STM JOURNALS

Emerging Trends in
Personalized Medicines

ISSN: 3049-1347
Volume 2, Issue 1, 2025
January–June
DOI: 10.37591/ETPM

https://journals.stmjournals.com/etpm

Review ETPM

Flaxseed-Based Drug Delivery Systems: Advancing Colon Cancer Treatment

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Abstract

Flaxseed (Linum usitatissimum) has long been appreciated for its rich nutritional profile, including essential fatty acids (such as α-linolenic acid), plant fibers, and lignans. Recent research has focused on its potential as a novel drug delivery system (DDS) for the treatment of colon cancer. This review explores the bioactive constituents of flaxseed, their pharmacological activities, and innovative approaches to the use of flaxseed extracts in drug delivery for the treatment of colon cancer. We highlight the promising pharmacokinetics, target delivery mechanisms, and therapeutic efficacy of flaxseed drug carriers, as well as challenges and future directions in the field. One of the main causes of cancer-related fatalities, colon cancer is a serious worldwide health concern. Effective drug delivery systems (DDS) are essential to target the disease while minimizing systemic toxicity. Flax, a natural product rich in lignans, omega-3 fatty acids, and fiber, has shown promise in cancer treatment due to its anti-inflammatory, antioxidant, and anticarcinogenic properties. This paper investigates the potential of flax extract as a novel drug delivery system (NDDS) for the targeted delivery of chemotherapeutic agents to colon cancer cells. We explore the bioactive compounds of flaxseed, their interactions with drug molecules, and the use of flax-based DDS to improve the bioavailability and therapeutic efficacy of anticancer drugs.

Keywords: Flaxseed, colon cancer, targeted therapy, *Linum usitatissimum*, Pharmacokinetics of flax-based DDS

INTRODUCTION

Colon cancer is among the top causes of cancer-related deaths worldwide. Current therapies, including chemotherapy and targeted therapies, may be limited by toxicity and systemic resistance. Alternative delivery methods and natural substances that can increase treatment efficacy while reducing negative effects are gaining popularity. Flax is an ancient medicinal plant known for its rich nutritional profile and its potential anti-cancer properties. Recent advances in drug delivery systems have emerged as promising solutions to improve efficiency and reduce the adverse effects of cancer treatments. Among many natural products, flax seed (*Linum usitatissimum*) has attracted attention for its rich composition of bioactive compounds, including lignans, omega-3 fatty acids and dietary fiber. These compounds are linked to several health benefits, including the prevention and treatment of cancer. This study aims to explore the application of flax extract as a drug delivery system for the treatment of colon cancer, examining its mechanisms of action, formulation strategies and potential for improvement the results. Through a comprehensive review of the current literature, this study highlights the promise of flax extract to overcome the challenges associated with traditional

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Received Date: December 14, 2024
Accepted Date: January 03, 2025
Published Date: February 01, 2025

Citation: Mohd. Wasiullah, Piyush Yadav, Mohit Vishwakarma, Nidhi Dubey. Flaxseed-Based Drug Delivery Systems: Advancing Colon Cancer Treatment. Emerging Trends in Personalized Medicines. 2025; 2(1): 54–59p.

anticancer therapies and paves the way for future research in this area. One of the most common cancers in the world, colon cancer, presents serious public health concerns. The rising rates of incidence and mortality associated with this disease emphasize the urgent need for more effective treatment approaches. Traditional therapies, such as surgery, chemotherapy, and radiotherapy, are often limited by factors, such as systemic toxicity, drug resistance, and suboptimal availability of therapeutic agents. Flax extract has shown potential as a new drug delivery system, due to its ability to encapsulate therapeutic agents, improve their stability and facilitate direct delivery to cancer tissues. Bioactive compounds in flax seeds not only exhibit anticancer properties but can also synergistically improve the effectiveness of conventional chemotherapy.

A significant worldwide health concern, colon cancer, contributes to elevated rates of morbidity and mortality. Conventional treatments, such as chemotherapy and radiation therapy, often fail to specifically target cancer cells, leading to unwanted side effects and reduced efficacy. Recent advances in nanotechnology and drug delivery systems (DDS) have enabled more targeted therapies, improving the specificity and bioavailability of anticancer drugs. Flax (*Linum usitatissimum*), traditionally used for its nutritional and medicinal properties, has attracted attention for its range of bioactive compounds, which possess anticancer, antioxidant, anti-inflammatory and anti-angiogenic properties. Cancer is the second leading cause of death worldwide, with most cancer-related deaths (around 90%) resulting from metastases [1]. Reducing metastases is crucial for improving patient survival rates. Recently, it has been suggested that cancer stem cells or cancer-initiating cells play a key role in generating highly metastatic cells [2–4]. Identifying and targeting specific cell populations responsible for metastasis is critical, regardless of the underlying mechanisms, as it will facilitate the development of more effective treatments. Metastases often occur in areas that are challenging to treat surgically, such as the bones and brain, making chemotherapy the primary treatment option. However, because it affects all rapidly dividing cells, conventional chemotherapy has serious adverse effects (Figure 1).

