

The dilemma of the Arthritis patient: Is there a solution?

A safe and well documented alternative.

- By CG. Nilsson MD, Senior Specialist in Rehabilitative Medicine, Sweden (Translated)

In my role as a medical doctor specializing in rehabilitation, I am confronted daily with people suffering from serious pain. For those whose bodies no longer perform adequately, the ability to complete simple daily activities that others take for granted would be a big victory. Many arthritis sufferers, dream of being able to wake up one morning, totally pain-free and able to walk around without discomfort.

Following the publicity regarding the risk of using traditional drugs for the treatment of Arthritis pain, I believe that many people are asking for alternatives that offer fewer side effects. To be able to postpone, reduce, or eliminate the drugs known for their many negative side effects is an ambition that I share with many of my medical colleagues.

I find the new, at least in Sweden, natural herbal extracts, called Avocado and Soy Unsaponifiables (ASU) the most promising. These herbal extracts are already approved by Health Authorities in many countries as a drug or a dietary supplement. In France, for example, ASU has been known for decades. As an approved medical remedy, ASU meets all the requirements for proper clinical documentation, effectiveness, and reliability.

CG Nilsson, MD

Arthritis and Rheumatic Disorders

Rheumatic disorders consist of a group of more than 100 different diseases. These diseases may stem from a single cause, or from multiple causes, and each form requires a different kind of treatment. Osteoarthritis (OA) is currently recognized as the most prevalent rheumatic disorder.

More than 25% of all Canadians suffer from some form of rheumatic disorder, the most common symptoms being joint and skeletal pain. Statistics show that 33% of people reporting to their employers as being sick and unable to work, as diagnosed by their physicians, do so due to joint and skeletal problems.

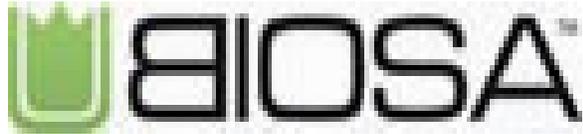
Types of Rheumatic Disorders

Rheumatic disorders are normally divided into 4 groups, each having different characteristics:

1. Deterioration of joints. E.g. Arthritis, most common is Osteoarthritis.
2. Inflammatory joint disorder, where the inflammation interferes with joint function. E.g. Rheumatic Arthritis.
3. Rheumatic system disorder, which may create inflammation not only in the joint, but also in the skin and various internal organs. E.g. Rheumatic fever and SLE (systemic lupus erythematosus) etc.
4. Other pain conditions related to the mobility of the frame. E.g. Fibromyalgia, nerve inflammations, etc.

The Problem with Conventional Treatment

The Arthritic process is often characterized by the deterioration of the cartilage. Currently there is no clinically proven drug that can cure this disorder. The current drugs used in the treatment of Arthritis are aimed at providing pain relief, alleviating joint stiffness, and reducing inflammation. The pharmaceutical industry is focused on developing effective drugs to relieve the symptoms; however these drugs do not treat the cause of the problem.



Treatment goals

With any disease, it is important to identify the goal of the particular treatment to be applied, and to determine which treatment method will offer the best results. It appears that no pharmaceutical drug available offers better results than the combination of a healthy diet and exercise program. In fact, a healthy diet, stress free lifestyle, and regular exercise may provide longer lasting and more effective results for the relief of pain and stiffness than conventional pharmaceutical drugs.

Despite this, millions of people are depending on so called “pain killers” just to overcome the daily struggle caused by OA. Even before the risks of Vioxx were published, the drug was thought to be the cause of several negative side effects that were experienced by 20% of its users.

Clinical studies show that the natural compound ASU not only leads to reduced pain and inflammation, but that it may restore joint mobility and reduce or completely eliminate the need for anti-inflammatory drugs. This fact is of great importance, because a reduced need for non-steroidal anti-inflammatory drugs (NSAIDs) and the newer Cox-2-selective inhibitors means fewer negative side effects will be experienced by their users.

