WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.63
Volume 15, Issue 5, 409-428. Review Article ISSN 2277–7105

TURNING WASTE INTO WELLNESS: THE EMERGING ROLE OF MODIFIED PECTIN FROM FRUIT PEELS IN MODERN DRUG DELIVERY SYSTEMS

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Article Received on 01 Feb. 2026,
Article Revised on 21 Feb. 2026,
Article Published on 01 March 2026,

https://doi.org/10.5281/zenodo.18800994

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How to cite this Article: Dr. Vandana Patil*[1], Shaikh Abubakar[2], Ms. Sana Tahreem Shaikh[3], Dr. Sachidanand Angadi[4]. (2026). Turning Waste Into Wellness: The Emerging Role Of Modified Pectin From Fruit Peels In Modern Drug Delivery Systems. World Journal of Pharmaceutical Research, 15(5), 409–428.

ABSTRACT

Pectin, a biodegradable and biocompatible polysaccharide mainly extracted from citrus peels and apple pomace, exhibits unique gelling and stabilizing properties due to its degree of esterification. These characteristics have enabled its wide application in pharmaceuticals as a natural carrier for controlled and targeted drug delivery systems. Pectin has also been considered an attractive natural polymer for biomedical and pharmaceutical applications outside of food uses. Pectin is non-toxic and has suitable physicochemical properties, which has led to research into the use of pectin as a carrier for targeted and controlled delivery of drugs (particularly in gastrointestinal systems); pectin has been investigated as a matrix tablet, gel beads, and film coated dosage forms. Pectin may have health promoting properties, potential for the use in active packaging systems, and potential compatibility with other biopolymers for the purpose of creating multifunctional materials for specific applications. Pectin has structural complexity and a variety of functions, including its crucial roles in plant growth, morphology, development, and defense.

KEYWORDS: Pectin, Natural polymers, Matrix-forming agent, Citrus peel.

1 INTRODUCTION

Natural polymers have been used in the formulation of pharmaceutical dosage forms for a number of reasons, including biocompatibility, biodegradability, safety and cost. Natural polymers are obtained from plants, animals and microbes, and include cellulose derivatives, starch, gums, alginates, chitosan, gelatin, and pectin.[1] Compared to synthetic polymers, natural polymers can provide advantages regarding non-toxicity, renewable sources, and acceptability to the patient population. As such, natural polymers serve as suitable materials in the creation of modern drug delivery systems.

Pectin is a ubiquitous naturally occurring complex hetero-polysaccharide constituting the main constituent of the primary cell wall of non-woody plants. It plays an important role in the growth and development of plants. In 1825, Heneri Braconnot coined the word pectin from the Greek word πηχτες (pektes) which means "Coagulated material". In higher plants, approximately one-third of the dry cell wall weight is corresponding to its pectin content. The concentration of pectin declines from the cell wall to the plasma membrane. The highest concentration is found in the middle lamella. Pectin has an array of functional and nutritional properties; therefore, it is highly popular in foods, cosmetics, textiles, drugs (drug delivery, wound healing, cholesterol-lowering, matrix tablets, gel beads, and film-coated dose form), and personal care products (paints, toothpaste and shampoos) due to its thickening, gelling, and stabilizing properties.[1]

Pectin offers a magnitude of biological and physiological properties like colon cancer, immune modulation, cell apoptosis induction, mouth-feel improver, and cholesterol reducing properties which are helpful in cardiovascular diseases management, and delayed gastric emptying to help in body weight reduction. Pectin was recommended as a safe ingredient by the FAO/World Health Organization (WHO) joint committee on food additives and the European Commission, with no acceptable daily intake limits, except for good manufacturing practices. The galacturonic acid content of pectin is advised to be at least 65% for use in food as an additive.

Chemically, pectin is a complex carbohydrate made of α-(1→4)-linked D-galacturonic acid units that are partly esterified with methanol as shown in Figure 1. Its ability to form gels, interact with ions, and control drug release has made it an appealing choice over synthetic polymers. Pectin is considered non-toxic, non-cancerous, biocompatible, and easily broken down by colonic bacteria, giving it special use in colon-targeted drug delivery systems. Additionally, it acts as a binder, stabilizer, thickener, and matrix-forming agent in various pharmaceutical forms like tablets, hydrogels, microspheres, nanoparticles, and films.

