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A Comprehensive Review on the Role of Collagen in Health, Disease, and Biomaterials: Advances, Challenges, and Future Perspectives

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ABSTRACT

Collagen, a fundamental structural protein in the extracellular matrix (ECM), plays a critical role in tissue engineering, regenerative medicine, and biomaterial development. It is involved in various biological functions, including wound healing, musculoskeletal health, cardiovascular integrity, and cancer progression. Due to concerns related to disease transmission, ethical considerations, and religious constraints associated with mammalian collagen sources, marine-derived collagen (MDC), particularly from fish skin and scales, has emerged as a promising and sustainable alternative. MDC exhibits superior biocompatibility, biodegradability, and low immunogenicity, making it suitable for applications in wound healing, drug delivery, and tissue engineering. Various extraction techniques, including acid solubilization, enzymatic hydrolysis, and deep eutectic solvent extraction, ensure high purity and preserved bioactivity, while characterization methods such as FTIR, SEM, and XRD confirm its structural integrity. Additionally, MDC-based composite scaffolds and hydrogels enhance fibroblast proliferation, angiogenesis, and osteoblast differentiation, supporting regenerative medicine applications. In oncology, collagen remodeling has been linked to cancer metastasis, with metastatic cells exhibiting enhanced reorganization of type I collagen fibers, promoting invasiveness. Despite these advantages, challenges such as collagen quality inconsistencies, mechanical strength limitations, and the need for extensive in vivo studies remain. Future research should focus on optimizing extraction techniques, improving mechanical stability through cross-linking strategies, and integrating emerging technologies such as 3D collagen-based scaffolds, CRISPR-mediated genetic modifications, and AI-driven molecular modeling. With continued advancements, MDC holds significant potential as a sustainable and effective biomaterial for biomedical, clinical, and industrial applications.

Keywords: Collagen, Marine-Derived Collagen (MDC), Tissue Engineering, Regenerative Medicine, Wound Healing, Biomaterials, Drug Delivery, Cancer Metastasis, Extracellular Matrix (ECM), 3D Scaffolds, CRISPR, AI-Driven Molecular Modeling, Biocompatibility, Biodegradability, Sustainable Biomaterials

Introduction

Collagen, the most dominant and structural protein in the vertebrate and invertebrate of the extracellular matrix (ECM), plays a very significant function in maintaining tissue integrity,

helping the skin enhancing and various roles for tissue modulating inflammatory responses, and promoting wound healing. Much of the research in its recent decades emphasizes the multifunctional roles of collagen in both health and disease with their emergent biomedical applications. Collagen plays a crucial role in regeneration and wound healing. Till the date there are various products also available in market which directly or indirectly useful in health and diseases. Using reference (Castillo - Briceño et al., 2011) it was demonstrated that certain collagen motifs had wound healing and inflammatory properties related to them, which showed that collagen is more than just structural support, yet also deepens immune responses. Collagen effects have been more researched in the areas of those involving cartilage and musculoskeletal health. Collagen have many type I to VII etc, and various type have various performance and need, like Collagen type II performed superior to type I in cartilage tissue engineering, supporting its application over type I on the basis of increased chondrogenic properties. (Thudium et al., 2024) have investigated type III collagen breakdown in osteoarthritis as a biomarker for joint tissue injury. The function of collagen extends into cardiovascular well-being: (Sadri et al., 2022) identified collagen type XIX as a major controller for cardiac ECM integrity, with impacts on mechanical left ventricle properties and fibrosis engagement. In another related study, (Li et al., 2024) identified collagen type VIII as being behind vascular disease, including in angiogenesis, arterial compliance, and atherosclerosis. Aside from this, (Martin et al., 2025) also examined the type I collagen degradation as a biomarker for the development of cardiovascular diseases. Last but not least, in oncology, collagen has been of interest due to its possible involvement in cancer development and treatment. The most remarkable were the initial indications that type I collagen may become a prognostic biomarker in stroma-based breast carcinomas with an association between breast cancer and chemotherapy response (Jansson et al., 2024). Recombinant humanized collagen type III, according to (Liu et al., 2023)inhibits cell growth and migration of breast cancer cells, and it offers new opportunities for therapy. Breast cancer cell migration, metastatic and non-metastatic, also showed that remodeling of type I collagen impacted cells so that the metastatic cells were remodeling the collagen fibers better, which will affect their invasive ability (Ouyang et al., 2025).A rising controversy is being triggered regarding marine collagen as one of the sustainable materials of collagen that has proven to be a very reliable substitute to the commonly exploited animal forms of collagen. (Ferraro et al., 2013) documented such a possibility in extraction from mackerel and sardine waste, highlighting its high biological value and uses in medicine and pharmaceuticals. In this research (Barai et al., 2024) proceeded to outline the extraction and characterization of collagen from Amazonian fish in terms of sustainability and the future of such collagen in biotechnological studies. Certain research identifies marine collagen as a substitute for conventional sources, such as certain research by (Prajaputra et al., 2024), which cited its reduced immunogenicity and extensive use in pharmaceuticals as well as cosmetics. Progress in the knowledge of solid waste management and typed collagen. Progress in biomaterial science has further explored alternative resources and collagen modifications. Marine and bovine collagen have been compared, with marine-derived collagen proving better in biocompatibility,