Figure 1. Flaxseed plant.

FLAXSEED EXTRACTS COMPONENTS AND HEALTH BENEFITS

Lignans

Flax seeds contain lignans, which are a class of polyphenolic chemicals. These compounds have demonstrated anti-cancer properties, particularly in colon cancer, through mechanisms, such as inhibiting cell proliferation, promoting apoptosis, and modulating estrogen receptors. The gut microbiota makes enterolignans from SDG, the most prevalent lignan in flaxseed. Through the

reduction of inflammation and oxidative stress, these enterolignans offer protective actions in the colon [5].

Omega-3 Fatty Acids

Alpha-linolenic acid (ALA), an omega-3 fatty acid, is abundant in flax seeds, one of the most abundant plant sources of ALA. ALA has been shown to suppress the growth and spread of colon cancer cells by influencing inflammation pathways, reducing cell proliferation, and promoting apoptosis. Omega-3 fatty acids also contribute to altering the tumor microenvironment by inhibiting angiogenesis.

Fiber

By encouraging improved digestion and regular bowel movements, flax seeds' high content of soluble and insoluble fiber may help reduce the risk of colon cancer. Additionally, fiber interacts with the gut microbiota to promote the growth of good bacteria and inhibit the growth of bad ones. Soluble fiber is fermented by intestinal bacteria to produce short-chain fatty acids (SCFAs), which possess anti-inflammatory and anticancer properties.

Proteins and Peptides

Flax proteins, which make up about 20–30% of the seed's total mass, exhibit anti-cancer effects. Peptides made from flax seeds may prevent colon cancer cells from proliferating by triggering apoptosis and cell cycle arrest, according to some research. Nevertheless, more research is required to completely examine their methods and possibilities.

MECHANISMS OF ACTION

1. *Antioxidant Activity:* Flax lignans have potent antioxidant properties that help neutralize free radicals, reduce oxidative stress, and protect cells from DNA damage. This is crucial in preventing cancer development and slowing tumor progression.
2. *Inhibition of Tumor Cell Proliferation:* Flaxseed components, particularly SDG, have been found to inhibit the proliferation of colon cancer cells by regulating key signaling pathways, such as PI3K/Akt and MAPK. When these pathways are inhibited, tumor growth is decreased because they are important in cell survival, proliferation, and differentiation.
3. *Induction of Apoptosis:* Both lignans and omega-3 fatty acids can trigger apoptosis (programmed cell death) in cancer cells. By lowering the expression of anti-apoptotic proteins like Bcl-2 and raising that of pro-apoptotic proteins like Bax and caspase-3, flax extract affects apoptotic signaling pathways.
4. *Anti-inflammatory Effects:* One known contributing factor to the development of colon cancer is chronic inflammation. Flaxseed components, particularly lignans and omega-3 fatty acids, exert anti-inflammatory effects that help mitigate this risk. Flax extract has anti-inflammatory properties through modulation of cytokine production (e.g., reduction of IL-6 and TNF-α levels) and inhibition of inflammatory enzymes, such as cyclooxygenase (COX). These actions can help reduce the inflammatory microenvironment that promotes tumor growth [6].
5. *Colon-Specific Drug Release:* The soluble fiber and mucilage present in flax seeds can be used to enhance the release of colon-specific therapeutic agents. By forming a gel-like structure in the gastrointestinal tract, flax mucilage can protect drugs from premature degradation, ensuring their effective delivery and absorption [7].
6. *Synergistic effects with chemotherapy:* Flax extract has shown potential as an adjunctive therapy to improve the effectiveness of conventional chemotherapy. Its bioactive components can sensitize cancer cells to chemotherapeutic agents by modifying drug metabolism, improving their absorption and reducing their resistance. mature breakdown in the stomach and facilitate their direct release into the colon [8].
7. *Targeted Delivery:* Functionalization of Lino transporters with targeting ligands (such as antibodies or peptides) can facilitate the preferential accumulation of drugs in tumor sites, thus improving the therapeutic index of anticancer drugs [9].
8. *Controlled release:* The polysaccharides in flaxseed can form microcapsules or nanocapsules,

which allow a controlled and sustained release of the encapsulated drug over time, thus improving therapeutic efficacy and reducing side effects [10].

