



Genacol[®]

AN INNOVATIVE RESEARCH LEADER

Collaborative research project with



Who we are

Genacol® is a leading brand of joint care supplements in Canada. Our mission is to offer the best innovative natural health products to help people age healthy and stay active longer.

Although our products are now available in over 40 countries, Genacol® remains a human-size family-owned company dedicated to customers' well-being through their joint health since 2000.

The Genacol® difference:

A unique collagen hydrolyzate



AminoLock Collagen®, the main component of all of our supplement products, is a bioactive complex of collagen hydrolyzate made with **AminoLock® Sequence Technology**.

This patented method makes it possible to obtain, from bovine collagen proteins, peptides (small chains of amino acids) weighing less than 1,000 daltons (Da). This is the smallest molecular weight used among all the collagen products available on the world market.

Proven results



With this low weight, our product is better absorbed by the body than those of the competition. This characteristic may likely result in better effects on the joints and better control of pain associated with osteoarthritis.

Scientifically proven effectiveness



The effectiveness of **AminoLock Collagen®** products in reducing joint pain associated with osteoarthritis is supported by three clinical studies, carried out in Belgium and the Philippines on patients suffering in particular from osteoarthritis.

High manufacturing standards



Our collagen products are all made in GMP certified facilities. We also abide by the highest standards in the natural supplement industry in order to always deliver the highest quality products.



McGill Collaborative Research Project

At **Genacol®**, we care about the joint health and well-being of our patients. This is why we have been committed for more than 20 years in a quest for excellence driven by a strong desire for innovation.

This is what prompted us to develop a unique product: **AminoLock® Collagen**. Although the creation of this collagen hydrolyzate is a great achievement, our desire for innovation and better understanding our AminoLock collagen was not satisfied.



McGill
UNIVERSITY

Therefore, we continuously invest in research and development and we create collaborations with teams from recognized universities, such as McGill University, which ranks number 1 in Canada for medical research according to the McLean Magazine ranking.

Genacol®: An Innovative Research Leader

In order to maintain our position in the market and to provide our patients with the best natural supplements, we are constantly pursuing our technical and scientific innovation initiatives. In addition to our investments in internal research and development, we maintain external partnerships with recognized teams.

To date, three independent clinical studies (the Bruyère, Parm and Suarez studies conducted in Liège, Belgium and the Philippines) have demonstrated the effectiveness of **AminoLock® Collagen** in reducing joint pain associated with osteoarthritis. One of these studies (Suarez study) also demonstrated that taking **AminoLock® Collagen** combined with physical activity led to functional joint improvements, in addition to inducing beneficial intra-articular and periarticular structural changes.



BRUYÈRE STUDY

Bruyère O, et al. Effect of collagen hydrolysate in articular pain: A 6-month randomized, double-blind, placebo controlled study. Complement Ther Med (2012).



PARM STUDY

Maria Lourdes R. Bernardo and Alfredo C. Azarcon, Jr. Effects of Oral Collagen Treatment on the Media Knee Joint Space and Functional Outcome among Veterans Memorial Medical Center Patients Diagnosed with Osteoarthritis of the Knee (2012).



SUAREZ STUDY

Chan, R., & De Los Reyes, M. F. Effect of Collagen Hydrolysate as adjuvant treatment to Exercise for Knee Osteoarthritis (2016).

To consult our clinical studies in their entirety, visit our website: www.genacol.ca/en/clinical-studies/

The Beginning of the McGill Collaboration

These clinical studies have been able to demonstrate that our product has beneficial effects on joints. However, they could not investigate a direct link between the precise characteristics of **AminoLock® Collagen** (sequencing method, low molecular weight, etc.) and these benefits. To do so, the analysis of the process of absorption and metabolism of our product would have been necessary, although impractical.

This is what prompted us to develop a scientific partnership with the team of **Dr. Stan Kubow** of the **School of Human Nutrition at McGill University**, an institution whose biomedical research stands out nationally and internationally. This association, started in 2017, seemed natural to us given Dr. Kubow's vast experience in the development of natural supplements derived from food-derived products and in the development of innovative analysis models.