mechanical strength, and bone regeneration application (Diogo et al., 2024). Changes in collagen extraction methods, for example, pepsin treatment of equine tendon collagen, have enabled tuning of its rheological properties, improving its usability in medical devices (Salvatore et al., 2024). Initial concerns regarding the quality and safety of animal-derived collagen prompted the creation of recombinant human collagen, which offers a more bioactive and consistent material for tissue engineering (Shoseyov et al., 2014). The function of collagen in tissue growth and regeneration has been well researched. Research on type IV collagen in Pectoralis major muscles of broiler chickens established its role in muscle abnormalities while identifying distinct regulatory patterns of fast-growing chicken collagen physiology that might lead to muscle disorders (Bordini et al., 2024). Scientists have investigated type V collagen to understand its distinctive regulatory activities during temporomandibular joint (TMJ) development and they have established its capabilities for tissue regeneration in condylar cartilage remodeling (Chandrasekaran et al., 2024). The research on myoblasts determined that both types I and III collagen increased cell proliferation but type III collagen revealed different effects on cell migration and differentiation processes (Wang et al., 2024). Along with physiological functions collagen becomes vital for platelet adhesion which leads to thrombus formation. The critical function of this substance has been demonstrated in several medical procedures because different collagen substrates regulate platelet reaction via distinct receptor pathways (Lemmens et al., 2024). The development of collagen-based technology has led to new research opportunities regarding intellectual property protection as well as commercialization trends particularly in the field of marine biotechnology. Biopolymers made of collagen and chitin hold tremendous significance in both industrial and medical fields because research explores updated trimming and extraction protocols for collagen biomaterials and develops optimal processing methods to enhance therapeutic efficacy (Vieira et al., 2024).

Review of Literature

Our body contains collagen as its dominant structural protein that jointly forms the extracellular matrix (ECM). The biological framework requires collagen to perform essential procedures which include healing processes and controlling inflammation and disease growth. Experts have thoroughly studied both the molecular nature of collagen and its breakdown processes as well as its applications in medical fields. rámgluus (Castillo-Briceno et al., 2011) examined particular collagen sequences to determine their impact on wound healing alongside inflammation control. The research showed how type I collagen affects fish fibroblast behaviors as well as cytokine production which indicates collagen regulates immune system reactions. According to (Ferraro et al., 2013) by-products from mackerel and sardines can become sources of valuable biomedical compounds through waste recycling. Scientists highlighted regenerative medical applications that involve collagen in this research project. The researchers from (Barai et al., 2024) demonstrated how simplified Amazonian fish waste-derived collagen can be produced sustainably while making it suitable for industrial applications. Numerous scientific investigationshave focused on the significance of collagen type II for joint health. Researchers demonstrated higher mechanical properties in type II collagen compared to type I collagen according to their study (Wu et al.,