Pectin is a naturally abundant biopolymer sourced from fruit peels and pomace, which has spurred rapid large-scale manufacturing as a sustainable biopolymer. Due to advancements in green extraction techniques and pectin modifications (including amidation and esterification control), pharmaceutical applications are being developed beyond traditional gelling agents toward the use of pectin-based smart drug delivery carriers. A complete understanding of Pectin sources, classifications, structural diversity, and the functions is required to maximize Pectin use in modern pharmaceutical formulations.[1]

The purpose of this review is to provide a thorough valuation of pectin as a medicinal polymer. First, it will highlight the classification and sources of pectin to understand its functional behaviour. Second, it will then cover its role as a disintegrant, hydrogel for tissue engineering, matrix former for controlled release, binder, and targeted delivery extension for colonic drug targeting.

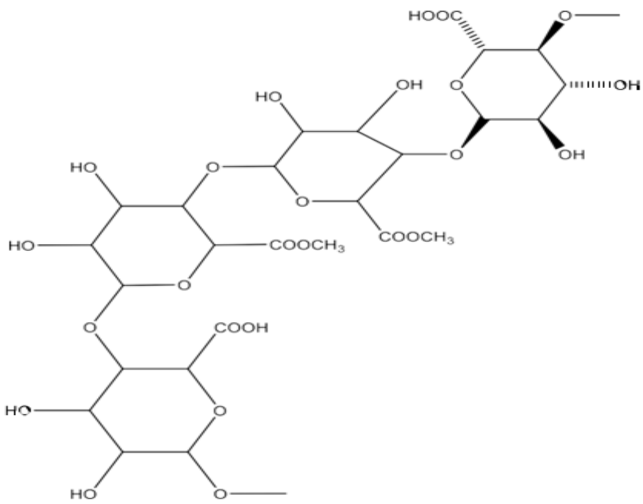

Figure 1: Structure of Pectin.

1.2 Sources of pectin

Usually, pectin is obtained from various sources, which are composed of citrus peel (85%), lemons (56%), limes (30%), oranges (13%) and apple pomace (14%).

Pectin is commonly produced from apple pomace, citrus peels, and sugar beetroot pulp. Food and agriculture industry wastes are also being used for pectin extraction. This solution can help solve the waste disposal and also provide more variety of materials to the industry. Pectin is used in non-processed fruit wastes for example banana peels, kiwifruit pulp, papaya peels, grapefruit peels, sugar beetroot peel etc. In dry matter apple pomace is made up of about 10%−15% pectin, from fruit, whereas citrus peel is relatively higher in pectin from 20% to 30% when compared to apple as shown in Table 1. In addition, the colour of the pectin from citrus is light cream to light tan, while apple pectin colour is normally dark.

Table 1: Sources of Pectin, Plant Parts, Yield along with Phytoconstituents.

Sr. No.	Source	Plant Part Used	Pectin Yield (%)	Phytoconstituents	References
1	Apple (Malus domestica)	Pomace (peel + pulp residues)	10–20	Pectin (homogalacturonan), polyphenols (catechin, chlorogenic acid), fibres	[2]
2	Jackfruit (Artocarpus heterophyllus)	Peel	9–15	Pectin, flavonoids, tannins	[2]
3	Banana (Musa spp.)	Peel	2–21	Pectin, tannins, dopamine, serotonin, starch	[6]
4	Papaya (Carica papaya)	Peel	11–50	Pectin, papain enzyme, carotenoids	[7]
5	Passion fruit (Passiflora edulis)	Peel	10–30	Pectin, polyphenols, flavonoids	[8]
6	Watermelon (Citrullus lanatus)	Rind	3–28	Pectin, lycopene, citrulline	[9]
7	Durian (Durio zibethinus)	Rind	2–10	Pectin, fibres, flavonoids	[10]
8	Citrus fruits (orange, lemon, grapefruit, lime)	Peel (albedo & flavedo), pulp residues	15–30	Pectin (galacturonic acid, arabinose, galactose, rhamnose), flavonoids (hesperidin, naringin), essential	[13];[9]
9	Cocoa (Theobroma cacao)	Husk	3–10	Pectin, polyphenols, theobromine	[13]
10	Sugar beet (Beta vulgaris)	Pulp (sugar extraction residue)	10–20	Pectin (acetylated galacturonic acid), betalains, cellulose	[14]
11	Dragon fruit (Hylocereus spp.)	Peel	2–27	Pectin, betalains, anthocyanins	[15]
12	Blueberry wine pomace	Pomace (peel + pulp residue)	~3	Pectin, anthocyanins, phenolics	[16]
13	Mango (Mangifera indica)	Peel (processing waste)	18	Pectin, carotenoids, Mangiferin, phenolic acids	[17]

Pectin extraction from fruit waste includes the following steps:

1. Collection of fruit waste material.
2. Selection of extraction methods and conditions.
3. Pectin extraction from the fruit waste through an appropriate extraction met.
4. Purification of pectin molecule

Pectin acts as a processing aid in the food processing process. Pectin is favoured because it is a food ingredient that is typically underutilized as a processing aid. Most wastes from the food processing and manufacturing sector contain some degree of pectin content. It is suggested that the pectin content of seasonal fruits that are under-utilized or wasted can have pectin levels as follows: melon rinds (8.03%), kiwifruit (6.54%), and pomegranate (6.13%) as shown in Table

2. A small amount of pectin (2%) can be found from sugar beet waste. This suggests that there are numerous fruit waste streams that can not only provide acceptable yields for production but also be a great avenue for the recovery of pectin in the food processing industry.

