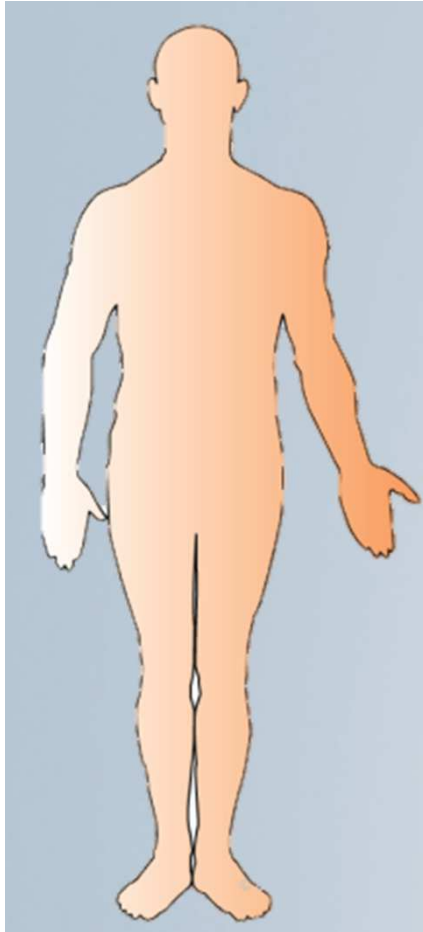


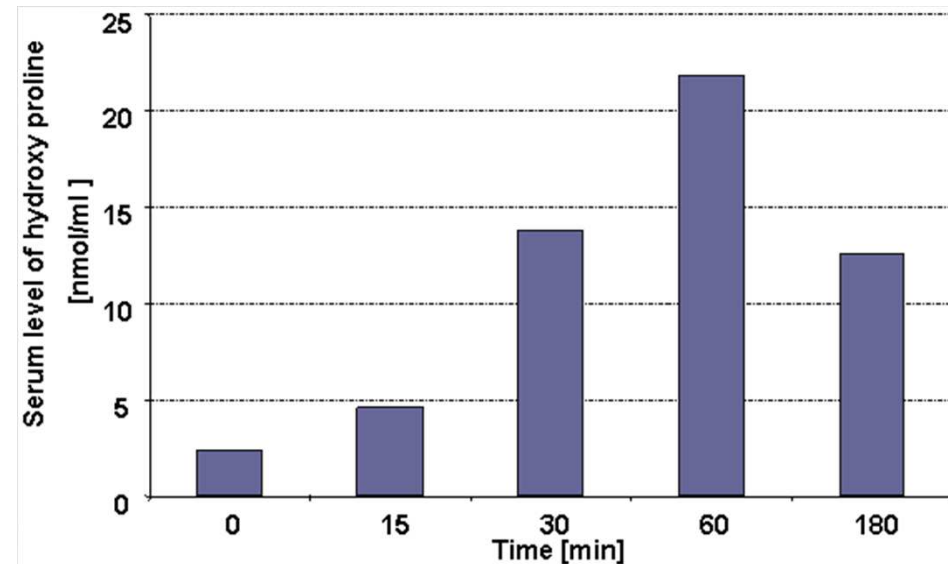
Nutra Botanicals Protein+ Collagen in the Human Body



- Collagen – the most abundant protein in humans
 - About 30% of the body's protein is collagen
- Structural protein
 - Up to 80% of dry skin mass
 - Main component of tendons (>85%) and ligaments (>70%)
 - Up to 70% of dry cartilage mass (joints)
 - About 20% of bone structure
 - Abundant in blood vessels & intervertebral discs
 - Accounting for about 6% of the weight of strong, tendinous muscles

Collagen Peptides: Highly Available Protein Source

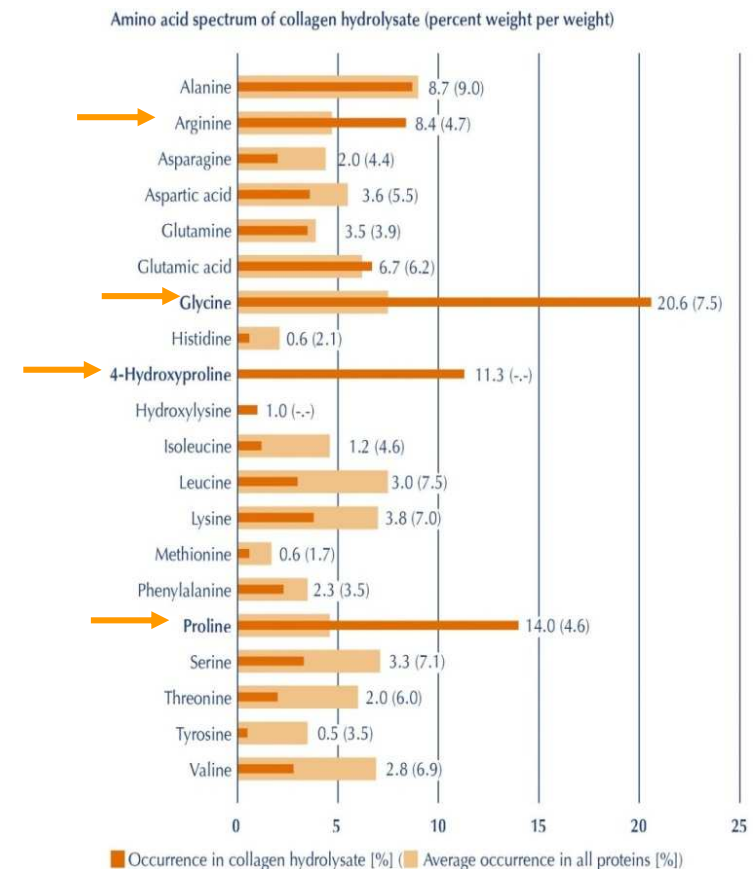
- Excellent and rapid absorption of collagen peptides after oral uptake
- Significant and continuous increase of collagen-specific amino acids in human blood after collagen peptide supplementation
- Rapid absorption important for post-exercise recovery



