Chapter 4

Design and Application of Plant Protein-Based Materials For Controlled Phytochemical Delivery in Bone Cancer Therapy-Review

Mehtap Demirel[1]

Abstract

Phytochemicals from plants offer considerable potential for bone cancer treatment because of their anticancer properties. Their clinical effectiveness is frequently restricted by low bioavailability, systemic distribution, and quick elimination. This review focuses on plant protein-based drug delivery systems engineered for the controlled and targeted release of phytochemicals, specifically in bone tissue applications. These systems, prized for their biocompatibility and ability to break down naturally, provide dual functionality as both drug delivery systems and regenerative platforms.

Natural biopolymers like silk fibroin, sisal fibers, and bamboo fibers, in addition to widely used plant proteins such as soy, zein, and gliadin, are receiving increasing attention. Silk fibroin aids in the adhesion and growth of bone cells, whereas sisal and bamboo fibers provide mechanical strength and the potential for bone growth, suggesting that they could be effective in bone-regenerative treatments. These materials can be developed into carriers of various micro/nano-scale dimensions, allowing for both sustained release and bone healing.

The review also emphasizes key mechanisms such as post-implantation bone-targeted delivery, enhanced osteoconductivity, localized delivery of anticancer drugs, and bioactive surface modifications. In contrast to conventional synthetic polymers, these natural biomaterials display reduced toxicity, environmentally friendly manufacturing processes, and compatibility with the structural framework of bone microenvironments.

In conclusion, biomaterials based on plant protein and fiber exhibit significant potential as dual-functional systems for the controlled release of phytochemicals and the regeneration of bone tissue in the context of bone cancer treatment.

1 Doç. Dr., Adiyaman University, Vocational School of Technical Sci, Adiyaman, Turkey
ORCID: 0000-0003-2362-314X, E Mail: mdemirel@adiyaman.edu.tr

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INTRODUCTION

Cancers of the bone, including osteosarcoma and bone metastases from breast or prostate cancer, are among the most aggressive and resistant to treatment types of malignancies. Conventional treatments, such as chemotherapy, surgical removal, and radiation therapy, frequently lead to severe side effects, limited selectivity in targeting cancer cells, and reduced effectiveness in preventing cancer from recurring or promoting bone repair. The restrictions have led to an increasing interest in alternative and complementary therapeutic methods that are safer, more environmentally friendly, and capable of targeting the bone microenvironment more accurately.

Bioactive compounds from plants, which include several phytochemicals, are being studied more extensively for their potential to combat cancer. Compounds such as curcumin, resveratrol, epigallocatechin gallate (EGCG), and quercetin show anti-inflammatory, pro-apoptotic, antiproliferative, and antioxidant characteristics. Promising outcomes have been observed with several phytochemicals, which have demonstrated the ability to inhibit osteosarcoma growth, decrease bone resorption, and regulate the tumor microenvironment's dynamics. Their clinical applications are restricted due to problems like low water solubility, chemical instability, quick removal from the body, and the inability to be absorbed effectively by the body—especially in the dense, mineralized bone matrix.

In order to overcome the challenges associated with pharmacokinetics and delivery, advanced biomaterial-based controlled release systems have been developed. Plant- and animal-derived proteins and fibers have been identified as effective carrier materials due to their natural composition, compatibility with living tissues, ability to break down naturally, and versatility in formulations. Besides the more commonly examined materials like soy protein isolate, pea protein, and zein, natural structural fibers such as silk fibroin, sisal fibers, and bamboo fibers are also receiving attention. These materials possess high mechanical strength, inherent porosity, and the ability to coexist with osteogenic cells, rendering them suitable for use as both drug delivery agents and structural components for bone regrowth.

Plant- and fiber-based biopolymers can be processed into microcapsule structures, coatings, or composite scaffolds that allow for the localized and sustained delivery of phytochemicals. In addition, combining these materials with bioactive ceramics like hydroxyapatite or calcium phosphate can improve their ability to foster bone growth, making them especially appealing for use

in bone grafts, implant coatings, and multifunctional scaffolds that support bone repair while also offering localized anticancer properties.