The effects of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

The drugs referred to as “pain killers” consist mainly of a group of compounds known as NSAIDs. Long-term treatment with NSAIDs can lead to several negative side effects, including stomach ulcers, stomach bleeding, respiratory problems, liver and kidney impairment, circulatory disturbances, headaches, and nausea. Studies from Norway have shown that NSAIDs can even inhibit cartilage regeneration and accelerate cartilage attrition, leading to the further progression of Osteoarthritis. (Source: Knowledge Database, University of Stockholm)

What are Avocado-Soybean Unsaponifiables (ASU)?

ASU, a natural plant-based compound without any significant side effects, helps to reduce joint pain and stiffness caused by OA and other rheumatic disorders. ASU was approved as a Natural Health Product by Health Canada in June 2006, and is available under the brand name Avosol.

ASU works by balancing the forces that cause deterioration of cartilage, and enhancing those that are responsible for rebuilding cartilage. ASU is an extract composed of one third avocado oil, and two thirds soybean oil. The non-saponifiable parts of the oil, which make up approximately 1% of the total fraction, contain the active ingredients that are of interest for the treatment of rheumatic disorders.

An aspect often overlooked by Physicians

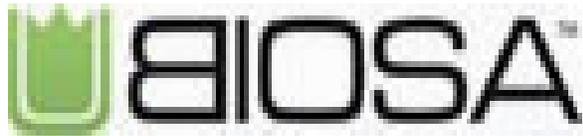
People suffering from OA or other Rheumatic Disorders generally experience an impact in **lifestyle** and **finances**, as well.

The effect on lifestyle may be:

- Depression
- Anxiety
- Feelings of helplessness
- Job limitation
- Difficulty in participating in personal and family joys and responsibilities

The effect on finances may be:

- Cost of treatment
- Lost income because of disability



ASU: Clinically proven results

At least four clinical studies have been published documenting the beneficial effects of ASU. The studies were all double blind with control and placebo groups, lasting between 3 months and 2 years. In addition to the clinical studies, a number of lab and animal research initiatives have been conducted, and several review articles have also been published.

Three of the studies indicated that 300 mg of ASU per day is sufficient to provide improved joint mobility, decrease pain, and reduce the need for NSAIDs. The studies found that ASU both stimulates the formation of new cartilage, and may consequently stop the ongoing erosion of cartilage at the same time.

Improvement of joint mobility

The aim of one two-year clinical study was to measure the change in joint space of OA patients who were either given ASU or a placebo. The study also investigated the effects of ASU on joint mobility, and monitored the level of pain experienced by the participants taking ASU compared to those taking the placebo.

When dividing the group according to seriousness of the disease, the participants with the most severe Arthritis that were receiving ASU showed significantly less change in the joint space compared to the placebo group. The differences between the two groups were statistically significant, with the researcher concluding that ASU may have a preserving effect on joint cartilage.

Neutralization of Interleukin 1 (IL-1)

ASU has a neutralizing effect on the inflammation-causing cytokine (signalling molecule) Interleukin 1 (IL-1). An increased production of IL-1 in the cellular membrane and cartilage plays an important role in the progression of Arthritis, as this inflammatory molecule can cause degeneration of bone joints. Intra-articular (between joints) injection of IL-1 in animals showed cartilage damage similar to that observed in Arthritis participants.

Review of the studies

There are a many alternative therapies for Arthritis, including herbal medicine, massage therapy, chiropractic treatments, and acupuncture. While these therapies enjoy great popularity with those who seek them out, they are less investigated by majority of the population. Due to the lack of traditional random placebo controlled double-blind studies regarding these alternative treatments, the effects that these alternative approaches have on Arthritis are virtually unknown.

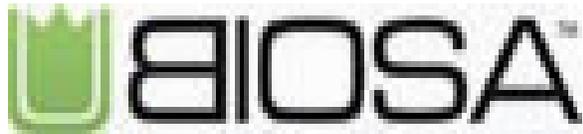
The Institute of Health and Community Studies in Bournemouth, UK, performed a meta-analysis on a number of studies founded on herbal therapies. The meta-analysis showed that the herbal treatments were well tolerated by the participants without any significant side effects. When looking for convincing documentation for the effects of herbal treatments in regard to mobility and reduction of pain, however, the Institute concluded that ASU alone provided sufficient and trustworthy documentation. In addition to this, ASU has a comprehensive safety record.

