state in the host that contributes to the development of obesity and associated chronic metabolic diseases





Major Points where Dietary or Bacterial Metabolites Intersect with the Immune System

Immunity 2014 40, 833-842DOI: (10.1016/j.immuni.2014.05.014)

Cell. 2005 Sep 9;122(5):659-67.
Cellular and molecular signatures of muscle regeneration: current concepts and controversies in adult myogenesis.
Wagers AJ, Conboy IM.

Muscle remodeling involves myogenesis, reinnervation, and revascularization and is regulated by multiple biochemical pathways, including those initiated by inflammatory cytokines, growth factors. Muscle repair coincides with injury-induced inflammation, and some inflammatory cytokines, such as IL-4, LIF, TGF-β, IL-6, and TNF-α regulate myogenic potential (Tidball, 2005).

FANS (exc. COX2 inib).

Damaged muscle produces monocyte and macrophage chemoattractants, and blockade of inflammatory cell infiltration impairs muscle regeneration (Chazaud et al., 2003; Jejurikar and Kuzon, 2003; Lescaudron et al., 1999), possibly due to a reduction in macrophage-secreted factors inducing myoblast proliferation (Bondesen et al., 2004; Robertson et al., 1993).

Annals of Nutrition & Metabolism

Ann Nutr Metab 2010;57(suppl 2):43–53
DOI: 10.1159/000322703

Published online: February 22, 2011

Nutrition for Acute Exercise-Induced Injuries

Kevin D. Tipton

SOCIETÀ ITALIANA Nutrizione Sport e Salute

can be considered to have two main stages, either of which may be influenced by nutrition.

Stage 1:
Tissue Repair, Immobilization and Atrophy

Stage 2:
Rehabilitation and Hypertrophy

Stage 1: Tissue Repair, Immobilization and Atrophy

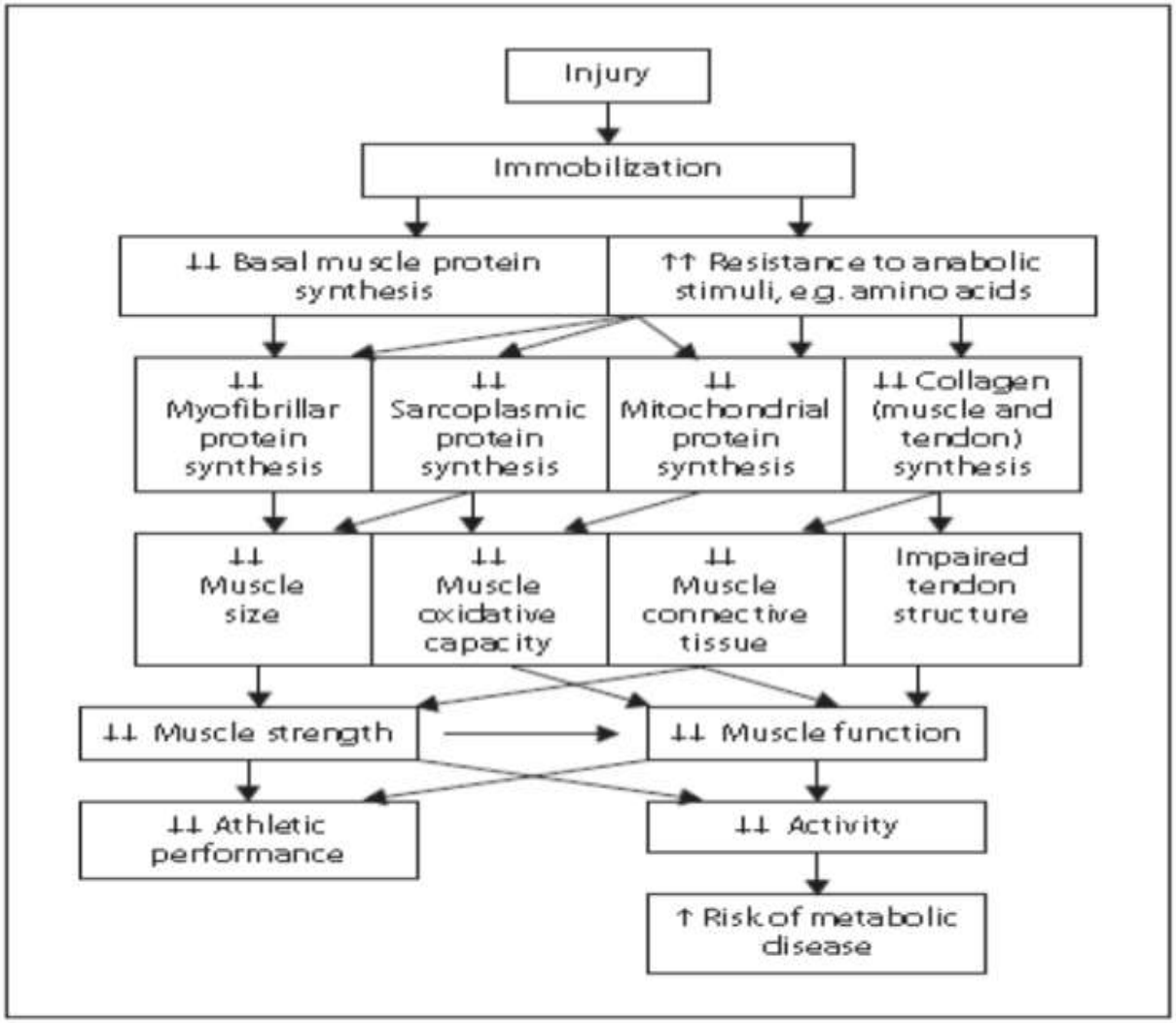


Fig. 1. Flow diagram of the metabolic and functional changes during immobilization due to exercise-induced injury. Decreased basal synthesis of muscle and tendon proteins, as well as decreased stimulation from amino acids leads to a quick and dramatic decrease in muscle size and strength, tendon structure and function.

Immediately following a severe injury, an inflammatory response is initiated. The inflammatory response is necessary for proper healing

muscle loss is a decrease in the rate of muscle protein, particularly <u>myofibrillar protein synthesis.</u> Interestingly – perhaps unexpectedly to many – protein breakdown also decreases, at least in humans

J *Interferon Cytokine Res. 2010 May;30(5):329-37.*
Cytokine responses to carbohydrate ingestion during recovery from exercise-induced muscle injury.
Ross ML, Halson SL, Suzuki K, Garnham A, Hawley JA, Cameron-Smith D, Peake JM.

Carbohydrate ingestion during early recovery from exercise-induced muscle injury may promote proinflammatory reactions within skeletal muscle

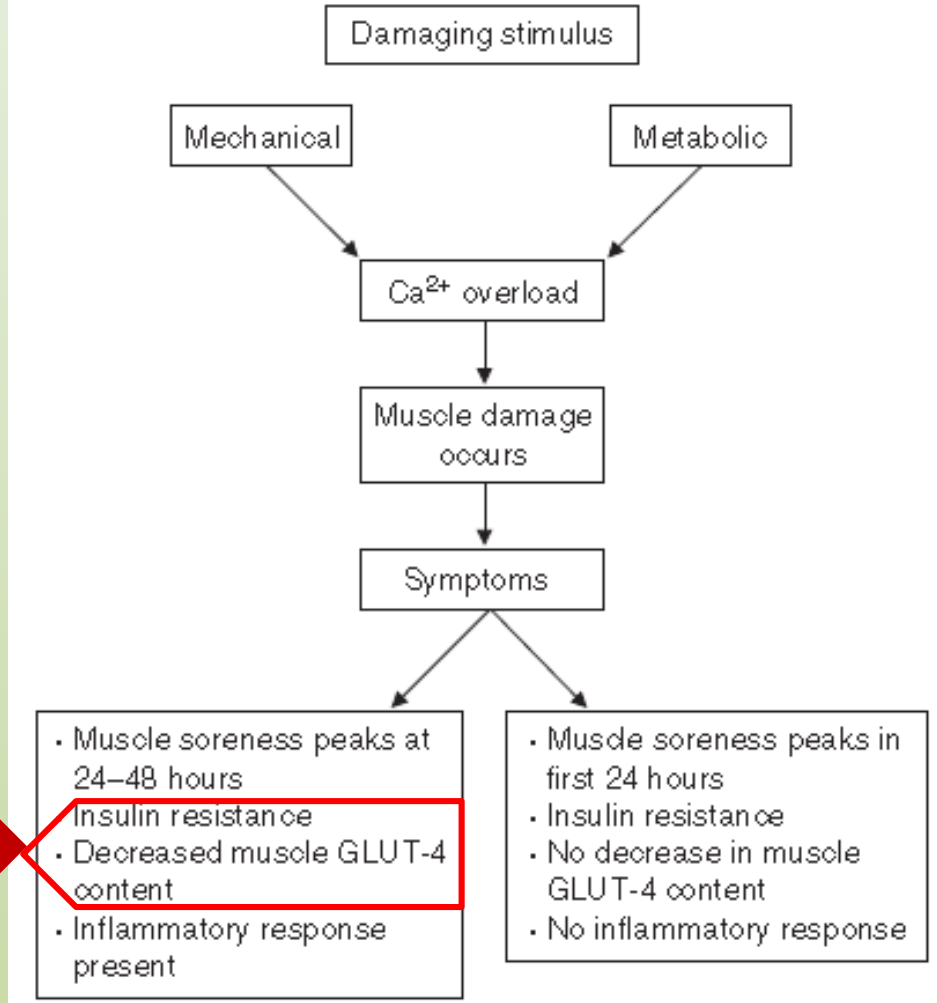
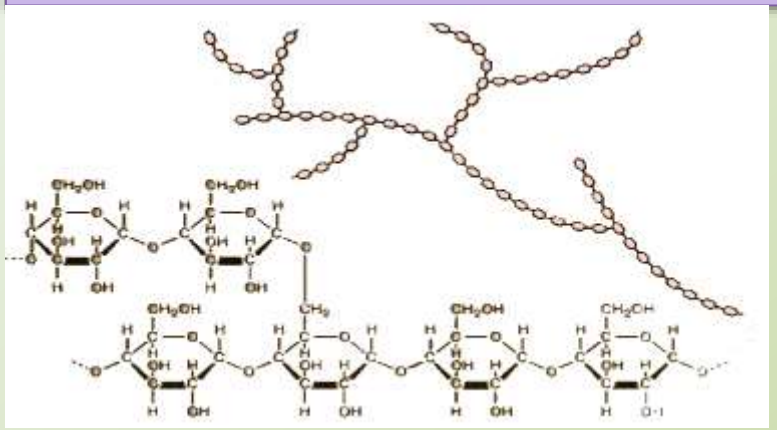


Fig. 1. Muscle damage characteristics as determined by stress profile.

Sports Med. 2007;37(10):827-36.
Metabolic consequences of exercise-induced muscle damage.
Tee JC, Bosch AN, Lambert MI.

delay in the restoration of muscle glycogen is likely due to a decrease in insulin sensitivity. Eccentric exercise causes damage to the sarcolemma and it is likely that this **alteration in membrane integrity** decreases the rate of insulin-stimulated glucose transport.



muscle requires a **prolonged period of time to recover** from damage and that athletes should be cautious about competing too soon after an event that may have caused damage.

