Collagen and Joints

A double-blind, placebo-controlled, randomised, clinical study on the effectiveness of collagen peptide on osteoarthritis.

"Recent studies show that enzymatically hydrolysed collagen, the collagen peptide, is absorbed and distributed to joint tissues and has analgesic and anti-inflammatory properties. A double-blind, placebo-controlled, randomised trial with collagen peptides isolated from pork skin (PCP) and bovine bone (BCP) sources was carried out to study the effectiveness of orally supplemented collagen peptide to control the progression of osteoarthritis in patients diagnosed with knee osteoarthritis...The study demonstrated that collagen peptides are potential therapeutic agents as nutritional supplements for the management of osteoarthritis and maintenance of joint health."


Oral administration of type-II collagen peptide 250-270 suppresses specific cellular and humoral immune response in collagen-induced arthritis.

"These observations suggest that oral administration of chicken collagen II (CII) can suppress the cellular and humoral immune response in collagen-induced arthritis."


Change in knee osteoarthritis cartilage detected by delayed gadolinium enhanced magnetic resonance imaging following treatment with collagen hydrolysate: A pilot randomized controlled trial

“Single center, prospective, randomized, placebo-controlled, double-blind, pilot trial of collagen hydrolysate for mild knee osteoarthritis (OA)...These preliminary results suggest that the dGEMRIC technique may be able to detect change in proteoglycan content in knee cartilage among individuals taking collagen hydrolysate after 24 weeks.”


Effects of Pro-Hyp, a collagen hydrolysate-derived peptide, on hyaluronic acid synthesis using in vitro cultured synovium cells and oral ingestion of collagen hydrolysates in a guinea pig model of osteoarthritis

“The results suggest that collagen hydrolysates have therapeutic potential for treatment of osteoarthritis.”


Efficacy and tolerance of enzymatic hydrolysed collagen (EHC) vs. glucosamine sulphate (GS) in the treatment of knee osteoarthritis (KOA).

"This was a 13-week, multicentre, randomised, parallel, double-blind study...Clear improvement was observed in both joint pain and symptoms in patients with KOA treated with EHC and significant differences were observed...pain intensity reduction in the target knee for EHC... WOMAC index decrease ≤ 15 points at the last visit for EHC (34.04%) and for glucosamine (13.04%)...patient's global assessment of efficacy as the sum of improvement good + ideal: 80.8% for EHC and 46.6% for glucosamine. EHC showed superior improvement over GS in the SF-36 Questionnaire in the Physical Health Index."


Collagen hydrolysate for the treatment of osteoarthritis and other joint disorders: a review of the literature.

"According to published research, orally administered collagen hydrolysate has been shown to be absorbed intestinally and to accumulate in cartilage. Collagen hydrolysate ingestion stimulates a statistically significant increase in synthesis of extracellular matrix macromolecules by chondrocytes (p < 0.05 compared with untreated controls). These findings...showed collagen hydrolysate to be safe and to provide improvement in some measures of pain and function in some men and women with OA or other arthritic conditions...A growing body of evidence provides a rationale for the use of collagen hydrolysate for patients with OA."

Control of rheumatoid arthritis by oral tolerance
“This randomized, double-blind, controlled trial examined the therapeutic effect of bovine type II collagen (CII) tablets in rheumatoid arthritis... Treatment with 0.5 mg/day of bovine CII is well tolerated and produces small, but significant, disease improvement in RA... There were no side effects associated with CII treatment.”

Oral administration of an immunodominant human collagen peptide modulates collagen-induced arthritis.
"Arthritis severity was reduced markedly in mice orally tolerized with Human type II collagen (HuCII) 250-270 peptide both at early and effector phases. Suppression of CIA at the effector phase by oral administration of HuCII peptide suggests a potential immunotherapeutic use of collagen II peptide in the treatment of human RA."

24-Week study on the use of collagen hydrolysate as a dietary supplement in athletes with activity-related joint pain
“The results of this study have implications for the use of collagen hydrolysate to support joint health and possibly reduce the risk of joint deterioration in a high-risk group... the results suggest that athletes consuming collagen hydrolysate can reduce parameters (such as pain) that have a negative impact on athletic performance.”

Effect of collagen hydrolysate in articular pain: a 6-month randomized, double-blind, placebo controlled study
“At 6 months, the proportion of clinical responders to the treatment, according to VAS scores, was significantly higher in the collagen hydrolysate (CH) group... This study suggests that collagen hydrolysate 1200 mg/day could increase the number of clinical responders (i.e. improvement of at least 20% on the VAS) compared to placebo.”

