

# Chemistry of Pectin and Its Pharmaceutical Uses : A Review

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## Abstract

Pectin, a naturally occurring polysaccharide, has in recent years gained increasingly in importance. The benefits of natural pectin are also more and more appreciated by scientists and consumer due to its biodegradability. Pectin is the methylated ester of polygalacturonic acid. It is commercially extracted from citrus peels and apple pomace under mildly acidic conditions. Pectins are divided into two major groups on the basis of their degree of esterification. The association of pectin chains leads to the formation of the three-dimensional networks that is to gel formation. The pectin, by itself or by its gelling properties, was employed in pharmaceutical industry, health promotion and treatment. It has been used potentially as a carrier for drug delivery to the gastrointestinal tract, such as matrix tablets, gel beads, film-coated dose form. This review will discuss the important chemistry and general properties of pectin, and its gel formation mechanism and properties. The example of the pharmaceutical uses of pectin will be given.

## Introduction

Pectin is a naturally occurring biopolymer that is finding increasing applications in the pharmaceutical and biotechnology industry. It has been used successfully for many years in the food and beverage industry as a thickening agent, a gelling agent and a colloidal stabiliser. Pectin also has several unique properties that have enabled it to be used as a matrix for the entrapment and/or delivery of a variety of drugs, proteins and cells. This review will first describe the source and production, chemical structure and general properties of pectin. The methods of gel formation and properties of the gels will then be discussed. Finally, some examples of the pharmaceutical uses of pectin will be given.

## Chemistry of pectin

### Source and production

Pectin is a complex mixture of polysaccharides that makes up about one third of the cell wall dry substance of higher plants. Much smaller proportions of these substances are found in the cell walls of grasses. The highest concentrations of pectin are found in the middle lamella of cell wall, with a gradual decrease as one passes through the primary wall toward the plasma membrane (Kertesz, 1951). Although pectin occurs commonly in most of the plant tissues, the number of sources that may be used for the commercial manufacture of pectins is very limited. Because the ability of pectins to form gel depends on the molecular size and degree of esterification (DE), the pectin from different sources does not have the same gelling ability due to variations in these parameters. Therefore, detection of a large quantity of pectin in a fruit alone is not in itself enough to qualify that fruit as a source of commercial pectin (Thakur et al., 1997). At present, commercial pectins are almost exclusively derived from citrus peel or apple pomace, both by-products from juice (or cider) manufacturing. Apple pomace contains 10-15% of pectin on a dry matter basis. Citrus peel contains of 20-30% (May, 1990). From an application point of view, citrus and apple pectins are largely equivalent. Citrus pectins are light cream or light tan in colour; apple pectins are often darker.

Alternative sources include sugarbeet waste from sugar manufacturing, sunflower heads (seeds used for edible oil), and mango waste (Rolin, 1993).

Commercially, pectin is extracted by treating the raw material with hot dilute mineral acid at pH about 2. The precise length of extraction time varies with raw material, the type of pectin desired, and from one manufacturer to another. The hot pectin extract is separated from the solid residue as efficiently as possible. This is not easy since the solids are by now soft and the liquid phase are viscous. The viscosity increases with pectin concentration and molecular weight. There is a compromise between efficient extraction and solids separation and operating cost. The pectin extract may be further clarified by filtration through a filter aid. The clarified extract is then concentrated under vacuum. Powdered pectin can be produced by mixing the concentrated liquid from either apple or citrus with an alcohol (usually isopropanol). The pectin is separated as a stringy gelatinous mass, which is pressed and washed to remove the mother liquor, dried and ground.

