

AMWC

AESTHETIC & ANTI-AGING
MEDICINE WORLD CONGRESS

AMWC Monaco, April 2020

COLLAGEN BENEFITS FOR JOINTS

Recent data

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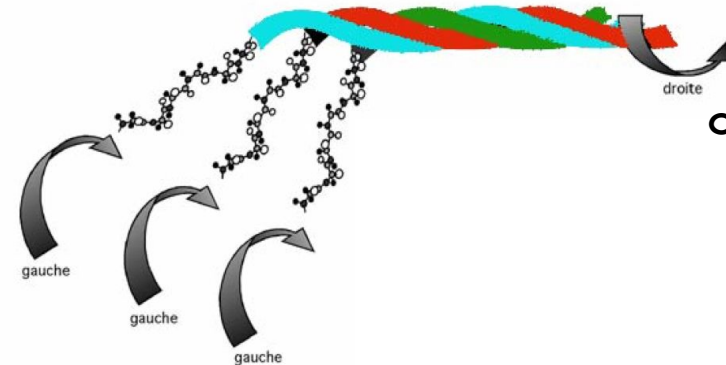
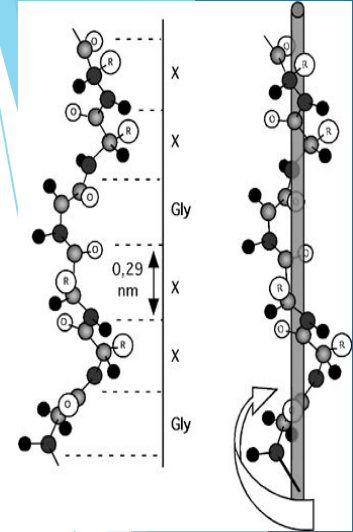
COLLAGEN

from Greek: *kólla*, meaning "glue",
and suffix *-gen*, denoting "producing"

- Collagen consists of amino acids bound together to form a **triple helix of elongated fibril** (= collagen helix).
- **Most abundant protein in Mammals** (25-35% of whole-body protein content).
- Mostly found in the **extracellular matrix of fibrous connective tissues** such as tendons, ligaments, joints and skin.
- **Essential role in maintaining their structural integrity:** Ensures cohesion, strength, elasticity and regeneration.
- Collagen is inextensible and **resists to traction forces.**

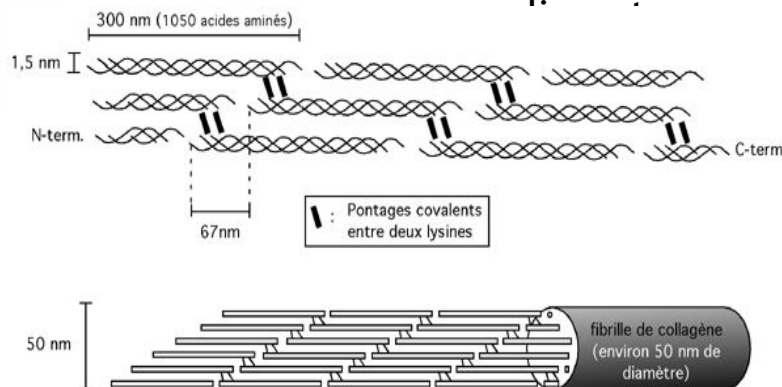
COLLAGEN MOLECULE, STEP BY STEP

- Composed of 3 polypeptide chains, organized in different ways.
- **TERTIARY STRUCTURE**
 - Repeated sequences with **Gly-X-Y** (often X = Proline, Y = Hydroxyproline).
 - Polypeptide chains assemble in triple helix.
 - 3 sub-units (1050 AA each) bundled together to form micro-fibril.
 - Tropocollagen = mature form of the triple helix (300 nm), stabilized by hydrogen bridges and very dependent on hydroxyproline bounds.



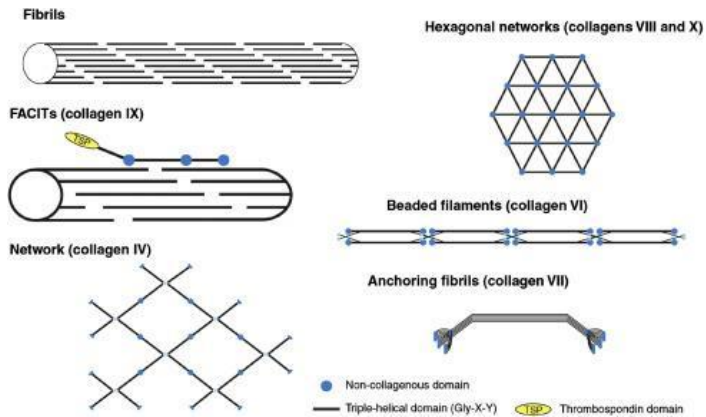
○ SPATIAL ASSEMBLY IN FIBRILS AND FIBRES

Tropocollagen molecules assemble into a 50 nm diameter fibril, that aggregates into a higher order fibril of 500nm diameter, which in turn, can form a collagen fiber of 1 - 10 μm in

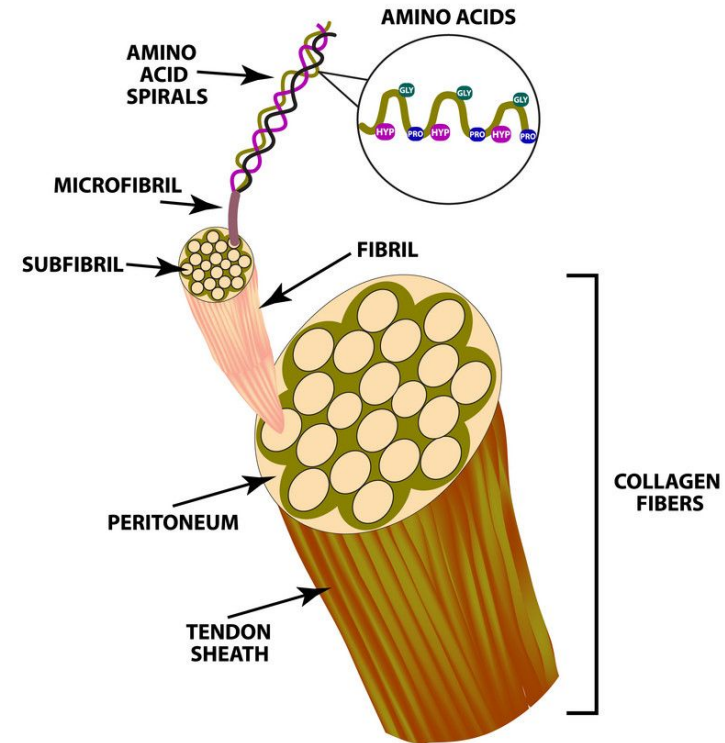


SPECIALIZED COLLAGEN STRUCTURES

- Different properties depending supra-molecular organization
- 12 main types of collagen (out of 28) are grouped in 7 families:



