Collagen Treatment

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Collagen, the most abundant protein in our bodies, plays a crucial role in maintaining the structural integrity of various tissues and organs. Collagen treatment offers a range of advantages, including antioxidant and anti-inflammatory properties, wound healing support, benefits for hair and nail health, improvement in gut health, support for joint health, skin rejuvenation, and potential support for musculoskeletal disorders and cardiovascular health.

collagen disease inflammation tissue damage treatment

1. Introduction

Collagen, a vital protein synthesized within the body, is a fibrillar protein and is the primary structural component in the skin, tendons, and bone. Collagen constitutes a major component of the conjunctive and connective tissues, providing mechanical stability, elasticity, and strength to organisms [1][2]. The extracellular matrix (ECM) is the non-cellular component of all tissues, shaping the physical environment surrounding cells, and plays crucial roles in both providing structural support and facilitating cellular signaling processes [3]. In the human body, collagen constitutes one-third of the total protein content, accounts for approximately three-quarters of the dry weight of the skin, and stands as the predominant constituent within the ECM [4].

Collagen has a unique structure formed with three polypeptide chains (α-chains) that wind around each other to create a strong triple helix. Each of these chains has a specific repeating sequence (Gly-X-Y), where Gly is glycine, and X and Y are often proline and hydroxyproline, which makes it similar to a polyproline helix. This triple helical arrangement gives collagen its distinctive properties, contributing to its strength and function in various tissues [5]. The distinct collagen structure may play a significant role in ensuring its mechanical stability.

Collagen exhibits a variety of applications and demonstrates positive medical effects [6][7]. The superior properties of collagen-based biomaterials include biocompatibility, biodegradability, mechanical strength, and cellular activity. These attributes render collagen highly suitable for various biomedical applications, including wound healing, tissue engineering, surface coating of medical devices, and skin supplementation [8]. Collagen-based supplements have emerged as a fundamental component in addressing the effects of the aging process, demonstrating their established capacity to repair skin damage and bestow a rejuvenated and healthy appearance sought after in the pursuit of beauty [9]. Collagen has been recognized as a drug carrier possessing numerous benefits, including non-toxicity, superior biocompatibility, and favorable interactions with pharmaceutical agents [10][11]

Collagen could impact tumor cell behavior by interacting with integrins, discoidin domain receptors, tyrosine kinase receptors, and various signaling pathways, and extensive collagen deposition is the primary pathological hallmark of certain cancers [12][13].

Comorbid diseases refer to the simultaneous presence of two or more medical conditions in an individual. Collagens are implicated in the pathogenesis of a multitude of diseases, and the observed associations among these disorders indicate a compelling association between the comorbidity of these conditions and an underlying deficiency in collagen [6].

2. Types and Sources of Collagen

There are five primary types of collagen, which are classified as types I–V. **Table 1** presents the tissues or organs composed of the five predominant types of collagen.

Table 1. The tissues or organs composed of the five predominant types of collagen.

Collagen	α-Chains	Tissue or Organ
Type I	$[\alpha 1\,(\mathbf{I})]_2\alpha 2(\mathrm{I})$	skin, bone, teeth, tendons, ligaments, vascular ligature
Type II	$[\alpha 1\,(\mathbf{II})]_3$	cartilage
Type III	$[\alpha 1\,(\mathbf{III})]_3$	muscle, blood vessels
Type IV	$[\alpha 1\,(\mathrm{IV})]_2\alpha 2(\mathrm{IV})$ $[\alpha 3\,(\mathrm{IV})]_2\alpha 4(\mathrm{IV})$ $[\alpha 5\,(\mathrm{IV})]_2\alpha 6(\mathrm{IV})$	basal lamina, the epithelium-secreted layer of the basement membrane
Type V	$\alpha 1\,(\mathbf{V}), \alpha 2\,(\mathbf{V}), \alpha 3(\mathbf{V})$	hair, cell surfaces, placenta, skin, tendons, ligaments

Type I collagen is the most abundant form of collagen in the human body [14] and acts as the primary organic scaffold, undergoing mineralization to support the process of bone development. This collagen is continuously synthesized and deposited in the ECM and subsequently broken down by enzymes in a finely balanced cycle that enables growth. During development, the turnover of collagen is rapid, which later stabilizes during adulthood. However, in later life, collagen turnover increases once more to counteract the cumulative detrimental effects associated with chronological aging and photoaging [9]. The principal components comprising the EMC of cartilage consist of type II collagen, proteoglycans, and several proteins, which include certain minor collagens [15]. Loss of type II collagen led to an acceleration of chondrocyte hypertrophy, mediated with the BMP-SMAD1 signaling pathway [16].

Type III collagen is extensively cross-linked with type II collagen, playing a vital role in regulating the fibrillar structure and biomechanical properties of cartilage tissue [17]. It is expressed during early embryonic development and remains prevalent throughout the process of embryogenesis. Type III collagen plays a crucial role in facilitating

the proper fibrillogenesis of type I collagen in various organs. Type I and III collagens are two major subtypes in the female pelvic tissues, with type I collagen affecting tissue stiffness, while type III collagen is related to tissue elasticity [18].

