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Review

Deciphering Pectin: A Comprehensive Overview of Its Origins, Processing, and Promising Utility

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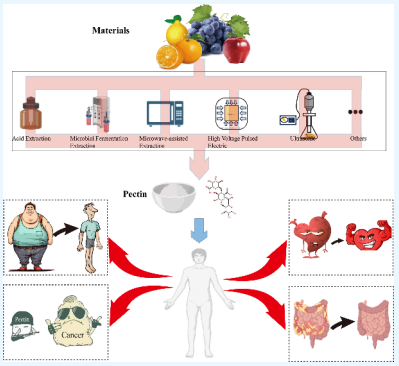
ABSTRACT: Pectin is an acidic heteropolysaccharide, a natural high molecular weight compound primarily found in higher plants. It consists of four major structural domains: homogalacturonan (HG), rhamnogalacturonan II (RG-II), rhamnogalacturonan I (RG-I), and xylogalacturonan (XGA). Various methods are currently employed for pectin extraction, including acid extraction, microbial fermentation, microwave-assisted extraction, and ion extraction, each with unique advantages and disadvantages. Pectin is sourced from fruits and vegetables, such as citrus fruits, apples, beets, and carrots. In terms of regulating human health, pectin enhances antioxidant activity, promotes beneficial microorganisms, and stimulates the production of short-chain fatty acids (SCFAs) through microbial metabolism. Additionally, pectin interacts directly with the mucosa, inhibits Toll-like receptor 2 (TLR2) signaling, and modifies the glycosylation of intestinal mucosal proteins. In disease models, pectin shows preventive and therapeutic effects in inflammatory bowel disease, type 2 diabetes, obesity, cardiovascular disease, and cancer. This review covers recent research, summarizing the sources and extraction methods of pectin, and emphasizes its role as a modulator of human health.



1. INTRODUCTION

Pectin, a natural polymer compound present in all higher plants, plays a critical role in maintaining the structure and integrity of various cell tissues. Comprised of different structural types known as pectin domains, this heterogeneous polysaccharide includes homogalacturonan (HG), rhamnogalacturonan II (RG-II), rhamnogalacturonan I (RG-I), and xylogalacturonan (XGA).[1] Among these domains, HG stands as the most abundant pectic polysaccharide. Pectin was first discovered in 1824 by Bracennot, who extracted it from carrots.[2,3]

Pectin is widely sourced from diverse fruits and vegetables, including citrus fruits, apples, beets, and sweet potatoes.[4] Citrus pectin, extracted from the peels and pulps of fruits, such as grapefruits, oranges, and lemons, demonstrates enhanced emulsifying ability and stability when extracted under ultrasound-assisted conditions. Apple pectin, obtained from apple waste, exhibits excellent gel properties, stability, thickening, and emulsifying capabilities.[5] Other pectins derived from sources such as beet pulp, sunflower heads, watermelon rind, and passion fruit rind also hold potential value as byproducts.[6]

Several methods are employed for pectin extraction, including acid extraction, microbial fermentation extraction, microwave-assisted extraction, high voltage pulsed electric field extraction, enzymatic extraction, and ultrasonic extraction.[7−13] The acid extraction method is commonly used in industrial extraction, where hot acidic aqueous solutions convert protopectin into water-soluble pectin, followed by precipitation using ethanol or polyvalent metal salts.[14] Microbial fermentation extraction selectively breaks down complex polysaccharides through the use of microbial enzymes.[15] The microwave-assisted extraction method utilizes microwaves to enhance the interaction between the medium and promote pectin dissolution.[16] The high voltage pulsed electric field method involves the application of high voltage pulses to disrupt the cell wall and release pectin.[17] Enzymatic extraction and ultrasonic extraction are clean and efficient methods with shorter extraction cycles, requiring less energy and solvent.[18]

Pectin offers several beneficial effects on gut immunity. It exhibits antioxidant activity by reducing the production of free radicals and enhancing the antioxidant capacity. Pectin also regulates the intestinal microbiota by promoting the growth of beneficial bacteria while inhibiting harmful ones. It increases the abundance of bacteria associated with positive effects on colon cancer and ulcerative colitis. In the gut, pectin fermentation produces short-chain fatty acids (SCFAs) that contribute to gut health and peristalsis.[19] SCFAs also bind to

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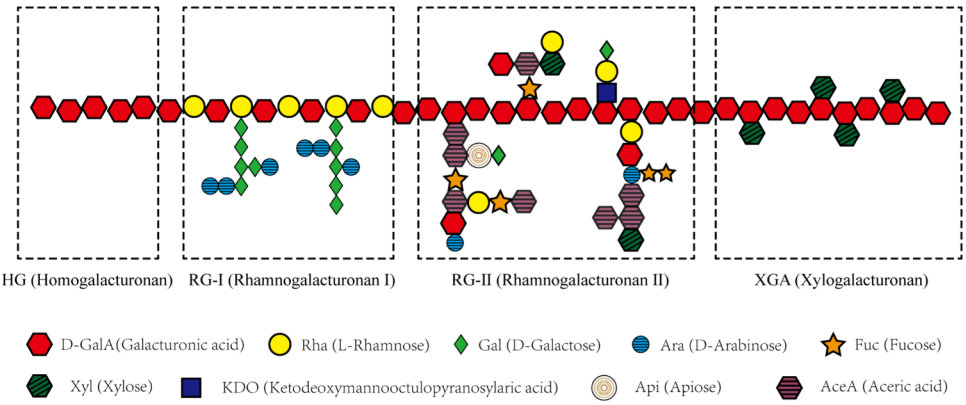

Figure 1. Pectin has four structural domains, including homogalacturonan (HG), a linear pectic polysaccharide of α-1,4-linked galacturonan, followed by rhamnogalacturonan I (RG-I), which consists of a repeating backbone of (α-1,2)-l-rhamnose-(α-1,4)-d-galacturonic acid, with various side chains; rhamnogalacturonan-II (RG-II) is the most complex type of fructose, consisting of a HG backbone of at least eight 1,4-linked α-D-GalA residues, decorated with 12 different types of side chains. The primary structure of XGA is composed of a linear polymer composed of α-1,4-D-GalAp residues, and the C-3 hydroxyl group of GalA on the polymer backbone is covered by monosaccharide D-Xyl to form the XGA domain.

receptors, regulating gut homeostasis and inflammatory responses. Pectin affects tryptophan metabolism, leading to the production of indole derivatives, which promote intestinal health. Additionally, pectin interacts directly with the mucosal barrier, blocking specific immune pathways and modulating mucin glycosylation.[20,21] Pectin has shown promise in disease models, particularly in inflammatory bowel disease, where it can alleviate inflammation and promote healing. However, the effects of pectin on bile acid metabolism and cholesterol levels are still subject to debate. Overall, the various effects of pectin on gut immunity contribute to its potential as a valuable dietary component for maintaining mammalian health.

