BLUE STAR®

THE SCIENCE BEHIND JOINT ARMOUR™

Protect Your Joints

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THE SCIENCE BEHIND JOINT ARMOUR™

Painful joints are common for individuals of all ages, activities or experience level. At one time or another many of us have suffered anything from unexplained joint pain to overt joint injuries. As we continue to age, this problem only gets worse as our resilience to injury declines, and our time to recovery lengthens.

Joint pathologies are particularly troublesome due to their lack of innervation and vascularity, which renders them slow to repair themselves. With the lack of healing capabilities, improper treatment may lead the ailment to continue to degrade and worsen.

Loading an injured joint with excessive weight may exacerbate the injury through increased inflammation, swelling and additional trauma. However, while resting an injury seems to be the intuitive solution, without adequate movement of the joint, the rate of recovery may be further delayed. There is therefore a fairly narrow window for which the natural treatment of exercise is beneficial.

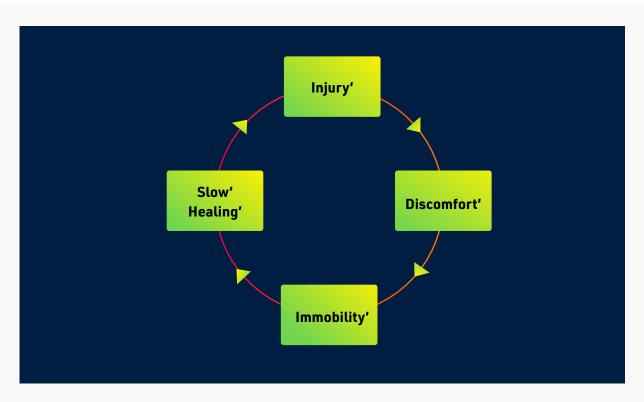


Figure 1. A common path to recurring joint injury.

All too often, joint injuries persist through discomfort causing immobility, hindering the healing process rather than exercise exacerbating the original injury. Joint $Armour^{M}$ is a product that can support joint issues that already persist, and also hinder future injuries from occurring in the first place using scientifically-backed natural joint supporting ingredients.

The core ingredients in Joint Armour[™] have been strategically formulated to intervene at three major mechanisms:

- 1) Inhibiting the enzymes responsible for joint degradation.
- 2) Stimulating the synthesis of new tissue to strengthen and/or repair the joints.
- 3) Modifying the symptoms of poor joint function.

These combined features in the Joint Armour[™] can be used at any point of the injury cycle to protect from future injuries, alleviate discomfort of current injuries and also accelerate the healing process to aid quicker recovery from joint injuries.

Joint Protection Before Injury

As the name Joint Armour $^{\mathsf{M}}$ implies, a great place to start is to reduce the incidence of injuries in the first place. For those particularly prone to injury, consuming the following two ingredients every day may help reduce the global risk of joint injury.

Cissus quadrangularis is a natural perennial plant used in traditional medicine for bone and joint health. Cissus quadrangularis contains antioxidant compounds that activate an enzyme called heme oxygenase-1 (HO-1), which is a major player in the protection of joint deterioration. It is well known that reactive oxygen species (ROS) participate in the progression of joint deterioration and several antioxidant systems may protect cartilage components. Cissus quadrangularis protects against the proinflammatory and oxidative ROS in chondrocytes, osteoblasts and synoviocytes, all of which are components of healthy bone and joints. Cissus quadrangularis has specifically been shown to promote strengthening of bone and cartilage via osteoblastic proliferation and differentiation in addition to promoting collagen synthesis in osteoblasts. In fact animal studies show that, oral intake of cissus quadrangularis can fully prevent losses of bone strength and prevent losses in bone thickness.

The joint strengthening abilities of cissus quadrandularis is just one aspect related to injury prevention. The protection of synovial fluid production is critical for joint health.

AvoVida® is a combination of unsaponifiable oils from avocado and soybeans. Mechanistic studies have indicated that AvoVida® inhibits the inflammatory marker called IL-1, known to cause destruction in many

aspects of the joints. Most significantly, AvoVida® prevents the deleterious action of IL-1 on synovial cells, which are necessary for the production of natural joint lubrication called synovial fluid. Like engine oil in a car, any reduction in lubrication can cause major damage to moving parts. In the case of joints, a healthy production of synovial fluid is absolutely critical to the prevention of joint damage.