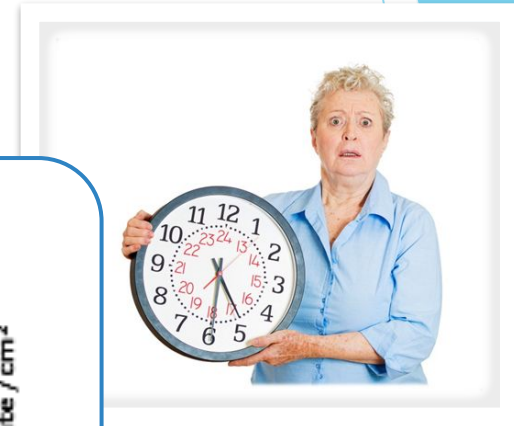
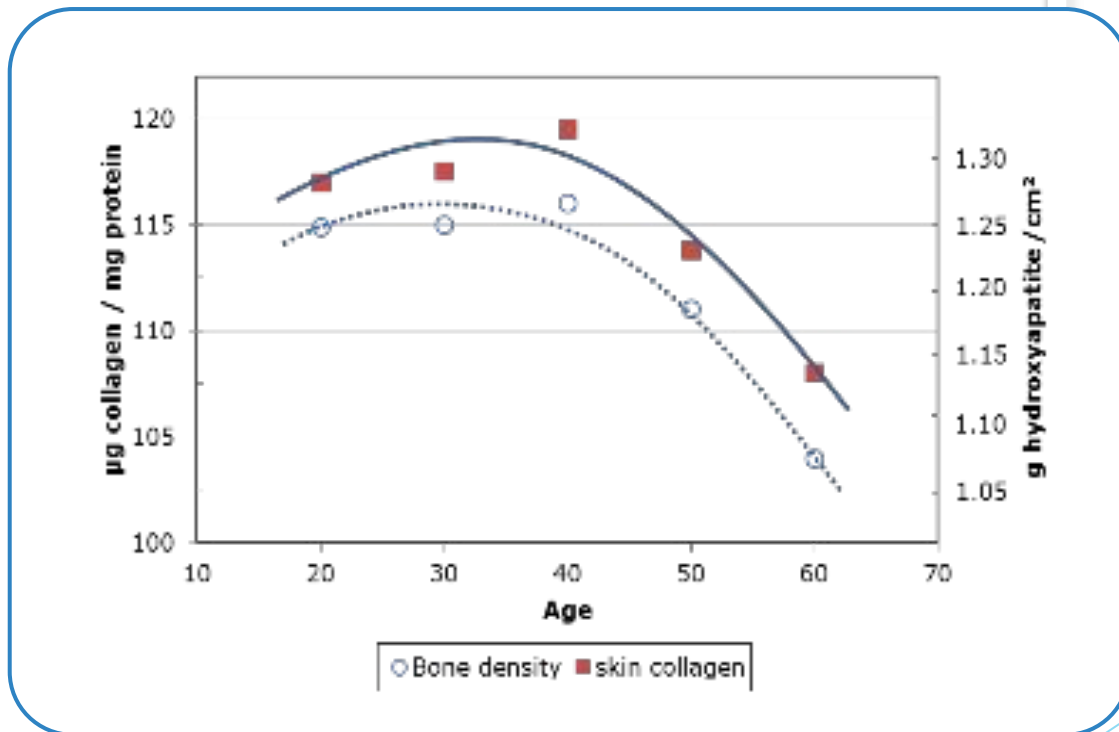
Fibrillar (Type I, II,
 Facit (Type IX, XII,
 Short chain (Type V
 Basement membrar
 Other (Type VI, VII,



- **FIBRILLAR COLLAGEN IS MOST ABUNDANT**
 ~ 90% of all types.
 Most important types in this group:
 collagens I, II, III and V.

COLLAGEN SYNTHESIS REDUCES IN TIME

- Collagen turn-over impairs from the age of 25 years old
- By then, 1% of collagen mass is lost every year.
- After 40, collagen loss increases, reaching 25% loss per year after the age of 50
- Up to 40% loss per year after 70 years old !



COLLAGEN LOSS RESULTS IN:

Deficit of cellular balance, sagging, weakening...

Visible and invisible signs of aging set in !

ACCELERATING FACTORS:

- Unhealthy lifestyle,
- UVs,
- Pollution,
- Free radicals,
- Junk food,
- Excess sugar intake (collagen is very sensitive to glycation stress)
- AGE's, Advanced-glycation-Endproducts (triggerring collagen degradation)

COLLAGEN IN BONE TISSUES

○ COMPOSITION

Collagen type I = 80% of the organic matrix

Collagen type III = 10%

Rich in proline and hydroxyproline

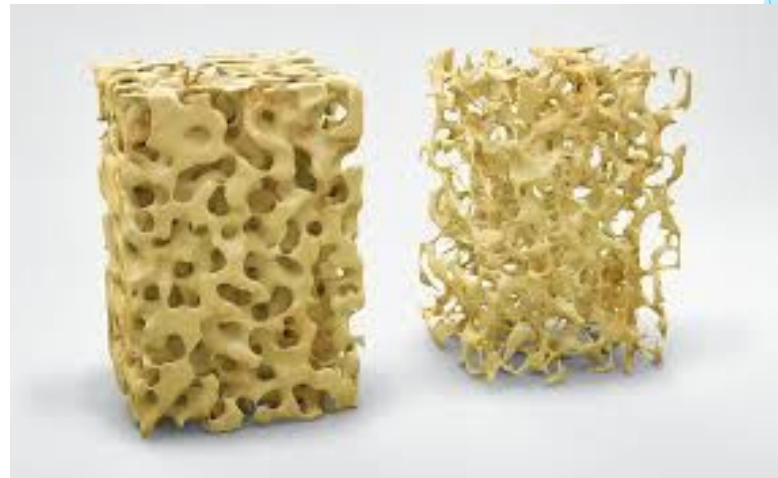
Associated with non-collagen proteins collagen molecules tend to associate with crystals of calcium phosphates, and will form very hard structures.