This review aims to provide a comprehensive review of recent research progress in the field of pectin. It will summarize the sources and extraction methods of pectin while emphasizing its significant impact as a modulator of human health. By exploring the diverse applications and potential benefits of pectin, we can further understand its role in promoting overall well-being and its potential in disease prevention and treatment.

2. MONOSACCHARIDE COMPOSITION, STRUCTURE, AND PROPERTIES OF PECTIN

2.1. Monosaccharide Composition. Pectin, a natural polymer compound present in all higher plants, plays a critical role in maintaining the structure and integrity of various cell tissues.[22,23] It consists of an α-(1,4)-linked d-galacturonic acid (d-GalA) backbone, along with alternating regions of L-rhamnose and d-GalA.[3] Pectin exhibits a heterogeneous structure comprising four structural types known as pectin domains: HG, RG-II, RG-I, and XGA.

HG, the most abundant pectic polysaccharide, is a linear homopolymer of α-1,4-linked galacturonic acid, constituting approximately 65% of pectin (Figure 1). RG-I, the second largest fraction (20−35%), features a repeating backbone of (α-1,2)-l-rhamnose-(α-1,4)-d-galacturonic acid, along with various side chains.[24] RG-II, with a complex structure comprising about 10% of pectin, consists of an HG backbone adorned with side branches composed of 12 different types of sugars in over 20 different linkages.[25] XGA, another structural type, is primarily composed of a linear polymer of α-1,4-D-GalAp residues, with the C-3 hydroxyl groups of GalA substituted with monosaccharide D-Xyl to create the XGA domain[26,27] (Figure 1).

2.2. Physical−Chemical Properties of Pectin. The composition and physical−chemical properties of pectins vary greatly due to factors such as the type of raw source material and the extraction method. These properties include solubility, emulsifying, esterification degree, Gal-A content, and monosaccharide composition.[28−31]

2.2.1. Solubility. Pectins can be classified into water-soluble and nonwater-soluble pectins based on their solubility characteristics.[32] Various factors influence the solubility of pectin, such as the degree of esterification and the distribution of the methoxy sites.[29,33] Pectins with a lower relative molecular mass and a higher degree of esterification generally exhibit better solubility.[34] Additionally, pectin particles need to swell prior to dissolution, similar to hydrophilic colloids.[35]

2.2.2. Degree of Esterification. The esterification degree of pectin, also known as methoxylation, refers to the sum of the proportion of methyl esterification, acetylation, and amidation in the pectin. Its esterification degree affects the morphology and conformation of the pectin. Increasing the esterification degree can decrease the extension and curvature of pectin molecules while increasing hydration volume.[36] Conversely, decreasing the esterification degree can reduce chain flexibility and increase rigidity.[37] Pectin can be classified into high ester pectin (DE > 50%) and low ester pectin (DE < 50%) based on esterification degree, which is influenced by differences in raw materials and processing technology.[38] The esterification degree also affects the ability of pectin to form a complex with other substances. Stone et al. (2018) found that high ester pectin has a stronger interaction with pea protein isolate under optimal mixing conditions.[39] Pillai et al. (2020) found that as the esterification degree decreases the critical pH for pectin to form a complex with other substances significantly increases.[40]

2.2.3. Gal-A Content and Monosaccharide Composition in General. Pectin is primarily composed of D-GalA, along with neutral sugars such as L-rhamnose, D-galactose, and D-arabinose.[41] The composition of individual sugars can indirectly reflect the structure of pectin, and some scholars use the GalA content to indicate the purity of pectin.[42] The majority of neutral sugars in pectin are present in side chains; therefore, a high GalA content indicates a high content of side

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Table 1. Differences in the Properties of Pectin from Different Sources

Type of pectin	Source	Pectin content	Properties
Citrus Pectin	Grapefruits, oranges, lemons	Up to 30%	-Enhanced emulsifying ability and stability under ultrasound-assisted conditions. -Good gel formation, thickening, and emulsifying properties. -Ideal viscosity and protein stability (lemon and orange pectin). (Vogt et al., 2016; C. Wang et al., 2021)
Apple Pectin	Apple waste	15−18%	-Excellent gel properties, stability, thickening, and emulsifying properties. - Suitable for use as a gel agent. -Enhanced antioxidant activity through acid−base and thermal modifications (Lyu et al., 2020).
Beet Pulp Pectin	Beet pulp (byproduct of beet sugar production)	15−30%	-Good flowability and gel properties. -Small molecular weight, low viscosity, and strong thermal stability for regulating gel properties (Fissore et al., 2013).
Sweet Potato Pectin	Sweet potato residue	20−30%	-Acidic heteropolysaccharide extracted from sweet potato residue. -Derived from sweet potato industrial processing and production (Abang Zaidel et al., 2017).
Sunflower Head Pectin	Sunflower heads	15−24%	-Good gelling properties, high molecular mass and high viscosity.
Watermelon Pectin	Watermelon rind	19−21%	-A high degree of methyl esterification (about 60%). -Higher viscosity and good foaming and emulsifying properties.
Passion Fruit Pectin	Passion fruit rind	6.2−18.2%	-Exhibited medium to high degree of esterification (50.00%−64.56%).

chains. A low content of neutral sugars in pectin means a lower content of side chains.[43]

2.3. Source of Pectin. The sources for pectin are composed of a wide variety of fruits and vegetables. Popular sources include citrus fruits (oranges, grapefruits, lemons, and limes - known as citrus pectin), apples, beets, carrots, apricots, plums, blackberries, and cherries (Table 1).

2.3.1. Citrus Pectin. Citrus pectin is a polysaccharide compound extracted from the peels and pulps of various fruits such as grapefruits, oranges, and lemons, and its molecules exist out of long-chain carbohydrates.[4] Recent studies have shown that citrus pectin extracted under ultrasound-assisted conditions has an enhanced emulsifying ability and stability when compared with untreated pectin. This is especially the case for lemon peel, which has a pectin content of up to 30%.[44,45] This pectin has a good gel formation, thickening, and emulsifying properties, while both lemon and orange pectin show an ideal viscosity and protein stability, which can provide a good texture for food.[2,46]

2.3.2. Apple Pectin. Apple pectin is a high molecular weight polysaccharide extracted from apple waste, which contains 15% to 18% pectin, making it another commercially produced fruit pectin besides citrus pectin.[5] As a natural food additive, it possesses excellent gel properties, stability, thickening, and emulsifying properties.[47] The optimized apple pectin extracted through the process has gel and viscosity properties suitable for use as a gel agent.[48] Furthermore, acid−base modifications and thermal modifications of apple pectin result in a rich dehydrated GalA content, which enhances its antioxidant activity, possibly due to an increased level of GalA.[49]

2.3.3. Other Pectins. Beet pulp is a byproduct of beet sugar production, and its raw materials are readily available.[50] The pulp content ranges from 15 to 30% of the dry weight of the beet. The research on the effects of beet pulp pectin emerged later than that of the two previously mentioned types of pectins.[51] It however has good flower-like activity and gel properties. Studies have shown that beet pulp pectin has a small molecular weight, low viscosity, and strong thermal stability, making it effective in regulating gel properties.[52,53]

Sweet potato pectin is an acidic heteropolysaccharide extracted from a sweet potato residue. Sweet potatoes are an important food crop worldwide, and their industrial processing and production generate a significant amount of sweet potato residue, which contains 20−30% of pectin-like substances.[54]

Furthermore, there are other pectins derived from different sources, such as sunflower head pectin obtained from sunflower heads,[6,55] watermelon pectin extracted from watermelon rind,[56] and passion fruit pectin obtained from passion fruit rind.[56,57] These pectins are mainly derived from byproducts, which not only avoids waste of resources but also exploits their potential value.