Iwai et al.(2005) J.Agric.Food Chem.; modified

Collagen Peptides – Unique Amino Acid Profile

- About 30% of body's protein is collagen
- Collagen is the main component of connective tissue
- High content of conditionally essential & glycogenic amino acids, e.g.:
 - Arginine → precursor for nitric oxide (Nitric Oxide NO; i.a. an important mediator in satellite cell stimulation)
 - Glycine → most simple amino acid and building block / precursor for several molecular pathways, e.g. of glutathione (endogenous antioxidant)
 - Glycine & Arginine → Creatine precursor (nitrogenous organic acid that helps to supply energy to all cells in the body, primarily muscle)



Comparison between AAs of average food proteins considered “complete proteins” versus food sources of collagen proteins.

Bioactive Collagen Peptides[®]

Special composition of collagen peptides

- Obtained by specific enzymatic hydrolysis
- Optimized to stimulate extracellular matrix formation = physiological functionality
- Scientifically substantiated by clinical studies

Skin
Pharmacology
and
Physiology

Original Paper

Skin Pharmacol Physiol 2014;27:47–55
DOI: 10.1159/000351376

Received: November 2, 2012
Accepted after revision: March 24, 2013
Published online: August 14, 2013

Oral Supplementation of Specific Collagen Peptides Has Beneficial Effects on Human Skin Physiology: A Double-Blind, Placebo-Controlled Study

Osteoarthritis and Cartilage

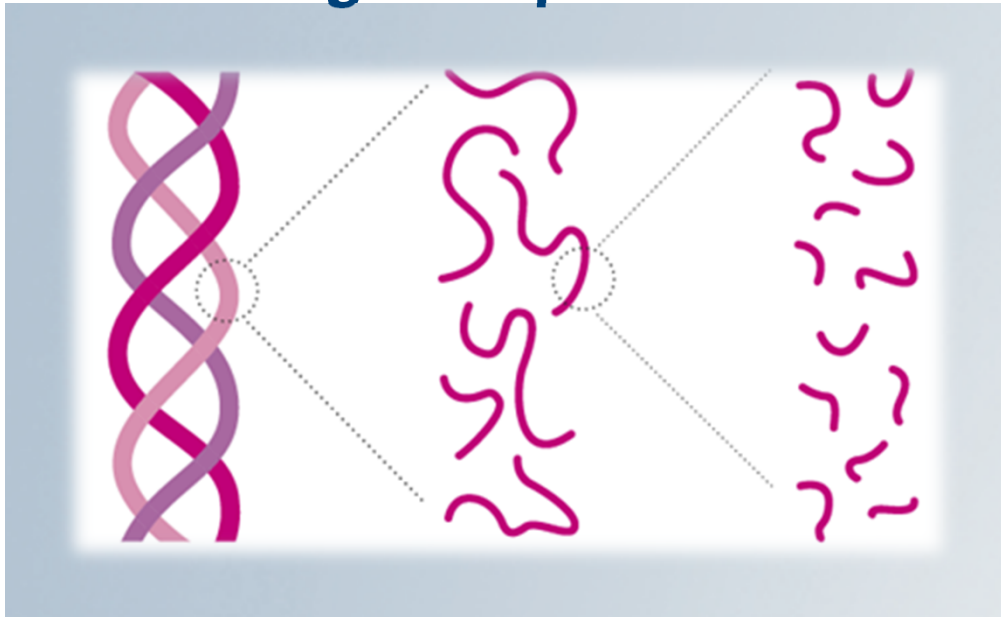


OARSI
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RESEARCH SOCIETY
INTERNATIONAL

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

T.E. McAlindon †*, M. Nuite †, N. Krishnan ‡, R. Ruthazer §, L.L. Price §, D. Burstein ||, J. Griffith ¶, K. Flechsenhar #

All Collagen Peptides ≠ *Bioactive Collagen Peptides*[®]



Significant variance in peptide composition of different collagen peptides, which are often very unspecific

≠

***Bioactive Collagen Peptides*[®]**
Optimized to stimulate specific tissue formations

- Collagen Peptides with similar specification sheets don't have a similar physiological functionality

Bioactive Collagen Peptides®

Preclinical Research Path

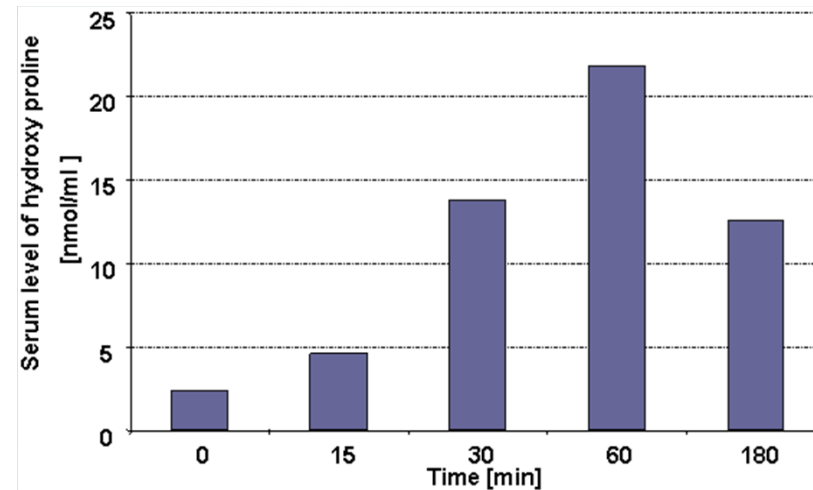
Rapidly absorbed, partially in intact form



