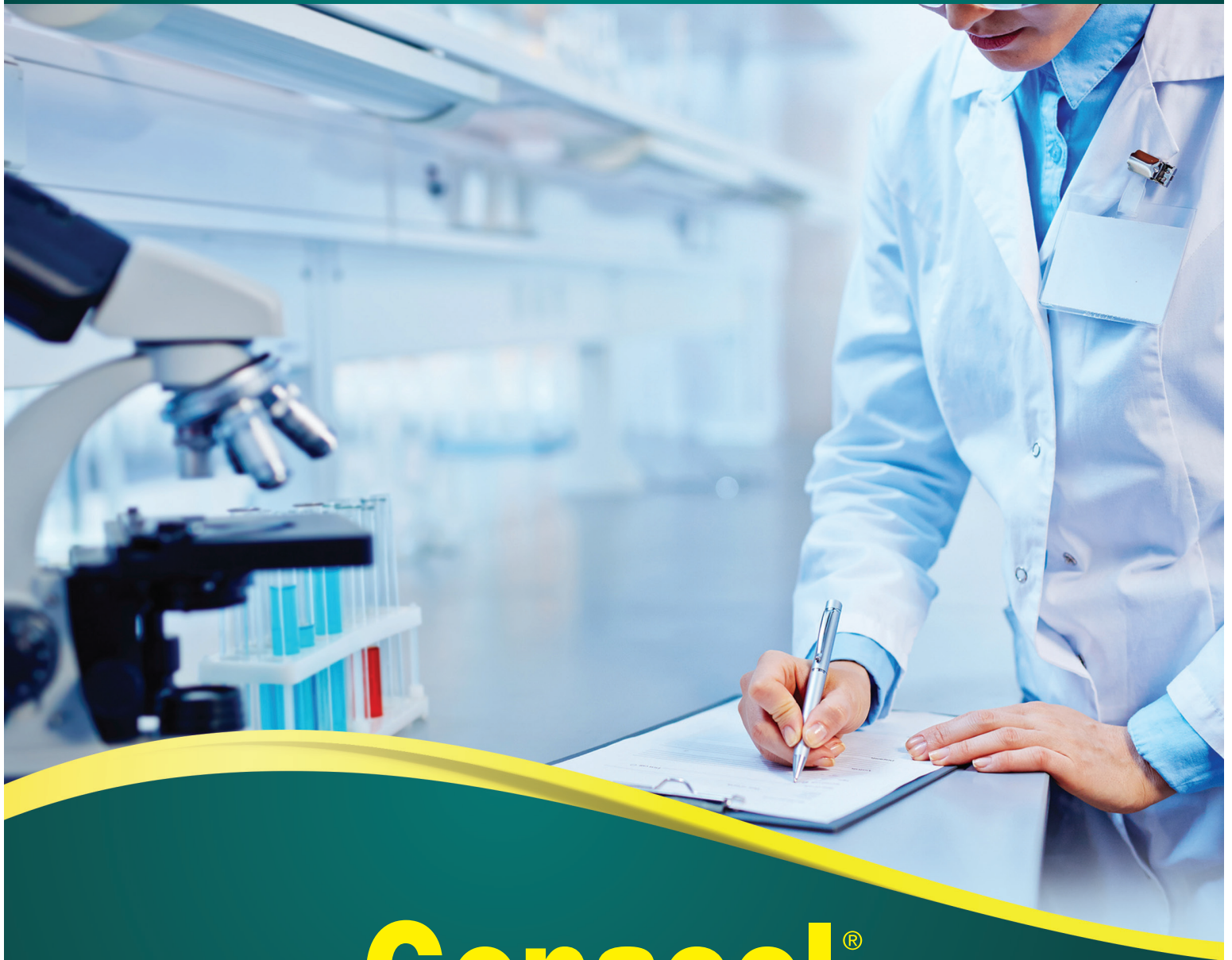


Scientifically proven
to improve joint health



Genacol[®]

AminoLock[®] Collagen

#1 ABSORBABLE
FORM OF
COLLAGEN



3 CLINICAL
STUDIES

Canadian technology



JOINTS, CARTILAGE AND COLLAGEN

Joints exist wherever two bones meet. They play a key role to ensure smooth and safe movements between the bones involved. Joints must thus deal with two major forces, namely load (including shock absorption) and friction. Synovial fluid present in the joint space acts as a hydraulic cushion in this context.