2.4. Extraction of Pectin. There are various extraction methods for obtaining pectin, each with its unique mechanism, effectiveness, usability, and potential drawbacks (Table 2).

2.4.1. Acid Extraction Method. The acid extraction (AE) method is commonly used as an industrial extraction method. The basic principle is to convert protopectin in plant cells into water-soluble pectin by using a hot acidic aqueous solution, then extract it, and finally add ethanol or polyvalent metal salts to precipitate the pectin.[8] Both inorganic and organic acids can be used as acid mediums. Inorganic acids mainly include sulfuric acid, hydrochloric acid, and nitric acid.[11,58,59] They are low in price, have strong stability, and have a low molecular weight, making them less prone to decomposition when heated. However, their acidity is strong, and this can easily cause structural destruction of the pectin. Another option are organic acids including oxalic acid, ammonium oxalate,[14] tartaric acid,[60] etc. The acidity of these organic acids is relatively mild, making it less likely to cause denaturation of the pectin. However, its volatility can lead to unstable pH values, which can affect the quality of pectin. Raji et al. (2017) used citric acid to extract pectin from melon peel. Their research showed that with a pH value of the extract of 1, a temperature of 95 °C, and an extraction time of 3.2 h the yield of pectin reached 31.18%, and the obtained pectin had a good emulsifying activity and emulsion stability.[61] Virk et al. (2004) used hydrochloric acid and citric acid to extract pectin from fresh apple peel. The experimental results showed that the yield after extraction with citric acid was 0.9% higher than

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Table 2. Comparison of Different Pectin Extraction Processes

Extraction Method	Advantages	Disadvantages	Examples of Studies
Acid Extraction Method	Commonly used industrial extraction method	-Strong acidity may cause structural destruction of pectin	-Raji et al. (2017): Used citric acid for melon peel extraction, achieving a 31.18% yield and good emulsifying activity.
	-Relatively low cost	-Volatility of organic acids can lead to unstable pH values	-Virk et al. (2004): Compared organic and inorganic acid extraction from apple peel, showing better extraction with organic acid.
	-Strong stability of inorganic acids		
	-Milder acidity of organic acids		
Microbial Fermentation	-Selectively breaks down complex polysaccharides in plant tissues	-Potential depolymerization and denaturation of pectin during extraction	-Sakai et al. (1980): Used Trichosporon penicilatum for pectin extraction from plant peels.
	-Relatively large molecular weight and high gelation degree of extracted pectin	-Enzyme cost and variable results due to strain differences	-Gomashe et al. (2019): Used Trichosporon penicillatum enzymes for orange peel fermentation, minimizing production cost.
	-No need for crushing, heat treatment, or acid treatment		-Thibault et al. (1988): Used complex enzyme for pectin extraction from citrus fruit.
Microwave-assisted Extraction	-Low energy consumption	-Requires careful control to protect pectin structure and avoid overheating	-Maran et al. (2017): Used MAE to extract pectin from watermelon rind with a 25.8% yield.
	-Short processing time		-Hosseini et al. (2016): Extracted pectin from citrus peel using MAE with a 29.1% yield.
	-High efficiency and cleanliness of extraction		
Ion Extraction Method	-Yields pectin with high quality and desirable color	-Pectin prone to depolymerization and denaturation during extraction	-Torkova et al. (2018): Extracted pectin from pumpkin, citrus, and apple using cation exchange resin with 5% (wt) resin amount.
		-Relatively expensive and complex operation, limiting industrial application	-Davara et al. (2017): Used cationic resin for pectin extraction from apple pomace with higher yield and gel strength.
High Voltage Pulsed Electric Field Method	-Effective in disrupting plant cell membranes	-Requires high-frequency electromagnetic field, limiting application for heat-sensitive materials	-Chongguang et al. (2009): Used pulsed electric field for pectin extraction from apple pomace, showing higher efficiency than other methods.
		-Potential fragmentation of pectin molecules during extraction	
Enzymatic Assay	-High extraction efficiency	-Higher reaction time and cost of enzymes	-Vasco-Correa et al. (2017): Extracted pectin from passion fruit peel using fungal enzyme PPase-SE, achieving a high yield
	-Precise control of enzyme quantity	-Variable results due to enzyme strain differences	-Kazemi et al. (2019): Determined optimal conditions for pectin extraction from subskins using an ultrasonic power of 50 W and 30 min
	-Better quality and less solvent required		
Ultrasonic Method	-Clean, efficient, and environmentally friendly	-Excessive ultrasonic time can lead to pectin overhydrolysis and fragmentation	-Karbuz et al. (2021): Extracted pectin from fruit peels using ultrasonic waves, showing optimal conditions for maximum yield
	-Short extraction cycle and low energy and solvent requirements	-Optimal conditions required for maximum pectin yield	

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that extracted with hydrochloric acid, and the extraction effect of the organic acid was thus better than that of the inorganic acid.[62] Nevertheless, the extraction with either organic or inorganic acids generates acidic wastewater, which can cause serious environmental problems.[63] It also has the disadvantage of simultaneously having a high cost and low output.[64]

2.4.2. Alkaline Extraction of Pectin. Alkaline extraction, using chelating agents in alkaline solutions, has been shown to yield higher pectin quantities compared to acidic extraction.[64,65] As early as 2013, a study demonstrated that suspending 2 g of potato in 200 mL of 0.02 M $NaBH_4$ and incubating the suspension in a 60 °C water bath for 24 h resulted in the extraction of pectin. After centrifuging the supernatant at 15,000*g* for 20 min the collected extract was filtered, neutralized, dialyzed, and freeze-dried.[66] Another study conducted by Zhang et al. (2018) utilized citrus peel waste as the raw material, and extraction was performed using 0.6% NaOH at 32 °C with stirring for 10 min.[67] Interestingly, the highest pectin yield (24.2%) was achieved at an NaOH concentration of 50 mM, while increasing NaOH concentrations to 100 and 200 mM resulted in decreased pectin yields.[65] Despite variations in the extraction conditions, the obtained pectin shared certain characteristics: low molecular weight, RG-1 content 2−5 times higher than conventional methods (reaching up to 82.5%),[67] retention of neutral side chains, and a higher content of arabinoxylans. However, it was found that this extraction method might lead to the breakdown of the HGA main chain.[68]

