RELIEF+

All-Natural Pain Relief
& Recovery*

amare® GLOBAL
THE MENTAL WELLNESS COMPANY

Technical Data Sheet

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RELIEF+

The key ingredients in Relief+ have been scientifically shown to improve sports recovery and joint health, while also providing fast-acting and long-lasting relief from occasional aches and pains.*

KEY INGREDIENTS

Pain Relief Proprietary Blend:

Turmeric Root (Meriva®) — a patented formulation of turmeric, with curcumin derived from the rhizomes (underground stems) of the plant Curcuma longa and combined with Indena's phospholipid phytosome technology to ensure the most efficient absorption, delivery, and retention in the body. People throughout India have benefited from the healthful effects of curcumin for centuries, including natural balance of inflammatory compounds and alleviation of occasional aches and pains.*

Boswellia Gum (Casperome®) — a highly purified extract, obtained from the gum resin of Boswellia serrata, a large branching tree native to India, Northern Africa, and the Middle East. Boswellia resin has a pleasant herbal scent (also known as frankincense) that was highly valued for its medicinal qualities in ancient times. Indena's phospholipid phytosome technology ensures the most efficient absorption, delivery, and retention in the body. Boswellia has demonstrated effectiveness in the management of various inflammatory response functions including those that occur in the bowel, joints and bones, and in the brain.*

Papain — a proteolytic enzyme found in concentrated amounts in unripe papaya fruit. It helps reduce pain and inflammation, as well as fluid retention following soft-tissue trauma and surgery.*

Bromelain — a proteolytic enzyme derived from pineapples, with pain relieving and anti-inflammatory effects comparable to NSAIDS (e.g. aspirin, ibuprofen, etc).*

Cayenne — a variety of hot pepper that is extremely high in a substance called capsaicin, which has positive effects on both the digestive system (reducing gut inflammation) and the nervous system (reducing pain sensations).*

White Willow Bark — has been used since the time of Hippocrates (400 BC) to ease pain and inflammation. The synthetic drug aspirin (acetyl salicylic acid) was created in 1828 by isolating the active ingredient in white willow bark (salicin).*

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Sports Recovery & Joint Health Proprietary Blend:

Univestin® — is a combination of extracts prepared from two medicinal plants "Scutellaria baicalensis" (Chinese Skullcap, huangqin, Baikal, scutellaria) and "Acacia catechu." (black cutch, katchu, wadalee gum)

1. Clinically proven to provide rapid and long-lasting relief from joint discomfort.*
2. Improves range of motion, flexibility and physical function.*
3. Great for musculoskeletal recovery, inflammatory response, and relaxant. *
4. Alleviate joint discomfort and stiffness.*
5. Improve mobility and range of motion.*
6. Enhance flexibility and physical function.*
7. Clinically shown to reduce joint stiffness within 3 days.*
8. Clinically shown to reduce joint discomfort within 5 days.*
9. Clinically shown to increase range of motion and physical function within 7 days.*
10. Supports joint health through a multi-pronged mechanism of action.*
11. Backed by two randomized, double-blind human clinical trials.*

Chamomile — a popular herb used in "calming" teas for both the digestive system and nervous system. Chamomile has been shown to relax the smooth muscles in both the digestive tract and the vascular system (blood vessels) – which may explain its reputation and traditional usage as a general calming and relaxation herbal to alleviate both stress and tension. Some studies have shown chamomile to be effective in naturally calming pain associated with soft-tissue injuries such as back pain.*

CLINICAL STUDIES

A combination of Scutellaria baicalensis and Acacia catechu extracts for short-term symptomatic relief of joint discomfort associated with osteoarthritis of the knee

Bahram H Arjmandi 1, Lauren T Ormsbee, Marcus L Elam, Sara C Campbell, Nader Rahnama, Mark E Payton, Ken Brummel-Smith, Bruce P Daggy

PMID: 24611484 PMCID: PMC4060778 DOI: 10.1089/jmf.2013.0010

Abstract

The extracts of Scutellaria baicalensis and Acacia catechu have been shown in previous studies to alleviate joint discomfort, reduce stiffness, and improve mobility by reducing the production of proinflammatory molecules over long periods of supplementation. The acute effects of intake of these extracts have not yet been investigated. Thus, we carried out a 1 week clinical trial to examine the extent to which UP446-a natural proprietary blend of S. baicalensis and A. catechu (UP446)-decreases knee joint pain, mobility, and biomarkers of inflammation in comparison to naproxen. Seventy-nine men and women (40-90 years old) diagnosed as having mild to moderate osteoarthritis (OA) consumed either 500 mg/day of the UP446 supplement or 440 mg/day of naproxen for 1 week in a double-blind randomized control trial. Pain, knee range of motion (ROM), and overall physical activity were evaluated at the start and at the end of treatment. Fasting blood was collected to determine serum interleukins 1β and 6, tumor necrosis

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factor-α, C-reactive protein, and hyaluronic acid. The UP446 group experienced a significant decrease in perceived pain (P=.009) time dependently. Stiffness was significantly reduced by both treatments (P=.002 UP446, P=.008 naproxen). Significant increases in mean ROM over time (P=.04) were found in the UP446 group. These findings suggest that UP446 is effective in reducing the physical symptoms associated with knee OA.

Burke DW, Zakhary B, Pinelis E (2014). Hepatotoxicity associated with baikal skullcap (Scutellaria baicalensis). Am J Respir Crit Care Med 189(Conference Suppl.) [abstract A6118].

A medicinal extract of Scutellaria baicalensis and Acacia catechu acts as a dual inhibitor of cyclooxygenase and 5-lipoxygenase to reduce inflammation

B P Burnett 1, Q Jia, Y Zhao, R M Levy

PMID: 17887937 DOI: 10.1089/jmf.2006.255

Abstract

A mixed extract containing two naturally occurring flavonoids, baicalin from Scutellaria baicalensis and catechin from Acacia catechu, was tested for cyclooxygenase (COX) and 5-lipoxygenase (5-LOX) inhibition via enzyme, cellular, and in vivo models. The 50% inhibitory concentration for inhibition of both ovine COX-1 and COX-2 peroxidase enzyme activities was 15 microg/mL, while the mixed extract showed a value for potato 5-LOX enzyme activity of 25 microg/mL. Prostaglandin E2 generation was inhibited by the mixed extract in human osteosarcoma cells expressing COX-2, while leukotriene production was inhibited in both human cell lines, immortalized THP-1 monocyte and HT-29 colorectal adenocarcinoma. In an arachidonic acid-induced mouse ear swelling model, the extract decreased edema in a dose-dependent manner. When arachidonic acid was injected directly into the intra-articular space of mouse ankle joints, the mixed extract abated the swelling and restored function in a rotary drum walking model. These results suggest that this natural, flavonoid mixture acts via "dual inhibition" of COX and LOX enzymes to reduce production of pro-inflammatory eicosanoids and attenuate edema in an in vivo model of inflammation.