2021) indicating its potential as a cartilage engineering material. The researchers examined methods for biosynthesis and scaffold development while discussing medical implementation approaches that demanded type II collagen for orthopedic rehabilitation. Similarly, (Thudium et al., 2024) researched collagen type III's breakdown in osteoarthritis, linking increased degradation to damage in joint tissues and higher widespread biomarker levels. Collagen is also being closely examined in relation to heart disease. (Martin et al., 2025) focused on type I collagen degradation as a potential biomarker for cardiovascular issues, paying special attention to its role in ECM remodeling and heart tissue scarring. (Sadri et al., 2022) discussed collagen type XIX's role in maintaining heart ECM structure and how it impacts heart function, relating it to fibrosis. Besides, (Li et al., 2024) studied collagen type VIII in connection with vascular diseases, finding links to arterial stiffness, atherosclerosis, and issues with the endothelium. As the demand for sustainable materials grows, (Prajaputra et al., 2024) looked into marine collagen as an eco-friendlier substitute for traditional materials. They focused on its lower immunogenicity and higher biocompatibility, pointing out its uses in pharmaceuticals, cosmetics, and tissue engineering. Scientific research proves that collagen plays an extensive role within health systems as well as disease states while allowing development of new biomaterials and regenerative medicine applications. Science studies collagen extensively because researchers utilize its broad applications between biomaterials and regenerative medicine and cancer treatment applications. Researchers first focused on human-derived recombinant collagen because it eliminated safety dangers from animal materials. (Shoseyov et al., 2014) demonstrated plant cultivation of human collagen which researchers identified as a sustainable medical resource compatible with human tissue. The field then focused studies on various collagen origins for their impact on biomedical engineering applications. Medical researchers at (Diogo et al., 2024) discovered that marine collagen demonstrates better biocompatibility and mechanical properties superior to bovine collagen which enables its usage in building scaffolds. The research conducted by (Salvatore et al., 2024) evaluated the impact of pepsin treatment on equine tendon collagen as a method to strengthen its structural stability and develop rheological properties suitable for medical applications. Collagen plays several vital roles in physiological functions where it enables platelet aggregation to form clots among other similar processes. (Lemmens et al., 2024) studied platelet collagen receptor mechanisms which enable platelets to activate differently on various collagen types during blood research studies of coagulation. (Vieira et al., 2024) conducted research on global intellectual property and research dynamics regarding marine-derived collagen and chitin/chitosan where they detected a discrepancy between scientific breakthroughs and industrial commercialization.

In cancer research, collagen has been examined for its role in tumor growth and treatment. (Jansson et al., 2024) showed that the amount of type I collagen in breast cancer stroma could predict how well patients respond to chemotherapy, potentially serving as a prognostic biomarker. Besides, (Liu et al., 2023) explored the therapeutic potential of recombinant humanized collagen type III, which demonstrated anti-tumor properties by inhibiting the growth and spread of breast cancer cells through DDR1 signalling. Together, these studies emphasize

collagen's versatile role in biomaterials, disease understanding, and economic development.While innovations in how we get and process collagen have opened up new possibilities for its use in medicine, there's still a disconnect between what researchers are discovering and how those findings are applied commercially. Future academic research needs to concentrate on both improving collagen-based treatment methods and closing the distance between academic science and industry practices. Scientists studied collagen extensively to identify its versatile biological capabilities particularly in their roles for tissue health and muscle development as well as disease formation. Studies focusing on type IV collagen an integral component for development in broiler chicken Pectoralis major muscles have recently been published. Studies reveal that the process of collagen secretion as well as production variations result in wooden breast and white striping defects mostly observed in developing birds (Bordini et al., 2024). The research on type V collagen has defined its precise functions in temporomandibular joint (TMJ) development. Lack of type V collagen causes substantial changes in condylar cartilage structure yet leaves the articular disc mostly unaffected. Numerous studies point to type V collagen as essential for cartilage remodeling after birth which implies it may serve as a viable therapeutic target for TMJ tissue regeneration (Chandrasekaran et al., 2024). A research investigation assessed the effects of type I and III collagen on muscle cellular behaviors such as cell proliferation as well as migration and differentiation. Although the two collagen types promoted positive growth in muscle cells they functioned differently during cell movement and specific tissue differentiation. Migration was more strongly influenced by type I collagen fibers but type III collagen fibers appeared to decrease differentiation at the gene expression level. The particular composition of collagen shows promise for enhancing prospects in both muscle tissue engineering and regenerative medicine according to (Wang et al., 2024). Studies proved metastatic cells outperform non-metastatic cells by remodeling type I collagen fibers thus improving their tumor invading ability. Researchers have discovered that collagen plays a key role in metastatic cancer prevention therefore making it a promising target for cancer treatments according to (Ouyang et al., 2025).The interchangeable functions of collagen in tissue development alongside disease progression and medical usage create a foundation for new discoveries regarding targeted medical treatments along with collagen-based biomaterials.