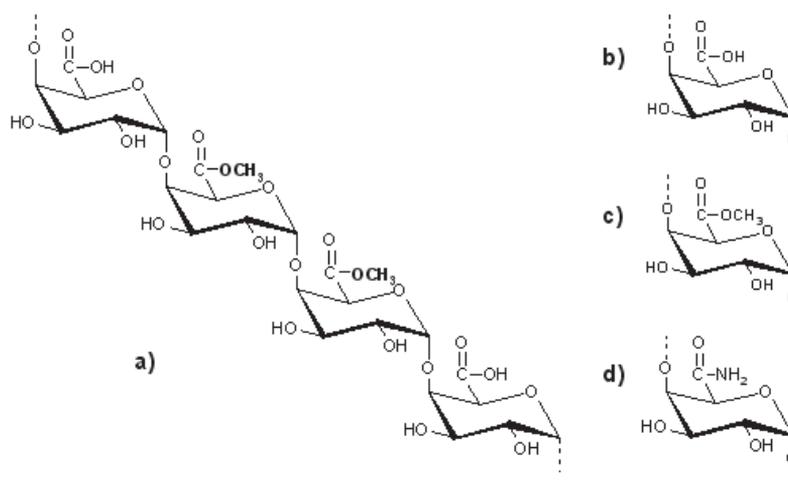
This process yields pectin of around 70% esterification (or methoxylation). To produce other types, some of the ester groups must be hydrolysed. This is commonly carried out by the action of acid, either before or during a prolonged extraction, in the concentrated liquid, or in alcoholic slurry before separation and drying. This process can produce a range of calcium reactive low methoxyl pectins. Hydrolysis using ammonia results in the conversion of some of the ester groups into amide groups, producing 'amidated low methoxyl pectins' (May, 1990).

### **Chemical structure**

Pectin is an essentially linear polysaccharide. Like most other plant polysaccharides, it is both polydisperse and polymolecular and its composition varies with the source and the conditions applied during isolation. In any sample of pectin, parameters such as the molecular weight or the content of particular subunits will differ from molecule to molecule.

The composition and structure of pectin are still not completely understood although pectin was discovered over 200 years ago.

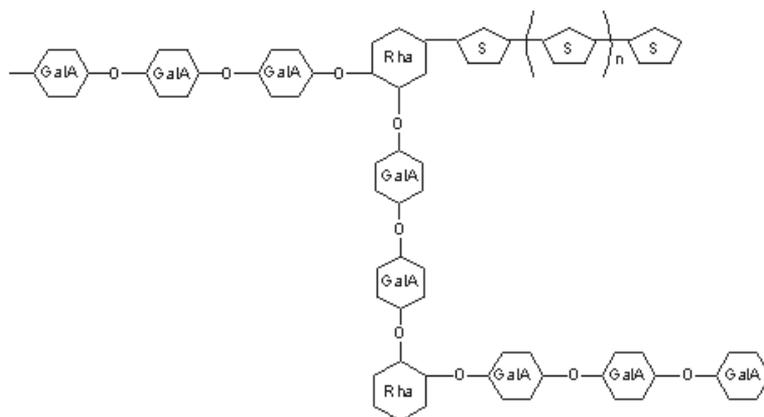
The structure of pectin is very difficult to determine because pectin can change during isolation from plants, storage, and processing of plant material (Novosel'skaya et al., 2000). In addition, impurities can accompany the main components. At present, pectin is thought to consist mainly of D-galacturonic acid (GalA) units (Mukhiddinov et al., 2000), joined in chains by means of  $\alpha$ -(1-4) glycosidic linkage. These uronic acids have carboxyl groups, some of which are naturally present as methyl esters and others which are commercially treated with ammonia to produce carboxamide groups (Fig. 1).



**Fig. 1** (a) A repeating segment of pectin molecule and functional groups: (b) carboxyl; (c) ester; (d) amide in pectin chain.

Pectin contains from a few hundred to about 1000 saccharide units in a chain-like configuration; this corresponds to average molecular weights from about 50,000 to 150,000 daltons. Large differences may exist between samples and between molecules within a sample, and estimates may differ between methods of measurement.