SAFETY EVALUATION OF A COMBINATION, DEFINED EXTRACT OF SCUTELLARIA BAICALENSIS AND ACACIA CATECHU

BRUCE P. BURNETT, STACIA SILVA, MICHAEL H. MESCHES, STEVEN WILSON, QI JIA

First published: 21 November 2007 https://doi.org/10.1111/j.1745-4514.2007.00142.xCitations: 31

Abstract

A combined extract containing primarily baicalin from Scutellaria baicalensis and (+)-catechin from Acacia catechu used in both joint supplements and a prescription medical food was tested for safety. Cytotoxicity testing in THP-1 monocytes showed limited cell death compared to nonsteroidal anti-inflammatory drugs (NSAIDs). Acute and subchronic toxicity testing demonstrated no abnormalities in any toxicological end points examined including animal body weights, gross organ pathology and tissue histology, and blood chemistries or serology. The extract, when dosed in Fischer 344 rats, a model for gastric toxicity of NSAIDs, showed no evidence of ulceration. No mutagenicity or drug interactions were seen by AMES and cytochrome P450 enzyme inhibition, respectively. When the extract was compared with placebo after administration to a healthy human population, no changes in blood chemistry or serology were observed. Based on these findings, the combined extract with baicalin and catechin appears to possess a safety profile that justifies further testing in humans.

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"Effect of Univestin (Scutellaria baicalensis root & Acacia catechu heartwood) on Post-Exercise Muscle Soreness and Range of Motion in Healthy Adults"
By Shawn M Talbott, Julie A Talbott, Don Hantla

Abstract

Introduction

Intense exercise is known to increase post-exercise pain and result in delayed-onset muscle soreness (DOMS) lasting for several days. Muscle soreness and soft tissue pain is a frequent complaint among recreational exercisers and a significant obstacle to continued participation in regular physical activity.

Objective

Our study examined the effects of an herbal dietary supplement (Univestin; combination of Scutellaria baicalensis root & Acacia catechu heartwood) versus a look-alike placebo on subjective pain and range of motion (ROM) following intense exercise.

Subjects & Methods

Twenty-three (N=23) healthy men and women were recruited to participate in an intense 60-minute "boot camp style" resistance training workout designed to induce DOMS across all major muscle groups (quadriceps, hamstrings, gluteals/hips, shoulders, biceps, triceps). Subjects were randomly divided in double-blind fashion to receive either the supplement (Univestin) at 250 mg b.i.d. (N=12) or placebo (N=11) for 1-week post-exercise. We measured range of motion (ROM), joint pain (WOMAC; Western Ontario & McMaster Universities Osteoarthritis Index), and muscle pain/stiffness (VAS; visual analog score) daily during the 1-week post-exercise period.

Results

Subjective evaluation of pain/stiffness (VAS) was noticeably lower across several muscle groups (calves, gluteals/hips, biceps, triceps) at day-1 and significantly lower ($p<0.05$) by the 2nd day post-exercise in the Univestin group compared to Placebo. ROM scores were significantly higher across both shoulder and hip movements (flexion/extension) at all time points from day-1 to day-6 post-exercise in Univestin compared to Placebo ($p<0.05$). Measures of joint pain (WOMAC) were also lower in Univestin versus Placebo at some, but not all, timepoints.

Conclusion

Univestin has previously been reported to reduce the pain and stiffness associated with osteoarthritis (1–3). These clinical results further demonstrate Univestin's effectiveness to reduce post-exercise muscle pain and improve range of motion in a population of healthy non-arthritic adults. Therefore, Univestin may be viewed as an effective dietary supplement to facilitate healthy pain-free participation in regular physical activity.

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Nutrients. 2017 Jan 16;9(1). pii: E70.
Phytomedicine in Joint Disorders.
Dragos D, Gilca M, Gaman L, Vlad A, Iosif L, Stoian I, Lupescu O.

Abstract

Chronic joint inflammatory disorders such as osteoarthritis and rheumatoid arthritis have in common an upsurge of inflammation, and oxidative stress, resulting in progressive histological alterations and disabling symptoms. Currently used conventional medication (ranging from pain-killers to biological agents) is potent, but frequently associated with serious, even life-threatening side effects. Used for millennia in traditional herbalism, medicinal plants are a promising alternative, with lower rate of adverse events and efficiency frequently comparable with that of conventional drugs. Nevertheless, their mechanism of action is in many cases elusive and/or uncertain. Even though many of them have been proven effective in studies done in vitro or on animal models, there is a scarcity of human clinical evidence. The purpose of this review is to summarize the available scientific information on the following joint-friendly medicinal plants, which have been tested in human studies: Arnica montana, Boswellia spp., Curcuma spp., Equisetum arvense, Harpagophytum procumbens, Salix spp., Sesamum indicum, Symphytum officinalis, Zingiber officinalis, Panax notoginseng, and Whitania somnifera.

Inflammopharmacology. 2016 Dec;24(6):377-388.
Curcuma longa extract reduces inflammatory and oxidative stress biomarkers in osteoarthritis of knee: a fourmonth, double-blind, randomized, placebo-controlled trial.
Srivastava S, Saksena AK, Khattri S, Kumar S, Dagur RS.

Abstract

BACKGROUND AND PURPOSE:

Curcuma longa L. (CL), an Indian herb, has been used to treat many disorders because of its wide spectrum of pharmacological activities. It has been shown to exhibit anti-oxidant and anti-inflammatory properties, and is being used as herbal remedy since ancient times. Osteoarthritis of knee (KOA) is a chronic painful disorder in which prolong use of non-steroidal anti-inflammatory drugs (NSAIDs) or steroids may result into many serious side effects; hence, there is a need to develop herbal drugs, having good analgesia without side effects. Therefore, we planned to evaluate the efficacy of CL in KOA.