A randomized controlled trial on the efficacy and safety of a food ingredient, collagen hydrolysate, for improving joint comfort
“There was a significant improvement in knee joint comfort as assessed by visual analogue scales to assess pain and the Womac pain subscale. Subjects with the greatest joint deterioration, and with least intake of meat protein in their habitual diets, benefited most.”

Chemotactic attraction of human fibroblasts to type I, II, and III collagens and collagen-derived peptides
"Since collagen is degraded and remodeled at sites of tissue injury and inflammation, these findings suggest that collagen and collagen-degradation peptides might function as chemotactic stimuli for fibroblasts in vivo and attract these cells to effect repair of damaged tissue."

Stimulation of type II collagen biosynthesis and secretion in bovine chondrocytes cultured with degraded collagen
“These results clearly indicate a stimulatory effect of degraded collagen on the type II collagen biosynthesis of chondrocytes and suggest a possible feedback mechanism for the regulation of collagen turnover in cartilage tissue.”

Type III collagen, a fibril network modifier in articular cartilage.
"The present findings emphasize the role of type III collagen, which is synthesized in mature articular cartilage, as a covalent modifier that may add cohesion to a weakened, existing collagen type II fibril network as part of a chondrocyte healing response to matrix damage."
Oral administration of (14)C labeled gelatin hydrolysate leads to an accumulation of radioactivity in cartilage of mice (C57/BL).
"In cartilage, measured radioactivity was more than twice as high following gelatin administration compared to the control group...These results demonstrate intestinal absorption and cartilage tissue accumulation of gelatin hydrolysate and suggest a potential mechanism for previously observed clinical benefits of orally administered gelatin."

Effects of ingestion of collagen peptide on collagen fibrils and glycosaminoglycans in Achilles tendon.
"These results suggest that the ingestion of collagen peptide affects the size of collagen fibrils and composition of glycosaminoglycans in the Achilles tendon and thus may improve the mechanical properties of the Achilles tendon."

The effects of collagen hydrolysate on symptoms of chronic fibromyalgia and temporomandibular joint pain.
"It was concluded that patients with fibromyalgia and concurrent temporomandibular joint problems may gain symptomatic improvement in their chronic symptoms by taking collagen hydrolysate."

Phenotypic re-expression of near quiescent chondrocytes: The effects of type II collagen and growth factors.
"The data showed that exogenous type I collagen and type II collagen at 1:1 ratio stimulate cell proliferation greatly while type II collagen alone was enough to revive most of cartilaginous functions of near quiescent P9 chondrocytes. Exogenous type II collagen by itself was more effective in restoring cell proliferation rate, elevating glycosaminoglycan (GAG) accumulation and promoting the re-expression of type II collagen mRNAs in the near quiescent chondrocytes."

Chondroprotective effect of the bioactive peptide prolyl-hydroxyproline in mouse articular cartilage in vitro and in vivo.
"In vivo, CH and Pro-Hyp inhibited the loss of chondrocytes and thinning of the articular cartilage layer caused by phosphorus-induced degradation...Moreover, CH and Pro-Hyp caused two and threefold increases, respectively, in the staining area of glycosaminoglycan in the extracellular matrix of ATDC5 cells."

Collagen and Bone

The role of collagen in bone strength.
"Bone is a sophisticated composite material with complex relationships between mineral and collagen that influence bone strength. A change in collagen properties may alter the amount and disposition of the mineral, which would by itself affect bone mechanics... Several studies suggest that part of the large variation in bone strength may be related to differences in the quality of the collagenous matrix... Type I collagen comprises approximately 95% of the entire collagen content of bone and about 80% of the total proteins present in bone... In bone, a large body of evidence indicates that type I collagen molecules are involved in mechanical properties of bone. Several studies indicate that collagen plays a substantial role in its toughness (capacity to absorb energy), while the mineral content is mainly involved in determining bone stiffness... the collagen network may become weaker with age, leading to decreased toughness... After menopause, hormonal and systemic factors may also directly or indirectly modify type I collagen properties. For example, estrogen deficiency has been suggested to affect the stability of collagen by decreasing LOX activity."
Vigué-Carrin S1, Garnero P, Delmas PD. Osteoporos Int. 2006;17(3):319-36.
Early gene and protein expression associated with osteoblast differentiation in response to fish collagen peptides powder.
"After one, three, five and seven days of culture, the number of FCP-treated cells increased significantly compared with untreated cells. In a real-time PCR analysis, the expression of osteocalcin, osteopontin, BMP-2 and integrin β3 mRNAs in FCP-treated cells showed increases compared with untreated cells after three days of culture...The production of osteocalcin, osteopontin and integrin β3 proteins in FCP-treated cells also showed increases after seven days of culture. Furthermore, FCP accelerated matrix mineralization in the cultures."