Meet the Research Team



Dr Stan Kubow
Associate Professor,
School of Human Nutrition,
McGill University

Senior investigator



Christina Larder
Doctorate Candidate
Mcgill University Department
of Human Nutrition

Research Assitant



Dre Michele Iskander
Research Associate
and Lecturer

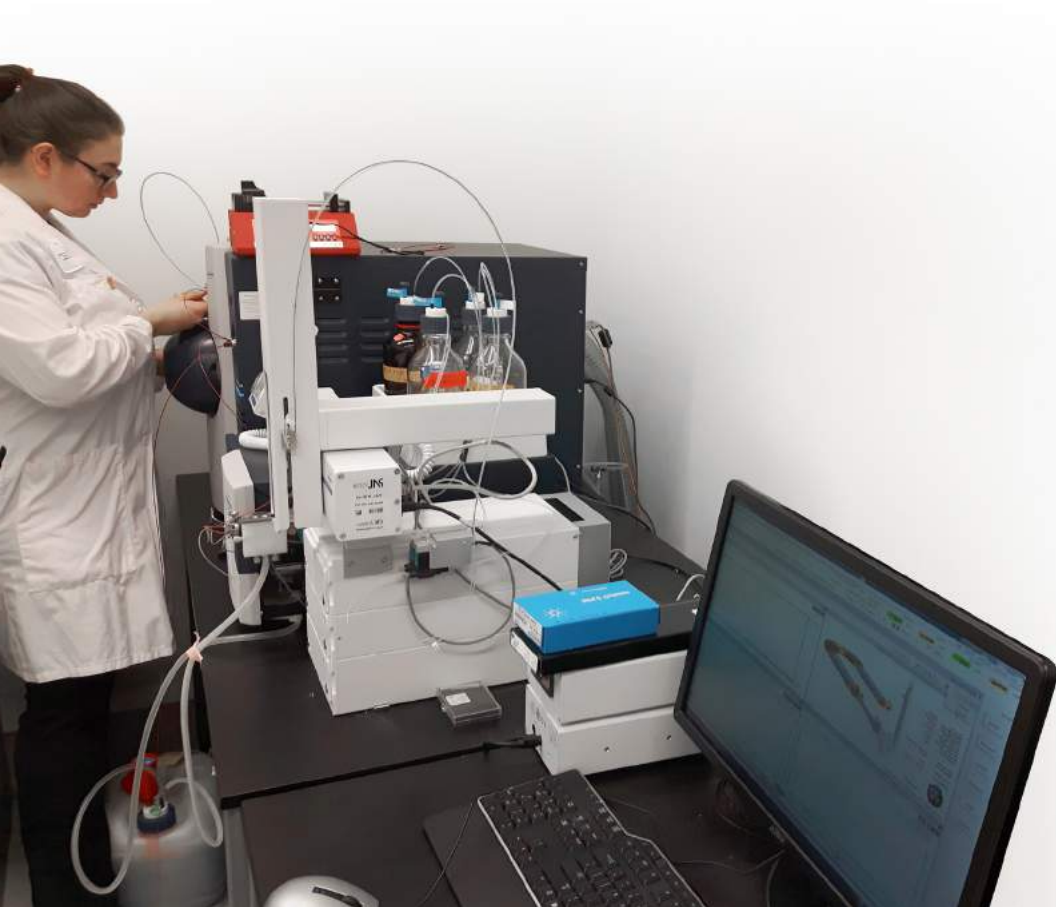
Associated Researcher

Bioavailability under study

Together with doctoral candidate Christina Larder and Dr. Michele Iskander, a research associate and lecturer trained in gastrointestinal digestion models, cell culture analyzes and peptide characterization, Dr. Kubow created and then implemented in practice, a study aimed at investigating the bioavailability of **AminoLock® Collagen**.

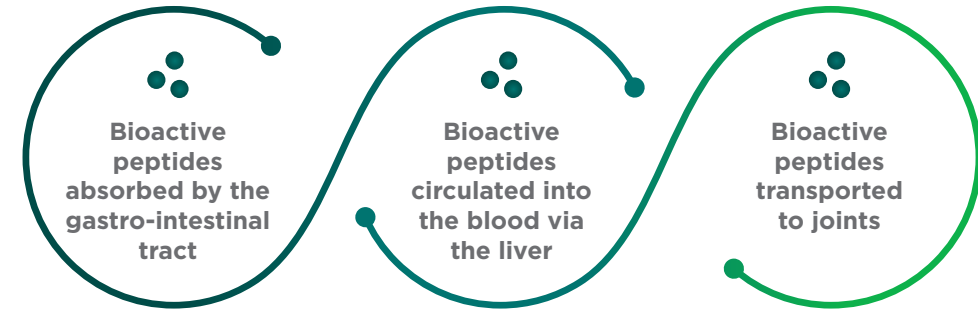
The partnership between Genacol® and this McGill University research team was based on the limitations of studies properties and mechanisms of action of hydrolyzed collagen products.

Most of the current work published up to now have primarily used collagen hydrolysates or bioactive peptides directly on the tissues of interest (e.g. cartilage) without first having assessed their degree of digestion by the gastrointestinal system, as well as accounting for bioavailability (absorption) and the effects of their metabolism by the liver.

