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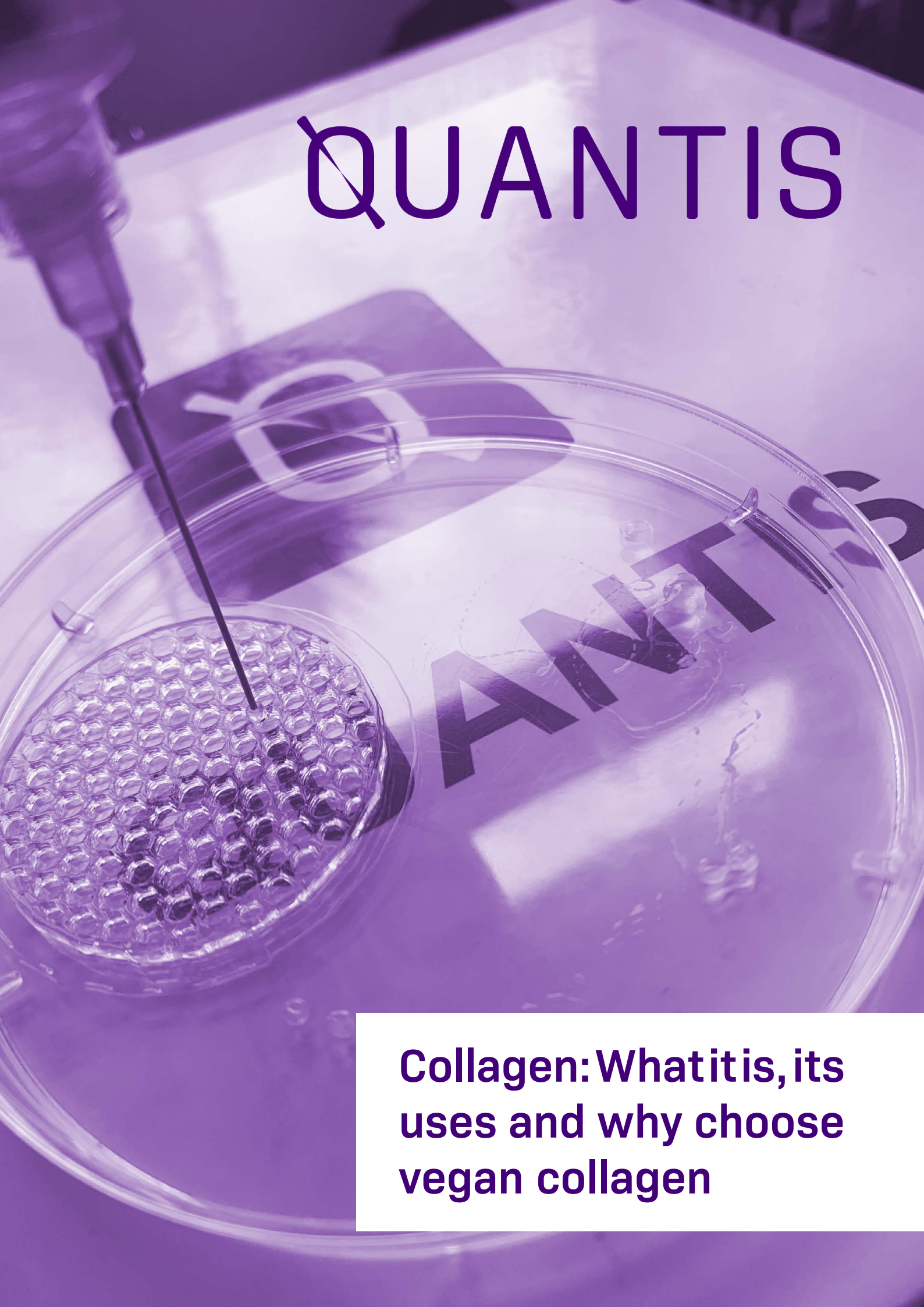

Collagen: What it is, its uses and why choose vegan collagen

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Original Publication BIOTECHTOWN

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What is Collagen

Collagen is a fibrous protein, commonly found in mammals, being 25-30% of the total protein content. The triple helix protein is composed by proline, lysine and glycine. In addition, there are hydroxypoline and hydroxylyzine, amino acids modified by ascorbic-acid dependent enzymatic processes.

