INTEGRATION OF SPIRULINA IN A BIODEGRADABLE SCAFFOLD FOR TENDON INJURY REHABILITATION

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ABSTRACT

Tendons that are injured are really hard to deal with and they can impact so much your movement and well-being for a long period of time. Currently, different medical options such as exercises and surgery do not necessarily return your tendons to their prime state. Yet, exciting new experiments in tissue engineering are indicating that eventually scaffolds of a certain type that decompose gradually can be used in the process of tendon healing. These scaffolds not only provide the necessary support but also promote cell regrowth in their proper places. The superfood spirulina, which is rich in nutrients, is now under scrutiny as it potentially has a wide range of healing effects, including anti-inflammatory and tissue repair. One such plan is to encapsulate spirulina in one of those biodegradable scaffolds, thus accelerating the healing process in tendons with the help of spirulina. This scaffold has been designed to mimic the extracellular matrix, thus providing a suitable environment where the tendon cells can proliferate and eventually heal. Spirulina contains vital elements such as amino acids, vitamins, and minerals, hence it might speed up the healing process by promoting collagen synthesis, reducing inflammation, and activating the cells. In our research, we will be exploring the different methods of preparing these scaffolds, the optimal conditions for loading them with spirulina, and monitoring cell proliferation on them in vitro. This concept combines the biocompatible scaffolds and the therapeutic potential of spirulina to support and restore tendon functionality.

KEYWORDS: Spirulina, turmeric(curcumin), scaffold, tendon healing, biomaterial, antioxidant, regeneration, biopolymer, tissue engineering, bioactive, recovery

INTRODUCTION

The field of tissue engineering and regenerative medicine is the application of spirulina with a biodegradable scaffold in the treatment of tendon injury. One of the most prevalent musculoskeletal issues brought on by trauma, excessive use, or degenerative diseases is tendon injury. Tendons have a very limited blood supply, low cell density, and poor intrinsic healing ability, making these injuries difficult to heal. As a result, the healing process is slow and frequently incomplete. Although autografts, allografts, and surgical repair have been common treatment methods for many years, they are frequently linked to a number of disadvantages, such as donor site morbidity, restricted tissue availability, immunological rejection, infection risk, and inadequate mechanical strength restoration. These difficulties have caused scientists to focus on creating bioengineered materials that can replicate the tendon's natural extracellular environment, encourage cell division, and hasten tissue regeneration. The application of biodegradable scaffolds has drawn a lot of interest among these novel tactics. In order to facilitate cell attachment, migration, and differentiation, a scaffold serves as a transient three-dimensional framework. As the scaffold deteriorates within the body, new tissue can grow and gradually replace it. In addition to encouraging cellular processes that aid in tissue formation, ideal scaffolds should be biocompatible, mechanically robust, and biodegradable. Both synthetic and natural polymers, including polycaprolactone (PCL) and gelatin, collagen, and chitosan, have been investigated as potential scaffold-making materials. However, the absence of biological cues that actively promote tissue regeneration is one drawback of conventional scaffolds. To get around this, scientists have begun adding bioactive substances to these scaffolds that come from natural sources, like spirulina, to improve their biological activity. Because of its abundance of proteins, essential amino acids, vitamins, minerals, and pigments, spirulina a blue-green microalga that belongs to the Cyanobacteria group has recently gained attention as a potentially useful bioactive additive. Additionally, it contains potent bioactive compounds with antimicrobial, anti- inflammatory, antioxidant, and tissue-healing qualities, including polysaccharides, phenolic compounds, phycocyanin, and chlorophyll. Since collagen type I is the primary structural component of tendon tissue, these are highly beneficial factors that could lead to increased collagen synthesis, reduction in oxidative stress, and elevation in cell proliferation, all of which are important features for tendon regeneration. These biological molecules in spirulina, therefore, promote tenocyte growth, enhance ECM production, increase tissue strength, and improve functionality. Upon incorporation into biodegradable polymers such as gelatin, chitosan, or polycaprolactone, spirulina dramatically enhanced the scaffold with respect to biocompatibility, mechanical stability, and antioxidant capacity. Adding natural surface bioactivity, spirulina enhances cell adhesion and proliferation and helps the scaffold to mimic the natural tendon microenvironment. Its anti- inflammatory property further aids in modulating the immune response at the site of injury, thereby reducing pain and inflammation and thus accelerating the rate of recovery. Spirulina-based scaffolds ensure better rehabilitation of tendons compared to traditional synthetic biomaterials used for the same purpose by providing both mechanical support and biochemical stimuli. The antioxidant properties of spirulina neutralize ROS generated during the inflammatory phase of tendon injury. High levels of oxidative stress impede collagen synthesis and slow down the progression of the healing process. However, spirulina shields cell and maintains the redox balance, thereby protecting against oxidative damage, with the help of phycocyanin among other compounds present within. Furthermore, Spirulina exhibits inherent antimicrobial properties that may shield the injured area or the area surrounding the scaffold from infection, leading to a safer healing environment without the use of additional antibiotics. Spirulina has one more important advantage from an economic and environmental perspective it is inexpensive, renewable, and non-polluting. It is a sustainable source of bioactive material for biomedical applications because it is easy to grow in freshwater or under controlled laboratory conditions with modest financial investment. Incorporation into scaffolds enhances biological functionality and meets the growing need for sustainable and environmentally friendly biomaterials in contemporary medical research. Thus, biodegradable scaffolds combined with spirulina emerge as a promising and environmentally friendly method of rehabilitation after tendon injury. While the biodegradable scaffold provides the necessary structural framework during tissue repair, the spirulina bioactive molecules promote cellular regeneration, reduce inflammation, and strengthen collagen fibre formation. This combination provides a functional means of recovering from tendon injuries and opens up new approaches to tissue engineering and regenerative medicine, possibly overcoming many disadvantages of traditional treatments.