This chapter offers a thorough examination of plant protein and natural fiber-based materials, focusing on their design and biomedical applications in controlled anticancer phytochemical delivery, especially in the context of bone cancer treatment. The forthcoming chapter will explore the therapeutic applications of the chosen plant-derived compounds, the physical and operational characteristics of the carrier substances, encapsulation methods, and their implementation in targeted delivery systems aimed at the bone tissue. Future challenges and clinical translation prospects will be explored.

PHYTOCHEMICALS IN BONE CANCER THERAPY

Bone cancers, particularly osteosarcoma and metastatic bone lesions, pose significant clinical challenges because of their highly aggressive behavior and intricate microenvironment (Lu et.al., 2025). Treatment options for the current scenario usually involve finding a delicate balance between surgically removing the entire tumor and maintaining the structural integrity of the bone (Bădilă et al., 2021)

Naturally occurring bioactive compounds in plants have significant therapeutic potential for cancer prevention and treatment. In the context of bone cancer, numerous plant-derived compounds show significant anticancer potential by triggering cell death, suppressing the formation of new blood vessels, reducing oxidative damage, and adjusting inflammatory response pathways.

The most thoroughly investigated phytochemicals associated with bone cancers are composed of the following:

Curcumin is a polyphenolic compound that originates from the plant Curcuma longa, also known as turmeric. Curcumin has demonstrated robust anticancer properties by triggering apoptosis in osteosarcoma cells, limiting cell division, and blocking the NF-κB signaling pathway. This also has potent anti-inflammatory and antioxidant effects, as demonstrated (Wang et.al.,2021).

Resveratrol, which can be found in grapes, peanuts, and berries, has been shown to inhibit the growth of osteosarcoma cells, decrease bone loss caused by tumors, and affect bone remodeling markers like RANKL and OPG (Shakibaei et.al., 2011). Green tea's main catechin, Epigallocatechin Gallate (EGCG), has cytotoxic effects on osteosarcoma cell lines, hampers the growth of new blood vessels in tumors, and reduces the activity of matrix

metalloproteinases (MMP-2/9), two key enzymes involved in tumor spread and bone breakdown (Li et.al., 2023).

A flavonoid called quercetin is commonly found in various foods, including apples, onions, and leafy greens.

It triggers apoptosis and halts the cell cycle in osteosarcoma cells through mitochondrial and caspase-driven mechanisms and was demonstrated to increase the efficacy of standard chemotherapy treatments (Granado-Serrano et. al., 2010). It induces apoptosis and cell cycle arrest in osteosarcoma cells via mitochondrial and caspase-mediated pathways and has been shown to enhance the effectiveness of conventional chemotherapeutics treatments (Granado-Serrano et. al., 2010).

A neolignan derived from Magnolia officinalis, honokiol, has shown antiproliferative and anti-angiogenic properties in various cancers, such as osteosarcoma. The compound induces apoptosis while preventing tumor growth and the spread of cancer to other parts of the body (Arora et.al., 2012). Research has demonstrated that the phenolic compound gingerol, which is present in ginger (Zingiber officinale), can prevent the spread of cancer cells, cause cancer cell death, and halt cell division in bone tumor cells, thereby underscoring its value as a complementary treatment in bone cancer therapy (Lee et.al., 2008).

Most phytochemicals with potent biological properties are hindered by pharmacokinetic drawbacks, including low water solubility, chemical instability, and swift removal from the body. The restrictions imposed by these limitations significantly impede the accumulation of drugs in the bone tissue, a dense and mineralized area that poses a barrier to therapeutic delivery. Despite their potent biological activities, most phytochemicals suffer from pharmacokinetic limitations such as poor water solubility, chemical instability, and rapid systemic elimination. These limitations particularly hinder drug accumulation in the bone tissue, which is dense and mineralized, creating a barrier for therapeutic delivery. Over the past few years, a number of natural products have been studied for their potential to slow the progression of osteosarcoma, regulate bone metabolism, and counteract chemoresistance mechanisms, as reported (Zhang et.al., 2020). Various delivery systems including nanoparticles, liposomes, hydrogels, and natural polymer-based microcapsules have been investigated to overcome these challenges. The goal of these approaches is to increase the uptake of phytochemicals by cells, prolong their circulation within the body, and enhance their accumulation at the tumor site (Liu et. al., 2019).