○ AGING EFFECTS

Bone becomes fragile

Higher occurrence of bone fracture

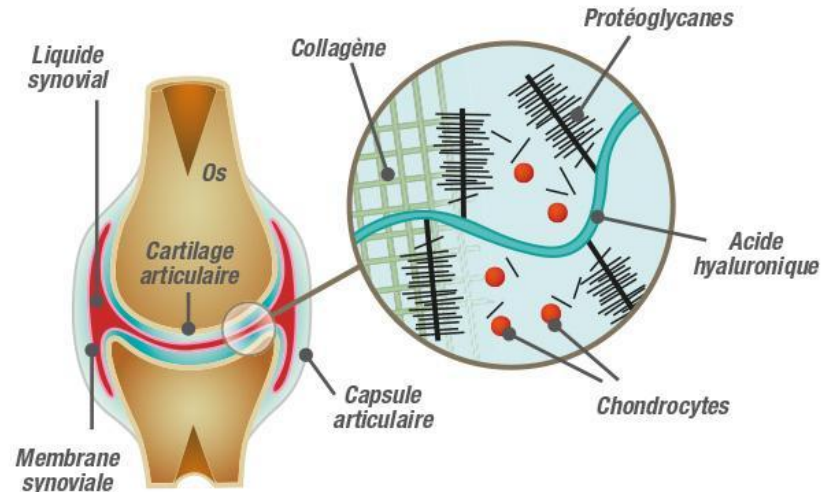
Osteoporosis



COLLAGEN IN JOINTS (1/2)

○ COMPOSITION

- Extracellular Matrix = water (70%) with proteoglycans (PGs) and type I, II and IX collagen fibers produced by chondrocytes.
- Collagen fibers are bringing strength to cartilage.
- Network of solid fibers which gives shape to cartilage and which retains proteoglycans.
- Proteoglycans attract and retain water which creates a kind of gel that can regain its shape after being deformed



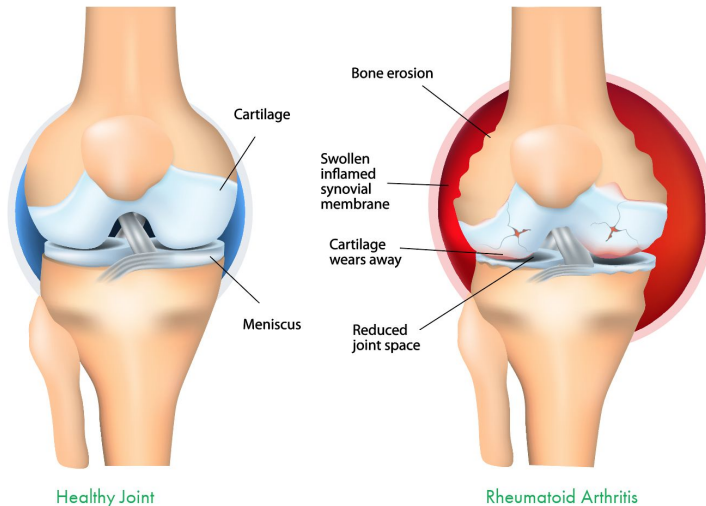
COLLAGEN IN JOINTS (2/2)

○ AGING EFFECTS

Mature chondrocytes slow down production of collagen, leading to: limited turn-over and modest maintenance process.

Lost of joint flexibility and mobility

Caramelization of cartilage



14 years



68 years

Loeser et al.

COLLAGEN IN TENDONS

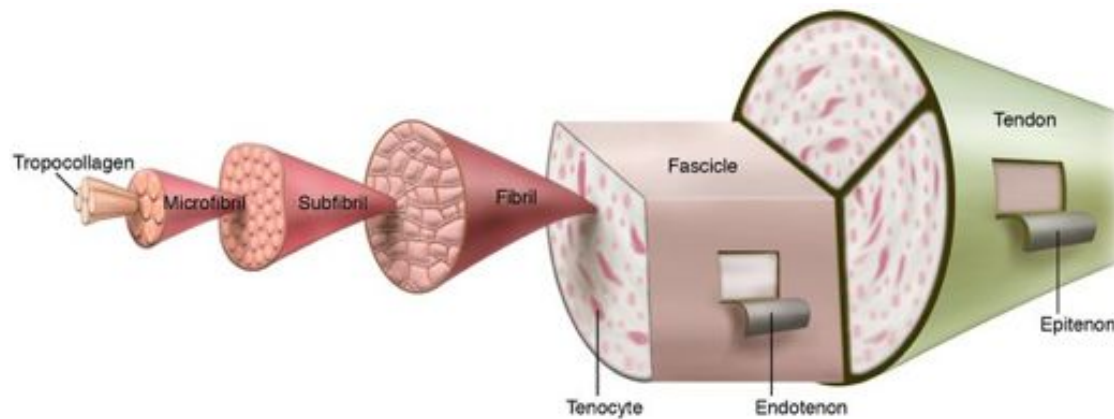
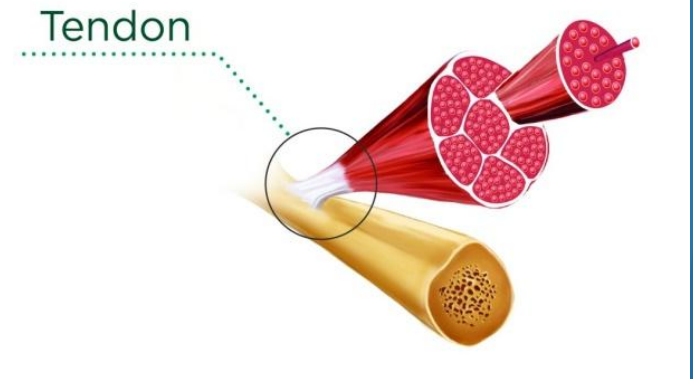
○ COMPOSITION

More than 90% of collagen type I

The enthesis is almost 99% of collagen molecules forming flexible fibers with high tensile strength.