Collectively, the oral ingestion of Cissus quadrangularis and AvoVida® are involved with diminishing the susceptibility to joint injury through improving the cellular conditions for bone, cartilage and synovial cells.



Symptom Management with Joint Injury

Physical discomfort is at the forefront of limitations endured in the face of a joint injury. The physical discomfort impedes most movements around that joint and thus limits the delivery and removal of fluids and healing factors into the affected area. Without adequate movement, swelling and inflammation remains contained rather than being dissipated and resolved in a timely fashion.

White willow bark comes from the species Salix alba and consists of the active chemical, Salicin, that when consumed is converted to salicylic acid. Being similar to the chemical makeup of aspirin, salicylic acid reduces the production of prostaglandins in the nerves, resulting in the reduction of discomfort. The anti-inflammatory activity of salicylic acid has been laboratory tested and has been shown clinically to impact symptoms of discomfort.

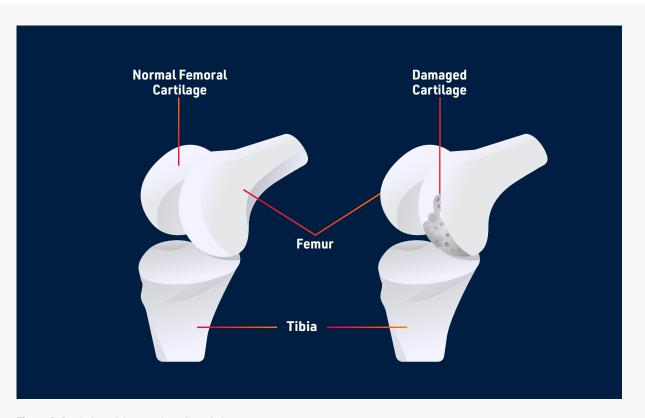


Figure 2. Depiction of damaged cartilage in knee.

Cissus quadrangularis ingestion has also been shown to reduce symptoms of discomfort as well. In a human study assessing the effects on joint pain due to excessive exercise, Cissus quadrangularis reduced the symptoms of discomfort by 31%.

Expedited Joint Recovery

What makes Joint Armour™ truly unique is not only the ability to reduce the discomfort of joint injury, but also the powerful abilities to positively affect the recovery process. This attribute separates Joint Armour™ from all other joint supplements. The most significant component to most chronic joint pain lies at the level of the articular cartilage, the tissue that covers the ends of bones where they come together and form joints. The articular cartilage is responsible for allowing the bones to glide over each other with very little friction. This surface can be easily damaged through exercise or even normal wear and tear. It is quite common with many joint injuries including those with meniscus or ligament involvement as well. The troubling conundrum is that damaged cartilage is very difficult to heal on its own. Cartilage is composed of cells called chondrocytes that surround themselves with a protein called collagen. Therefore, damage to cartilage occurs from either degradation of collagen and/or the cell death of the chondrocytes themselves.



AvoVida® has been shown to stimulate the synthesis of collagen in articular chondrocytes as well as an increase in the growth factor (TGF-β) used to accelerate chondrocyte replication. These data suggest that AvoVida® initiates and accelerates the repair process of damaged cartilage. Moreover, AvoVida® reduces the production of cartilage catabolic factors such as IL-8 and PGE2 in chondrocytes indicating an anticatabolic action as well. Applying this mechanism in a clinical population has led to the discoveries of functional joint improvements. A clinical study in 260 osteoarthritic patients over 3 months showed that a 300 mg daily dose of AvoVida® caused a 43% decrease in functional disability which correlated with a 55% decrease in joint pain.

YOU SHOULD KNOW

Painful joints are common for individuals of all ages, activities, or experience level and loading an injured joint with excessive weight only adds to the problem. At one time or another many of us have suffered from unexplained joint pain to overt joint injuries. As we continue to age, this problem only gets worse as our resilience to injury declines, and our time to recovery lengthens.