A diverse assortment of delivery systems, including nanoparticles, liposomes, hydrogels, and natural polymer-based microcapsules, have been investigated to address these challenges. One notable option is plant protein-based microcapsules, which offer a biocompatible, biodegradable, and sustainable approach to safeguard phytochemicals and facilitate targeted, long-lasting delivery. In addition, these systems can be paired with osteoinductive substances or incorporated into frameworks, thereby serving a dual purpose in bone tissue regeneration and targeted cancer treatment.

According to Isakoff et al. (2022), approximately 6% of childhood malignancies are bone cancers, with osteosarcoma being the most frequent primary bone cancer. Several current clinical challenges exist:

Recurrence of the condition can occur in 30-40% of patients following surgical removal (Bielack et al., 2002).

Sclerotic bone tumors exhibit limited drug penetration (Roodman et al., 2004, Chow et.al., 2013).

A mechanical incompatibility exists between implants and the host's natural bone (Huiskes et al., 1993, Ryan et. Al, 2006).

Conventional metallic implants and synthetic bone grafts often fail to meet three essential requirements for treating bone cancer. Delivery of medication directly to the site of a tumor to inhibit its recurrence. Bone regeneration facilitated through mechanical assistance. Compatibility of biological materials with adjacent healthy tissue.

In addition to those mentioned, another category of compounds used in bone tumors includes plant-based material compounds. Composites made from natural fibers and plant proteins have become potential solutions that tackle these challenges simultaneously, as noted in the research three of these fibers specifically demonstrate a promising potential for bone cancer applications (Faheed, 2024, Liu et.al., 2023, Jouyandeh et. al., 2022). Coconut shell fibers possess hydrophobic regions that are well-suited for encapsulating poorly soluble anticancer agents. Additionally, their lignin and polyphenolic content—including catechins and tannins—contribute significant antioxidant and anticancer properties. Notably, lignocellulosic-derived nanoparticles such as lignin nanoparticles demonstrate high efficiency in loading hydrophobic drugs and exhibit strong antioxidant activity (Wijaya et al., 2021). Moreover, studies on coconut shell extracts have confirmed the presence of tannins and catechins with documented cytotoxic effects against cancer cell lines (Mohd Effendi Mohamed Nor et al., 2023; Koschek et al., 2007).

Pineapple Leaf Fiber (PALF) systems provide distinct advantages:

- Pineapple Leaf Fiber (PALF)-based composites exhibit inherently porous structures, which are advantageous for facilitating drug diffusion in biomedical applications, as highlighted in recent studies. (Sethupathi et al., 2024; Brailson et al., 2022)
- Research indicates that the biodegradable nature of PALF composites aligns with the time frames associated with early-stage bone tissue healing, making them suitable for use in temporary or dissolvable scaffolds.(Sethupathi et al., 2024)
- PALF-containing biocomposites have also shown promising results in promoting angiogenesis, a critical factor for bone healing and integration, particularly when combined with bioactive polymer matrices.(Liu et al., 2023; Sethupathi et al., 2024)

Silk fibroin composites demonstrate considerable potential owing to the following:

- The tensile strength of this material is 158 ± 12 MPa, which meets the mechanical strength requirements of cortical bone, as confirmed by Rockwood et al., who demonstrated that regenerated silk fibroin films and scaffolds exhibit tensile strengths ranging from 120 to 200 MPa depending on processing conditions (Rockwood et. al., 2011).
- Osteoconductivity was found to support 92% osteoblast adhesion, which is significantly higher than the 68% observed for polycaprolactone (PCL), as reported by Nazarov et al., where silk nanofiber mats significantly outperformed synthetic polymers in supporting cell attachment (Nazarov et. al. 2004).
- Research has shown that the rate of drug release achieves 80% curcumin release at a pH level of 6.8, as opposed to 35% at a pH level of 7.4, indicating a pH-responsive release profile that enhances bioavailability in tumor microenvironments, as demonstrated by Wang et al. (Wang et.al., 2008).

Sisal Fiber Reinforcements Exhibit Clinical Benefits

- Sisal fibers offer a cost-effective and sustainable alternative to synthetic fibers. Numerous studies have highlighted that the price per kilogram of natural fibers, including sisal, is significantly lower than that of synthetic counterparts, making them attractive for both industrial and biomedical applications (Li et al., 2020).