In addition to the galacturonan segments shown in Fig. 1, neutral sugars are also present. Rhamnose (Rha) is a minor component of the pectin backbone and introduces a kink into the straight chain (Fig. 2) and other neutral sugars such as arabinose, galactose and xylose occur in the side chains (Oakenful, 1991). A chain of several hundred  $\alpha$ -(1-4)-bonded GalA units with a varied DE is a typical fragment.



**Fig. 2** Schematic diagram showing how rhamnose (Rha) insertions cause kinking of galacturonic acid (GalA) chain; S = neutral sugars (adapted from Sriamornsak, 2002).

The X-ray fibre diffraction studies showed that the galacturonan segments in sodium pectate form helices with three subunits per turn and an identity period of 1.31 nm. The conformation of GalA units as determined by NMR spectroscopy is  ${}^4C_1$  (Rees & Wright, 1971). Calculations indicate that the helix is probably right-handed (Rees & Wright 1971; Walkinshaw & Arnott, 1981a). Walkinshaw & Arnott (1981a,b) indicated that X-ray fibre diffraction patterns of sodium and calcium pectates, pectic acids, and pectinic acids show the same helix structure, but the ways in which these helices were arranged relative to each other in the crystals seemed to differ. They suggested that helical pectinic acid molecules pack in a parallel arrangement, whereas the pectates pack as corrugated sheets of antiparallel helices.

## Degree of esterification

The polygalacturonic acid chain is partly esterified with methyl groups and the free acid groups may be partly or fully neutralised with sodium, potassium or ammonium ions. The ratio of esterified GalA groups to total GalA groups is termed as the DE. Pectin might be formed initially in a highly esterified form, undergoing some deesterification after they have been inserted into the cell wall or middle lamella. There can be a wide range of DEs dependent on species, tissue, and maturity. In general, tissue pectins range from 60 to 90% DE. It seems that the distribution of free carboxyl groups along the pectin chains is somewhat regular, and the free carboxyl groups are largely isolated from one another (DeVries et al., 1986).

The pectin classes based on the DE are high methoxyl (HM) pectins, and the low methoxyl (LM) pectins which are either the conventionally demethylated or the amidated molecule. DEs values for commercial HM-pectins typically range from 60 to 75% and those for LM-pectins range from 20 to 40%. These two groups of pectin gel by different mechanisms. HM-pectin requires a minimum amount of soluble solids and a pH within a narrow range, around 3.0, in order to form gels. HM-pectin gels are thermally reversible. In general, HM-pectins are hot water soluble and often contain a dispersion agent such as dextrose to prevent lumping. LM-pectins produce gels independent of sugar content. They also are not as sensitive to pH as the HM-pectins are. LM-pectins require the presence of a controlled amount of calcium or other divalent cations for gelation.

## General properties of pectin

Pectins are soluble in pure water. Monovalent cation (alkali metal) salts of pectinic and pectic acids are usually soluble in water; di- and trivalent cations salts are weakly soluble or insoluble. Dry powdered pectin, when added to water, has a tendency to hydrate very rapidly, forming clumps. These crumps consist of semidry packets of pectin contained in an envelope of highly hydrated outer coating. Further solubilisation of such crumps is very slow. Clump formation can be prevented by dry mixing pectin powder with water-soluble carrier material or by the use of pectin having

improved dispersibility through special treatment during manufacturing (Rolin, 1993; Hercules Incorporated, 1999).