High dietary carbohydrate for 3 days after eccentric exercise did increase intramuscular carbohydrate storage.

carbohydrate administration has little or no effect in attenuating signs and symptoms of muscle damage.

Nat Med. 2015 March ; 21(3): 263–269. doi:10.1038/nm.3804.

Ketone body β-hydroxybutyrate blocks the NLRP3 inflammasome-mediated inflammatory disease

Yun-Hee Youm[1,*], Kim Y. Nguyen[1,*], Ryan W. Grant[2], Emily L. Goldberg[1], Monica Bodogai[3], Dongin Kim[4], Dominic D'Agostino[5], Noah Planavsky[6], Christopher Lupfer[7], Thirumala D. Kanneganti[7], Seokwon Kang[8], Tamas L. Horvath[1], Tarek M. Fahmy[4], Peter A. Crawford[9], Arya Biragyn[3], Emad Alnemri[8], and Vishwa Deep Dixit[1,10]

The anti-inflammatory effects of caloric restriction or ketogenic diets may be mechanistically linked to BHB-mediated inhibition of the NLRP3 inflammasome, and point to the potential use of interventions that elevate circulating BHB against NLRP3-mediated proinflammatory diseases.

Stage 2: Rehabilitation and Hypertrophy

Primary nutritional goal will be to support muscle growth and increased strength with rehabilitation and training

Increased synthesis of myofibrillar proteins in response to resistance exercise will lead to hypertrophy of atrophied muscles. Moreover, tendon collagen synthesis is increased during rehabilitation from immobilization Since, the energy cost of muscle protein synthesis is high, energy requirements will increase

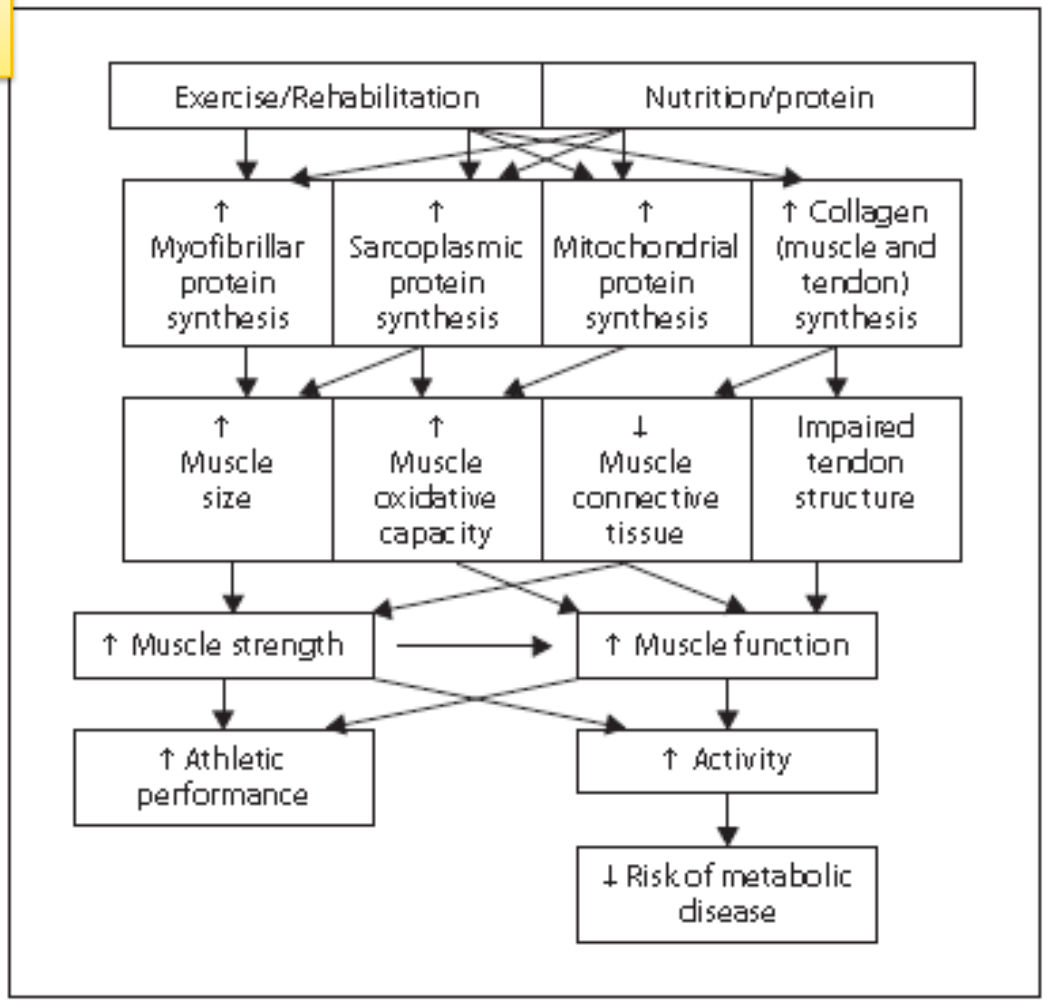


Fig. 3. Flow diagram of the metabolic and functional changes in muscle and tendon when activity is restored following immobilization due to injury. Exercise and amino acids stimulate muscle and exercise stimulates tendon synthesis, thus restoring muscle size and function. Note that the time course of the return of muscle mass and strength is often much slower than the loss during immobilization.

how much protein?

Appl Physiol Nutr Metab. 2009 Jun;34(3):403-10.
Physiologic and molecular bases of muscle hypertrophy and atrophy: impact of resistance exercise on human skeletal muscle (protein and exercise dose effects).
Phillips SM.

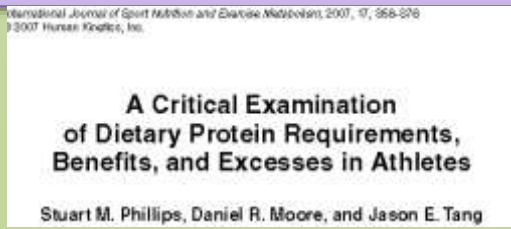
the notion that dramatically increasing protein intake results in a proportional increase in muscle size and function is not supportable

J Sports Sci. 2004 Jan;22(1):65-79. Protein and amino acids for athletes. Tipton KD, Wolfe RR.

occurs with much less dietary protein than many believe necessary (e.g. approx. 1.4 g/kg/day)

Appl Physiol Nutr Metab. 2009 Jun;34(3):403-10. Physiologic and molecular bases of muscle hypertrophy and atrophy: impact of resistance exercise on human skeletal muscle (protein and exercise dose effects). Phillips SM.

The high-quality protein dose that appears to maximally stimulate muscle protein synthesis is close to 20–25 g; above this point protein synthesis is not additionally stimulated,


A Critical Examination of Dietary Protein Requirements, Benefits, and Excesses in Athletes

Stuart M. Phillips, Daniel R. Moore, and Jason E. Tang

Activity level	Grams of protein (P)/Kg body weight/day
Sedentary (adult)	0,8 g P/Kg di peso
Recreational exerciser (adult)	1,0 – 1,4 g P/Kg di peso
Resistance-trained (maintenance)	1,2 – 1,4 g P/Kg di peso
Resistance-trained (gain muscle mass)	1,4-1,8 g P/Kg di peso
Endurance-trained	1,2-1,4 g P/Kg di peso
Intermittent, high-intensity training	1,2-1,8 g P/Kg di peso
Weight-restricted sports	1,4 – 2,0 g P/Kg di peso

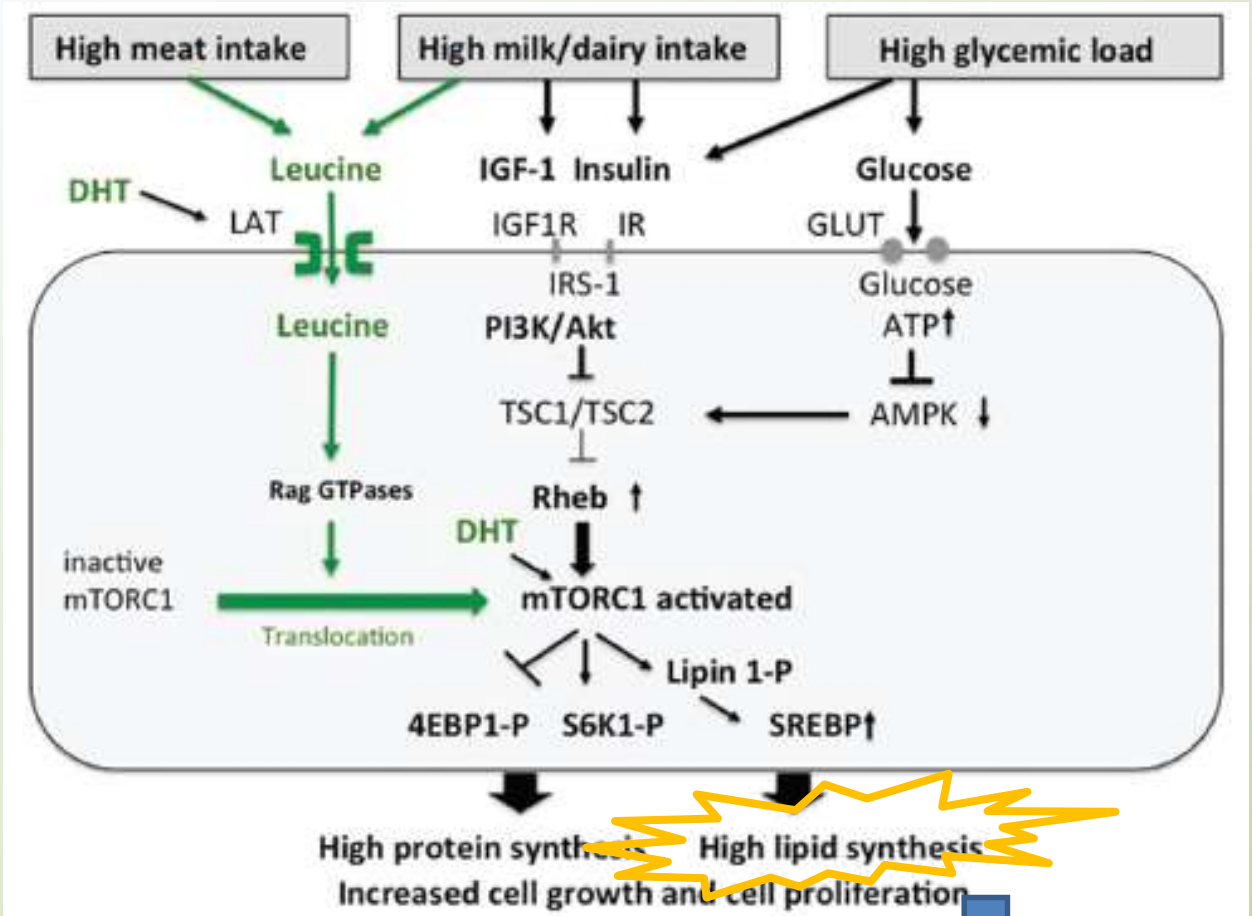
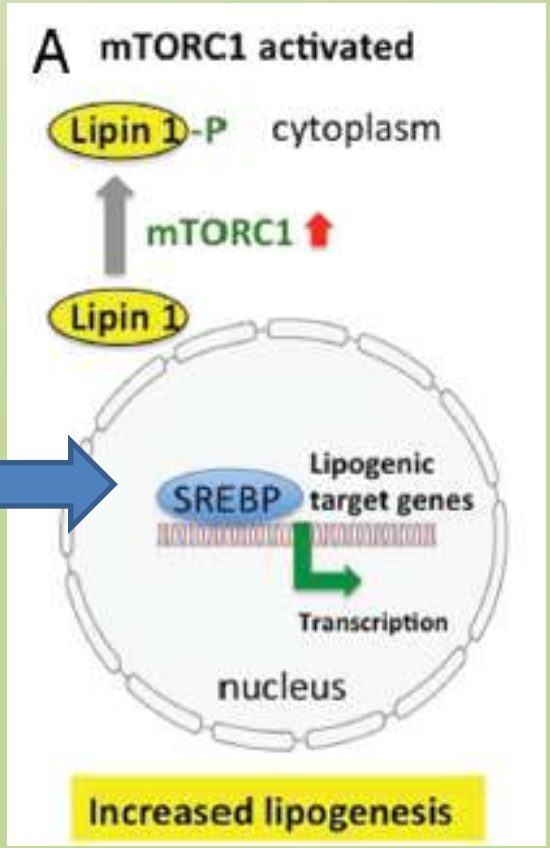