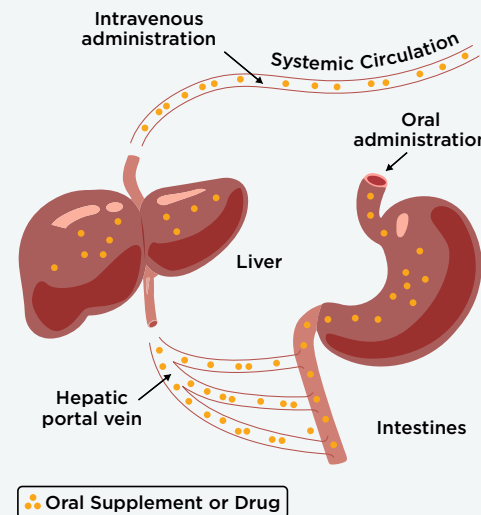


Research Problem

Dr. Kubow's team observed a lack of data on the bioavailability of collagen supplements (and bioactive peptides) after absorption by the small intestine and metabolism by the liver.



FIRST PASS METABOLISM



In this process, known as the **first pass metabolism**, the hydrolyzed collagen products are absorbed by the small intestine and metabolized by the liver before entering into the systemic circulation.

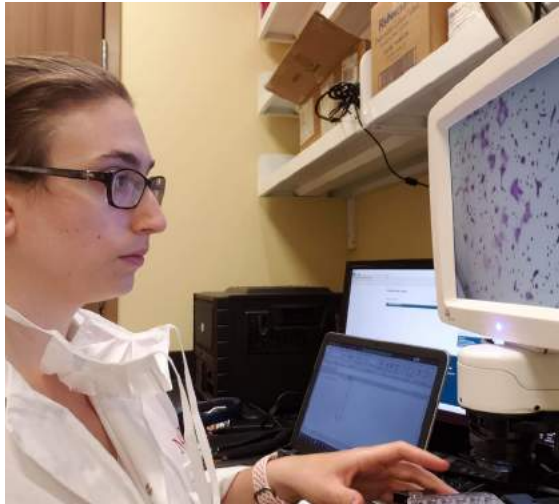
Once the collagen peptides reach the systemic circulation they travel throughout the body and carried to the joint tissues, where they exert their bioactivity. The shape of peptides (weight, properties, composition) that arrive at the joints is different from what they originally had.

The challenge for the team was therefore to find a way to measure the bioavailability of peptides generated by hydrolyzed collagen products (**AminoLock® Collagen** in particular) once absorbed and metabolized.

An Innovative Process

As a result, an innovative research study was developed to overcome the limitations of current published work and obtain convincing results regarding the bioavailability of collagen hydrolysate peptides.

Dr. Kubow and his collaborators have thus implemented a model to identify and quantify key bioactive peptides as they are when they enter the joints.

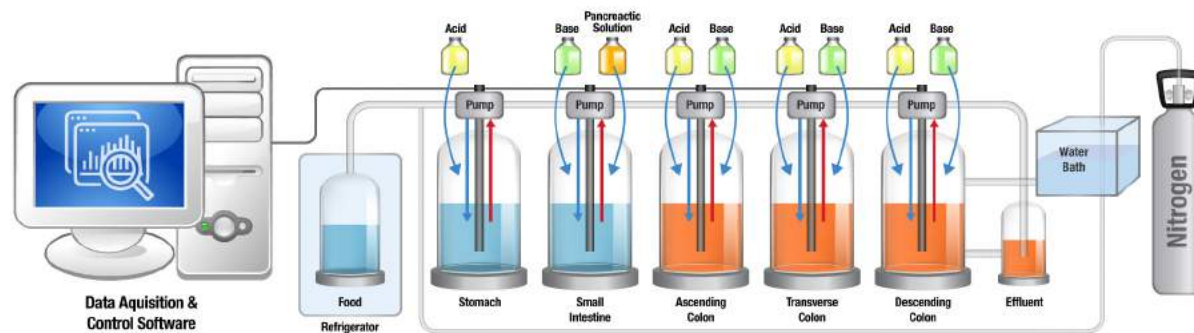


The analytical data was obtained by first simulating human digestion and then using a novel cell culture method to replicate the human small intestine and liver system.

The bioavailability of key peptides generated from **Genacol**[®]'s collagen hydrolyzate and a generic bovine collagen product is analyzed.

The results were also compared with data available in the literature obtained from other collagen products, as no studies of this type have used bovine before.

