IAA Journal of Biological Sciences 13(2):95-102, 2025
©IAAJOURNALS
https://doi.org/10.59298/IAAJB/2025/13295102
www.iaajournals.org
ISSN:2636-7254
IAAJB132

Biopolymer-Based Nanocarriers for Synergistic Delivery of Anti-Obesity and Anticancer Phytochemicals

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ABSTRACT

Obesity and cancer are two globally prevalent and interrelated diseases that share several pathophysiological mechanisms, including chronic inflammation, oxidative stress, and altered lipid metabolism. Phytochemicals derived from medicinal plants have shown promising therapeutic potential in both anti-obesity and anticancer interventions. However, their clinical applications are often limited by poor solubility, low bioavailability, and rapid degradation. Biopolymer-based nanocarriers have emerged as innovative platforms for enhancing the delivery, stability, and targeted action of these bioactive compounds. This article provides an overview of biopolymer-based nanocarriers and their advantages in delivering phytochemicals with dual action against obesity and cancer. We explore the synergistic potential of such phytochemicals, discuss commonly used biopolymers such as chitosan, alginate, and gelatin, and examine recent advances in nanoformulation strategies. The integration of biocompatible nanotechnology with plant-based therapeutics offers a promising approach for managing complex diseases and improving patient outcomes.

Keywords: Biopolymers; Nanocarriers; Phytochemicals; Obesity; Cancer

INTRODUCTION

Obesity and cancer are increasingly recognized as interlinked global health challenges, both characterized by complex etiologies involving genetic, environmental, and lifestyle-related factors[1–3]. Obesity, defined by excessive fat accumulation that impairs health, has reached epidemic proportions worldwide and significantly contributes to the burden of various non-communicable diseases, including type 2 diabetes, cardiovascular disorders, and notably, cancer[2–4]. Cancer, in turn, remains one of the leading causes of mortality globally[5, 6]. A growing body of epidemiological and experimental evidence suggests that obesity is a strong risk factor for the development and progression of several malignancies, particularly breast (especially postmenopausal), colorectal, pancreatic, liver, endometrial, and kidney cancers[7–9]. The biological link between these two conditions is underscored by shared pathophysiological mechanisms, such as chronic inflammation, insulin resistance, hormonal dysregulation, and oxidative stress. These mechanisms not only facilitate tumorigenesis but also worsen prognosis and complicate treatment responses, making it imperative to explore therapeutic strategies that can address both obesity and cancer concurrently[10–12].

In this context, phytochemicals like bioactive compounds derived from plants have emerged as promising candidates for the prevention and management of both obesity and cancer[13, 14]. Numerous in vitro and in vivo studies have documented the beneficial effects of phytochemicals such as curcumin, resveratrol, quercetin, and epigallocatechin gallate (EGCG), which exhibit potent antioxidant, anti-inflammatory, anti-proliferative, and metabolic regulatory properties[15–17]. These compounds modulate multiple cellular pathways, including those involved in cell cycle regulation, apoptosis, lipid metabolism, and angiogenesis, thereby demonstrating a capacity to intervene in the pathogenesis of both obesity and cancer[13]. Despite their therapeutic promise, however, the clinical translation of phytochemicals has been significantly hindered by several pharmacokinetic challenges. Many phytochemicals suffer from poor water solubility, limited gastrointestinal absorption, rapid metabolic degradation, and low bioavailability, which limit their therapeutic concentrations at target tissues and compromise their clinical efficacy.

To overcome these limitations, innovative drug delivery systems have been explored, with biopolymer-based nanocarriers gaining increasing attention[18, 19]. These nanocarriers, made from natural or synthetic biodegradable polymers such as chitosan, alginate, gelatin, and polylactic acid, offer multiple advantages for the delivery of phytochemicals. By encapsulating phytochemicals within these nanostructures, it is possible to

enhance their solubility, protect them from enzymatic degradation, and control their release over time[20, 21]. Moreover, biopolymer-based nanocarriers can be engineered for targeted delivery, enabling the accumulation of therapeutic agents at specific disease sites, such as inflamed adipose tissue or tumor microenvironments[18]. This dual-targeted approach not only maximizes therapeutic efficacy but also minimizes systemic side effects. Thus, the integration of phytochemicals with nanotechnology represents a novel and potentially transformative strategy for the simultaneous management of obesity and cancer. This article reviews current knowledge on the pathophysiological link between these two diseases and explores the therapeutic potential of biopolymer-based nanocarriers for delivering phytochemicals with dual anti-obesity and anticancer properties.