Table 2. Mechanisms of mTORC1 activation by Western diet

Compound of Western diet	Mechanisms of mTORC1 activation
High total calories (= high energy)	Reduced activity of AMPK
High glycemic load (= high energy)	Reduced activity of AMPK Increased insulin signaling
High fat intake (= high energy)	Reduced activity of AMPK
High alcohol intake (= high energy)	Reduced activity of AMPK
High dairy protein intake (= high leucine)	Increased insulin/IGF-1 signaling and leucine-mediated mTORC1 activation
High meat intake (= high leucine)	Leucine- and IGF-1-mediated mTORC1 activation

Eccessiva introduzione di proteine e di energia



J Appl Oral Sci. 2015 Mar-Apr;23(2):135-44..
Evaluation of protein undernourishment on the condylar process of the Wistar rat mandible correlation with insulin receptor expression.
Cavalli MA1, Gonçalves A1, Pereira JN1, Silva JB1, Boldrini Sde C2, Liberti EA2.

Protein Under nourishment

our results suggest vitamin K is implicated in progression of several distinct pathologies of OA affected joint tissues.

Osteoarthritis Cartilage. 2015 Mar;23(3):370-8. The association between vitamin K status and knee osteoarthritis features in older adults: the Health, Aging and Body Composition Study.
Shea MK1, Kritchevsky SB2, Hsu FC3, Nevitt M4, Booth SL5, Kwoh CK6, McAlindon TE7, Vermeer C8, Drummen N8, Harris TB9, Womack C10, Loeser RF11; Health ABC Study.

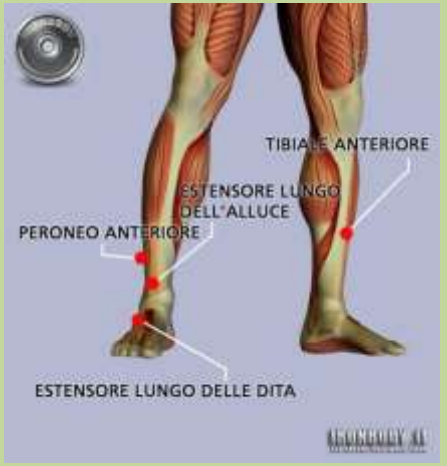
Stage 2:
Rehabilitation and Hypertrophy

how much protein?

Increased protein intake may support increased protein turnover, but the amount necessary may not be as high as many believe … A recent study suggested that increased protein intake enhances recovery from immobilization but other results are somewhat equivocal

TIMING

within total energy requirements and does not restrict the amount of carbohydrate or essential fat intake, then elevating protein intake may not be a problem. There seems little reason to increase protein intake with the goal of increasing tendon collagen synthesis. Neither muscle nor tendon collagen synthesis responds to provision of amino acids



J Orthop Res. 2006 Nov;24(11):2114-23. The effect of protein and carbohydrate supplementation on strength training outcome of rehabilitation in ACL patients. Holm L, Esmarck B, Mizuno M, Hansen H, Suetta C, Hölmich P, Krogsgaard M, Kjaer M.

Sintesi proteica e rigenerazione muscolare

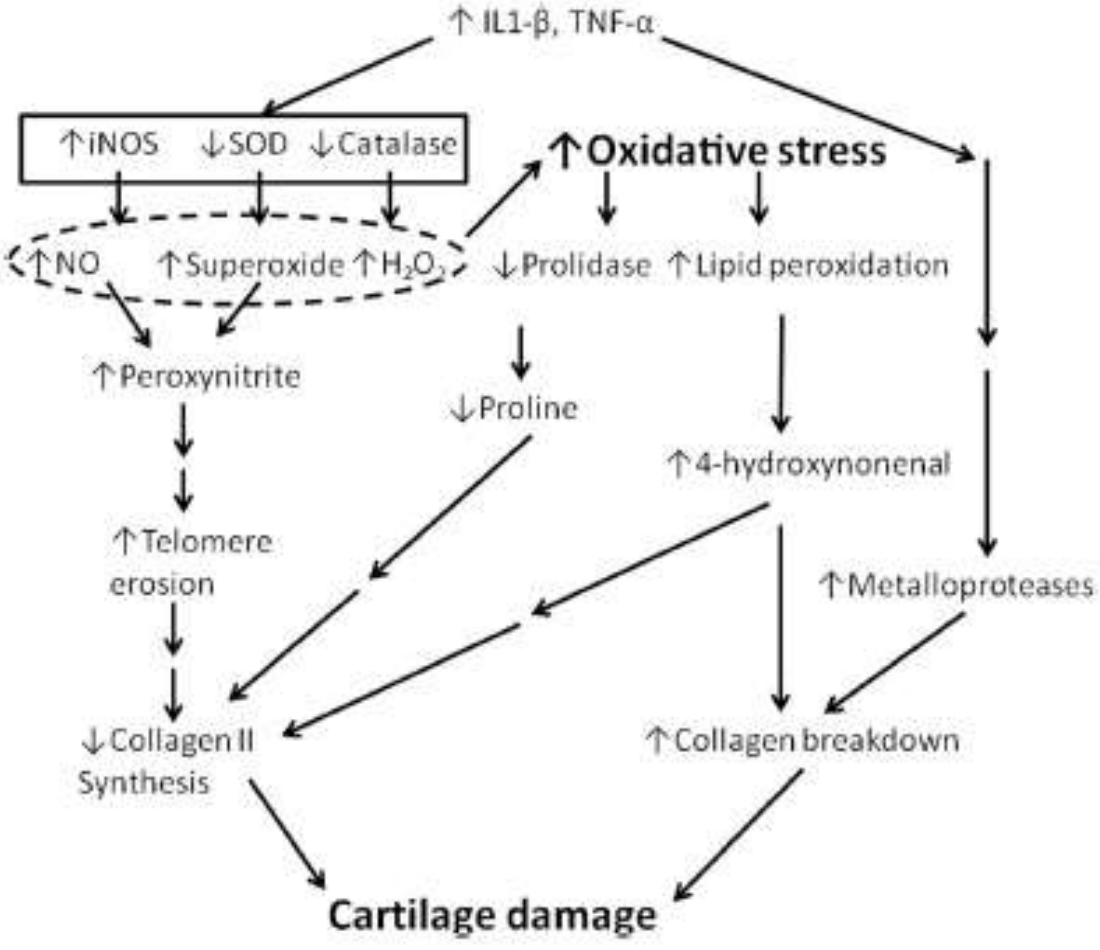
Grover and Samson Nutrition Journal (2016) 15:1
DOI 10.1186/s12937-015-0115-z

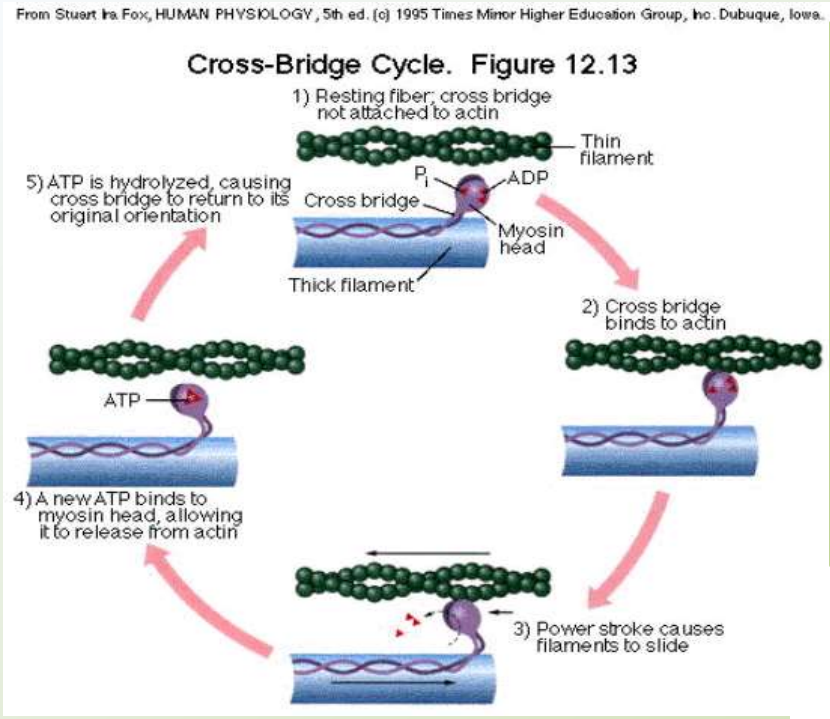
Nutrition Journal

REVIEW Open Access

Benefits of antioxidant supplements for knee osteoarthritis: rationale and reality