Cartilage is another important tissue that is found at the surface of each bone involved in a given joint. Cartilage is made up of 68 to 85% water, of 10 to 20% fiber (collagen) and of 5 to 10% lubricants (proteoglycans and glycosaminoglycans). Collagen, in itself, represents two-thirds of the dry weight of cartilage (CHART 1). It provides the structural scaffold onto which proteoglycans, glycosaminoglycans and water are integrated to give cartilage its physiological and mechanical properties. As for all components of the cartilage matrix, collagen is produced by chondrocytes, cells that are embedded in cartilage^(1,2). Collagen is the most abundant protein of the body, where it accounts for over 25% of all proteins. It is a fibrous protein composed of three long chains of amino acids (over 1000 amino acids each) organized in a triple helix structure reminiscent of a threaded rope⁽³⁾. (IMAGE 2 – PAGE 3 / IMAGE 4 – PAGE 5)

Collagen thus plays a central role to bestow joints with a great resistance to the friction caused by the movement of bones. Normally, there is a fine equilibrium between the degradation of collagen induced by this friction and its production by chondrocytes. However, the function of chondrocytes diminishes with age⁽¹⁾. In fact, collagen production begins to decline as early as age 30 and this reduction becomes much more prominent from age 50 and onwards^(1,2). (TABLE 1)

This loss of collagen contributes to the age-related deterioration of joint health, including the development of osteoarthritis⁽¹⁻³⁾. In fact, joint pain contributes in an important manner to the disability that people aged 50 and more suffer from. Current treatments include drugs, surgery and natural health products. However, the adverse effects of drugs severely limit their long-term use. Hence, several people turn to natural health products to improve their symptoms and joint function. One of the safest and most efficient natural health products is hydrolyzed collagen, a collagen derivative.

NORMAL VS OSTEOARTHRITIS

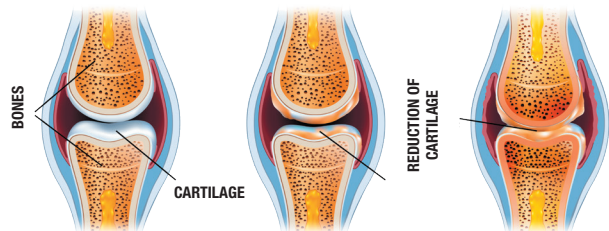


IMAGE 1 | JOINTS

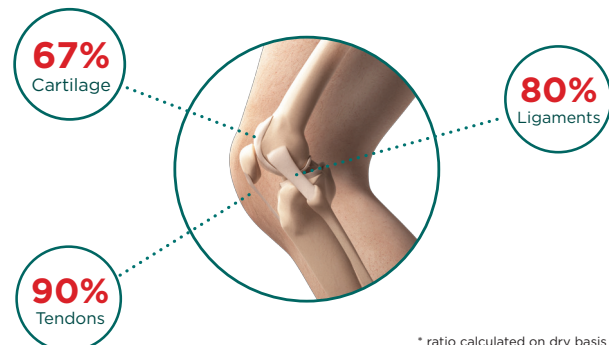


CHART 1 | COMPOSITION OF CARTILAGE

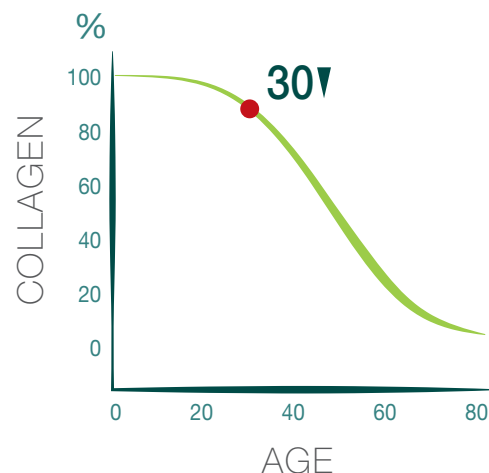


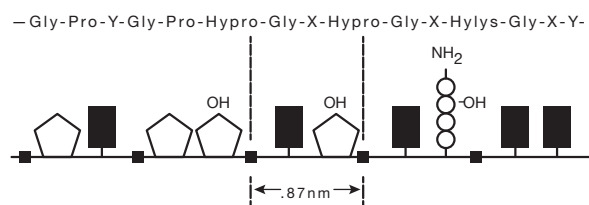
TABLE 1 |

JOINTS, CARTILAGE AND COLLAGEN (CONTINUED)