METHODS:

The study was designed as a randomized, double-blind, placebo-controlled trial in patients of KOA. After obtaining ethical clearance and written informed consent, a total of 160 patients of KOA were randomly enrolled into two groups to receive either CL extract or placebo along with the standard drug regimen. The patients were assessed on day 0, day 60, and day 120. On the days of their visit, the clinical prognosis was assessed by visual analog scale (VAS) and Western Ontario and McMaster Universities (WOMAC) Osteoarthritis index. On these days, the radiographs were also taken for Kellgren and Lawrence grading and blood samples were collected for assessing the changes in levels of IL-1β and biomarkers of oxidative stress, such as reactive oxygen species and malondialdehyde (MDA).

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RESULTS:
Over all significant improvement was observed in the patients of CL extract group as compared to placebo group. Clinically, the VAS and WOMAC scores became better, and simultaneously, the levels of biomarkers, viz., IL-1β, ROS, and MDA, were also significantly ($p < 0.05$) improved.

CONCLUSION:
It may be concluded that on chronic administration, CL suppresses inflammation and brings clinical improvement in patients of KOA, which may be observed by decreased level of IL-1β and VAS/WOMAC scores, respectively. At the same time, CL decreases the oxidative stress also.

Drug Des Devel Ther. 2016 Sep 20;10:3029-3042.
The spice for joint inflammation: anti-inflammatory role of curcumin in treating osteoarthritis.
Chin KY.

Abstract

Osteoarthritis is a degenerative disease of the joint affecting aging populations worldwide. It has an underlying inflammatory cause, which contributes to the loss of chondrocytes, leading to diminished cartilage layer at the affected joints. Compounds with anti-inflammatory properties are potential treatment agents for osteoarthritis. Curcumin derived from Curcuma species is an anti-inflammatory compound as such. This review aims to summarize the antiosteoarthritic effects of curcumin derived fromclinical and preclinical studies. Many clinical trials have been conducted to determine the effectiveness of curcumin in osteoarthritic patients. Extracts of Curcuma species, curcuminoids and enhanced curcumin, were used in these studies. Patients with osteoarthritis showed improvement in pain, physical function, and quality of life after taking curcumin. They also reported reduced concomitant usage of analgesics and side effects during treatment. In vitro studies demonstrated that curcumin could prevent the apoptosis of chondrocytes, suppress the release of proteoglycans and metal metalloproteases and expression of cyclooxygenase, prostaglandin E-2, and inflammatory cytokines in chondrocytes. These were achieved by blocking the activation of nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) system in the chondrocytes, by preventing the activation of nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha, phosphorylation, and translocation of the p65 subunit of NF-κB complexes into the nucleus. In conclusion, curcumin is a potential candidate for the treatment of osteoarthritis. More well-planned randomized control trials and enhanced curcumin formulation are required to justify the use of curcumin in treating osteoarthritis.

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J Med Food. 2016 Aug;19(8):717-29.
Efficacy of Turmeric Extracts and Curcumin for Alleviating the Symptoms of Joint Arthritis: A Systematic Reviewand Meta-Analysis of Randomized Clinical Trials.
Daily JW, Yang M, Park S.

Abstract

Although turmeric and its curcumin-enriched extracts have been used for treating arthritis, no systematic review and meta-analysis of randomized clinical trials (RCTs) have been conducted to evaluate the strength of the research. We systemically evaluated all RCTs of turmeric extracts and curcumin for treating arthritis symptoms to elucidate the efficacy of curcuma for alleviating the symptoms of arthritis. Literature searches were conducted using 12 electronic databases, including PubMed, Embase, Cochrane Library, Korean databases, Chinese medical databases, and Indian scientific database. Search terms used were "turmeric," "curcuma," "curcumin," "arthritis," and "osteoarthritis." A pain visual analogue score (PVAS) and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) were used for the major outcomes of arthritis. Initial searches yielded 29 articles, of which 8 met specific selection criteria. Three among the included RCTs reported reduction of PVAS (mean difference: -2.04 [-2.85, -1.24]) with turmeric/curcumin in comparison with placebo ($P < .00001$), whereas meta-analysis of four studies showed a decrease of WOMAC with turmeric/curcumin treatment (mean difference: -15.36 [-26.9, -3.77]; $P = .009$). Furthermore, there was no significant mean difference in PVAS between turmeric/ curcumin and pain medicine in meta-analysis of five studies. Eight RCTs included in the review exhibited low to moderate risk of bias. There was no publication bias in the meta-analysis. In conclusion, these RCTs provide scientific evidence that supports the efficacy of turmeric extract (about 1000 mg/day of curcumin) in the treatment of arthritis. However, the total number of RCTs included in the analysis, the total sample size, and the methodological quality of the primary studies were not sufficient to draw definitive conclusions. Thus, more rigorous and larger studies are needed to confirm the therapeutic efficacy of turmeric for arthritis.

J Evid Based Complementary Altern Med. 2017 Jan;22(1):156-165.
Efficacy of Curcuma for Treatment of Osteoarthritis.
Perkins K, Sahy W, Beckett RD.

Abstract

The objective of this review is to identify, summarize, and evaluate clinical trials to determine the efficacy of curcuma in the treatment of osteoarthritis. A literature search for interventional studies assessing efficacy of curcuma was performed, resulting in 8 clinical trials. Studies have investigated the effect of curcuma on pain, stiffness, and functionality in patients with knee osteoarthritis. Curcuma containing products consistently demonstrated statistically significant improvement in osteoarthritis related endpoints compared with placebo, with one exception. When compared with active control, curcuma-containing products were similar to nonsteroidal anti-inflammatory drugs, and potentially to glucosamine. While statistical significant differences in outcomes were reported in a majority of studies, the small magnitude of effect and presence of major study limitations hinder application of these results. Further rigorous studies are needed prior to recommending curcuma as an effective alternative therapy for knee osteoarthritis.

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Curr Gastroenterol Rep. 2016 Apr;18(4):19.
Chili Peppers, Curcumins, and Prebiotics in Gastrointestinal Health and Disease.
Patcharatrakul T, Gonlachanvit S.