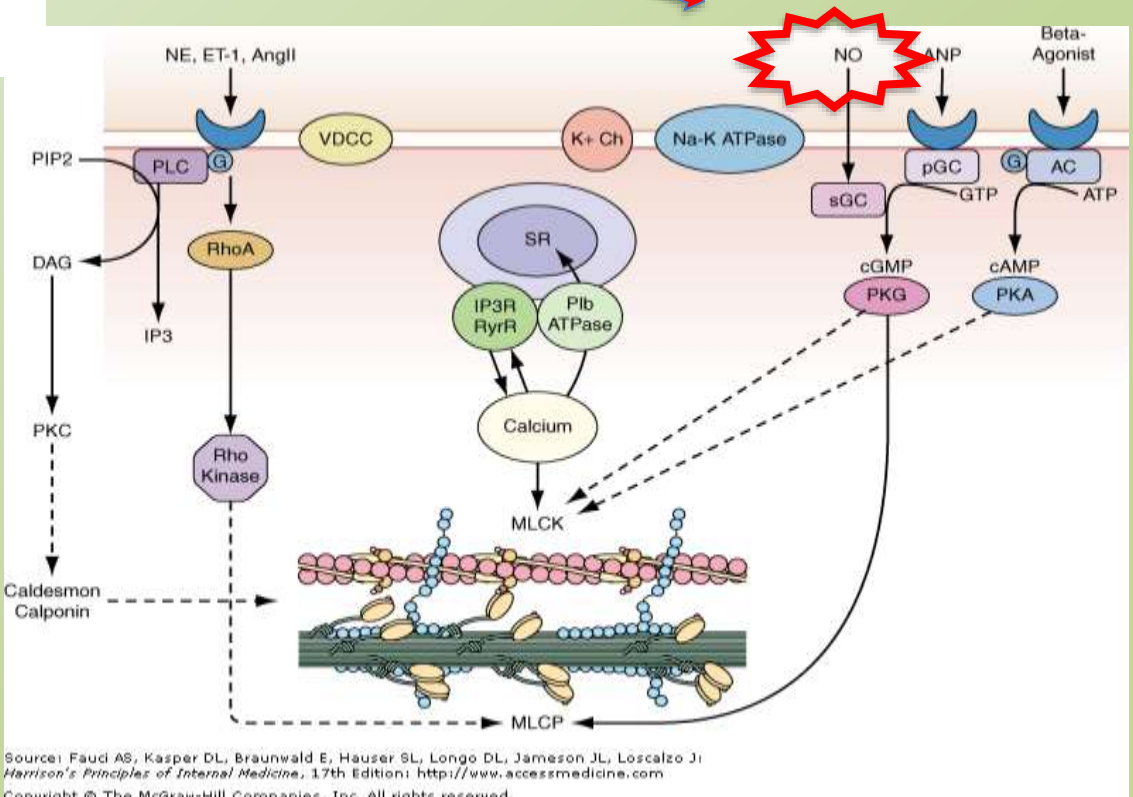
Ashok Kumar Grover* and Sue E. Samson





sarcoplasmic reticulum Ca2+-ATPase (SERCA) as the plausible site downstream of dietary nitrate

NO riduce Ca^{2+} cycling e rallenta "cross-bridge cycling kinetics"



NUTRITIONAL SUPPORT

Vitamin C

Vitamin A

Vitamin D

Omega-3 FA?

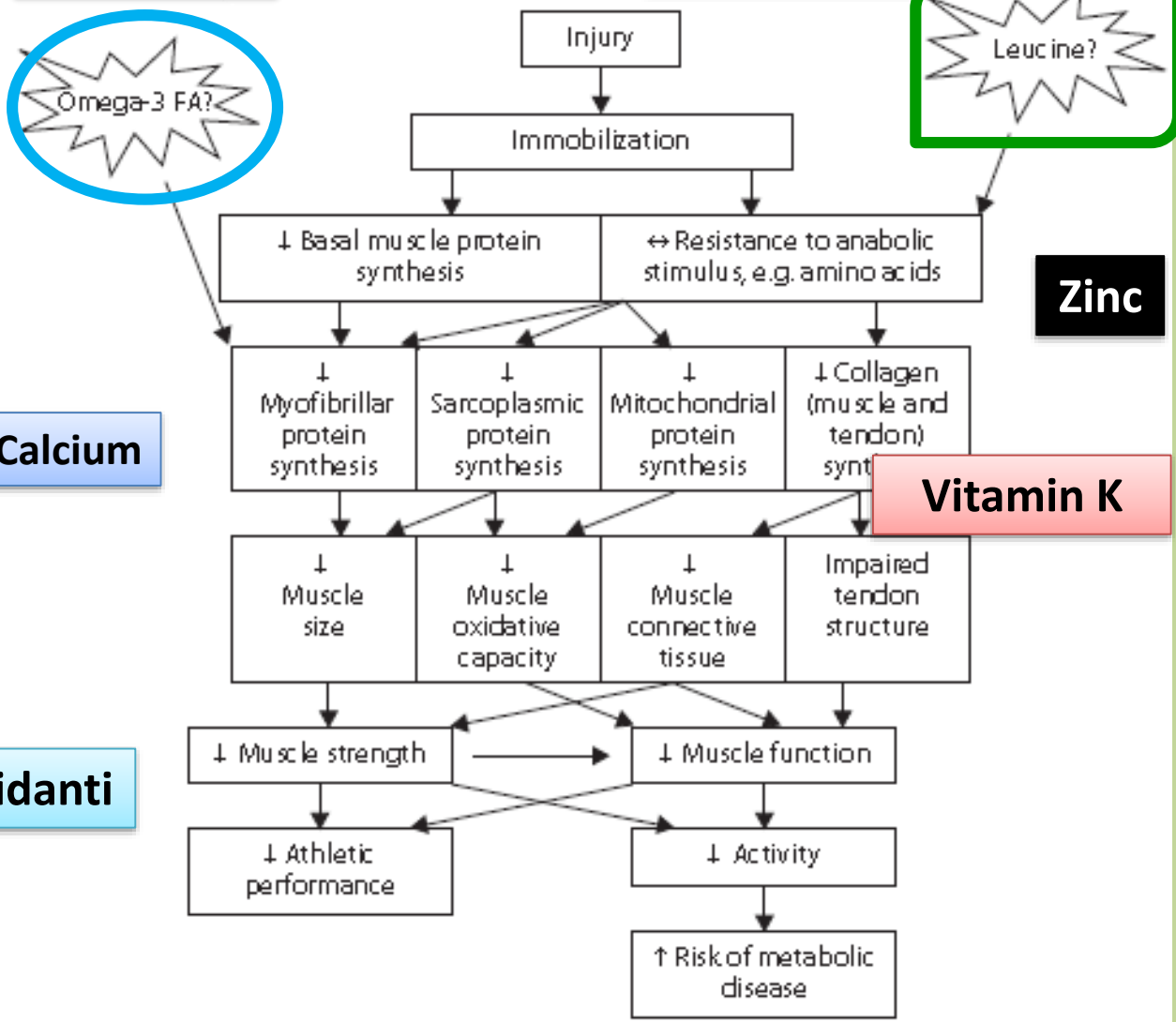
Leucine?

Zinc

Calcium

Vitamin K

antiossidanti



Nutraceutical Support

Glucosamine - Chondroitin

Methyl-Sulfonyl-Methane

Omega 3

Arginine

Boswellia Serrata

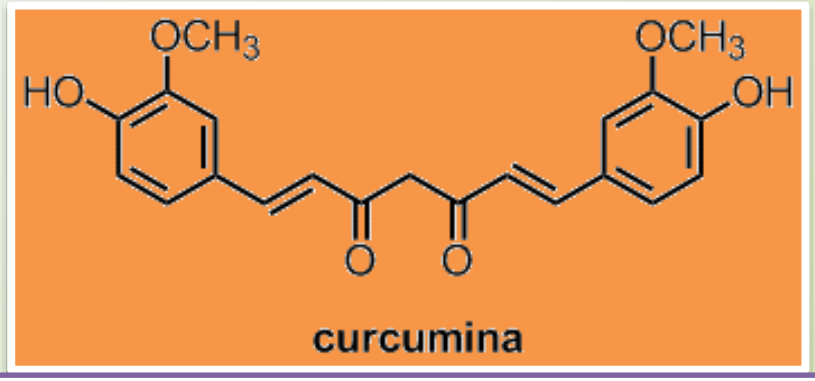
Superox Dismutase

Curcumin

Nutrition. 2009 February ; 25(2): 125–129. doi:10.1016/j.nut.2008.09.002.

CURCUMIN AND MUSCLE WASTING – A NEW ROLE FOR AN OLD DRUG?

Nima Alamdari, **Patrick O'Neal**, and **Per-Olof Hasselgren**



curcumina

Curcumin (diferuloylmethane), a component of the spice turmeric (Curcuma longa) and responsible for the yellow color of curry

results suggest that curcumin may be a potentially useful drug to prevent loss of muscle mass,

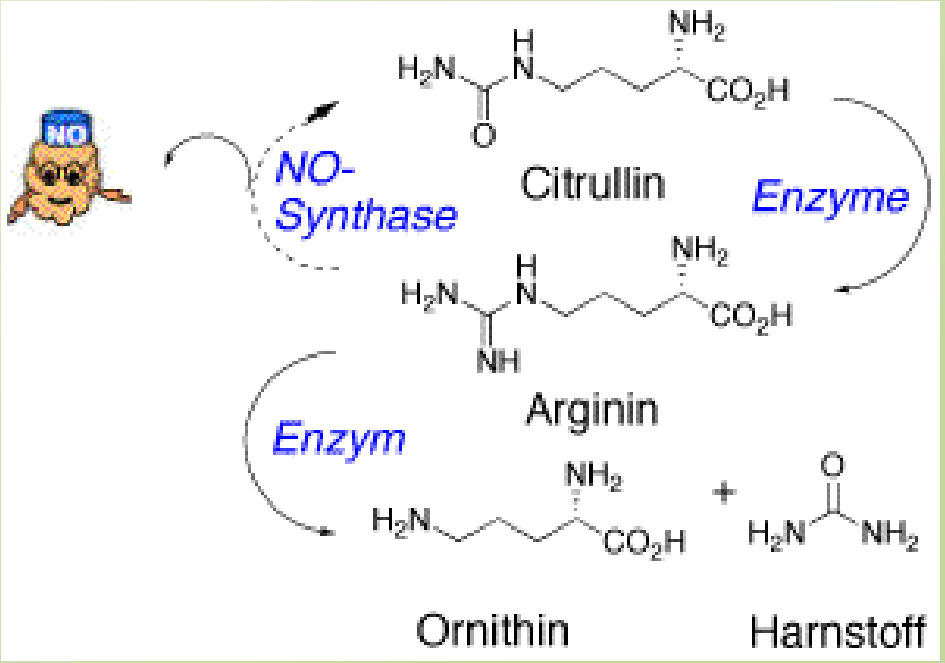
only if it is easily assimilated

previous observations provide strong evidence that NF-kB is involved in muscle wasting during different catabolic conditions and that NF-kB inhibitors may be efficacious in the management of muscle-wasting conditions. Of note, inhibition of NF-kB activity is an important mechanism by which curcumin may exert beneficial effects.

