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Review Article

Advances in Pectin-Based Drug Delivery Systems: Applications and Future Perspectives

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Abstract

Pectin is an acidic structural heteropolysaccharide primarily composed of galacturonic acid units. It is mainly extracted from citrus fruits, apples, pears, guavas, and other plant sources using acidic hot-water extraction methods within a pH range of 1.5–3.5. Due to its biocompatibility, biodegradability, and non-toxic nature, pectin has gained significant attention as a promising natural polymer in the pharmaceutical, nutraceutical, and biomedical fields. Pharmacologically, pectin exhibits various therapeutic properties, including hypoglycaemic, hypocholesterolemic, antibacterial, antioxidant, and antitumor activities. It helps regulate blood glucose, reduce cholesterol levels, inhibit microbial growth, and suppress tumour progression. Nutraceutically, pectin functions as both a prebiotic and a probiotic agent, serving as a bioactive dietary fibre that promotes cardiovascular and metabolic health. In biomedical applications, pectin-based formulations have demonstrated great potential for controlled and targeted drug delivery. A wide range of pectin-based systems—such as hydrogels, films, microparticles, nanoparticles, beads, pellets, and tablets—have been developed for oral, buccal, nasal, and ocular delivery. Future research will likely focus on chemical modification, crosslinking, and nano-structuring approaches to enhance pectin's mechanical strength, stability, and site-specific release properties. Moreover, combining pectin with other biopolymers, such as chitosan, alginate, or gelatin, may yield hybrid or composite systems with improved bioadhesion and controlled-release properties. This study highlights the drug delivery applications of pectin and discusses its future research prospects.

Keywords: Pectin, drug delivery, pharmaceutical applications.

1. Introduction:

Pectin is an acidic heteropolysaccharide made up mostly of galacturonic acid, which itself is a sugar acid derived from galactose. It was first isolated and described by Henri Braconnot in 1825. Commercially, pectin is often obtained from citrus peels and similar plant sources, and is widely used in the food industry as a gelling or thickening agent—for example, in jams, jellies, and dessert fillings¹.

2. Sources:

Fruits such as pears, apples, guavas, quinces, plums, gooseberries, and citrus fruits like oranges contain relatively high levels of pectin, whereas softer fruits — for example, cherries, grapes, and strawberries — have much lower pectin content. Commercially, most of the world's pectin is extracted from citrus peels (about 85 %), followed by apple pomace (around 14 %), and a small fraction is derived from sugar-beet pulp (less than 1 %) ^{2,3}

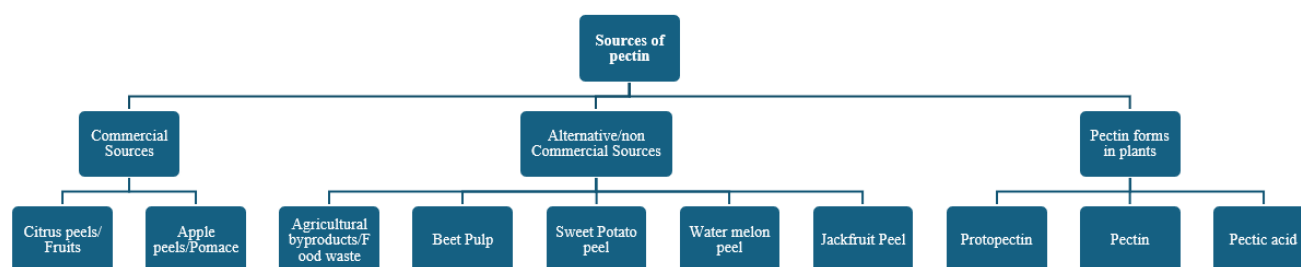


Figure 1: Sources of Pectin⁴

3. Extraction:

Pectin is extracted from plant-derived feedstocks via hot dilute-acid hydrolysis (pH ~1.5–3.5), which solubilises protopectin by cleaving side-chains and reducing chain length over several hours of extraction⁵. After filtration, the resulting extract is concentrated under vacuum, and the pectin is precipitated with ethanol or isopropanol. Use of aluminium-salt precipitation is now obsolete. The precipitated pectin is isolated, washed, and dried. Exposure of the crude pectin to dilute acid produces low-esterified pectins, whereas treatment involving ammonium hydroxide (NH₃(aq)) yields amidated pectins. Finally, the dried and milled pectin is standardised with sugar—and often with calcium salts or organic acids to optimise its functionality for specific applications.⁶