Frequently Asked Questions

Who may benefit from taking ASU?

People who:

- Have been diagnosed with, or are at risk of developing, Arthritis.
- Use pain killers such as NSAIDs for joint pains and/or joint stiffness
- Are genetically predisposed to the development of Arthritis



- Have a history of traumatic joint damage
- Have undergone joint surgery
- Are using Glucosamine sulphate and/or Chondroitin sulphate without getting the expected relief from symptoms
- Would like to use a dietary supplement based on natural components
- Are interested in preventive joint health
- Have a problem with Gingival diseases, e.g. Parodontitis

In addition to the beneficial effects of ASU on Arthritic conditions and Parodontal disease, ASU also has cholesterol-lowering effects, due to its content of plant phytosterols.

Who should avoid taking ASU ?

The effects of ASU have not been studied in the following groups:

- Pregnant women
- Breastfeeding mothers
- Children under 17 years of age

Are there any side effects from taking ASU?

ASU FROM BIOSA has a proven record as both a safe and effective treatment. Studies show that ASU is well tolerated by those taking it, and side effects are rare and very mild. There are no documented instances of interactions with ASU and other drug treatments.

How soon will I see results?

People begin seeing results, such as loss of pain and stiffness, within 3 weeks to 2 months of taking ASU.

How long will the effect last once I stop taking ASU?

The beneficial effects can last up to two months after stopping treatment with ASU.

Is it possible to substitute ASU by eating avocado and soy instead?

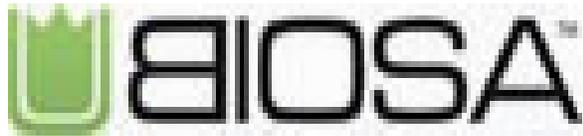
The oil portion makes up 20-30% of the avocado and soy, and less than 1% of this oil is made up of unsaponifiables. It is practically impossible to eat the amount of avocados and soy beans required to achieve the same result as with the intake of ASU.

Published Clinical Studies on Avocado and Soybean Unsaponifiables (ASU)

Blotman F, Maheu E, Wulwik A, Caspard H, Lopez A

Rev Rhum Mal Osteoartic (Eng. Ed) 1997; 64:12, 825-834

Efficacy and safety of avocado/soybean unsaponifiables in the treatment of symptomatic osteoarthritis of the knee and hip. A prospective, multicenter, three-month, randomized, double blind, placebo-controlled trial.



Objective: To evaluate the efficacy of avocado/soybean unsaponifiables as a symptomatic slow-acting agent against OA in terms of NSAID use reduction.

The investigators conducted a three-month, prospective, randomized, double blind, placebo-controlled, parallel-group trial including 164 participants suffering from OA (verified by X-ray) of either the knee (101 participants) or the hip (62 participants). Each participant had OA for at least 6 months, with regular pain requiring NSAID therapy for at least 3 months.

During the first 45 days of the study, all participants received one of seven predefined NSAIDs. Participants also received either 300 mg of ASU or a placebo. Of the 164 participants included, 163 were evaluable, with 80 participants in the ASU group, and 83 participants in the placebo group.

During the first half of the study, the use of NSAIDs was similar in both groups. After 45 days, patients receiving ASU significantly reduced their use of NSAIDs for pain management compared to the placebo group. Measurements of joint mobility showed significant improvements in the ASU group compared to the placebo group.

Conclusion: After six weeks, ASU reduced the need for NSAIDs in participants with lower limb OA. Safety was optimal in both the ASU and placebo groups

Maheu E, Mazieres B, Valat JP, Loyau G, Le Loet X, Bourgeois P, Grouin JM, Rozenberg S.

Arthritis Rheum 1998; 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 follow up demonstrating a persistent effect.

Objective: To determine whether ASU might be a symptomatic slow-acting drug in the treatment of OA by assessing the efficacy and safety of ASU in the treatment of participants with symptomatic OA of the knee or hip, as well as the residual effects of ASU after stopping the treatment.