Amino Acids. 2009 May;37(1):153-68. Epub 2008 Nov 23.
Arginine metabolism and nutrition in growth, health and disease.
Wu G, Bazer FW, Davis TA, Kim SW, Li P, Marc Rhoads J, Carey Satterfield M, Smith SB, Spencer TE, Yin Y

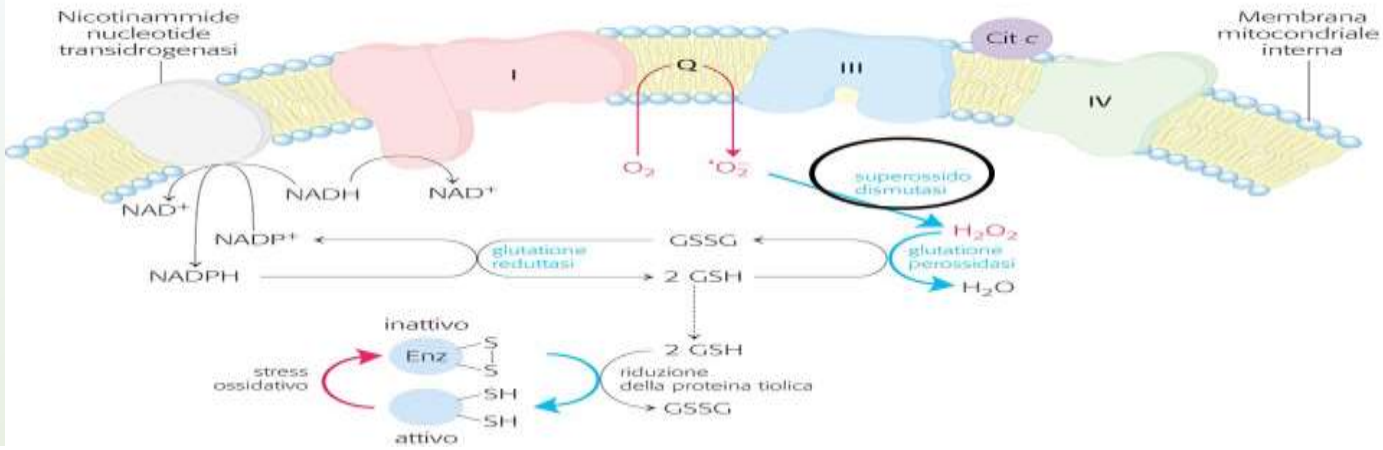
SOCIETÀ ITALIANA Nutrizione Sport e Salute

Arginine degradation occurs via multiple pathways that are initiated by arginase, nitric-oxide synthase, Arg:glycine amidinotransferase, and Arg decarboxylase. These pathways produce nitric oxide, polyamines, proline, glutamate, creatine, and agmatine with each having enormous biological importance.



a growing body of evidence clearly indicates that dietary supplementation or intravenous administration of Arg is beneficial in improving reproductive, cardiovascular, pulmonary, renal, gastrointestinal, liver and immune functions, as well as facilitating wound healing, enhancing insulin sensitivity, and maintaining tissue integrity.

La superossido dismutasi (SOD)



Superoxide dismutases (SODs) are the major antioxidant defense systems against O2•−, which consist of three isoforms of SOD in mammals: the cytoplasmic Cu/ZnSOD (SOD1), the mitochondrial MnSOD (SOD2), and the extracellular Cu/ZnSOD (SOD3), all of which require catalytic metal (Cu or Mn) for their activation.

In addition, SODs play a critical role in inhibiting oxidative inactivation of nitric oxide, thereby preventing peroxynitrite formation and endothelial and mitochondrial dysfunction.

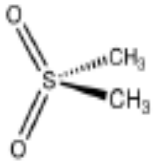
Enzymatic activity of SOD1 depends on the presence of the Cu and Zinc

SOD is commercially obtained from marine phytoplankton,bovine liver, horseradish, cantaloupe and by fermenting certain bacteria, though it is found in most living forms at diverse concentrations.

Muller FL, Song W, Liu Y, Chaudhuri A, Pieke-Dahl S, Strong R, Huang TT, Epstein CJ, Roberts LJ, Csete M, Faulkner JA, Van Remmen H (Jun 2006). "Absence of CuZn superoxide dismutase leads to elevated oxidative stress and acceleration of age-dependent skeletal muscle atrophy". *Free Radical Biology & Medicine*. **40** (11): 1993–2004. doi:10.1016/j.freeradbiomed.2006.01.036. PMID 16716900.

MSM Metil-Sulfonil-Metano

SOCIETÀ ITALIANA Nutrizione Sport e Benessere



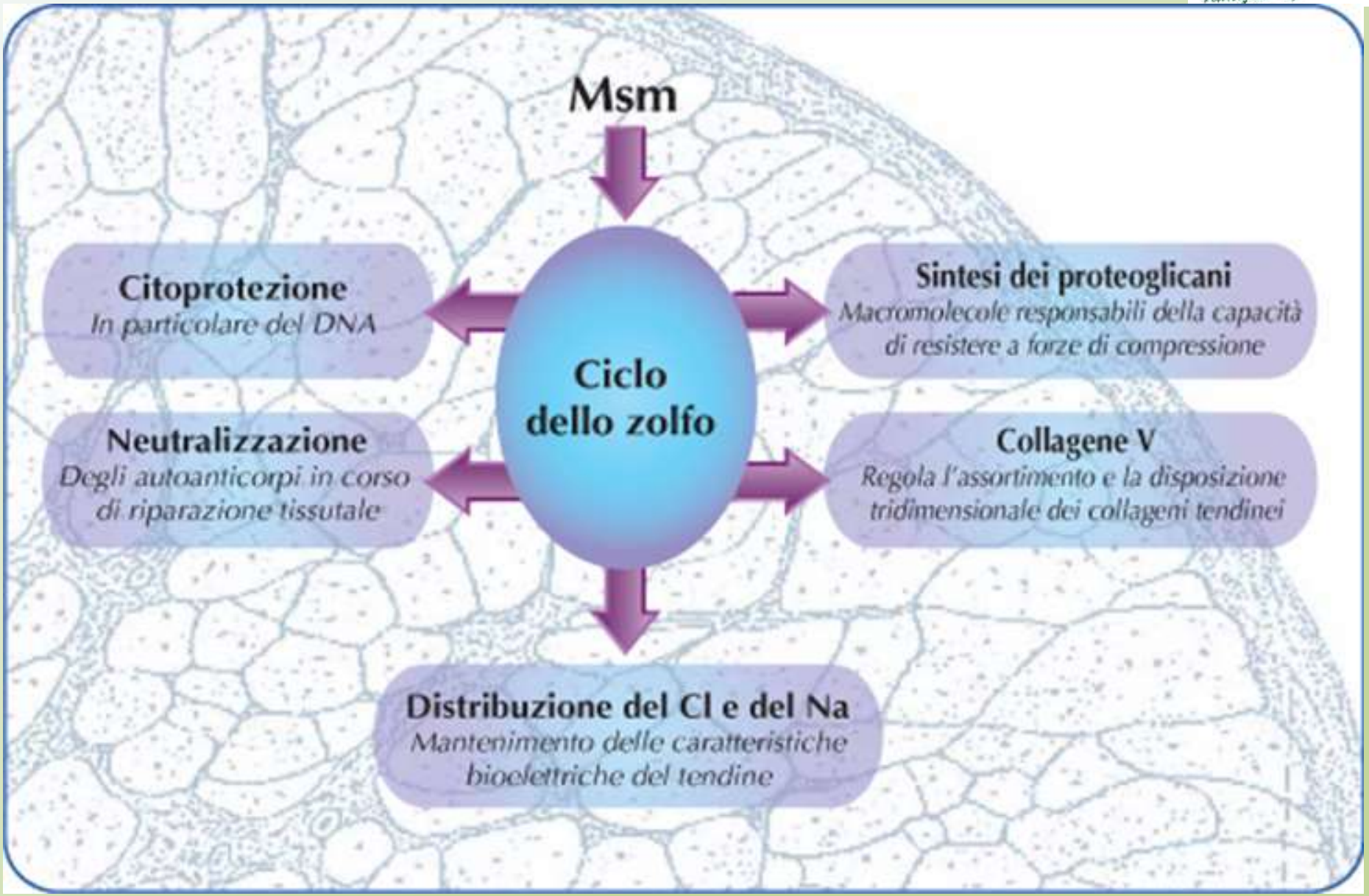
Methylsulfonylmethane

Methylsulfonylmethane (**MSM**) is an organosulfur compound with the formula $(CH_3)_2SO_2$. It is also known by several other names including **$DMSO_2$**, **methyl sulfone**, and **dimethyl sulfone**.[2] This colorless solid features the sulfonyl functional group and is considered relatively inert chemically. It occurs naturally in some primitive plants, is present in small amounts in many foods and beverages, and is marketed as a dietary supplement

Oxidative stress and inflammation[edit]

Multiple human and animal trials indicate MSM may reduce oxidative stress and inflammation, although it is not a direct antioxidant.[30] In human studies, MSM has been shown to protect muscles from damage by reducing the amount of oxidative stress damage incurred through exercise.[31][32] The total antioxidant capacity was significantly increased after taking MSM.[33] Studies in animals indicate a hepatoprotective effect of MSM against several toxins including acetaminophen, paraquat, and carbon tetrachloride.[34][35][36][37] Animal models of experimental colitis and pulmonary hypertension indicate a protective effect as well.[38][39]

DOSING: Typical doses adult dosages range from 500 to 8,000 mg daily with or after meals.


Msm
Citoprotezione
In particolare del DNA
Sintesi dei proteoglicani
Macromolecole responsabili della capacità di resistere a forze di compressione
Ciclo dello zolfo
Neutralizzazione
Degli autoanticorpi in corso di riparazione tissutale
Collagene V
Regola l'assortimento e la disposizione tridimensionale dei collageni tendinei
Distribuzione del Cl e del Na
Mantenimento delle caratteristiche bioelettriche del tendine

J Sports Med (Hindawi Publ Corp). 2016;2016:7498359. Epub 2016 Oct 23.
The Influence of Methylsulfonylmethane on Inflammation-Associated Cytokine Release before and following Strenuous Exercise.
van der Merwe M1, Bloomer RJ1.

Physically active men were supplemented with either placebo or MSM (3 grams per day) for 28 days before performing 100 repetitions of eccentric knee extension exercise

MSM appears to dampen the release of inflammatory molecules in response to exercise, resulting in a less incendiary environment, allowing cells to still have the capacity to mount an appropriate response to an additional stimulus after exercise

J Int Soc Sports Nutr. 2012 Sep 27;9(1):46. doi: 10.1186/1550-2783-9-46.
Influence of methylsulfonylmethane on markers of exercise recovery and performance in healthy men: a pilot study.
Kalman DS1, Feldman S, Scheinberg AR, Krieger DR, Bloomer RJ.

Before and after the 28 day intervention period, subjects performed 18 sets of knee extension exercise in an attempt to induce muscle damage (and to be used partly as a measure of exercise performance). Sets 1-15 were performed at a predetermined weight for 10 repetitions each, while sets 16-18 were performed to muscular failure. Muscle soreness (using a 5-point Likert scale), fatigue (using the fatigue-inertia subset of the Profile of

MSM, especially when provided at *3.0 grams per day*, may favorably influence selected markers of exercise recovery

Arthritis Foundation℠

Indian Frankincense

[Frankincense, Boswellia, Boswellin, Salai Guggal] Boswellia serrata

Origin: Gum resin from the bark of the Boswellia tree found in India.

Claims: Reduces inflammation and treats rheumatoid arthritis (RA), osteoarthritis (OA) and bursitis symptoms. It may also be used to treat symptoms of ulcerative colitis and Crohn's disease.