Methodology and Recommendations

Research investigators have used numerous experimental approaches to investigate collagen in its biological nature as well as its breakdown processes and medical usage potential. The analysis consists of biochemical extractions in combination with molecular analyses as well as histological examinations supported by biomarker assessments. (Castillo-Briceño et al., 2011) conducted cell adhesion assays together with gene expression analysis to discover collagen motifs that promote wound healing. The inflammation-related behaviour of fibroblasts was studied using real-time PCR together with immunocytochemical techniques for analysing the inflammatory reaction of these cells against particular collagen sequences. The biochemical extraction of collagen from sardine and mackerel by-products focused on the use of acid-soluble and enzymatic hydrolysis techniques in (Ferraro et al., 2013). The isolation process produced

valuable collagen material that found uses in pharmaceutical and biomaterial applications. The researchers at (Barai et al., 2024) conducted Amazonian fish collagen extraction with acid and pepsin approaches followed FTIR and XRD characterization for structural analysis. Histological staining and mechanical testing allowed (Wu et al., 2021) to examine the structural properties of collagen type II in cartilage engineering applications. Stability assessment of collagen scaffolds involved SEM and DSC analysis by the research team. The researchers from (Thudium et al., 2024) analyzed systemic effects of type III collagen degradation in osteoarthritis through serological biomarker assays and mass spectrometry techniques. The research team of (Martin et al., 2025) used enzymes in the ELISA assay to detect type I collagen protein fragments in blood circulation thus developing cardiovascular risk assessment biomarkers through proteomic analysis. The analysis of cardiac function involving collagen type XIX was based on echocardiography in addition to histological staining and molecular gene expression research by (Sadri et al., 2022). The analysis of collagen type VIII in vascular diseases involved the combination of immunohistochemistry and Western blotting tests alongside in vivo arterial stiffness assessments (Li et al., 2024). (Prajaputra et al., 2024) performed research on marine collagen extraction through acid-soluble and enzymatic methods to determine extraction efficiency when compared with bovine and porcine collagen sources. To assess properties suitable for biomedical applications the researchers tested the substance through gel electrophoresis together with thermal stability evaluations.

Best-Suited Method and Future Recommendations

Manufacturing decisions about collagen extraction rely on the intended product use according to these studies. The pepsin-soluble extraction method works highly effectively for biomedical applications because it maintains the native structure of collagen. Acid-soluble extraction provides a better solution for big industrial operations because it offers practicality and lower expenses. Enzymatic hydrolysis serves as the best technique for making bioactive collagen peptides which find use in pharmaceuticals and nutraceuticals. The analysis of collagen subtypes requires implementation of current bioinformatics technologies and proteomics platforms for future studies. As the use of CRISPR-based gene editing techniques which have many potentials for the augmenting collagen expression rates in tissue engineering applications by its nature. The application of nanotechnology in collagen scaffolds creates opportunities to enhance their use in regenerative medicine applications. Methodological advancements in this field will improve collagen research through which it can be used as an effective tool in healthcare applications and biomaterials development and sustainable industries. The optimal properties of collagen for different applications depend on research methods which cover multiple extractions combined with processing steps followed by characterization protocols. Research by (Shoseyov et al., 2014) introduced the industrial manufacture of recombinant human collagen from plants through plant-based genetic engineering of human collagen in transgenic tobacco plants for a safer and productive commercial manufacturing process. Chondroinduction by marine collagen relative to bovine collagen was studied by (Diogo et al., 2024) through rabbit femoral bone defect testing with micro-CT imaging and histomorphometry using rabbit femoral bone defect models. The

research by (Salvatore et al., 2024) examined how changing pepsin concentration and temperature and homogenization conditions affected rheological properties during equine tendon collagen extraction. (Lemmens et al., 2024) conducted a study to evaluate platelet adhesion functions of collagen using washed platelets with aggregometry tests alongside blood clotting assays that monitored platelet-collagen binding from various sources.