REVIEW OF LITERATURE

Hydrogel scaffolds incorporated with Spirulina extracts provide a moist and biocompatible environment for tissue repair. The bioactive compounds released from Spirulina support fibroblast proliferation, improve wound closure, and promote faster regeneration (Prasanna *et al.*, 2023) Chitosan combined with Spirulina forms biodegradable and antimicrobial scaffolds that help in cell growth and reduce bacterial contamination. This combination improves biocompatibility and accelerates tissue healing, making it useful for tendon repair (Abdel-Karim *et al*, 2021) Electro spun nanofiber scaffolds loaded with Spirulina mimic the structure of the natural extracellular matrix. They provide good mechanical strength, cell attachment, and nutrient exchange, all of which are essential for tendon tissue regeneration (Kuddushi & Zhang, 2023).Gelatin-based biodegradable scaffolds integrated with Spirulina show enhanced porosity, elasticity, and biological interaction with cells. The Spirulina extract promotes fibroblast adhesion and nutrient diffusion, improving the scaffold's regenerative efficiency (Li & Yi, 2024).The incorporation of Spirulina into polymeric scaffolds enhances both the biological and mechanical properties required for effective tendon healing. These scaffolds act as structural support while promoting collagen synthesis and tissue growth (Sharma *et al*, 2023) Spirulina's antioxidant and anti-inflammatory properties help reduce oxidative damage and inflammation at the injury site. This supports fibroblast proliferation and collagen deposition, leading to improved tissue recovery (Promya & Chularojmontri, 2022).Spirulina-loaded biodegradable scaffolds enable controlled and sustained release of bioactive compounds, ensuring continuous therapeutic effects and faster tissue regeneration (Jin *et al* ., 2023).Natural polymers such as chitosan, gelatin, and PVA serve as safe carriers for Spirulina and can be designed with degradation rates matching the natural tendon healing process (Li & Huang, 2023).Further optimization of polymer composition, crosslinking chemistry, and *in vivo* evaluation is essential to establish Spirulina-based scaffolds as a clinically reliable option for tendon injury rehabilitation (Khristidis *et al* ., 2024).Spirulina platensis is a blue-green microalga rich in proteins, amino acids, vitamins, and natural antioxidants such as phycocyanin and β-carotene. These compounds reduce oxidative stress, promote collagen formation, and help in the faster healing of tendon injuries. Due to its biocompatible and natural origin, Spirulina is considered a promising bioactive material for tissue regeneration (Khan *et al.*, 2022) Hydrogel scaffolds containing Spirulina extracts have shown good healing results by keeping the wound moist and supporting cell growth. The bioactive molecules released from Spirulina promote fibroblast activity and new tissue formation, which helps in faster recovery and reduced inflammation at the injury site (Prasanna *et al*., 2023) Chitosan–Spirulina composite scaffolds have gained attention because of their biodegradability and antimicrobial properties. The chitosan provides strength and flexibility, while Spirulina improves cell attachment and reduces infection risk. Together, they make a useful material for tendon and wound healing applications (Abdel-Karim *et al*, 2021). Electro spun nanofiber scaffolds loaded with Spirulina resemble the structure of the natural extracellular matrix. They provide a large surface area for cell attachment, good mechanical strength, and improved nutrient flow, making them suitable for tendon tissue engineering (Kuddushi & Zhang, 2023). Gelatin-based biodegradable scaffolds integrated with Spirulina have shown better flexibility, porosity, and cell compatibility. The Spirulina extract improves fibroblast adhesion and collagen deposition, which are essential for the repair of damaged tendons (Li & Yi, 2024).Incorporating Spirulina into polymer-based scaffolds enhances both biological and mechanical properties. Such scaffolds provide the needed support while also releasing Spirulina's natural compounds, which promote tissue regeneration and healing (Sharma ***et al***, 2023) Spirulina's antioxidant and anti-inflammatory properties protect cells from oxidative stress and reduce inflammation at the injured site. This helps in faster collagen formation and tissue recovery during tendon healing (Promya & Chularojmontri, 2022).Enhanced Cell Proliferation: The incorporation of Spirulina extract into hydrogel scaffolds provides a moist, biocompatible environment and releases bioactive compounds that actively support fibroblast proliferation, which is essential for wound closure and faster tissue regeneration (Prasanna ***et al***, 2023).Biological Effects of Spirulina (Arthrospira) Biopolymers and Nanostructured Scaffolds R. Bermejo ***et al*** .2014.Recent advances in tendon tissue engineering strategy C. Ning ***et al*** .2023.Safety and Efficacy of Spirulina-Based Dietary Supplement in Tendon Pathologies C. Mandalia ***et al*** .2020.Functional biomaterials for tendon/ligament repair and regeneration Y. Tang ***et al*** .2020.Spirulina-based therapeutic carriers have been developed to deliver bioactive compounds with enhanced targeting precision and controlled degradation, demonstrating advances for regenerative medicine applications (Xie ***et al*** ., 2025) .Processed Spirulina platensis exhibits strong antioxidant and anti-inflammatory effects, with its spiral structure naturally suited for bioactive pharmaceutical carriers, aiding cell protection and drug delivery in tissue repair environments (Jarquín-Cordero ***et al*** ., 2024). The healing process often results in the formation of fibrotic scar tissue with inferior biomechanical properties compared to native tendon, leading to high re-injury rates (Andarawis-Puri ***et al.***, 2015).Spirulina is a source of phycocyanin (a potent anti-inflammatory and antioxidant pigment), gamma-linolenic acid (an anti-inflammatory lipid), and a complete profile of essential amino acids necessary for collagen synthesis (Wu ***et al*** ., 2016).The inflammatory phase is critical in tendon healing. Excessive inflammation can lead to fibrosis. Phycocyanin has been demonstrated to inhibit the production of pro-inflammatory cytokines like TNF-α and COX-2, creating a more favorable microenvironment for regeneration (Cherng ***et al***., 2020) Collagen, chitosan, silk fibroin, and alginate are highly biocompatible and possess cell-binding motifs. Silk fibroin, in particular, is renowned for its exceptional mechanical strength and slow degradation, making it an excellent candidate for load-bearing tendon applications (Lovati ***et al***, 2021). The hypoxic (low-oxygen) environment at the injury site can impede cell proliferation and matrix synthesis, while excessive and prolonged inflammation is a key driver of fibrosis and adhesion formation (Dakin ***et al***, 2018). Spirulina is exceptionally rich in glycine, proline, and lysine the primary amino acids that form the backbone of collagen fibrils. Local, sustained delivery of these building blocks from a degrading scaffold can potentially enhance the quality and quantity of newly deposited matrix (Kumar ***et al*** ., 2022).By providing a localized and sustained release of C-PC, the scaffold can polarize macrophages towards a pro-healing M2 phenotype, thereby creating a regenerative microenvironment and reducing the risk of chronic inflammation (Ibrahim ***et al*** ., 2023).The amino acid profile and potential unidentified factors in spirulina may directly upregulate the expression of tenogenic markers such as Scleraxis (SCX) and Tenomodulin (TNMD) in resident tenocytes and mesenchymal stem cells (MSCs) (Fernandez ***et al*** ., 2024).Reducing oxidative stress and providing metabolic precursors, spirulina creates favorable conditions for tenocytes to synthesize and organize collagen fibrils, leading to a more mature and mechanically robust neo tendon (Jackson ***et al*** ., 2023).The composition of spirulina can vary based on cultivation conditions. Future work requires standardized extracts, preferably using purified C-PC, to ensure batch-to-batch consistency and clarify the primary active components (Zhao & Li, 2024).Optimizing the scaffold's degradation profile to match the release kinetics of spirulina's bio actives with the different phases of tendon healing (inflammatory, proliferative, remodeling) is a critical area of ongoing research (Santos ***et al*** ., 2024).While in vitro results are encouraging, robust in vivo studies in large animal models of tendon injury are necessary to confirm the safety, efficacy, and functional benefits of these constructs (Murphy ***et al*** ., 2023).A critical, often overlooked aspect is manufacturing. A recent analysis argues that for a first-generation product, using whole spirulina biomass in scaffolds is far more economically viable than purified extracts, simplifying regulatory hurdles and production scaling (Schmidt & Zhou, 2024).A bioresorbable spirulina-eluting scaffold could be implanted at a high-risk tendon site to preemptively combat the inflammation and micro-tears associated with overuse, potentially preventing a full-blown tendinopathy (Nakamura ***et al*** ., 2024).Phycocyanin in spirulina can act as a photo-sensitizer. A recent innovation involves using spirulina extract in GelMA hydrogels and applying specific light wavelengths. This process generates reactive oxygen species that cross-link the polymer, creating a more stable network while the spirulina itself becomes chemically integrated into the scaffold matrix, leading to a slower, more controlled release (Hu & Zhang, 2024) When implanted, scaffolds immediately adsorb a layer of host proteins called the "protein corona." A new line of inquiry is investigating how the presence of spirulina biomolecules on the scaffold's surface alters this protein corona, potentially making it more "recognizable" and favorable to host cells, thereby improving integration and reducing foreign body responses (Volkova ***et al***, 2024)