Dilute pectin solutions are Newtonian but at a moderate concentration, they exhibit the non-Newtonian, pseudoplastic behaviour characteristics. As with solubility, the viscosity of a pectin solution is related to the molecular weight, DE, concentration of the preparation, and the pH and presence of counterions in the solution. Viscosity, solubility, and gelation are generally related. For example, factors that increase gel strength will increase the tendency to gel, decrease solubility, and increase viscosity, and vice versa. These properties of pectins are a function of their structure, which is that of a linear polyanion (polycarboxylate). As such, monovalent cation salts of pectins are highly ionised in solution, and the distribution of ionic charges along the molecule tends to keep it in an extended form by reason of coulombic repulsion (Paoletti, 1986). Furthermore, this same coulombic repulsion between the carboxylate anions prevents aggregation of the polymer chains. (The number of negative charges is, of course, determined by the DE.) In addition, each polysaccharide chain, and especially each carboxylate group, will be highly hydrated. Solutions of monovalent salts of pectins exhibit stable viscosity because each polymer chain is hydrated, extended, and independent.

As the pH is lowered, ionisation of the carboxylate groups is suppressed, and this results in a reduction in hydration of the carboxylic acid groups. As a result of reduced ionisation, the polysaccharide molecules no longer repel each other over their entire length, and as a result, they can associate and form a gel. Apparent pK-values (pH at 50% dissociation) vary with the DE of the pectin (Plaschina et al., 1978); a 65% DE pectin has an apparent pK of 3.55, while a 0% DE pectic acid has an apparent pK of 4.10. However, pectins with increasingly greater degrees of methylation will gel at somewhat higher pH, because they have fewer carboxylate anions at any given pH.

Dissolved pectins are decomposed spontaneously by deesterification as well as by depolymerisation; the rate of this decomposition depends on pH, on water activity, and on the temperature. In general, maximum stability is found at pH 4. The

presence of sugar in the pectin solution has a certain protective effect while elevated temperatures increase the rate of degradation. At low pH-values and elevated temperatures degradation due to hydrolysis of glycosidic linkages is observed. Deesterification is also favoured by low pH. By deesterification a HM-pectin becomes slower setting or gradually adapts LM-pectin characteristics. At near-to-neutral pH (5-6), HM-pectin is stable at room temperature only. As the temperature (or pH) increases, a so-called  $\alpha$ -elimination starts which results in chain cleavage and very rapid loss of viscosity and gelling properties. LM-pectins show a somewhat better stability at these conditions. At alkaline pH-values pectin is rapidly deesterified and degraded even at room temperature (Rolin, 1993).

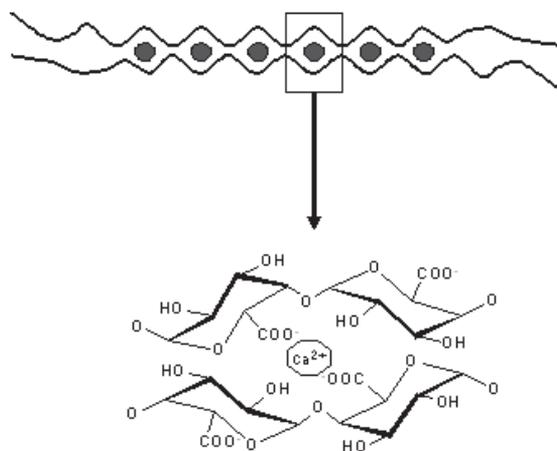
Powdered HM-pectins slowly lose their ability to form gels if stored under humid or warm conditions while LM-pectins are more stable and loss should not be significant after one year storage at room temperature (Hercules Incorporated, 1999).

## Gel formation properties of pectin

The most important use of pectin is based on its ability to form gels. HM-pectin forms gels with sugar and acid. This can be seen as a partial dehydration of the pectin molecule to a degree where it is in a state between fully dissolved and precipitated. The particular structure of pectin imposes some specific constraints. HM-pectin, unlike LM-pectin, does not contain sufficient acid groups to gel or precipitate with calcium ions, although other ions such as aluminium or copper cause precipitation under certain conditions. It has been suggested by Oakenfull (1991) that hydrogen bonding and hydrophobic interactions are important forces in the aggregation of pectin molecules. Gel formation is caused by hydrogen bonding between free carboxyl groups on the pectin molecules and also between the hydroxyl groups of neighbouring molecules. In a neutral or only slightly acid dispersion of pectin molecules, most of the unesterified carboxyl groups are present as partially ionised salts. Those that are ionised produce a negative charge on the molecule, which together with the hydroxyl groups causes it to attract layers of water. The repulsive forces between these groups, due to their