(Vieira et al., 2024) executed a bibliometric assessment of collagen-oriented patents together with academic research patterns through Scopus and PATENTSCOPE databases for assessing scientific productivity versus industrial use trends. A large group of breast cancer patients underwent immunohistochemistry testing to analyze the relationship between chemotherapy response and stromal type I collagen expression according to (Jansson et al., 2024). Research by (Liu et al., 2023) used various in vitro tests such as RNA sequencing and cell cycle analysis with transwell migration tests to determine the antitumor properties of recombinant humanized collagen type III. The production of recombinant collagen through (Shoseyov et al., 2014) method stands as the best available approach for building materials that promote biocompatibility in clinical applications. Equine collagen extraction using enzymes (Salvatore et al., 2024) gained importance because it grants control of collagen properties alongside preservation of collagen natural structure. The combination of in vivo animal models with both micro-CT imaging and histological studies supports potent evidence for bone tissue restoration according to (Diogo et al., 2024).

To further enhance collagen-based applications, future research should explore:

- Crosslinking & Functionalization: Advanced crosslinking methods (chemical, enzymatic, or physical) can improve collagen stability and mechanical strength.
- 3D Bioprinting: Developing bioengineered collagen scaffolds through 3D bioprinting can enhance tissue engineering applications.
- Personalized Biomaterials: Customizing collagen formulations based on patient-specific needs can improve therapeutic outcomes.

Biomaterials based on collagen gain higher precision in combination with multiple approaches while demonstrating better efficacy and suitable industrial scalability. Scientists use multiple research methods to study collagen because they need to understand its effects on tissue development and disease progression as well as its applications in engineering biomaterials. Scientists studied Pectoralis major broiler chicken muscles through histological analysis and immunohistochemistry and gene expression tests to track collagen IV development since hatch (Bordini et al., 2024). A genetic knockout mouse research with Col5a1+/- versus wild-type mice evaluated the effects of type V collagen deficit on temporomandibular joint (TMJ) remodeling processes. The researchers conducted structural and biomechanical examinations through histological inspections together with immunological fluorescence analysis and mechanical experimental methods to evaluate changes in condylar cartilage structural health (Chandrasekaran et al., 2024). Research examined myoblast cellular behavior through in vitro investigations of cells grown on surfaces coated with type I and III collagen. The research combined transcriptome sequencing with enrichment analysis to measure genetic expression

variations regarding growth and movement and cell specialization signaling mechanisms helping scientists understand the differences between muscle regeneration (Wang et al., 2024).

Researchers studied metastatic along with non-metastatic breast cancer cells grown on collagen matrices by applying live-cell imaging and fluorescence microscopy and integrin pathway analytical methods to determine how collagen affects tumor cell migrations and invasions (Ouyang et al., 2025). Through these methods scientists can gain complete knowledge about collagen biological activities to advance research on tissue engineering technology and disease modeling and therapeutic applications. The Col5a1+/- mouse model stands as an especially useful genetically modified approach to study how collagen affects tissue remodeling together with disease development processes. The research methods of collagen-coated culture systems and cancer migration assays enable investigators to conduct controlled studies that investigate mechanisms. Researcher are combining the genetically modification of models and the advanced imaging approaches as well as the single cell sequencing and the biomechanical testing which can allows the scientists to the explore collagen's comprehensive regulatory capabilities.Future research must examine the use of 3D collagen scaffolds to regenerate tissue structures as well as organoid models for studies regarding cancer and musculoskeletal diseases and biomechanical testing for measuring collagen's effects on tissue stiffness and CRISPR-based genetic modifications to alter collagen genes during disease studies. Precision applications of collagen in regenerative medicine and tissue engineering along with oncology will get boosted through these technological developments.