In addition, S. Yeoh (Awad, Ghareeb, Abdel-Raheem, and Bohm) pointed out other potential drawbacks of alkaline extraction, particularly the lower yield. The reason behind this lies in the instability of GalA caused by alkali, leading to pectin decomposition and subsequent yield reduction.[69] However, contradictory findings exist in the research of Nurdjanah et al. (2013) and Pérez-Martínez et al. (2013), indicating that the chelating agent-assisted extraction in an alkaline solution resulted in higher pectin content compared to acidic extraction.[64,70]

Furthermore, pectin obtained from alkaline extraction can be directly used for the production of pectin oligosaccharides through β-elimination and saponification reactions.

2.4.3. Microbial Fermentation Extraction Method. Microbial fermentation selectively breaks down complex polysaccharides in plant tissues, facilitating pectin extraction. Sakai et al. (1980) developed a systematic research method in which washed peels were suspended in a sterile water fermenter and inoculated with a seed culture of a strain of *Trichosporon penicilatum*, SNO-3. After fermenting at 25 to 30 °C for 15 to 20 h, pectin powder was obtained by filtering, concentrating the precipitate, and drying it.[15] Pectin extracted by microbial fermentation has a relatively large molecular weight, a high gelation degree, and stable quality. The extraction process does not require crushing, heat treatment, or acid treatment, making it easy to separate and extract completely, with low cost and low pollution as a result. Therefore, microbial pectin extraction has broad prospects for further development.

2.4.4. Microwave-Assisted Extraction Method. Microwave-assisted extraction (MAE) is an innovative alternative method to traditional techniques for extracting organic compounds from various organic substances by combining microwave energy with a solvent.[16] This technology offers several advantages, such as low energy consumption, easy control, short processing time, low solvent requirements, low cost, high efficiency, and cleanliness.[71] The mechanism of action involves the absorption of microwave radiation by polar molecules within plant tissue cells, leading to a rapid increase in the temperature within the cells. As the liquid within the cell tissue vaporizes, it creates a vapor pressure that ruptures the cell membrane and cell wall, facilitating the release of intracellular substances into the extraction fluid.[7]

For example, Maran et al. (2017) used MAE to extract pectin from watermelon rind under the conditions of 477 W microwave power at 2 min, achieving a maximum yield of 25.8%.[72] Similarly, Hosseini et al. (2016) extracted pectin from citrus peel using MAE with 700 W microwave power at 3 min, obtaining a maximum yield of 29.1%.[73]

2.4.5. Ion Extraction Method. The ion exchange process technique (IEP) is a method that utilizes ion exchange resins to reduce the intermolecular forces between atoms of similar properties during the extraction process, thus improving the efficiency of pectin extraction. This method yields pectin with a high quality and desirable color. However, during the extraction process, pectin is prone to depolymerization and denaturation. Moreover, the ion exchange process is relatively expensive and has a complex operation, which limits its industrial application.

Torkova et al. (2018) extracted pectin from pumpkin, citrus, and apple using cation exchange resin with a 5% (wt) resin amount.[12] Double extractions at 85−88 °C for 1 h using a cationic resin for the extraction of pectin from apple pomace have been reported to give higher yield and better gel strength of the product when compared with single extractions.[74]

2.4.6. High Voltage Pulsed Electric Field Method. The high intensity pulsed electric fields technique (HIPEF) is an innovative nonthermal technology that has gained traction in recent years for processing heat-sensitive materials. HIPEF is particularly effective in disrupting plant cell membranes and has demonstrated promising results in enhancing the solubilization of intracellular substances.[17]

Pectin is a large molecule composed of galacturonic acid and possesses some polarity, which allows it to dissolve in water. When a high-frequency electromagnetic field is applied, the pectin and water molecules inside the cell rotate, leading to molecular thermal motion and an increase in the material's overall temperature.[75] This heating process occurs without the need for thermal conduction or convection, which allows for uniform heating of the material without a temperature gradient. Additionally, pectin inside plant cells can rapidly absorb energy, resulting in a swift temperature increase within the cell.[10] This temperature increase facilitates the separation of hydrolyzed pectin and cellulose, thereby increasing the efficiency of the extraction process.

A study by Chongguang et al. (2009) has found that the optimal conditions for extracting pectin from apple pomace using a strong pulsed electric field are an electric field strength of 15 kV/cm, pH value of 3, 10 electric pulse repetitions, a solid−liquid ratio of 1:19, and a temperature of 62 °C. This method has shown to be highly effective, surpassing other extraction techniques such as the acid extraction method, the ultrasonic extraction method, and the microwave extraction method.[76]

Overall, HIPEF offers a promising alternative to traditional thermal processing methods, particularly for heat-sensitive materials, and has demonstrated impressive results in enhancing the extraction efficiency of pectin.[77]