Osteoporosis, a unitary hypothesis of collagen loss in skin and bone.
"Changes in skin collagen correspond to changes in bone density...thus a loss of collagen in skin and bones with aging is the causal counterpart to loss of bone density in senile osteoporosis... skin collagen and the production of collagen by skin fibroblasts could be used for the assay and industrial development of more potent, if not less toxic treatments and prevention of loss of bone (and skin) substance."

Osteogenic activity of collagen peptide via ERK/MAPK pathway mediated boosting of collagen synthesis and its therapeutic efficacy in osteoporotic bone by back-scattered electron imaging and microarchitecture analysis.
"Collagen hydrolysate (CH) increased osteoblastic cell proliferation and alkaline phosphatase activity in a dose-dependent manner. Collagen synthesis and collagen, type1, alpha1 (COL1A1) gene expression were also increased by CH treatment...OVX rats supplemented with CH showed osteoprotective effects as the BMD levels were increased compared with control. Moreover, CH prevented the trabecular bone loss induced by OVX and improved the microarchitecture of lumbar vertebrae...The present study suggests that CH isolated in this study is a promising alternative to current therapeutic agents for the management of osteoporosis."

Increase in bone mineral density through oral administration of shark gelatin to ovariectomized rats.
"Administering collagen to the ovariectomized rats resulted in the bone mineral density of the femur epiphysis being higher than that in the sham-operated rats. The contents of type I collagen and glycosaminoglycan in the epiphysis were increased by administering shark skin gelatin. These results indicated that shark skin gelatin would be useful as a dietary supplement for treating osteoporosis."

A Calcium-Collagen Chelate Dietary Supplement Attenuates Bone Loss in Postmenopausal Women with Osteopenia: A Randomized Controlled Trial.
"The loss of whole body BMD in women taking CC was substantially lower than that of the control group at 12 months in those who completed the study...These results support the use of CC in reducing bone loss in osteopenic postmenopausal women."

Absorption and effectiveness of orally administered low molecular weight collagen hydrolysate in rats
“Our findings show that LMW-CH exerts a beneficial effect on osteoporosis by increasing the organic substance content of bone.”

Skin wrinkling and rigidity are predictive of bone mineral density in early postmenopausal women
“In a population of early postmenopausal women, study of the skin is observed to provide a glimpse into the status of the skeleton, a relationship not previously described.”
Hydrolyzed collagen improves bone status and prevents bone loss in ovariectomized C3H/HeN mice.
"Moreover, hydrolyzed collagen (HC) ingestion for 1 month before surgery prevented BMD decrease...Ingestion of 25 g/kg of HC for 3 or 6 months reduced bone loss significantly in, respectively, 3- and 6-month-old OVX mice...HC ingestion for 3 months is as efficient as raloxifene to protect 3-month-old OVX mice from bone loss...This study confirms that dietary collagen reduces bone loss in OVX mice by increasing the diameter of the cortical areas of femurs and can have a preventive effect."

Hydrolyzed collagen intake increases bone mass of growing rats trained with running exercise
“The present study demonstrated that moderate HC intake (where the diet contains 20% protein, of which 30% is HC) increased bone mass during growth period and further promoted the effect of running exercise.”

Effects of fish collagen peptides on collagen post-translational modifications and mineralization in an osteoblastic cell culture system.
"These results indicate that FCP exerts a positive effect on osteoblastic cells in terms of collagen synthesis, quality and mineralization, thereby suggesting the potential utility of FCP for bone tissue engineering."

Postmenopausal osteoporosis. Treatment with calcitonin and a diet rich in collagen proteins.
"Forty-nine of these women took an oral collagen hydrolysate, 10 g per day, for the same period of time...oral administration of collagen proteins enhanced and prolonged the effect of calcitonin."

Assessment of effectiveness of oral administration of collagen peptide on bone metabolism in growing and mature rats
"These results suggest that orally administered collagen peptide may provide beneficial effects on bone metabolism, especially in the calcium-deficient condition, without obvious undesirable effects."

