Bibliography report on how ingredients of Helix original 30 caps help the function of the joints

Turmeric rhizome powder: *Curcuma longa L.* (*Curcuma domestica*)

Kuptniratsaikul V et al. Efficacy and Safety of *Curcuma domestica* Extracts in Patients with Knee Osteoarthritis. The Journal of Alternative and Complementary Medicine. 2009;15(8):891-7.

Patients with primary knee osteoarthritis were randomized to *C. domestica* extracts and ibuprofen groups. The main outcomes were improvement in joint complaints on level walking, on stairs, and functions of knee assessed by time spent during 100-m walk and going up and down a flight of stairs. *C. domestica* extracts seem to be similarly helpful and safe as ibuprofen for the management of knee osteoarthritis.

Chandran B et al. A Randomized, Pilot Study to Assess the Efficacy and Safety of Curcumin in Patients with Active Rheumatoid Arthritis. Phytother Res. 2012;26(11):1719-25.

Patients diagnosed with rheumatoid arthritis (RA) were randomized into three groups with patients receiving curcumin and diclofenac sodium alone or their combination. The curcumin group showed the highest percentage of improvement in overall joint problems and these scores were significantly better than the patients in the diclofenac sodium group. This study provides the first evidence for the safety and superiority of curcumin benefits in active RA.

Belcaro G et al. Meriva®+Glucosamine versus Condroitin+Glucosamine in patients with knee osteoarthritis: an observational study. European Review for Medical and Pharmacological Sciences. 2014;18: 3959-63.

A 'real-life' scenario compared the association of Meriva® (a lecithin delivery form of curcumin) and glucosamine with chondroitin sulphate+glucosamine in patients with grade 1-2 osteoarthritis (OA) of the knee. The Meriva®+glucosamine group showed significantly higher performance and improved benefits (both in the physical and emotional domains), compared to those in the chondroitin+glucosamine group.

Panahi Y. et al. Curcuminoid Treatment for Knee osteoarthritis: A Randomized Double-Blind Placebo-Controlled Trial. Phytother Res. 2014;28(11):1625-31.

Patients with mild-to-moderate knee osteoarthritis (OA) were assigned to curcuminoids or matched placebo for 6 weeks. Supplementation with curcuminoids was associated with significantly greater

reductions in joint complaints compared with placebo. Curcuminoids represent a helpful and safe alternative approach to minimize articular discomfort in OA.

Nakagawa Y et al. Short-term effects of highly bioavailable curcumin for treating knee osteoarthritis: a randomized, double-blind, placebo-controlled prospective study. J Orthop Sci (2014) 19:933-9.

Patients with knee osteoarthritis (OA) of Kellgren–Lawrence grade II or III were randomized into two groups with patients receiving placebo or Theracurmin® (containing 180 mg/day of curcumin) for 8 weeks. Mostly, knee discomfort was significantly lower in the Theracurmin® group than in the placebo group.

Kuptniratsaikul V et al. Efficacy and safety of *Curcuma domestica* extracts compared with ibuprofen in patients with knee osteoarthritis: a multicenter study. Clinical Interventions in Aging. 2014;9:451-8.

Primary knee osteoarthritis patients were randomized to receive ibuprofen or *C. domestica* extracts for 4 weeks. Several parameters related to articular inconveniences and function were assessed. *C. domestica* extracts were as helpful as ibuprofen minimizing articular discomfort of knee osteoarthritis, and patients' global assessment and satisfaction at week 4 also was no different between groups.

Appelboom T et al. A New Curcuma Extract (Flexofytol®) in Osteoarthritis: Results from a Belgian Real-Life Experience. The Open Rheumatology Journal. 2014;8:77-81.

Retrospective observational approach that summarizes the experiences of >800 patients supplemented with a Curcuma extract (Flexofytol®), for more than 6 months for various forms of osteoarthritis. Flexofytol® improved patient articular difficulties, articular mobility, and quality of life. Excellent tolerance was reported, and more than half of these patients were able to discontinue analgesic and anti-inflammatory drugs.