Computer Controlled Dynamic multi-stage gastrointestinal digestion model



- ▶ Validated to generate peptide profiles matching human gastric/duodenal aspirates
- ▶ Assess prebiotic potential (microbiome)

The Stages and Particularities of the Analysis System



The analysis is based at quantifying the bioavailability of the peptides generated during the first-pass metabolism effect.

The McGill team used a small batch digestion model, which simulated the digestive effects of the stomach and the small intestine. Samples are taken and applied to cell cultures to assess the bioavailability of the peptides.

The purpose of this step (cell culture) is to simulate the first-pass metabolism, i.e., the absorption of peptides by the gastrointestinal cells then their metabolism by the liver. Samples from the digestion experiment are applied to the cell culture system.

The samples from the cell culture system are then assessed using a capillary electrophoresis device to identify and quantify peptides, to calculate the bioavailability.

The two models used (simulated digestion model, and cell culture first pass metabolism model) are both characterized by high sensitivity. While this attribute provides specific results, it presents its share of challenges. For example, the operation of this this modelling process requires permanent monitoring; even the slightest change in pH or temperature may affect results.

Furthermore, cell culture is always at risk for contamination, even with standardized and strict protocols.

In addition, any necessary manipulations must be done with care in order to avoid fluctuations and contamination of cell cultures.

This unique and complex model has therefore made it possible to understand how Genacol[®] exclusive collagen hydrolyzate reaches a patient' joint after being ingested orally.

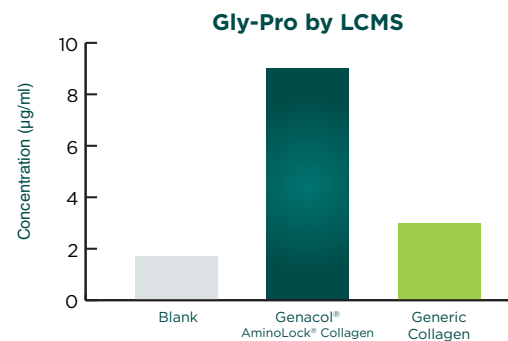
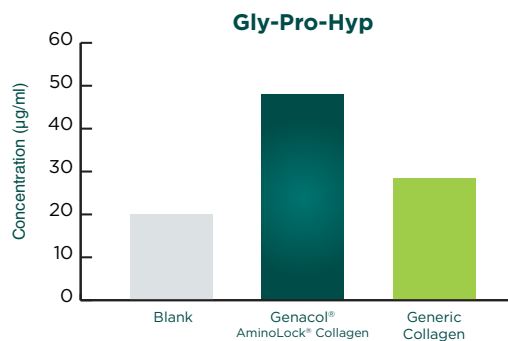
Note that the accuracy of these results and the validity of these findings owe a great deal to the method used for identification and quantification, which is sensitive enough to detect small peptides without interference from other molecules (digesta and metabolites).

Convincing results

More specifically, research has identified and quantified the bioavailability of key peptides after the complete process of digestion, absorption, and metabolism.

Dr. Kubow and his team have made certain observations:

- The bioactive peptides Pro-Hyp, Gly-Pro, Hyp-Gly, and Ala-Hyp and Gly-Pro-Hyp from **AminoLock® Collagen** are absorbed and then transferred into the systemic circulation (first pass metabolism);
- Only the Gly-Pro-Hyp present in **AminoLock® Collagen** is absorbed and then transferred into the systemic circulation. The peptide Gly-Pro-Hyp from the generic product does not undergo the first pass effect and is therefore not bioavailable and will not reach the joints, so the effects associated with this peptide chain are therefore lost);
- The peptides that reach the systemic circulation have significant permeability (absorption capacity). **AminoLock® Collagen** products also have better permeability of Gly-Pro-Hyp peptides compared with other collagen hydrolyzates from bovine sources and those from fish, which were compared;
- Peptides are also metabolized by the liver before being released into the systemic circulation, but to different degrees depending on the product;
- Genacol® unique collagen hydrolyzate is better metabolized than the generic: changes in the composition of the peptide chains, as well as a significant increase (around 40%) in the contents of Pro-Hyp are observed there, but not in the generic collagen.



Genacol®
AminoLock® Collagen

Generic
Collagen

BIOAVAILABILITY (the contents after absorption by the intestine and metabolism by the liver)

Significant absorption of Pro-Hyp, Gly-Pro, Hyp-Gly, and Ala-Hyp and Gly-Pro-Hyp peptides.

Gly-Pro-Hyp peptides are not absorbed.

LIVER METABOLISM

40% increase in Pro-Hyp peptide content

No significant increase in peptide content.