Distribution & accumulation in the target organ



Stimulatory and regulatory effect in bones, joints and the skin



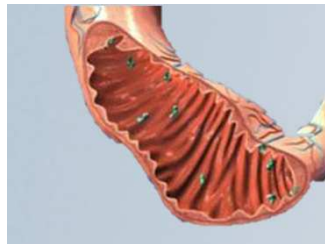
- Excellent and rapid absorption of collagen peptides after oral uptake (Iwai et al. 2005)
- Significant and continuous increase of collagen-specific amino acids in human blood after collagen peptide supplementation (Beuker et al. 1993)

Bioactive Collagen Peptides®

Preclinical Research Path



Rapidly absorbed, partially in intact form

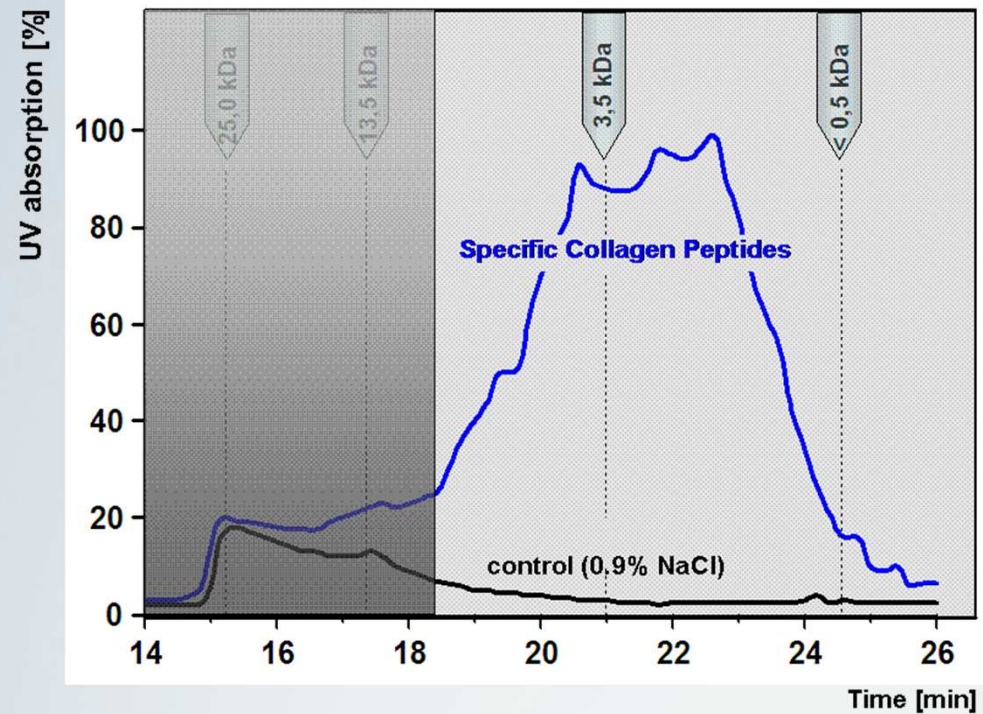


Distribution & accumulation in the target organ



Stimulatory and regulatory effect in bones, joints and the skin

Absorption profile of SCP

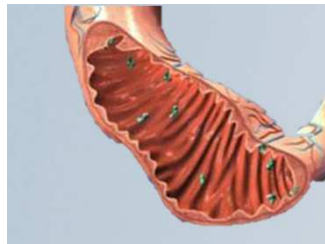


Oesser et al. J. Nutr. (1999) 129:

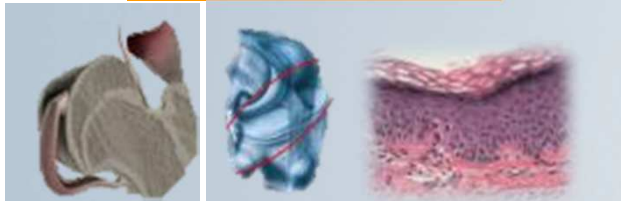
Bioactive Collagen Peptides®

Preclinical Research Path

Rapidly absorbed, partially in intact form

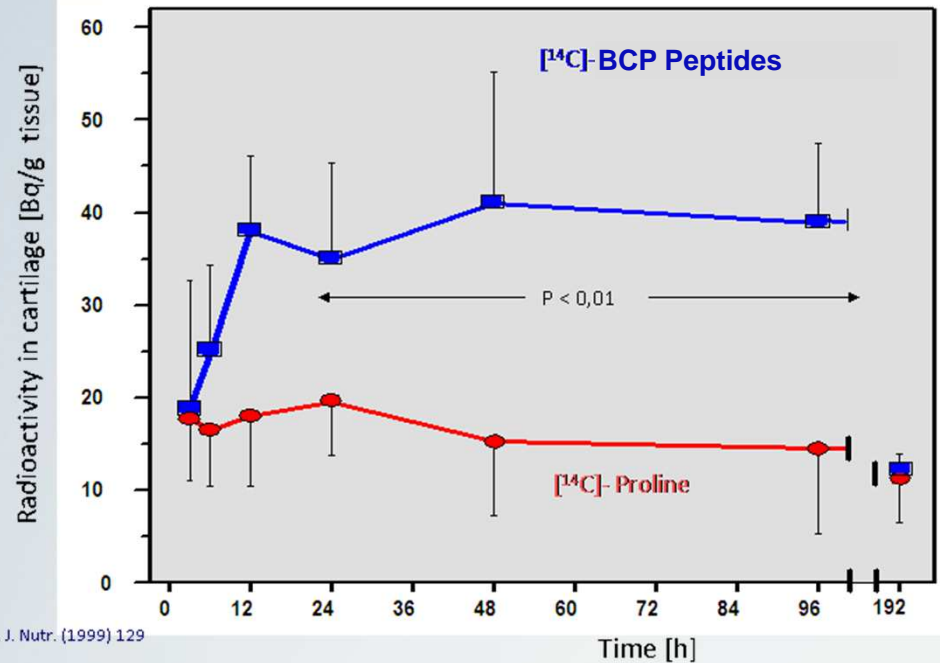


Distribution & accumulation in the target organ



Stimulatory and regulatory effect in bones, joints and the skin

Accumulation of Bioactive Collagen Peptides® in mice cartilage

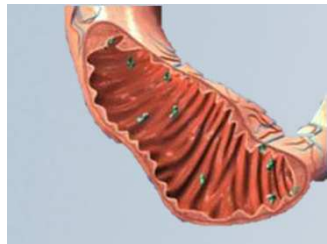


Oesser et al. J. Nutr. (1999) 129

Bioactive Collagen Peptides®

Preclinical Research Path

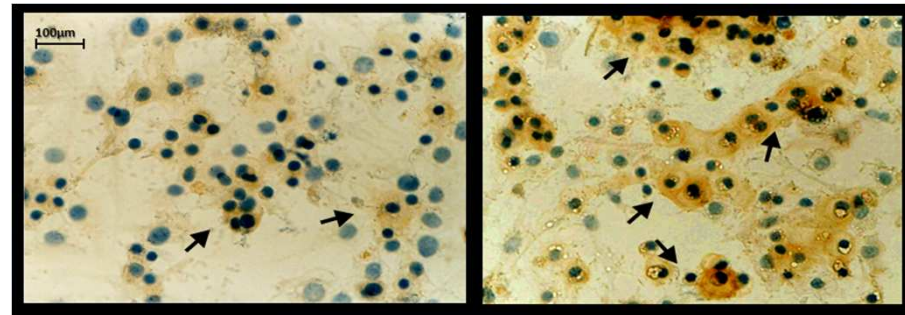
Rapidly absorbed, partially in intact form



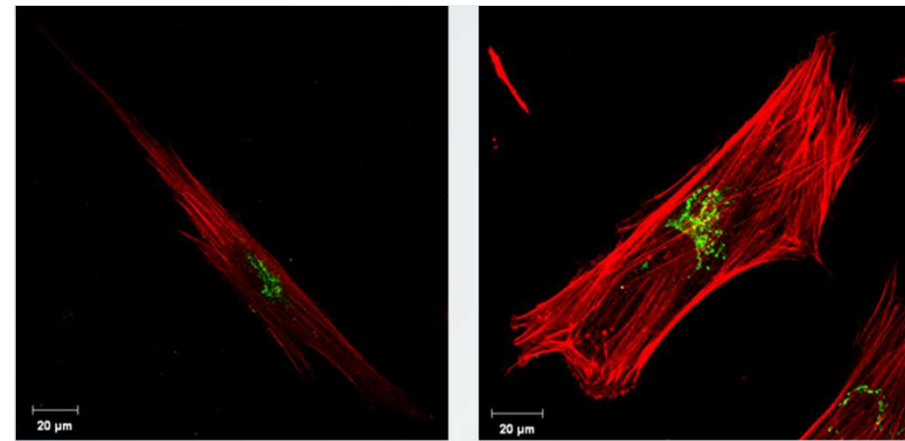
Distribution & accumulation in the target organ