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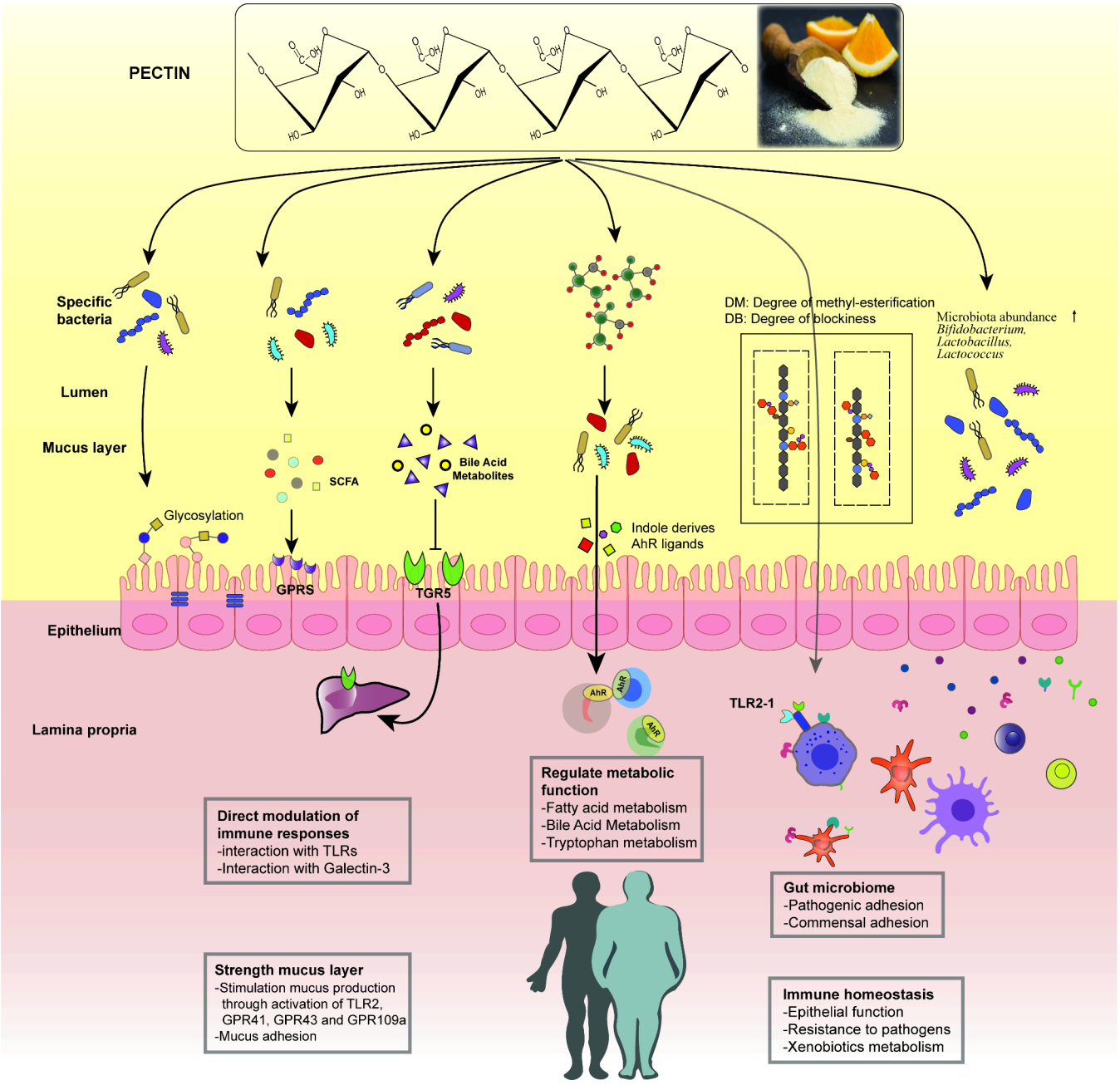

Figure 2. Possible ways in which the body's immunity can be affected when the body ingests pectin. The pathways in which pectin is directly involved in mediating immune responses include galectins and TLRs; indirect effects include stimulating microbial diversity (interfering with the adhesion of pathogens, etc.), stimulating glycosylation of mucins (strengthening the mucus layer, stimulating lymphocytes to produce IL-22), short-chain fatty acids (stimulate epithelial integrity and mucus secretion by binding to GPR41, GPR43, or GPR109a and participate in intestinal immune regulation), indoles (metabolites of tryptophan, which can act as AhR receptors ligands, stimulate and activate type III lymphocytes, promote intestinal health), and bile acid metabolites (bile acids can regulate blood sugar levels, cholesterol metabolism, and immune signaling by activating receptors in the liver and gut).

2.4.7. Enzymatic Assay. Enzyme-assisted extraction (EAE), also known as biological extraction, is a method that utilizes microorganisms or biological enzymes to break down the cell walls of plant materials under appropriate conditions, facilitating the release of natural products into the extraction medium. The general steps include adding an enzyme-containing buffer to ground raw materials, extracting and reacting in a constant temperature water bath shaker, followed by ethanol precipitation, filtration, separation, drying, and pulverization to obtain the finished product of pectin.[18] The advantages of biological extraction include a high extraction efficiency, almost no reverse reactions during the extraction process, and the ability to precisely control the quantity of biological enzymes used, better quality, and less solvent required. The disadvantages include the higher reaction time, the high cost of the enzymes, which prohibits their implementation by industries, and the variable results obtained due to enzyme strain differences.

Recently, Vasco-Correa et al. (2017) demonstrated that pectin could be extracted from fresh passion fruit peel using a

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crude extract of the fungal enzyme PPase-SE. The process achieved a high yield of 26% GalA of dried passion fruit peel, which was 40% higher than conventional chemical methods involving high temperatures and strong acids. The production of GalA is significantly affected by factors, such as temperature, pH, and enzyme load. To achieve the maximum yield, it is recommended to use 30 U/mL of raw pectinase-SE at a pH of 3.0 and a temperature of 37 °C.[78−80] Similarly, Gomashe et al. (2019) used *Trichosporon penicillatum* enzymes, which can produce protopectinase SE (PPase-SE), an endogalacturonase with pectin-releasing activity, to ferment orange peel substrate at 40 °C for 24 h, thus minimizing the cost of pectin production.[13] Additionally, Thibault et al. (1988) extracted a certain amount of pectin from citrus fruit using a complex enzyme containing endoarabinanase, endogalactanase, and a small amount of endopectate lyase that was activated at 30 °C and a 0.03 M sodium acetate buffer (pH = 5).[81]

2.4.8. Ultrasonic Method. Ultrasonic-assisted extraction is a clean, efficient, and environmentally friendly technology that can be completed in a few minutes and provides a final product of higher purity. The method utilizes ultrasonic waves to enhance the interaction between the medium and promote the dissolution of substances in plant tissues.[9] Compared to traditional acid extraction methods, this method has a shorter extraction cycle and needs less energy and solvent. However, excessive ultrasonic time can lead to overhydrolysis of the raw materials, resulting in an increase in the fragmentation of pectin molecules. On the other hand, if the time is too short, the pectin yield may be reduced. Karbuz et al. (2021) showed that during the extraction time from 15 to 45 min ultrasound waves caused an increase in the cavitational effect in the solvent medium, promoting the solvent penetration into the fruit peels and the release of pectin into the solvent, resulting in an increase in the pectin yield.[36] Beyond 45 min, modification and fragmentation of the pectin polysaccharide structure occurred, leading to a decrease in the pectin yield. Studies by Karbuz et al. (2021) show that the maximum pectin yield is obtained after 45 min at a temperature of 75 °C.[36] Kazemi et al. (2019) determined the optimal process conditions for extracting pectin from subskins as an ultrasonic power of 50 W and an ultrasonic time of 30 min, with a pectin yield of 33.64%.[82]

3. EFFECTS OF PECTIN ON GUT IMMUNITY

Pectin has been demonstrated to have various beneficial effects on mammalian health, including immune modulation, antitumoral effects, and antioxidant activities.

3.1. Regulation of the Intestinal Microbiota. Pectin exhibits the ability to withstand the conditions of the upper digestive tract, and upon reaching the colon, it optimizes the gut microbiota. This unique characteristic serves as the foundation for pectin's regulation of the gut microbiota[83] (Figure 2).