Although more than **30 types of collagen** are known today, type I is the most common one, found in the human body comprising tendons, fibrous cartilage, loose and dense connective tissue, bones, tendons and skin. Its thick fibers are responsible for providing resistance, cohesion and elasticity to the skin and tendons.

Collagen classification is made according to the **structure and function**, which can be:

Long fibrils: collagens that form aggregated structures, visible through electron microscopy. Examples: type I, II, III, V and XI collagens.

Associated with fibrils: collagens responsible for connecting the fibrils to each other or other components of the extracellular matrix. Examples: type IX, XII and XIV collagens.

Network formation: collagens capable of associating and creating a network, as seen in the connective tissue. Example: type IV collagen.

Anchorage: collagens responsible for anchoring type I collagen fibers in the basal layer. Example: type VII collagen.

Collagen's Uses and Applications

Collagen is **widely used** in food, cosmetics and pharmaceutical industries due to its properties, such as: biocompatibility, biodegradability and low antigenicity. In the pharmaceutical area, collagen is used for the manufacture of vitreous implants, drug carriers, support for enzymes, production of biologically active compounds. In the medical field, this protein can be applied in the treatment of angiogenic diseases and in the treatment and prevention of diseases such as arthrosis and osteoporosis. Another area in which it stands out is beauty and cosmetics, due to its repairing properties on skin tissues.

One of its best known actions is related to aging. The main characteristic of skin aging is the fragmentation of collagen matrix in the dermis by the action of specific enzymes. The fibroblasts that produce and organize the matrix of this protein cannot insert the fragmented collagen. The loss of its insertion, that is the reduced production of collagen, prevents the fibroblast from receiving mechanical information, causing an imbalance between its production and the action of enzyme , degrading it. In aging skin, there is less protein production by the fibroblasts and greater action of enzymes that degrades it, and this imbalance speeds up the aging process.

Currently, it is **clinically proven** that anti aging treatments, such as retinoic acid, laser, CO2 and intradermal injection of hyaluronic acid (HA) stimulate the production of new non-fragmented collagen. These treatments balances the production of collagen and the action of enzymes that degrades it, delaying the aging process and consequently improving skin's appearance and health.

Collagen Sources

The main source of commercial collagen extraction today is animal by-products, mainly bovine tendons and rat tails. For collagen extraction, it is necessary to remove numerous intra and intermolecular covalent cross-links, which makes this process costly and complex. Furthermore, due to the recurrent cases of zoonoses originating from the animal source of collagen, the search for alternative and safer sources of this compound has become an attractive option.

It can be **obtained by different methods**, such as the extraction from animal source, vegetable source, microorganisms, synthetic source and human source. Thus, all medical or pharmaceutical grade collagen used today are from animal origin and needs to go through very expensive processes to become ultrapure and not suffer from immunotoxicity. Furthermore, the availability of this input today is only in highly broken proteins (peptides) and not in its structured format (fibrous).

The recent processes of tissue bioengineering (outside the body) show very conclusive results in relation to tissue regeneration (skin and cartilage) using structured and fibrous collagen (type I and II) in engineered tissues composition. Therefore, the possibility of producing collagen in this structured and fibrous format in the laboratory opens up a new possibility for the creation of various products in regenerative medicine, either for beauty or the creation of new therapies for tissue reconstruction in the human body.

Production of Animal Free or Vegan Collagen

It is known that the processes of obtaining, extracting and purifying collagen from animal sources are costly, generates insecurities regarding existing zoonoses and, mainly, aggressive or even toxic chemical products are used, requiring safer sources of this biomaterial. Considering the new trends in bioengineering, nutraceuticals, vegan products and advances in beauty products and alternative methods, it is imperative to search for alternative processes.

There is an understanding that collagen production, extraction and cross-linking methods (animal and human) **do not provide effective results in the body**, as they use cross-linking molecules that can produce by-products that causes reactions, not efficiently cross-linking the fibers, avoiding signaling primordial cells for lasting and/or biostimulating properties and will not have an effect on the molecular modifications of the collagen fibers, as the probability of being damaged due to the extraction process is high.

There are already companies and startups in the market working towards this challenge. The startup Quantis, for example, uses an innovative bioprocess to manufacture human collagen, using the most advanced methods in bioprinting and genetic engineering. The differentiated properties of the final solution are purity, fibrous structure and the fact that the final input is bioidentical to human collagen.