Stimulatory and regulatory effect in bones, joints and the skin



Chondrocytes



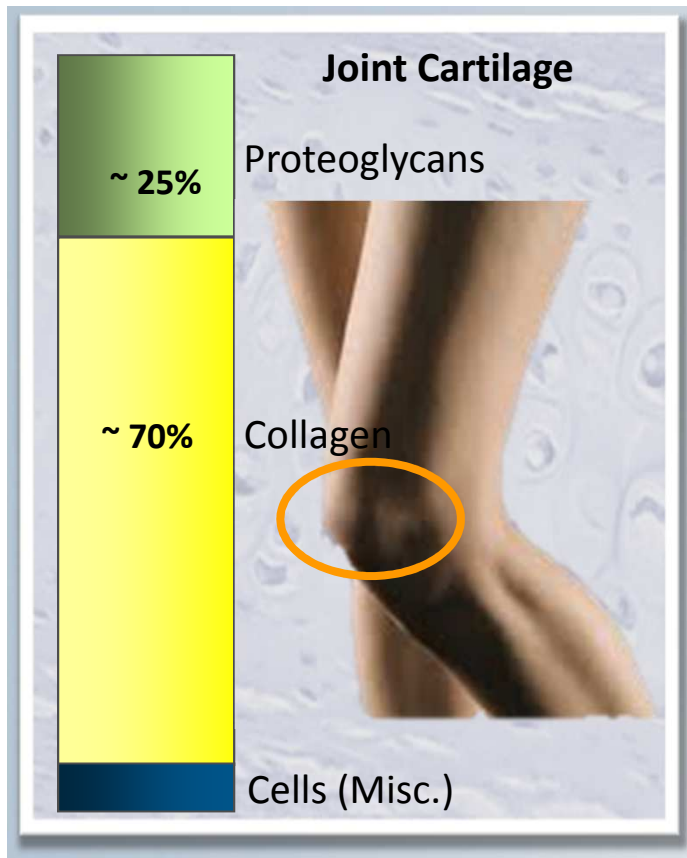
Fibroblasts

Without VERISOL®

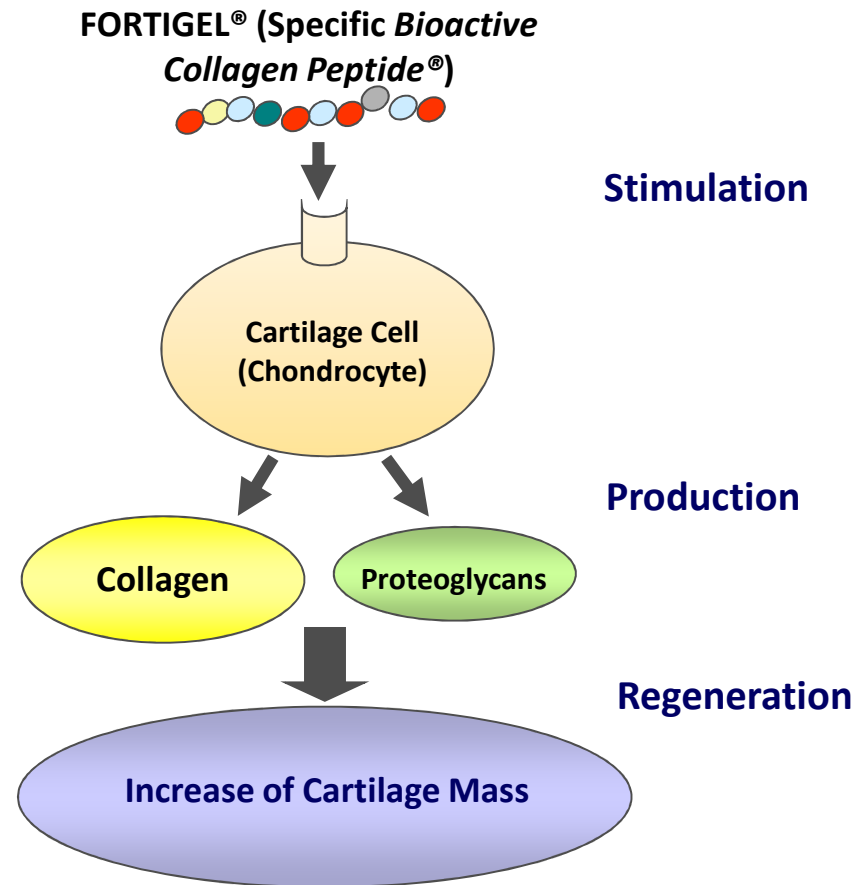
With VERISOL®

Bioactive Collagen Peptides®

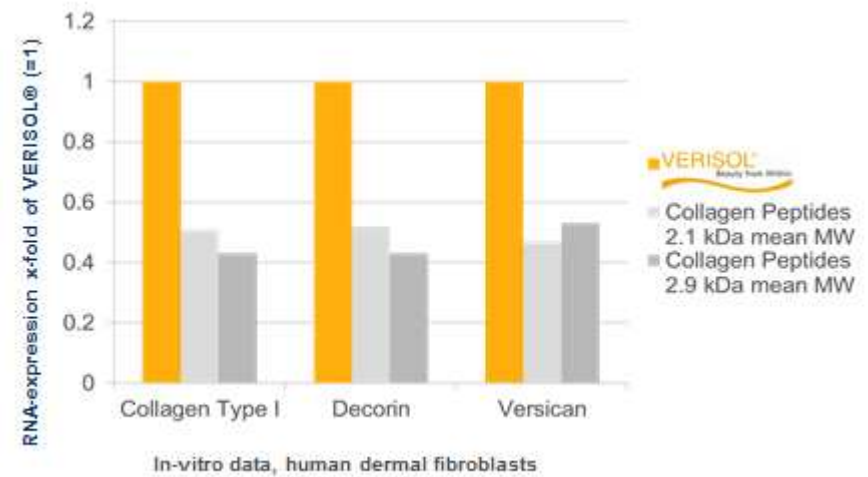
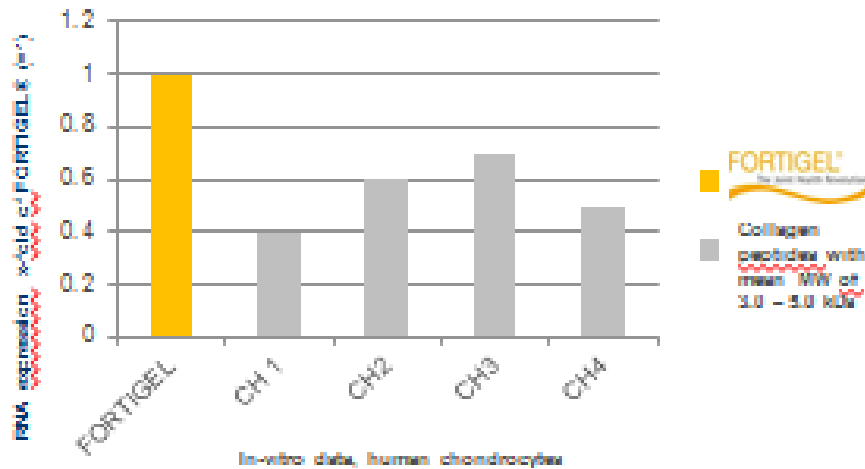
Mode of Action (as in cartilage)