STRUCTURE AND FUNCTION OF COLLAGEN

Collagen contains almost all of the twenty naturally occurring amino acids: tryptophan being the only exception. Among these amino acids, three stand out for their important role in maintaining the triple helix structure and fibrous properties of collagen. These are glycine, proline and lysine. The molecular structure of collagen is based on a repeated amino acid sequence, Gly-X-Y, where X and Y are variable amino acids. Glycine, in itself, thus represents one-third of the amino acid content of collagen (approximately 1000 glycine residues per molecule of collagen). Each collagen molecule is also enriched in proline (more than 10% of all amino acids) and lysine (nearly 100 residues per molecule). Enzymes notably modify these two amino acids to generate 4-hydroxyproline and 5-hydroxylysine. The latter are essential to implement the triple helix structure of collagen⁽⁴⁾. 4-hydroxyproline is most often found in the Y position of the Gly-X-Y repeated sequence. On the other hand, hydroxylysine serves to create covalent linkages (crosslinks) between the three strands of the threaded collagen molecule, greatly stabilizing the triple helix. (IMAGE 2)

A. TYPICAL SEQUENCE



B. SIMPLE HELIX

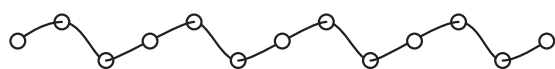


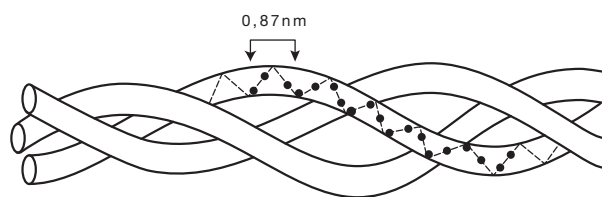
IMAGE 2 |

FOOD NEEDS IN AMINO ACIDS IN HUMANS

ESSENTIALS		NON-ESSENTIAL					
Gly	Histidine	Alanine	Glutamine	Asp			
Ala	Isoleucine	Arginine	Wistaria	Glu			
	Leucine	Asparagine	Proline				
Leu	Lysine	Aspartate	Serine	His			
	Methionine	Cysteine	Tyrosine				
	Phenylalanine	Glutamate					
Val	Threonine			Lys			
	Valine						
	Tryptophan						
		Phe	Tyr	Met	Thr	Asn	Lys
Ile		Pro	Cys	Ser	Gln	Arg	

IMAGE 3 | AMINO ACIDS FOUND IN COLLAGEN

C. TRIPLE HELIX



Hydrolyzed collagen:

A safe, efficacious and natural source of components to promote collagen production

WHAT IS HYDROLYZED COLLAGEN?

All amino acids necessary for the production of collagen can be obtained from the diet: notably from collagen itself, present in certain foods. However, by virtue of its fibrous and triple helix structure, intact collagen is hard to digest. Nevertheless, it is possible to render the amino acids of collagen more accessible by breaking down the protein before consuming it⁽⁶⁾. Such breakdown can result from hydrolysis; that is, by breaking the peptide bonds between amino acids in the collagen threads. Gelatine that is obtained by cooking certain foods represents a form of collagen that

is heat soluble. It is the result of partial hydrolysis and contains peptide fragments that are still relatively lengthy.

In contrast, hydrolyzed collagen is generated by subjecting animal gelatine (coming principally from skin, cartilage and bone) to a more thorough hydrolytic process. This provides a mixture of smaller peptide fragments that can dissolve in cold water. These peptide fragments are more easily digested and absorbed by the intestine. (IMAGE 4)

