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Pharmaceutical Applications of Pectin

Olufunke D. Akin-Ajani and Adenike Okunlola

Abstract

Pectin, a natural ionic polysaccharide found in the cell wall of terrestrial plants undergoes chain–chain association to form hydrogels upon addition of divalent cations. Based on its degree of esterification, pectin has been classified into two main types. The high methoxyl pectin with a degree of esterification greater than 50%, which is mainly used for its thickening and gelling properties and the low methoxyl pectin, which is widely used for its low sugar-content in jams, both applications being in the food industry. Pectin is mostly derived from citrus fruit peels, but can also be found in other plants such as waterleaf leaves, cocoa husk, and potato pulps. Pectin has been used as an excipient in pharmaceutical formulations for various functions. This chapter will focus on the various applications to which pectin has been used in the pharmaceutical industry.

Keywords: Pectin, Degree of Esterification, Drug Delivery, Polymer Matrix, Excipients

1. Introduction

In the pharmaceutical industry, plants and plant products are continually used as sources of drugs and excipients. In particular, plant-derived polymers have contributed significant roles in drug delivery systems where they function as excipients [1]. Excipients refer to the non-pharmacological ingredients that are required to convert the Active Pharmaceutical Ingredient (API) into a dosage form. The International Pharmaceutical Excipients Council (IPEC, 1995) defines excipients as all substances contained in a dosage form other than the active substance or finished dosage form, which have been appropriately evaluated for safety and are included in a drug delivery system [2]. Excipients are included in drug delivery systems to assist in processing during manufacture, protect, support, enhance stability, bioavailability and patient acceptability, help in product identification, or enhance any other aspects of the drug delivery system's overall safety and effectiveness during use or storage [2–4]. Far from being just a random combination of ingredients, a pharmaceutical formulation is a well-rationalized formulation designed to satisfy quality and performance. Excipients are essential in the drug development process, as well as the formulation and administration of stable dosage forms [2]. Excipients are required in drug formulations to guarantee the potency, safety, predictability and reproducibility of the release of the API as well as its palatability and suitability for the patients [3].

The interest in excipients of plant origin over semi-synthetic or synthetic excipients is not far-fetched: low toxicity, relative abundance, cost-effectiveness

and non-irritant nature make them preferable to others sources [5]. Plant-based polymeric excipients can be used in different pharmaceutical formulations where they act as diluents or bulking agents, thickeners, binders, disintegrants, suspending agents, emulsifiers, film formers, matrix formers, release modifiers, sweeteners and mucoadhesive polymers [6–9]. These natural polymers would have to fulfill the requirements of an ideal excipient to be successful candidates for use as excipients in various formulations for pharmaceutical use. The requirements for an ideal excipient includes being pharmacologically inert, non-toxic and non-irritant as well as being non-reactive with drug or with other substances present in the formulation and the packaging. In addition, they must be easy to handle, cost-effective and readily available for the sustainable manufacture of the pharmaceutical product. Numerous plant polymers fulfill many of these requirements and have found application in pharmaceutical formulations. These include Inulin; a polysaccharide obtained from plant sources like; onion, garlic, artichoke and chicory, starches which are polymeric carbohydrates with large glucose units joined by glycosidic bonds, gums, and mucilage such as: acacia gum, tragacanth gum, locust bean gum, okra mucilage, seaweed polysaccharides which include carrageenan, agar and alginates, microbial polysaccharides such as: xanthan gum and pullulan obtained by the fermentation of carbohydrate products by specific bacteria or fungus, and polysaccharides of the plant cell wall with cellulose, hemicelluloses, pectin being the main polymers of this group [10–16].

Pectin, a structural heteropolysaccharide, is considered the second most abundant component of the cell wall of all terrestrial plants [17, 18]. It is a hydrophilic polymer that is biodegradable, biocompatible and non-toxic, making it a good biomaterial for packaging, coating and various pharmaceutical applications. Pectin is normally produced during the initial stages of growth of the primary cell wall and constitutes about one-third of the dry substance of the cell wall of some monocotyledonous and dicotyledonous plants [19]. A white to light brown powder, pectin is found in numerous fruits and vegetables. The main raw materials for pectin production are dried citrus peels or apple pomace, both by-products of juice production that are often discarded as waste. Alternative sources of pectin extraction include sugar beet waste from sugar manufacturing, mango waste from mango canning factories and sunflower seeds used for extracting edible oil, waterleaf leaves, cocoa husk, and potato pulps [20–23].