negative charge, can be sufficiently strong to prevent the formation of a pectin network. When acid is added, the carboxyl ions are converted to mostly unionised carboxylic acid groups. This decrease in the number of negative charges not only lowers the attraction between pectin and water molecules, but also lowers the repulsive forces between pectin molecules. Sugar further decreases hydration of the pectin by competing for water. These conditions decrease the ability of pectin to stay in a dispersed state. When cooled, the unstable dispersing of less hydrated pectin forms a gel, a continuous network of pectin holding the aqueous solution. The rate at which gel formation takes place is also affected by the degree of esterification. A higher DE causes more rapid setting. Rapid-set pectins (i.e. pectin with a DE of above 72%) also gel at lower soluble solids and higher levels than slow-set pectins (i.e. pectin with a DE of 58-65%).

LM-pectins require the presence of divalent cations (usually calcium) for proper gel formation. The mechanism of LM-pectin gelation relies mainly on the well-known 'egg-box' model (Grant et al., 1973). The mechanism involves junction zones created by the ordered, side-by-side associations of galacturonans, whereby specific sequences of GalA monomer in parallel or adjacent chains are linked intermolecularly through electrostatic and ionic bonding of carboxyl groups (Fig. 3).

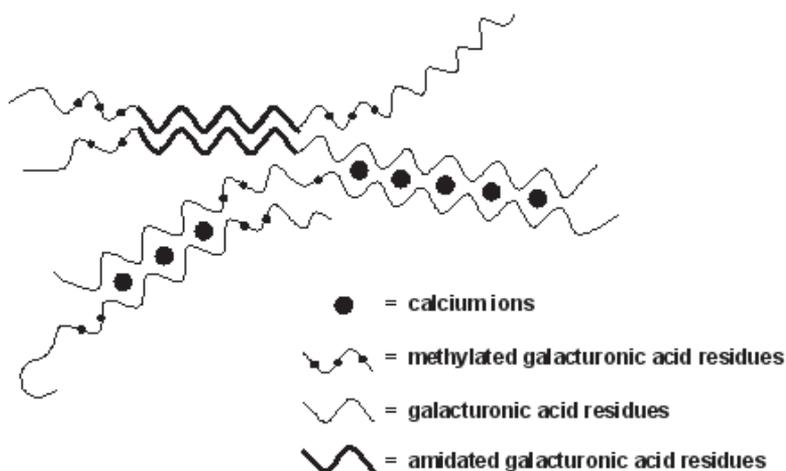


**Fig. 3** Schematic representation of calcium binding to polygalacturonate sequences: ‘egg box’ dimer and ‘egg-box’ cavity (adapted from Axelos & Thibault, 1991).

It is generally accepted that the junctions consist of dimers in  $2_1$  helical symmetry, similar to the  $2_1$  model proposed for alginates (Axelos & Thibault, 1991). The oxygen atoms of the hydroxyl groups, the ring oxygen atoms, and the bridging oxygen atoms of the component sugar units participate in the bonding process through their free-electron pairs (Kohn, 1987). The life of the junction depends on the strength of the electrostatic bonds. The bonds are stable when there are at least seven consecutive carboxyl groups on the interior of each participating chain (Powell et al., 1982). The occurrence of methyl ester groups in the primary backbone limits the extent of such junction zones leading to formation of the gel. Other models for LM-pectin gelation (e.g.  $3_2$  helical model) have been proposed (Walkinshaw & Arnott, 1981a,b), but they are currently unconfirmed by experimentation. Nevertheless, all LM-pectin gels seem to develop similar, if not identical, junction zones (Filippov et al., 1988).

