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Nutrition and health effects of pectin: A systematic scoping review of human intervention studies

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Abstract

Pectin is composed of a group of complex polysaccharides that are naturally found in various plants and are associated with a range of beneficial health effects. Health outcomes from dietary pectin can vary depending on botanical origin, dietary dose and structure of pectin. The objective of this scoping review is to build a comprehensive overview of the current evidence available on intervention studies conducted in humans and to better understand the possible knowledge gaps in terms of structure–function relationships across the different health-related effects. PubMed and Embase databases were searched using PRISMA-ScR guidelines, yielding 141 references (from the initial 3704), representing 134 intervention studies performed between 1961 and 2022 that met inclusion criteria. Studies were divided into six categories, which included gut health, glycaemic response and appetite, fat metabolism, bioavailability of micronutrients, immune response and other topics. Review of these human intervention studies identified a variety of cohort characteristics and populations (life stage, health status, country), sources/types of pectin (i.e. citrus, sugarbeet, apple, other and non-defined), intervention timeframes (from one single intake to 168 d) and doses (0.1–50 g/d) that were tested for health outcomes in people. Gut health, post-prandial glucose regulation and maintenance of blood cholesterol represented the largest categories of studied outcomes. Further research to strengthen the structure–function relationships for pectin with health properties and associated outcomes is warranted and will benefit from a more precise description of physico-chemical characteristics and molecular compositions, such as degree of esterification, weight, degree of branching, viscosity, gel formation and solubility.

Key words: **blood cholesterol: dietary fibre: galacturonic acid: glucose regulation: gut health: human intervention studies: immune response: pectin**

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Introduction

Health benefits related to high-fibre diets have been acknowledged for many years; however, average intakes for adults still do not reach dietary recommendations to consume 25–30 g/d in many countries across the globe[1]. Moreover, not all fibres are the same, and the structures, characteristics and interactions with other food ingredients and beverages differ from one another regarding impact on the host physiological functions[2].

Pectin, a well-known dietary fibre, is a group of complex polysaccharides naturally occurring in many plants[3] and is acknowledged by various health authorities, including the European Food Safety Agency (EFSA) and the Food and Drug Administration (FDA) in the USA. Not digested in the small intestine but fermented in the large intestine, pectin is recognised for its benefits on the regulation of post-prandial blood glucose and the reduction of blood total and/or low-density lipoprotein (LDL) cholesterol levels[3–6]. Recent observational studies have highlighted the specific association of pectin with various markers of health in diverse populations. Interestingly, intake of pectin during pregnancy is one of the dietary components that was associated with a higher secretion of human milk oligosaccharides in breast milk[7] and positively correlated with improved accuracy response during cognitive tests among prepubertal children[8]. Physiological effects of pectin may be related to its physico-chemical properties (i.e. for blood cholesterol modulation[9]), whereas other benefits might also be linked to its direct interaction with various receptors located in the gut or via its fermentation by gut microbiota[10–12].

Not all pectin is the same, and the variety of pectin chemical structures mainly depends on the botanical origin, part of the plant and extraction method. The backbone of the polysaccharides is composed of galacturonic acid (GalA) linked by α(1,4) bonds. Pectin is formed of three blocks: homogalacturonan (HG), rhamnogalacturonan (RG-I) and substituted galacturonan (RG-II), the most complex structure (Figure 1). The ratio between the different blocks is plant-specific and can be modified by enzymes during the extraction process. Most commercially available pectin is obtained by up-cycling citrus peels and apple pomace generated by the juice industry, as well as sugarbeet pulp from the sugar industry. Besides botanical

Abbreviations: DE, Degree of methyl esterification; HG, Homogalacturonan; RG, Rhamnogalacturonan; LM, Low-methoxyl; HM, High-methoxyl; MW, Molecular weight.

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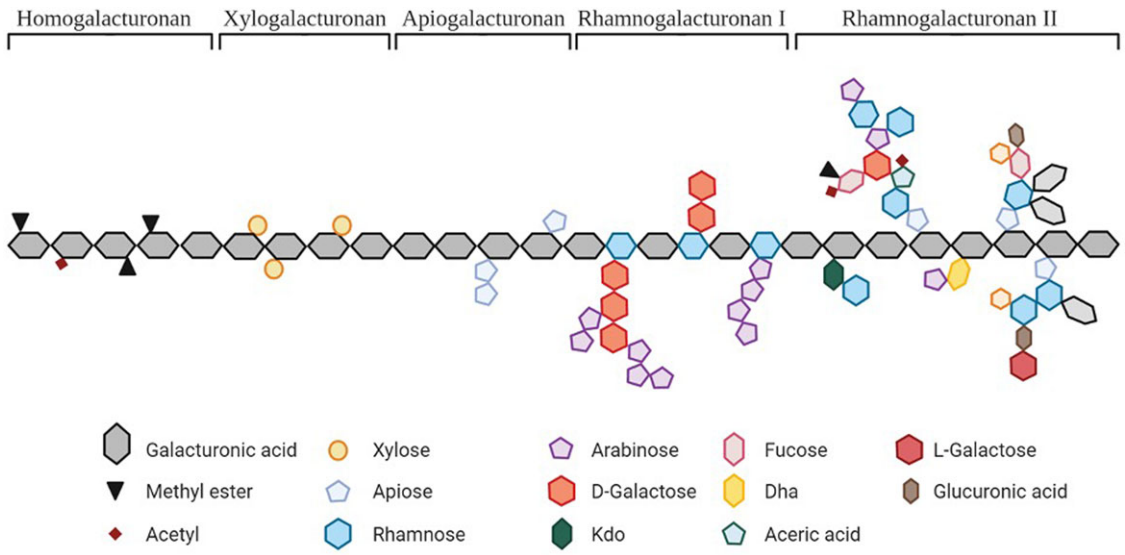