- Alkali-treated sisal fibers demonstrate notable improvements in mechanical performance. Treatments using 5% NaOH have been shown to enhance fiber–matrix interfacial bonding, thereby increasing tensile and flexural strength. This enhancement can result in performance levels approaching those of certain metallic materials, such as titanium meshes. (Bekele et.al., 2023)
- Sisal-based materials have also shown promising biological effects, particularly in reducing the viability of osteosarcoma cell lines such as Saos-2. Studies involving plant-derived reinforcements suggest that these materials can exert cytotoxic effects on cancerous cells, indicating their potential for biomedical and therapeutic use.). (Ağan et.al., 2020)

Challenges in Clinical Translation

Gamma radiation exposure has been shown to negatively affect the mechanical integrity of sisal fibers, with several studies demonstrating a reduction in tensile strength following irradiation.(Dorneles de Castro et.al.,2020)

To date, there are no plant protein–based implants that have received FDA approval for cancer therapy applications. Although plant-derived biomaterials show great promise in preclinical stages, none have progressed to regulatory clearance for oncological implant use, underscoring this translational gap. (Wu et.al., 2024)

Tablo1. Preliminary Testing Outcomes of Composites Reinforced with Natural Fibers for Treating Bone Cancer

Material – Model	Outcome Summary	Supporting References
Silk–Curcumin (murine OS)	Curcumin-loaded silk scaffolds showed significant reduction in tumor volume and mass in osteosarcoma-bearing murine models.	Ouyang et al. (2024) – "significant reduction in tumor volüme"
Sisal–Dox (Saos-2 xenograft)	Doxorubicin-loaded sisal fiber carriers resulted in marked reduction in tumor growth and cell viability in Saos-2 xenografts.	Orel et al., 2024 – observed ~61 % decrease in Saos-2 cell viability
PALF scaffold (rabbit tibia)	Pineapple leaf fiber–based scaffold promoted robust bone regeneration, supporting effective defect repair in rabbit tibial models.	Rabbit tibia defect scaffolding studies with plant fiber composites show strong osteointegration-Sethupathi et.al.(2024)

PLANT PROTEIN-BASED MATERIALS FOR BONE-TARGETED PHYTOCHEMICAL DELIVERY

Phytochemical delivery to bone-targeted sites utilizing plant-derived protein-based materials plant-based protein materials present a promising foundation for creating sustainable and functional drug delivery systems. These biopolymers, sourced from natural materials including legumes, cereals, and oilseeds, exhibit superior film-forming, encapsulating, and biodegradable characteristics. Their compatibility with bone regeneration strategies makes these compounds particularly valuable for the localized treatment of bone malignancies such as osteosarcoma and bone metastases. Their compatibility with bone regeneration strategies makes them particularly valuable for the localized treatment of bone malignancies such as osteosarcoma and bone metastases.

Plant proteins commonly found in use include:

Soy protein isolate (SPI) has undergone thorough investigations into its mechanical properties, controlled breakdown, and ability to create microspheres and hydrogels. The material's surface can be altered to enhance its bioactivity and increase its capacity for carrying drugs, making it suitable for use in bone scaffolds (Li et.al., 2019).

Pea protein is becoming increasingly popular as a matrix for controlled release systems due to its well-balanced amino acid profile and low potential for causing allergic reactions. Research has demonstrated its ability to work well with calcium phosphate composites in the field of bone tissue engineering, as found in the study (Wang et.al., 2021).

Zein is a protein found in maize, characterized by its high hydrophobic nature, which facilitates prolonged drug release. Good biocompatibility and structural integrity have been achieved in the fabrication of bone-targeted nanocarriers using this method (Zhang et.al., 2022).

These proteins can be developed into microcapsules, coatings, or scaffold composites using methods like spray drying, ionic gelation, coacervation, and emulsion-based techniques. These systems can be used to provide a dual function when incorporated into bone tissue engineering scaffolds or applied as implant coatings—supporting bone regeneration and facilitating the localized release of anticancer phytochemicals.

In addition, composites based on plant protein can be augmented with osteoconductive fillers like hydroxyapatite (HAp), calcium phosphate (CaP), or bioactive glass to increase the mechanical strength and bone bonding. These hybrid systems not only enhance cell attachment and growth but also

facilitate the targeted and prolonged delivery of therapeutic agents directly to the bone tumor site (Chen et.al., 2020).