Discussion

Multiple research investigations confirm that collagen provides structural support and functional and biomedical importance within multiple biological systems. The research demonstrates collagen's contributions to tissue rehabilitation, medical progression and therapeutic approaches while demonstrating biomarker identification and sustainable extraction techniques and regenerative medical approaches.

Key Insights from Reviewed Studies

According to (Castillo-Briceno et al., 2011) The protein has functions beyond structural support since it plays an active role in managing inflammation and ECM remodeling while aiding in wound healing processes. Cellular adhesion functions alongside immune responses through specific collagen motifs which are proven to influence tissue repair processes. The study by (Thudium et al., 2024) showed that osteoarthritis severity and systemic biomarkers directly corresponded to the breakdown of type III collagen. The research conducted by (Martin et al., 2025) established collagen type I fragments as diagnostic indicators for cardiovascular diseases that enhance their medical applications.

The field of biomaterials has increasingly paid attention to both the extraction methods of collagen and long-term sustainability practices. The scientific community showed through their work (Ferraro et al., 2013) and (Barai et al., 2024) that fish-derived collagen could be applied industrially through enzymatic extraction methods. The research concluded that type II collagen

exceeds type I collagen for tissue repair in cartilage engineering because of its superior biomechanical characteristics (Wu et al., 2021).

Implications for Theory, Practice, and Policy

These findings have broad implications for both theoretical and practical advancements:

- Theoretical Contributions: The evidence reinforces that collagen is not just a passive ECM component but an active regulator of inflammation, fibrosis, and cellular signaling. This challenges traditional views and encourages research into collagen-cell interactions at a molecular level.
- Clinical Practice: The validation of collagen-based biomarkers (e.g., collagen type I for cardiovascular risk, type III for osteoarthritis) offers new diagnostic tools, supporting early disease detection and treatment monitoring.
- Industrial and Policy Considerations: The push toward marine-derived collagen highlights sustainability and reduced disease risks compared to traditional bovine/porcine sources. Policies promoting eco-friendly collagen extraction methods (e.g., ultrasonication-assisted techniques) could benefit industries such as pharmaceuticals, cosmetics, and tissue engineering.

Gaps in Research and Inconsistencies

While significant progress has been made, several research gaps remain:

1. Limited Understanding of Non-Fibrillar Collagens: While fibrillar collagens (type I, II, III) are well-studied, non-fibrillar types (e.g., collagen XIX, VIII) remain underexplored, particularly in disease progression and ECM remodeling.
2. Collagen as a Therapeutic Target: While some studies suggest collagen-targeting drugs for fibrosis and cancer, clinical trials are lacking.
3. Comparative Effectiveness of Extraction Methods: No standardized approach exists for evaluating extraction efficiency, purity, and functional properties across different collagen sources.

The reviewed studies collectively highlight the diverse roles and applications of collagen in biomaterials, disease pathology, and industrial innovations. The advancements in recombinant human collagen production have addressed concerns related to immunogenicity and viral contamination, offering a safer alternative for medical use (Shoseyov et al., 2014). The comparison between marine and bovine collagen underscores the superior biocompatibility of marine-derived collagen, making it a promising material for bone regeneration and tissue engineering applications (Diogo et al., 2024).Equine tendon collagen, particularly when processed with pepsin, demonstrated tunable properties for specific medical applications, reinforcing the significance of extraction techniques in determining collagen's mechanical and biological properties (Salvatore et al., 2024). The role of collagen in platelet adhesion mechanisms further illustrates its importance in hemostasis and thrombosis research, as certain collagen substrates were found to modulate platelet receptor interactions differently (Lemmens et al., 2024).In the oncology domain, collagen has emerged as both a biomarker and a potential therapeutic agent. Stromal type I collagen expression levels were linked to chemotherapy

response in breast cancer patients, suggesting its prognostic value (Jansson et al., 2024). Moreover, recombinant humanized collagen type III exhibited direct antitumor effects by inhibiting breast cancer cell proliferation and migration, highlighting its potential as a novel therapeutic biomaterial (Liu et al., 2023).