Fig. 1. Overview of the pectin structure[11]. Copyright: Creative Commons—Attribution 4.0 International—CC BY 4.0. Kdo, 3-deoxy-D-manno-2-octulosonic acid. Dha, -3-deoxy-D-lyxo-2-heptulosaric acid.

origin, pectin is qualified according to its degree of methyl esterification (DE), that is, the percentage of GalA units esterified. Pectin structures can be defined as high-methoxyl (HM) for DE of 50% and above, or low-methoxyl (LM) for DE below 50%[10,13]. Pectin is often used as food additives (E440/INS440) for gelling and viscosifying properties. A reason to distinguish pectin according to DE is the different functional properties and ability to gel in different food applications that vary in pH and heat treatment. Sugarbeet pectin can also be acetyl-esterified on the GalA residues of HG having, for instance, a negative impact on gelling but offering other properties[13]. Several authors suggest that the molecular structure of pectin can influence its impact on health[9,10,12]. Also, a recent systematic review on *in vitro* fermentation studies performed using human faecal samples as inoculum highlighted the impact of the molecular structure of pectin, and especially the DE, the ratio between HG and RG and the molecular weight, on the modulation of the gut microbiome composition[11].

Few published reviews have focused on pectin and human health-related outcomes, as most have concentrated on *in vitro* or animal studies. To the best of our knowledge, there is no scoping review of dietary pectin in human intervention trials. Therefore, the objective is to build a comprehensive overview of the current evidence available on intervention studies conducted in humans and to better understand the possible knowledge gaps in terms of structure–function relationship across different health-related effects. Pectin is present in many plant-based foods that are associated with other beneficial nutrients such as polyphenols, minerals and vitamins. This scoping review focused on intervention studies where commercial pectin was tested and would potentially have been characterised to highlight the variety of botanical sources, wide range of dosages, intervention duration, study designs and specific categories of health outcomes.

Methods

This scoping review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR)[14] guidelines (**Supplementary Table 1**).

Information sources

A systematic search to map the available evidence on nutrition and health effects of pectin in humans was performed. A comprehensive literature search was performed using both PubMed and Embase to identify human intervention studies published until March 2023. Additional citations listed within studies assessed for eligibility were also screened, as well as European Food Safety Agency (EFSA) opinions from 2010 and 2021[4,15], Food Standards Australia New Zealand (FSANZ), 2016[16], Food and Drug Administration (FDA) report on dietary fibre in 2018[5], Institute for the Advancement of Food and Nutrition Sciences (IAFNS) 'Diet-Related Fibers and Human Health Outcomes Database'[17] and grey literature. The final comprehensive search was performed on 31 July 2023.

Search and selection criteria

The search strings applied to conduct this search can be found in **Supplementary Table 2**. All identified records were imported into Covidence software[18], which was used to remove duplicates. The titles and abstract were screened by two independent reviewers, and conflicts were solved jointly with the option for review by a third author who was not involved in the screening. The remaining full-text papers were screened again by two independent reviewers. Any remaining duplicates were removed at this stage.

Inclusion criteria were the following: human intervention study; dietary supplementation or enteral feeding; pectin-derived

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ingredient (pectin, hydrolysed pectin, pectin oligosaccharides, rhamnogalacturonan) was tested as a single ingredient or there was an appropriate control treatment (for instance, the same food/blend of ingredients without added pectin) or baseline comparison; full text availability; and in the English language. Studies were excluded if they were *in vitro*, *ex vivo* or animal studies, were testing plant extracts/plant fibres, were epidemiological or observational studies, were testing non-oral intake, or were conference abstracts or reviews or medical case reports. Authors that did not report the exact amount of pectin used in the study were contacted for these details, and if there was no clarification, these articles were excluded.

Data extraction and synthesis

Data extraction was performed by first importing the list of included studies from Covidence into an Excel spreadsheet. The data were extracted and collated from the selected publications by a single reviewer (F.R., N.P., A.M.W.), with review of the data by all researchers. The studies were categorised according to the following categories and their related reported outcomes: gut health: gut function (transit, symptoms), gut microbiota composition, fermentation (short-chain fatty acids (SCFA), pH, breath gas); glycaemic response and appetite: gastric emptying, post-prandial blood glucose and insulin, hormones related to glycaemia and appetite, and measures of satiety; fat metabolism: measurements of blood cholesterol, measurement of triacylglycerol, fat absorption and bile acid changes; bioavailability of minerals/vitamins/other micronutrients; immune health: immune markers, response to vaccination and infections; and others for all other outcomes. The extracted data also included type of population studied (i.e. life stage, health status and enteral feeding), product type and dose, duration of intervention, study country, and study design and size. Populations were listed as 'healthy' if stated by the author and were absent of known disease. As study design, we considered the following: randomised controlled trial (RCT) parallel, RCT crossover, and non-randomised: comparison with baseline only/single-arm studies. If the study did not specify randomisation, it was classified as 'non-randomised'[19].

A full list of the charting data extracted can be found in **Supplementary Table 3**. The results were analysed and summarised by the categories listed above and together as a whole in Excel.