Pectin is the methylated ester of polygalacturonic acid which contains 1, 4-linked α-D-galacturonic acid residues and a variety of neutral sugars like arabinose, galactose, rhamnose and lesser amounts of other sugars [24, 25]. It can be classified into different types based on the degree of esterification or the number of methoxy groups that substitutes the carboxylic acid moiety on the galacturonic acid residues [26]. The degree of esterification influences the gelation mechanism, processing conditions and properties of the pectin [18, 27]. High methoxyl pectin is primarily used for gelation and has a degree of esterification greater than 50%. It requires a large amount of sugar and is acid-sensitive. Because of hydrogen bonding and hydrophobic interactions between the pectin chains, high methoxyl pectin forms a gel at low pH and a high concentration of soluble particles [28]. Low methoxyl pectin has a degree of esterification of less than 50% and is widely used in the food industry to form low sugar jams since it does not require a large amount of sugar for gelation. It shows less sensitivity toward acidity and requires Ca^{2+} ions to form gel [29]. Low methoxyl pectin is generally formed by the de-esterification of high methoxy pectin using acids, alkali, pectin methylesterase and ammonia in alcohol or concentrated aqueous ammonia. Monovalent cation i.e. alkali metal salts of pectin is normally soluble in water while di- and trivalent cations are partially or completely insoluble in water. When dissolved, pectin decomposes rapidly by

de-esterification or depolymerization. The rate of decomposition depends on the pH and temperature of the solution. The maximum stability of pectin is at pH 4 [30]. Low pH and high temperature increase the rate of degradation due to hydrolysis of the glycosidic linkage. At alkaline pH, pectin is rapidly de-esterified and degraded even at room temperature [31].

In this Chapter, the sections that follow would review in detail, some important pharmaceutical applications of pectin and possible modifications to enhance the future uses of pectin in pharmaceutical formulations.

2. Pharmaceutical uses of pectin

2.1 Drug delivery systems

The polymer pectin has been put to several uses since its discovery over 200 years ago. Though its major application has been in the food industry where it has been used as a gelling agent, emulsifier, stabilizer, thickener, and more recently as a food packaging material, where they as used as edible films on fruits and vegetables etc. The most important use of pectin is based on its ability to form gels, hence its potential as an excipient; pectin has been used as a binding agent [32, 33] in tablets, carrier for drug delivery to the gastrointestinal tract from matrix tablets, and as a controlled-release matrix in tablet formulations [34–36]. It has also been used as a sustained release drug delivery system in gel beads prepared by the ionotropic gelation method [19, 37, 38], colon-specific drug delivery vehicle [39], and film-coated dosage forms. Gel formation is caused by hydrogen bonding between free carboxyl groups on the pectin molecules and between the hydroxyl groups of neighboring molecules [40]. Most of the unesterified carboxyl groups in pectin occur as partially ionized salts in a neutral or very slightly acid dispersion of pectin molecules. [41]. Those that are ionized produce a negative charge on the molecule, which together with the hydroxyl groups causes it to attract layers of water [38]. Because of their negative charge, the repulsive forces between these groups can be strong enough to preclude the creation of a pectin network. When acid is added, the carboxyl ions are converted to mostly unionized carboxylic acid groups [38]. The attraction between pectin and water molecules is lowered by a reduction in the number of negative charges, which also lowers the forces of repulsion between pectin molecules. Sugar further decreases the hydration of the pectin by competing for water [41]. These conditions decrease the ability of pectin to stay dispersed. When cooled, the unstable dispersion of less hydrated pectin forms a gel, a continuous network of pectin holding the aqueous solution. High methoxyl pectin produces gels with sugar and acid. Unlike Low methoxyl pectin, high methoxyl pectin does not contain sufficient acid groups to gel or precipitate with calcium ions, although other ions such as aluminum or copper cause precipitation under certain conditions [25]. The degree of esterification (DE) affects the rate at which gel formation takes place [38]. A higher DE causes a more rapid setting. Slow-set pectins (with DE 58–65%) gel at lower soluble solids and greater levels than rapid-set pectins (DE > 72 per cent). Low methoxyl pectins require the presence of divalent cations (usually calcium) for proper gel formation [38].