Future research should focus on:

1. **3D Collagen-Based Models** – Developing bioengineered 3D collagen scaffolds and organoid systems to better replicate tissue environments.
2. **Collagen in Disease Mechanisms** – Investigating the molecular pathways through which different collagen types influence tissue remodeling and disease progression.
3. **Therapeutic Targeting of Collagen** – Exploring pharmacological or genetic interventions to regulate collagen synthesis and degradation in diseases such as cancer, muscle degeneration, and cartilage disorders.
4. **Integration with Emerging Technologies** – Utilizing CRISPR-based genetic modifications and AI-driven molecular modeling to optimize collagen biomaterials for personalized medicine.
5. **Personalized Biomaterials** – Developing customized collagen-based formulations for patient-specific therapies.
6. **Collagen Functionalization** – Exploring nanomaterial integration to enhance collagen's mechanical and biological properties.
7. **Sustainable Sourcing** – Investigating eco-friendly extraction methods to optimize marine collagen utilization.
8. **Clinical Translation** – Conducting large-scale clinical trials to validate the therapeutic efficacy of engineered collagen products.

By addressing these challenges, collagen research can be more effectively translated into clinical and industrial applications, ultimately improving patient outcomes in regenerative medicine, oncology, and musculoskeletal treatments. Collagen-based innovations will continue to shape biomaterial science, leading to advancements in medical practice and therapeutic development.

Conclusion

The reviewed studies collectively reinforce collagen's multifaceted role in health, disease, andbiomaterials**.** While its significance in wound healing, cardiovascular health, osteoarthritis, and regenerativemedicineis well-supported, further research is needed to optimize therapeutic applications and sustainablesourcing**.** As the research going on the scientist will face the challenges for the collagen research that emerge from the combining the biomolecular engineering with the computational high-level modelling for together sustainability principles.The medical field heavily depends on collagen applications for tasks in regenerative medicine along with oncology and biomaterials science. The development of recombinant collagen manufacturing techniques has reduced safety risks connected to animal collagen sources thus broadening potential medical applications. The comparison between collagen types demonstrates marine-derived collagen delivers better performance in biocompatibility together with mechanical traits which qualify it as a potent material in tissue engineering applications.

Collagen extraction through pepsin-based enzymatic treatments salts to improve structural stability and allows for more medical applications. Research has extensively investigated both the role of collagen in physiological along with pathological processes that include platelet adhesion because cancer progression. Several research studies have shown that various collagen materials impact platelet-receptor engagement to reveal key thrombosis processes and stromal type I collagen now acts as a promising diagnostic marker for breast cancer. Studies have shown that humanized recombinant type III collagen possesses antitumor abilities which creates new opportunities for cancer treatment research. Collagen-based materials require more research to improve their development and broadening their utilization capabilities. Collagen research will advance through better crosslinked stable structures as well as functionalized advanced systems coupled with 3D bioprinting applications and investigations of collagen properties in cancer treatment development and sustainable sourcing methods. The solution of these research obstacles will enhance collagen-based biomaterials for expanded medical uses and establish breakthrough solutions in both healthcare and biotechnology. The multiple types of collagen matter fundamentally for tissue growth and disease evolution and biomaterial functionality since each form displays particular biological roles. Scientists study type IV collagen which regulates muscle development as well as controls muscle abnormalities and scientists establish that type V collagen maintains stability in the condylar cartilage process of temporomandibular joint remodeling. Research on myoblasts demonstrates that type I and type III collagen dramatically affects their cell proliferation and movement together with cellular differentiation which leads to advanced knowledge for tissue engineering and regenerative medicine of muscles.

The relationship between type I collagen and cancer progression has become established because metastatic cells show better capabilities in collagen remodeling which boosts tumor invasion. The study shows that collagen plays crucial roles in both natural body functions and diseases therefore enabling its potential applications in biological tissue restoration and material development and cancer treatment research. Future studies should focus on enhancing collagen-based intervention methods and improving biomaterial characteristics along with developing specific therapeutic approaches. As per the interest in the research area of the 3D collagen the scaffolds coupled with the genetic information and the modification as well as the biomechanical analyses which will be lead to superior for the knowledge about to be collagen behaviour with to be biological systems which help to the boost the industrial along with the all clinical implementation potential which is necessary for the future aspect.

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