Composition of Joint Cartilage



All Collagen Peptides ≠ Bioactive Collagen Peptides®



- Stimulation effect on in-vivo collagen synthesis widely varies between different collagen peptides
- each clinical study is conducted with respective dedicated *Bioactive Collagen Peptides®*

Collagen Peptides for Specific Solutions



Collagen Peptides for Specific Solutions



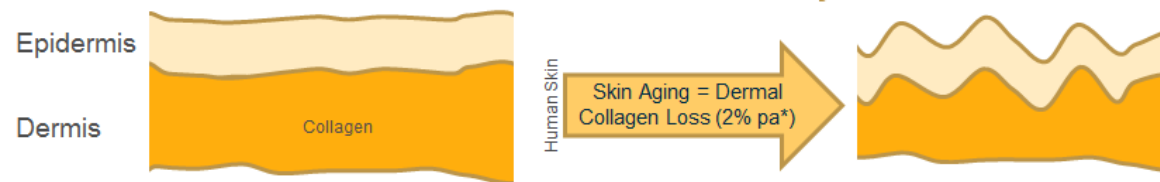
Skin Aging



Why Collagen is Important

- Major structural component of skin, comprising ~80% of dry skin weight
- Influences skin's water binding capacity, elasticity and outside appearance (wrinkles)
- Loss begins at ~ 30 years old and significantly increases after menopause (~2% per year)*

* Chung et al 2001; Li et al 2005, Patriarca et al 2007



Collagen Peptides for Specific Solutions



Nutra Collagen Clinical Scientific Substantiation

- Studies in >2,500 patients showing Nutra Collagen® effects in joint cartilage
- Bioactive Collagen Peptides® proven to stimulate growth of connective tissue in joints with an effective dose of 5g to 10g/day

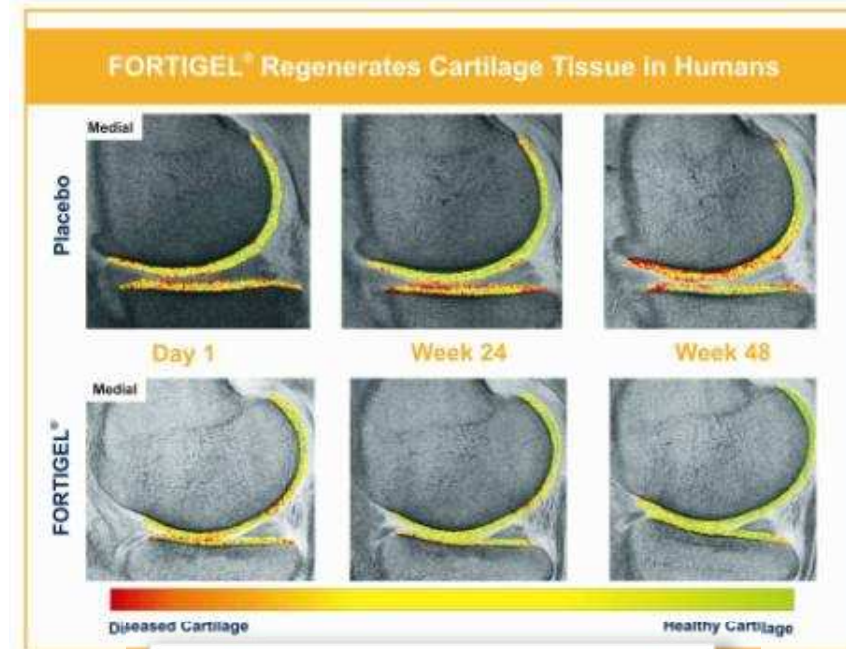


Investigator	Published	Subjects
Krug	1979	193
Götz	1982	60
Oberschelp	1985	154
Seeligmüller	1989	356
Adam	1991	81
Seeligmüller	1993	519
Beuker, Eck	1996	40
Beuker, Rosenfeld	1996	100
Moskowitz	2000	389
Zukley	2004	250
Carpenter	2005	102
Alf	2005	100
Clark	2008	147
McAlindon	2011	30

Tufts Medical Center Study (2011): Visual Effect

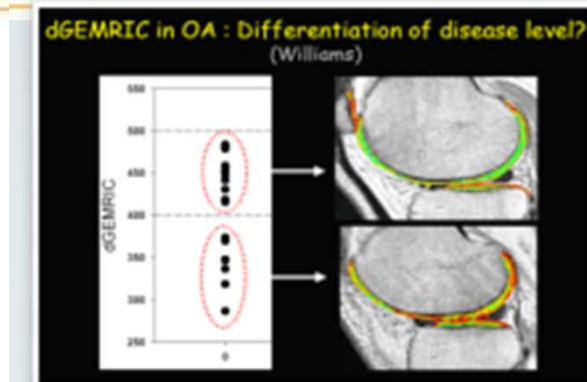
Study Design

- Prospective, randomized, double blind, placebo controlled
- 30 individuals with mild osteoarthritis (Kellgren grade 1–2)
- 10g FORTIGEL® or placebo
- 11 months trial
- dGEMRIC data