Recent studies have shown that the microarchitecture of these protein-based carriers, including factors like porosity, swelling behavior, and degradation rate, can be precisely adjusted to match the dynamics of bone remodeling and pathological environments, as demonstrated in research (Deng et.al., 2023).

Beyond traditional plant proteins like zein and soy protein, naturally occurring structural proteins and fibers such as silk fibroin, sisal, and coconut shell fibers have garnered increasing attention for use as biomaterials in drug delivery systems. Silk fibroin nanoparticles have been extensively investigated within tumor microenvironments due to their advantages, including controlled drug release, high biocompatibility, and low toxicity (Foppiani et al., 2024; Pollini et al., 2024). These protein-based systems show promise for the encapsulation and targeted delivery of therapeutic agents (Chemis Group, 2024). The use of natural fiber composites (e.g., sisal) as biomaterials for bone-supporting applications has also grown due to their high mechanical strength and environmentally friendly characteristics (PMC, 2023; Springer, 2023).

Sisal fibers, specifically from the plant Agave sisalana, possess a high cellulose content and stiffness, which enable them to provide mechanical support in drug delivery systems. Although direct evidence regarding their application in bone cancer treatment is limited, their potential as reinforcing components in biomedical composites is well documented. Sisal-reinforced biocomposites have been investigated for orthopedic applications due to their high tensile and compressive strength; however, their use specifically in bone cancer therapy remains in the early stages of research (Zamora-Mendoza et.al., 2023).

Coconut shell fibers possess hydrophobic regions that are well-suited for encapsulating poorly soluble anticancer agents. Additionally, their inherent lignin content provides antioxidant properties, which may enhance therapeutic outcomes. Lignocellulosic-derived nanoparticles, such as lignin nanoparticles, have demonstrated high efficiency in loading hydrophobic drugs and exhibit strong antioxidant activity (Wijaya et al., 2021).

ENCAPSULATION TECHNIQUES AND BONE-TARGETED DELIVERY STRATEGIES

The effectiveness of plant protein-based delivery systems is heavily reliant on the selected encapsulation method and the specific targeting approach

employed to guide therapeutic agents to the bone tissue. For anticancer phytochemicals to be effective in treating cancer in the bones with minimal side effects, it is crucial to deliver them in a controlled, sustained way that is specific to the bone environment.

MICROENCAPSULATION TECHNIQUES WITH PLANT PROTEINS

Plant-Based Microencapsulation Methods Utilizing Proteins Methods have been created to manufacture microcapsules or nanoparticles from plant proteins such as soy, zein, and pea protein.

These methods not only maintain the structural integrity and biological activity of the encapsulated phytochemicals but also facilitate their controlled release. These methods not only preserve the structural integrity and activity of the encapsulated phytochemicals but also allow controlled release.

Spray drying is a commonly applied and highly scalable technique. The plant proteins are mixed with the medication, and then they are transformed into a fine, dried powder through atomization into hot air. The method offers good control over particle size and cost-effectiveness, although the thermal sensitivity of certain phytochemicals needs to be considered (Patel et.al., 2019).

Coacervation: This process is based on the electrostatic interactions between the positively and negatively charged polymers that occur through coacervation. Coacervates made with zein or SPI can trap non-water-soluble plant compounds such as curcumin or resveratrol and be hardened into stable delivery vehicles (Chen et.al., 2021).

Ionic Gelation: This process involves cross-linking of plant proteins using calcium ions. This procedure is a gentle approach, especially well-suited for compounds that are sensitive to heat, and produces uniform microspheres that are suitable for use in injectable delivery systems (Nunes et.al., 2020).

These encapsulation methods can be customized to regulate the particle size, surface charge, degradation rate, and drug release profiles in order to align with the pathological and regenerative properties of the bone tissue environments.

BONE-TARGETING STRATEGIES

To achieve effective bone accumulation, delivery systems typically need to be modified to be more bone-targeting. The primary methods employed involve

Bisphosphonate functionalization involves compounds like alendronate, which exhibit a high affinity for hydroxyapatite and are often attached to drug delivery systems to ensure targeted deposition in mineralized bone tissue (Wang et.al., 2017).

Short peptides, such as Asp-Ser-Ser, or molecules with a high affinity for hydroxyapatite can be attached to proteins to enhance their adhesion to bone surfaces, as demonstrated (Zhou et. al., 2021).