Table 2: Pectin Yield from Different Sources.[21-41]

Sr. No.	Source	Pectin Yield (%)	References
1	Apple pomace	4.60 – 20.92	[21]
2	Citrus: Orange peel	10.90 – 24.80	[22]
3	Grapefruit peel	21.60 – 28.00	[23]
4	Lemon peel	20.96 – 30.60	[24]
5	Lime peel	9.00 – 33.60	[25]
6	Sugar beet pulp	4.10 – 24.96	[26]
7	Banana peel	2.40 – 21.70	[27]
8	Carrot peel	8.90 – 9.10	[25]
9	Mango peel	9.20 – 31.80	[29]
10	Papaya peel	11.00 – 50.00	[30]
11	Pomelo peel	6.00 – 24.00	[31]
12	Watermelon peel	3.00 – 28.00	[32]
13	Durian rinds	2.00 – 10.00	[33]
14	Blueberry wine pomace	3.00	[34]
15	Passion fruit peel	10.00 – 30.30	[39]
16	Jackfruit peel	8.94 – 14.50	[36]
17	Rapeseed cake	6.85	[37]
18	Cocoa husk	3.38 – 12.60	[38]
19	Dragon fruit peel	2.00 – 27.00	[39]
20	Creeping fig seeds	5.00 – 6.00	[40]
21	Mangosteen rind	12.00	[41]

1.2 Classification of Pectin

Pectin is a complex heteropolysaccharide primarily composed of galacturonic acid units. The flow diagram classification of pectin (Figure 2) is usually based on degree of esterification, amidation, and chemical modifications, as these parameters strongly influence its gelling behaviour, solubility, and pharmaceutical applications.

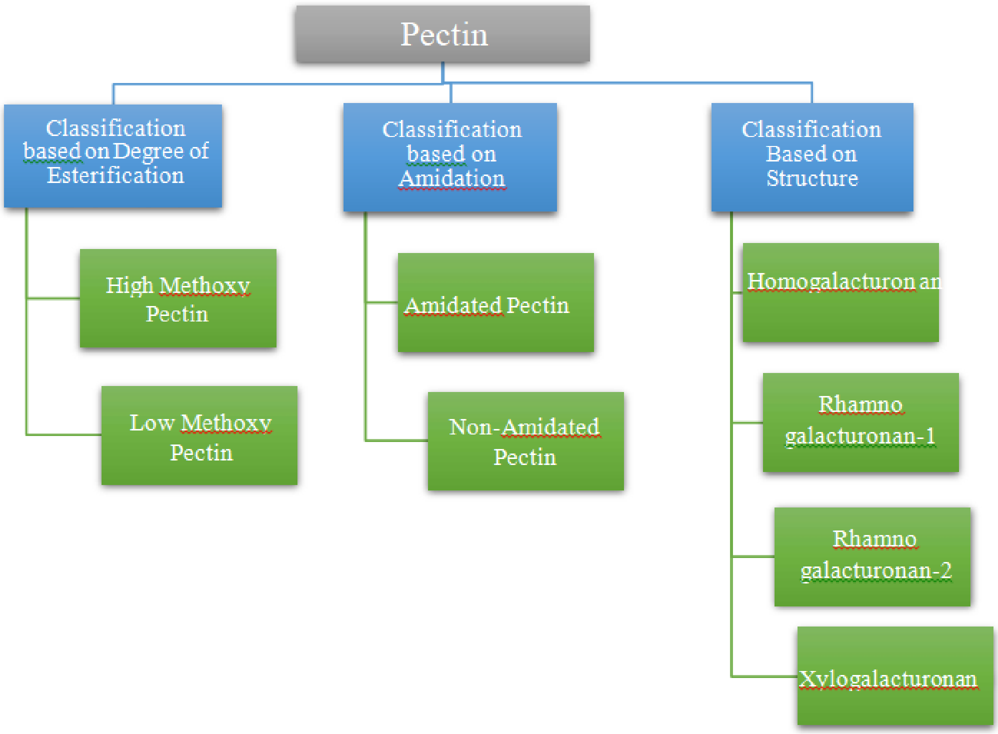

Figure 2: Classification of Pectin.