Snail powder (allantoin-rich)

Lira Cortés AJ. Allantoin determination in Chilean snail secretion (*Helix aspersa* Müller). [Date of consultation: October 2020]
Available: http://cybertesis.uach.cl/tesis/uach/2008/fcl768d/doc/fcl768d.pdf

The concentrated extract of snail secretions, naturally rich in components such as **allantoin**, glycolic acid, proteins, collagen and elastin, is obtained by specialized processes in which the animals are stimulated to secrete the fluids. Subsequently, the quality and quantity of the active components present in the secretion is guaranteed by purification and concentration techniques.

Conte R. Recent advances on nano delivery of Helix mucus pharmacologically active components. Int. J. Nano Dimens.2016;7(3):181-5.

Snails are members of the phylum Mollusca. Specifically, the main Helix species are *Helix aspersa* and *Helix Pomatia*. The land helix use in health is described by several authors since antiquity. Importantly, **Allantoin**, Helicidine, Helix pomatia agglutinin, Collagen, Elastin, Natural antibiotics and Glycolic acid show beneficial properties.
Allantoin is a substance broadly used as active ingredient in over-the-counter cosmetics, thanks to its moisturizing and keratolytic effects, the ability to increase the water content of the extracellular matrix the capacity to enhance the desquamation of upper layers of dead skin cells and the aptitude to promote cell proliferation and wound healing. Moreover, Allantoin is a soothing, anti-irritant, and skin protectant agent by forming complexes with irritant and sensitizing substances.

Tsoutsos D et al. The efficacy of Helix aspersa Müller extract in the healing of partial thickness burns: a novel treatment for open burn management protocols. J Dermatolog Treat. 2009;20(4):219-22.

Snail extracts are used in many dermatological conditions for their anti-inflammatory, calming and regenerating properties. *Helix aspersa* protein extract is an effective approach in the management of open wounds caused by partial thickness burns in adults.

Giannetti BM et al. Efficacy and safety of a Comfrey root extract ointment in the treatment of acute upper or low back pain: results of a double-blind, randomised, placebo-controlled, multicentre trial. Br J Sports Med. 2010;44(9):637-41.

A phytotherapeutic cream rich in allantoin is an effective method to relieve acute back inconveniences and discomfort. The analgesic effect of the topical application of creams rich in allantoin, obtained from root extracts of *Symphytum officinale L.*, has been described in various episodes, such as knee osteoarthritis and ankle injuries.

Lope-Lopez J et al. Efficacy of chlorhexidine, dexpanthenol, allantoin and chitosan gel in comparison with bicarbonate oral rinse in controlling post-interventional inflammation, pain and cicatrization in subjects undergoing dental surgery. Curr Med Res Opin. 2015;31(12):2179-83.

Prospective sequential cross-over, randomized controlled study in patients undergoing surgical removal of at least two impacted mandibular third molars to determine the effect of Bexident Post (BP) (containing chlorhexidine, dexpanthenol, allantoin and chitosan) in comparison with bicarbonate (BC) oral rinse, both used three times daily. BP performed better than BC in controlling discomfort and inflammation in subjects undergoing dental surgery, reducing the consumption of analgesics, and helping better cicatrization.

Boswellia Oleoresin extract (*Boswellia serrata*)

Kimmatkar N et al. Efficacy and tolerability of *Boswellia serrata* extract in treatment of osteoarthritis of knee – A randomized double-blind placebo-controlled trial. Phytomedicine. 2003;10:3-7.

Assessment of the efficacy, safety and tolerability of *Boswellia serrata* extract in patients suffering from knee osteoarthritis (active ingredient or placebo) for eight weeks. All patients receiving oral supplementation of *Boswellia serrata* extract reported decrease in knee discomfort and increased knee functionality (flexion and increased walking distance). The frequency of swelling in the knee joint was also reduced.

Haroyan A et al. Efficacy and safety of curcumin and its combination with boswellic acid in osteoarthritis: a comparative, randomized, double-blind, placebo-controlled study. BMC Complementary and Alternative Medicine. 2018;18(1):7.

