Pectin: New science and forthcoming applications of the most valued hydrocolloid

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A B S T R A C T

From first-hand understanding of pectin molecular structure and physiological effects up to new production methods and applications, significant insightful knowledge of pectin polysaccharide and pectin-derived oligosaccharides has emerged in the last decade (2010–2020). These developments open the route to new and unexpected applications of this uniquely complex heteropolysaccharide ubiquitous in plants and fruits, well beyond its traditional use as food hydrocolloid. This study provides a unified perspective on the new science and technology of pectin and its extraction by-products. Furthermore, we offer an insight into forthcoming pectin uses from an expanded perspective, taking into account selected technology and economic factors that we believe will shortly impact the pectin production and uptake in many countries.

1. Introduction

Abundant in the cell wall of non-graminaceous plants and fruits (more abundant in the pericarp) where it acts as glue facilitating cell adhesion and separation (BouDaher and Braybrook Siobhan, 2015) but also modulates cell growth and shape (Yang et al., 2020), pectin is nature's structurally most complex polysaccharide. The molecule is a galacturonic acid polymer comprising homogalacturonan (HG), rhamnogalacturonan-I (RG-I), rhamnogalacturonan-II (RG-II), arabinogalacturonan (AG), and xylogalacturonan (XGA) regions. Approximately, the polymer consists of repeating units of $(1 \rightarrow 4)$-α-D-GalA (galactopyranosyluronic acid) residues, partly methyl-esterified at O-6 position (and at lower extent also acetyl-esterified at O-2 or O-3), interrupted by branched regions composed of $(1 \rightarrow 2)$-α-L-rhamnose units (RG-I regions) further binding neutral sugars including galactose, arabinose, xylose, and fructose (Ropartz et al., 2020).

Commercial production started in the early 1900s. The first plant extracting pectin from citrus fruit peel started in California in 1926 (Kertesz, 1951), and from dried apple pomace in 1934 in Germany (Herbstreith&Fox, 2009). Readily forming a gel in the presence of sugar, pectin was mostly used for the production of jam obtained from fruits poor in pectin such as gooseberries and redcurrants.

Since about a century (the world's first large-scale plant using hydrolysis of protopectin with hot dilute mineral acid started operations in France's Redon in 1941) a highly degraded form of the biopolymer is extracted from citrus peels or apple pomace via prolonged hydrolysis promoted by dilute mineral acid (most often nitric acid) at relatively high temperature (70–80 °C), followed by precipitation with isopropyl alcohol (Ciriminna et al., 2016a).

In general, pectin extracted via the conventional acid-extraction process is high methoxyl (HM) pectin, namely pectin with degree of esterification (DE)>50%. Low methoxyl (LM) pectin having degree of esterification (DE) < 50% (produced by controlled hydrolysis of HM pectin) is more valued than HM pectin, because it is able to gel without requiring sugar in a broad pH range in the presence of small amounts of Ca^{2+} ions coordinating with free carboxylate groups via the "egg box" cross-linking mechanism (Han et al., 2017).

Gelling of HM pectins, on the other hand, requires both high concentration of sugar (usually >55%) and acidic conditions (pH < 3.5), which enhanced the demand of LM-pectins as low-calorie thickener and stabilizer in products such as dessert fillings, fruit juices, ice creams, drinking yogurt and dairy drinks. In low-calorie beverages, for example, LMP is successfully used to impart mouthfeel to the sugar-deprived beverage, being able to "build back body" in acidic beverages (Gelski,

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2018).

Besides safety and environmental issues related to the use of highly flammable alcohol and vacuum installations posing explosion risks due to explosive alcohol vapor, significant degradation of the original molecular structure of the pectic polysaccharide takes place during the acidic hydrolysis. A significant portion of the "hairy" RG regions of the polymer is lost during the extraction leaving most of the "smooth" HG regions with a few neutral sugar units bound to the main galacturonic acid chain (Wang et al., 2017).

Though degraded, commercial pectin is a versatile and safe hydrocolloid widely used by the food and beverage industries as texturizer and gelling agent (Zeeb et al., 2021). Due to its unique physiological activity and exceptional versatility, however, its use is rapidly growing also in many other sectors, including the nutraceutical industry (Ciriminna et al., 2015).

Driven by the expanding consumer demand for low-calorie and safe food products of good palatability preferably of vegetable origin, in the last decade (2010–2020) the pectin demand has been growing at fast pace. "Despite increases in the raw material prices and shortages of raw material supply" we wrote in 2016 "pectin will replace a number of hydrocolloids that have been used on large scale due to their much lower cost" (Ciriminna et al., 2016a). Five years later, reputed hydrocolloid market analysts reported that pectin had become the third food hydrocolloid in terms of revenues (after gelatin and starches), with sales in 2020 exceeding $1.25 billions, and a global output of 70,000 tonnes, having become by far the most valued natural hydrocolloid (Seisun & Zalesny, 2021).