1.2.1 Classification Based on Degree of Esterification (DE)

1.2.1.1 High Methoxy (HM) Pectin

1.2.1.2 DE > 50% of galacturonic acid residues esterified with methanol.

1.2.1.3 Forms gels in acidic medium (pH < 3.5) in the presence of high sugar concentration (>55%).

1.2.1.4 Commonly used in food gels, jellies, and some pharmaceutical coatings.[12]

1.3 Low Methoxy (LM) Pectin

1.3.1.1 Degree of Esterification < 50%.

1.3.1.2 Gelation occurs via ionic crosslinking with divalent cations, especially **Ca^{2+}** ("egg-box"model).

1.3.1.3 More suitable for controlled-release drug delivery (colon-targeted, mucoadhesive formulations).[1]

1.4 Classification Based on Amidation

1.4.1.1 Amidated Pectin (AMP)

1.4.1.2 A derivative of LM pectin where some of the ester groups are replaced by amide groups.

1.4.1.3 Exhibits improved gel strength, stability, and calcium sensitivity compared to nonamidated LM pectin.

1.4.1.4 Useful in pharmaceutical gels, film coatings, and colon-targeted drug delivery.[2]

1.5 Structural Classification

1.5.1 Homogalacturonan (HG)

1.5.1.1 This is the most abundant part of pectin, making up about 65% of the molecule. It is a linear polymer made of α-(1→4)-linked D-galacturonic acid residues. The galacturonic acid units may be methyl-esterified in varying degrees, influencing pectin's behavior.

1.5.2 Rhamnogalacturonan 1 (RG-1)

1.5.2.1 Constituting about 20–35% of pectin, RG-I contains a backbone of alternating galacturonic acid and rhamnose residues with various side chains of neutral sugars like arabinose and galactose. These side chains give the molecule a "hairy" appearance.

1.5.3 Rhamnogalacturonan 2 (RG-2)

1.5.3.1 A less abundant but structurally complex domain, RG-II has a homogalacturonan backbone decorated with a variety of unusual sugars in highly branched side chains. Despite its low abundance, RG-II is crucial for cross-linking and structural stability.

1.5.4 Xylogalacturonan (XGA)

1.5.4.1 Another substituted form of homogalacturonan where xylose units are attached, contributing to the diversity of pectic substances.

1.6 Applications

1.6.1 Applications of Pectin in Food Industry

- Pectin is one of the most functional hydrocolloids commonly used in the food industry due to its abilities to gel, stabilize, and thicken. Usually extracted from sources of citrus peel, apple pomace, and other fruit news, pectin has historically been considered useful in commercial food applications for more than a century and continues to expand uses in the field of food technology.[1]
- Pectin's application in food is pectin in the production of jams, jellies, and marmalades.
- In this case, pectin acts as a gelling agent and in the presence of sugar and acid pectin creates a three-dimensional network which captures water to create a firm, gel-like consistency.[1,4]
- Pectin acts as a stabilizer or suspending agent in many beverages, particularly juices and

dairy products, including products like orange juice, in which pectin resists pulp and serum separation thereby leading to a more visually appealing drink with better mouthfeel. In acidified milk beverages, pectin protects proteins from precipitation by providing protective colloidal layers so the beverage can remain stable and uniform**.**

- Within the confectionery sector, pectin is involved in the manufacture of gummies, fruit pastes and chewy candies. When pectin is formed into thermo-reversible gels, it is possible for manufacturers to manipulate gummy texture and chewiness properties, ultimately altering the gel setting time of the candy.
- Meat and plant-based alternatives, pectin is emerging as a fat replacer and texturizer. By forming gels that mimic the juiciness of fats, pectin can be used to reduce the fat content of sausages, burgers, and meat substitutes without compromising sensory attributes. This aligns with current consumer demand for healthier, low-fat foods.
- Figure 3 shows general applications of pectin in Food Industry.

Figure 3: Application of Pectin in Food Industry.

1.6.2 Applications of Pectin in Pharmaceutical Industry

- Pectin has attracted considerable attention in the pharmaceutical and biomedical fields owing to its biocompatibility, non-toxicity, biodegradability, and ability to form gels and films. Its diverse physicochemical properties make it suitable for applications ranging from conventional formulations to advanced drug delivery systems.
- Pectin has been used a lot in the drug delivery area as a drug delivery carrier, in particular, colon-targeted delivery systems. Pectin would be a natural carrier, as colonic microflora degrade it but it would remain stable in the upper gastrointestinal tract! Thus, it can be used for the local treatment of colonic diseases, such as ulcerative colitis, Crohn's disease, and colon cancer. There are many types of formulations, including pectin matrix tablets, gel

beads, and film-coated dosage forms that have been developed using this principle. For example, controlled-release tablets (pectin-based) can successfully release indomethacin, metformin, and diclofenac slowly, and directly within the colon.