The study included 164 participants with regular painful, OA of the knee (114 participants) or the hip (50 participants) for a 6-month treatment period, followed by a 2-month post-treatment follow-up. Efficacy of the treatment was based on improvement of joint mobility, pain, and disability patterns in participants.

The participants were divided into two parallel groups. Eighty-five participants received 300 mg of ASU and 79 participants received a placebo. After 6 months, a total of 144 participants were evaluable, consisting of 75 participants in the ASU group, and 69 participants in placebo group.

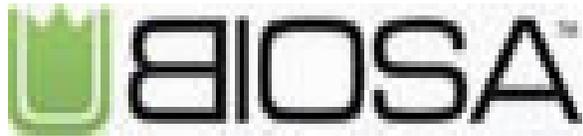
The ASU group showed improvement in mobility, decreased pain, decreased NSAIDs use and an overall decrease in functional disability compared to the placebo group, as soon as 2 months into treatment. A residual effect was observed in the ASU group 2 months after the treatment period was finished.

Conclusion: After two months of treatment, ASU showed a significant symptomatic improvement over the placebo in the treatment of OA, with beneficial effects persisting after the end of treatment.

Appelboom T, Schuermans J, Verbruggen G, Henrotin Y, Reginster JY.

Scan J Rheumatol 2001; 30(4): 242-7

Symptoms modifying effect of avocado/soybean unsaponifiables (ASU) in knee Osteoarthritis. A double blind, prospective, placebo controlled study.



Objective: To compare the symptomatic effects of 300 mg or 600 mg of ASU in participants with knee Osteoarthritis.

A total of 260 participants of both genders, aged 45 to 80, with at least a 3 month old diagnosis of OA of the knee were selected to participate in a 3 month long multicenter, double-blind, randomized and placebo controlled study. Participants were divided into three parallel groups, receiving either 300 mg of ASU, 600 mg of ASU, or a placebo. A reference period of 15 days was used in which all participants received between 90 and 110 mg of NSAIDs daily.

The intake of NSAIDs among all participants continued unchanged during the first 30 days of the study. The dose of NSAIDs was adjusted upon request for the second and third month of the study. The evaluation parameter was seen as the participants' need for NSAIDs and other anti-inflammatory drugs during the test period. The extent of pain felt and the general wellbeing of the participants were monitored by the participants and medical doctors.

A significant difference in NSAID use and pain felt by the participants was seen in the ASU groups compared to the placebo group. There was no difference seen in the amount of NSAIDs used by participants in the ASU 300 mg and the ASU 600 mg groups. During the second and third months of treatment, the consumption of NSAIDs was reduced by at least 50% compared to the reference period in both ASU groups, and both groups showed a decrease in the request of NSAIDs compared to the placebo group.

Conclusion: The efficacy of ASU at a dosage of 300 mg per day and 600 mg per day was consistently superior to that of placebo at all endpoints with no difference observed between the two dose levels. There was no difference in

the efficacy between those receiving 300 mg and 600 mg of ASU per day, confirming that the previously recommended dosage of 300 mg per day is the most appropriate.

Lequesne M, Maheu E, Cadet C, Dreiser RL.

Arthritis Rheum. 2002; 47 (1): 50-8

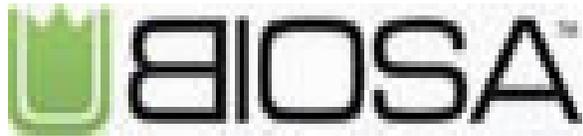
Structural effect of avocado/soy unsaponifiables on joint space loss in Osteoarthritis of the hip.

Objective: To evaluate the structural effect of ASU in the treatment of participants with symptomatic OA of the hip.

A total of 163 participants with a 6 month history of painful OA were included in a multicenter, randomized, double blind, and placebo controlled study with a duration of 2 years. Two criteria were used in the assessment of participants: a decrease in the joint space width measured by X-ray of the front of the hip with the participant in a standing position; and clinical outcome measures consisting of assessment of pain and discomfort under various conditions, maximum walking distance, the need for pain relief drugs (NSAIDs), plus a global evaluation by both doctors and participants.