Attracting significant interest (ResearchGate, 2021), the pectin market study published in 2016 offered an insight into a poorly known market amid contradictory information. As mentioned above, in the subsequent five years the global production of pectin has substantially expanded. New pectin plants started operations, while incumbent companies expanded the capacity of their plants.

Since more than a decade research on pectin is flourishing at unprecedented levels. Recently named "a universal medicine" in light of its broad physiological activity (Zaitseva et al., 2020), pectin also exerts antibacterial activity, a most important property which has been literally rediscovered (Ciriminna et al., 2020). Recently, for example the broad-scope antibacterial activity of a new citrus pectin ("IntegroPectin", obtained from lemon and grapefruit processing waste via hydrodynamic cavitation) against harmful Gram-positive and Gram-negative bacteria has been demonstrated, suggesting the origin of said enhanced antimicrobial activity (Presentato et al., 2020). Similarly, the antibacterial activity towards several bacteria, and particularly against *Staphylococcus aureus*, of a whole pectin extracted from banana peel was lately reported by scholars in India (Tripathi & Mishra, 2021).

"Tremendous progress in our understanding of the very complex fine structure of pectic polymers" wrote in 2006 researchers at a large pectin manufacturer, allow producers "to develop a new generation of sophisticated designer pectins with specific functionalities". (Willats et al., 2006)

In this study, we offer a unified perspective on the new science and technology of pectin. Accordingly, we offer an insight into forthcoming pectin uses from an expanded perspective taking into account selected technology and economic factors that we believe will shortly impact the pectin production and uptake in many countries.

2. New insight on structure and physiological role

Following the determination of the primary structure and early X-ray diffraction studies in the 1940s (Palmer & Hartzog, 1945), research on the structure of pectin, especially related to conformation, re-started in the 1990s, using new diffraction and microscopy techniques. For instance, using small-angle neutron scattering Perez and co-workers in

1996 showed the main difference between the two main commercial pectins (Cros et al., 1996). Having a significantly higher degree of branching imparted by neutral sugars on more numerous RG-I chains, apple pectin in solution is more flexible than citrus pectin of similar degree of methylation, forming more viscous hydrogels.

Almost concomitantly, in a series of studies started in the mid 1990s shortly after the introduction of single molecule atomic force microscopy (AFM) imaging able to produce subnanometer scale images of a biopolymer, Morris and co-workers revealed the morphologies of individual polymers within pectin samples. In general, as stated by Zdunek, whose team in Poland has made substantial contrbutions to the study of the structure of pectins using the same technique, AFM unveils pectin conformation since it allows to measure the force-extension curve of the pectin molecules deposited on mica, which is directly related to its stiffness or flexibility (Zdunek et al., 2021).

For example, AFM imaging of pectin extracts from mature green tomatoes subjected to acid hydrolysis in 0.1 M HCl at 80 °C for 1, 8, 24 and 72 h unveils the structure of pectin in solution (Round et al., 2010) The polymer structures observed show (Fig. 1) individual strands of lengths ranging from 20 to 400 nm with diameters in the range 0.5–0.8 nm, commensurate with the expected diameters of single polysaccharide strands adopting a helical conformation when imaged by AFM, and complexes with widths or heights greater than those measured for single strands. The complexes range in size in all three dimensions from one to tens or even hundreds of nm.

Fig. 1e, f and 1g show these complexes sharing two common features: the presence of a backbone structure in the aggregate and the emergence of one or more polymer strands resembling the individual polymer
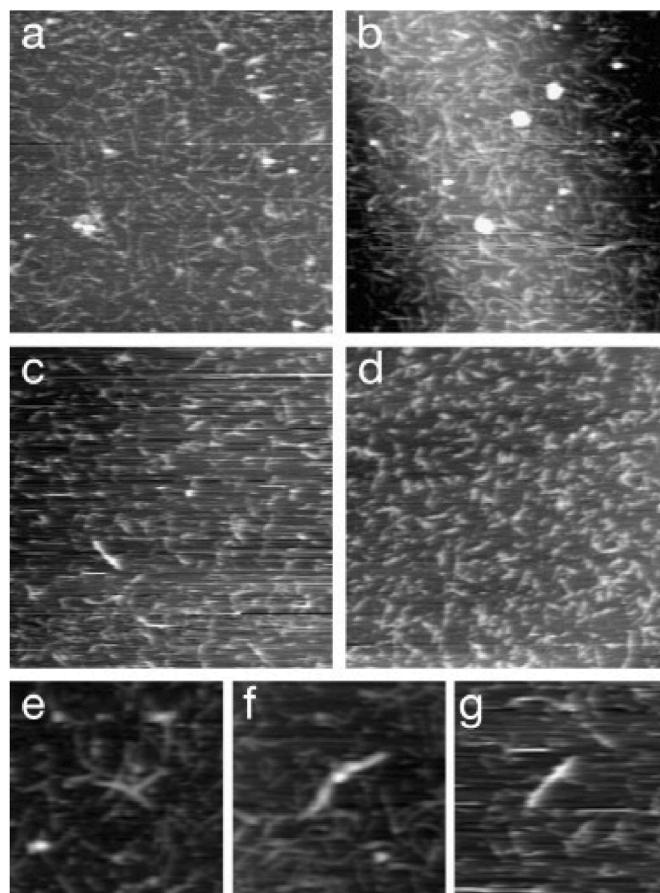