Results and discussion

Selection of sources of evidence and characteristics of the studies

The number of retrieved publications and the selection is illustrated in the PRISMA flow diagram (Figure 2). Overall, 134 studies (published in 141 scientific references, due to duplicate publications on the same study, and instances of multiple studies in a single publication) published between 1961 and 2022 were selected. The studies included were conducted in thirty different countries around the world (Figure 3). The participant characteristics of the human intervention studies included in this scoping review are displayed in Table 1.

The majority of studies covered outcomes related to gut health ($n = 50$; reported in fifty-two publications) followed by glycaemic response and appetite ($n = 47$), fat metabolism ($n = 34$; reported in thirty-six publications), bioavailability of micronutrients ($n = 20$; reported in twenty-two publications) and other topics (e.g. radioactivity, heavy metals, cancer-related, bioavailability of drugs, infant growth parameters, cardiovascular health) ($n = 21$). Immune health-related studies ($n = 8$; reported in nine publications) are a more recent subject, with the first paper published on this topic in 2008 (Figure 4). The most common reference to pectin source was non-defined; however, other prevalent botanical origins included citrus and apple (Figure 5). Citrus was the most common botanical origin of pectin tested for fat metabolism and bioavailability of micronutrient studies and was widely used for gut health studies. Types of pectin included in the 'other' pectin category included carrot RG-I and other RG-I sources (e.g. potato).

The maximum reported dose was 50 g/d of HM pectin for 14 d[20]. Seven other studies also tested daily doses above 30 g/d for 1–42 d[21–29] (Figure 6). The longest studies evaluated the consumption of 1 g/d of citrus pectin oligosaccharides for 127 d in infants[30] and 0.4–20 g/d of citrus pectin, hydrolysed citrus pectin and apple pectin for 168 d in healthy and non-healthy adults[31–35] (Figure 7).

Among the ninety-one studies that were randomised controlled trials, thirty-three were conducted with parallel groups and fifty-nine in a crossover manner. Another forty-two studies were not randomised: thirty-one of them were conducted before 2000, and the more recent ones were pilot single-arm studies that explored new areas for potential health benefits related to pectin consumption (Figure 8).

Summary for gut health

Fifty studies (reported in fifty-two publications) evaluated markers related to gut health dating back to 1976. Of these studies, thirty-one were conducted before 2000. The botanical origin of the pectin used was not described in more than half of the studies, citrus was the second most frequently evaluated, followed by apple ($n = 3$) and sugarbeet ($n = 2$, Figure 5). The dose of pectin tested in studies ranged from 0.4 g/d to 50 g/d (Figure 6), with an average and median tested dose of 13.5 g/d and 12.6 g/d, respectively. The average duration of pectin intervention was 22 d, and the median 9 d (Figure 7). Most of the studies evaluated markers related to gut function (i.e. transit time, faecal output, digestive symptoms, gut barrier)[20,23–27,30–32,36–68] or gut fermentation (i.e. breath gas, faecal pH, SCFA, microbial enzymes)[23–25,36,38–40,43,48–50,54,55,58,60,61,64,66,67,69–75] (Figure 8).

Most of the studies were conducted in healthy subjects ($n = 2$ in infants, $n = 25$ in adults, $n = 1$ in elderly >65 years). The two RCT parallel studies in infants have specifically evaluated the digestive tolerance and other gut-related effects of approximately 1 g/d of citrus pectin oligosaccharides (95% < 3.8 kDa) supplemented via the infant formula (in replacement of equivalent dose of maltodextrin) for 50–127 d[30,38]. The study in elderly compared, in an RCT parallel design, the effect of 15 g/d of sugarbeet pectin versus maltodextrin on the gut

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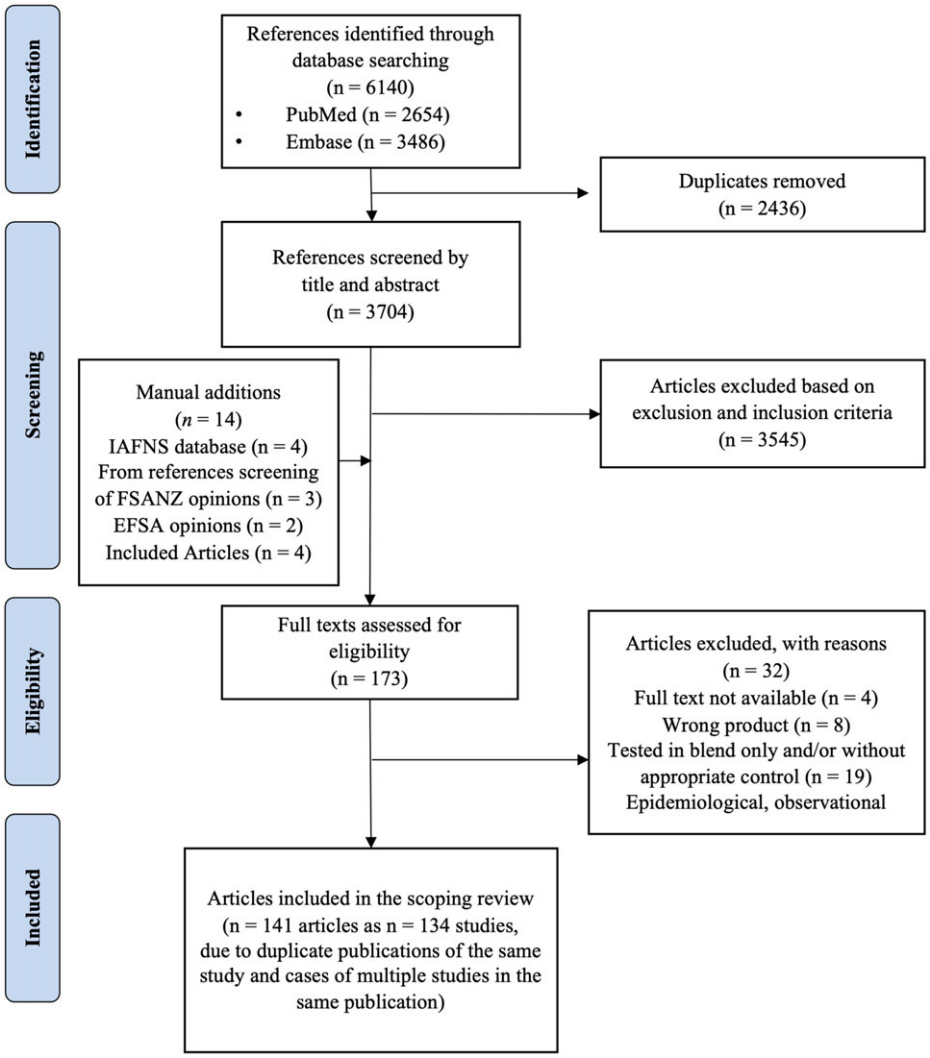