4. Types of Pectin³

Pectin is categorized based on the number of methoxy groups either low methoxyl (LM) or high methoxyl (HM) that substitute the carboxylic acid (COOH) groups on the galacturonic acid residues. The degree of esterification (DE) significantly influences the gelation behavior, processing characteristics, and functional properties of pectin.

i High Methoxyl Pectin (HMP):

In high methoxyl pectin, the DE is greater than 42.9%. This form of pectin is primarily utilized for conventional gel formation and stabilization processes, requiring high sugar concentrations and acidic conditions. HMP forms gels through hydrogen bonding and hydrophobic interactions between pectin chains, typically at low pH and high soluble solid content. It is widely applied in the preparation of jams, jellies, and other confectionery products that depend on high-sugar environments for proper texture and firmness.

ii Low Methoxyl Pectin (LMP):

Low methoxyl pectin has a DE below 42.9%. Unlike HMP, it does not require a large amount of sugar for gelation, making it suitable for low-sugar or dietetic food products. LMP is less sensitive to acidic conditions and can form gels in the presence of divalent cations such as calcium ions (Ca²⁺), which crosslink the pectin chains. LMP is typically produced through the de-esterification of HMP using chemical (acids, alkalis, ammonia) or enzymatic agents such as pectin methyl esterase (PME).

HMP vs. LMP

Feature	High Methoxyl Pectin (HMP)	Low Methoxyl Pectin (LMP)
Degree of Methoxylation	50%	50%
Gelling Mechanism	High sugar, low pH	Calcium ions
Sugar Requirement	High	Low or none
pH Sensitivity	High	Low
Typical Applications	Jams, jellies, confectionery	Low-sugar products, dairy, fillings
Gel Texture	Clear, firm	Can be brittle

Figure 2: Functional Properties of High-Methoxyl vs Low-Methoxyl Pectin¹

5. Structure of Pectin:

Homogalacturonans are chains of D-galacturonic acid linked by α -(1→4) bonds. In addition to D-galacturonic acid, pectins often contain neutral sugars such as D-galactose, L-arabinose and D-xylose; the types and amounts of these vary with the source of the pectin. Another structural form of pectin, although less common,

is rhamnogalacturonan II (RG-II) — a highly branched, complex polysaccharide. The molecular weight of pectins isolated from various sources typically ranges from about 60 000 to 130 000 g/mol, although this depends on both the plant source and the extraction method used.⁴

6. Functional and Physical Properties

A. Rheological Properties

Rheological studies help to understand the flow behaviour of pectin solutions.

- **Flow Behaviour**
- **Viscosity**
- **Viscoelasticity**

B. Thermal Properties

Thermal properties of pectin are commonly analysed using Differential Scanning Calorimetry (DSC) to assess its thermal stability.

- **Thermal Degradation:** Pectin generally shows exothermic degradation peaks between 230 °C and 255 °C, indicating its decomposition temperature range.