Fig. 1. AFM images of pectin during acid hydrolysis. (a) 1 h, (b) 8 h, (c) 24 h, (d) 72 h of hydrolysis, all images 1 μm × 1 μm, height 3 nm. (e–g) High resolution images of examples of complexes, all images 200 nm × 200 nm, height 3 nm [Reproduced from (Round et al., 2010), with kind permission].

strands. In brief, progressively smaller complexes are observed as the hydrolysis proceeds, suggesting that hydrolysis initially disrupts the associations that give rise to the complexes. Finally, the images of the polymers after 72 h hydrolysis show a clear reduction in average polymer length with only a few small complexes present in the samples.

In brief, the AFM imaging analysis confirms that acid hydrolysis degrades the RG-I polymer chains with the complexes being decomposed into their constituent parts, whereas the individual HG chains retain molecular weights similar to their initial values. After 72 h of hydrolysis only trace amounts of arabinose, galactose and rhamnose remain and the observable pectin structures consist of individual HG polysaccharides and HG aggregates.

Ten years later, Zdunek and co-workers reported that apple pectin instead is chiefly composed of long linear chains of homogalacturonan with bend points with arabinan-rich structures amorphously aggregated around the linear HG chains clearly visible on AFM images (Fig. 2) (Pieczywek et al., 2020) Arabinan was found to be the second most abundant polysaccharide in apple pectin.

The structural characterization of bend points showed that linear molecules are formed by two sections of homogalacturonan separated by a single rhamnose unit, that AFM imaging shows to be a common feature of the molecular structure of apple pectin, suggesting a possible role in the networking of pectic polysaccharides.

In agreement with simulations suggesting that arabinan exhibits a very high degree of flexibility, the team proposed that branch and bend points having similar values of experimental (bend and branch) angles and similar lengths (of bend and branch sections) are formed by single interspersions of rhamnose connecting three homogalacturonan chains of rhamnogalacturonan-I with the homogalacturonan side branch (Fig. 3).

Rhamnose interspersions within the HG chains lead to kinked rods with higher degree of mobility, as well as the greater number of segments increasing the number of possible interactions with surrounding molecules and thus increase the tendency of gel formation. This model
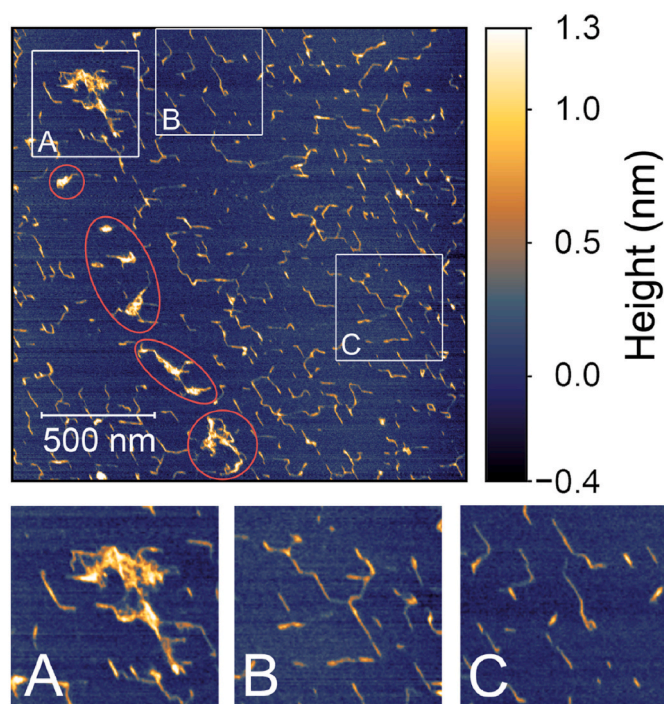

Fig. 3. Hypothetical pectic structures responsible for the occurrence of branch points in alkaline-extracted apple pectin. [Reproduced from (Pieczywek et al., 2020), with kind permission].

would also explain the key role of rhamnose in apple pectin regardless of its low abundance.

New research on the primary and secondary structure of pectins is driven by the now well established finding that the structure of pectin is eminently affected both by the fruit/plant *and* by the extraction procedure, which in its turn alters both the rheological properties of the hydrogels (so far the main commercial applications) and the bioactivity of the extracted pectin.