Aside from the chondrocytes regulating collagen production, an independent enzyme called MMP-3 plays a significant role in the inflammatory response to injury and contributes to the degradation of collagen protein. MMP-3 is highly expressed in many joint diseases as a pathological mediator of joint deterioration through activating a cascade of other catabolic factors. Therefore, attenuating the effects of MMP-3 would have a major impact on preventing further joint degradation and thus expediting recovery.

5-Loxin® is the newest and most exciting ingredient in Joint Armour™ making the most significant impact on joint improvement from a functional level. 5-Loxin® is a novel Boswellia serrata extract enriched with 30% 3-O-acetyl-11-keto-betaboswellic acid (AKBA), which inhibits a wide array of inflammatory cytokines including TNF-a, IL-1B and specifically, MMP-3.

In a clinical study with 75 osteoarthritic patients, daily ingestion of 100 mg of 5-Loxin® caused a 27% decrease in MMP-3 expression. This reduced MMP-3 expression was associated with a 56% decrease in joint stiffness and a 41% decrease in functional limitation after 90 days. Consequently, this also led to a 63% decrease in joint discomfort. In fact, 5-Loxin® was so impactful, the improvements in symptoms were significantly detectable within the first 7 days. For this express reason, Joint Armour™ contains the full research-backed dose of 100 mg of 5-Loxin®.

To put these results into perspective, the current standard to improve joint health that is widespread in the joint health industry is the combination of glucosamine and chondroitin. However, when measured in the same populations, and length of time, the combination of glucosamine and chondroitin was only associated with a 5.9% decrease in functional disability and a 15% decrease in pain, making AvoVida® 592% more effective at improving joint function and 270% more effective at reducing the symptoms of joint discomfort.

An alternative supplement in the industry is an undenatured type-II collagen called UC-II. While this ingredient has been growing in popularity, both AvoVida® and 5-Loxin® show strikingly stronger improvements on both joint discomfort and functional limitation. A comparison of the benefits from these ingredients as analyzed with identical measures over identical time frames is shown below.

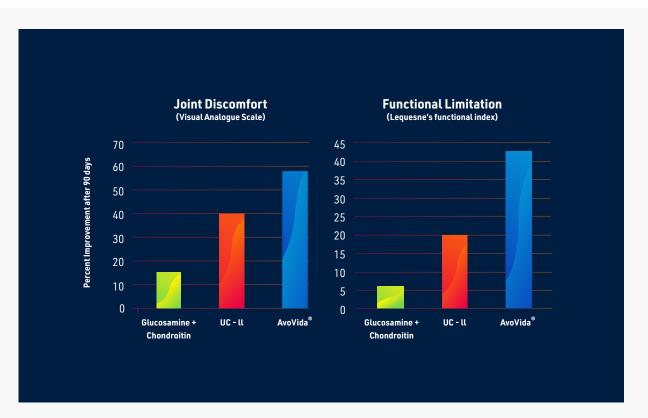


Figure 3. Percent improvement in A. joint discomfort and B. functional limitations with respect to three treatments, glucosamine + chondroitin, UC-II (undenatured type-II collagen) and AvoVida®

CONCLUSION

In regards to the common cycle of joint injury, Joint Armour[™] is equipped to support aid at any, and all points of the cycle. The combination of Cissus quadrangularis, White Willow bark, AvoVida® and 5- Loxin® work synergistically to help manage discomfort, manage symptoms and support faster recoveries.

The strengthening of the bone and cartilage while preserving the function of synovial cells provides the ultimate defense by actively reducing the risk of joint injury first. Warming up prior to exercise is important, but without healthy synovial cells producing adequate quantities of synovial fluid, joint injury is inevitable. If significant joint damage does occur, daily intakes of Joint Armour™ can support the symptoms of discomfort within the first 7 days. More importantly, to facilitate injury healing, low impact joint movement is necessary. The unmatched improvement in functional mobility by Joint Armour™ is an asset to improved recovery. However, the real power behind Joint Armour™ is the ability to intervene at the cellular level and help prevent the enzymes responsible for tissue damage, and boost the mechanisms involved with tissue healing. Joint Armour™ is therefore, the ultimate product for all aspects of joint health, from just trying to keep healthy and preventing injuries from occurring, to the management and recovery from severe joint impairments, and everything in between.