○ AGING EFFECT

Tendon becomes fragile with appearance of micro tears
Triggering inflammation (Tendinitis) or degeneration (Tendinosis)



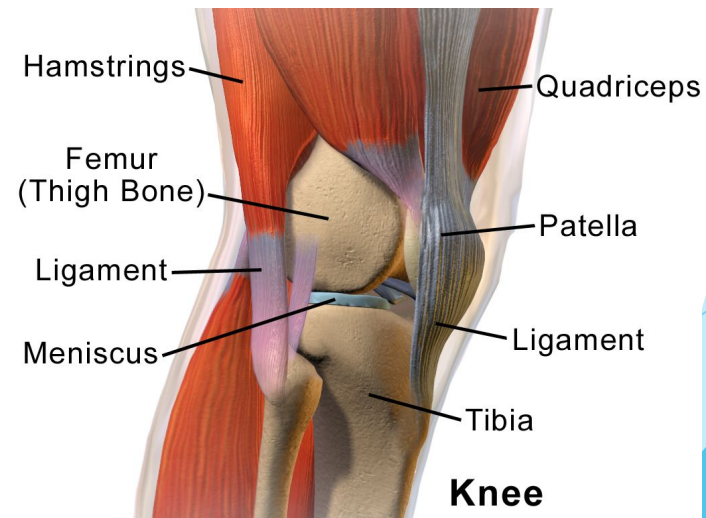
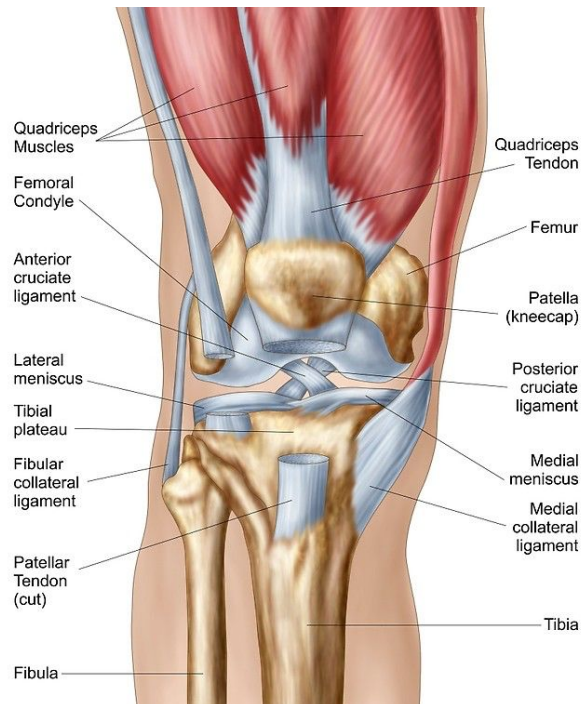
COLLAGEN IN LIGAMENTS

○ COMPOSITION

80% type I collagen

○ AGING EFFECT

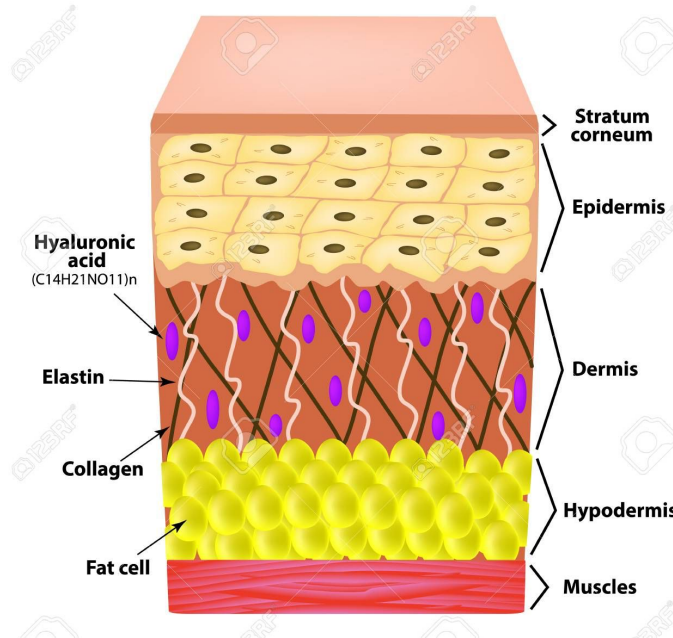
Lost of elasticity over time, resulting in lost of strength and flexibility



COLLAGEN IN SKIN

○ COMPOSITION

- Collagen = most important component of the dermis (> 90%).
- Collagen is synthesized by fibroblasts under the form of a tropocollagen precursor.
- Type I (60 to 80%), Type III (15 to 25%) and Type V collagen types (2 to 5%).
- These fibrillar collagens assemble into thick fibers and provide strength and thickness of skin



COLLAGEN IN SKIN

○ AGING EFFECTS

Collagen down-graded by enzymes: metalloproteinases and collagenases.

Accelerating factors: UV, pollution, smoking

Appearance of fine lines and wrinkles

Thinner skin, lack of gloss ...



COLLAGEN IN BLOOD VESSEL

○ COMPOSITION

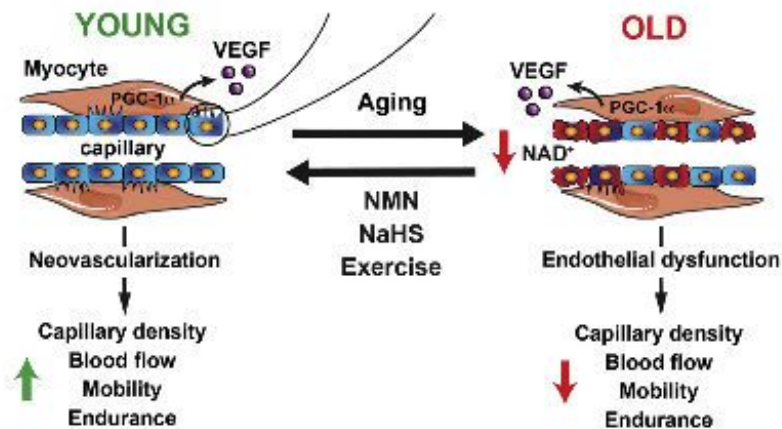
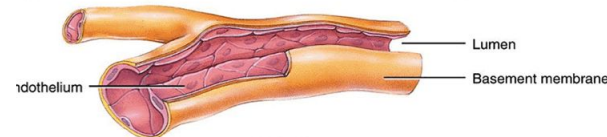
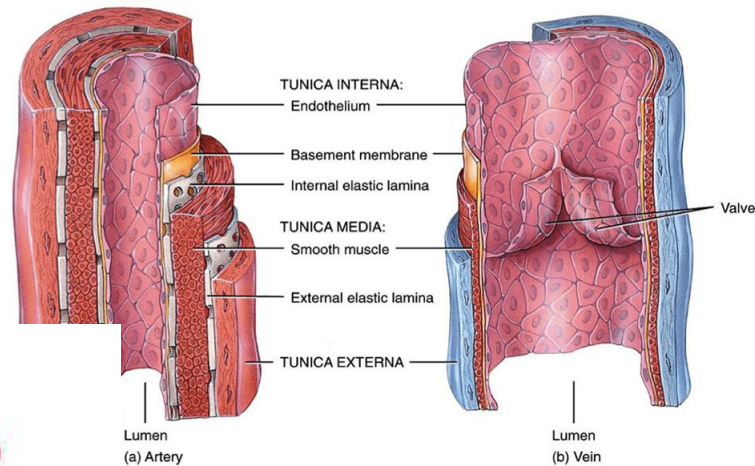
Collagen is found in the 3 layers of the vessel wall