2.2 Bioadhesive systems

The ability of pectin to absorb water, swell and form bioadhesive bonds with biological tissue has found application in the preparation of mucoadhesive formulations such as patches [42]. Pectin has also been found useful as a demulcent in

Brand Name	Ingredients/strength	Dosage form	Manufacturer
Berry Breezer Throat Drop	7 mg/1	Lozenge	Topco Associates USA
Burts Bees Throat Soothing	10.5 mg/1	Lozenge	L. Perrigo Company USA
CVS Clean Label Throat Relief Pops	12 mg/1	Lozenge	CVS Pharmacy USA
Grape Throat Relief Lollipop	10 mg/1	Lozenge	Topco Associates USA
Little Remedies Sore Throat Pops	5.4 mg/1	Lozenge	Medtech Products Inc. USA
Ludens Assorted Flavors	2.8 mg/1	Lozenge	Prestige Brands Holdings, Inc. USA
Sundown Honey Soothers Lollipops	0.1 g/100 g	Lozenge	The Nature's Bounty Company USA
Throat Coat Lemon Ginger Echinacea	5 mg/4.2 g	Lozenge	Traditional Medicinals, Inc. USA
Axcel Kaopec Suspension	Pectin (20 mg/5ml) + Kaolin (1 g/5ml)	Suspension	Kotra Pharma (M) Sdn. Bhd.
Benylin DM With Pectin Freezer Pops	Pectin (150 mg/unit) + Dextromethorphan hydrobromide (7.5 mg/unit)	Liquid	Mcneil Consumer Healthcare Division of Johnson & Johnson Inc
Cepacol Sore Throat and Coating	Pectin (5 mg/1) + Benzocaine (15 mg/1)	Lozenge	Reckitt Benckiser
Cepacol Sore Throat Plus Coating	Pectin (5 mg/1) + Benzocaine (15 mg/1)	Lozenge	Combe Incorporated
Diaret Liq	Pectin (150 mg/30 mL) + Kaolin (3.078 g/30 mL)	Liquid	Produits Francais Labs Inc. Canada
Diaret Tab	Pectin (45 mg/tab) + Aluminum hydroxide (70 mg/tab) + Attapulgite (350 mg/tab) + Zinc phenolsulfonate (30 mg/tab)	Tablet	Produits Francais Labs Inc. Canada
Diban Cap	Pectin (71.4 mg) + Atropine sulfate anyhdrous (9.7 mcg) + Attapulgite (300 mg) + Hyoscyamine sulfate (0.0519 mg) + Opium (12 mg) + Scopolamine (3.3 mcg)	Capsule	Wyeth Ayerst Canada Inc.
Orabase Paste	Pectin (13.3%) + Carboxymethylcellulose sodium (13.3%) + Gelatin (13.3%)	Paste	Convatec Inc.
Organix Complete	Pectin (1.7 mg/1) + Levomenthol (2.5 mg/1)	Lozenge	Pro Phase Labs, Inc.
Herbon Berry Buddies	Pectin (10 mg/1) + *Echinacea purpurea* (50 mg/1)	Lozenge	Purity Life Division of SunOpta

Table 1.
Some commercial drug products containing pectin.

throat lozenges where it gives temporary relief for minor discomfort and protects irritated areas in sore mouth and sore throat [43]. The antihemorrhagic effect of pectin has also been utilized in wound healing as medical adhesives [44].

2.3 Disperse systems

Pectin has been shown to have foam stabilizing and emulsification potential since the protein and hydrophobic acetyl groups of pectin can act as anchors on the oil particle surface, thus decreasing the surface tension [45]. Other areas of use have been as an emulsifier in oil: water emulsions [46, 47], and as a viscosity enhancer in lipid digests [48]. Pectin slows gastric transit thus helps control energy intake and hence its use by weight-watchers, since the large water-binding capacity of pectin reduces contact between intestinal enzymes and food, thus prolonging gastric emptying half-life, allowing a marked reduction in quantity and frequency of eating [49]. Furthermore, its interaction with polyphenolic compounds leads to systemic anti-inflammation [50].

2.4 Health benefits

In the pharmaceutical industry, pectin has been used both for its health benefits and as an excipient. Pectin as an active agent was formerly used in diarrhea mixtures, in conjunction with kaolin and sometimes bismuth compounds, and in wound dusting powders and ulcer dressings where pectin appears to have some specific activity in promoting healing [25]. It has been found to have certain health benefits such as reducing cancer development, lowering blood cholesterol and blood glucose level through the different domains of the pectin structure, and stimulating the immune response [51–55].