Pathophysiological Links Between Obesity and Cancer

The connection between obesity and cancer is rooted in a complex network of biological processes, many of which are initiated or exacerbated by the excessive accumulation of adipose tissue[22, 23]. One of the most prominent features of obesity is chronic low-grade inflammation [24]. As adipose tissue expands, it becomes infiltrated by immune cells, particularly macrophages, which shift toward a pro-inflammatory phenotype. This triggers the release of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and monocyte chemoattractant protein-1 (MCP-1), which together create a microenvironment conducive to cancer development[25]. This inflammatory milieu can promote genomic instability, inhibit apoptosis, and stimulate angiogenesis—key hallmarks of cancer. Furthermore, the persistent inflammatory state alters the immune surveillance mechanisms that normally suppress tumor formation, enabling malignant cells to proliferate and evade immune destruction[25].

Another key contributor to obesity-associated carcinogenesis is oxidative stress, characterized by an imbalance between the production of reactive oxygen species (ROS) and the body's antioxidant defenses[26]. In obesity, increased mitochondrial activity, enhanced fatty acid oxidation, and inflammatory signaling pathways collectively elevate ROS levels. These reactive molecules cause DNA damage, promote mutations, and activate oncogenic signaling cascades, such as the PI3K/Akt and MAPK pathways[11, 26, 27]. Over time, this oxidative burden accelerates the transformation of normal cells into malignant ones. Moreover, insulin resistance and hyperinsulinemia, common in obese individuals, further contribute to cancer risk. Elevated insulin and insulin-like growth factor-1 (IGF-1) levels stimulate cell proliferation and inhibit programmed cell death, favoring tumor growth[28]. These hormones also interact with inflammatory and oxidative stress pathways, compounding their carcinogenic potential.

Dysregulated lipid metabolism is yet another vital link between obesity and cancer. In obesity, excess free fatty acids and altered lipid profiles promote lipotoxicity and disrupt cellular homeostasis[28]. These changes activate nuclear receptors such as peroxisome proliferator-activated receptors (PPARs) and sterol regulatory element-binding proteins (SREBPs), which modulate genes involved in lipid synthesis, storage, and oxidation. Such metabolic reprogramming not only supports energy demands of rapidly dividing tumor cells but also enhances their invasive and metastatic potential[11, 12]. Furthermore, adipokines—hormones secreted by adipose tissue such as leptin and adiponectin—are markedly dysregulated in obesity. Leptin, which is elevated in obesity, has pro-inflammatory and pro-tumorigenic effects, whereas adiponectin, which exerts anti-inflammatory and anti-proliferative actions, is typically reduced[28]. This hormonal imbalance adds another layer of complexity to the obesity-cancer axis. Together, these interrelated mechanisms underscore the importance of developing integrated therapeutic strategies that can concurrently address both metabolic dysregulation and tumor progression, highlighting the promise of phytochemical-based nanotherapies in this dual context[29].

Phytochemicals with Dual Anti-Obesity and Anticancer Activities

Several phytochemicals have demonstrated potential in modulating both obesity and cancer pathways:

Phytochemical	Source	Mechanisms	Therapeutic Actions	References
Curcumin	*Curcuma longa*	NF-κB inhibition, AMPK activation	Anti-inflammatory, pro-apoptotic	[30–32]
Resveratrol	Grapes, berries	SIRT1 activation, ROS scavenging	Antioxidant, anti-proliferative	[33–35]
EGCG	Green tea	Lipogenesis inhibition, angiogenesis suppression	Anti-obesity, anti-metastatic	[17]
Quercetin	Apples, onions	Lipid metabolism modulation, apoptosis induction	Anti-adipogenic, cytotoxic	[36–38]
Berberine	*Berberis vulgaris*	AMPK activation, glucose uptake	Anti-obesity, anti-cancer	[39–41]