Type I and III collagen mostly, with IV and V in medium and inner layers

○ AGING EFFECTS

Thinner blood walls, brittleness

Reduced wound healing capability

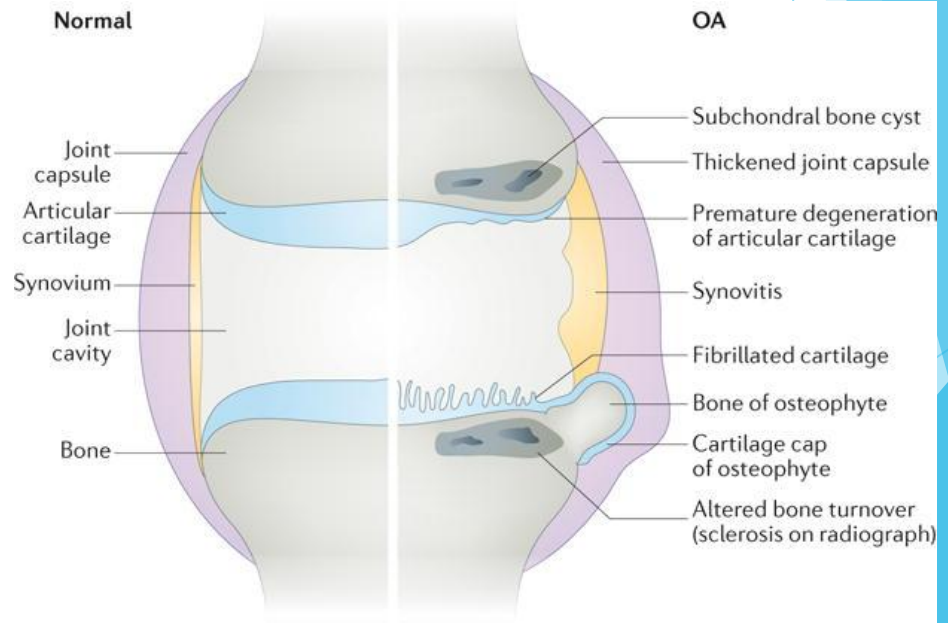
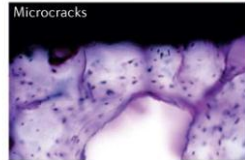
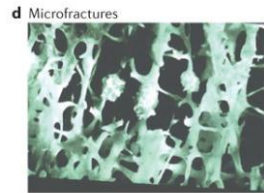
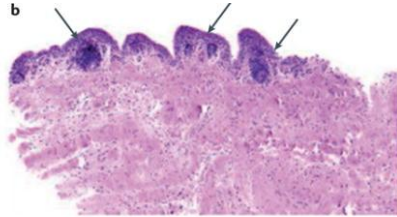


MOST COMMON ARTICULAR PATHOLOGY: OSTEO ARTHRITIS



OSTEO ARTHRITIS

- Long considered a simple wear of cartilage and fatality linked to aging, it only benefits from symptom treatments, intended to relieve pain.
- Prevalence: >50 million people , 5 out of 10 after 45 years old
- More than 78 million expected to be diagnosed by 2040 !
- Side-effects on : sub-chondral bone, synovial membrane



ROLE OF AGE'S IN OSTEO ARTHRITIS

Advanced Glycation End-products

Caramelization of cartilage

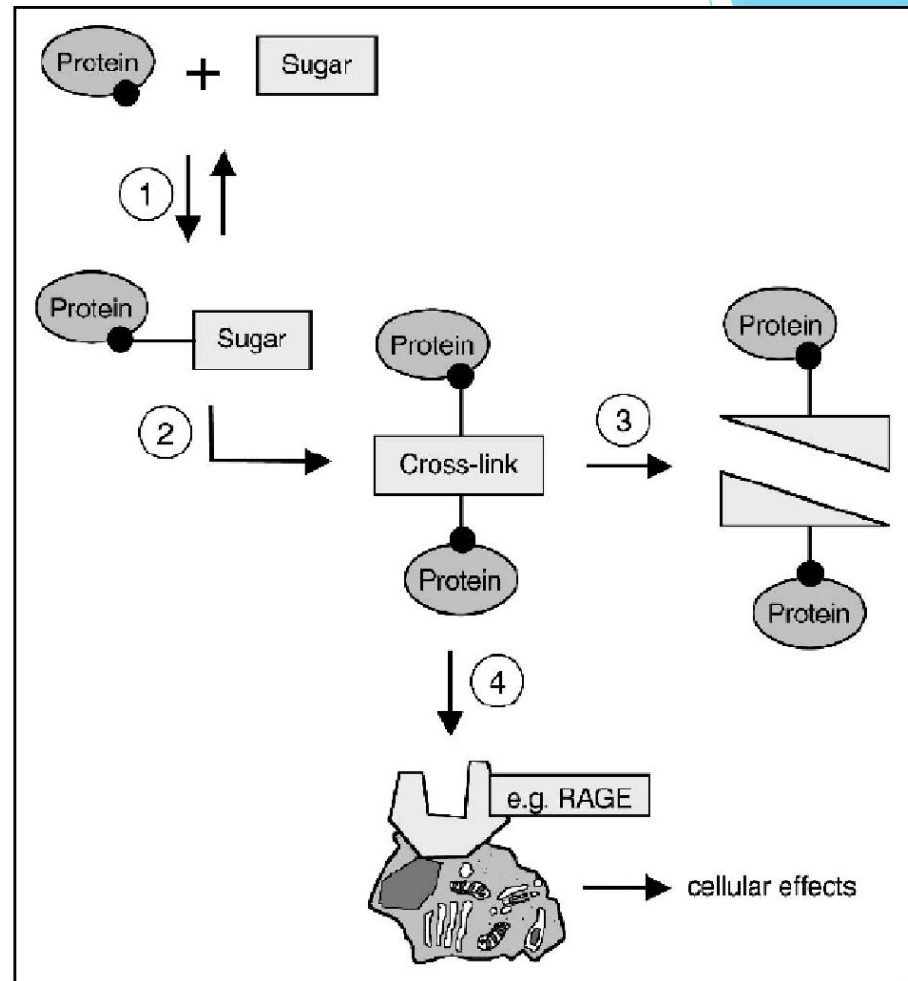


14 years



68 years

Loeser et al.