Abstract

There is growing evidence for the role of several natural products as either useful agents or adjuncts in the management of functional GI disorders (FGIDs). In this review, we examine the medical evidence for three such compounds: chili, a culinary spice; curcumin, another spice and active derivative of a root bark; and prebiotics, which are nondigestible food products. Chili may affect the pathogenesis of abdominal pain especially in functional dyspepsia and cause other symptoms. It may have a therapeutic role in FGIDs through desensitization of transient receptor potential vanilloid-1 receptor. Curcumin, the active ingredient of turmeric rhizome, has been shown in several preclinical studies and uncontrolled clinical trials as having effects on gut inflammation, gut permeability and the brain-gut axis, especially in FGIDs. Prebiotics, the non-digestible food ingredients in dietary fiber, may serve as nutrients and selectively stimulate the growth and/or activity of certain colonic bacteria. The net effect of this change on colonic microbiota may lead to the production of acidic metabolites and other compounds that help to reduce the production of toxins and suppress the growth of harmful or disease-causing enteric pathogens. Although some clinical benefit in IBS has been shown, high dose intake of prebiotics may cause more bloating from bacterial fermentation.

Nutr J. 2016 Jan 5;15:1.
Benefits of antioxidant supplements for knee osteoarthritis: rationale and reality.
Grover AK, Samson SE.

Abstract

Arthritis causes disability due to pain and inflammation in joints. There are many forms of arthritis, one of which is osteoarthritis whose prevalence increases with age. It occurs in various joints including hip, knee and hand with knee osteoarthritis being more prevalent. There is no cure for it. The management strategies include exercise, glucosamine plus chondroitin sulfate and NSAIDs. In vitro and animal studies provide a rationale for the use of antioxidant supplements for its management. This review assesses the reality of the benefits of antioxidant supplements in the management of knee osteoarthritis. Several difficulties were encountered in examining this issue: poorly conducted studies, a lack of uniformity in disease definition and diagnosis, and muddling of conclusions from attempts to isolate the efficacious molecules. The antioxidant supplements with most evidence for benefit for pain relief and function in knee osteoarthritis were based on curcumin and avocado-soya bean unsaponifiables. Boswellia and some herbs used in Ayurvedic and Chinese medicine may also be useful. The benefits of cuisines with the appropriate antioxidants should be assessed because they may be more economical and easier to incorporate into the lifestyle.

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Musculoskelet Surg. 2015 Sep;99 Suppl 1:S43-52.
Co-analgesic therapy for arthroscopic supraspinatus tendon repair pain using a dietary supplement containing
Boswellia serrata and Curcuma longa: a prospective randomized placebo-controlled study.
Merolla G, Dellabiancia F, Ingardia A, Paladini P, Porcellini G.

Abstract

BACKGROUND:
The cuff tendon that is most prone to full-thickness rotator cuff tears is the supraspinatus (SSP). Arthroscopic SSP repair ensures good to satisfactory mid- to long-term clinical outcomes. However, the intense postoperative pain reduces rehabilitation compliance and is cause of patient dissatisfaction. Many natural compounds act by inhibiting inflammatory pathways in a similar way to anti-inflammatory drugs

MATERIALS AND METHODS: This was a prospective randomized trial designed to assess the analgesic effect of a dietary supplement (DS) containing Boswellia serrata and Curcuma longa in a population of subjects with full-thickness SSP tendon tear treated by arthroscopy. Three weeks before surgery, patients were randomized to receive Tendisulfur(®) (group T) or a placebo (group P) for 2 months. The primary outcome measure was subjective VAS pain. Secondary outcomes measures were Constant-Murley score simple shoulder test, and patient global assessment (PGA) scores. Patients were assessed immediately at baseline and subsequently at 1, 2, 4, 6, 8, 12, and 24 weeks.

RESULTS: Stratification of pain scores and subscores demonstrated significantly lower overall pain scores in group T versus group P at 1 week ($p = 0.0477$), and lower but not significantly different scores on week 2 ($p = 0.0988$); at subsequent time points, differences were not significant ($p > 0.05$). PGA scores were good in all subjects.

CONCLUSIONS: In conclusion, this study provides objective data on the effect of a DS containing natural substances, added to standard analgesics, on postoperative RC pain. DS alleviated short and partially mid-term pain, while long-term pain was unchanged. This limitation can probably be addressed by a dosage increase over the first 4 weeks and by extending treatment by 1 or 2 months.

Clin Interv Aging. 2014 Mar 20;9:451-8. Efficacy and safety of Curcuma domestica extracts compared with ibuprofen in patients with knee osteoarthritis: a multicenter study. Kuptniratsaikul V, Dajpratham P, Taechaarpornkul W, Buntragulpoontawee M, Lukkanapichonchut P, Chootip C, Saengsuwan J, Tantayakom K, Laongpech S.

Abstract

OBJECTIVE: To determine the efficacy and safety of Curcuma domestica extracts in pain reduction and functional improvement. METHODS: 367 primary knee osteoarthritis patients with a pain score of 5 or higher were randomized to receive ibuprofen 1,200 mg/day or C. domestica extracts 1,500 mg/day for 4 weeks. The main outcomes were Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) total, WOMAC pain, WOMAC stiffness, and WOMAC function scores. Adverse events (AEs) were also recorded. RESULTS: 185 and 182 patients were randomly assigned into C. domestica extracts

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and ibuprofen groups, respectively. The baseline characteristics were no different between groups. The mean of all WOMAC scores at weeks 0, 2, and 4 showed significant improvement when compared with the baseline in both groups. After using the noninferiority test, the mean difference (95% confidence interval) of WOMAC total, WOMAC pain, and WOMAC function scores at week 4 adjusted by values at week 0 of C. domestica extracts were noninferior to those for the ibuprofen group (P=0.010, P=0.018, and P=0.010, respectively), except for the WOMAC stiffness subscale, which showed a trend toward significance (P=0.060). The number of patients who developed AEs was no different between groups. However, the number of events of abdominal pain/discomfort was significantly higher in the ibuprofen group than that in the C. domestica extracts group (P=0.046). Most subjects (96%-97%) were satisfied with the treatment, and two-thirds rated themselves as improved in a global assessment.

CONCLUSION:
C. domestica extracts are as effective as ibuprofen for the treatment of knee osteoarthritis. The side effect profile was similar but with fewer gastrointestinal AE reports in the C. domestica extracts group.

Crit Rev Food Sci Nutr. 2013;53(5):507-16.
Plant food supplements with anti-inflammatory properties: a systematic review (II).
Di Lorenzo C1, Dell'Agli M, Badea M, Dima L, Colombo E, Sangiovanni E, Restani P, Bosisio E.