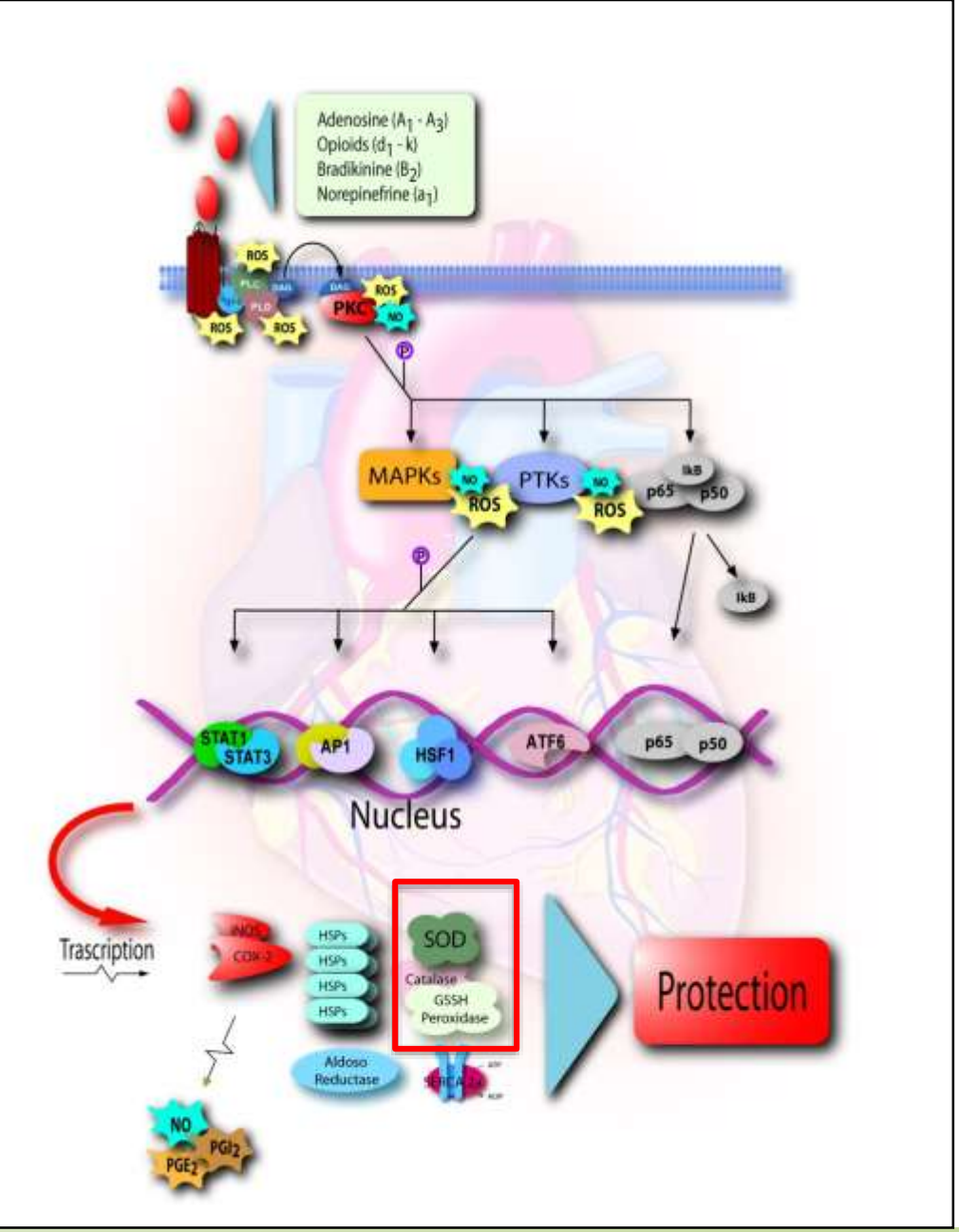
What we know: Boswellic acids – the active components – may have strong anti-inflammatory and analgesic properties. They may also help prevent cartilage loss and inhibit the autoimmune process, making Indian frankincense/boswellia a potential therapy for RA in addition to OA.

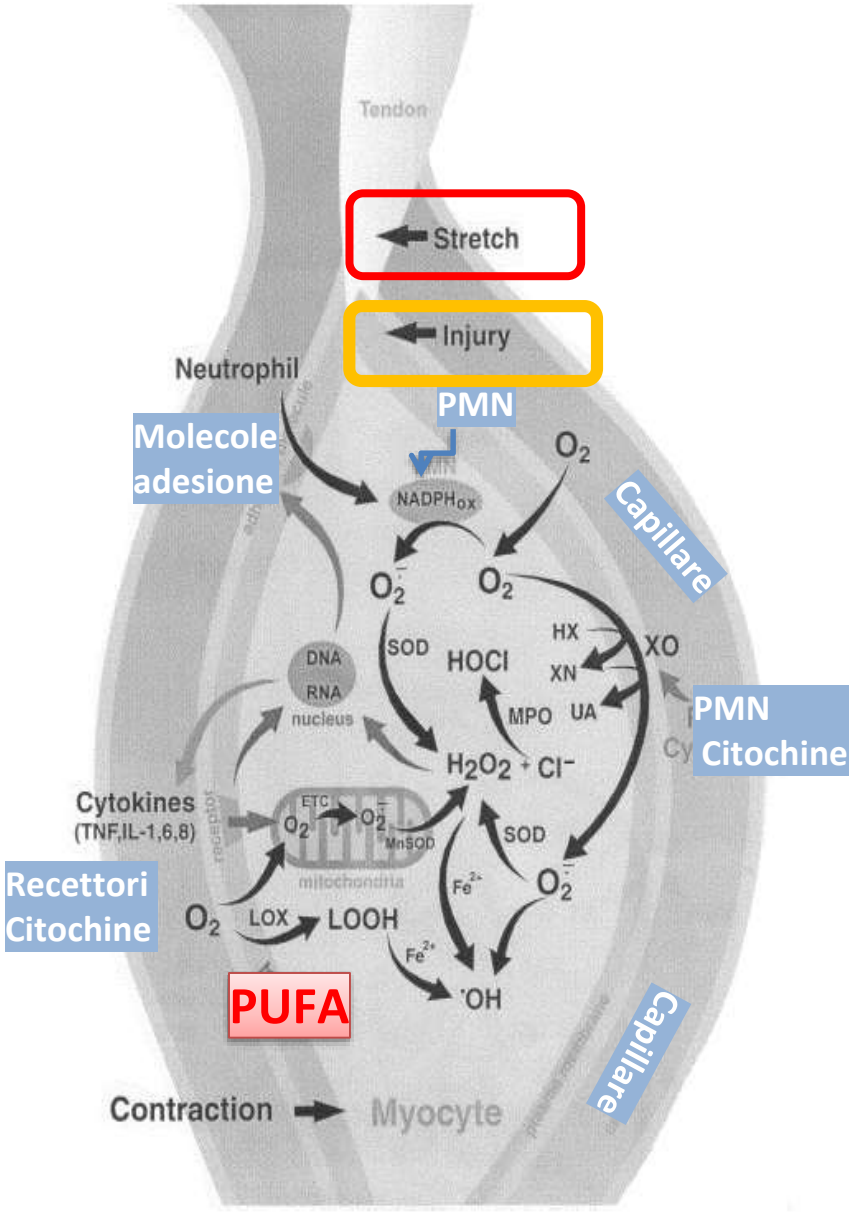
Studies: In a 2004 study, Indian frankincense/boswellia was tested as a treatment for knee OA. Researchers recruited 30 people with knee OA and gave half the group a daily supplement containing 333 mg of Indian frankincense/boswellia; others got placebo. People who took Indian frankincense/boswellia reported less knee pain, better mobility and an ability to walk longer distances than those taking placebo.

A 2008 study in India, where Indian frankincense/boswellia is a traditional remedy, found that a supplement called 5-Loxin significantly improved OA pain and function within seven days and slowed cartilage damage after 3 months.

A 2008 British review found Indian frankincense/boswellia safe and effective for both OA and RA, though results of RA trials have been mixed.

Dosage: Capsule or tablet; typically 300 mg to 400 mg three times per day. Look for products with 60-percent boswellic acids, the active ingredient.





Meccanismi di protezione dei PUFA

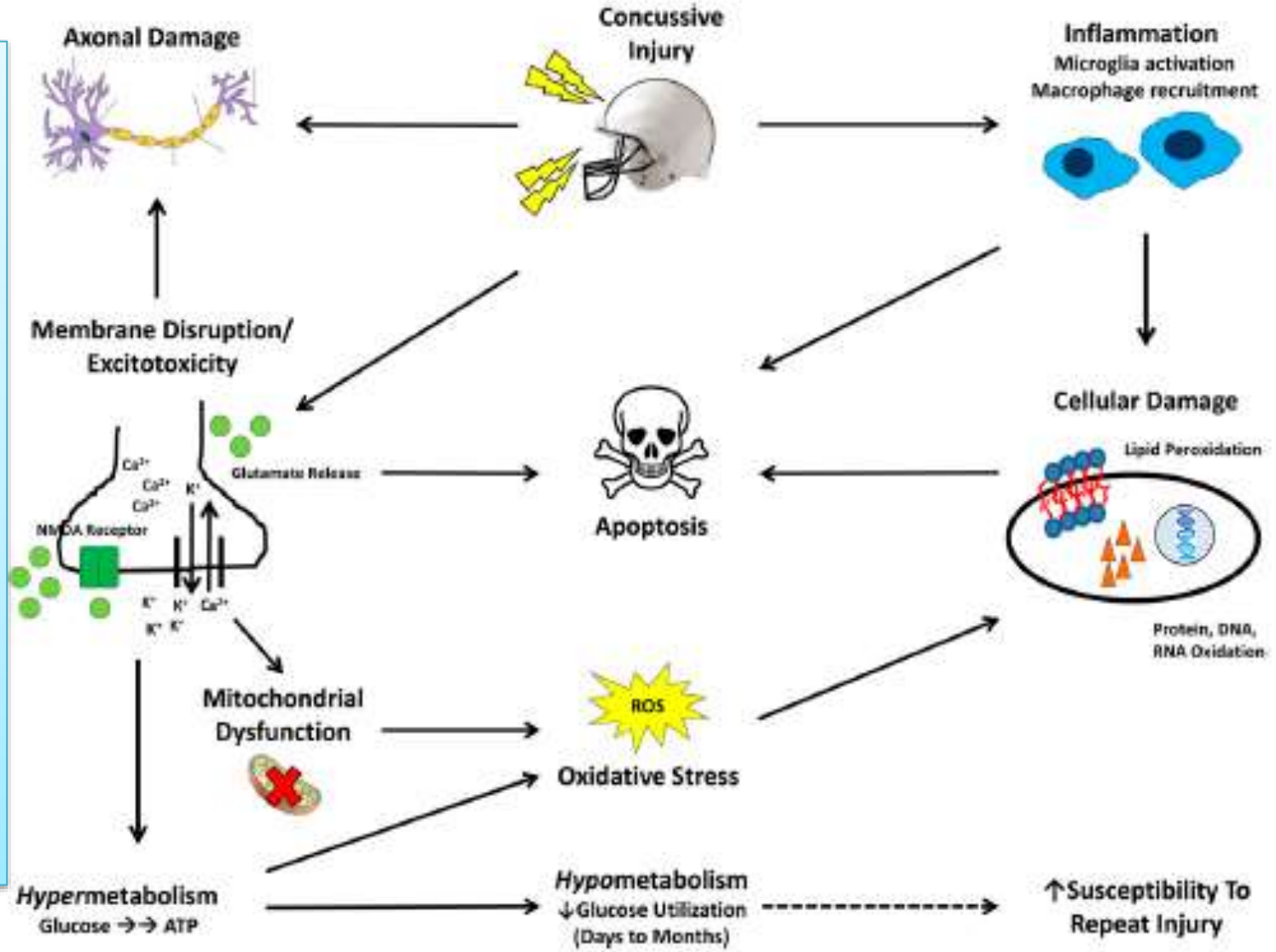
ω-3 Fatty Acid Supplementation as a Potential Therapeutic Aid for the Recovery from Mild Traumatic Brain Injury/Concussion[1,2]

Erin Cernkovich Barrett, Michael I. McBurney, and Eric D. Ciappio*
DSM Nutritional Products, Parsippany, NJ

SOCIETÀ ITALIANA

Molecular cascade of events after a mild traumatic brain injury.