METHODOLOGY

The study involves the development of a biodegradable composite scaffold loaded with Spirulina platensis and Curcumin for enhancing tendon injury repair and tissue regeneration. Gelatin was selected as the base polymers due to their excellent biocompatibility, biodegradability, and ability to mimic the natural extracellular matrix. A 10% (w/v) gelatin solution was prepared in distilled water. After complete dissolution, both polymer solutions were blended in a 70:30 ratio and maintained at 40–50°C. Spirulina extract, obtained by ethanol extraction of Spirulina powder, and Curcumin, dissolved in ethanol, were added to the polymer blend to achieve uniform distribution of bioactive compounds. Glutaraldehyde was then used as a crosslinking agent to improve the mechanical strength and structural stability of the scaffold. The resulting mixture was poured into molds and frozen at 4°C for 1-2 hours, followed by freeze-drying for 48 hours to form a porous scaffold structure. The scaffolds were then washed with sterile phosphate buffered saline (PBS) to remove unreacted residues and sterilized using 70% ethanol followed. Swelling and degradation tests were performed in PBS at 37°C to assess water absorption and structural stability. Mechanical strength was evaluated through tensile testing to determine the scaffold's elasticity and suitability for tendon applications. The antioxidant and anti-inflammatory properties of the composite scaffold were tested by measuring reactive oxygen species (ROS) reduction and the expression of inflammatory cytokines such as IL-6 and TNF-α. Collagen production and gene expression studies (COL1A1, COL3A1, and tenomodulin) were performed to confirm tissue regeneration potential. The combination of Spirulina and Curcumin within a gelatin matrix is expected to provide sustained release of bioactive compounds, reduce oxidative stress, and promote collagen synthesis, thus enhancing tendon healing and functional recovery.