- Pectin can also act as a mucoadhesive polymer and can increase retention time at a mucosal surface, e.g., buccal, nasal, and vaginal routes. The mucoadhesive property results in an increase in drug bioavailability through prolonged release at the absorption site. Moreover, amidated and modified pectin demonstrate improved Mucoadhesion and have been studied in buccal tablets and patches for drugs such as propranolol and insulin.
- Pectin hydrogels are emerging as attractive agents in wound healing and tissue engineering. Pectin has a high-water holding capacity, biocompatibility, and ability to form films. Due to these properties, pectin hydrogels have been studied for use in wound dressings. Pectin hydrogels can maintain a moist nature of the environment, retain and absorb exudates, and enhance healing time. When developing wound dressings, pectin hydrogels could play a role in infection prevention and tissue regeneration.
- Pectin's therapeutic applications range from its historical functions as a stabilizer and excipient to contemporary applications in colon-targeted systems, wound healing, cancer treatment, and nanomedicine. With increasing interest from researchers working in the field, pectin is on track to become an even more useful biopolymer within the pharmaceutical industry and meet the initiatives for natural, safe, and sustainable drug delivery systems□
- Pectin-based nanoparticles and microparticles are being investigated for advanced drug delivery, including the targeted delivery of anticancer drugs, vaccines, and biomolecules. The capability of pectin to create polyelectrolyte complexes with chitosan and other polymers expands its use in controlled release and gene delivery systems. The graphical representation of pharmaceutical applications of pectin is shown in Figure 4.

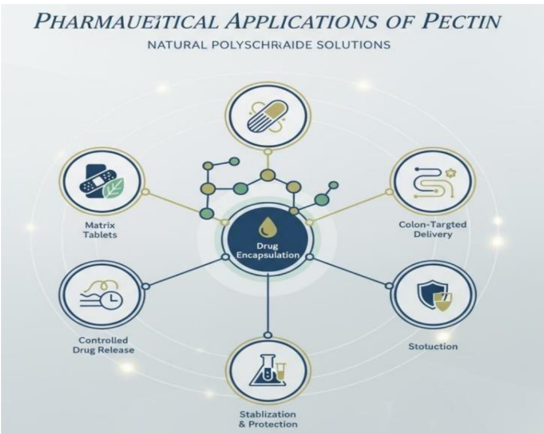

Figure 4: Application of pectin in pharmaceutical industry.

1.7 Properties of Pectin and Their Benefits

1.7.1 Gelling Property

High methoxy (HM) pectin, characteristically DE>50%, form gels in the presence of sugar and a low pH, while low methoxy (LM) pectin, DE<50%, gel in the presence of divalent cations such as calcium via the "egg-box" model. This makes pectin very useful in the food industry when producing jams, jellies, and marmalades. In pharmaceuticals, the gel formation aspect of pectin is useful in modulating drug release and allows pectin to entrap drugs to form viscous barriers, extending drug residence time in the GI as shown in Figure 5. LM pectin gels are resistant to gastric enzymes but degraded in the colon, making them an ideal candidate for controlled drug delivery systems targeting the colon. Overall, the ability to control drug release via gel formation demonstrates evidence towards the use of this attribute in sustained release and or site-specific drug-formulations.[2]

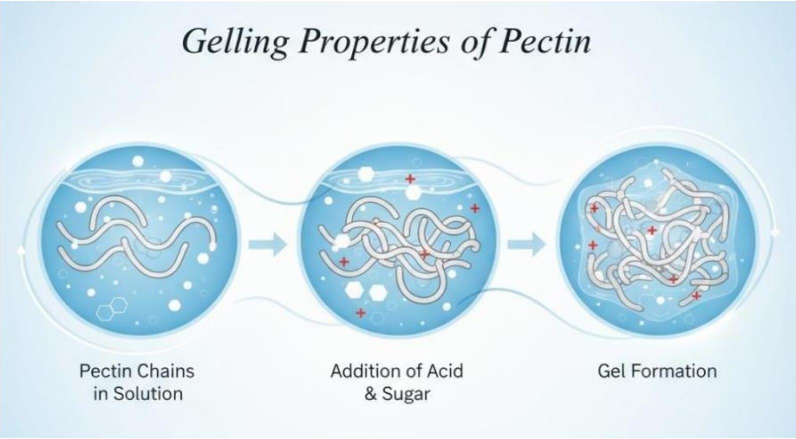

Figure 5: Gelling Properties of pectin.