References

Alcaraz MJ, Fernandez P, Guillen MI. Anti-inflammatory actions of the heme oxygenase-1 pathway. Curr Pharm Des. 9; 2541-2551, 2003.

Appelboom T, Scheumans J, Verbruggen G, Henrotin Y, Reginster J. Symptoms modifying effects of avocado/soybean unsaponifiables (ASU) in knee osteoarthritis. Scand J Rheumatol. 30; 242-247, 2001.

Biegert C, Wagner I,m Ludtke R, Kotter I, Lohmuller C, Gunaydin I, Taxis K, Heide L. Efficacy and Safety of Willow Bark Extract in the Treatment of Osteoarthritis and Rheumatoid Arthirits: Results of 2 Randomized Double-Blind Controlled Trials. J Rheumatol. 31; 2121-2130, 2004.

Bloomer RJ et al. Cissus quadrangularis reduces joint pain in exercise-trained men: A pilot study. Phys Sportsmed. 41; 29-35, 2013.

Buillen MI, Megaias J, Gomar F et al. Heme oxygenase-1 regulates catabolic and anabolic processes in osteoarthritic chondrocytes.

Chrubasik S, Eisenberg E, Balan E, Weinberger T, Luzzati R, Conradt C. Treatment of Low Back Pain Exacerbations with Willow Bark Extract: A Randomized Double-Blind Study. Am J Med 109; 9-14, 2000.

Clancy R, Rediske J, Koehne C et al. Activation of stress-activated protein kinase in osteoarthritic cartilage: evidence for nitric oxide dependence. Osteoarthritis Cartilage. 9; 294-299, 2001.

Crowley DC, Lau FC, Sharma P, Evans M, Guthrie N, Bagchi M, Bagchi D, Dey DK, Raychaudhuri SP. Safety and efficacy of undenatured type II collagen in the treatment of osteoarthritis of the knee: a clinical trial. Int J Med Sci. 6; 312-321, 2009.

Kobayashi H, Takeno M, Saito T, et al. Regulatory role of heme oxygenase 1 in inflammation of fheumatoid arthritis. Arthritis Rheum. 54; 1132-1142, 2006.

Manicone AM, McGuire JK. Matrix Metalloproteinases as Modulators of Inflammation. Semin Cell Dev Biol. 19; 34-41, 2008.

Sun S, Bay-Jensen A, Karsdal M, Siebuhr AS, Zheng Q, Maksymowych WP, Christiansen TG, Henriksen K. The active form of MMP-3 is a merker of synovial inflammation and cartilage turnover in inflammatory joint diseases. BMC Musculoskelet Disord 15; doi: 10.1186/1471-2474-15-93, 2014.

Sengupta K, Alluri KV, Satish AR, Mishra S, Golakoti T, Sarma KV, Dey D, Raychaudhuri SP. A double blind, randomized, placebo controlled study of the efficacay and safety of 5-Loxin® for treatment of osteoarthritis of the knee. Arthritis Res Ther. 10; doi10.1186/ar2461, 2008.

Sengupta K, Krishnaraju AV, Vishal AA, Mishra A, Trimurtulu G, Sarma KV, Raychaudhuri SK, Raychaudhuri SP. Comparative Efficacy and Tolerability of 5-Loxin® and Aflapin® Against Osteoarthritis of the Knee: A Double Blind, Randomized, Placebo Controlled Clinica Study. Int J Med Sci. 7; 366-377, 2010.

Zwerina J Txima S, Hayer S et al Heme oxygenase 1 (HO-1) regulates osteoclastogenesis and bone resorption. FASEB J. 19; 2011-2013, 2005.

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Dr. David Gundermann is an award winning nutritional product development scientist, clinical researcher, and known expert in muscle health and metabolism. He developed his passion for health & fitness at a very early age growing up in a family of accomplished competitive athletes.

As Director of Research and Development at Blue Star Nutraceuticals®, he leads all efforts concerning product formulation, key ingredient research, flavor science, long-term scientific assessment, and proprietary development.

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