POTENTIAL EFFECTS ONCE IN THE SYSTEMIC CIRCULATION

Pro-Hyp: a few effects

- Prevents thinning of cartilage;
- Helps reduce bone loss (in the subchondral bone, located below the cartilage);
- Stimulates the synthesis of hyaluronic acid;
- Pro-Hyp may help regulate and decrease inflammation.

Gly-Pro-Hyp is not bioavailable, therefore its effects are lost.

Pro-Hyp is bioavailable, but are metabolized at lower levels in the liver.

Gly-Pro-Hyp: a few effects

- Acts as an inhibitor of DPP-IV, an enzyme that helps control blood sugar in type 2 diabetes;
- Participates in the aggregation of platelets;
- Acts on the central nervous system;
- Like Gly-X-X, it promotes the bone healing process in the long term;
- Has the potential, if metabolized in this manner, to share the properties of Pro-Hyp and Gly-Pro. These effects are additive in addition to their individual effects.

Some definitions

Proteins

These are the macromolecules (large molecules), which make up the bulk of living things and the tissues that make them up. They are made of combinations of peptides, chains of even smaller molecules, amino acids. These combinations, which vary widely, determine the shape and function of proteins.

Amino acids

These are molecules that the body uses to form the proteins that make up its tissues and organs. There are 20 that are necessary for humans. The body is capable of producing some of them while others must come from external sources, either because they are not naturally present or because they are in insufficient quantity (due to age or to increased need).

Peptides

These are relatively long sequences of amino acids, held together by a peptide bond. These chains of multiple peptides (polypeptides) then bind together to form proteins according to a predetermined characterization (order, nature, number of sequences) in the DNA.

Bioavailability

This is the extent to which a drug, supplement, or compound taken by mouth becomes available when it enters the systemic circulation. It is measured as a percentage. This is the «amount» of the supplement available in the blood.

Metabolization

This term is used to describe chemical reactions, including those produced by enzymes, which break down complex foods and filter nutrients. The metabolization of peptides takes place during gastrointestinal digestion (in the stomach and small intestine) and in the liver. There they are broken down, that is, reduced into smaller chains, and transformed.

These are the chemical reactions the supplement goes through during digestion/before entering the bloodstream.

First pass metabolism

It is the process of absorption through the digestive tract (gastrointestinal tract) and metabolization by the liver of a drug, supplement or compound taken orally. The compounds are eventually released into the systemic circulation.

This is the process the supplement goes through.

Systemic circulation

Also called large circulation, it is through this system that the blood loaded with oxygen and nutrients is carried to the various tissues before being returned to the heart and lungs.



Major Conclusions

The results were obtained by performing an evaluation of the peptide profile of the collagen hydrolyzate products (**Genacol**[®] and the generic) analyzed before and after first pass metabolism.

The peptide profiles of **AminoLock**[®] **Collagen** and other collagen products were analyzed and confirmed that the **Genacol**[®] product is different and unique compared to a generic bovine source collagen hydrolyzate.



Greater Bioavailability

The study confirmed the greater bioavailability of key peptides generated from **AminoLock**[®] **Collagen** compared to a generic one.



Peptides with confirmed properties

The breakdown, absorption and metabolism of bioactive peptides were completed. Peptides with known bioactivity and benefits to joint and bone health were measured.



Better absorption

In other words, several important peptides of **AminoLock**[®] **Collagen** have been shown to be better absorbed and metabolized. These results help support and may explain why **Genacol**[®] continues to see positive clinical results.

Genacol[®] makes me feel so good!

Futures Implications of the Results

The results obtained so far thanks to this collaboration, which we intend to continue, are promising and encouraging, both for the field of research in nutrition and medicine as well as for our company.

Dr. Kubow's team successfully developed a unique analysis system to produce strong evidence of collagen hydrolysate bioavailability. This method, which represents a real scientific breakthrough, can be used in the context of other studies aimed at measuring the bioavailability of new drugs, supplements or nutrients.

For our part, this research has allowed us to confirm that our product contains bioactive peptides, which have known effects on bone and joint health. Furthermore, the effects of the unique composition of **AminoLock**[®] **Collagen** on its absorption and metabolism could also be observed.

To conclude, we have gained a better mechanical understanding of the properties of our collagen product. We have filed a second patent application in connection with these results. In addition, we are working on the development of a new generation of supplements with increased biopotential.

To sum up, now that we have a better understanding of the process of absorption and metabolism of **AminoLock**[®] **Collagen**, we are motivated to further improve our product to make it even more effective in reducing joint pain.

This research, and future research, will undoubtedly help us refine our innovative technology and its beneficial applications.

You want to learn more about **Genacol**[®]?

Visit our website genacol.ca