The ω-3 FA DHA has been shown to address several of the hallmark pathologic features of this injury, such as excitotoxicity, oxidative stress, antinflammation.



Nutraceutical supplement in the management of tendinopathies: a systematic review

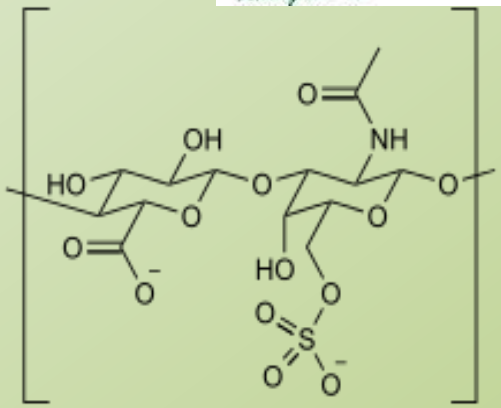
Muscles, Ligaments and Tendons Journal 2016;6 (1):48-57

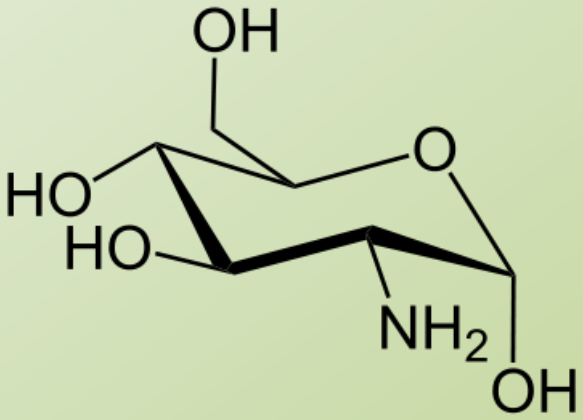
SOCIETÀ ITALIANA

Table 1. Overview of principal nutraceutical and their properties (Glc-N-CS: glucosamine and chondroitin sulphate; vit C: vitamin C; Col I: collagen type 1; Col III collagen type 3; AAKG: L-arginine-α-keto-glutarate; NOS: nitric oxide synthase; NO: nitric oxide; 5-LO: 5-lipoxygenase; TNFα: tumor necrosis factor α; IL-1/2/4/6: interleukin 1/2/4/6; IFNγ: interferon γ; MSM: methilsulfonil methane; MDA: malonyldialdehyde; GSSG: oxidized gluthation).

Nutraceutical	Biological effect
Glucosamine and chondroitin sulphate (GlcN-CS)	Increase collagen synthesis, ameliorate mechanical properties, organization of collagen bundles and resistence to fatigue, helpful in the management of pain.
Vitamin C (Vit C)	Stimulate hydroxyproline synthesis of procollagen, enhance angiogenesis and maturation of Col III to Col I fibers, anti-inflammatory and antioxidant effect.
Collagen I (Col I)	Increase mechanical properties, beneficial effects on collagen-rich tissues.
L-arginine-α-keto-glutarate	Substrate of NOS, increase NO levels and collagen synthesis.
Curcumin	Neoangiogenesis and apotosis inhibitor, antioxidant effect, stimulate tenocytes survival.
Boswellic acid	Elastase and 5-LO activity inhibition, reduce TNFα, IL-1, IL-2, IL-4, IL- 6 e INFγ levels.
Methilsulfonilmethane (MSM)	Analgesic, anti-inflammatory and antioxidant effects, reduce MDA and GSSG levels.
Bromelain	Decrease lymphocytes rolling, anti edema, antioxidant and immunosuppressive effects, reduce MDA levels.

Il ***solfato di condroitina*** *è un glicosaminoglicano (GAG) solfato, composto da una catena alternata di zuccheri (N-acetilgalattosamina e acido glucuronico). Si trova normalmente associata a proteine, a formare un proteoglicano. Una catena di condroitina può avere oltre 100 zuccheri, ognuno dei quali può legare ioni solfato in posizione e quantità variabili. Il solfato di condroitina è un importante componente strutturale della cartilagine, dandogli la quasi totalità della resistenza alla compressione*





La ***glucosammina*** *è un amminomonosaccaride (o glicosammina) e uno dei principali precursori della sintesi delle proteine glicosilate e dei lipidi. È uno dei maggior componenti del guscio dei crostacei e di altri artropodi, nei funghi e molti organismi superiori. È uno dei componenti del lipopolisaccaride dei batteri Gram-negativi. Non è un monosaccaride in senso stretto del termine, in quanto la sua formula molecolare non corrisponde alla formula generale Cn(H_2O)n.*

Citation: Ann Rheum Dis 2005;64(Suppl III):483

OSTEOARTHRITIS: CHONDROITIN SULFATE LONG TERM UTILIZATION REDUCES CONSUMPTION OF COXIBS, NSAIDS &ANALGESICS

SOCIETÀ ITALIANA

Arthritis Foundation

GLUCOSAMINE SULPHATE INDUCES CARTILAGE QUALITATIVE MORPHOLGICAL CHANGES IN OSTEOARTHRITIS: AN ULTRASONGRAPHIC AND MRI EVIDENCE

Citation: Ann Rheum Dis 2005;64(Suppl III):493

Origin: Chondroitin is a component of human connective tissues found in cartilage and bone. In supplements, chondroitin sulfate usually comes from animal cartilage.

Claims: Reduces pain and inflammation, improves joint function and slows progression of osteoarthritis (OA).

What we know: Believed to enhance the shock-absorbing properties of collagen and block enzymes that break down cartilage. Helps cartilage retain water and may reverse cartilage loss when used with glucosamine.

Studies: The largest study to date, the 2006 Glucosamine/chondroitin Arthritis Intervention Trial (GAIT) looked at 1,600 people with knee OA. The first phase found that a small subset of patients with moderate-to-severe arthritis experienced significant pain relief from combined glucosamine and chondroitin. The 2008 phase found that glucosamine and chondroitin, together or alone, did not slow joint damage. And in the two-year-long 2010 phase, glucosamine and chondroitin were found as effective for knee OA as celecoxib (*Celebrex*).

But a 2010 meta-analysis of 10 trials involving more than 3,000 patients published in *BMJ* found no benefit from chondroitin, glucosamine or both.

A separate 2011 study showed a significant improvement in pain and function in patients with hand OA using chondroitin alone. Benefits of chondroitin and glucosamine remain controversial, but the supplements appear extremely safe.

Associations Between Glucosamine and Chondroitin Supplement Use and Biomarkers of Systemic Inflammation

Elizabeth D. Kantor, PhD,[1–3] Johanna W. Lampe, PhD,[1,2] Sandi L. Navarro, PhD,[1] Xiaoling Song, PhD,[1] Ginger L. Milne, PhD,[4] and Emily White, PhD[1,2]

THE JOURNAL OF ALTERNATIVE AND COMPLEMENTARY MEDICINE
Volume 20, Number 6, 2014, pp. 479–485

SOCIETÀ ITALIANA Nutrizione Sport e Benessere

TABLE 2. DISTRIBUTION OF INFLAMMATORY BIOMARKERS AND ASSOCIATION BETWEEN EACH BIOMARKER AND AGE, SEX, AND BODY–MASS INDEX

Variable	*Geometric mean (geometric 25th, 75th percentile)*	*Ratio[a] per 10-y increase in age (95% CI)*	*Ratio[b] for sex: male vs. female (95% CI)*	*Ratio[c] per 5-unit increase in BMI (95% CI)*
CRP (mg/L)	1.75 (0.72, 4.03)	1.25 (1.04–1.50)	0.45 (0.34–0.59)	1.67 (1.42–1.95)
IL-1β (pg/mL)	0.77 (0.11, 2.58)	1.11 (0.85–1.46)	0.80 (0.53–1.21)	0.96 (0.76–1.22)
IL-6 (pg/mL)	3.62 (1.50, 12.0)	1.39 (1.06–1.83)	0.63 (0.42–0.95)	1.19 (0.94–1.50)
IL-8 (pg/mL)	2.24 (1.44, 3.47)	1.17 (1.04–1.33)	0.91 (0.75–1.10)	0.97 (0.87–1.08)
TNF-α (pg/mL)	5.77 (3.38, 11.6)	1.22 (1.05–1.43)	0.91 (0.72–1.15)	1.03 (0.90–1.18)
sTNFRI (pg/mL)	1430 (1186, 1732)	1.12 (1.06–1.19)	1.09 (1.00–1.20)	1.05 (1.00–1.11)
sTNFRII (pg/mL)	5677 (4768, 6683)	1.17 (1.11–1.23)	1.04 (0.97–1.12)	1.06 (1.02–1.11)
PGE-M (ng/mg creatinine)	5.43 (3.38, 8.55)	1.16 (1.04–1.30)	1.20 (1.01–1.42)	1.04 (0.94–1.16)

Use of glucosamine and chondroitin supplements is associated with lower concentrations of hsCRP and PGE-M. This study offers an important piece of evidence to suggest that these supplements might have anti-inflammatory potential.

Glucosamine Supplementation after Anterior Cruciate Ligament Reconstruction in Athletes: A Randomized Placebo-controlled Trial

Ali Eraslan[a] & Bulent Ulkar[b]

Research in Sports Medicine, 23:14–26, 2015

ISSN: 1543-8627 print/1543-8635 online
DOI: 10.1080/15438627.2014.975809

FIGURE 2 Study progress.

This is the first study investigating the effect of glucosamine supplementation on rehabilitation outcomes in athletes who underwent ACL reconstruction. It was found that glucosamine-sulfate (1000 mg/day, for 8 weeks) did not positively affect the rehabilitation outcomes.

SOCIETÀ ITALIANA
Nutrizione Sport e Benessere

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

Usha PR1, Naidu MU.