Abstract

The aim of this systematic review is to summarize the evidence for or against the efficacy of plant food supplements (PFS) for coping inflammatory conditions by considering epidemiological and human intervention studies. The review considers six botanical species commonly used as food supplements/ medicinals: Urtica dioica L., Symphytum officinalis L., Calendula officinalis L., Curcuma longa L., Boswellia serrata Roxb., and Harpagophytum procumbens L. The search retrieved 579 publications. By removing the duplicates and applying the inclusion/exclusion criteria, the final number of papers was 47. No epidemiological data were found. The bibliographic search found no paper regarding the anti-inflammatory effects of Calendula officinalis L. and Symphytum officinalis L. by oral use. In spite of the long-term traditional use for inflammatory disorders, Curcuma longa L. and Harpagophytum procumbens L. warrant further investigation, whereas the efficacy of Urtica dioica L, even if the available data on hard endpoints are promising, requires other trials. Boswellia serrata Roxb. was found to be the most promising, since it shows the best efficacy for the treatment of pain/inflammatory conditions. In conclusion, it is advisable to conduct further studies with more homogeneous population and larger number of subjects by avoiding the heterogeneity of the herbal preparations considered.

Inflammopharmacology. 2013 Apr;21(2):129-36. Safety and efficacy of Curcuma longa extract in the treatment of painful knee osteoarthritis: a randomized placebo-controlled trial. Madhu K, Chanda K, Saji MJ.

Abstract

Curcuma longa Linn. is widely used for the treatment of disorders associated with inflammation and was evaluated for its safety and efficacy in the treatment of painful knee osteoarthritis (OA). This was a randomized, single blind, placebo-controlled trial. Total of 120 patients (37 males and 83 females) with primary knee OA received either placebo (400 mg twice daily) or NR-INF-02 (500 mg twice daily) or

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glucosamine sulphate (GS) (750 mg twice daily) alone or combination of NR-INF-02 and GS for 42 days. The efficacy was assessed during treatment period, on day 21 and day 42. The decrease in severity of pain symptom and function of affected knee as primary efficacy outcome measure was assessed by Visual Analog Scale (VAS) and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scale, respectively. The clinical examination of affected joint was measured by an orthopaedic specialist and using a Clinician Global Impression Change (CGIC) scale. The analysis of post-treatment scores following administration of NR-INF-02 using VAS, WOMAC, and CGIC at each clinical visit showed significant decrease ($p < 0.05$) compared to placebo. NR-INF-02 treated group showed a significant ($p < 0.01$) decrease in use of rescue medication, along with clinical and subjective improvement compared to placebo. The tolerability and acceptability profile of NR-INF-02 was better during the trial period. The study demonstrates safety and efficacy of NR-INF-02 as a useful treatment option for patients with primary painful knee OA.

J Med Assoc Thai. 2012 Jan;95 Suppl 1:S51-8.
The efficacy of Curcuma Longa L. extract as an adjuvant therapy in primary knee osteoarthritis: a randomized control trial.
Pinsornsak P, Niempoog S.

Abstract

Nonsteroidal anti-inflammatory Drugs (NSAIDs) is one of the most commonly use medication for treatment of knee osteoarthritis which has the analgesic and anti-inflammation by inhibition of prostaglandin synthesis via COX-1 and COX-2 isoenzyme. The problem of prolong using NSAIDs has side effect on kidney, liver and GI system. Curcumin longa extract Curcumin) is the Asian herbal medicine that has the anti-inflammatory effect by down regulate activation of NF-kappaB and proinflammatory cytokines such as Tumor Necrotic Factor-alpha, Interleukin-1, Interleukin-8, and Nitric Oxide Synthase. Many research data had advocate for the combination therapy which can increase safety and efficacy with less side effect compare with monotherapy regimen especially when the medicine has the different mechanism of action. The present study is the double blind prospective randomized control trial to evaluate the efficacy of curcumin as an adjuvant therapy of diclofenac in primary knee osteoarthritis. 44 patients were randomized to take NSAIDs (diclofenac) 75 mg/d with placebo and the other 44 took NSAIDs (diclofenac) 75 mg/d with curcumin 1,000 mg/d for 3 months. The authors evaluated the Visual Analog Scale (VAS) for pain and Knee Injury and Osteoarthritis Outcome Score (KOOS) every month for 3 months. At the end of study 36 patients were completed for the first group and 37 for the study group. There was no difference in VAS [p-value = 0.923 (F = 0.009)]. The KOOS was analyzed in 5 categories symptom, pain, function in daily living, function in sport and recreation and knee related quality of life. The curcumin with diclofenac group had tendency to be better in Pain and Function in daily living, but there were no statistic different in all group [p-value = 0.412 (F = 0.683), p-value = 0.814 (F = 0.056), p-value = 0.446 (F = 0.589), p-value = 0.224 (F = 1.511) and p-value = 0.938 (F = 0.006)]. In conclusion, the adjuvant therapy of curcumin with diclofenac has the potential beneficial effect in comparison with diclofenac alone, but no statistical significance.

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Eur Rev Med Pharmacol Sci. 2016 Oct;20(19):4156-4161. A novel lecithin based delivery form of Boswellic acids (Casperome®) for the management of osteo-muscular pain: a registry study in young rugby players. Franceschi F, Togni S, Belcaro G, Dugall M, Luzzi R, Ledda A, Pellegrini L, Eggenhoffner R, Giacomelli L.

Abstract

OBJECTIVE:
Several experimental studies and clinical trials support the potential of Boswellia serrata extracts (BSE) for the treatment of various inflammatory diseases. The aim of this registry study was to assess the safety and the efficacy of a novel lecithin-based delivery form of Boswellia serrata extract (Casperome®) in the supportive management of osteo-muscular pain.

PATIENTS AND METHODS:
52 healthy young rugby players with acute knee pain and inflammation were recruited. Informed participants freely decided to follow either a standard management (SM) to control joint pain (control group = 27) or SM associated with oral daily supplementation with Casperome® (supplement group =25). Parameters associated with osteo-muscular pain and inflammation, and measurements of joint health and functions were assessed at the inclusion and after a 4-week supplementation.

RESULTS:
A significant beneficial effect of Casperome® vs SM alone was observed for all the parameters evaluated, namely: local pain on effort; pain-free walking distance (treadmill test); minimal joint effusion; structural damage (joint, tendons, muscles) and intramuscular hematomas; thermal imaging of the anterior knee; Visual Analog Scale for Pain (VAS Pain); need for concomitant drugs and medical attention; measurement of inflammatory biomarkers.