Recently for instance Kumar and co-workers in India used molecular docking investigation to mulberry pectin extracted from two fruit varieties (BR-2 and S-13) against six bacterial strains and two human cancer cell lines (HT-29 and Hep G-2) (Venkatesh Kumar et al., 2020). The BR-2 mulberry fruit had both the highest antibacterial and cytotoxic activity (against the Hep G-2 cell line, both tested pectins had no cytotoxicity on colon cancer cell line HT-29). Based on molecular interaction through docking, pectin would bind effectively with the 1e3g, 3t0c, 5czz, 6j7l, 6v40, 5ibs, 5zsy, and 6ggb receptors involved in bacterial infections and carcinogenesis.

Similarly, Ardestani and co-workers in 2018 demonstrated that both citrus and apple pectins selectively suppress viability in MDA-MB-231, MCF-7 and T47D human breast cancer cells, while being entirely nontoxic to L929 normal cells driving apoptosis in MDA-MB-231 cells by increasing the release of reactive oxygen species (ROS), which may be related to the mitochondrial apoptosis pathway, and direct interactions with DNA (Salehi et al., 2018). Concluding that both citrus and apple pectins "may be potentially useful in cancer treatment", they also clearly showed that both pectins are able to interact with DNA, with citrus pectin binding to double stranded DNA by intercalation, and apple pectin by groove binding/partial intercalation.

On the other hand, it is now clear that simplistic representations of pectin as a GalA tetramer of units (the model used in the aforementioned molecular docking simulation)(Venkatesh Kumar et al., 2020), or as a linear chain of GalA units such as that often portrayed by chemistry and food chemistry magazines (Bomgardner, 2013) are inadequate to represent the structure and the broad biological, chemical and rheological properties of pectins. For instance, in plant growth the RG-I and RG-II chains play a crucial role, suggesting "specificities in pectin-mediated cell adhesion that extend beyond a simple story where pectin-equals-glue" (BouDaher and Braybrook Siobhan, 2015).

Fig. 2. Alkaline-extracted apple pectin deposited on mica, with magnified characteristic structures in AFM imaging: A) amorphous aggregates around linear molecules, B) branched rod-like molecules, C) linear unbranched molecules with bend points. [Reproduced from (Pieczywek et al., 2020), with kind permission].
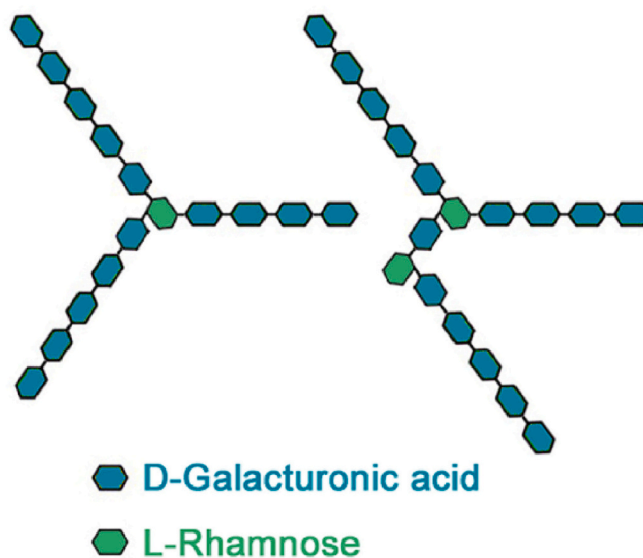
3. New advanced biomaterials

From pectin-based aerogels to pectin-based implants, a number of different pectin-based advanced materials have been developed in the last decade. Two examples, namely aerogels and implantable and prosthetic devices based on pectin, suffice to render the scope and the potential of this exceptional biomaterial in materials science and technology. Biobased pectin aerogels, for instance, have thermal conductivity values similar to those of silica aerogels, but they do not break under compression, suggesting their use for thermal insulation applications (Zou & Budtova, 2021).

The lowest value of conductivity, around 0.015 W/m K typical of thermal superinsulating materials (Fig. 4), was obtained for aerogels made from non-gelled pectin solutions, at pH 2 and pectin concentration of 2 wt%. Contrary to brittle silica aerogels requiring reinforcement strategies such as addition of glass or cellulose fibers or cross-linking, such modifications would not be required for pectin aerogels.

Budtova's team has made substantial contributions to advance the science of pectin-based aerogels. Asked to comment whether pectin could be suitable for the commercial production of biobased aerogels for thermal insulation, Budtova noted how "additional work is needed to replace drying with supercritical CO_2 with a less costly drying process as well as to avoid rapid aging of the pectin aerogel" (Prof. Budtova, 2021).

Silica-based aerogels prepared at low cost via ambient pressure drying from sodium silicate, rather than from expensive organosilane precursors, have been lately commercialized (Minju et al., 2021). The ambient pressure drying process could therefore be easily extended to dry biobased aerogels.

The real problem to be faced for these polysaccharide aerogels is to stabilize them against bacterial degradation. Pectin-based implantable and prosthetic devices seeking practical application, in their turn, only require enhancement of the mechanical properties of scaffold materials made of pectin only.