We have listed below the **main areas** of research and development studied for the application of Quantis vegan collagen:

Injectable in the Face: dermal filling line with the potential for way better results than hyaluronic acid and market leading biostimulators.

Reconstructive Cosmetic Surgery: same line of solution as dermal filler, but with evidence of tissue regeneration.

Animal Joints (Horses): injectable product for cartilage regeneration with expected results from 3 to 6 months.

Human Joints: injectable product for cartilage regeneration with expected results from 3 to 6 months. Focus on senior and high performance athletes.

Bone Implants: collagen solution with dental cements to improve adhesion and incorporation of the implant in the patient. Orthodontics can be an initial focus.

Hydrogel: gel solution to use in the production of artificial skins, biocures and pre-clinical tests in the cosmetic industry.

The table below presents the details of the characteristics, advantages and disadvantages of conventional methods, compared to the new proposal.

Conventional Methods	Problems Found	QUANTIS
Animal Source	Greater risk of adverse reaction of the body; High cost purification process - toxic by-products	Lower risk of adverse reaction because it is bioidentical to humans. Safe, sterile and ultra-pure process
Vegetal source and microorganisms	Collagen with incomplete structures and crosslinking difficulties	Collagen obtaining with fibrillar characteristics and efficient crosslinking
Synthetic source	Risks of adverse reaction; Non-reversibility	Lower risk of adverse reaction; Bioidentical to human. Organic product may be reversed by enzymatic action, physical and chemical processes
Human source	Current Non-Scalable Neonatal Cell Extraction Methods	Scalable

Vegan Collagen Usage in Cosmetic and Regenerative Medicine

In the regenerative medicine field, the fibrous collagen, which distinguishes the input of this new bioprocess, allows crosslinking processes, providing higher durability and bioactivity for injectable applications.

The most used products in aesthetics medicine as of today, hyaluronic acid and biostimulators, show **aggressive, not so safe and little durable results**. On the other hand, in osteoarthritis treatment, hyaluronic acid and stem cell treatments show several technical issues in cartilage recovery.

Utilizing *animal free* collagen, particularly Quantis' one, for comparison, this one has **higher structural capacity** in relation to hyaluronic acid, offering higher volumization potencial (face filling with a three-dimensional approach). However, the biggest differential in relation to HA is the collagen biostimulation capacity and dermis tissue regeneration, offering better long-term results.

Since the crosslinking capacity of fibrous collagen is much higher than that of hyaluronic acid, the hypothesis is that the durability of Quantis' collagen-based solution application has the potencial to be up o three times better than the HA-based one, highly attractive feature according to the aesthetics medicine experts consulted for the project.