Role of collagen hydrolysate in bone and joint disease
“Collagen hydrolysate is of interest as a therapeutic agent of potential utility in the treatment of osteoarthritis and osteoporosis. Its high level of safety makes it attractive as an agent for long-term use in these chronic disorders.”

A food supplement of hydrolyzed collagen improves compositional and biodynamic characteristics of vertebrae in ovariectomized rats.
"The vertebrae of the ovariectomized group that received the higher dosage of CH withstood a load four times greater and exhibited higher levels of protein and osteocalcin content than those receiving either gelatin or no supplement."

Porcine skin gelatin hydrolysate promotes longitudinal bone growth in adolescent rats.
"CHs dose-dependently promoted the longitudinal bone growth and height of the growth plate in adolescent male rats, whereas gelatin failed to affect longitudinal bone growth. Insulin-like growth factor-1 and bone morphogenetic protein-2 in the CH treated group were highly expressed in the growth plate. These results suggest that CHs isolated in this study may provide beneficial effects on bone metabolism of growing animals and humans."
HA, Glucosamine & Joints

**Oral Administration of Polymer Hyaluronic Acid Alleviates Symptoms of Knee Osteoarthritis: A Double-Blind, Placebo-Controlled Study over a 12-Month Period**

"Oral administration of HA may improve the symptoms of knee OA in patients aged 70 years or younger when combined with the quadriceps strengthening exercise."


**Oral administration of hyaluronan reduces bone turnover in ovariectomized rats.**

"Oral administration of HA resulted in approximately 50% (p < 0.05) increases in serum HA... HA gavage blunted the development of osteopenia in this model as determined by preventing the 30% increase in serum collagen N-terminal telopeptide levels (p < 0.001) and by reducing bone mineral content loss from 6 to 4%. These results show that oral supplements of HA (gavage solution, 0.12% solution) significantly reduce bone turnover associated with mild osteopenia in rats."


**Effect of a natural extract of chicken combs with a high content of hyaluronic acid on pain relief and quality of life in subjects with knee osteoarthritis: a pilot randomized double-blind placebo-controlled trial.**

"This pilot clinical trial showed that daily supplementation with oral hyaluronic acid from a natural extract of chicken combs... was useful to enhance several markers of quality of life in adults with osteoarthritis of the knee."


**Evaluation of the effect of a chicken comb extract-containing supplement on cartilage and bone metabolism in athletes.**

"These observations indicate that the test product is effective in inhibiting, not only cartilage degradation, but also bone remodeling. Thus, the CCE-containing supplement may be useful for the management of joint health in athletes."


**Structural and symptomatic efficacy of glucosamine and chondroitin in knee osteoarthritis: a comprehensive meta-analysis.**

"Our results demonstrated a highly significant efficacy of glucosamine on all outcomes, including joint space narrowing and WOMAC... Safety was excellent for both compounds."


**Glucosamine, chondroitin sulfate, and the two in combination for painful knee osteoarthritis.**

"The primary outcome measure was a 20 percent decrease in knee pain from baseline to week 24."


**Glucosamine and chondroitin for treatment of osteoarthritis: a systematic quality assessment and meta-analysis.**

"Quality scores ranged from 12.3% to 55.4% of the maximum, with a mean (SD) of 35.5% (12%)... Trials of glucosamine and chondroitin preparations for OA symptoms demonstrate moderate to large effects..."

Turmeric & Inflammation and Stress

Safety and anti-inflammatory activity of curcumin: a component of tumeric (Curcuma longa).
“Curcumin has been demonstrated to be safe in six human trials and has demonstrated anti-inflammatory activity. It may exert its anti-inflammatory activity by inhibition of a number of different molecules that play a role in inflammation.”

Anti-aging Role of Curcumin by Modulating the Inflammatory Markers in Albino Wistar Rats.
“Finding of the study suggests that Curcumin exhibits favorable influence in slowing down of ageing process by suppressing age-related changes in inflammatory indices.”

Curcumin supplementation improves vascular endothelial function in healthy middle-aged and older adults by increasing nitric oxide bioavailability and reducing oxidative stress.
“In healthy middle-aged and older adults, 12 weeks of curcumin supplementation improves resistance artery endothelial function by increasing vascular nitric oxide bioavailability and reducing oxidative stress, while also improving conduit artery endothelial function.”

Curcumin inhibits superoxide anion-induced pain-like behavior and leukocyte recruitment by increasing Nrf2 expression and reducing NF-κB activation.
“Curcumin inhibits superoxide anion-induced inflammatory pain-like behaviors and leukocyte recruitment by targeting inflammatory molecules and oxidative stress; and inducing antioxidant and anti-inflammatory pathways.”