As lately suggested by Indian scholars, beyond biocompatibility and porosity, successful application of biobased scaffolds in regenerative medicine depends on mechanical strength (Indurkar et al., 2021). Readily cross-linked with Ca^{2+} to form stable (insoluble) films and microparticles, cross-linked pectin is ideally suited to promote osteogenic activity. This was first shown by Wang and co-workers in 2016, using a calcium phosphate/pectin cement (CPCP) scaffold to promote bone tissue growth repair bone defects (Zhao et al., 2016).

We briefly remind that self-setting calcium phosphate cement (CPC) is a bone substitute commonly used in bone surgery to enhance the bone healing process. Its main component is α-tricalcium phosphate (α-TCP). Adding 6% pectin to CPC dramatically improved its poor compressive strength, with the compressive strength of the CPCP now approaching 29 MPa, similar to the mechanical strength of cancellous bone. As expected, the introduction of pectin promoted the attachment and proliferation of human adipose-derived stem cells (hADSCs) *in vitro* (Zhao et al., 2016). In addition, hADSCs seeded onto the CPCP scaffold showed higher osteogenetic efficacy than those seeded onto the CPC scaffold resulting in dramatically higher expression of osteogenic genes when compared to scaffolds formed with calcium phosphate alone.

A pre-clinical study on white rabbits using the cavity defect model clearly showed formation of new bone around the CPCP scaffold 8 weeks after the operation with CPCP maintaining its form in the cavity after two weeks, whereas CPC was deformed (Fig. 5).

This seminal work established the foundation of a new generation of technically and economically viable bone repair healing agents using pectin as key functional agent promoting better and faster bone repair.

Supporting this viewpoint, four years later Zima and co-workers in Poland used the same approach to enhance the injectability and leaching resistance of CPCP-based biomicroconcretes adding apple and citrus LM pectins to the biomaterial (Dziadek et al., 2020). Again, the α-TCP-based materials showed brittle behaviour, while the presence of apple and citrus LM pectin granules led to ductile characteristics. Furthermore, the addition of citrus pectin in small amount (0-5%–1%) significantly enhanced the mechanical strenght of the final biomicroconcretes. The latter did not lose their integrity after compression test, when compared to α-TCP-based materials, likely due to electrostatic interaction between the positively charged amino groups of chitosan in hybrid
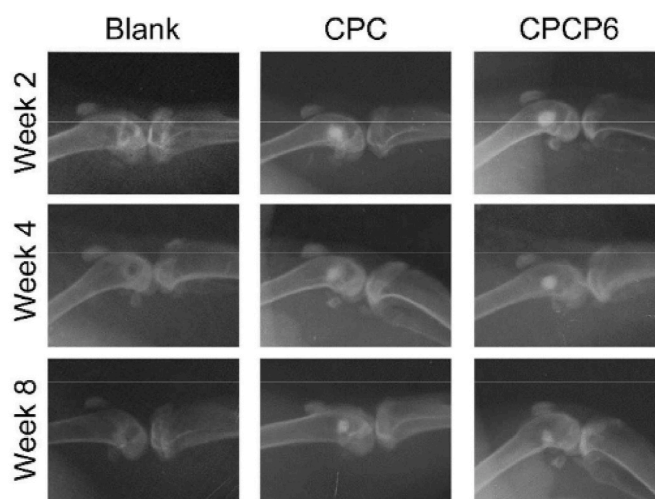

Fig. 5. X-rays images of rabbit femur condyle cavity following implantation of calcium phosphate/pectin cement (CPCP) scaffolds at different times. [Reproduced from (Zhao et al., 2016), with kind permission].
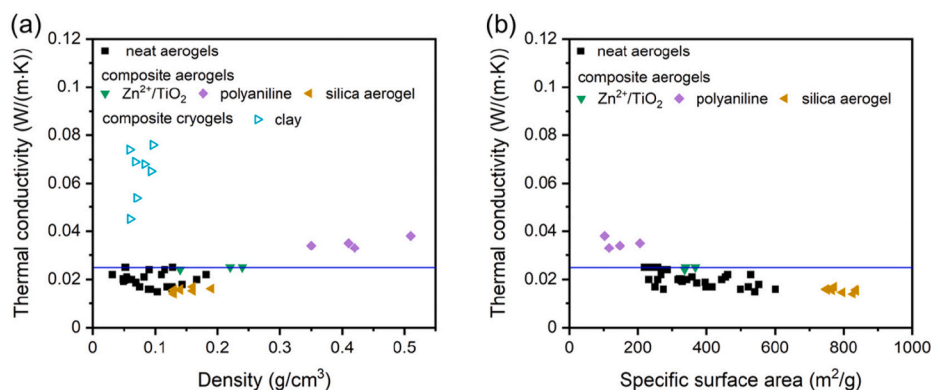

Fig. 4. Thermal conductivity of neat and composite pectin aerogels (filled points) and cryogels (open points) as a function of density (a) and specific surface area (b). Blue solid line corresponds to the thermal conductivity of air. [Reproduced from (Zou & Budtova, 2021), with kind permission]. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

hydroxyapatite/chitosan (HAp/CTS) granules used as a reinforcing phase in biomicroconcrete and the negatively charged carboxyl groups of LM pectin in the cement phase.