1.7.2 Solubility and Water Holding Capacity

Pectin is a hydrophilic polysaccharide with exceptional water binding and swelling properties. Its solubility depends on the degree of esterification, branching, and molecular weight. As pectin has such a high hydration capacity that it provides viscous solutions, it improves mouth feel, texture, and stability in various food products including yogurt, fruit beverages, and confectionery. From a health perspective, the water-holding property allows for slow gastric emptying, as well as nutrient absorption. This may provide satiety, along with potential improvements in weight management and lowering postprandial glucose spikes for diabetic patients. Pectin's solubility also gives it the ability to be a source of dietary fiber, positively influencing bowel health and constipation.[12] Figure 6 shows pictorial presentation of solubility behaviors of pectin.

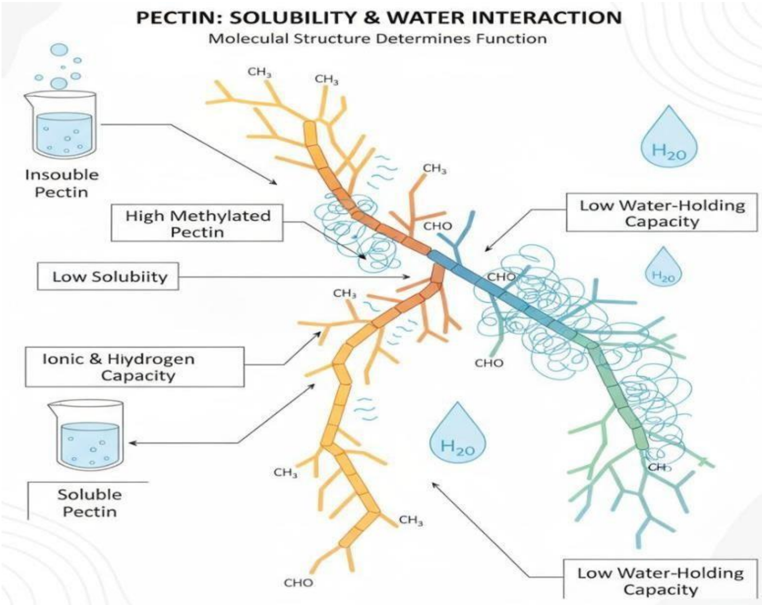

Figure 6: Solubility and Water-Holding Capacity of pectin.

1.7.3 Emulsifying and Stabilizing Ability

Certain types of pectin primarily sugar beet pectin, have strong surface activity due to the acetyl and ferulic acid groups associated with the galacturonic backbone. Because of these functional groups, pectin can behave as an emulsifier and stabilizing agent at the interface. In pharmaceutical formulations, pectin's emulsifying property promotes the development of nano emulsions and colloidal drug delivery systems, in which poorly water-soluble drugs can be made more soluble and bioavailable as shown in Figure 7. Pectin is also utilized for the encapsulation of bioactive compounds, providing protection to prevent degradation upon storage and during gastrointestinal transit.

Figure 7: Emulsifying and Stabilizing Ability.

1.7.4 Biodegradability and Biocompatibility

Pectin is a biodegradable and biocompatible polymer and can be considered a good choice for pharmaceutical and biomedical applications. It is resistive to digestion by human gastric and small intestinal enzymes but can be fully degraded by colonic microflora into short- chain fatty acids (SCFAs). Thus, pectin can be perfect for colon-targeted drug delivery as a vehicle or carrier to deliver therapeutic agents for the treatment of diseases such as ulcerative colitis, Crohn's disease, and colorectal cancer. Researchers have explored pectin- based hydrogels and scaffolds for applications related to wound healing, tissue regeneration, and drug encapsulation due to their low cytotoxicity, in addition, pectin interacts favourably with cells and is a suitable wound healing agent. It has the necessary biologic safety, eco-friendly/green, patient friendly attributes that can be used as an excipient in modern pharmaceutics as shown in Figure 8.[1]

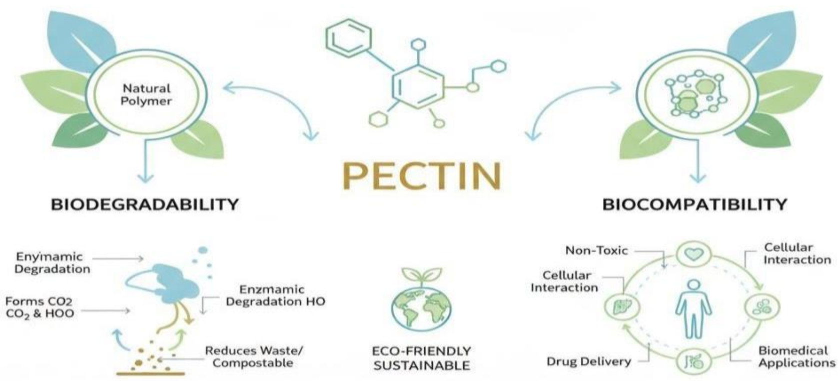

Figure 8: Emulsifying and Stabilizing Ability of pectin.