2.5 Other applications

Pectin's application has spread to water treatment where it is used as a biosorbent to remove heavy metals [47] and in urinary excretion of toxic minerals such as lead, cadmium, strontium, or arsenic [56–58]. In cosmetics, it is used as a plasticizer, texturizer and adhesive [59], and in biomedical applications, where it is used as a biomaterial ink to fabricate patient-specific scaffolds when cross-linked with 3-glycidyloxypropyl trimethoxysilane (GPTMS) [60]. Some examples of drug products that contain pectin are presented in **Table 1**.

3. Material properties of pectin

Pectin is an important biomaterial that has numerous pharmaceutical applications. Its application, however, largely depends on its material properties such as degree of esterification (DE), degree of blockiness (DB), ash value and solubility. This section will focus on these properties and how each affects the application of pectin pharmaceutically.

3.1 Degree of esterification

The DE of pectin is the ratio of esterified D-galacturonic acid (GalA) groups to total GalA groups [34, 61]. Depending on the species, tissue, and maturity of the plant, the DE can have a wide range. In general, the structure of pectin is mostly composed of homogalacturonan (HG), regions (partially 6-methylated and

2- and/or 3-acetylated poly-α(1–4)-D-galacturonic acid residues), alternating with rhamnogalacturonan I (RG-I), regions (branched α(1–2)-L-rhamnosyl-α(1–4)-D-galacturonosyl chains substituted with side chains of mainly α-L-arabinofuranose and α-D-galactopyranose) [18, 62]. The interconnection of HG "smooth" (responsible for the gelling capability) and RG-I "hairy" (play a gel-stabilizing role) regions, in relative proportions determine the flexibility and rheological properties of the polymer in solution [63, 64]. The gelling mechanism of pectin is dictated by its degree of esterification (total methoxyl content) [65]. Pectin based on the DE can be classified as high methoxyl (HM) pectin with DE > 50% or low methoxyl (LM) pectin DE < 50%, which are either the conventionally demethylated or the amidated molecule [66–68]. The two groups of pectin gel by different mechanisms. To form gels, high methoxyl pectin requires a minimum amount of soluble solids and a pH of around 3.0.

HM pectins are generally hot water-soluble, thermally reversible, and often contain dextrose (a dispersion agent) to prevent lumping. Conversely, LM pectins produce gels independent of sugar content, are less sensitive to pH compared to the HM pectins, and require the presence of a controlled amount of calcium or other divalent cations for gelation [41].

The specific application to which pectin will be put is a function of its gelling behavior, which is dependent on its DE, the monosaccharide content (HG), and the spatial disposition of the cross-linking blocks (RG) [69]. While HM pectins have been used in tablet formulations as a binder, controlled-release matrix and taste masker through complexation with bitter molecules, the LM pectins have been used as sustained-release matrices in microspheres produced by ionotropic gelation [19, 53, 69].

3.2 Degree of blockiness

Pectin, an anionic cell wall polysaccharide through its non-methyl esterified galacturonic acid units, interacts with divalent cations [40, 47]. At pH values above the pKa of pectin (2.8 to 4.1), non-methyl esterified GalA residues can be negatively charged, giving pectin the ability to interact with cations [34, 70]. Thus, the lower the DE of pectin, the higher the number of non-methyl esterified GalA residues present, the higher the cation-binding capacity. Due to LM pectin's higher number of negatively chargeable carboxyl groups (non-methyl esterified carboxyl groups) compared to HM pectin, it exhibits a higher charge density, further showing that the cation-binding capacity of pectin increases with decreasing DE [40, 70, 71]. Studies have shown that regardless of the method used, a stronger and higher bound interaction occurs between pectin with decreasing DE and cations (Fe^{2+}, Zn^{2+}, or Ca^{2+}) [47]. Furthermore, the DE and the intramolecular distribution of the non-methyl esterified carboxyl groups within the pectin determine pectin's anionic nature and associated functionality [72, 73]. Interestingly, less described in the literature is the influence of the distribution pattern of non-methyl esterified GalA units on the cation-binding capacity of pectin compared to DE [47].