Figure 3: Physicochemical Characterisation of Pectin

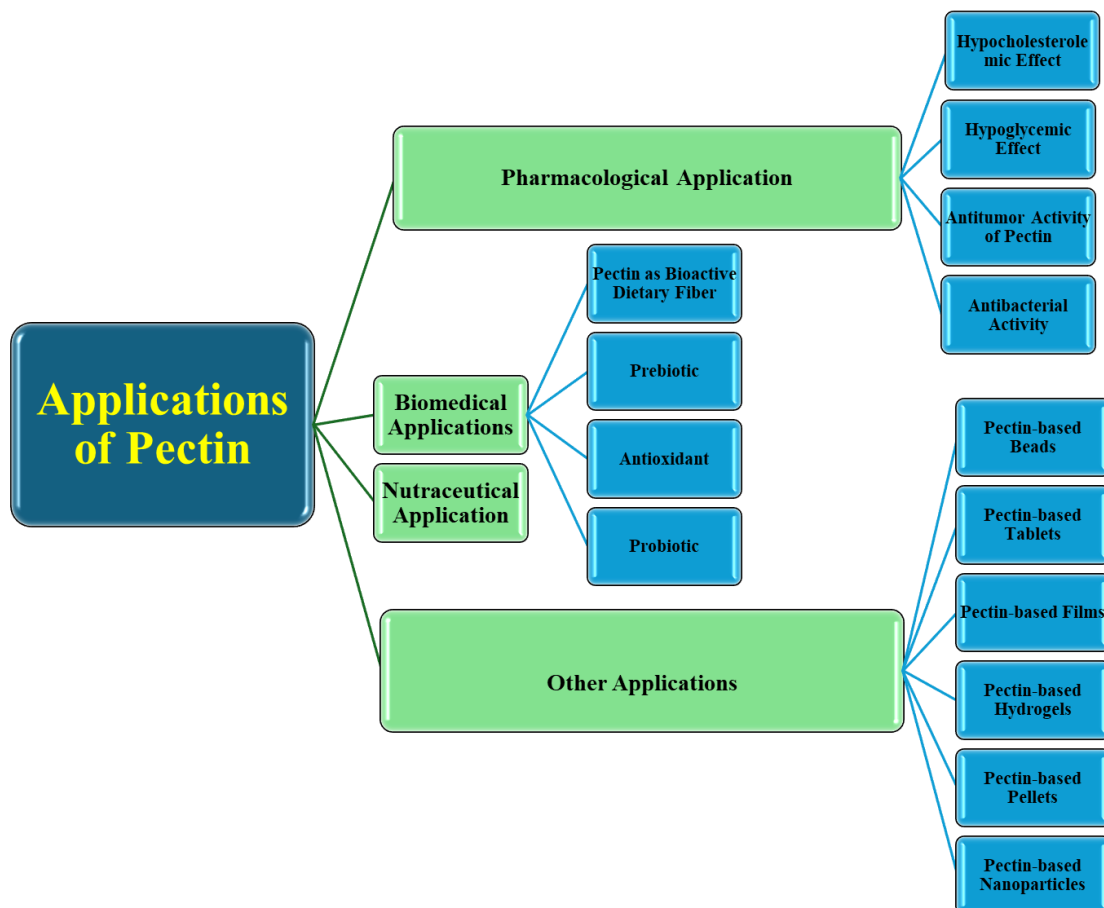


Figure 4: Applications of Pectin

6. Pharmacological Applications

a. Hypoglycemic Effect:

Diabetes mellitus is a serious metabolic disorder affecting millions worldwide. Approximately 90 % of these cases are classified as type 2 diabetes mellitus (T2DM), which manifests most commonly. In T2DM, insulin resistance leads to impaired glucose tolerance and persistent hyperglycaemia⁷. Although synthetic antidiabetic agents are widely used in treatment, they are often associated with adverse side-effects. In recent years, considerable attention has shifted toward the antidiabetic potential of dietary fibre, which may offer a safer complementary approach to conventional therapies.^{8,9}

Dietary fibres, including pectins, play a significant role in regulating hyperglycaemia. Their hypoglycaemic action is primarily attributed to the ability of viscous fibres to slow gastrointestinal transit, thereby reducing the rate of glucose absorption. Pectin-based composites have therefore been increasingly explored for controlled insulin delivery via the oral route, owing to the capacity of pectin to attenuate postprandial blood glucose levels. In this context, Maciel et al. developed nano- and microparticles prepared from a chitosan-pectin composite for insulin encapsulation, achieving an encapsulation efficiency of 62 % with particle sizes ranging from 240 to 1900 nm.^{10,11}