METHODS OF FORMULATION

A System Based on Nanoparticle Encapsulation

1. *Liposomes:* These spherical, lipid-based bilayer structures can contain both hydrophilic and hydrophobic medications. Flaxseed oil, rich in omega-3 fatty acids, can be incorporated into liposomal formulations for colon-specific drug delivery. Liposomes enable controlled release in the colon and shield the medication from deterioration in the digestive system [11].
2. *Polymer Nanoparticle:* Polymer nanoparticles made from biocompatible polymers, such as PLGA (polylactic-co-glycolic acid) can be used to encapsulate flax-derived compounds, such as lignans and ALA. These nanoparticles can improve the solubility and stability of drugs by providing controlled and targeted release to the tumor site in the colon. Polymers can be modified to respond to the acidic environment or enzymes present in the colon for site-specific drug release.
3. *Solid lipid nanoparticles (SLNs):* SLNs are nanoparticles made of solid lipids, which can improve the solubility of poorly soluble drugs. Linseed oil can be used as a lipid matrix in SLN form approach provides sustained drug release, protects drugs from environmental degradation, and facilitates targeted drug delivery in the colon [12].

HYDROGELS BASED ON SYSTEM

1. *Flax hydrogels:* Flax mucilage is a natural polymer that can form hydrogels. These hydrogels can encapsulate both hydrophilic and hydrophobic drugs, providing controlled release properties and improved stability. The gelatinous structure of flax mucilage also allows for localized drug release in the colon, thereby minimizing the risk of systemic toxicity.
2. *Polymeric hydrogels based on flax extract:* Flax extract can be combined with synthetic or natural polymers (for example, chitosan, alginate, or polyvinyl alcohol) to create hydrogel compounds. These formulations can improve the mechanical properties and drug release profiles of the system, while the bioactive compounds in the flax seeds contribute to the anticancer effects [13].

MICROSPHERES AND MICROPARTICLES

Flaxseed Oil-Loaded Microspheres

Flaxseed oil, rich in omega-3 fatty acids, can be used to prepare microspheres for drug delivery. These microspheres can encapsulate hydrophobic chemotherapeutic agents, such as paclitaxel, thus improving their solubility and bioavailability. Microspheres provide regulated drug release and can be designed to administer the medication for a long time. Alginate/Flaxseed Microspheres: Alginate, a natural polysaccharide, can be combined with flax extract to prepare microspheres for colon-specific drug delivery. Alginate is known for its ability to form gel-like structures in the gastrointestinal tract, which can improve the stability and controlled release of encapsulated drugs in the colon. The incorporation of flax extract into these microspheres may provide synergistic effects in terms of anticancer activity and targeted drug delivery [14].

EMULSION BASED SYSTEM

Linseed Oil Nanoemulsions

Nanoemulsions are fine dispersions of oil in water that can improve the solubility of lipophilic drugs. Linseed oil can be used as an oil phase in nanoemulsions, thus improving the delivery of hydrophobic compounds to colon cancer cells. These systems offer improved bioavailability and stability, as well as potential for targeted drug delivery [15].

ORAL DRUG DELIVERY SYSTEM

Oral delivery of drugs for the treatment of colon cancer involves overcoming several challenges, including gastric degradation, low bioavailability and poor colon drug targeting. To overcome these difficulties, several formulations have been created. Flax extract, with its intrinsic properties, can be used in some promising oral drug delivery systems for the treatment of colon cancer [16].

FLAXSEED-BASED NANOPARTICLES (NPS)

Polymeric Nanoparticles

Polymeric nanoparticles made from biodegradable polymers, such as PLGA (polylactic-co-glycolic acid) or chitosan can be used to encapsulate bioactive compounds from flaxseed, such as lignans and omega-3 fatty acids. These nanoparticles improve the solubility, stability, and bioavailability of hydrophobic drugs and can be designed to deliver drugs to the colon by exploiting the pH or enzyme-responsive characteristics of polymers [17].

- *Flaxseed oil nanoparticles:* Flaxseed oil-loaded nanoparticles, rich in omega-3 fatty acids, can improve the bioavailability of poorly soluble chemotherapeutic agents, such as paclitaxel. Nanoparticles loaded with linseed oil have the advantage of improving the therapeutic index by ensuring drug release especially in the colon, where omega-3 fatty acids exert anticancer effects [18].
- *Liposomes:* Flax extract liposomal formulations can protect the encapsulated drug from gastrointestinal degradation and improve the solubility and absorption of poorly water-soluble drugs (Figure 2). Liposomes are biocompatible and can be modified to deliver their payload specifically to the tumor site in the colon [19–25].

Figure 2. Flaxseed.

CONCLUSIONS

Flax extract holds great promise as a new drug delivery system for the treatment of colon cancer due to its rich bioactive profile, including lignans, omega-3 fatty acids and fiber. When used as part of advanced drug delivery platforms, such as nanoparticles, liposomes, and hydrogels, flax extracts can provide targeted, controlled, and sustained drug release, thus improving efficacy against colon cancer. However, challenges related to bioavailability, stability and regulatory approval need to be addressed before flax-based DDSs can be translated into clinical use. Future research should focus on optimizing flax formulations, conducting preclinical studies, and exploring combination therapies to maximize their therapeutic potential for the treatment of colon cancer.

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