A « LOW GRADE » INFLAMMATION

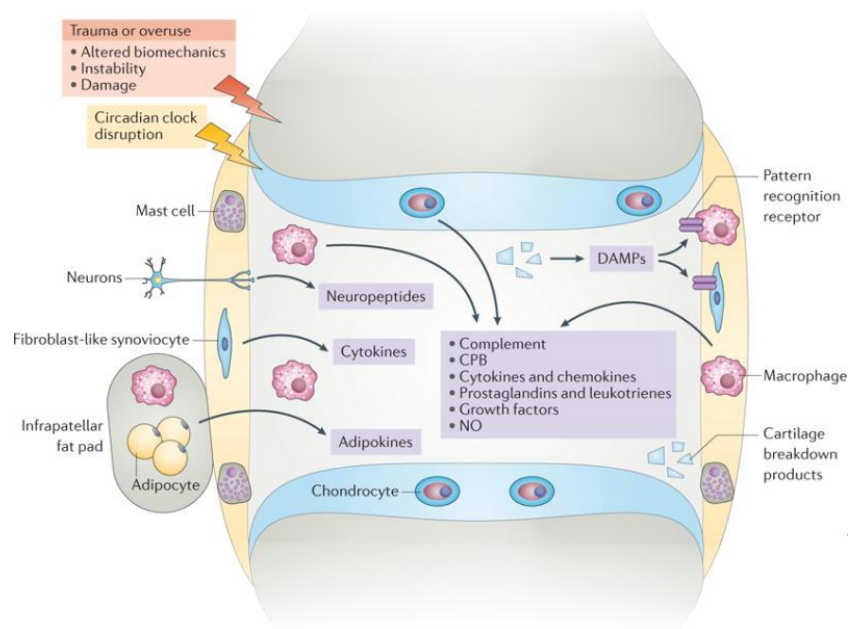
Many markers of inflammation induce cartilage depletion:

- Cytokines
- Chemokines
- Adipokines
- Growth Factors

Following chondral lesions, **release of cartilage matrix fragments** into the joint cavity causes **synovial inflammation** mediated by innate immunity.

(Source: Robinson WH et al: *Low-grade inflammation as a key mediator of the pathogenesis of osteoarthritis. Nat Rev Rheumatol 2016;12 (10): 580-592*)

Under the effect of inflammatory mediators, activation of **chondrocyte catabolism**: production of **proteases** causing **cartilage matrix lesions**.



HOW TO REMEDIATE ?

REGENERATE OWN COLLAGEN FROM INSIDE

- **Control low grade inflammation** (omega6 / omega3 balance),
- **Supply with cofactors:** vitamin C, zinc, magnesium,
- **Eat collagen-rich ingredients** (bone broth, fish skin, ...),
 - Traditional Chinese Medicine has been recommending for millennia of consuming animal cartilage and skin to treat joint disorders.
 - In Europe, Hildegard de Bingen, a 12th century mystic, mentioned the virtues of veal stock in this indication.
- **Do soft physical activities** on daily basis,
- **Supplement with highly digestible collagen peptides** (hydrolyzed collagen)



SCIENTIFIC EVIDENCE OF BENEFITS FROM COLLAGEN SUPPLEMENTATION



SCIENCE, OVER THE LAST 20 YEARS, PROVES INTEREST OF COLLAGEN SUPPLEMENTATION

- Essentially because of methodological reasons, the studies made in the 80's were inconclusive.

Sources:

- Moskowitz RW. Role of collagen hydrolysate in bone and joint disease. *Semin Arthritis Rheum.* 2000 Oct;30(2):87-99.
 - Bello AE, et al: Collagen hydrolysate for the treatment of osteoarthritis and other joint disorders: a review of the literature.. *Curr Med Res Opin.* 2006 Nov;22(11):2221-32. Review.
 - Arthritis Research Campaign. Complementary and alternative medicines for the treatment of rheumatoid arthritis, osteoarthritis and fibromyalgia, 2008.
-
- Because production of hydrolyzed collagen has significantly improved, **lots of scientific publications have proven, since the 2000's, that collagen supplementation plays a role in symptom relief and/or joint repair.**
 - Most significant studies are mentioned in coming slides...

- ❑ 2008: 97 Athletes. 10g Hydrolyzed Collagen vs. 10g Placebo / 3 months

Reduction in knee joint pain

Source: Clark KL et al: 24-Week study on the use of collagen hydrolysate as a dietary supplement in athletes with activity-related joint pain *Curr Med Res Opin.* 2008 May;24(5):1485-96.

- ❑ 2009: 52 advanced gonarthrotic subjects. 10g Hydrolyzed Collagen UCII vs. Glucosamin and Chondroitin (G+C)/ 9 months

Reduction Lequene's functional index by 20% vs 6% with G+C

Source: David C. Crowley, et al :Safety and efficacy of undenatured type II collagen in the treatment of osteoarthritis of the knee: a clinical trial. *Int J Med Sci.* 2009; 6(6): 312-321.

- ❑ 2009: Multicenter, Randomized & Double-blinded, 250 gonarthrotic subjects. 10g Collagen Peptides /day during 6 months.