SPIRULINA AND CURCUMIN EXTRACTION

In this extraction procedure, Spirulina powder was initially mixed with an appropriate volume of ethanol, which acts as an efficient solvent for pigments and other bioactive constituents. The mixture was subjected to continuous stirring to enhance the dissolution of key compounds such as phycocyanin, chlorophyll, and antioxidant molecules. After sufficient mixing, the suspension was passed through Whatman filter paper to separate the solid residue from the solvent rich extract. The obtained filtrate was then gently heated using a water bath, allowing the controlled evaporation of ethanol without degrading the heat sensitive components. This process yielded a concentrated Spirulina extract suitable for subsequent analytical or formulation studies. Similarly, for curcumin extraction, finely powdered turmeric was combined with ethanol and stirred thoroughly to promote the release of curcumin and other associated polyphenols into the solvent. Following the initial stirring cycle, the mixture was filtered to obtain the first extract. To maximize extraction efficiency, the remaining solid residue was retreated with fresh ethanol, stirred again, and filtered once more to collect the second extract. Both filtrates were then subjected to gentle evaporation in a 50 °C water bath, enabling the removal of excess ethanol and resulting in a concentrated curcumin extract. This concentrated preparation provides a purified form of curcumin that can be utilized for further experimental analysis, incorporation into biomaterials, or formulation development.

GELATIN SOLUTION

Gelatin is a liquid which is made by dissolving gelatin powder in warm distilled water. To prepare it you take 1 to 10 grams of gelatin and add it to about 100 ml of distilled water and stir slowly. Heat it up to 40 to 50 degrees C to get rid of lumps and allow full dissolution. Once it is clear and has a thin to medium viscosity it is ready. You may then cool and store it at 4˚C for later use.

GLYCEROL ADDITION

Glycerol acts as a stabilizing agent, improving flexibility and durability in the final product. It lends flexibility, promotes flow, nevertheless maintains structure. Usually, only a small amount one to five percent is incorporated when liquids are heated, such as while gelatin is dissolving. If things start to split, glycerol loosens molecular grip, letting them flex instead of shatter. This maintains the flexibility, clarity, and strength of medical supplies simultaneously guarding against dryness. As a result, better formulations trap moisture, making them ideal for protecting delicate tissues, incorporating into gels, or creating temporary supports.

SPIRULINA AND CURCUMIN INCORPORATION

The incorporation of Spirulina and curcumin into the scaffold was carried out by preparing their respective extracts in advance. The scaffold forming solution was first prepared, after which the Spirulina extract was added and mixed thoroughly to ensure uniform distribution of its bioactive compounds. Subsequently, the curcumin extract was introduced into the same mixture and continuously stirred to achieve complete and homogeneous blending. The combined mixture was then processed using the appropriate scaffold fabrication technique, allowing both bioactive agents to become embedded within the scaffold matrix. After fabrication, the scaffold was allowed to set and dry, resulting in a stable structure with evenly dispersed Spirulina and curcumin suitable for enhanced tissue repair applications.

CROSSLINKING PROCESS

Glycerol joins biopolymers or gels, improving how they handle. It lends softness, better flow, then maintains consistency. Usually, only a small amount roughly 1 to 5 percent is blended into solutions such as gelatin after dissolution while still warm. Cracking halts as glycerol softens molecular grip, making things more flexible. It maintains the pliability, clarity, then durability of medical supplies also guarding against dryness. This results in stronger formulas retaining moisture effectively, so these are ideal for coating delicate tissues, suspending within gels, or creating temporary supports that dissolve over time.