Biopolymer-Based Nanocarriers: Composition and Benefits

Biopolymers in Nanocarrier Systems

Biopolymers are naturally derived macromolecules known for their biocompatibility, biodegradability, and low toxicity, making them highly attractive in drug delivery systems, particularly for the encapsulation of bioactive compounds such as phytochemicals[42]. Their origin from renewable sources ensures environmental friendliness, while their intrinsic properties support safe interaction with biological tissues. In nanocarrier systems, biopolymers can be tailored for desired properties such as controlled release, target specificity, and increased solubility of poorly water-soluble compounds[43]. These characteristics make biopolymer-based nanocarriers ideal platforms for delivering therapeutic agents in both anti-obesity and anticancer interventions.
Among the commonly used biopolymers, chitosan stands out due to its mucoadhesive nature, positive charge, and pH-responsive behavior[44]. These properties facilitate adhesion to mucosal surfaces and improve drug permeation through epithelial barriers. Chitosan enhances the intestinal absorption of encapsulated agents and is particularly effective for oral drug delivery[44, 45]. Alginate, another polysaccharide derived from brown algae, possesses strong gel-forming capabilities in the presence of divalent cations like calcium. It is extensively used for encapsulating hydrophilic drugs and bioactives, forming hydrogels that provide sustained release and protection from gastric degradation[46]. Gelatin, a protein derived from collagen, is thermo-sensitive and well-suited for preparing temperature-responsive nanocarriers. It offers excellent biocompatibility and is often utilized in the sustained release of therapeutic agents[47].
Starch and dextran are plant-derived polysaccharides with a long history of safe use. They are not only abundant and cost-effective but also highly modifiable, making them versatile materials for targeted drug delivery[48]. Their chemical structure allows for easy conjugation with ligands or other functional groups to enhance specificity and efficacy. The modification of these polymers can lead to the development of nanocarriers that are sensitive to physiological stimuli such as pH or enzymes, thereby enabling targeted and controlled drug release[48]. Overall, biopolymers provide a sustainable and functional platform for the delivery of therapeutic phytochemicals, with the potential to revolutionize treatment strategies for complex conditions like obesity and cancer.

Benefits of Biopolymer-Based Nanocarriers

Biopolymer-based nanocarriers provide numerous advantages over conventional drug delivery systems, particularly in enhancing the bioavailability and therapeutic efficacy of poorly soluble phytochemicals[49]. One of the most significant benefits is the improved solubility and stability of these bioactive compounds[49]. Many natural phytochemicals, including curcumin, resveratrol, and quercetin, suffer from low aqueous solubility and rapid metabolic degradation. Encapsulating them in biopolymer nanocarriers protects them from harsh gastrointestinal conditions and enzymatic breakdown, thereby enhancing their systemic availability and prolonging their therapeutic action[49].
Another major advantage is the controlled and targeted release of the encapsulated compounds at the site of action. By modifying the surface properties or integrating targeting ligands, such as folic acid or transferrin, nanocarriers can selectively accumulate in specific tissues—such as tumor microenvironments or adipose tissue—thus reducing off-target effects.[50] This targeted delivery minimizes systemic toxicity and maximizes therapeutic outcomes. Controlled release also ensures that the drug is released in a sustained manner, maintaining therapeutic levels over a longer period and reducing the frequency of dosing.
Moreover, biopolymer-based nanocarriers have demonstrated the ability to enhance pharmacokinetic profiles, including absorption, distribution, metabolism, and excretion. This leads to improved tissue penetration and reduced clearance, resulting in higher drug accumulation in desired tissues[51]. Their compatibility with multiple routes of administration—including oral, transdermal, and injectable—further broadens their clinical applicability. Importantly, these systems reduce the likelihood of adverse side effects by limiting systemic exposure and allowing lower effective doses[51]. Collectively, these benefits underscore the transformative potential of biopolymer-based nanocarriers in precision medicine, especially in managing multifaceted diseases such as obesity and cancer.