4. Economic and industrial aspects

In the early years after its commercialization, pectin extracted from dried apple pomace was sold as a "jellying solution" in liquid form. Today, it is sold to customers in powder form, most often in "standardized" form adding sugar as functional additive.

As mentioned above, demand is rising at fast pace since more than a decade. For instance, between 2013 and 2018 close to 500 new food products launched had pectin as stabilizing ingredient (Møller, 2019). The second hydrocolloid used for said new products was carboxymethylcellulose, with slightly more than 100 new products, followed by agar, modified starch, guar, gellan, xanthan, alginate, and carrageenan as preferred stabilizer.

Highly pure pectin is also sold to biomedical and pharmaceutical companies producing medical products (wound dressings and ostomy care products), as well as an excipient or carrier for oral drug delivery systems (Sriamornsak, 2011). Such "pharmaceutical grade" pectin meeting demanding standards for microbiological and chemical purity is sold at prices exceeding $1000/kg for applications such as ostomy formulations improving pouch adhesion and to prevent adhesions after surgical interventions.

In 2002, the global annual pectin consumption was 45,000 tonnes with revenues exceeding $400 million (Savary et al., 2003). By 2015, driven by product shortage due to rapid rise in demand, the price of both pectins had crossed the $15.00/kg threshold (Ciriminna et al., 2016a). Another five years and the average price of pectin averaged $18/kg, with revenues exceeding $1.25 billions (Seisun & Zalesny, 2021). In brief, in less than 20 years the market value of pectin has more than tripled. This led to significant changes in the structure of the pectin industry (Table 1).

By 2009, there were a few large-scale pectin production plants, nearly all of them in Europe, with one in Mexico, one in Brazil and one in China (Staunstrup, 2009). Citrus peel (lemon, lime, orange) was the main (85.5%) raw material used, followed by apple pomace (14%). A minor fraction (0.5%) for specific applications was obtained from sugar beet. The five largest manufacturers included Yantai Andre Pectin, a joint venture between DSM, a Dutch chemical company, and Shandong Andre Group, a China-based company supplying the raw materials and utilities. Nearly all plants were (and are) highly profitable. For example, the latter China-based company in 2018 recorded sales of about €65 million with earnings before interest, taxes, depreciation, and amortization (EBIDTA) margin above 25% (DSM, 2019). A few months later, in early 2019, DSM acquired majority stake in Andre Pectin for €150 million (FoodBev Media, 2019).

Attracted by similar protability levels, in the subsequent decade a number of new companies started to produce pectin at several new plants located in many countries including Italy and Ukraine.

The top producers, in their turn, further consolidated their activities or sold their plants in a booming market. For example, DuPont in 2011 acquired Danisco (a large enzyme manufacturer producing also pectin).

In the same year, Naturex bought Pektowin, a Polish company with a plant producing apple and citrus pectins since 1963. In 2020, Herbstreith & Fox purchased all Naturex pectin plants from Givaudan (owner of Naturex). One year later, Cargill opened in Brazil its fourth and largest pectin production plant. Thanks to the $100 million investment, the company added 6000 t/a to its production capacity (Mano, 2021).

Other companies such as CP Kelco in Denmark and Ceamsa in Spain expanded their production capacity. The latter, for instance, brought capacity to 1380 t/a thanks to a new evaporator and a new dryer to separate the alcohol from the precipitated pectin (Ceamsa et al., 2017).

In general, pectin is costly but it is effective as hydrocolloid at low concentrations. Typical use levels vary between 0.1 and 0.6 per cent in weight, depending on the application (Dziadek et al., 2020). In 2004, the main customers of the pectin industry were the food and beverage companies (Table 2).

In the subsequent fifteen years, several new industrial uses of pectin emerged. Pectin is now widely used in to formulate diarrhoea treatment and wound healing treatments as well as by cosmetic companies for its anti-inflammatory effect on skin, water-holding and lift-restructuring properties (Akin-Ajani et al., 2021). In 2010 the European Food Safety Authority (EFSA) recognized pectin as a food supplement capable to reduce post-prandial glycaemic responses, maintain normal blood cholesterol concentrations, and increase satiety leading to a reduction in energy intake (EFSA, 2010). In agreement with the European regulation on food supplements, nutraceutical companies can therefore add these health claims in the of pectin-based food supplements commercialized in 27 European countries, thereby originating a completely new demand of pectin from the rapidly growing nutraceutical industry.

Growth of the market demand for pectin from pharmaceutical and nutraceutical is far from being over as new health benefits of pectin, including potential for the treatment of allergies (Blanco-Pérez et al., 2021), are reported almost on a monthly basis.