Fig. 2. PRISMA-ScR flow diagram of the publication search and screening process. IAFNS, Institute for the Advancement of Food and Nutrition Sciences; FSANZ, Food Standards Australia New Zealand; EFSA, European Food Safety Agency.

microbiome and associated outcomes between elderly and younger adults[60]. Overall, there is limited impact of a dietary supplementation with pectin on the gut function (full transit time, frequency and consistency of stools) of healthy individuals, illustrating a good digestive tolerance until 50 g/d, which is the maximum reported tested dose in humans. At this level and similar to what is observed in general with dietary fibres, there is a transient increase of flatus gas correlated with higher production of SCFA and, thus, microbial fermentation of pectin[46,47].

Several studies were also conducted in specific sensitive or non-healthy populations. Two RCT parallel studies evaluated pectin (non-defined origin) supplementation for 7 d on the improvement of digestive symptoms and intestinal permeability in infants and young children with recurrent diarrhoea[46,47]. Studies conducted in non-healthy adults ($n = 2$ RCT crossover, $n = 4$ RCT parallel and $n = 5$ non-randomised) included: gastro-oesophageal reflux disease ($n = 2$)[31], gastric surgery ($n = 2$)[61,76], other intestine surgery ($n = 2$)[49,53], small intestine-related issues ($n = 2$)[32,36], ulcerative colitis ($n = 1$)[56], hypercholesterolaemic adults ($n = 2$)[20,77]. Finally, nine RCT studies ($n = 7$ parallel, $n = 2$ crossover) evaluated the thickening effect of an equivalent daily dose of 1.4–16 g of pectin (mostly not described origin) to enteral feeding for 1–30 d during hospitalisation of patients. Frequency and severity of gut symptoms usually occurring with this type of feeding were evaluated[42,44,45,52,59,63,65,67]. There was a general decrease of digestive symptoms observed in fragile populations such as hospitalised patients with enteral feeding, who experienced fewer reflux and diarrhoea events. These benefits can be seen with a minimum of 2.5 g/d of pectin and are certainly explained by a thickening effect of pectin in the enteral formula especially when the pH starts to decrease in the stomach. This effect was also observed in formula-fed infants presenting frequent reflux symptoms when their usual formula was switched to a pectin-thickened (with other thickeners) formula[78]. Unfortunately, there is a general lack of description on the type of pectin that was tested, except that it is of citrus origin. However, LM pectin is known to react

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Table 1. Characteristics of the study participants, pectin daily dose and intervention duration from included studies ($n = 134$)

Study characteristics		Number of studies (% of total)	Daily dose (g/d) min–max	Duration (d) min–max
Life stage	Preterm/infants	5 (3%)	1–10	7–150
	Children	8 (6%)	5–15	7–84
	Adults	101 (76%)	0.1–50	1–168
	Elderly	2 (1%)	2.5–9.9	1–7
	More than 1	18 (14%)	0.4–15	1–168
Health status	Healthy	82 (61%)	0.1–40	1–168
	Healthy and non-healthy	3 (3%)	0.6–50	1–56
	Non-healthy	49 (36%)	0.4–20	1–168
Type of health condition*	Bariatric surgery	1 (2%)	4.2	1
	Cancer	2 (4%)	14.4–15	28–168
	Congenital disorder	1 (2%)	5	28
	Diabetes	6 (11%)	10–20	1–84
	Dumping syndrome	4 (7%)	5–14.5	1
	Gut-related disease	10 (20%)	0.4–20	1–168
	Haemochromatosis	1 (2%)	15.75	1
	Hypercholesterolaemic/hypertension	8 (15%)	9.6–50	14–168
	Infection/intensive care	8 (15%)	1.4–16	7–30
	Toxicant exposure	5 (10%)	3.6–15	7–28
	Undernutrition	1 (2%)	10	10
	Obesity	2 (4%)	0.6–15	1–56
	Osteoarthritis	1 (2%)	8	84
	Pancreatic deficiency	1 (2%)	5	1
	Stroke	1 (2%)	5.4	7
Consumption mode	Oral intake	122 (91%)	0.1–50	1–168
	Enteral feeding	12 (9%)	1.4–16	1–30

* Includes non-healthy participants in 'healthy and non-healthy' studies ($n = 3$), and 'non-healthy' studies ($n = 49$).