Results

- Proteoglycan density in knee joint cartilage significantly increased after FORTIGEL® treatment



GELITA Collagen Peptides for Specific Solutions



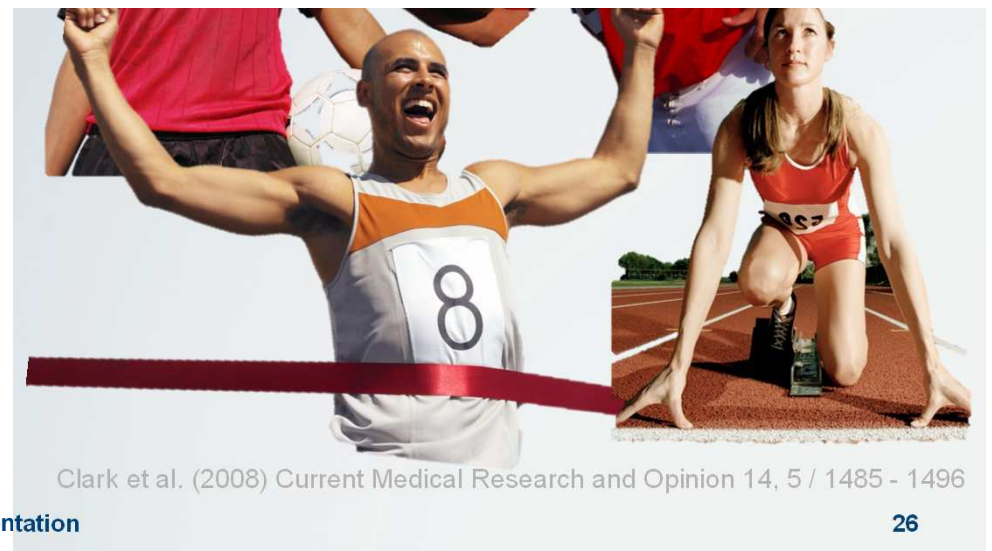
Penn State Study (2008): [®] in Athletes

Study Design

- 147 student athletes, randomized, placebo-controlled, double-blind
- Therapy: 10g FORTIGEL[®] or placebo over 24 weeks
- Parameters: pain, mobility, flexibility in different joints

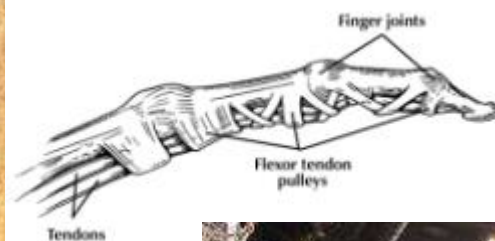
Results

- Significant improvements in joint problems (especially in the knee)
- Increase of performance & mobility
- Decrease of alternative therapies (massages / ice packs)



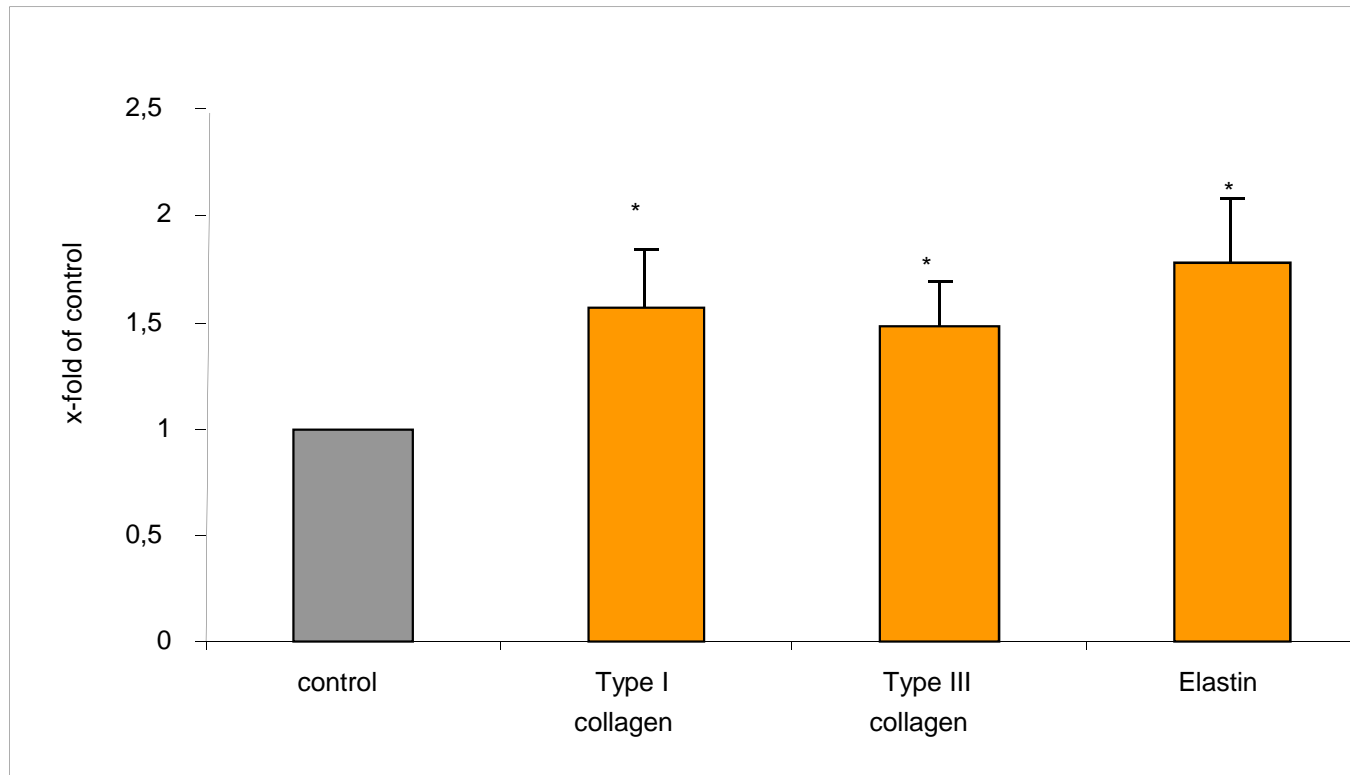
Tendons and Ligaments – Crucial for Performance