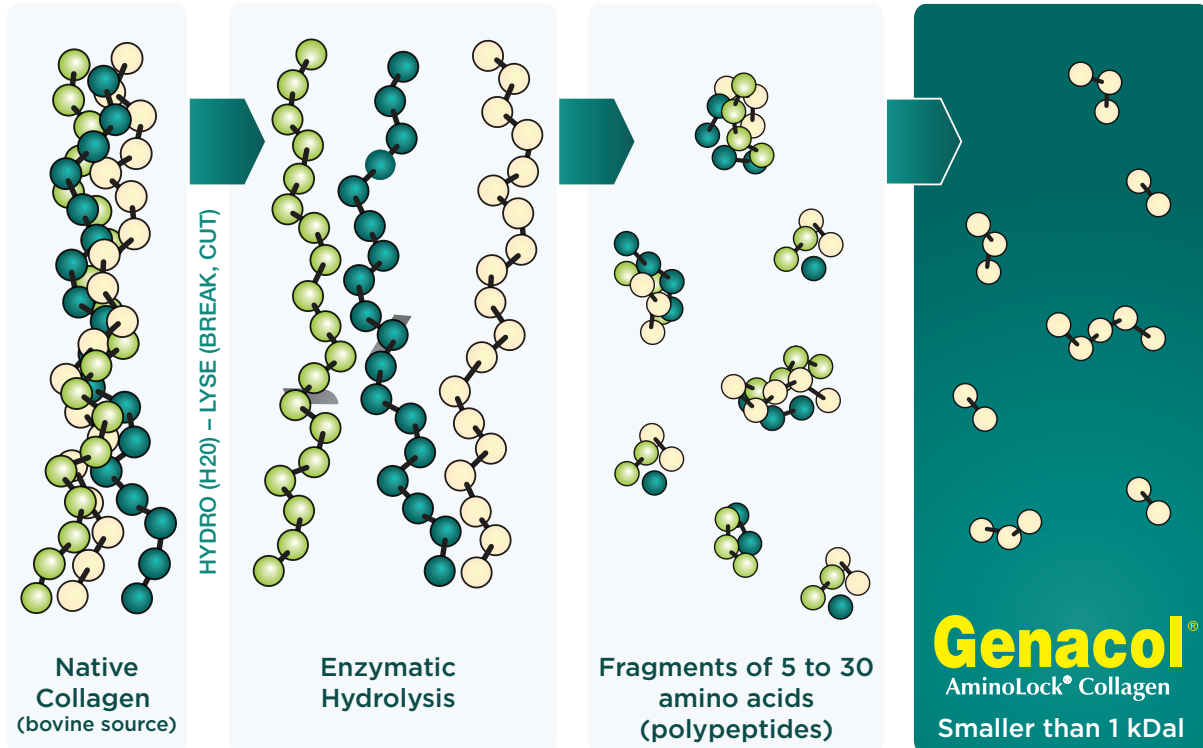


IMAGE 4 |

HYDROLYZED COLLAGEN (CONTINUED)

DIGESTION, ABSORPTION AND FATE OF HYDROLYZED COLLAGEN

Once ingested, pancreatic proteolytic enzymes (proteases) in the small intestine will digest hydrolyzed collagen. This digestion produces free amino acids as well as dipeptides (pairs of amino acids) that are readily absorbed through the gut. In fact, a human clinical study carried out by Iwai and collaborators clearly showed that such amino acids and dipeptides (notably proline-hydroxyproline combinations) reached maximal concentrations in the blood within 1-2 hours⁽⁷⁾. (IMAGE 5)

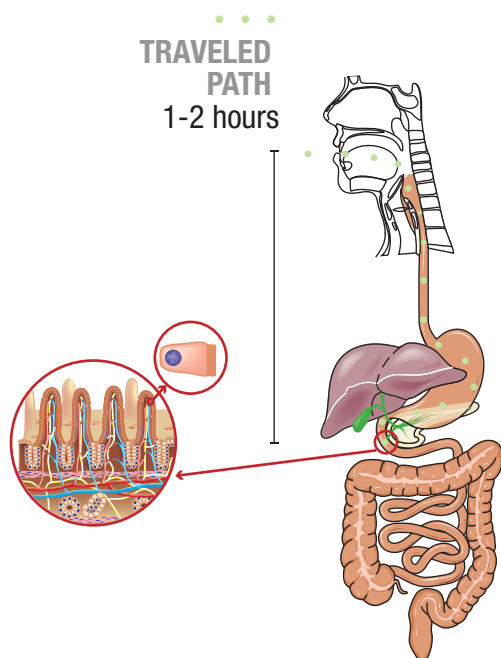


IMAGE 5 | DIGESTIVE SYSTEM

Another study used mice fed with hydrolyzed collagen that had been tagged with radioactive amino acids. Not only did amino acids and peptide fragments from hydrolyzed collagen make their way into the bloodstream, but they were also found incorporated into the cartilage of the mice within 12 hours⁽⁸⁾. (TABLE 3)