CONCLUSIONS:
Our registry study suggests that Casperome® supplementation could represent an effective and safe, integrated approach for the treatment of osteo-muscular pain and inflammation.

Eur Rev Med Pharmacol Sci. 2016 Jun;20(12):2695-700.
Managing ulcerative colitis in remission phase: usefulness of Casperome®, an innovative lecithin-based delivery system of Boswellia serrata extract.
Pellegrini L, Milano E, Franceschi F, Belcaro G, Gizzi G, Feragalli B, Dugall M, Luzzi R, Togni S, Eggenhoffner R, Giacomelli L.

Abstract

OBJECTIVE:
Boswellia serrata extracts (BSE) have been traditionally used for the treatment of several inflammatory diseases. The aim of this study was to evaluate the efficacy of a novel delivery form of BSE (Casperome®) in Ulcerative Colitis (UC) during minimally symptomatic remission phase.

PATIENTS AND METHODS:
In this open-label, observational, registry study, informed participants with UC in remission phase (n = 43) freely decided to receive the oral daily Casperome® supplementation (n = 22) or no supplementation

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(n = 21) for 4 weeks. Several parameters associated with minimally symptomatic UC in remission were evaluated at the inclusion and the end of the study.

RESULTS:
A significant beneficial effect of Casperome® was observed for all the parameters evaluated, namely: diffuse intestinal pain, evident and occult blood in stools, bowel movements and cramps, watery stools, malaise, anemia, rectal involvement, number of white blood cells as well as need for concomitant drugs and medical attention. Faecal concentration of calprotectin, a marker of bowel inflammation, resulted ameliorated in Casperome® supplemented patients.

CONCLUSIONS:
Our study showed that Casperome® supplementation attenuates symptoms associated with mild UC in remission, reducing the use of drugs and medical consultations. Therefore, our study suggests that Casperome® supplementation could represent a promising alternative approach to manage minimally symptomatic UC and maintain the remission phase.

Minerva Med. 2014 Dec;105(6 Suppl 2):9-16.
FlexiQule (Boswellia extract) in the supplementary management of osteoarthritis: a supplement registry.
Belcaro G, Dugall M, Luzzi R, Ledda A, Pellegrini L, Cesarone MR, Hosoi M, Errichi M, Francis S, Cornelli U.

Abstract

The aim of the present pilot, registry study was an assessment in a supplement study of FlexiQule (standardized Boswellia extract) capsules in the supplementary management of patients with symptomatic knee osteoarthritis (OA) also treated with the "standard management" (SM) in comparison with a group of patients only managed with SM.

METHODS:
This 4-week study included patients with symptomatic knee arthrosis (X-ray). Registry subjects were able to perform a treadmill walking test and to understand questions from the WOMAC questionnaire. Exclusion criteria were conditions requiring drug treatment, Body Mass Index >25, metabolic disorders, surgery within three months prior to inclusion, oncological condition or inability to walk.

RESULTS:
Twenty-seven registry subjects using the supplement+SM and 28 using only SM completed the registry; at inclusion, the two groups were comparable including Karnofsky scale, WOMAC Score and the Treadmill Test. Of the subjects completing the registry 24 preferred to use the combination SM and the supplement. Safety evaluation: no problems - indicating the suspension of the supplementation - were observed. Routine blood tests were normal at inclusion and did not significantly vary at 4 weeks. The Karnofski Scale at 4 weeks was improved in both groups: from 74.3;3.1 to 88.9;5.3 ($P<0.05$) in the Boswellia group in comparison with a variation from 75.3;5.2 to 79.4;3.3 ($P<0.05$) in the SM. The effects of the supplement were significantly higher ($P<0.05$). The WOMAC Score was decreased significantly more in the supplement+SM group in comparison with controls considering pain, stiffness and physical functions ($P<0.05$). Social/emotional functions improved better with the supplement ($P<0.05$). Both groups improved their walking distance at 4 weeks. The improvement was higher ($P<0.05$) in the

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Boswellia group. The need for other drugs or tests during the registry period was reduced more in the supplement group (P<0.05).

CONCLUSION:
The difference between SM and the supplementation associated to SM was significant) in favor of the supplementation with Boswellia for all target measurements evaluated in the registry at 4 weeks.

Indian J Pharmacol. 2014 Sep-Oct;46(5):475-9.
A randomized, double blind, placebo controlled, cross over study to evaluate the analgesic activity of Boswellia serrata in healthy volunteers using mechanical pain model.
Prabhavathi K, Chandra US, Soanker R, Rani PU.

Abstract

OBJECTIVE:
Experimental pain models in human healthy volunteers are advantageous for early evaluation of analgesics. All efforts to develop nonsteroidal anti-inflammatory drugs (NSAIDs) which are devoid of gastrointestinal and cardiovascular system effects are still far from achieving a breakthrough. Hence we evaluated the analgesic activity of an ayurvedic drug, Boswellia serrata by using validated human pain models which has shown its analgesic activity both in-vitro and preclinical studies to evaluate the analgesic activity of single oral dose (125 mg, 2 capsules) of Boswellia serrata compared to placebo using mechanical pain model in healthy human subjects.

MATERIALS AND METHODS:
After taking written informed consent, twelve healthy subjects were randomized (1:1) to receive single oral dose of Boswellia serrata (Shallaki (®)) 125 mg, 2 capsules or identical placebo in a crossover design. Mechanical pain was assessed using Ugo basile analgesymeter (by Randall Selitto test) at baseline and at 1 hr, 2 hrs and 3 hrs after test drug administration. Pain Threshold force and time and Pain Tolerance force and time were evaluated. Statistical analysis was done by paired t-test.

RESULTS:
Twelve healthy volunteers have completed the study. Mean percentage change from baseline in Pain Threshold force and time with Boswellia serrata when compared to placebo had significantly increased [Force: 9.7 ± 11.0 vs 2.9 ± 3.4 (P = 0.05) and time: 9.7 ± 10.7 vs 2.8 ± 3.4 (P = 0.04)] at third hr. Mean Percentage change from baseline in Pain Tolerance force and time with Boswellia serrata when compared to placebo had significantly (P ≤ 0.01) increased at 1 hr, 2 hrs and 3 hrs.

CONCLUSION:
In the present study, Boswellia serrata significantly increased the Pain Threshold and Pain Tolerance force and time compared to placebo. Both study medications were well tolerated. Further multiple dose studies may be needed to establish the analgesic efficacy of the drug.