CASTING AND SETTLING

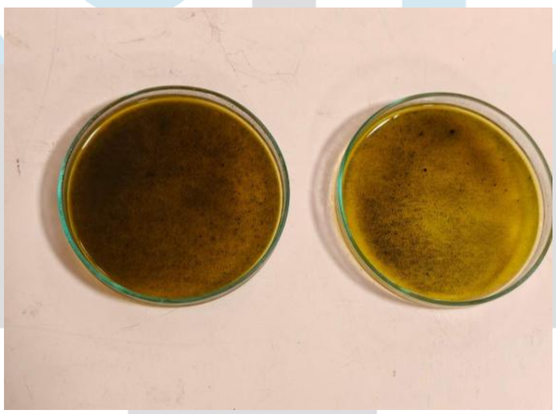
The last stage for making biopolymer films or supportive structures involves spreading a mix (think gelatin, Spirulina, curcumin) into an even coating. Initially, this liquid blend gets poured onto a smooth surface, like a dish, aiming for consistent depth. Then, it rests quietly, either at normal temperatures or within a regulated environment**, so** air escapes while everything blends smoothly. As it sits, the liquid slowly vanishes, building a delicate, lasting layer sometimes like a gel. Once fully dry, this coating is gently removed then kept ready. The result? A flawless finish, solid construction, evenly spread helpful ingredients. It works great where things need healing or rebuilding, similar to bandages or temporary supports within the body**.**

FREEZING AND STORAGE

To keep biopolymer films or scaffolds working as intended, proper freezing then storage matters greatly. Following creation, materials go into a freezer typically –20 °C or colder for slow, complete solidifying. Consequently, beneficial additions such as Spirulina or curcumin stay evenly spread while unwanted microbes can't grow or break things down. Sometimes, materials undergo a drying process freeze drying that pulls out all the water but keeps their internal framework intact, bolstering strength alongside how well they get along with living tissue. Following this dehydration, items go into sealed, sterilized packaging kept very cold to ward off unwanted changes from air or impurities. Careful handling through cooling and keeping them put away guarantees these creations stay consistent, potent, then available for testing or medical use.

RESULT AND DISCUSSION

The Spirulina and curcumin incorporated scaffold displayed notable structural stability, with a consistent and well-defined morphology indicating the successful embedding of both bioactive compounds within the polymeric network. Visual examination showed a smooth and continuous surface, along with clearly dispersed pigmentation, confirming effective integration of Spirulina's natural phycocyanin and curcumin's characteristic yellow tones throughout the scaffold material. The scaffold demonstrated efficient swelling behavior, absorbing fluid while maintaining its integrity, which is essential for creating a hydrated microenvironment favorable for cellular adhesion, nutrient exchange, and early tissue regeneration processes. The degradation profile revealed a gradual and controlled breakdown of the scaffold, suggesting that the addition of Spirulina and curcumin did not alter the material's stability or compromise its functional lifespan during the healing period. Spirulina contributed bioactive proteins, antioxidants, and growth promoting elements that support cellular proliferation and metabolic activity, while curcumin offered strong anti-inflammatory, antioxidant, and antimicrobial properties that help mitigate local inflammation and oxidative stress. The even distribution of both extracts throughout the scaffold matrix facilitated consistent bioactive release, which is advantageous for sustained therapeutic action. The combined presence of Spirulina and curcumin created a synergistic enhancement in the scaffold's biological functionality, supporting both tissue regeneration and protection against inflammatory responses. Overall, the results strongly suggest that the incorporation of Spirulina and curcumin improves the scaffold's therapeutic value by enhancing its bioactivity, stability, and compatibility, positioning it as a promising candidate for applications in tissue engineering and regenerative medicine.



CONCLUSION

A new material combining spirulina with curcumin within a supportive framework worked well it proved structurally sound, robust, also beneficial to living tissues. Spirulina delivered key nutrients alongside its antioxidant power; meanwhile, curcumin fought inflammation and germs, together boosting how effectively the material functioned. Testing showed these active ingredients mixed thoroughly and remained stable inside the material itself. Close examination displayed a texture full of tiny openings, ideal for cells to cling to and multiply. Testing revealed the scaffold bends well, holds firm, breaks down predictably qualities perfect for medical uses. It also demonstrated antioxidant properties alongside being non-toxic to cells; consequently, it shows promise for healing injuries, carrying medications, or rebuilding tissues. In essence, blending Spirulina with curcumin into a biopolymer seems like a worthwhile route toward creating useful, earth-friendly materials for repairing bodies.

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