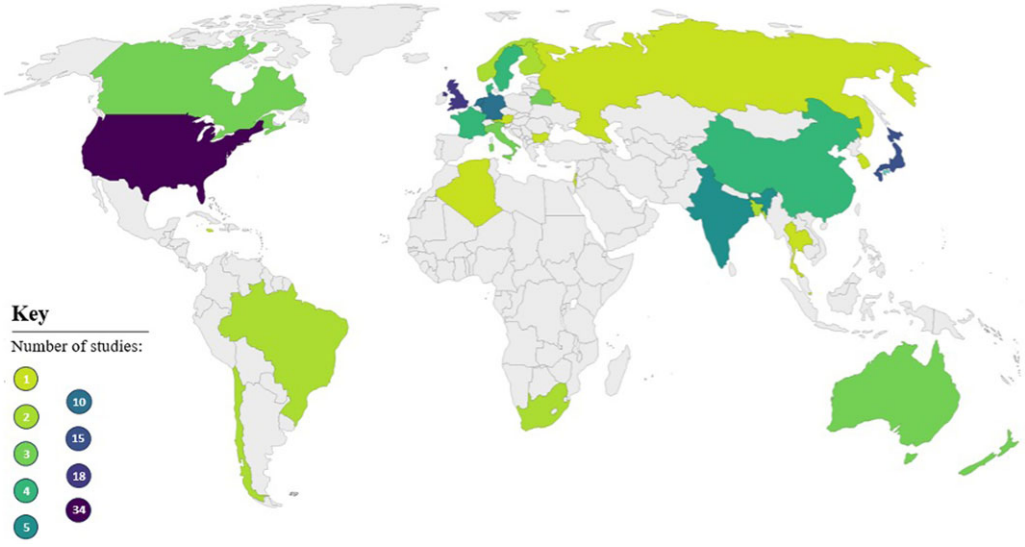

Fig. 3. World map depiction to highlight countries with human clinical investigations of dietary pectin ($n = 134$) included in the scoping review. Colours indicate the number of studies completed in each country.

with ionised calcium, especially in acidic conditions; thus, we can hypothesise that, as reported by Tabei *et al.* (2018), LM pectin could be favoured for enteral feeding[52].

Despite a significant amount of research conducted *in vitro* in human gut microbiome models[11], there is still a limited number of intervention studies that have evaluated the effects of pectin on the gut microbiota composition[30,38,43,54–56,60], and among them only three studies report composition obtained with 16S rRNA/DNA techniques[54,56,60]. In general, these studies reported limited effects, except for pectin-derived ingredients with the lowest molecular weight[30,54]. However, several intervention studies demonstrate that pectin is slowly but completely fermented by the bacteria in the human gut microbiome, which can relate to higher SCFA production, especially acetate[23,24,50,72]. Because of the relatively poor reporting of the characteristics of the pectin, it is not possible to confirm yet if there is a visible

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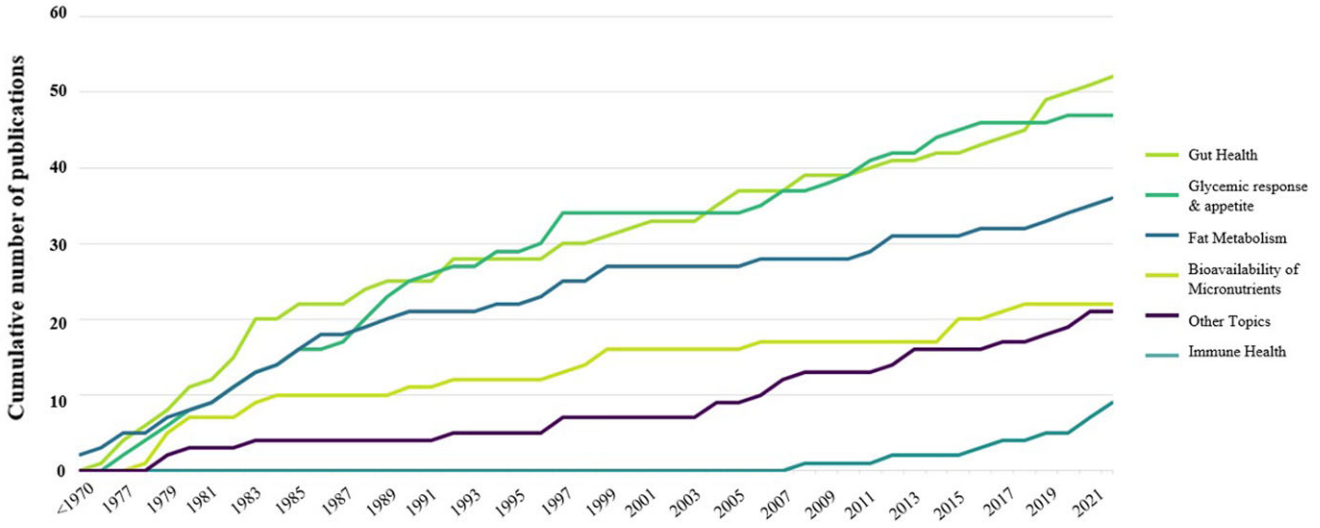

Fig. 4. Publications ($n = 141$) timeline for human intervention studies with dietary pectin ($n = 134$) for the six most common categories of health-related effects. One reference can include several categories.