In general, the use and role of pectin in the global current trend towards low-glycaemic foods is already significant (Muñoz-Almagro et al., 2021). The pectin industry, an oligopoly of less than 10 companies comprising an highly rewarding niche of the chemical market, underwent profound changes with several new entrants operating new extraction plants and market consolidation amid the top producers. New pectin plants consume a fraction of the water of older plants and use far better precipitation units, dryers, and evaporators reducing the overall energy costs. Yet, all existing plants continue to use the acid-assisted extraction with mineral acid followed by precipitation with alcohol first industrialized in 1941 France's Redon (where also LM pectin was first produced and commercialized).

Several alternative processes have been developed to extract less degraded pectin via acid-free technologies (see below). Whether or not these technologies will be commercialized will not be due to reduced environmental impact or better product quality (lesser degradation and higher purity), but to their higher profitability due to significantly lower capital and production costs. Such enhanced protability might originate also from the new industrial ability to recover the valuable phenolic

Table 1
The five pectin largest manufacturers in 2009 (Reproduced from (Ciriminna et al., 2016a), with kind permission).

Rank	Company
1	CP Kelco
2	Danisco
3	Cargill
4	Herbstreith & Fox
5	Andre Pectin

Table 2
Main pectin applications in 2004 (Reproduced from (Staunstrup, 2009), with kind permission).

Application	Market share (%)
High sugar jams	30
Acidified milk drinks	15
Low sugar jams	13
Bakery jams	9
Yoghurt fruit preparations	8
Fruit beverages	8
Confectionery	8
Pharma/Tobacco	5
Dairy	2
Other	1

compounds and pectin oligosaccharides (POS) that are lost, alongside arabinan and rhamnogalacturonan chains, in the acid-based industrial extraction process.

As put it by Muhidinov and co-workers (Muhidinov et al., 2021), separating these materials after the vacuum evaporation and alcohol precipitation (VEAP) adds cost to the overall production process. Furthermore, the standard process involving the VEAP purification technology poses significant safety issues arising from the use of flammable alcohol (to precipitate pectin) generating explosive vapors in the vacuum installation used to recover the alcohol.

5. Ending the loss of phenols and oligosaccharides

Several alternative processes have been developed to extract less degraded pectin via acid-free technologies, including microwave-assisted hydrodistillation and gravity (Ciriminna et al., 2016b), enzymatic degradation using pectin methyl esterase directly captured as recyclable biocatalyst from citrus processing waste (Talekar et al., 2020), and hydrodynamic cavitation in water only (Meneguzzo et al., 2019).

Being reproducible and scalable, these acid-free and "green" extraction processes hold practical (commercial) applicative potential. For instance, extraction based on hydrodynamic cavitation directly carried out on a semi-industrial scale (>30 kg citrus biowaste in 120 L water) affords pectin in solution alongside citrus flavonoids and emulsified terpenes ("IntegroPectin") and micronized cellulose of high value ("CytroCell") (Scurria et al., 2021) via an efficient, one-pot process requiring no chemical reactant to promote the extraction. Water is the only dispersion medium, and electricity the unique energy form employed to run the process affording plentiful amounts of two biomaterials (pectin and micronized cellulose) with numerous applications. The safe and robust hydrodynamic cavitation process for the extraction of natural products is easily scaled-up (Panda & Manickam, 2019).

Furthermore, advances in purification technology already allow to replace conventional VEAP technology with diaultrafiltration and concentration using a fiber membrane (Muhidinov et al., 2012). Comparison of the pectin structures extracted by flash hydrolysis in dilute mineral acid solution and isolated via VEAP and diaultrafiltration directly on pilot-scale shows that the latter purification process affords (in 2 cycles) pectin with decreased polydispersity and increased molar mass, thanks to the separation of pectin polymers with higher molar mass, at a fraction of the energy requirements of the VEAP process. In detail, the amounts of ethanol and power needed for the isolation of pectin when using the VEAP process are, respectively, twice and four times larger than those used for the isolation of pectin by diaultrafiltration (Muhidinov et al., 2021).

Regardless of the method used for pectin extraction, the latter isolation process is general and can be applied to any pectic aqueous solution.

POS in high amounts usually remain in the alcohol solution or permeates from the diaultrafiltration process of pectin production. Until now, no research has considered exploring POS by-products produced in the pectin hydrolysis and extraction process, even though they are well known prebiotics with multiple health-promoting roles. In general, POS can stimulate apoptosis process in human colonic adenocarcinoma cells, show protective functions for cardiovascular tissues, reduce the damage caused by metals, and have anti-obesity effects, antitoxic, antibacterial, and antioxidant activities (Gullon et al., 2013).