Daas et al. first quantified the relative occurrence of blocks of non-methyl esterified GalA units within a pectin chain as the degree of blockiness, DB [47, 74]. Apart from the DB, the absolute number of non-methyl esterified GalA units present in blocks can be expressed as the absolute degree of blockiness (DB_{abs}). Both parameters (DB and DB_{abs}) were established by exhaustive enzymatic degradation of pectin using endo-polygalacturonase (endo-PG) of *Kluyveromyces fragilis*, which required at least four consecutive non-methyl esterified GalA units to hydrolyze the linkage between two non-methyl esterified GalA units [70]. The DB is the proportion of galacturonic acid units (mono-, di-, and tri-) released by the enzyme to the total amount of non-methyl esterified GalA units, while DB_{abs} is the number of

GalA oligomers released in the endo-PG digest to the total number of GalA units in the pectin polymer, without adjustment of the DE [47, 74, 75]. Thus, to characterize the presence of blocks of non-methyl esterified GalA units, these parameters (DB and DB_{abs}) are used [70]. For most of the cations (divalent cations), the binding between them and pectin is known to follow the egg-box model [47]. The egg-box model of ´binding was mainly described for pectin-Ca^{2+} binding but assumed to be applicable for interaction between pectin and other divalent cations [76]. However, Assifaoui et al. [77] reported that the egg-box model was more appropriate for Zn^{2+} binding than Ca^{2+} as they found that Zn^{2+} interacts with both carboxyl and hydroxyl groups, comparable to the egg-box model, whereas Ca^{2+} binds only via carboxyl groups [40]. This egg-box model yields stronger gels [78, 79].

Applications to which a high DB is required would thus mean high cation-binding capacity and hence the use of LM pectins and the converse is true.

3.3 Ash value

The ash content of pectin is a valuable tool in determining the purity as well as the gel-forming capability of the polymer. The ash content of pectin has been found to increase as the yield of pectin decreases [80]. High levels of ash in pectin may be caused by elevated concentrations of negatively charged carboxylic groups of pectin and the counterions in solution during pectin precipitation [41]. However, for gel formation, low ash content ($\leq 10\%$) is a more favorable criterion as this will aid in determining the applicability of the polymer [47, 81, 80]. Ash content along with the anhydrouronic acid value of pectin has also been used to determine its purity [82, 83].

3.4 Solubility

Pectins are soluble in pure water. The solubility appears to depend on the valency of the cation salt; monovalent cation salts of pectin and pectic acids are usually soluble in water, while the di- and trivalent cation salts are weakly soluble or insoluble in water. Dry powdered pectin hydrates very rapidly when added to water, but tends to form clumps. These clumps are semidry packets of pectin within a highly hydrated outer coating. Dry mixing the powder with water-soluble carrier material can prevent the formation of clumps or by the use of specially treated pectin that has improved dispersibility [20, 83]. Studies have shown that pectin extracted with distilled water showed a high yield and low ash content when compared to other solvents [79]. High ash content and the drying process of the extracted pectin, however, may reduce the solubility of pectin [47]. It has been shown too that a decrease in the esterified carboxylic group reduced the solubility of extracted pectin; this insolubility of the extracted pectin is probably due to the presence of electrolytes in de-methylated pectic acid [47]. Thus, pectins with lower DE are less hydrophilic [69].

Dilute pectin solutions are Newtonian in behavior but at a moderate concentration, they exhibit the non-Newtonian, pseudo plastic behavior characteristics. Solubility, viscosity, and gelation are generally related. Whatever factors increase gel strength will increase the gelling tendency, viscosity, decrease solubility, and vice versa [84].

3.5 Antioxidant activity

Another property of pectin that could affect its application is its antioxidant activity. However, there are limited studies to show how this property may be applied to either the food industry or the pharmaceutical sector [85].

4. Modifications of pectin for future applications

The presence of several hydroxyl and carboxyl groups distributed along its backbone as well as a certain amount of neutral sugars presented as side chains gives pectin the capability of producing a broad spectrum of derivatives with modified or new functional properties. Various methods used for pectin modification include substitution (alkylation, amidation, quaternization, thiolation, sulfation, oxidation, etc.), chain elongation (cross-linking and grafting) and depolymerization (chemical, physical, and enzymatic degradation). Saponification (a process catalyzed by mineral acids, bases, salts of weak acids and primary aliphatic amines) can also be used to modify pectin chemically. Modification induced by pH changes can produce new fragments that have their solubility and biological activities altered [86]. Enzymatic modification of pectin has been achieved by using endo-polygalacturonase (Endo-PG), resulting in highly selective and specific structural changes in the polymer backbone. This modification leads to the cleavage of glycosidic linkages between two non-esterified α-D-galacturonic acid residues inside the HG fragment, which is depolymerisation. The enzymatic modification method can alter the macromolecular structure of pectin and can yield modified pectin with newer and improved properties and functionalities [87].