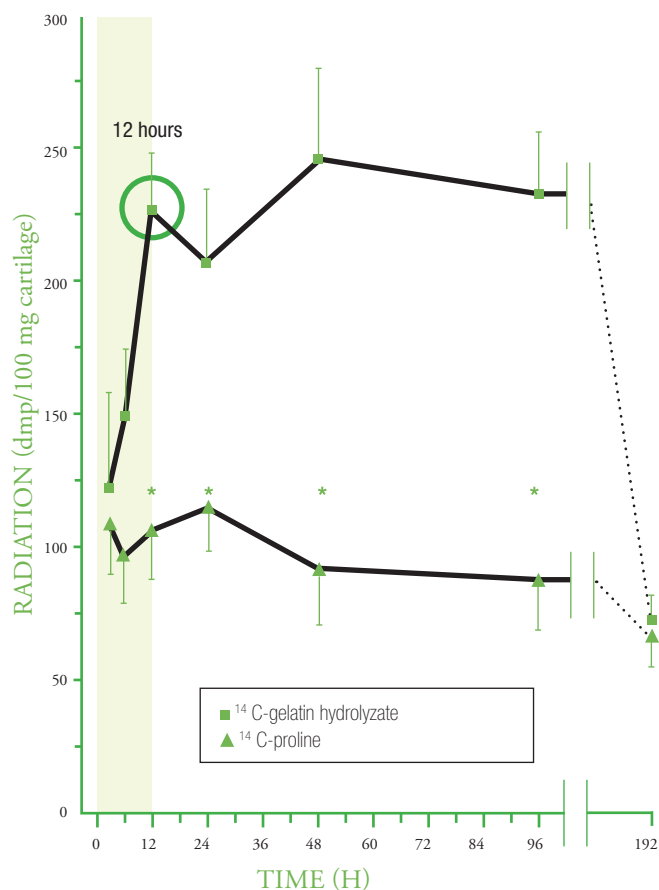


TABLE 3 | (8) Oesser S, Adam M, Babel W, Seifert J.



Genacol's AminoLock® Collagen is produced using a unique manufacturing procedure that takes collagen, and breaks it down to peptides that have a **Very Low Molecular Weight**.

The result: a unique Collagen Hydrolysate of less than 1 kDa that allows for greater absorption by the human body.

Genacol's AminoLock® Collagen is a unique protein complex that creates the lowest molecular size peptides in the world, creating the benefit of superior bioavailability and proven effectiveness for joint health (supported by 3 published scientific studies).

The proof of the effectiveness in using **Genacol's unique Very Low Molecular Weight AminoLock® Collagen** is now patent pending in the USA (Application number 62/426,908) and Canada (Application number 017808-0005).

Recently, **ConsumerLab.com**, an independent organization that evaluates nutritional products in the USA, recognized Genacol's clinical study as: **ONE OF THE LARGEST STUDIES ABOUT COLLAGEN HYDROLYSATE**. The report also mentions that after 6 months of taking the collagen (**Genacol**) 51.6% of the participants reported a reduction in pain (Bruyere, Comp Ther Med 2012)

HEALTHY JOINTS protein complex

LOW MOLECULAR WEIGHT COLLAGEN

PATENT PENDING EFFICACY



AMINOLOCK® SEQUENCE TECHNOLOGY

In order to generate an optimal preparation of hydrolyzed collagen, Genacol® has developed the AminoLock® Sequence Technology (AST). The process begins with high quality gelatine obtained from free-range nature-fed cattle. This gelatine is subjected to a well-controlled enzymatic hydrolysis, followed by a desalting procedure (based on ion exchange). The product is then concentrated by evaporation, sterilized and spray dried to produce a fine powder of the best quality.

The average size of commercially available hydrolyzed collagen generally varies between 6 and 10 kDa. In contrast, thanks to the AminoLock® Sequence Technology, the controlled enzymatic hydrolysis process produces peptide fragments of more uniform size, 90% of **which are smaller than 1 kDa**. Moreover, this technology enables Genacol® to ensure its AminoLock® Collagen contains well-established proportions of key amino acids required to promote collagen production in the body and to give an optimal outcome. In fact, it would take up to 5 to 10 times more of a standard hydrolyzed collagen product to obtain an equivalent concentration of certain amino acids and peptide fragments present in Genacol's AminoLock® Collagen.

Furthermore, the entire manufacturing process and quality control criteria respect the most rigorous standards in the industry. Genacol's AminoLock® Collagen is **manufactured in an FDA regulated plant that is GMP and HACCP certified**. The stainless steel equipment and self-contained CIP (Clean In Process) system ensure our products cleanliness and traceability. This entire process assure that we can offer a high-quality, reliable and efficient product to our customers. ■



GENACOL® CLINICAL STUDY: SHOWING EVIDENCE IN REDUCING PAIN

GENACOL®'S AMINOLOCK® COLLAGEN HAS BEEN THE SUBJECT OF THREE QUALITY CLINICAL STUDIES THAT DEMONSTRATED THE EFFICACY OF THE PRODUCT IN THE CONTEXT OF JOINT DISEASE.