Panax ginseng remains one of the most widely utilised medicinal plants for diabetes management. Its hypoglycaemic properties have been well-documented through extensive investigations in both preclinical and clinical models. Pectic polysaccharides have been extracted from different types of ginseng using a combination of ion-exchange chromatography, water extraction, and gel-permeation chromatography. These include polysaccharides isolated from red ginseng (GPR, steamed at 100 °C), white ginseng (GPW), and highly steamed ginseng (GPS, processed at 120 °C).^{12,13}

b. Hypocholesterolemic Effect:

Over the past five decades, extensive research has highlighted the hypocholesterolemic potential of dietary fibres. Recognition of these benefits has led the United States Food and Drug Administration (FDA) to endorse the use of dietary fibres as a nutritional strategy to lower serum cholesterol and reduce the risk of cardiovascular disease. Among these fibres, pectin has received particular attention. Gunness and Gidley proposed three mechanistic pathways through which pectin contributes to reductions in total cholesterol and low-density lipoprotein (LDL). The first mechanism involves the inhibition of bile salt reabsorption in the intestine. Secondly, pectin and other soluble fibres are suggested to attenuate post-prandial glycaemic response while simultaneously decreasing 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) activity, a key intermediate step in the mevalonate pathway responsible for endogenous cholesterol biosynthesis.¹⁴

Furthermore, following the consumption of pectins and other soluble fibres, fermentation by the colonic

microbiota leads to the production of short-chain fatty acids (SCFAs), which have been reported to down-regulate endogenous cholesterol biosynthesis. Evidence from animal studies also indicates that the physicochemical characteristics of pectin influence its hypocholesterolemic efficacy. Notably, the chemical structure of pectin plays a decisive role; high-methoxyl pectins have been shown to reduce cholesterol concentrations in both plasma and liver more effectively than low-methoxyl pectins. In addition, highly viscous pectins can modify the enterohepatic circulation of bile acids derived from cholesterol, ultimately increasing their faecal elimination and thereby contributing to an indirect “excretion of cholesterol” from the body.^{15,16,17}

c. Antibacterial Activity:

Antibacterial agents are substances capable of inhibiting or eliminating bacterial growth. Pectin has demonstrated antibacterial activity against both Gram-positive and Gram-negative microorganisms. In one study, citrus pectin served as a reducing and stabilising agent in the green synthesis of silver nanoparticles (AgNPs). Fourier-transform infrared (FTIR) spectroscopy confirmed the presence of a pectin layer on the nanoparticle surface, indicating successful functionalisation. The resulting AgNPs exhibited potent antibacterial effects against both Gram-negative *Escherichia coli* and Gram-positive *Staphylococcus aureus*. These findings support the substantial potential of pectin-mediated AgNPs as antibacterial candidates for biomedical applications.^{18,19}

Biodegradable materials derived from pectin—including pectin-oleate, pectin-linoleate, and pectin-palmitate—have shown notable antimicrobial activity against a range of bacterial pathogens, particularly *Staphylococcus aureus* and *Escherichia coli*. Among these derivatives, pectin-linoleate and pectin-oleate demonstrated the highest inhibitory performance, suppressing microbial growth by approximately 50–70%, with *S. aureus* exhibiting the greatest susceptibility.

In a related development, a pectin-cadmium sulphide nanocomposite (Pc/CSNC) was synthesised in an aqueous medium at 60 °C using pectin as the stabilising and linking component. The resulting Pc/CSNC displayed pronounced antibacterial activity, especially against *E. coli*, indicating its strong potential as an antimicrobial nanomaterial.²⁰

d. Antitumor Activity of Pectin

The antitumor potential of pectin is attributed in part to the presence of galactan-rich segments within the rhamnogalacturonan-I (RG-I) domains, which are thought to interact with the carbohydrate-recognition domain of Galectin-3 (Gal-3), a lectin implicated in metastasis, apoptosis regulation and angiogenesis. Evidence from studies by Ellen G. Maxwell and colleagues shows that pectins derived from various botanical sources (such as citrus, sugar beet and potato) can inhibit proliferation of colon cancer cell lines. For example, an RG-I enriched extract from potato pectin significantly reduced viability of colon cancer cells in a dose-dependent manner. Moreover, alkaline-treated sugar-beet-derived pectin—characterised by increased RG-I to