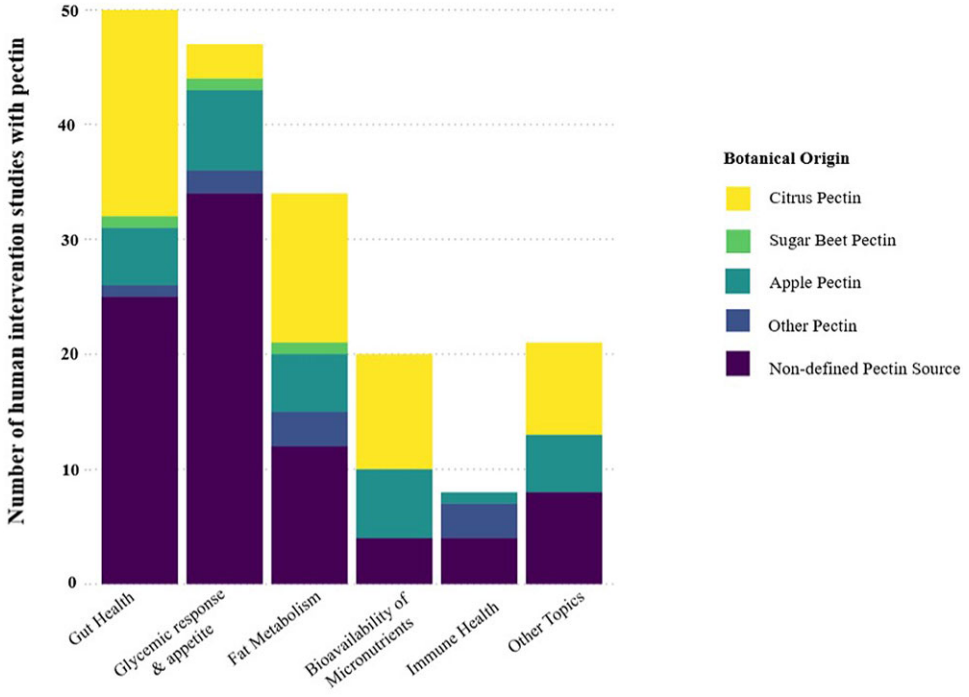

Fig. 5. Human intervention studies ($n = 134$) and pectin botanical origin by health topic.

structure–function relationship in human studies as it was found for *in vitro* studies conducted with human gut microbiome[11], nor what the minimum dose and duration of supplementation are to observe the increased production of SCFA.

Summary for glycaemic response & appetite

The effect of pectin on glycaemic response has been widely studied, with interventions related to glycaemic response and appetite being the second largest health topic and including forty-seven studies. The publication date of these studies ranged from 1977 to 2020, though only thirteen of these forty-seven studies were published after the year 2000. The pectin botanical origin tested in these studies consisted primarily of non-defined pectin sources ($n = 34$), as well as apple ($n = 8$) and citrus ($n = 2$) (Figure 5). The dose of pectin tested in studies related to glycaemic response ranged from 0.1 g/d to 40 g/d (Figure 6), with an average and median tested dose of 13.2 g/d and 14.5 g/d, respectively. The average duration of pectin intervention was 11 d, though the median was 1 d, as twenty-nine of the forty-seven studies were 1-d, single-intake studies (Figure 7).

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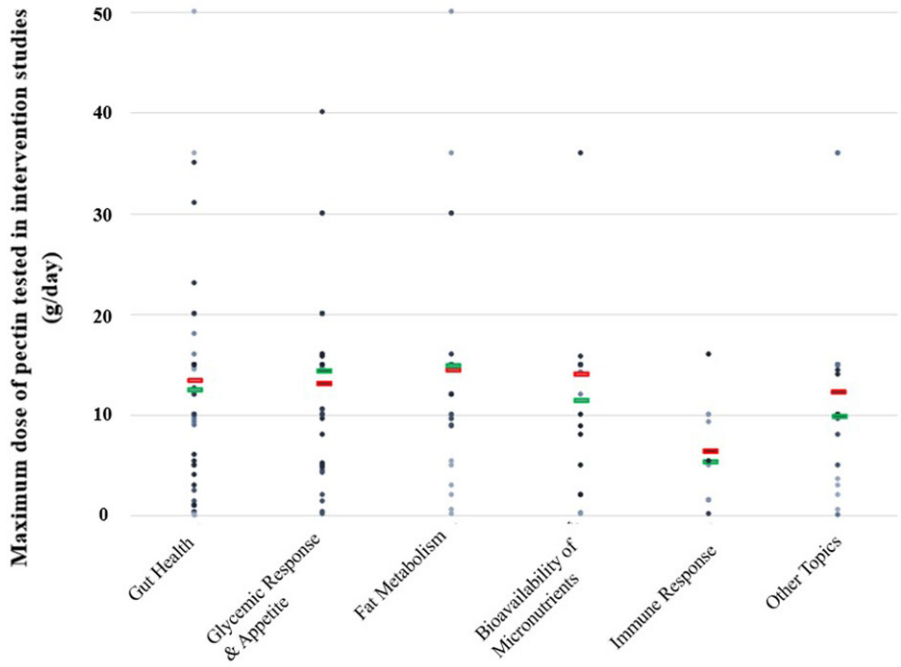

Fig. 6. Maximum daily dose of pectin evaluated in human intervention studies ($n = 134$) according to health topic. Average (red line) and median (green line) pectin daily dose.