Type IV collagen, being the principal collagen constituent of the basement membrane, plays a vital role in forming a network that underlies both epithelial and endothelial cells, functioning as a critical partition between tissue compartments. This collagen type is extensively involved with various binding partners, forming the foundational structure of the basement membrane [19].

Type V collagen plays a role in modulating the formation of fibrils and tissue characteristics, thereby contributing to the composition of the bone matrix, corneal stroma, and interstitial matrix of muscles [20]. Type V collagen is typically found in association with type I collagen. It helps control the diameter and organization of collagen fibrils, thus influencing the overall strength and stability of tissues.

The most common sources of collagen used in biomaterial or biomedicine applications include human collagen, as well as collagen derived from bovine, porcine, and marine organisms. Collagen could be readily obtained from animal tissues, particularly bones [21]. Fibrillar collagen extracted from a bovine Achilles tendon demonstrated the potential for creating 3D printed scaffolds [22]. Collagen extracted from an ovine Achilles tendon exhibited a significant enhancement in human dermal fibroblast attachment and proliferation [23]. Marine organisms and their wastes could be a sustainable, environmentally friendly collagen source for various applications [24]. The mechanical characteristics of marine-derived collagen exhibited a general inferiority when compared to those of porcine-derived collagen in tissue engineering [25].

Although animals make up the majority of collagen sources used in biomaterial science, the occurrence of outbreaks of bovine spongiform encephalopathy, transmissible spongiform encephalopathy, and foot-and-mouth disease in recent decades has resulted in restrictions and limitations on the utilization of collagens from these particular sources [26]. Furthermore, animal-derived collagen has several drawbacks, such as immunogenicity, batch-to-batch variation, and the risk of pathogenic contamination. In light of these challenges, recombinant collagen might be a promising resolution to address these concerns [27].

3. Collagen Treatment

Collagen treatment offers a range of advantages, including antioxidant and anti-inflammatory properties, wound healing support, benefits for hair and nail health, improvement in gut health, support for joint health, skin rejuvenation, and potential support for musculoskeletal disorders and cardiovascular health.

The impact of collagen peptides isolated from milkfish scales, known as milkfish scale collagen peptides (MSCP), and extracted using the pepsin-soluble collagen method on cell viability was investigated [28]. MSCP exhibited anti-inflammatory effects by reducing lipoxygenase activity and nitric oxide radicals. MSCP demonstrated strong antioxidant properties as indicated with its ability to scavenge DPPH· and ABTS·+ radicals, as well as reduce

cellular reactive oxygen species. An approach known as Subcision was introduced as a minimally invasive technique to treat scars, involving the use of extremely fine needles to disrupt dermal collagen and stimulate dermal remodeling and skin resurfacing [29][30]. The efficacy of the microneedling-delivered irradiated amniotic collagen matrix (IACM) compared to platelet-rich plasma (PRP) in facial rejuvenation was investigated [31]. The result showed that both approaches demonstrated effectiveness and safety in treating skin aging. However, microneedling with IACM yielded superior results compared to PRP, clinically, pathologically, and through an Antera camera analysis.

Collagen can decrease the levels of matrix metalloproteinases (MMPs) by acting as a sacrificial substrate for excessive proteases in chronic wounds. Targeting broad-spectrum excessive MMP levels through collagen dressings could potentially have a positive effect on the healing rates of challenging wounds [32]. The primary health benefits of collagen are associated with dermatological and orthopedic conditions [33]. The effects of bioactive collagen peptide intake on hair thickness and metabolism were investigated [34]. After the consumption of bioactive collagen peptides, a notable increase in hair thickness was observed, which could be attributed to a direct impact of the supplemented peptides on hair metabolism.

The efficacy and tolerability of undenatured type II collagen (UC-II) in regulating joint function and joint pain resulting from strenuous exercise in healthy subjects were investigated with a randomized, double-blind, and placebo-controlled study on healthy volunteers [35]. The findings indicated that the daily intake of 40 mg of UC-II was well tolerated and resulted in enhanced knee joint extension among healthy participants.

Purified porcine atelocollagen (PAC) showed promise as a potential treatment option for managing refractory chronic musculoskeletal pain in a study that recruited patients with chronic refractory pain, where musculoskeletal damage or defects were suspected based on evidence from imaging studies [36]. PAC has the potential to facilitate tissue recovery, act as a scaffold for repair, or directly alleviate inflammation. A new recombinant human type III collagen (hCOLIII) with thromboprotective properties was developed for cardiovascular stents [37]. It supported endothelial cell growth, inhibited smooth muscle cell proliferation, and enhanced healing. Injectable recombinant human collagen type I (rHCI) and type III (rHCIII) matrices were used to treat myocardial infarction in a mice study, restoring mechanical properties, reducing scar size, and preventing heart enlargement [38]. rHCI could promote healing, enhance cardiomyocyte survival, and reduce pathological remodeling.

Collagen has the potential to treat comorbid diseases, including rheumatoid arthritis, osteoarthritis, osteoporosis, psoriatic arthritis, sarcopenia, gastroesophageal reflux, periodontitis, skin aging, and diabetes mellitus.

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