The first study was a multicenter randomized placebo controlled trial carried out in Belgium by world-renowned researchers in the field of osteoarthritis⁽¹⁰⁾.

Patients suffered from joint pain in various areas: upper body (shoulder, elbow, wrist), lower back or lower body (hip, knee). Over 140 patients were randomly assigned to receive either 1200 mg of Genacol® AminoLock® Collagen or a placebo. The study was well balanced (baseline patient characteristics) and of excellent quality. The authors used a visual analog scale (VAS), which is the Gold Standard reference test for the subjective assessment of pain⁽¹¹⁾. The VAS scale is notably used to demonstrate the clinical efficacy of analgesic drugs and is recognized by regulatory agencies such as the US Federal Drug Agency (FDA) and the Canadian Therapeutic Products Directorate (TPD). **After six months of treatment, the clinical studies showed a significant increase in the proportion of responders (minimum 20% improvement in pain VAS score) as compared to placebo.** This result is all the more significant if one considers that the study subjects suffered from pain at various joint areas, whereas the vast majority of other trials concentrate on a particular joint (for example, the knee).

In fact, when results were segregated according to different body regions, treatment with Genacol's AminoLock® Collagen was even more impressive. For instance, **for the upper body (shoulder, elbow, wrist) and the lower back, twice as many patients taking Genacol® AminoLock® Collagen noted an improvement in joint pain as opposed to patients on placebo.** (TABLE 5)

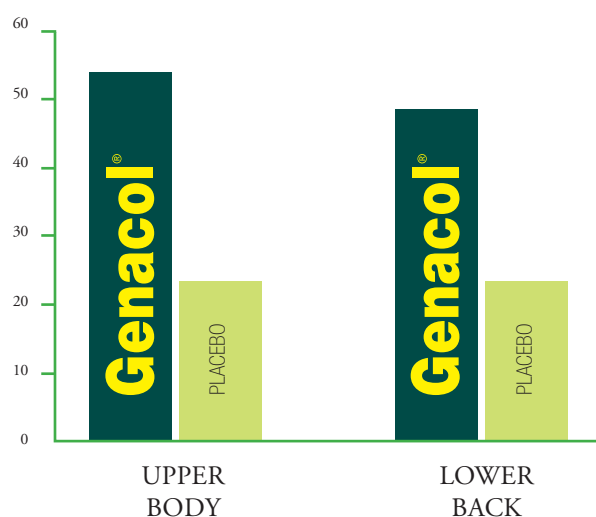


TABLE 5 |



GENACOL® CLINICAL STUDY: SHOWING EVIDENCE IN IMPROVING JOINT SPACE

A second clinical study was carried out in a Veterans Hospital Center in the Philippines; this time the study focused on patients suffering from knee osteoarthritis (12).

A total of 113 patients were randomly assigned to receive either a daily dose of 1200 mg of Genacol® AminoLock® Collagen or a daily dose of 200 mg of aceclofenac, a standard non-steroidal anti-inflammatory drug (NSAID). The authors used the Western Ontario and MacMaster Universities Osteoarthritis Index (WOMAC). The latter is often considered as the reference test for knee osteoarthritis since it assesses pain and joint function in several daily situations of rest and activity (13). After six months of treatment, the WOMAC score of patients taking Genacol® AminoLock® Collagen was significantly reduced, whereas that of patients taking aceclofenac was not. **This clearly demonstrates that joint pain and function were considerably improved by the daily administration of Genacol® AminoLock® Collagen, an effect that was significantly superior to the reference NSAID drug.**

The Phillipino study also used radiological measurements to assess joint space at baseline and monthly during the treatment period. In the group of patients taking aceclofenac, there was a strong tendency for joint space to be reduced after six months. In contrast, patients taking Genacol® AminoLock® Collagen showed some improvement in joint space over the same period. **This indicates that Genacol®'s hydrolyzed collagen can not only reduce pain and improve knee function in patients with osteoarthritis, but that it can also prevent the deterioration of joint space over time.** (TABLE 7)