Orange peel albedo (white part), for example, is an excellent source of POS with prebiotic properties (Hotchkiss et al., 2008); whereas bacterial fermentation of pectooligosaccharides obtained from lemon peel in a *in vitro* colon model affords the highest butyrate cumulative production and the lowest branched chain fatty acid cumulative production when compared to commercial fructooligosaccharides (FOS) and standard ileal efflux medium, resulting in shifts in the elderly microbiota similar to those observed using FOS (Míguez et al., 2020). FOS is

considered as the best available prebiotic, leading Alonso and co-workers to conclude that lemon POS is an excellent prebiotic candidate targeting gut health in the elderly (Míguez et al., 2020).

This and related previous findings suggest the opportunity to fully exploit the prebiotic potential of pectic oligosaccharides to re-balance the microbiota towards an anti-inflammatory profile (Chung et al., 2017).

Progress, even at clinical level, is now rapid. For example, Japanese scholars recently completed a randomized clinical trial administering 201 stable patients receiving intragastric tube with either POS or a standard polymeric formula (SPF) as a control for one week. Results clearly supported the use of POS rather than SPF as diarrhea treatment had a significantly lower incidence in the POS group compared with the SPF group (occurring only in 2 patients *vs.* 13 patients in the SPF group). (Maruyama et al., 2020).

6. Outlook and conclusions

Pectin, the plant heteropolysaccharide once used as main ingredient of the "jellying solution" to gelify jams, actually is a biomolecule of exceptionally broad physiological properties and uniquely complex primary and secondary structures, which make it suitable for widely different applications, from advanced biomaterials through new antimicrobials of broad scope.

As it happened with glycerol, and as usual in chemistry research when a substance knows a quick expansion in demand, intense new research carried out in the last decade (2010–2020) has shed new light on its molecular structure and physiological role, up to new production methods and completely new applications, such as pectin aerogels for thermal insulation, and calcium phosphate pectin cements for bone repair.

Investigating the market sustainability of pectin productions taking into account selected economic aspects we found analyses dating back to the early 1990s reporting that oversupply due to increased capacity and lower worldwide demand drove prices downward (Bahner, 1993). Yet, driven first by the unique performance of pectin in stabilizing milk proteins in acidic dairy beverages such as drinking yoghurts, in only ten years the situation turned out to be completely the opposite.

The worldwide consumption of pectin quickly went from 18,000–19,000 tonnes of the early 1990s to 30,000 tonnes in 2009 (Zhao et al., 2016). Another decade, and in 2020 the overall amount of pectin delivered to ever more numerous customers reached 70,000 tonnes (Seisun & Zalesny, 2021).

The world's largest country, Russia, which is also the world's third country in terms of apple production, does not yet host a pectin production plant. So does India, which is a huge producer of both citrus and apple fruits. It is likely that new pectin producers in these countries, but also in other huge countries harvesting large amounts of citrus fruits such as Argentina, Brazil, Mexico and South Africa, will start producing pectin using new extraction and purification (*i.e.*, diaultrafiltration and concentration using a fiber membrane) (Muhidinov et al., 2012) technologies. These new plants will co-exist with plants of incumbent producers that will continue to rely on the acid-based extraction technology in modern plants.

The pectin industry produces large amounts of by-products, chiefly comprised of valued biophenols and pectic oligosaccharides, so far disposed of as waste. Integration of green chemistry technology allows the conversion of these by-products into high-value products with relevant potential applications for human consumption, such as antioxidant extracts, functional foods, prebiotics and even drugs.

Pagliaro has argued elsewhere that reduced "capex" and "opex" (capital and operational expenses) due to new green chemistry production (synthetic or extraction) technologies in much smaller production units operated in continuous mode is a common feature of these technologies that will shortly impact many productions of the global chemical industry (Pagliaro, 2019). Some of the "green extraction of

natural products" (Chemat et al., 2012) technologies based on green chemistry and green engineering share these properties since, along with dramatically reduced energy and solvent consumption, they have lately become scalable at relatively low capital cost.

Indeed, selected chemical engineering firms now commercialize the first pectin extractors based, for example, on acoustic cavitation. Remarkably, one reads on the website of one of these companies, a family of new "small footprint" acoustic cavitation extractors is already available "for producing large volumes of pectin" via "inline processing" which is "highly efficient, rapid and requires significantly less labour" (Hielscher, 2021).

In this rapidly evolving context, the pectin industry, including many new players using the aforementioned new green extraction technologies, will progressively start supplying the valued biomaterial and its derivatives, such as pectin-derived oligosaccharides no longer to customers in the food and beverage industries only, but also to companies using pectin to produce advanced biobased materials, nutraceutical, medical and pharmaceutical products.

From new understanding of pectin molecular structure and physiological effects up to new production methods and applications, this study provides a unified perspective on the new science and technology of pectin, with the aim to provide guidelines for future research in the utilization of this uniquely complex and versatile polysaccharide and its by-products.

Author statement

Rosaria Ciriminna, Mario Pagliaro, Alexandra Fidalgo and Laura M. Ilharco: conceptualization, supervision, writing - original draft, writing - review & editing, validation, project administration; Antonino Scurria: investigation; data curation; formal analysis.

Declaration of competing interest

The authors declare no competing financial interest.

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