Pectin has been shown to promote the growth of certain beneficial microorganisms, such as those in *Clostridium cluster XIV*, *Clostridium butyricum*, and *Clostridium beijerinckii* groups. At the same time, it can inhibit the growth of harmful bacteria.[84−86] It has also been reported that pectin increases the abundances of *Faecalibacterium prausnitzii* and *Roseburia intestinalis* in the gut. These two species have been linked to positive effects on colon cancer and ulcerative colitis.[87] Pectin could increase the relative abundance of *Bifidobacterium adolescentis*, *Prevotella spp*,and *Bacteroides*. Acetate and butyrate, SCFAs derived from the fermentation of pectin in the gut, have been shown to enhance digestibility.[55] Probiotics may feed on pectin and produce secondary metabolites that inhibit the growth of nonprobiotic microorganisms. A study by Gómez et al. (2016) reported that pectic oligosaccharides isolated from sugar beet pulp and lemon peel waste increased the populations of *Bifidobacteria* and *Lactobacilli* by up to 34% and 29%, respectively.[88] Research has also indicated that highly methylesterified pectin from oranges and lemons can increase the colonization of *Bifidobacteria*,[89−91] *Lactobacillius*,[92,93] and *Lactococci*.[88,94] In contrast, low DE pectin is more easily metabolized by the body than high DE pectin,[95] with reports suggesting that high DE pectin stays in the gut for a longer duration of 24 h than low DE pectin.[88] In addition to its impact on the microbial population, pectin also exerts its gel-forming properties, promoting gut health and peristalsis, as well as facilitating the formation of feces through its water-binding activity.[96]

3.2. Regulation of Mucosal Immunity through Metabolites. The fermentation of dietary fiber into nutritious metabolites such as SCFAs is one of the important benefits that the gut microbiota provides to its host. Furthermore, pectin also effects the tryptophan metabolism as well as bile acid metabolism, which is important for many biochemical functions and overall health.

3.2.1. Effects of Pectin on Short-Chain Fatty Acid Metabolism. Pectin can increase the volume of chyme and accelerate the gastrointestinal motility. Unlike insoluble fibers such as cellulose, pectin is almost 100% fermented in the colon,[19] leading to the production of SCFAs.[97] SCFAs are the main energy source for colon cells and can lower colon pH, thus preventing colon cancer.[98] Soluble dietary fiber apple pectin, after fermentation by intestinal microbiota, produces SCFAs, among which propionic acid may inhibit histone deacetylase (HDAC) expression, reduces the release of pro-inflammatory cytokine IL-6, alleviates tissue inflammation, and assists in the treatment of ulcerative colitis.[99] Different genera can produce different SCFAs; for example, acetate can be produced by many genera' propionate is mainly produced by Bacteroidetes and Firmicutes; and butyrate is mainly produced by *Clostridium spp.* SCFAs bind to "metabolism-sensing" G protein-coupled receptors, such as GPR41, GPR43, and GPR109A, which promote the regulation of gut homeostasis and inflammatory responses[100] (Figure 2). GPRs and their metabolites affect Treg activation, epithelial integrity, gut homeostasis, dendritic cell activation, and the IgA antibody response. By inhibition of HDAC expression or function, SCFAs also affect gene transcription in many cells and tissues.

3.2.2. Effects of Pectin on Tryptophan Metabolism. The ingestion of pectin also affects tryptophan metabolism. Tryptophan is an essential amino acid for mammals and serves as a biochemical precursor for metabolites that significantly influence mammalian physiological functions, including gastrointestinal function, immune response, metabolism, and nervous system activity.[101] Studies have shown that pectin administration significantly increases the abundance of *Bacteroides*, which is capable of metabolizing tryptophan into indole derivatives.[102−104] Research conducted by Wrzosek et al. (2021) has demonstrated that supplementing pectin in the diets of mice leads to a significant reduction in fecal tryptophan levels and promotes tryptophan metabolism.[105,106] Moreover, pectin can reshape the gut microbiota of piglets, altering the

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direction of tryptophan metabolism and promoting the production of indole derivatives.[94,107]

3.2.3. Effects of Pectin on Bile Acid Metabolism. According to several studies, pectin can promote heart health by improving cholesterol metabolism[108−111] (Figure 2). In the liver, cholesterol is a precursor to bile acids. Apple pectin optimizes blood cholesterol levels by binding with bile acids in the small intestine.[112] As more bile acids are lost in the feces, more cholesterol is converted to bile acids, helping to optimize the blood cholesterol levels. Research shows that pectin lowers low-density lipoprotein cholesterol without affecting high-density lipoprotein cholesterol. As a soluble dietary fiber, pectin can lower cholesterol by 5% to 16% when the daily intake reaches 5 g.[113] However, there is also a different opinion, as Singh et al. (2018) suggest that long-term addition of soluble dietary fiber such as inulin or pectin to the diet of mice with dysregulation can lead to an abnormal bile acid metabolism, bile stasis, and eventually liver cell cancer.[114]

3.3. Pectin Can Interact Directly with the Mucosal Barrier. Before dietary fiber is degraded by microbiota in the hindgut, it also interacts directly with the immune barrier cells in the small intestine.[115] The small intestine has a thin and loose layer of mucus that not only facilitates nutrient absorption but also allows dietary fiber molecules to directly interact with intestinal epithelial and immune cells, contributing to the regulation of gut immunity[116] (Figure 2).

3.3.1. Pectin Directly Blocks the Toll-Like Receptor 2 (TLR2)-TLR1 Pathway. Research has demonstrated that in addition to recognizing dietary fibers through pattern recognition receptors (PRRs) pectin can also directly interact with the intestinal tract by inhibiting the binding of bacterial lipopolysaccharide to TLR2. TLR2 forms heterodimers with TLR1, and it is the prerequisite to recognize a wide spectrum of microbial pathogen-associated molecules, thereby blocking the TLR2−TLR1 heterodimer formation. Pectin can effectively inhibit TLR2−1-induced IL-6 response.[21] This indicates that pectin not only affects TLR2−1 signaling, but also has an inhibitory effect on the initiation of its downstream IL-6 secretion.[117,118] This inhibitory effect helps to prevent intestinal diseases that result from TLR2 activation, as TLR2 activation can exacerbate intestinal inflammation and produce certain cytokines that combat infection.[21] Moreover, the efficacy of pectin is related to its degree of methylation (DM), with low-DM pectin being more effective than high-DM pectin. Similar studies have shown that low-DM pectin can directly interact with TLR2−1 receptors through electrostatic forces, reducing Toll-like receptor-2 mediated immune activation and decreasing peri-capsular fibrosis in mice.[92,119] In summary, dietary fibers can reduce inflammatory responses by directly interacting with TLR2−TLR1 receptors in the intestinal tract.