1.7.5 Hypocholesterolaemic and Hypoglycaemic Effects

Pectin is a soluble dietary fiber with significant hypocholesterolaemic and hypoglycemic effects. When consumed, pectin forms a gel-like material that is viscous in the gut. This will block and bind bile acids, cholesterol and triglycerides and thus reduce absorption and promotes excretion. This will also lead to reduced serum cholesterol which is beneficial for cardiovascular disease as shown in figure 9. Additionally, composition of meals affect absorption and in particular, pectin reduces gut absorption of glucose. Pectin may also lead to lower postprandial blood glucose spikes and therefore improve insulin-regulation especially in diabetic patients. Thus, these unique contributions of pectin make it particularly useful when combined with functional foods, nutraceutical supplements and therapeutic diets aimed at providing for weight loss and managing the metabolic syndrome, obesity and type- 2 diabetes.[18]

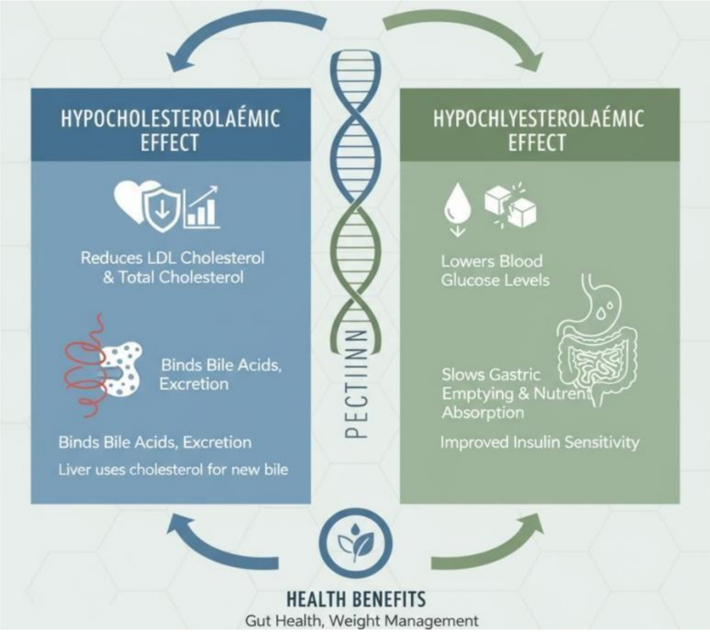

Figure 9: Hypocholesterolaemic and Hypoglycaemic Effects of pectin.

1.7.6 Anti-Cancer and Immunomodulatory Activity

Modified citrus pectin (MCP) has gained interest as an inhibitor of galectin-3, a β-galactoside-binding lectin involved in tumour progression and metastasis, and angiogenesis. MCP inhibits cancer cell adhesion, migration, and invasion (ischemic damage), blocking metastatic processes by binding to galectin-3. Experiments and clinical studies show MCP has anti-proliferative activity against prostate, breast, and colon cancers. Furthermore, pectin can modulate the immune response by stimulating macrophages, lymphocytes, and natural killer cells to enhance host defence. These bioactivities suggest that pectin is not just a dietary fibre, but also a potential therapeutic agent in cancer, immunotherapy, and overall health. With its natural origin, low toxicity, and feasible administration form, pectin is an appealing adjunctive therapy option for cancer prevention and treatment.[19] The graphical representation of anti-cancer and immunomodulatory activity of pectin is shown in Figure 10.