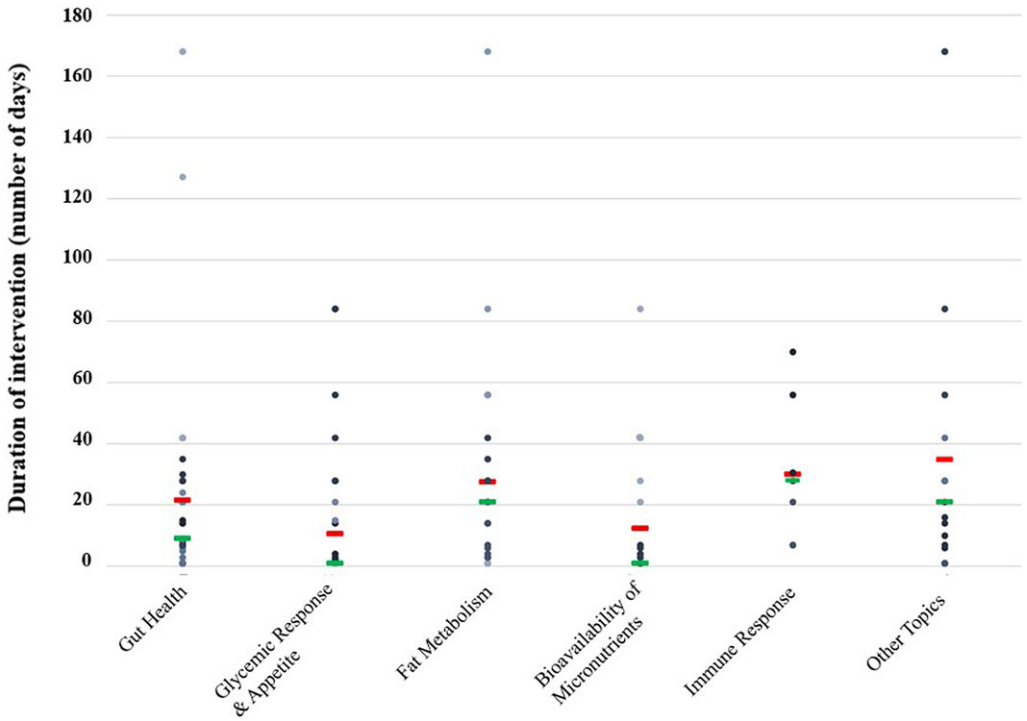

Fig. 7. Study duration for human intervention studies ($n = 134$) with pectin (number of days) for each health topic category, including average (red line) and median (green line).

Within this health topic, measured outcomes related to glycaemic response commonly included post-prandial glucose and insulin response[21,28,54,71,79–96]. Other measures included gastric emptying[36,64,67,80,81,84,86–88,95,97–104], satiety[54,67,80,85,87,95,98,105–108], fasting glucose[54,67,77,85,109–112], other hormonal responses related to glycaemic response[29,67,80,84,86–88,98,110,113], and haemoglobin A1C (HbA1C)/Homeostatic Model Assessment for Insulin Resistance (HOMA-IR)[85,109,110,113] (Figure 8). Overall outcomes found pectin to be related with a reduction in post-prandial

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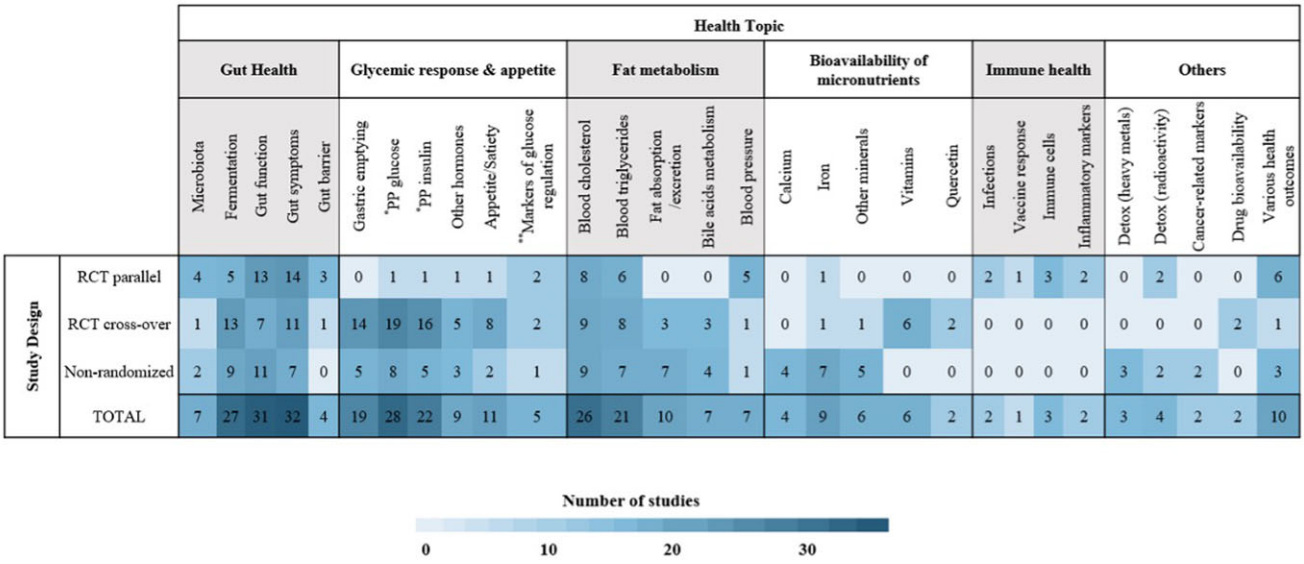

Fig. 8. Heatmap visualisation for types of human study design by health topic. Multiple health topics may be covered in one study. *PP, post-prandial. **Markers of glucose regulation: fasting blood glucose, HOMA-IR, glycated haemoglobin.

blood glucose and insulin peaks, increased satiety and delayed gastric emptying in both healthy and non-healthy individuals. Study design consisted mainly of RCT crossover ($n = 32$), followed by non-randomised studies ($n = 11$) and RCT parallel ($n = 5$). Furthermore, most of the RCT crossover studies were single intake ($n = 24$).