homogalacturonan ratio and enriched neutral sugar side-chains—induced apoptosis in HT-29 colon cancer cells; enzymatic removal of the galactan side-chains markedly diminished its anti-proliferative effect, thereby highlighting the functional importance of those neutral sugar residues.²¹ The anticancer effect of pectin may involve down-regulation of the intercellular adhesion molecule-1 (ICAM-1) gene. For example, reduction of ICAM-1 expression via small-interfering RNA (siRNA) in colon cancer cells decreased their proliferation, suggesting a novel mechanistic pathway for pectin's activity.²²

6.1 Nutraceutical applications of pectin -

a. Prebiotic effect

A prebiotic is defined as a non-digestible food ingredient that confers a health benefit on the host by selectively stimulating the growth and/or activity of beneficial colonic bacteria. Pectin qualifies for this role because it resists digestion in the small intestine but is amenable to fermentation by colonic microbiota, yielding short-chain fatty acids (SCFAs) such as acetate, propionate, and butyrate.²³

Numerous studies demonstrate that pectinolytic bacteria—including genera such as *Lactobacillus brevis*, *Bifidobacterium bifidum* and *Bifidobacterium longum*—can utilise pectin and its oligosaccharides. Meanwhile, growth of potentially harmful taxa such as *Escherichia coli* and *Clostridium perfringens* is suppressed under these conditions.²⁴ Furthermore, co-fermentation of pectin with probiotic strain *Bifidobacterium longum* BB-46 has demonstrated a synergistic effect: combined treatment reduced intestinal ammonium levels while increasing butyric-acid-producing bacteria, indicating a favourable modulation of gut ecology and potential downstream health benefits.²⁵

Pectins are complex heteropolysaccharides whose structural complexity has drawn significant interest in research exploring how partial degradation by colonic microbiota may release bioactive fragments with prebiotic functions. For instance, intestinal fermentation of pectins produces short-chain fatty acids (SCFAs) such as acetate and butyrate, which not only reflect enhanced digestibility and microbial utilization of the pectic material but may also contribute to host health benefits²⁶ Importantly, low-molecular-weight pectin derivatives (i.e., oligosaccharides) appear to exhibit greater prebiotic potential than their native high-molecular-weight counterparts. Nonetheless, it can be hypothesized that the colonic microbiota's degradation of long-chain pectins in situ yields low-molecular fragments which may exert prebiotic effects especially in the distal colon.²⁷ Probiotic microorganisms must not only survive passage through the upper gastrointestinal tract but also

effectively colonise the colon, compete for nutrients and attachment sites, and persist to confer health benefits. Genera such as *Bifidobacterium* and *Lactobacillus* are well-studied in this regard, as they contribute to host health by inhibiting pathogenic bacteria, stimulating immune responses, and enhancing nutrient digestion including the production of short-chain fatty acids (SCFAs).²⁸

b. Probiotic:

Apples are rich in dietary fibre, especially pectin, which acts as a prebiotic by promoting beneficial gut bacteria and increasing butyrate production. The gastrointestinal tract contains both harmful and beneficial microbes; while harmful bacteria can cause disease, beneficial bacteria help maintain gut health. Probiotics such as *Lactobacillus* and *Bifidobacterium* improve digestion, immunity, and nutrient absorption, especially when combined with prebiotics. However, their effectiveness is limited because many probiotics are stressed by gastric acid and bile before reaching the colon.²⁹

c. Antioxidant:

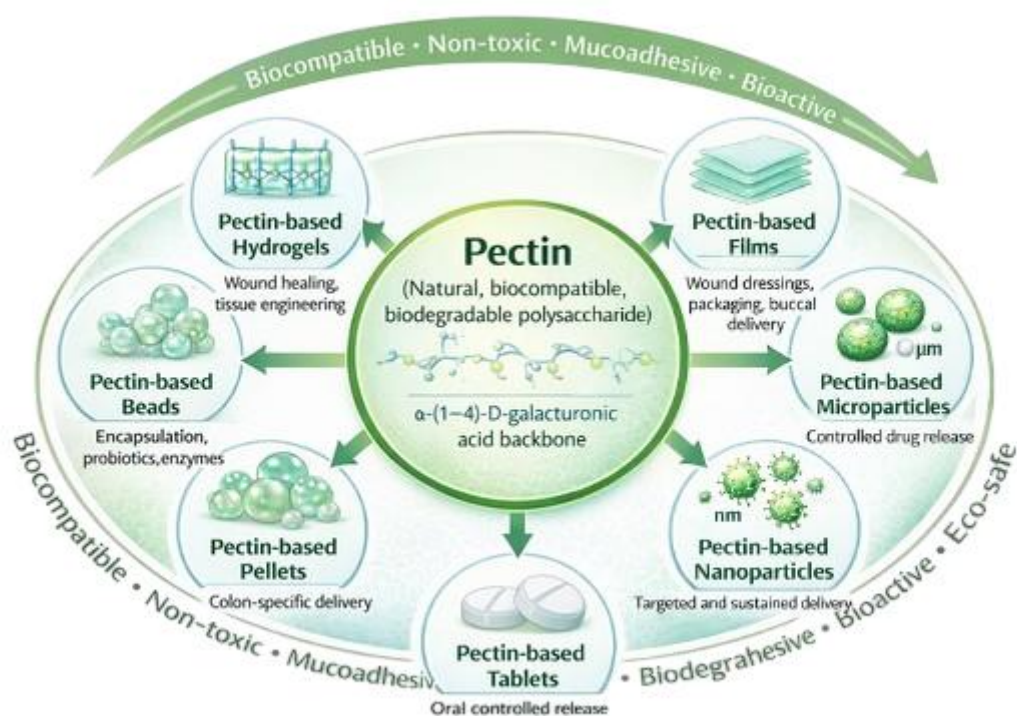
Pectic polysaccharides from plant sources such as oil pumpkin and horsetail exhibit notable antioxidant activity by scavenging free radicals and reactive oxygen species. Their antioxidant effectiveness is strongly influenced by phenolic content, monosaccharide composition, and molecular structure. Pectin fractions rich in galactose and galacturonic acid, especially in branched side chains and lower molecular weight forms, show enhanced radical-scavenging capacity compared to unmodified pectin. Overall, the structural features of pectin play a decisive role in determining its antioxidant potential.³⁰

d. Pectin as Bioactive Dietary Fiber:

Pectin is a naturally occurring bioactive dietary fiber predominantly located in the cell walls of higher plants. Structurally, it is a heterogeneous, anionic polysaccharide composed mainly of linearly linked α -(1 \rightarrow 4)-D-galacturonic acid units. Minor sugar residues such as rhamnose, arabinose, and xylose are also present, introducing branching and conformational irregularities within the otherwise linear backbone.

Owing to its diverse botanical sources and structural variability, pectin exhibits a broad spectrum of physical, chemical, and biological properties. Beyond its conventional role as a dietary fiber, pectin demonstrates notable bioactivities, including antibacterial, antioxidant, antifungal, and antitumor effects. Importantly, its non-cytotoxic and biocompatible nature supports its extensive use in medicinal, nutraceutical, and biomedical applications, highlighting pectin as a multifunctional and safe biopolymer for health-related formulations.³¹

6.3 Pectin-based Formulation for Biomedical Applications³²



Schematic representation of pectin-based formulations for biomedical applications.