Furthermore, amidation increases or improves the gelling ability of LM-pectin: amidated pectins need less calcium to gel and are less prone to precipitation at high calcium levels (May, 1990).

Racape and coworkers (1989) suggested that the gelation of amidated pectins could not be explained by the 'egg-box' model alone, as blocks of amide groups along the chain promote association through hydrogen bonding. As expected for any polymer, the lower the molecular weight, the weaker the gel. Fig. 4 illustrated the model for gelation of amidated LM-pectins.



**Fig. 4** Model for the gelation of amidated LM-pectins showing ionic interactions between galacturonic acid residues and hydrogen bonding between amidated galacturonic acid residues (adapted from Sriamornsak, 2002).

The gel structure is a net-like formation of cross-linked pectin molecules. The cross-linkages formed by ionic bonds between the carboxyls are strong and produce a rather brittle, less elastic than those formed by hydrogen bonding as in regular pectin. With pectins of lower DE, there is an increasing probability for the formation of cross-links with a given amount of calcium. As the number of reactive carboxyl groups that can form a salt bridge increases, the greater the chances are that the bridge will be formed. Furthermore, because of the larger amount of charged groups, de-esterified molecules are straighter than the esterified ones, so they will be more likely to form calcium linkages (Thibault & Rinaudo, 1985).

The amount of LM-pectin required for the formation of such gel decreases with the DE. The strengths of such ionic bonded gels are strongly dependent on the DE. Monovalent ions such as sodium, which can also react with free carboxyl groups, can affect gel formation because they decrease the cross-linking reaction of calcium and improve the solubility of LM-pectin in the presence of calcium (Axelos, 1990). Although sugar is not essential for gel formation with LM-pectins, the presence of small amounts (10-20%) of sugar tends to decrease syneresis and adds desirable firmness of these gels (Christensen, 1986). When some sugar is present, the amount of calcium required to form gel is reduced. High concentrations of sugar (60% or higher) interfere with gel formation because the dehydration of the sugar favours hydrogen bonding and decreases cross-linking by divalent ion forces.

## Pharmaceutical uses of pectin

Pectin has applications in the pharmaceutical industry. Pectin favourably influences cholesterol levels in blood. It has been reported to help reduce blood cholesterol in a wide variety of subjects and experimental conditions as comprehensively reviewed (Sriamornsak, 2001). Consumption of at least 6 g/day of pectin is necessary to have a significant effect in cholesterol reduction. Amounts less than 6 g/day of pectin are not effective (Ginter et al., 1979). Mietinnen & Tarplia (1977) reported a 13% reduction in serum cholesterol within 2 weeks of treatment.

Pectin acts as a natural prophylactic substance against poisoning with toxic cations. It has been shown to be effective in removing lead and mercury from the gastrointestinal tract and respiratory organs (Kohn, 1982). When injected intravenously, pectin shortens the coagulation time of drawn blood, thus being useful in controlling hemorrhage or local bleeding (Joseph, 1956). Pectin and combinations of pectin with other colloids have been used extensively to treat diarrheal diseases, especially in infants and children. Although a bactericidal action of pectin has been proposed to explain the effectiveness of pectin treating diarrhea, most experimental results do not support this theory. However, some evidence suggests that under certain *in-vitro* conditions, pectin may

have a light antimicrobial action toward *Echerichia coli* (Thakur et al., 1997).

Pectin reduces rate of digestion by immobilising food components in the intestine. This results in less absorption of food. The thickness of the pectin layer influences the absorption by prohibiting contact between the intestinal enzyme and the food, thus reducing the latter's availability (Wilson & Dietschy, 1974; Dunaif & Schneeman, 1981; Flourie et al., 1984). Due to its large water-binding capacity, pectin gives a feeling of satiety, thus reducing food consumption. Experiments showed a prolongation of the gastric emptying half-time from 23 to 50 minutes of a meal fortified with pectin (Holt et al., 1979). These attributes of pectin are used in the treatment of disorders related to overeating (Di Lorenzo et al., 1988).