After 2 years, a total of 108 participants, consisting of 72 men and 36 women with a mean age of 64 years, could be radiologically evaluated, with 55 participants in the ASU group and 53 participants in the placebo group. Overall comparison of the two groups showed no difference in the change in joint space width. However, when participants were divided into 2 subgroups based on the severity of the disease, the subgroup containing the most severe cases showed significantly less loss of joint space in the ASU group compared to the placebo group.

Conclusion: The results suggest that ASU may have a structural effect on OA of the hip, but a larger placebo-controlled study is required for confirmation.



Published Laboratory Studies on Avocado and Soybean Unsaponifiables (ASU)

Henrotin Y.E, Deberg M.A, Crielaard JM, Piccardi N, Msika P, Sanchez C.

J. Rheum. 2006; 33:8

Avocado/Soybean unsaponifiables prevent the inhibitory effect of osteoarthritis subchondral osteoblasts on aggrecan and type II collagen synthesis by chondrocytes.

Objective: To determine the effects of avocado/soybean unsaponifiables (ASU) on osteoblast-induced dysregulation of chondrocyte metabolism.

OA may be characterised by both cartilage degradation, and sclerosis (hardening) of subchondral bone, which is the area of bone below the cartilage. There is a clearly documented increase in subchondral bone growth with disease progression. This indicates that a dysregulation of bone remodelling may be part of OA.

The investigators isolated human chondrocytes (cells responsible for cartilage formation) from OA cartilage and cultured them in alginate beads for 4 or 10 days in absence or presence of osteoblasts (cells responsible for bone formation) isolated from non-sclerotic (NSC) or sclerotic (SC) zones of OA subchondral plate in monolayer.

The study found that sclerotic subchondral osteoblasts (bone building cells in the area of bone affected with OA) produced an increased production of certain factors that may be responsible for the altered bone remodelling found in OA patients. Cells treated with ASU were able to decrease this abnormal production of growth factors, suggesting that ASU could return subchondral bone to a steady-state.

Conclusion: ASU prevented the inhibition of cartilage matrix molecule production, suggesting that this compound may promote OA cartilage repair by acting on subchondral bone osteoblasts. The findings constitute a new mechanism of action for this compound, known for its beneficial effects on cartilage.

Boumediene K, Felisaz N, Bogdanowicz P, Galera P, Goullou GB, Pujol JP.

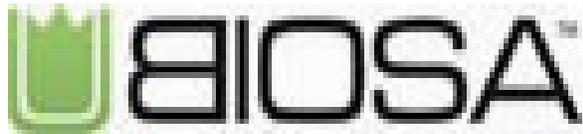
Arthritis Rheum 199; 42(1): 148-56.

Avocado/Soya unsaponifiables enhance the expression of transforming growth factor beta 1 and beta 2 cultured articular chondrocytes.

Objective: To determine the mechanism of action of ASU on articular chondrocytes that may account for its beneficial effect on cartilage metabolism.

ASU have been reported to stimulate the deposition and repair of the cartilage matrix, a gel-like substance made up of a special protein-carbohydrate complex that bathes the cartilage cells. This study was designed to determine the effect of ASU on transforming growth factor beta 1 and beta 2 (TGF β -1, TGF β -2), to determine whether these two growth factors are responsible for the beneficial effects of ASU on the treatment of osteoarthritis.

Conclusion ASU was capable of stimulating TGF β -1 and TGF β -2 expression, which provides a potential explanation for the beneficial effects of ASU on OA cartilage repair. ASU also increased the production of Plasminogen activator-inhibitor-1 (PAI-1), which has an influence on preventing the erosion of the cartilage.



Henrotin YE, Sanchez C, Deberg MA, Piccardi N, Guillou GB, Msika P, Reginster JY.

J. Rheumatol. 2003; 30(8):1825-34

Avocado/Soybean unsaponifiables increase aggrecan synthesis and reduce catabolic and pro-inflammatory mediator production by human osteoarthritic chondrocytes.