Figure 4: Pectin-based formulations for biomedical applications

a. Pectin-based Hydrogels:

Hydrogels are three-dimensional, crosslinked polymeric networks capable of absorbing and retaining large quantities of water within their structure. Their soft, elastic, and tissue-like mechanical properties allow close contact with biological tissues while causing minimal irritation or inflammatory response. Owing to these characteristics, hydrogels are widely regarded as suitable materials for artificial skin substitutes and tissue engineering scaffolds. In addition, hydrogels serve as versatile matrices for controlled and safe drug delivery, soft contact lenses, protein separation systems, and cell encapsulation platforms, highlighting their broad utility in biomedical and pharmaceutical applications.^{33,34}

b. Pectin-based Films:

Polymer blending is widely used to improve the physicochemical and functional properties of polymeric materials. Blends of natural polysaccharides with synthetic or protein-based polymers have been extensively explored for diverse biomedical applications, including films, hydrogels, wound dressings, and drug delivery systems. Pectin, a water-soluble and biodegradable polysaccharide, is particularly well suited for film formation due to its safety and film-forming ability. Recent pectin-based composite films, especially those blended with polymers such as polyvinylpyrrolidone or gelatin, exhibit enhanced mechanical properties and biocompatibility, making them promising materials for controlled drug delivery and wound-healing applications.³⁵

c. Pectin-based Microparticles:

Microencapsulation is a widely explored strategy in drug delivery for improving drug stability and achieving controlled and sustained release of bioactive agents. Microparticle-based systems, particularly microspheres, can enhance drug residence time and therapeutic performance when designed with high encapsulation efficiency, preserved drug activity, and well-controlled release profiles. Pectin-based microspheres have gained considerable interest due to their biodegradability and selective degradation by colonic microflora, making them especially suitable for site-specific and colon-targeted drug delivery applications.³⁶

d. Pectin based Nanoparticles:

Polymeric nanoparticles have attracted substantial interest in recent years due to their significant role in the delivery of anticancer agents and gene-based therapeutics. Among these systems, thiolated pectin-based nanoparticles have been recently developed and evaluated for their potential in ocular drug delivery. These nanoparticles were prepared using the ionotropic gelation technique, employing magnesium chloride as an ionic crosslinking agent and timolol maleate as a model drug. The formulation studies demonstrated that the concentration of the crosslinker plays a dominant role in controlling nanoparticle size, whereas the polymer concentration primarily influences drug entrapment efficiency. These findings highlight the importance of formulation parameters in optimizing thiolated pectin nanoparticles for efficient and controlled drug delivery.³⁷

e. Pectin-based Tablets:

Pectin, a naturally occurring polysaccharide, has been widely investigated as a carrier polymer in matrix tablet formulations for colon-specific drug delivery. Due to its biodegradability, biocompatibility, and selective susceptibility to enzymatic degradation by colonic microflora, pectin-based matrices have been extensively studied to achieve delayed release in the gastrointestinal tract until the dosage form reaches the colon. Matrix tablets prepared with pectin, alone or in combination with other polymers or cross-linking agents, remain intact in the upper GI environment and undergo microbial degradation in the colon, making them promising vehicles for site-specific therapeutic delivery.³⁸

f. Pectin based Pellet:

Pellet cores for colon-specific applications are commonly prepared by extrusion-spheronization, typically using microcrystalline cellulose (MCC) as a processing aid blended with the active pharmaceutical ingredient. The extrusion-spheronization method yields spherical, mechanically robust pellets that support further functional coatings.³⁹

g. Pectin based Beads:

Pectin hydrogel beads are promising carriers for colon-targeted oral drug delivery because they form ionically cross-linked gels that resist degradation in the stomach and small intestine but break down in the colon due to microbial activity, enabling site-specific release. In beads formed by calcium ion gelation, cross-linking density and initial drug load are key factors affecting release behavior, with stronger cross-linking slowing drug diffusion and higher drug content accelerating it, while pectin concentration has less impact. To enhance site specificity and stability, pectin is often combined with cationic polymers like chitosan through polyelectrolyte complexation, which improves mucoadhesion and protects the drug during upper GI transit. Studies have demonstrated successful colon-targeted delivery using pectin-chitosan bead systems, and further control of release profiles can be achieved by co-formulating with other polymers or selecting pectin types such as high- or low-methoxy variants to modify gel structure and morphology.⁴⁰