Clin Drug Investig. 2004;24(6):353-63

Online version at http://www.minervamedica.it

European Journal of Physical and Rehabilitation Medicine 2016 June;52(3):321-30

ORIGINAL ARTICLE

The efficacy and safety of a combination of glucosamine hydrochloride, chondroitin sulfate and bio-curcumin with exercise in the treatment of knee osteoarthritis: a randomized, double-blind, placebo-controlled study

RESEARCH ARTICLE

PLOS ONE February 26, 2015

Randomized Trial of Glucosamine and Chondroitin Supplementation on Inflammation and Oxidative Stress Biomarkers and Plasma Proteomics Profiles in Healthy Humans

Sandi L. Navarro[1]*, Emily White[1], Elizabeth D. Kantor[2], Yuzheng Zhang[1], Junghyun Rho[1], Xiaoling Song[1], Ginger L. Milne[3], Paul D. Lampe[1], Johanna W. Lampe[1]

Table 2. Inflammatory and oxidative stress biomarker concentrations after placebo and glucosamine and chondroitin intervention.

Biomarker	Placebo (N = 18) Mean (SD)[1]	Glucosamine & Chondroitin (N = 18) Mean (SD)[1]	*P*
CRP (mg/l)	1.17 (0.17)	0.90 (0.13)	0.048
IL-6 (pg/ml)	0.89 (0.10)	0.81 (0.09)	0.27
sTNFRI (pg/ml)	871.3 (15.6)	901.6 (15.7)	0.17
sTNFRII (pg/ml)	5558 (103)	5633 (104)	0.34
PGE-M (ng/mg creatinine)	6.15 (0.41)	5.89 (0.39)	0.60
F_2-isoprostane (ng/mg creatinine)	1.20 (0.08)	1.10 (0.08)	0.38

Glucosamine and chondroitin supplementation may lower systemic inflammation

Table 4. Top 100 (of 508) individual protein antibodies significantly different after glucosamine and chondroitin supplementation versus placebo intervention periods (n = 18).

Gene[1]	Function[2]	Effect size[3]	*P* value*
CEACAM1	Cell-cell adhesion	-2.45	8.7×10^{-15}
SUZ12	Proliferation and histone methyltransferase activity [50,51]	1.09	1.7×10^{-14}
THBS4	Cell-to-cell and cell-to-matrix interactions, extracellular mitogen	-1.88	2.1×10^{-14}
GADD45A	Induced in response to DNA damage	-1.37	2.8×10^{-14}
ITGA5	Adhesion and cell-surface mediated signaling	-1.54	9.7×10^{-14}
ITGB4	Adhesion and cell-surface mediated signaling	-1.89	1.2×10^{-13}
CSF3(GCSF)[§]	Cytokine involved in hematopoiesis and induction of granulocytes	-3.06	2.1×10^{-13}
PKNOX1	RNA polymerase II distal enhancer	1.43	2.8×10^{-13}
IL13[§]	Immunoregulatory cytokine involved in inhibition of allergic reaction, particularly in the airways	-6.29	3.5×10^{-13}
C1orf38	Mediates macrophage inflammatory response	3.67	4.6×10^{-13}
SON	Splicing co-factor for cell-cycle progression and DNA-repair, involved in differentiation of hematopoietic cells	1.02	6.4×10^{-13}
MUC3B	Provides protective barrier against infectious agents at mucosal surfaces	3.83	1.3×10^{-12}
RUNX1	Subunit of transcription factor that binds to many enhancers and promoters, involved in development of normal hematopoiesis	3.93	1.4×10^{-12}
IL17D	Cytokine involved in the stimulation of other cytokines, e.g., IL6, IL8, and CSF	-2.27	1.6×10^{-12}
BCAS2	Component of pre-mRNA splicesome complex	1.72	2.3×10^{-12}
KCNE3	Modulates gating kinetics of potassium voltage channel complexes	1.75	3.2×10^{-12}
CD44	Cell adhesion and migration, receptor for hyaluronic acid	1.50	3.3×10^{-12}
VEPH1	Function unknown	1.80	3.7×10^{-12}
HBEGF	Normal heart function, smooth muscle cell proliferation, may be involved in macrophage mediated proliferation	-1.47	5.2×10^{-12}
VCP	Putative ATP-binding protein in vesicle transport and fusion, 26S proteasome function and assembly of peroxisomes	-2.10	6.8×10^{-12}
COMP	Structural integrity of cartilage, potent suppressor of apoptosis in chondrocytes	-2.08	7.4×10^{-12}
IL8[§]	Chemokine, chemoattractant and potent angiogenic factor	-2.35	9.9×10^{-12}
CAPN3 (NCL1)	Intracellular protease, binds to titin	-2.09	1.0×10^{-11}
GCM2	Transcription factor regulating parathyroid development	1.23	1.0×10^{-11}
PKC	Regulation of cell growth and immune responses	-0.89	1.3×10^{-11}
LASP1	Regulation of actin-based cytoskeletal activities	-1.42	1.4×10^{-11}
SPP1 (Osteopontin)	Attachment of osteoclasts to the mineralized bone matrix; also a cytokine that upregulates expression of interferon-gamma and interleukin-12	-6.45	1.7×10^{-11}
EFNB3	Ligand for Eph receptors involved in migration, repulsion and adhesion during neuronal, vascular and epithelial development	-3.24	1.9×10^{-11}
HOXA4	Transcription factor that may regulate gene expression, morphogenesis and differentiation	1.88	2.3×10^{-11}
IL1β	Cytokine involved in inflammatory response	-2.65	2.3×10^{-11}
EGFR[§]	Cell proliferation	1.80	3.1×10^{-11}
PRKCQ	Kinase involved in diverse cellular signaling pathways including T-cell activation, proliferation, differentiation and survival	-1.68	3.1×10^{-11}

pharmaceuticals

MDPI

Article

Systematic Analysis of Pharmaceutical Preparations of Chondroitin Sulfate Combined with Glucosamine

Gustavo R.C. Santos, Adriana A. Piquet, Bianca F. Glauser, Ana M.F. Tovar, Mariana S. Pereira, Eduardo Vilanova and Paulo A.S. Mourão *

SOCIETÀ ITALIANA Nutrizione Sport e Benessere

The mechanisms of action of neither CS nor GlcN in cartilage and subchondral bone tissues affected with osteoarthritis still not fully determined

Table 1. Declared and observed contents of glucosamine (GlcN) and chondroitin sulfate (CS) on pharmaceutical preparations.

Formulation	Component	Declared Content (mg)	Observed Content (mg) [a]
Capsule	GlcN [b]	500	465 ± 20 [b]
	CS [c]	400	376 ± 8 [c]
Sachet	GlcN	1500	1500 ± 60 [b]
	CS	1200	1211 ± 179 [c]

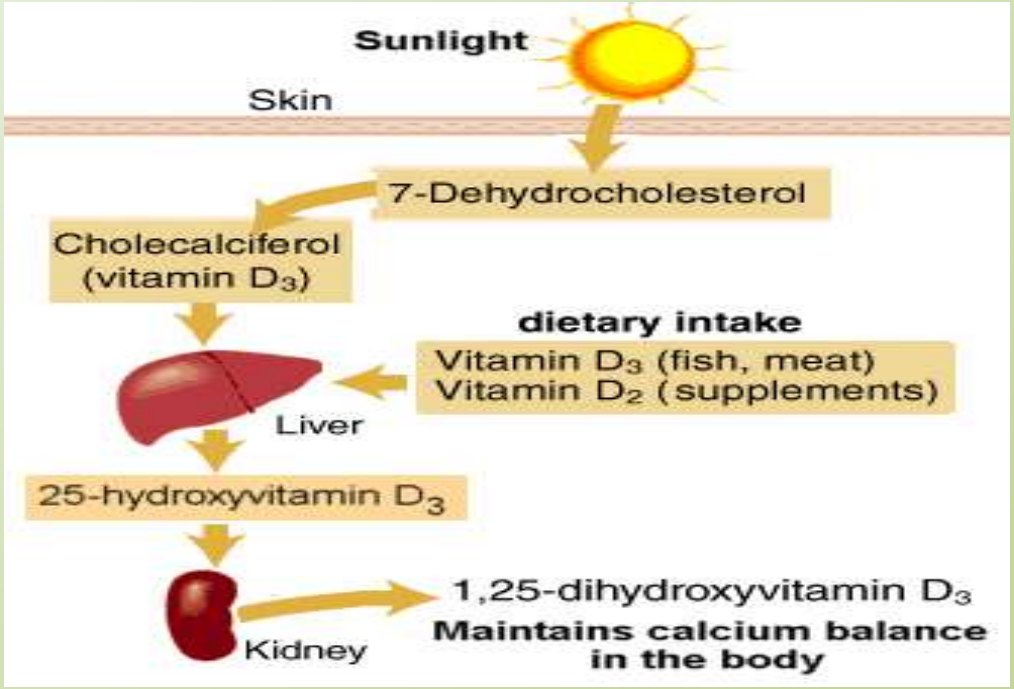
[a] Results as mean ± SD of three determinations; [b] Content of free GlcN determined by a colorimetric reaction [27]; [c] Content of CS determined by the carbazole reaction [26] using standard curves obtained with the international standard of CS from US Pharmacopeia.

Nevertheless, it is a challenging task to understand how a carbohydrate-based compound with high molecular weight like CS (20–50 kDa) could be absorbed after oral administration and then remain sufficiently undegraded

necessity of a precise and detailed determination of the chemical structures of the CS and GlcN present in these pharmaceutical preparations to support clinical and preclinical studies

Nutraceutici in medicina dello sport

- Epidemiologically, vit D is linked to decr risk of cancer, multiple sclerosis, flu, hypertension, diabetes, & mood disorders.
- Most human diets contain little vit D, unless wild-caught fatty fish is eaten.
- Age, latitude, time of day, season of the year, use of sunblock, and pigmentation can dramatically affect the production of vit D in the skin.
- If vit D affects athletic performance, then measurements of physical performance should peak in the late summer, start to decline in early autumn, and reach their nadir in late winter. ***Guess what…?***



Main Benefits:
- **Strengthens bones**
- **Helps prevent/treat cold & flu**
- **Inhibits tumor proliferation**
- **Protects against CVD**
- **Enhances NM function**

Google: Vitamin D Council, Vitamin D Society

AJCN. First published ahead of print November 16, 2016

Vitamin C–enriched gelatin supplementation before intermittent activity augments collagen synthesis[1,2]

*Gregory Shaw,[3] Ann Lee-Barthel,[5] Megan LR Ross,[3,4] Bing Wang,[7] and Keith Baar[5,6,8]**

How to use gelatin to promote collagen synthesis

mysportscience
Unlock the Power of Science to Optimise Performance
@jeukendrup
www.mysportscience.com

Gelatin: a food source with similar amino acids found in collagen.

Consuming **15 grams of gelatin** one hour before 6 minutes of jump rope resulted in a 2-fold greater increase in collagen synthesis than intermittent exercise for 6 minutes on its own.

Ingest gelatin **1 hour before** 5-6 minute protective session

At least 6 hours before or after other training

Jumping rope for 6 min with gelatin resulted in 2-fold greater increase in collagen synthesis than jumping only.


Grazie per la vostra
ITALIA
Cortese Attenzione