Objective: To investigate the effect of ASU on the metabolism of human OA chondrocytes cultured in alginate beads over 12 days.

The cartilage matrix consists of a gel made up of aggrecan, which are large protein-carbohydrate molecules. Matrix metalloproteinase (MMP) molecules are involved in the degradation of the cartilage matrix, and tissue inhibitor of metalloproteinase (TIMPs) inhibits the action of these MMPs.

The investigators observed that ASU stimulated the synthesis of aggrecan and TIMP-1, promoting cartilage repair, and inhibited the production of MMP-3 (stromelysin-1), thus inhibiting cartilage degradation.

Conclusion: The results suggest that ASU could have structure-modifying effects in OA by inhibiting cartilage degradation and promoting cartilage repair.

Cake MA, Read RA, Guillou B, Ghosh P.

Osteoarthritis and Cartilage 200; 8, 404-411

Modification of articular cartilage and subchondral bone pathology in an ovine meniscectomy model of osteoarthritis by avocado and soya unsaponifiables (ASU)

Objective: To examine the effect of an oral preparation of ASU on the development of joint pathology in an ovine model of OA, using computer-assisted histomorphometric methods.

OA was induced in sheep knee joints by bilateral lateral meniscectomy, a procedure in which a portion of the knee meniscus is removed. ASU (900 mg) was given to half of the group, while the other half received a placebo. Sixteen animals were not operated on, and served as a control group. Cuts were taken from the upper shank chondrals and the joint shank surface and examined histologically to determine pathology of the cartilage.

Results found a reduced loss of cartilage in ASU-treated animals compared to animals in the placebo or control groups.

Conclusion: ASU treatment following meniscectomy appeared to confer a subtle, but statistically significant protective effect on joint cartilage. The findings support other studies, which have proposed that ASU may exhibit disease-modifying anti-OA activity.

Desk review

Little CV, Parsons T, Logan S

(Cochrane Review) In: The Cochrane Library, Issue 1, 2004. Chichester, UK: John Wiley & Sons, Ltd

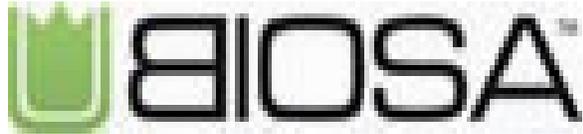
Herbal therapy for Treating Osteoarthritis

Background

The increasing popularity of complementary and alternative medicine appears to be particularly evident amongst people with chronic diseases. In the treatment of OA, one therapy that has been identified as having potential benefit is plant and herbal medicine (phytotherapy).

Objectives

To determine the effectiveness of herbal therapies in treating OA.



Strategy

Databases for mainstream and complementary medicine were searched using terms to include all forms of Arthritis combined with herbal medicine. The following electronic databases were searched: Cochrane Musculoskeletal Group register, Cochrane Complementary Medicine Field register, Cochrane Controlled trial Register (CCTR), MEDLINE, EMBASE, CISCOP, AMED, CINAHL, Dissertation Abstracts, and BIDS ISA. Reference lists from retrieved trials were also searched.

Selected Criteria

All randomized trials of herbal interventions in Osteoarthritis, compared to placebo. Studies were included according to an a priori protocol and agreement was reached between two reviewers who independently read each selected paper for content an assessment of quality. Papers of any language were included.

Data collection

Data were extracted independently by the same two reviewers.

Main Result

Five studies (four different herbal interventions) met the review criteria. Two studies were suitable for data pooling. It was not possible to draw firm conclusions from the single studies but for the two combined studies of avocado/soybean unsaponifiables showed beneficial effects on functional index, pain, intake of non-steroidal anti-inflammatory drugs (NSAIDs) and global evaluation. No serious side effects were reported.

Reviewers' conclusions

The evidence for avocado/soybean unsaponifiables in the treatment of OA is convincing, but evidence for other herbal interventions is insufficient to either recommend or discourages their use.

Further information: Biosa, Inc / 455 W Charlton Ave., / Hamilton, ON / Canada, L8P 2E9 / T: 1-905-357-0800 / info@biossa.com