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Rheumatology (Oxford). 2013 Aug;52(8):1408-17. doi: 10.1093/rheumatology/kes414. Epub 2013 Jan 30.
Ayurvedic medicine offers a good alternative to glucosamine and celecoxib in the treatment of symptomatic knee osteoarthritis: a randomized, double-blind, controlled equivalence drug trial.

Cephalalgia. 2012 Jul;32(9):719-22.
Long-term efficacy of Boswellia serrata in four patients with chronic cluster headache.
Lampl C, Haider B, Schweiger C.

Abstract

BACKGROUND:
Cluster headache is an extremely severe and debilitating trigemino-autonomic pain syndrome. About 10% of patients with cluster headache manifest a chronic form (CCH).The present case series study aims to evaluate the long-term efficacy of Boswellia serrata (Sallaki H15) on headaches and disturbed sleep in patients with CCH.

CASE RESULTS:
In an open-label study, four patients with CCH and disturbed sleep received oral B. serrata.

CONCLUSION:
The results provide Class IV evidence that oral B. serrata reduces the intensity and frequency of headaches in patients with CCH.

Phytomedicine. 2003 Jan;10(1):3-7.
Efficacy and tolerability of Boswellia serrata extract in treatment of osteoarthritis of knee--a randomized double blind placebo controlled trial.
Kimmatkar N, Thawani V, Hingorani L, Khiyani R.

Abstract

Osteoarthritis is a common, chronic, progressive, skeletal, degenerative disorder, which commonly affects the knee joint. Boswellia serrata tree is commonly found in India. The therapeutic value of its gum (guggulu) has been known. It posses good anti-inflammatory, anti-arthritic and analgesic activity. A randomized double blind placebo-controlled crossover study was conducted to assess the efficacy, safety and tolerability of Boswellia serrata Extract (BSE) in 30 patients of osteoarthritis of knee, 15 each receiving active drug or placebo for eight weeks. After the first intervention, washout was given and then the groups were crossed over to receive the opposite intervention for eight weeks. All patients receiving drug treatment reported decrease in knee pain, increased knee flexion and increased walking distance. The frequency of swelling in the knee joint was decreased. Radiologically there was no change. The observed differences between drug treated and placebo being statistically significant, are clinically relevant. BSE was well tolerated by the subjects except for minor gastrointestinal ADRs. BSE is recommended in the patients of osteoarthritis of the knee with possible therapeutic use in other arthritis.

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Planta Med. 2001 Jul;67(5):391-5.
Effects of gum resin of Boswellia serrata in patients with chronic colitis.
Gupta I, Parihar A, Malhotra P, Gupta S, Lüdtke R, Safayhi H, Ammon HP.

Abstract

Patients studied here suffered from chronic colitis characterized by vague lower abdominal pain, bleeding per rectum with diarrhea and palpable tender descending and sigmoid colon. The inflammatory process in colitis is associated with increased formation of leukotrienes causing chemotaxis, chemokinesis, synthesis of superoxide radicals and release of lysosomal enzymes by phagocytes. The key enzyme for leukotriene biosynthesis is 5-lipoxygenase. Boswellic acids were found to be non-redox, non-competitive specific inhibitors of the enzyme 5-lipoxygenase. We studied the gum resin of Boswellia serrata for the treatment of this disease. Thirty patients, 17 males and 13 females in the age range of 18 to 48 years with chronic colitis were included in this study. Twenty patients were given a preparation of the gum resin of Boswellia serrata (900 mg daily divided in three doses for 6 weeks) and ten patients were given sulfasalazine (3 gm daily divided in three doses for 6 weeks) and served as controls. Out of 20 patients treated with Boswellia gum resin 18 patients showed an improvement in one or more of the parameters: including stool properties, histopathology as well as scanning electron microscopy, besides haemoglobin, serum iron, calcium, phosphorus, proteins, total leukocytes and eosinophils. In the control group 6 out of 10 patients showed similar results with the same parameters. Out of 20 patients treated with Boswellia gum resin 14 went into remission while in case of sulfasalazine remission rate was 4 out of 10. In conclusion, this study shows that a gum resin preparation from Boswellia serrata could be effective in the treatment of chronic colitis with minimal side effects.

Eur J Med Res. 1997 Jan;2(1):37-43. Effects of Boswellia serrata gum resin in patients with ulcerative colitis.
Gupta I, Parihar A, Malhotra P, Singh GB, Lüdtke R, Safayhi H, Ammon HP.

Abstract

Ulcerative colitis is a chronic inflammatory disease of the colon where leukotrienes are suggested to play an important role for keeping inflammation active. Boswellic acids, the biologically active ingredients of the gum resin of Boswellia serrata (Sallai guggal), have been shown to be specific, nonredox and noncompetitive inhibitors of 5-lipoxygenase, the key enzyme of leukotriene biosynthesis. In patients suffering from ulcerative colitis grade II and III the effect of Boswellia serrata gum resin preparation (350 mg thrice daily for 6 weeks) on stool properties, histolopathology and scan microscopy of rectal biopsies, blood parameters including Hb, serum iron, calcium, phosphorus, proteins, total leukocytes and eosinophils was studied. Patients receiving sulfasalazine (1 g thrice daily) served as controls. All parameters tested improved after treatment with Boswellia serrata gum resin, the results being similar compared to controls: 82% out of treated patients went into remission; in case of sulfasalazine remission rate was 75%.