Assessment of the efficacy of the Curamin® (*Boswellia serrata*) and CuraMed® (*Curcuma longa L*) supplements in patients diagnosed with degenerative hypertrophic osteoarthritis (OA) of knee bone joints. 12-week supplementation of curcumin complex or its combination with boswellic acids reduced articular inconveniences in patients with OA. Combining *Curcuma longa* and *Boswellia serrata* extracts in Curamin® increased the efficacy of management of OA presumably due to synergistic effects of curcumin and boswellic acid.

Majeed M et al. A pilot, randomized, double-blind, placebo-controlled trial to assess the safety and efficacy of a novel *Boswellia serrata* extract in the management of osteoarthritis of the knee. Phytother Res. 2019;33(5):1457-68.

Evaluation of the safety and efficacy of a standardized oral supplementation of Boswellin®, a novel extract of *Boswellia serrata* extract (BSE). Patients with osteoarthritis of the knee were randomized and allocated to the BSE and placebo groups for 120 days. BSE helped the physical and functional articular ability and contributed to ameliorate the joint difficulties and stiffness.

Italiano G et al. Benefits of a Food Supplement Containing *Boswellia serrata* and Bromelain for Improving the Quality of Life in Patients with Osteoarthritis: A Pilot Study. J Altern Complement Med. 2020;26(2):123-9.

Patients with osteoarthritis (OA) took a Boswellia- and bromelain-based supplement for a period between 1 and 6 months. The use of the gastroresistant formulation containing the combination of Boswellia and bromelain supplements can represent a valuable nonpharmacological tool for improving the QoL and independence (in conducting daily activities) of patients experiencing bone and joint difficulties.

Sengupta K et al. A double blind, randomized, placebo-controlled study of the efficacy and safety of 5-Loxin® for treatment of osteoarthritis of the knee. Arthritis Research & Therapy. 2008;10:R85.

Osteoarthritis patients received 5-Loxin® (novel *Boswellia serrata* extract enriched with 30% 3-O-acetyl-11-keto-beta-boswellic acid) daily or a placebo for 90 days. Both doses of 5-Loxin® tested improved joint health and physical function by helping to diminish joint discomfort.

L-ascorbic acid - Vitamin C

McAlindon TE et al. Do antioxidant micronutrients protect against the development and progression of knee osteoarthritis? Arthritis and Rheumatism. 1996;39(4):648-56.

Reactive oxygen species can be generated by both chondrocytes and neutrophils and can cause damage to hyaluronan and cartilage matrix components such as proteoglycans and collagen, the integrity of which are important for the mechanical properties of articular cartilage. Prospective observational study with participants in the Framingham Osteoarthritis Cohort Study that underwent complete radiographic and nutritional data assessments. High intake of antioxidant micronutrients, especially vitamin C, may contribute to lessen the risk of cartilage loss and disease progression in people with osteoarthritis.

Hall MG et al. The vitamin C requirement in rheumatoid arthritis. Annals of Internal Medicine. 1939;13(3):415-23.

Patients with rheumatoid arthritis show an apparent vitamin C deficiency as indicated by low concentration of the vitamin in the blood. Patients with rheumatoid arthritis have a much greater demand for vitamin C than the normal individual.

Carr AC et al. The role of vitamin C in the treatment of pain: new insights. J Transl Med. 2017;15:77.

The vitamin C deficiency disease scurvy is characterized by musculoskeletal complaints and recent epidemiological evidence has indicated an association between suboptimal vitamin C status and spinal discomfort. Furthermore, accumulating evidence indicates that vitamin C administration can exhibit analgesic properties in some clinical conditions. Overall, vitamin C appears to be a safe and beneficial supplement for acute and chronic discomfort relief in specific patient groups.

DePhillipo NN et al. Efficacy of Vitamin C Supplementation on Collagen Synthesis and Oxidative Stress After Musculoskeletal Injuries. The Orthopaedic Journal of Sports Medicine. 2018 6(10):2325967118804544.

Systematic review, with the inclusion criteria of animal and human studies, on vitamin C supplementation after a musculoskeletal injury specific to collagen (a crucial matrix component of articular cartilage) cross-linking, collagen synthesis, and biologic healing of the bone, ligament, and tendon. Vitamin C supports bone healing after a fracture, helps type I collagen synthesis, and reduces oxidative stress parameters.