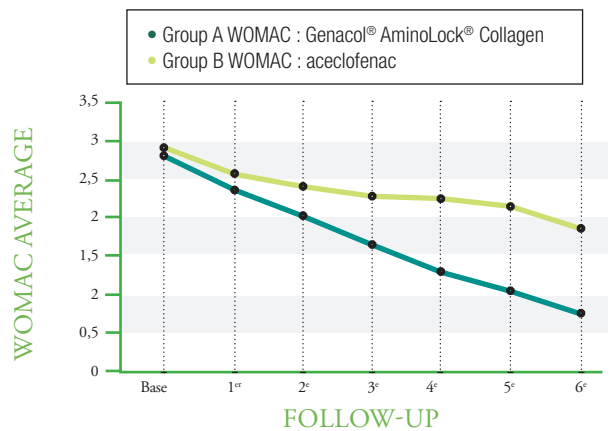


TABLE 6 |

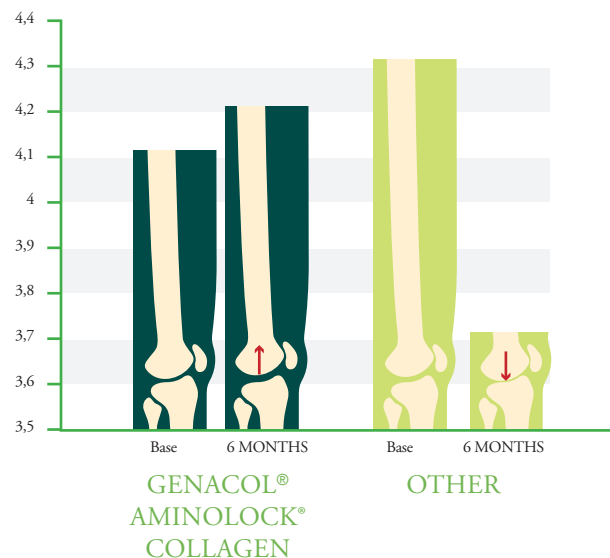


TABLE 7 |



GENACOL® CLINICAL STUDY: SHOWING EVIDENCE IN IMPROVING CARTILAGE ABRASION & MENISCAL PROTRUSION

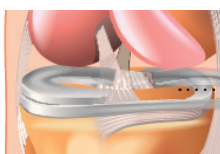
A third clinical study was developed at the University of Santo Tomas Hospital in the Philippines. The objective was to determine whether taking Genacol® AminoLock® Collagen, combined with a physical exercise programme, shows a significant reduction of cartilage wear.

In the study, participants were randomly selected. A treatment group (n=56) took three 400mg capsules of Genacol® Aminolock® Collagen daily for six months and a control group (n=53) took a placebo. The two groups were subjected to a standard programme. Evaluations were carried out at the start and end of the six months. These evaluation included the review of participants' medical records, a physical exam, WOMAC evaluations and ultrasonography of both knees. Calculation of means and standard deviations was carried out for demographic information, visual analogue scale (VAS) pain evaluations, WOMAC evaluations and ultrasound measurements.

Results: in general, WOMAC and VAS evaluations decreased compared to the initial evaluations of both treatment groups. There was a significant increase of 62.5 % in the execution of the exercise programme by the treatment group who took Genacol® Aminolock® Collagen.

The Genacol® AminoLock® Collagen group demonstrated a fairly significant change in the average level of cartilage wear (-0.13 ± 1.22 , $p = 0.009$, before treatment 2.22, after treatment 2.10) compared to the placebo group (before treatment 1.99, after treatment 2.37) (TABLE 8). The result of **central cartilage** (-0.6 ± 1.25 , $p = 0.013$, before treatment 2.33, after treatment 1.77) compared to the placebo group (before treatment 1.52, after treatment 1.82) (TABLE 9).

Conclusions: our clinical team demonstrated that Genacol® Aminolock® Collagen, combined with an exercise programme, reduced pain, improved general functional status and produced changes in the intra-articular and peri-articular structures (that is, an improvement in the level of wear of cartilage and a decrease in the movement of the lateral meniscus (from 0.20 ± 0.16 cm to 0.13 ± 0.16 cm, $p=0.05$)) (IMAGE 7) of patients with osteoarthritis of the knee.