A new hydrolyzed polyacrylamide-graft-sodium alginate (PAAmg-SA) and diclofenac sodium-loaded interpenetrating polymer network (IPN) beads of pectin were developed using the ionic gelation method. The results of the investigation verified that hydrolyzed PAAm-g-SA and pectin cross-linked with aluminum ion (Al^{3+}) and glutaraldehyde could form an optimal matrix material for the production of IPN beads to support the sustained release of diclofenac sodium [88]. In another study, for the nasal administration of tacrine hydrochloride (an anti-Alzheimer drug), mucoadhesive microparticles based on chitosan/pectin polyelectrolyte complexes were prepared. The microparticles were produced by spray drying followed by lyophilization and direct spray drying. The study thus demonstrated the potential of the chitosan/pectin polyelectrolyte complexes to function variously in mucoadhesive microparticles [89, 90]. The chitosan/pectin molar ratio influenced the water uptake and tacrine hydrochloride permeation [90, 91].

Emerging advanced manufacturing technology in the field of tissue engineering and pharmaceutical formulations is the use of 3D bioprinting technology. 3D printing is an additive manufacturing technology in which objects are constructed in a layer-by-layer manner achieved by heat fusion, ultraviolet light (UV), and chemical bonding [91]. Spritam®, a fast disintegrating orodispersible tablet containing levetiracetam for epilepsy was the first 3D printed drug product approved by the US Food and Drug Administration (FDA) in 2015 [91]. To sustain the manufacturing of these types of drugs using this new technique, biomaterials that are green and non-toxic, derived from renewable sources and can be processed through 3D bioprinting are being developed [42, 60]. Common techniques include powder bed printing, vat polymerization (VP), and fused deposition modeling (FDM) [92]. A major disadvantage of the FDM technology is the need to insert printing materials into a nozzle in the form of a solid filament, which is non-existing for many pharmaceutical materials, thus necessitating the transformation of pharmaceutical-grade materials, including active pharmaceutical ingredients (API), into FDM-suitable filaments using techniques like hot-melt extrusion (HME). However, thermolabile therapeutics are not suitable for extrusion via FDM, due to potential degradation concerns [93]. The use of bio-inks for extrusion-based bioprinting at room or body temperature has shown clinical potential in achieving personalized treatment [92]. For example, Long et al. developed a personalized 3D printed wound dressing composed of chitosan and pectin with the ability to

control dimensional properties such as thickness and pore size using an extrusion-based bioprinter [91, 92], while allowing for facile lidocaine incorporation for immediate pain relief [94]. Pectin from citrus peels has also been cross-linked with (3-glycidyloxypropyl)trimethoxysilane (GPTMS) through a one-pot procedure to obtain freeze-dried porous pectin sponges with varying porosity, water uptake, and compressive modulus [42]. The addition of GPTMS improved the printability of pectin due to an increase in viscosity and yield stress [95]. Without the use of any additional support material, three-dimensional woodpile and complex anatomical-shaped scaffolds interconnected with micro and macro pores were, therefore, bioprinted [96]. Thus showing the great potential of pectin cross-linked with GPTMS as biomaterial ink to fabricate patient-specific scaffolds that could be used to promote tissue regeneration *in vivo* [42]. In another study, gelatin, another natural biopolymer has had its rheological properties improved to aid its bio-printing performance by using pectin as a rheology modifier of gelatin and GPTMS as a gelatin-pectin crosslinking agent [95]. Pectin played a key role in increasing the viscosity and the yield stress of low viscous gelatin solutions as shown through investigation of the rheological properties, as well as bioprinting assessments [96]. Water stable, three-dimensional, and self-supporting gelatin-pectin-GPTMS scaffolds with interconnected micro- and macro- porosity were successfully obtained by combining extrusion-based bioprinting and freeze-drying which did not require any additional temperature control to further modulate the rheological properties of gelatin solutions [95]. Patient-centric dosage forms have been produced through additive manufacturing techniques, which enable its design with precise control over dimension and microstructure, factors that are known to ultimately play key roles in modulating drug release kinetics, a feat not achieved through compression; traditional manufacturing techniques [92, 96, 97].

5. Conclusions

Pectin over the years has "metamorphosed" from just being a gelling agent for the production of jam and confectionaries to a biomaterial with health benefits to being useful as an excipient in drug delivery systems and more recently even personalized 3D printed medicine. This is as a result of a better understanding of its structure, mechanism by which it gels, and its properties such as degree of esterification and degree of blockiness, which has aided its classification and application.

The pharmaceutical industry has a material that can be explored in different functional dimensions as the usefulness and functionality of pectin unfolds.

Conflict of interest

The authors declare no conflict of interest.

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