Curcumin supplementation likely attenuates delayed onset muscle soreness (DOMS).
“Oral curcumin likely reduces pain associated with DOMS with some evidence for enhanced recovery of muscle performance.”

The Attenuation of Pain Behavior and Serum COX-2 Concentration by Curcumin in a Rat Model of Neuropathic Pain.
“A considerable decline in pain behavior and serum COX-2 levels was seen in rat following administration of curcumin in CCI model of neuropathic pain.”

Reduction of delayed onset muscle soreness by a novel curcumin delivery system: a randomised, placebo-controlled trial.
“Subjects in the curcumin group reported less pain in the lower limb as compared with subjects in the placebo group…Significantly fewer subjects in the curcumin group had MRI evidence of muscle injury in the posterior or medial compartment of both thighs…Curcumin has the potential for preventing DOMS, as suggested by its effects on pain intensity and muscle injury.”
Turmeric & Arthritis and Osteoporosis

A randomized, pilot study to assess the efficacy and safety of curcumin in patients with active rheumatoid arthritis.

“Forty-five patients diagnosed with RA were randomized into three groups with patients receiving curcumin (500 mg) and diclofenac sodium (50 mg) alone or their combination...Interestingly, the curcumin group showed the highest percentage of improvement in overall DAS and ACR scores (ACR 20, 50 and 70) and these scores were significantly better than the patients in the diclofenac sodium group. More importantly, curcumin treatment was found to be safe and did not relate with any adverse events. Our study provides the first evidence for the safety and superiority of curcumin treatment in patients with active RA, and highlights the need for future large-scale trials to validate these findings in patients with RA and other arthritic conditions.”


Anti-inflammatory effect of Curcuma longa (turmeric) on collagen-induced arthritis: an anatomico-radiological study.

“Collagen-induced arthritis (CIA) is a well established experimental auto-immune mediated polyarthritis in susceptible strains of rodents. The main aim of the study was to observe the inflammatory, macroscopic and radiological changes in the arthritic ankle joints of experimentally collagen-induced arthritis animals treated with or without CL extract...Treatment with 110 mg/ml/kg CL showed significant mean difference in the ESR (p<0.01), AS (p<0.05) and radiological scores (p<0.01) on day-28 compared to the vehicle treated group...The administration of CL extract arrested the degenerative changes in the bone and joints of collagen-induced arthritic rats.”


Decrease of a specific biomarker of collagen degradation in osteoarthritis, Coll2-1, by treatment with highly bioavailable curcumin during an exploratory clinical trial.

“The treatment with curcumin was globally well tolerated. It significantly reduced the serum level of Coll2-1 (p<0.002) and tended to decrease CRP...This study highlighted the potential effect of curcumin in knee OA patient. This effect was reflected by the variation of a cartilage specific biomarker, Coll2-1 that was rapidly affected by the treatment. These results are encouraging for the qualification of Coll2-1 as a biomarker for the evaluation of curcumin in OA treatment.”


Curcuminoid treatment for knee osteoarthritis: a randomized double-blind placebo-controlled trial.

“Treatment with curcuminoids was associated with significantly greater reductions in WOMAC (p = 0.001), VAS (p < 0.001) and LPFI (p = 0.013) scores compared with placebo...To conclude, curcuminoids represent an effective and safe alternative treatment for OA.”


Attenuation of Oxidative Stress-Induced Osteoblast Apoptosis by Curcumin is Associated with Preservation of Mitochondrial Functions and Increased Akt-GSK3β Signaling.

“Osteoblast apoptosis induced by oxidative stress plays a crucial role in the development and progression of osteoporosis. Curcumin, a natural antioxidant isolated from Curcuma longa, has highly protective effects against osteoporosis...Curcumin was cytoprotective because it greatly improved the viability of Saos-2 cells exposed to H2O2 and attenuated H2O2-induced apoptosis. Curcumin treatment also preserved the mitochondrial redox potential, decreased the mitochondrial oxidative status, and improved the mitochondrial membrane potential and functions. Furthermore, curcumin treatment markedly increased levels of phosphorylated protein kinase B (Akt) and phosphorylated glycogen synthase kinase-3β (GSK3β)...Curcumin administration ameliorates oxidative stress-induced apoptosis in osteoblasts by preserving mitochondrial functions and activation of Akt-GSK3β signaling. These data provide experimental evidence supporting the clinical use of curcumin for prevention or treatment of osteoporosis.”