Pectin hydrogels have been used in tablet formulations as a binding agent (Slany et al., 1981a,b) and have been used in controlled-release matrix tablet formulations (Krusteva et al., 1990; Naggar et al., 1992). Recently, Sungthongjeen et al. (1999) have investigated HM-pectins for their potential value in controlled-release matrix formulations. The application of a binary polymer system, i.e. HM-pectin and hydroxypropyl methylcellulose, in drug release rate modulation for oral administration was studied by Kim & Fassihi (1997a,b,c). Pectin beads prepared by the ionotropic gelation method (Aydin & Akbuga, 1996) were used as a sustained release drug delivery system. However, the use of these beads has some drawbacks due to their rapid *in-vitro* release. By changing the DE of LM-pectin, Sriamornsak & Nunthanid (1998) modified the drug release pattern from calcium pectinate gel beads.

Since pectin can react with calcium ions, calcium pectinate has been investigated as an insoluble hydrophilic coating for sustained release delivery by interfacial complexation process (Sriamornsak 1996; Sriamornsak et al., 1997a,b). The spherical pellets, which contain calcium acetate, were prepared using an extrusion-spheronisation method and then coated in a pectin solution. An insoluble and uniform coating of calcium pectinate gel was formed around the pellets. The use of pectin to develop other oral controlled release drug delivery systems has been reported by some authors (Table 1).

Pectin has a promising pharmaceutical uses and is presently considered as a carrier material in colon-specific drug delivery systems (for systemic action or a topical treatment of diseases such as ulcerative colitis, Crohn's disease, colon carcinomas), as indicated by the large number of studies published over the last few years (Table 2). The potential of pectin or its salt as a carrier for colonic drug delivery was first demonstrated by two studies, i.e. Ashford et al. (1993) and Rubinstein et al. (1993). The rationale for this is that pectin and calcium pectinate will be degraded by colonic pectinolytic enzymes (Englyst et al., 1987), but will retard drug release in the upper gastrointestinal tract due to its insolubility and because it is not degraded by gastric or intestinal enzymes (Sandberg et al., 1983). Rubinstein et al. (1992) demonstrated that pectin-degrading bacteria, *Klebsiella oxytoca*, could adhere to a film casted of low methoxylated pectin. The ability of the bacteria to adhere to the films, however, was not correlated with their ability to degrade pectin. When the dissolution of pectin matrix tablets was analysed with and without *K. oxytoca*, a significant retardation in the dissolution rate was observed in the presence of *K. oxytoca*, suggesting the formation of a biofilm on the matrix or sedimentation of insoluble pectin salts.

Pectin is an interesting candidate for pharmaceutical use, e.g. as a carrier of a variety of drugs for controlled release applications. Many techniques have been used to manufacture the pectin-based delivery systems, especially ionotropic gelation and gel coating. These simple techniques, together with the very safe toxicity profile, make pectin an exciting and promising excipient for the pharmaceutical industry for present and future applications.