The bone tumor microenvironment frequently exhibits acidic conditions. Under specific conditions, plant protein carriers that can detect changes in pH levels release their cargo in a targeted manner, thereby enhancing the delivery of therapy to the correct site and reducing the impact of unintended side effects (Ramasamy et.al., 2022).

The concept of encapsulation can be expanded by incorporating fibrous biopolymers such as silk and lignocellulosic fibers. Electrospun silk fibroin scaffolds and composite systems that combine sisal or coconut fibers can improve both the mechanical strength and bone bonding of delivery platforms [16, 18,19]. The fabrication of nanofibrous silk fibroin mats has been made possible through electrospinning, which is used to create materials for targeted drug delivery in bone cancer research. These structures enable a controlled release over time and can be modified to incorporate targeting molecules [16].

Encapsulation of phytochemicals directly into fibers such as sisal or coconut is relatively uncommon, yet these fibers can serve as structural frameworks in hybrid systems, thereby improving the mechanical stability of devices designed for bone-targeted delivery. [17,19]

CONTROLLED RELEASE KINETICS AND THERAPEUTIC OUTCOMES IN BONE CANCER MODELS

The success of plant protein-based delivery systems in treating bone cancer hinges on their ability to release therapeutic compounds in a controlled and targeted fashion. The release dynamics of these systems have been extensively examined in both laboratory-based and living-organism models.

Release Kinetics Profiles

Plant-based carriers derived from proteins can release phytochemicals according to different kinetic models. Zein-based nanoparticles enable the gradual and prolonged release of hydrophobic phytochemicals, which facilitates effective delivery within the bone tumor microenvironment (Zhang et.al., 2022). Pea protein-based microgel capsules have also shown

the capability to manage the release of both water-loving and water-fearing compounds (Dinh et.al., 2024).

Plant-based protein systems can be designed to have two main functions through the integration of microencapsulation techniques with targeted approaches for bone tissue, thereby enabling the simultaneous promotion of bone repair and the controlled release of anticancer medication in specific areas over time.

Silk fibroin is notable among different biomaterials for its ability to degrade at a tunable rate and release substances in a controlled manner. In bone cancer models, silk-based drug carriers have demonstrated sustained drug presence at the tumor site. Only limited studies on sisal and coconut fibers exist, but their antioxidant properties and structural characteristics indicate possible future therapeutic applications (Florczak et. Al., 2021). Specifically, silk fibroin carriers have shown favorable release kinetics in bone cancer research models, maintaining therapeutic concentrations within the tumor and reducing systemic toxicity in several studies (Zheng et.al., 2025). Additionally, the inherent antioxidant activity of coconut-derived lignocellulosic fibers may enhance treatment efficacy by reducing oxidative stress within the tumor microenvironment, although further research is necessary to clarify their controlled-release behavior (Zheng et.al., 2025, Morsali et.al., 2022).

IN VITRO AND IN VIVO THERAPEUTIC EFFECTS

Research conducted in a laboratory setting has demonstrated that delivery systems based on plant proteins have an inhibitory effect on the proliferation of osteosarcoma cells in culture. Curcumin-loaded zein nanoparticles were found to cause apoptosis and suppress tumor growth in osteosarcoma cells (Shakori Poshteh et.al., 2024). In vivo studies have shown that these carriers tend to accumulate in areas where bone tumors occur, thereby lowering the risk of systemic side effects while increasing the effectiveness of the treatment (Wu et.al., 2024).

FUTURE PERSPECTIVES

Interest in plant protein–based delivery systems for bone cancer therapy has increased notably in recent years due to their inherent biocompatibility, biodegradability, and drug-loading capability. Recent reviews highlight the development of protein nanoparticles from plant sources—including zein, soy, and albumin—for biomedical applications, demonstrating improved targeting and controlled release profiles (Muraleedharan et.al., 2024,

Karnwal et.al., 2024). Additionally, nanoparticle-based systems designed specifically for bone targeting have been shown to enhance osteogenesis and local drug retention in bone cancer models (Guan et al., 2024). Finally, the incorporation of novel bacterial proteins with self-assembling tubular structures has enhanced targeting precision and encapsulation efficiency in bone tumor delivery designs (Bergeron et al., 2025).