Tendons subject to many types of injuries. [...] The extrinsic factors are often related to sports and include excessive forces or loading, poor training techniques, and environmental conditions ¹



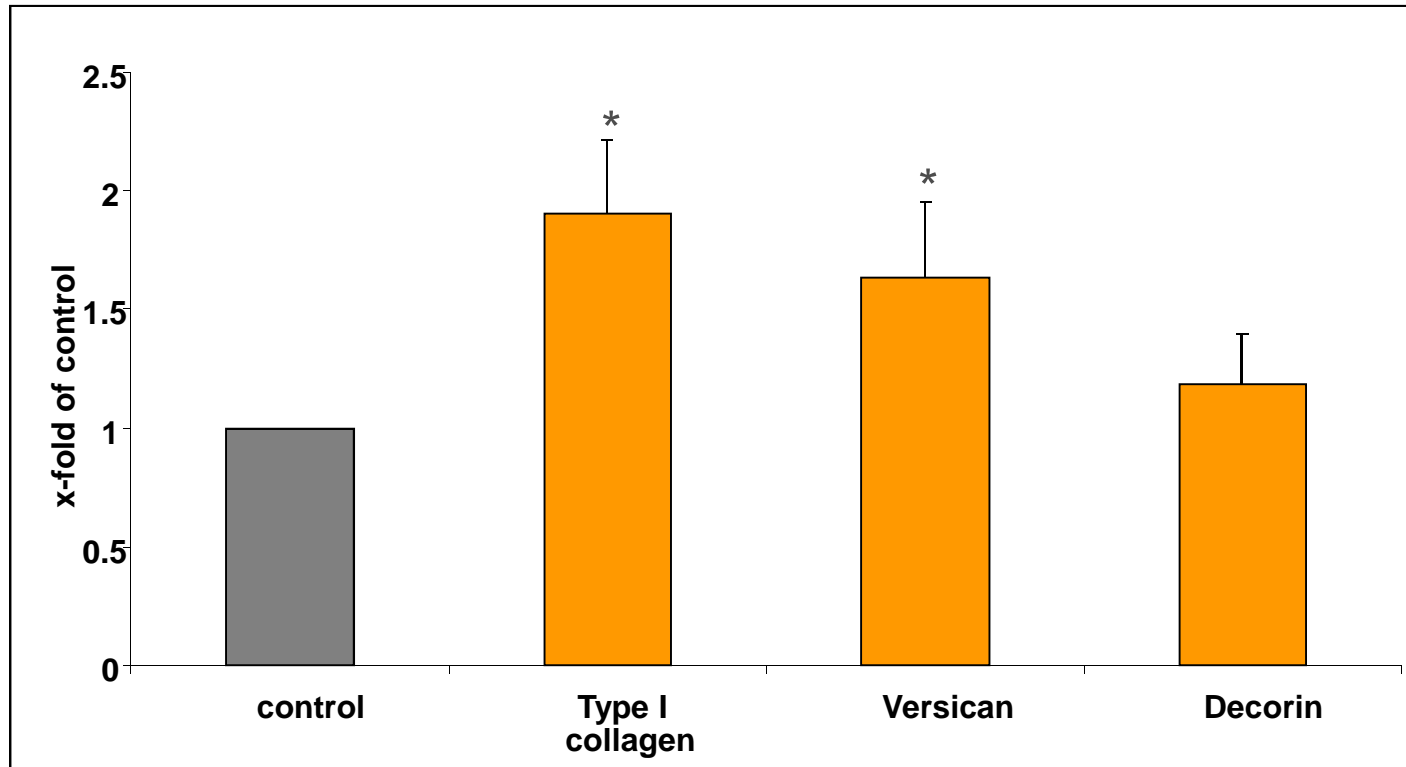
¹ Riley, G. (2004). "The pathogenesis of tendinopathy. A molecular perspective". *Rheumatology* 43 (2): 131–142

Human Cruciate and Hip Ligament Cells



A significantly increased collagen and elastin expression measured with treatment nuta protein and collagen[®] (n > 14; *p < 0.05) data: In-vitro test; RNA expression with FORTIGEL[®]

Extracellular Matrix molecules in Tenocytes



Significant increases of collagen, proteoglycan expression after treatment (n > 12; *p < 0.05)