Nanoformulation Strategies

Nanoformulation techniques are crucial for the successful incorporation of phytochemicals into biopolymer-based delivery systems[52]. One of the most widely used methods is nanoprecipitation, which involves the precipitation of the polymer and drug from an organic phase into an aqueous phase under controlled conditions[52]. This method is particularly suitable for hydrophobic phytochemicals such as curcumin and resveratrol. It allows the formation of uniform nanoparticles with high encapsulation efficiency and small particle size, which improves solubility and cellular uptake. Nanoprecipitation is simple, scalable, and does not require high-energy input, making it attractive for industrial applications.
Another important technique is ionic gelation, which exploits the electrostatic interaction between oppositely charged polymers. For instance, chitosan (positively charged) and alginate (negatively charged) can form stable nanoparticles through ionic cross-linking in the presence of counter-ions such as calcium[53]. This method is particularly advantageous for the encapsulation of hydrophilic compounds and biomolecules. It is performed under mild conditions without the use of organic solvents, thus preserving the activity of sensitive

phytochemicals. Additionally, the resulting nanoparticles exhibit good mucoadhesive and controlled-release properties, making them ideal for oral delivery[53].
Other techniques include emulsion solvent evaporation, where an oil-in-water or water-in-oil emulsion is formed, and the organic solvent is gradually evaporated to form nanoparticles. This method ensures uniform particle formation and is useful for both hydrophobic and hydrophilic drugs[54]. Spray drying, a technique widely employed in the food and pharmaceutical industries, offers scalability and cost-effectiveness[55]. It involves atomizing a solution or suspension into a hot drying chamber, leading to the rapid formation of dry particles. Each of these methods allows for further surface functionalization of nanocarriers with ligands like folic acid, peptides, or antibodies to enhance targeting to specific cells or tissues, such as cancer cells, while retaining anti-obesity activity[55]. This strategic approach to nanoformulation facilitates the development of multifunctional therapeutic platforms.

Synergistic Effects and Preclinical Evidence

Recent preclinical studies have shown that co-delivering anti-obesity and anticancer phytochemicals using biopolymer-based nanocarriers produces synergistic effects far superior to administering each compound alone[56]. These co-loaded systems allow for the simultaneous targeting of molecular pathways involved in both adipogenesis and tumorigenesis. For example, nanoparticles made from chitosan loaded with curcumin and epigallocatechin gallate (EGCG) have been shown to reduce fat cell formation while inducing apoptosis in breast cancer cells[15, 16]. This dual functionality is attributed to the ability of the phytochemicals to modulate signaling pathways such as AMPK, PPARγ, and NF-κB that are common to both obesity and cancer pathophysiology.
Similarly, resveratrol-loaded gelatin nanocarriers have demonstrated promising results in both adipocyte and colon cancer models[57]. In vitro and in vivo experiments reveal that these nanocarriers inhibit lipid accumulation, reduce inflammatory markers, and suppress tumor growth. Gelatin, being biodegradable and thermo-sensitive, allows for sustained release, thus maintaining consistent therapeutic levels over time. These effects underscore the advantage of using responsive biopolymer carriers for long-term management of obesity-associated cancers, particularly in tissues where inflammation and metabolic dysfunction intersect with tumor progression.[57]
Furthermore, quercetin encapsulated in alginate-based nanogels has been shown to significantly enhance the oral bioavailability of the flavonoid, enabling more effective targeting of both adipose and cancer cells. In animal studies, this formulation resulted in reduced body weight gain, decreased fat accumulation, and inhibition of tumor proliferation[58]. The synergistic effects observed stem from the coordinated action of phytochemicals on oxidative stress, inflammation, cell proliferation, and lipid metabolism—all critical in both disease contexts[58]. These findings suggest that multifunctional biopolymer-based nanocarriers offer a promising therapeutic strategy by combining the anti-obesity and anticancer properties of natural compounds into a single, targeted delivery system.
Certainly! Here's an expanded version of your section into approximately 700 words across three coherent and informative paragraphs:

Challenges and Future Perspectives

Despite the remarkable advancements and promising potential of biopolymer-based nanocarriers in drug delivery systems, several significant challenges hinder their widespread clinical application and commercialization. One of the primary obstacles is the scalability and reproducibility of manufacturing processes. Laboratory-scale synthesis of biopolymeric nanoparticles is often well-controlled and yields consistent results. However, translating these procedures to an industrial scale without compromising the physicochemical properties, bioactivity, or stability of the nanocarriers remains a daunting task. Achieving uniform particle size, surface characteristics, and drug loading efficiency on a large scale demands highly optimized and cost-effective techniques, which are still under development. Furthermore, stability during storage and in biological environments poses another major concern. Nanocarriers must maintain their structural integrity and functional capabilities under varying environmental conditions, including temperature, pH, and exposure to enzymes or serum proteins. The potential for premature drug release, aggregation, or degradation over time could drastically reduce therapeutic efficacy and safety, thereby limiting shelf-life and clinical usability.
Another critical challenge lies in the regulatory and safety evaluation landscape for these novel nanoformulations. The complexity of biopolymer-based nanoparticles, including their dynamic interactions with biological systems, complicates standardization for regulatory approval. Most national and international regulatory bodies, such as the FDA or EMA, require comprehensive preclinical and clinical data demonstrating the safety, efficacy, and biocompatibility of nanocarrier systems. However, standardized guidelines for nanoparticle evaluation are still evolving, leading to ambiguity and delays in clinical translation. Additionally, toxicological concerns must be rigorously addressed through in vitro and in vivo studies to evaluate potential long-term toxicity, immunogenicity, and bioaccumulation. Given that biopolymers often degrade into natural

or biologically compatible products, they are generally considered safer than synthetic polymers. Nonetheless, each formulation's specific composition, size, surface charge, and degradation profile could elicit varied biological responses, necessitating case-by-case evaluation. The lack of universally accepted toxicological benchmarks further complicates safety assessment, creating a bottleneck in the regulatory pipeline.

Looking ahead, future research directions must aim to overcome these limitations through innovative, interdisciplinary approaches. One exciting avenue is the development of personalized nanomedicine strategies, whereby nanocarriers are tailored to individual patient profiles based on genomic, proteomic, or metabolomic biomarkers. This approach promises higher therapeutic precision and minimized adverse effects. Moreover, the integration of artificial intelligence (AI) and machine learning (ML) algorithms into the design and optimization of nanocarriers represents a transformative shift. These tools can rapidly analyze large datasets to predict nanoparticle behavior, optimize formulations, and streamline preclinical testing. Another burgeoning field is the creation of multifunctional nanocarriers capable of simultaneous drug delivery, imaging, and therapeutic monitoring—a concept known as *theranostics*. These platforms can potentially provide real-time feedback on drug distribution, efficacy, and disease progression, leading to adaptive and dynamic treatment strategies. In conclusion, while biopolymer-based nanocarriers are poised to revolutionize targeted drug delivery and personalized medicine, addressing current limitations through collaborative research and technological integration is essential for their successful clinical realization.

CONCLUSION

Biopolymer-based nanocarriers represent a cutting-edge solution for enhancing the delivery and efficacy of phytochemicals with dual anti-obesity and anticancer potential. By overcoming pharmacokinetic barriers and enabling targeted, synergistic action, these systems offer a promising strategy for managing complex, comorbid conditions. Continued interdisciplinary efforts in material science, pharmacology, and nanomedicine will be pivotal in translating these innovations from bench to bedside.

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CITE AS: Masika Anna Mahinda (2025). Biopolymer-Based Nanocarriers for Synergistic Delivery of Anti-Obesity and Anticancer Phytochemicals. IAA Journal of Biological Sciences 13(2):95-102. https://doi.org/10.59298/IAAJB/2025/13295102