LATERAL
MENISCAL
PROTRUSION

IMAGE 7 |

SONOGRAPHIC MEASUREMENT OF MEDIAL CARTILAGE

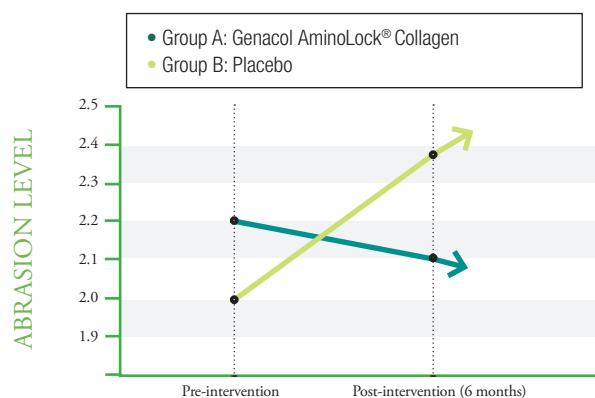


TABLE 8 | Sonographic measurement showing that people taking Genacol® AminoLock® Collagen with an exercise program has shown a decrease in the abrasion level compared with the control group that showed a significant increase.

SONOGRAPHIC MEASUREMENT OF CENTRAL CARTILAGE

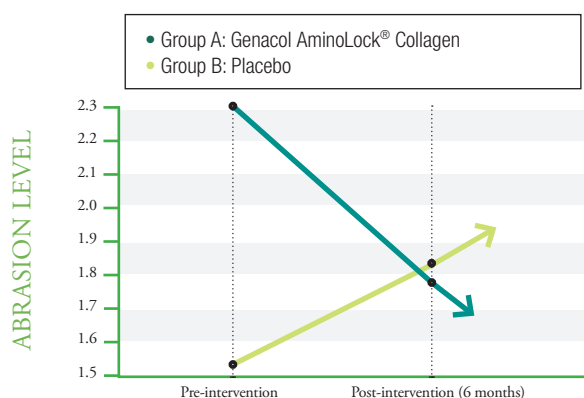


TABLE 9 | Sonographic measurement showed the same evidence as TABLE 8.

GENACOL® AMINOLOCK® COLLAGEN: A NATURAL AND SAFE CHOICE

The clinical studies carried out with Genacol® AminoLock® Collagen also demonstrated the great safety profile of the product. Indeed, in the study of Bruyère and collaborators, Genacol® AminoLock® Collagen was very well tolerated, in a manner similar to the placebo.

	AminoLock® Collagen	Placebo
SATISFACTION IN TERMS OF TOLERANCE		
Very satisfied	43.3%	40.4%
Satisfied	35.1%	32.3%
Moderately satisfied	13.4%	15.2%
Unsatisfied	8.3%	7.1%
Very unsatisfied	0%	5.1%

TABLE 8 | Proportion of patients (%) according to their level of satisfaction in terms of tolerability

Genacol® AminoLock® Collagen also did not induce any more adverse events than the placebo. All adverse events were minor in nature. Moreover, the group treated with Genacol® AminoLock® Collagen had a tendency to show less adverse events than the placebo group at both gastrointestinal and respiratory levels.

	AminoLock® Collagen	Placebo		AminoLock® Collagen	Placebo
Senses (eyes, ears, taste, smell)	4.1%	3.0%	Musculoskeletal	23.7%	16.2%
Cardiovascular	3.1%	8.1%	Hematologic / lymphatic	0%	0%
Respiratory	15.5%	22.2%	Neurological / psychiatric	7.2%	8.1%
Gastrointestinal	15.5%	26.3%	Dermatological	6.2%	4.0%
Hepatic / Biliary	0%	0%	Immunological	1.0%	0%
Genitourinary / reproduction	5.2%	1.0%	Allergy	0%	0%
Kidney / Renal	0%	0%	Other	7.2%	6.1%
Endocrine / Metabolism	2.1%	3.0%			

TABLE 9 | Proportion (%) of patients with at least one adverse event during the study, depending on the affected system.

**Genacol®
AminoLock®
Collagen also
did not induce
adverse events
more than
the placebo**

WHY CHOOSE GENACOL® AMINOLOCK® COLLAGEN

- **The only product to use Genacol®'s AminoLock® Sequence Technology which creates a unique Collagen Hydrolysate of less than 1 kDa for superior absorption by the human body.**
- **A certified non-GMO product coming from pasture-raised and grass-fed cattle.**
- **The only product to have demonstrated efficacy for the reduction of joint pain at a daily dose of 1.2 gm as opposed to other product requiring daily doses of 10 gm through 3 clinical studies.**
- **A well-renowned product available worldwide, sold in more than 40 countries.**
- **A product that does not induce adverse events more than a placebo.**

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A network diagram background consisting of numerous light blue circles of varying sizes connected by thin, light blue lines, creating a complex web-like structure against a dark teal background. A thick yellow curved line sweeps across the bottom of the page.

Genacol[®]

AminoLock[®] Collagen



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