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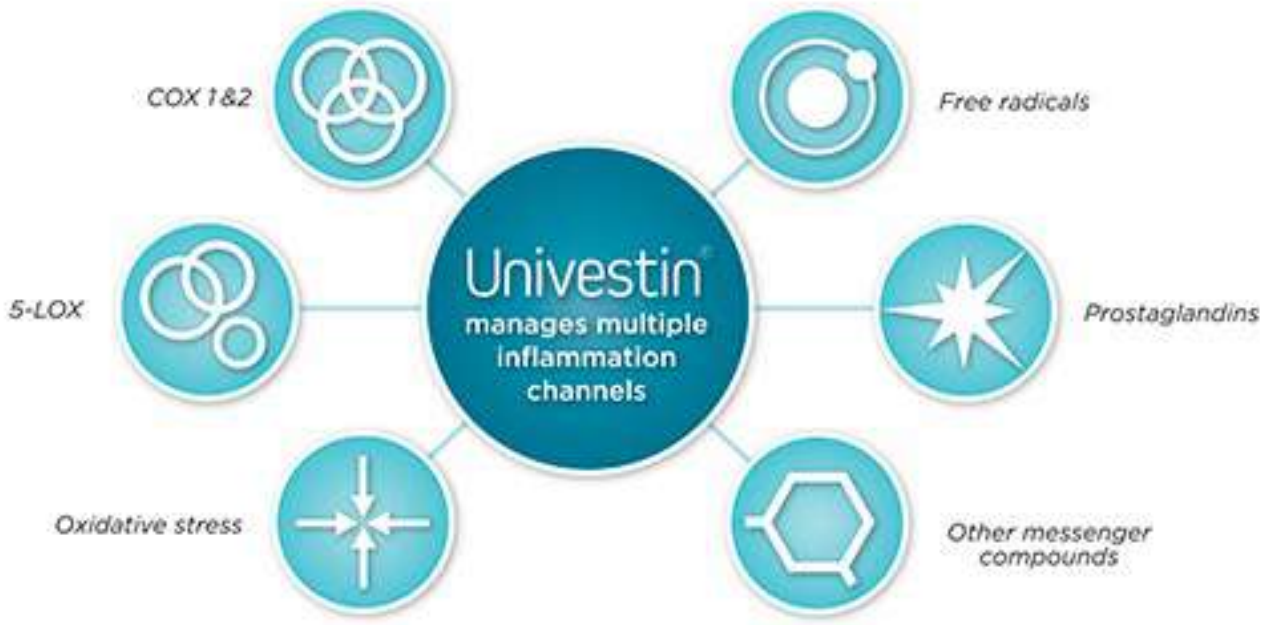
Univestin Additional Info



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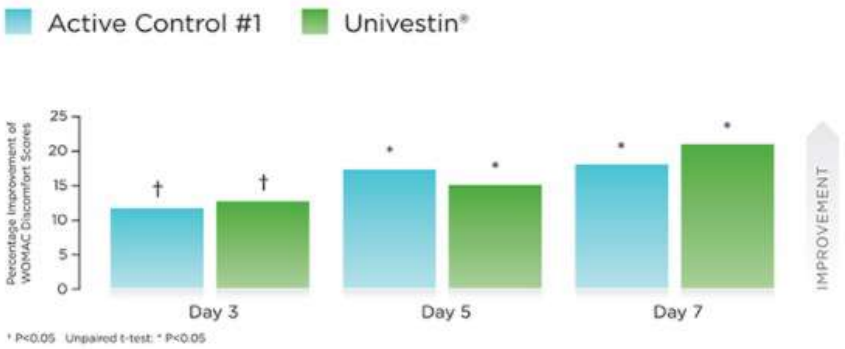
Results in 3 days*

With Univestin, consumers feel results fast.* The product's multi-pronged mechanism of action (MOA) modulates multiple reactions at once, helping prevent escalation.* As a result, oxidative stress and processes that cause joint discomfort are neutralized more rapidly.*

How fast? A human clinical trial comparing Univestin to an active control demonstrated that Univestin delivers results in as few as 3 days.*

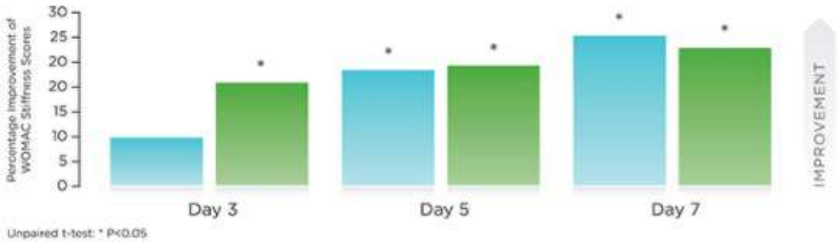
Joint Discomfort

Univestin reduces joint discomfort within 5 days*



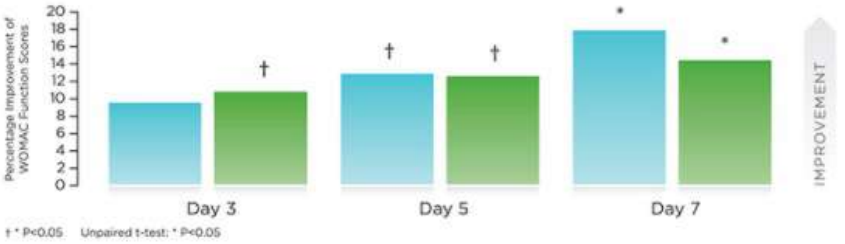
Joint Stiffness and Mobility

Univestin reduces joint stiffness and increases joint mobility within 3 days*



Joint Function

Univestin improves joint function within 7 days*



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2 Lasting Comfort

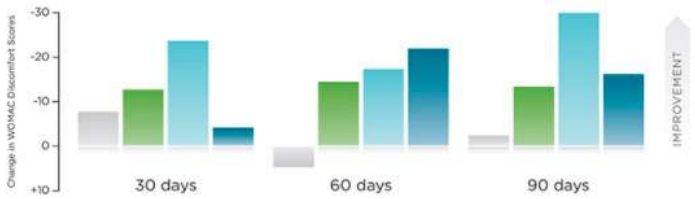
Proven effective for 90 days*

Consumers choose a joint health supplement they can continue to take on a recurring basis, one whose long-term effectiveness is backed by clinical results. Univestin's continued efficacy has been clinically proven in a randomized, double-blind placebo-controlled 90-day trial.* Univestin was compared to both a placebo and an active control, WOMAC scores for joint discomfort, stiffness and physical function all showed increasing improvement from 30 to 90 days.*

Placebo | Univestin® 250 mgs/d | Univestin® 500 mgs/d | Active Control #2 200 mgs/d

Joint Discomfort

Univestin continues to reduce joint discomfort in 90-day clinical trial*

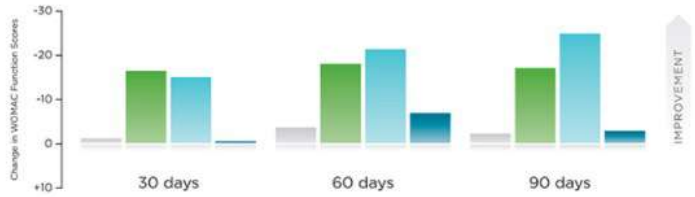


Joint Stiffness and Mobility

Univestin continues to reduce joint stiffness & increase mobility in 90-day clinical trial*

Joint Function

Univestin continues to improve joint function in 90-day clinical trial*



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