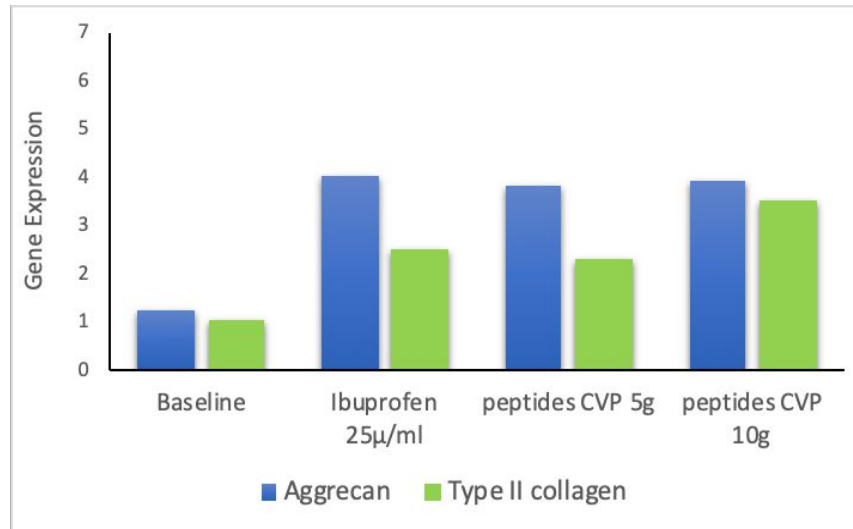
Improved joint comfort, confirmed by EVA and WOMAC score. Result even better with higher degree of joint damage

Source: Benito-Ruiz P et al. A randomized controlled trial on the efficacy and safety of a food ingredient, collagen hydrolysate, for improving joint comfort. *Int J Food Sci Nutr.* 2009 Feb 12:1-15.

- 2009: Randomized & Double-blinded, 250 gonarthrotic subjects. 10g Collagen Peptides /day during 6 months.

Chondrocytes were collected and grown in cell cultures 8 days. mRNAs were extracted from the chondrocytes and concentration measured by optical density. Gene expression was then measured by quantitative PCR

Enhanced expression of mRNA for aggrecan and type II collagen (2 major constituent of extracellular matrix)



Note: The study shows similar effect of collagen peptides on joint cells as Ibuprofen

(CVP = collagen peptides of Collagen Vital Power)

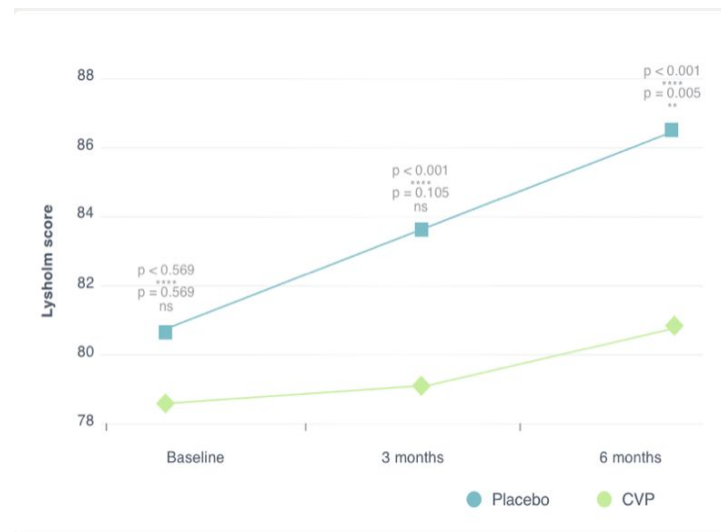
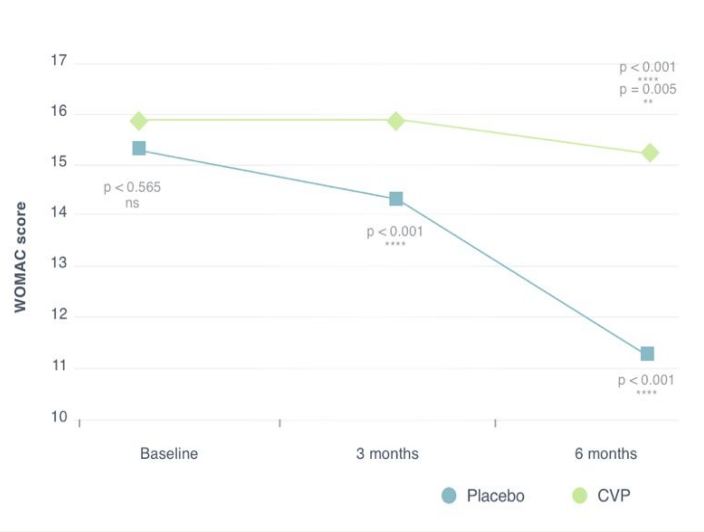
Source: Benito-Ruiz P et al. A randomized controlled trial on the efficacy and safety of a food ingredient, collagen hydrolysate, for improving joint comfort. *Int J Food Sci Nutr.* 2009 Feb 12:1-15.

- 2013 & 2014: Randomized, double-blind and placebo-controlled. 100 women (40-70 years old) diagnosed with knee osteoarthritis (X-Ray assessment + quantifying using the Kellgren-Lawrence grading system). 8 g Collagen Peptides /day during 6 months.

Improvement of joint functions (Lyshom score)

Reduction in joint discomfort (WOMAC score)

Note: A low WOMAC score indicates a low degree of osteoarthritis. A high Lyshom score indicates a low degree of osteoarthritis.



(CVP = collagen peptides of Collagen Vital Power)

Source: J.X. Jiang et al., Peptan Collagen Peptides for Treatment of Knee Osteoarthritis: A Double-Blind, Randomized, Placebo-Controlled Study, *Agro Food Industry Hi Tech*, Vol 25(2):19-23 (2013)+*Agro Food Industry Hi Tech* 25(2), 20-21 (2014)

And with bone tissues ...

- ❑ 2018: Randomized, double-blind. 131 postmenopausal women. Collagen hydrolysate 5g vs. Placebo. 12 months

➔ **Improvement in bone mineral density (femur & spine)**

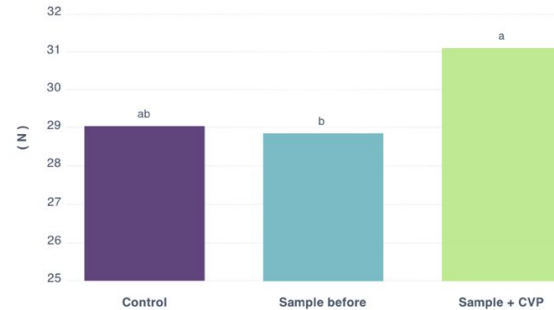
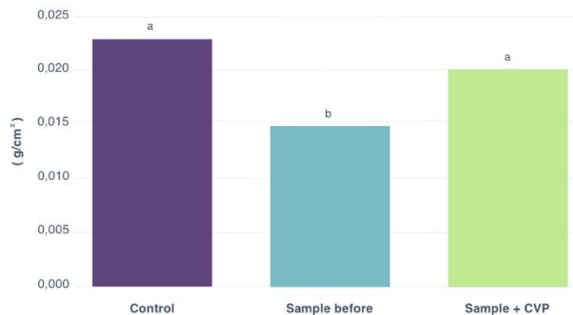
Source: Daniel König et al: *Specific Collagen Peptides Improve Bone Mineral Density and Bone Markers in Postmenopausal Women—A Randomized Controlled Study.* *Nutrients* 2018 Jan; 10(1): 97

- ❑ 2010 & 2012: Animal model mimicking the loss of bone mass during the onset of menopause. Supplementation with Collagen Peptides vs. placebo.