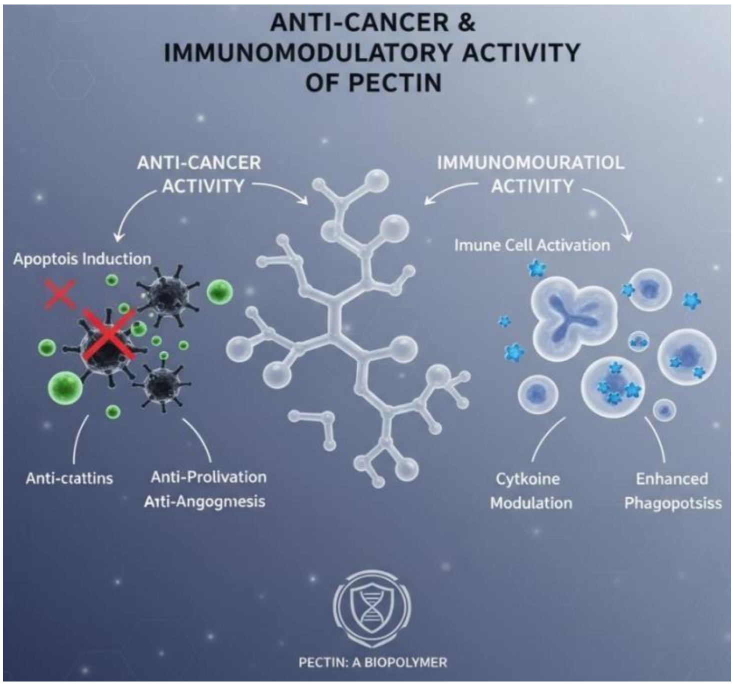

Figure 10: Anti-Cancer and Immunomodulatory Activity of pectin.

1.7.7 Film-Forming and Hydrogel Properties

Pectin has excellent properties for forming films and hydrogels (Figure 11) because it can crosslink with divalent cations or interaction with other biopolymers. This property of pectin is relevant to the food sector to formulate edible films and coatings that can extend shelf-life of fresh produce as moisture and oxygen barrier properties. Pectin-based hydrogels can provide moist environment suited to wound healing and provide thermotherapeutic agent delivery. Properties include the ability of active compounds to be incorporated into pectin hydrogels which are advantageous in drug delivery and regenerative medicine.

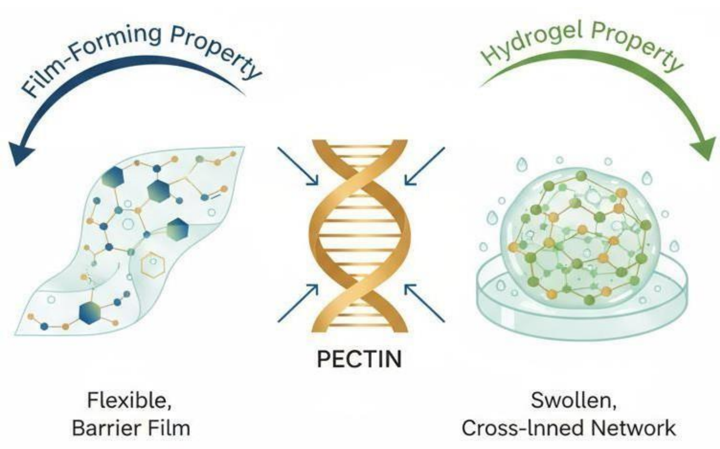

Figure 11: Film-Forming and Hydrogel Properties of pectin.

DISCUSSION

Pectin's structural diversity, biocompatibility, and biodegradability have made it a versatile natural polymer with a wide range of pharmaceutical uses. It is ideal for controlled and targeted drug delivery because of its capacity to form gels, function as a mucoadhesive agent, and degrade enzymatically in the colon. Modified pectins also exhibit encouraging biomedical uses, such as wound healing, hypoglycemic, and anticancer effects. Notwithstanding these benefits, there are still issues with variation in pectin yield, extraction methods, and physicochemical characteristics among sources. To completely realize pectin's medicinal and pharmacological potential, more investigation into environmentally friendly extraction techniques, chemical alterations, and clinical validations is necessary.

CONCLUSION

This study shows how useful pectin can be as a natural polymer in pharmaceutical formulations. It is a good excipient for controlled and colon-targeted drug delivery systems because it gels, stabilizes, and adheres to mucus, and it is also biodegradable and biocompatible. Pectin also looks promising for more advanced uses, like hydrogels for healing wounds, nanoparticles for targeted therapy, and film-forming agents for long- lasting release. Moreover, its bioactivities, encompassing hypocholesterolaemic, hypoglycaemic, and anticancer properties, augment its function beyond that of a standard excipient. The study finds that pectin is a sustainable and promising polymer for new drug delivery and biomedical innovations because it is abundant in nature, safe, and can be used in many different ways.

ACKNOWLEDGEMENT

The authors gratefully acknowledge their gratitude to The Principal, Yash Institute of Pharmacy, Dr. Babasaheb Ambedkar Marathwada University, Chh.Sambhajinagar (Aurangabad) for providing ICT facility.

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All authors have read and agreed to the published version of the manuscript

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