6.4 Buccal Delivery:

Pectin-based wafers were developed as mucoadhesive buccal matrices for diphenhydramine hydrochloride, investigating how crosslinking type and processing sequence affect structure and drug release. Crosslinking with divalent salts (Ca^{2+} , Ba^{2+} , Zn^{2+}) before or after lyophilization modified pore architecture and mechanical properties, with post-lyophilization crosslinking producing the most sustained release. Larger cations, such as Ba^{2+} , formed more extensive ionic bridges, influencing porosity and drug transport. These results demonstrate that optimizing crosslinker identity and application sequence can effectively control matrix porosity, strength, and release kinetics in pectin-based buccal wafers.⁴¹

6.5 Nasal Delivery:

Nasal inserts composed of chitosan/pectin polyelectrolyte complexes were formulated to enhance the systemic bioavailability of antipsychotic agents by exploiting the nasal route, which bypasses first-pass metabolism and provides rapid drug absorption through the richly vascularized nasal mucosa. In these systems, chitosan and pectin were combined at pH 5.0 in varying polycation/polyanion ratios and lyophilized in the presence of chlorpromazine hydrochloride to form small, porous inserts. Variations in the proportion of pectin altered the physicochemical properties of the complexes; higher pectin content increased porosity and water uptake, leading to greater interaction with the drug and formation of less readily hydratable matrices, which in turn reduced drug release and permeation. These findings demonstrate that adjusting the polymer composition within chitosan/pectin complexes can modulate hydration behavior, mucoadhesive capacity, and drug release profiles, supporting their potential utility for efficient nasal delivery of antipsychotics.^{42,43}

6.6 Ocular Drug Delivery:

Topical eye drops are simple and widely used, but most of the drug is rapidly washed away by tearing, blinking, and drainage, which results in poor ocular bioavailability and frequent dosing. To address this, hydrophilic polymers such as pectin are being explored for in situ gel systems that transform from liquid to gel upon contact with tear fluid, increasing residence time on the eye surface. Pectin-based gels and microspheres, including systems loaded with piroxicam, have shown prolonged precorneal retention and improved drug availability compared with conventional drops. Overall, pectin-based ocular systems offer a promising strategy to enhance retention, penetration, and therapeutic effectiveness.⁴⁴

6.7 Cancer Targeted Drug Delivery:

Modified pectins are gaining attention in cancer therapy because they can bind to galectin-3, a protein that is overexpressed in many aggressive and metastatic tumors. Galectin-3 supports several processes that promote cancer progression, including cell adhesion, invasion, angiogenesis, and resistance to apoptosis. Chemically or thermally modified citrus pectin shows stronger binding to galectin-3 and can block its activity, thereby interfering with key pathways involved in tumor growth and metastasis. Experimental studies indicate that modified citrus pectin reduces tumor spread, limits angiogenesis, and increases tumor sensitivity to chemotherapy-induced apoptosis. Overall, structurally optimized pectins represent promising multifunctional agents and supportive platforms for targeted cancer therapy.⁴⁵

Conclusion:

Pectin has emerged as a versatile, biocompatible, and multifunctional biopolymer capable of supporting a broad spectrum of advanced drug-delivery platforms, ranging from hydrogels and films to micro- and nanosystems. Its intrinsic biodegradability,

mucoadhesion, and capacity for chemical modification enable site-specific, controlled, and stimuli-responsive release. However, despite promising laboratory outcomes, translation into clinically approved products remains limited. Major challenges include batch-to-batch variability, insufficient structure–function correlation, limited in-vivo mechanistic validation, and the lack of robust manufacturing and regulatory frameworks for pectin-based systems. Future research should prioritize precise molecular engineering, reproducible green extraction and modification strategies, integration with hybrid and smart materials, and systematic in-vivo and clinical evaluation. Coupling pectin with nanotechnology, responsive crosslinking chemistries, and personalized delivery approaches may ultimately bridge the gap between bench innovation and therapeutic reality, positioning pectin as a next-generation platform for safe, targeted, and sustainable drug delivery.

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