3.3.2. Effect of Pectin on Glycosylation Modification of Intestinal Mucin. Glycosylation refers to the process of attaching sugar molecules to protein molecules and is an important regulatory pathway for cellular signal transduction, protein stability, and function.[120] As a dietary fiber, pectin has emerged as a new research area with regulatory effects on the glycosylation modification of intestinal mucosal proteins. Studies have demonstrated that pectin can regulate the expression of glycosylation-related genes, such as galectin and glycocalyx genes, and inflammation genes in intestinal epithelial cells, thus potentially preventing pathogen adhesion.[121] Moreover, pectin can also affect the structure and composition of the gut microbiota, leading to regulation of the glycosylation modification process in the intestine. Additionally, pectin can bind to specific proteins in the intestine and interfere with their glycosylation modification process, promoting the transformation of the O-glycosylation modification pattern of the jejunal mucosa to a Core 3 type glycan chain structure and affecting the expression of fucosyltransferase 2 (FUT2) and O-GlcNAcase (OGA). These research findings suggest that pectin has the potential to alleviate the damage caused by LPS stress to the piglet intestine by regulating the glycosylation modification pattern.[122]

4. REGULATORY ROLE OF PECTIN IN DISEASE MODELS

4.1. Inflammatory Bowel Disease. Inflammatory bowel disease (IBD) is a chronic and recurring condition that causes inflammation of the intestinal lining.[123] The two primary types of IBD, ulcerative colitis (UC) and Crohn's disease (CD), are characterized by their specific locations and patterns of inflammation within the digestive tract.[124] Pectin has shown promising results in the treatment of IBD through various mechanisms. Colitis is well-represented by the dextran sulfate sodium (DSS) model.[125] It is known that DSS is a negatively charged sulfated polysaccharide that can damage epithelial cells when taken orally. Afterward, nonspecific immune cells release cytokines that lead to inflammation of the colon.[126] A study by Fan et al. (2020) demonstrated that pectin was capable of downregulating myeloperoxidase (MPO) induced by DSS, alleviating inflammation-associated oxidative stress.[127]

Additionally, it has been discovered that pectin can improve the efficacy of fecal microbiota transplantation (FMT) by delaying the reduction of gut microbiome diversity in cases of UC. Pectin is currently being investigated as a potential carrier material for colon-specific drug delivery systems.[128] Further research has shown that pectin can promote the enrichment of beneficial gut bacteria (*Lactobacillus* and *Bifidobacterium*) and improve serum levels of glycerophospholipid phosphatidylcholine (PC) and phosphatidylethanolamine (PE). These were found to be increased after the pectin was added, and PC serves as barrier for intestinal epithelial cells and protects them from injury and the consequential inflammatory responses.[129] PE has recently been proven as an effective guardian of the epithelial permeability and intestinal homeostasis in DSS-stressed mice.[104,130,131] This suggests that the preventive effects of low-esterified pectin on DSS-induced colitis were likely initiated by the enrichment of probiotics in the gut and serum glycerophospholipids.[104] These findings have important implications for the treatment of IBD and highlight the potential of pectin as a therapeutic agent.

4.2. Type 2 Diabetes. Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder that primarily affects adults by inhibiting insulin action in the body, resulting in elevated blood glucose levels and damaging multiple organs.[132] Recent studies have brought attention to the potential preventive role of dietary fiber, particularly pectin, in the development of diabetes.[133] Research by Sánchez et al. (2008) showed that apple pectin effectively enhanced insulin resistance and improved insulin sensitivity in rats with metabolic disorders.[134] Additionally, administering pectin reduced the amount of triglycerides in the plasma and lowered total cholesterol and low-density lipoprotein cholesterol levels, suggesting that citrus pectin can reduce fasting blood glucose levels, improve hyperlipidemia, and enhance glucose tolerance and hepatic

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glycogen content in diabetic rats.[29] Studies have also revealed that pectin inhibits starch digestion, resulting in a lower absorption of glucose and decreased starch digestion rates.[135] The intake of fermented apple pectin has been found to suppress hyperglycemia-related enzyme activity, resulting in a 24% reduction in the concentration of glucose in the blood of diabetic rats.[136] Pumpkin flour with high starch and pectin content also depends on the complex network of pumpkin polysaccharides, with pectin acting as a barrier between amylase and starch during digestion.[137] These findings suggest that pectin has the potential to improve insulin resistance, reduce blood glucose levels, and enhance glucose tolerance in diabetic rats.[136] However, further research is needed to understand the underlying mechanisms and therapeutic applications of pectin in the prevention and treatment of T2DM.

4.3. Obesity. Obesity prevalence has increased dramatically during recent decades and is a global pandemic.

Numerous studies have established a positive correlation between high-fiber diets and improved glycemic control, as evidenced by the reduced absorption of glucose and cholesterol and a decrease in serum triglyceride levels.[137] Notably, specific dietary fibers have been observed to slow down the absorption of glucose and fatty acids from the upper small intestine, thus reducing the availability of substrates for triglyceride synthesis.[138] In the context of human consumption, pectin intake at a dosage of 15 g per day over a four-week period has been linked to a modest 3−7% reduction in blood LDL cholesterol levels.[139] Feeding pectin to high-cholesterol mice has been found to improve lipid distribution and reduce atherosclerotic plaque formation.[140]

Furthermore, as already mentioned, pectin can be fermented by microbiota in the colon to produce SCFAs.[94] Studies have shown that propionate can activate AMP-activated protein kinase (AMPK), which in turn inhibits acetyl-CoA carboxylase, leading to a reduction in lipid synthesis.[141]

Feeding hawthorn pectin to obese mice has been shown to decrease the expression of the farnesoid X receptor (FXR) in the small intestine and render the fibroblast growth factor 15 (FXR-FGF15) axis inactive, resulting in an upregulation of the rate-limiting enzyme CYP7A1 in the bile acid synthesis pathway. Additionally, the levels of apical sodium-dependent bile acid transporter (ASBT) in the small intestine were found to be increased.[142] This suggests that pectin may act as a competitive inhibitor of ASBT, which could lead to inhibition of ileal bile acid reabsorption and improvement in cholesterol metabolism.[143]

In 2010, the European Food Safety Authority (EFSA) acknowledged that the intake of pectin can effectively mitigate postprandial glycemic responses.[144] This assertion is substantiated by numerous subsequent studies. Notably, an in vivo investigation on diabetic rats revealed the hypoglycemic potential of low-methoxyl pectin (35%) and high molecular weight (1.6 × 105 g/mol) pectin extracted from passion fruit (*Passiflora edulis*). The study further ascertained that this pectin did not have any adverse impact on the liver, kidney, and pancreas.[145] In another study, Makarova et al. (2015) evaluated the glucose metabolism of healthy volunteers who consumed pectin-rich apple powder and found that it led to an increase in the excretion of glucose in urine.[146]