**Table 1** Controlled release formulation using pectin.

Dose form	Types of pectin	Application	References
Tablets	Pure and standardised pectin	Binding agents and delayed drug release	Slany et al., 1981a,b
Tablets	HM-pectin	Monolithic bioerodible system	Krusteva et al., 1990
Tablets	HM-pectin	Sustained release properties of direct compression tablets	Naggar et al., 1992
Tablets	HM-pectin (pure and standardised)	Hydrogel matrix system	Sunghongjeen et al., 1999
Tablets	HM-pectin	Direct compression of the mixture of HM-pectin and HPMC	Kim and Fassihi, 1997a,b,c
Gel beads	LM-pectin	Pectin beads prepared by ionotropic gelatin	Aydin and Akbuga, 1996
Gel beads	LM-pectin (amidated)	Sustained release drug delivery using calcium pectinate gel beads	Sriamornsak and Nunthanid, 1998, 1999
Gel beads	LM-pectin (amidated)	<i>In-vitro</i> and <i>in-vivo</i> studies of pectin hydrogel beads	Munjeri et al., 1998; Musabayane et al., 2000
Gel beads	LM-pectin	A crosslinked calcium-alginate-pectinate-cellulose acetophthalate gel spheres.	Pillay et al., 2002
Pellets	LM-pectin	Calcium petinate or calcium alginate-pectinate prepared by ionotropic gelation	Pillay and Fassihi, 1999
Particulates	LM-pectin	Alginate-pectin-polylysine system	Liu and Krisnan, 1999
Microspheres	LM-pectin	Pectin-based microspheres prepared by emulsification technique	Esposito et al., 2001; Wong et al., 2002
Coated pellets	LM-pectin (amidated and non-amidated)	Insoluble calcium pectinate gel coating for sustained release delivery prepared by interfacial complexation	Sriamornsak et al., 1997a,b

HM-pectin = high methoxy pectin; LM-pectin = low methoxy pectin.

**Table 2** Colon-specific drug delivery using pectin.

Dose form	Types of pectin	Application	References
Tablets	Calcium pectinate	Compression of calcium pectinate (matrix system)	Rubinstein et al., 1993
Tablets	HM-pectin	Compression coat	Ashford et al., 1993
Tablets	HM-pectin and LM-pectin	Matrix system	Ashford et al., 1994
Tablets	Calcium pectinate	Matrix system and compression coat	Rubinstein and Radaï, 1995
Tablets	HM-pectin and LM-pectin	Direct compression of HM-pectin or LM-pectin alone or combined with MCC	Kim et al., 1998
Tablets	HM-pectin	Compression coated with HM-pectin/ethylcellulose mixtures	Semde et al., 1999
Tablets	Amidated LM-pectin and calcium salt of pectin	Direct compression of amidated or calcium of pectin alone or incorporated with ethylcellulose	Ahrabi et al., 2000
Gel beads	LM-pectin (amidated)	Formation of a chitosan polyelectrolyte complex around calcium pectinate beads	Munjeri et al., 1997
Gel beads	LM-pectin (amidated)	Calcium pectinate gel beads for protein delivery	Sriamornsak, 1998, 1999
Film coated tablets	HM-pectin	Coating with mixtures of HM-pectin and ethylcellulose aqueous dispersion	Wakerly et al., 1997; Macleod et al., 1997
Film coated tablets	HM-pectin or LM-pectin	Coating with HM-pectin or LM-pectin combined with commercially aqueous polymer dispersion	Semde et al., 1998, 2000a,b
Film coated tablets	HM-pectin	Coating with HM-pectin or HM-pectin/chitosan mixtures	Fernandezhervas and Fell, 1998; Macleod et al., 1999a
Film coated tablets	HM-pectin	Coating with mixtures of HM-pectin/chitosan/HPMC	Macleod et al., 1999b
Capsule with plug	LM-pectin	Direct compression of pectin/pectinase-plug	Krogel and Bodmeier, 1999

HM-pectin = high methoxy pectin; LM-pectin = low methoxy pectin; HPMC = hydroxypropyl methylcellulose.

## Conclusion

The chemistry and gel-forming characteristics of pectin have enabled this naturally occurring biopolymer to be used in pharmaceutical industry, health promotion and treatment. It has also been used potentially in pharmaceutical preparation and drug formulation as a carrier of a wide variety of biologically active agents, not only for sustained release applications but also as a carrier for targeting drugs to the colon for either local treatment or systemic action. By selection of the appropriate type of pectin, gelation conditions, added excipients, and coating agents, the dosage forms of various morphology and characteristics can be fabricated. As research and development continues with delivery system using pectin, we expect to see many innovative and exciting applications in the future.

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