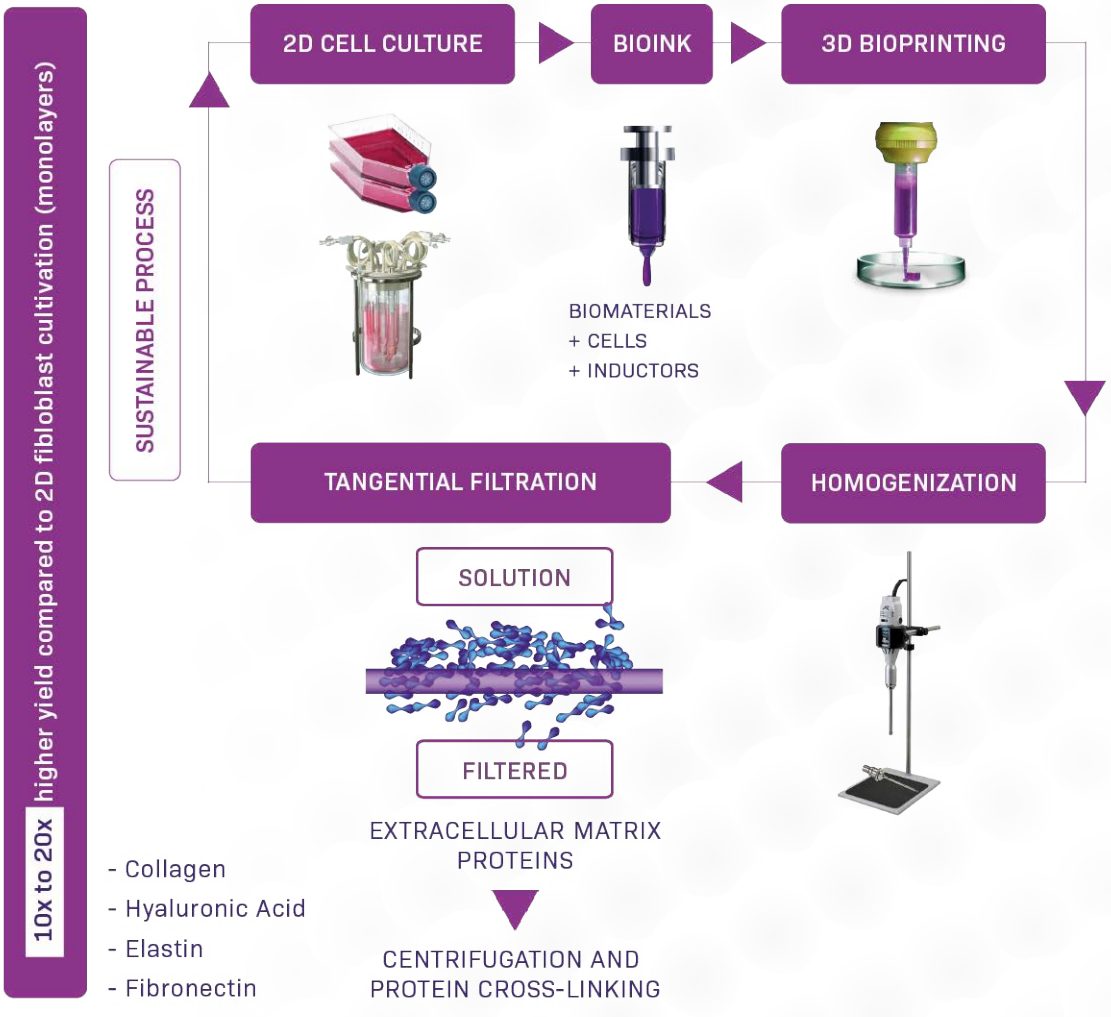
Therefore, the solution is capable to maintain fundamental **medical usage features** (in comparison to Hyaluronic Acid) as safety (antidote) and application flexibility (possibility of application in several tissue layers), in addition to have double durability, bringing features like biostimulation and regeneration of both skin cells and cartilage (fibroblasts and chondroblasts).

Technology and Benefits of Vegan Collagen

The new technology for the production of vegan collagen, especially the one developed by Quantis, involves a process of bioprinting fibroblasts, which are induced to overexpress collagen through genetic engineering techniques (without gene modification). This construct, called QuantumTissue, is responsible for producing the structural proteins and enzymes that make up the extracellular matrix, where there is a predominant presence of type I collagen, in addition to elastin, fibronectin, proteoglycans, glycosaminoglycans, enzymes, etc.

After a little abrasive centrifugation process, it is possible to separate the collagen matrix from the cells in the construct, allowing cell reuse to compose other constructs, obtaining the final product in a purer way, without the presence of chemical/enzymatic purification agents.

3D Tissue Biofabrication for collagen-based solution
Production - Processes involved - Patent



The benefits, compared to the traditional way of collagen obtention, are related to product composition factor. Most collagen gels on the market, whether animal, vegetal or synthetic origins, are composed only by collagen as the structural protein, in addition to some chemical/enzymatic agents from collagen peptides extraction. Quantis gel includes a huge variety of components naturally present in human extracellular matrix, in addition to great molecular biocompatibility, since they are bioidentical to human protein.

In addition, the process is completely animal free, with **no components of animal origin at any stage**, being a highly innovative biotechnological product that aims to replace animal collagen with human collagen in a highly competitive way, focusing on increasingly reducing the use of animals in research and development.

Today, there are several bioprinting companies around the world, but none of them uses artificially constructed tissues as intermediaries for the production of biotechnological products. Because of this, Quantis has **patented its revolutionary production methodology**, establishing itself as a pioneer in this innovative model with enormous potential in the bioprocesses area.

Thus, there are several markets that can be approached, such as aesthetics and food, in addition to large national and international industries, such as pharmaceuticals and cosmetics, for example. It is possible to provide inputs for several branches of research and development, inside and outside universities.•