4.4. Cardiovascular Disease. Cardiovascular disease (CVD) refers to a group of diseases that affect the heart and blood vessels, such as coronary heart disease, hypertension, heart failure, and arrhythmia.[147] CVD can cause vascular obstruction, myocardial ischemia, and myocardial infarction, which can be life-threatening.[148] Pectin can prevent cardiovascular disease by regulating the bile acid metabolism, as already mentioned. Studies have shown that pectin can reduce the intestinal reabsorption of bile acids, promote their excretion in feces, and thus hinder the enterohepatic circulation of cholesterol, reducing the concentration of total cholesterol in the serum.[149]

Citrus dietary fiber has good cation exchange capacity, which can exchange with Na+ and K+ in the gastrointestinal tract and promote the excretion of Na+ and K+ in urine and feces, thus lowering the Na+/K+ ratio in the blood and playing a role in lowering blood pressure. Furthermore, pectin can also break down and decompose lipids, reduce lipid absorption, and thus prevent the occurrence of cardiovascular disease.[150]

Studies have also shown that pectin can significantly downregulate TLR4 expression by acting on Gal-3. Since TLR4 is known to cause myocardial infarction, interstitial fibrosis, and myocardial hypertrophy,[151] downregulating TLR4 expression is preferable. Due to the administration of pectin, a reduction in oxidative stress and myocardial hypertrophy was observed in rats.

4.5. Prevention of Cancer. Cancer is a disease caused by the abnormal growth and division of cells, and it is one of the primary causes of death worldwide.[152] Traditional treatment methods for cancer include surgery, radiation therapy, chemotherapy, and targeted therapy. However, recent research has brought attention to the potential of pectin in improving cancer outcomes.

Citrus fiber, for example, has been found to prevent various types of cancer, such as prostate, colon, breast, and ovarian cancer. This is due to its water-holding and oil-holding properties that promote bowel movement, reduce transit time, increase stool mass and volume, and reduce the concentration of carcinogens in the intestine.[153,154] Studies have shown that consuming 25 g of citrus dietary fiber per day for more than 2 weeks can increase stool volume by 33%, decrease intestinal transit time by 21%, and dilute carcinogenic concentrations in the intestine, contributing to the prevention of colon cancer.[153]

Moreover, citrus dietary fiber can inhibit cancer cell proliferation and metastasis by regulating the expression of galactose lectin-3, which promotes cancer cell regulation.[150] Inhibiting galactose lectin-3 expression and thus reducing the survival of macrophages in a hypoxic environment has been found to inhibit the development of mammary carcinoma in mice.[155] Citrus fiber has also been found to inhibit the metastatic ability of cancer cells, preventing cancers such as prostate, ovarian, and gastrointestinal tract cancers. Pectin also reduces activator protein 1 (AP-1) and NF-κB signaling[156] and inhibits the expression of the galactose lectin-3 protein, which is known to be a potential mediator of cancer cell adhesion, migration, and invasion. Citrus pectin and apple pectin have been found to not only inhibit the development of breast cancer cells in the S and G1 phases of the cell cycle but also reduce the expression of the cell adhesion, cycle, and death-related lectin Gal-3.[157] Pectin guar gum zinc oxide nanocomposites could increase the expression of pro-inflammatory cytokines and lead to increased mortality of cancer cells.[158]

Finally, low molecular weight citrus pectin has been found to suppress intestinal cancer cell proliferation and metastasis by downregulating the expression of B-cell lymphoma-extra-large (Bcl-xL) and cyclin B, as well as inhibiting the epithelial−

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mesenchymal transition (EMT) process, thus preventing stomach cancer.[159,160]

In summary, citrus fiber and pectin have shown promising potential in preventing various types of cancer through different mechanisms, such as inhibiting cancer cell proliferation, metastasis, and angiogenesis. Further research is necessary to fully understand the extent of their effectiveness and their potential applications in cancer prevention and treatment.

5. CONCLUDING REMARKS AND FUTURE PERSPECTIVES

In this review, we summarize the preparation of pectin and its potential use as a functional food or feed additive for both human and animal health. Pectin has the ability to reduce the abundance of potentially pathogenic bacteria by promoting the proliferation of beneficial microorganisms in the gut. Moreover, pectin can regulate intestinal homeostasis by promoting the production of microbial-derived metabolites such as short-chain fatty acids, bile acids, and tryptophan metabolites. It also exhibits anti-inflammatory and immunomodulatory effects, influencing inflammation and tumor development by directly acting on pattern recognition receptors such as TLR2−1 and TLR-4 to regulate the body's immune response. However, several bottlenecks still exist in the preparation and application of pectin. One crucial aspect requiring attention is the need to further explore and clarify the structure−activity relationship of pectin. Currently, there are differences in the composition of pectin from different batches and sources, including HG, RGI, and RGII. Understanding how these structural differences influence the functional properties of pectin is essential for optimizing its applications. Additionally, pectin, as a typical acidic and easily fermentable dietary fiber, serves as a valuable nutrient source for microorganisms in the hindgut, promoting the proliferation of beneficial bacteria and contributing to improved gut health. Moreover, pectin plays a role in the development of goblet cells and pattern recognition receptors in the mucosal barrier of the foregut, further supporting gut health. However, to fully harness its potential, more research is needed to elucidate the specific molecular regulation mechanisms of pectin in the foregut. Advancements in these research fields will not only enhance our understanding of pectin's functionality but also contribute to its application value in various areas, including the prevention and treatment of human diseases and its potential benefits in animal production.

■ ASSOCIATED CONTENT

Data Availability Statement

No data were used for the research described in the review.

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Notes

The authors declare no competing financial interest.

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■ ABBREVIATIONS

AE, Acid extraction; AMPK, AMP-activated protein kinase; AP-1, Activator protein 1; ASBT, Apical sodium-dependent bile acid transporter; Bcl-xl, B-cell lymphoma-extra-large; CD, Crohn's disease; CVD, Cardiovascular disease; DM, Degree of methylation; DPPH, 2,2-Diphenyl-1-picrylhydrazyl; DSS, Dextran sulfate sodium; EAE, Enzyme-assisted extraction; EFSA, European Food Safety Authority; EMT, Epithelial-mesenchymal transition; FMT, Fecal microbiota transplantation; FUT2, Fucosyltransferase 2; FXR, Farnesoid X receptor; HDAC, Histone deacetylases; HG, Homogalacturonan; HIPEF, High intensity pulsed electric field technique; IBD, Inflammatory bowel disease; IEP, Ion exchange process technique; MAE, Microwave-assisted extraction; MPO, Myeloperoxidase; OGA, O-GlcNAcase; OH, Hydroxy radical; PC, Phosphatidylcholine; PE, Phosphatidylethanolamine; ppase-SE, Protopectinase SE; PRRS, Pattern recognition receptors; RG-I, Rhamnogalacturonan I; RG-II, Rhamnogalacturonan II; SCFAs, Short-chain fatty acids; T2DM, Type 2 diabetes mellitus; TLR2, Toll-like receptor 2; UC, Ulcerative colitis; XGA, xylogalacturonan

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