The dual-loading capability of plant-protein-based microgel systems for both water-loving and water-repelling drugs offers promising opportunities for combination therapy applications (Dinh et.al, 2024)

CHALLENGES AND FUTURE PERSPECTIVES

Bone cancer therapy may be enhanced by protein-based drug delivery systems. Several hurdles still need to be overcome in order to effectively translate these systems into practical clinical uses.

CLINICAL APPLICATION AND REGULATORY CHALLENGES

Standardizing and scaling up fabrication techniques for plant-protein-based nanoparticles is essential for their clinical application (Zhang et.al., 2022). In addition, more extensive in vivo studies are needed to assess the long-term biocompatibility and safety of these systems (Dinh et.al., 2024).

TARGETING AND CONTROLLED RELEASE STRATEGIES

Creating targeted strategies that specifically focus on bone development is crucial for improving the effectiveness of treatments. Conjugating bone-affinitive molecules like bisphosphonates to delivery vehicles can greatly enhance the precision of targeting (Wang et.al., 2017). Developing stimulus-sensitive systems like pH-sensing drug carriers that release medication in tumor environments with low pH can decrease side effects and improve treatment accuracy (Chen et.al., 2021).

FUTURE RESEARCH DIRECTIONS

Research in the future should concentrate on designing multi-functional systems based on plant proteins. Platforms capable of serving two purposes, namely promoting bone growth and releasing anticancer medications, may provide substantial clinical advantages (Dinh et.al., 2024). Genetic engineering could enhance the structural optimization of plant proteins, thereby potentially improving their bioavailability, stability, and ability to target effectively (Zhang et.al.,2022).

Further investigation is required to fully leverage the promising outcomes and maximize the potential of silk, sisal, and coconut shell fibers in bone-targeted drug delivery systems. The key steps toward the clinical adoption of these natural fibers as biofunctional components in advanced drug delivery systems will include standardizing the processing methods, increasing the drug-loading efficiencies, and improving the targeting capabilities. Replicating and increasing the manufacturing of silk fibroin-based systems consistently is a major problem to overcome. Obtaining regulatory approval necessitates comprehensive biocompatibility and safety evaluations [Hcini, 2023, Zamora-Mendoza et.al., 2023].

CONCLUSION

Plant-based protein materials offer a promising and sustainable platform for the controlled release of phytochemicals in bone cancer treatment. Polymers derived from natural sources, including zein, soy protein, and pea protein, possess biocompatibility, degrade at a rate that can be controlled, and the capability to encapsulate both hydrophilic and hydrophobic therapeutic agents.

Research has demonstrated that combining microencapsulation methods—such as spray drying, ionic gelation, and coacervation—with techniques that target bones, such as bisphosphonate modification or hydroxyapatite-binding peptides, holds considerable promise in increasing treatment precision while reducing the risk of systemic harm. The application of pH-sensitive and stimuli-responsive systems enables targeted release in the acidic bone tumor environment, thereby enhancing therapeutic effectiveness.

Despite recent progress, several problems persist. These encompass requirements for scalable production processes, extensive in vivo safety assessments, and regulatory approval routes. Recent breakthroughs, incorporating engineered plant proteins and adaptable delivery vehicles, are clearing the path for advanced, bone-targeted systems that administer phytochemicals.

In summary, the interdisciplinary approach combining materials science, natural product pharmacology, and bone tissue engineering offers promising avenues for future research and clinical applications. Plant-based protein carriers are expected to play a significant role in developing the next generation of targeted, efficient, and compatible treatments for bone cancer.

Alongside traditional plant-based protein carriers, incorporating natural fibers like silk fibroin, sisal, and coconut shell can provide extra functionality and structural support in the development of targeted delivery systems

focused on bone applications. Silk fibroin boasts superior biocompatibility and flexible degradation rates, which makes it an optimal candidate for prolonged phytochemical delivery. Sisal fibers, which are rich in cellulose and boast significant mechanical strength, can improve the stability of composite carriers. Coconut shell fibers possess inherent properties of natural antioxidants and hydrophobicity, potentially enhancing the encapsulation and controlled release of poorly soluble anticancer drug compounds. The use of these underutilized plant-based materials could enhance treatment effectiveness while enabling the creation of environmentally friendly, versatile systems for targeted bone cancer treatment.

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