Restored bone mineral density

➔ **Improved bone microarchitecture and solidity.**

Therapeutic, but also preventive effect



(CVP = collagen peptides of Collagen Vital Power)

Source: F. Guillerminet et al, *Hydrolyzed Collagen Improves Bone Metabolism and Biomechanical Parameters in Ovariectomized Mice: An In Vitro and In Vivo Study,* *Bone* 46(3), 827-834. (2010) / *Hydrolyzed Collagen Improves Bone Status and Prevents Bone Loss in Ovariectomized C3H/HeN Mice,* *Osteoporosis International* 23, 1909- (2012).

And with exercise recovery (tendons, muscles) ...

- ❑ 2019: Selected subjects exposed to Stanish-type exercise protocol, PEMF, Radial shock waves, medium energy, plasma enriched in platelets or PRP, resumption of exercise program.

May accelerate the clinical benefits of a well-structured calf-strengthening and return-to-running program in Achilles tendinopathy

Source: Praet SFE et al., Oral supplementation of specific collagen peptides combined with calf-strengthening exercises enhances function and reduces pain in Achilles tendinopathy patients. Nutrients, 2019, Jan 2;11(1).

- ❑ 2018: Randomized, double-blind and placebo-controlled. Newcastle University. 24 young athletes. 10g Collagen Peptides twice day during 9 days and 7 days before intense exercise. Subjects exposed to a serial of intense physical exercises with 150 drop jumps aimed at inducing muscle damage.

Muscle soreness is lower with collagen group

Faster recovery and better performance after 24h

Source: Clifford, T., et al., The effects of collagen peptides on muscle damage, inflammation and bone metabolism following exercise: a randomized, controlled trial. Submitted for publication. (2018).

SUCCESS FACTORS FOR EFFECTIVE COLLAGEN SUPPLEMENTATION



WIDE VARIETY OF PRODUCT ON THE MARKET PLACE ...

- **Animal origin:**

Bovine, Porcine, Chicken / Poultry, Marine

Frequent diseases with Mammalian origins (EU ban on use of bovine vertebrae and derived gelatin in 2001,

- **Sales channels:**

Internet, retails, pharmacies

No control of on-line sales. Recommend pharmacy circuit

- **Different quality:**

Safer quality from EU and US manufacturing

Registration to Health Authorities, Regulation for dietary supplement with positive list of approved and safe ingredients.

WHAT ARE THE KEY CRITERIA FOR EFFECTIVE SUPPLEMENTATION ?

- **Bioavailability**

Collagen must be hydrolyzed to enable rapid assimilation.
Low Molecular Weight and Purity are thus key success factors.

- **Dosage**

8 g minimum per day.
Recommended: 10 g per day.

- **Pharmaceutical Form**

Capsule, Tablet, Liquid shot, or Powder. Only powder could give a high dosage.

Recommended: powder in precisely dosed packs

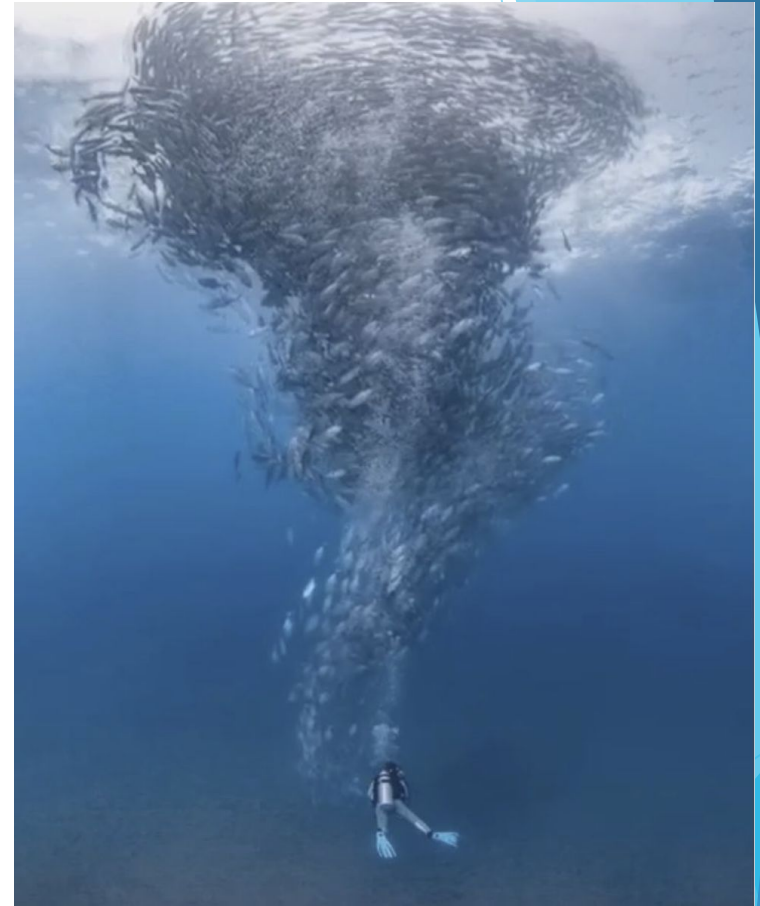
- **Posology**

1 to 3 months - To be renewed at least once in a year.

WHY MARINE SOURCE IS PREFERRED ?

- Higher bioavailability than other origins
- Mostly type I and III collagen.
- Safety vs mammalian sources
- Higher degree of purity

Fisk skin collagen has a superior quality than bone & skin marine origins



MY TESTIMONIAL

Collagen supplementation with my patients

- Fisk skin collagen, powder in sachet with 10g collagen peptides, highly bioavailable, Made in France
- Type of pathology
- Posology
- Results

Thanks for your attention

The background features abstract, overlapping geometric shapes in various shades of blue, ranging from light sky blue to deep navy blue. These shapes are primarily located on the right side of the frame, creating a modern, layered effect against the white background.