Fifteen studies within this health topic were conducted in adults with various health complications. Participants with short bowel syndrome and jejuno-colonic anastomosis, when consuming ~10 g/d of citrus pectin, did not experience differences in gastric emptying time[36]. Three studies of hypercholesterolaemic participants[77,110,112] found no effect of pectin consumption on fasting glucose levels, nor on gastric emptying. However, Sirtori *et al.* (2012) found hypercholesteraemic participants consuming bars with casein + apple pectin had significant reductions in post-prandial insulin levels[110]. In a study of adults with obesity, it was reported that consuming 15 g/d of pectin with a test meal significantly delayed gastric emptying time and also increased satiety[98]. Outcomes in those with diabetes found some improvement in glucose tolerance related to pectin consumption[82,86,114], though some found no significant change with pectin consumption related to glycaemic control[96,109,113]. The type of test meals consumed with pectin in the trials may lead to different results, especially in 'non-healthy' individuals. In the study by Vaaler *et al.* (1980), pure pectin lowered post-prandial blood glucose in insulin-dependent diabetics; however, the same effect was not seen in a barley/citrus fibre mix which included pectin along with other fibre types[114], highlighting the impact of the difference in structures and composition of fibres, especially in those with diabetes. Other health complications included dumping syndrome[76,81,97] and post-bariatric surgery[93]. For those experiencing dumping syndrome, in which after eating there is a rapid emptying of bowel contents into the colon alongside and rebound hypoglycaemia, pectin was generally related to prolonged gastric emptying and reduction in hypoglycaemia[81]. Two studies also tested pectin in healthy adults through enteral feeding and found that pectin increased viscosity of enteral nutrition as well as was related to reduced glucose ingestion[88,115].

These findings on glycaemic response have also been summarised by EFSA (2010) which states the finding of a 'cause and effect relationship has been established between the consumption of pectin and reduction of post-prandial glycemic responses', with at least 10 g of pectin per meal in adults[4]. Possible mechanisms of action related to pectin and controlled glycaemic responses are likely due to delayed gastric emptying, reduced sugar diffusion and absorption, and slowed release of digestion-related gut hormones[116,117]. However, many of the studies in this review related to post-prandial glucose response were single-intake studies. Future work is needed to identify relationships between long-term regulation of glycaemic response and pectin intake.

Summary for fat metabolism

There were thirty-four studies (reported in thirty-six publications) included in this review related to the health topic of fat metabolism, with publications dating from 1961 to 2022. Of these studies, twenty-five were published prior to 2000 (Figure 4). Pectin botanical origin tested in these studies was commonly citrus and non-defined sources (Figure 5). The dose of pectin tested in these studies ranged from 0.1 g/d to 50 g/d, with the average and median dose being 14.6 g/d and 15 g/d, respectively (Figure 6). The duration of the interventions was on average 28 d, though many were single-intake studies, and the median was 21 d (Figure 7).

Major outcomes studied in these publications were related to measures of blood cholesterol[9,20,22,26,29,35,37,40,41,44,51,54,55,74,77,85,109–112,118–125], blood triacylglycerol[9,20,22,26,37,40,41,54,55,74,77,85,109–112,119,120,122–124], fat absorption/excretion[20,28,36,40,41,48,49,51,115,126,127], bile acid metabolism[20,40,41,48,51,121,126] and blood pressure[34,51,54,77,85,110–112] (Figure 8). Most studies in this health

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topic were non-randomised study designs ($n = 14$), followed by RCT crossover ($n = 11$) and RCT parallel design ($n = 9$). Furthermore, fourteen studies tested pectin consumption in non-healthy adults and elderly populations, with obesity[118], diabetes[109], gut-related symptoms[36,49,126], hypercholesterolaemia/hypertension[20,34,74,77,110,112,124], pancreatic insufficiency[127] or severe stroke[44].

Of the thirty-four studies related to fat metabolism, twenty-eight reported positive effects of pectin on lowering cholesterol, triacylglycerol or fat absorption. Brouns *et al.* (2012) examined the cholesterol-lowering properties of pectin derived from various botanical sources with differing DE and molecular compositions[9]. Here, both citrus (DE 70%) and apple pectin (DE 70%) were most efficacious in lowering cholesterol, compared with citrus and apple pectin of low MW and DE, indicating pectin cholesterol-reduction properties to be dependent on molecular structure.

Several studies that measured cholesterol and triacylglycerol in relation to pectin consumption found that pectin was related to serum cholesterol reduction but had no effect on serum triacylglycerol[20,22,28,29,36,37,40,41,49,109,118–120]. These results were found conclusive by EFSA Scientific Opinion (2010), and it has since been stated that 'a cause-and-effect relationship has been established between the consumption of pectin and maintenance of normal blood cholesterol concentrations', with at least 6 g/d of pectin in one or more serving in adults[4]. This is likely due to the increased gut viscosity from pectin, which limits the reabsorption of bile acids, increases cholesterol elimination in faeces as bile acids, upregulates bile acid synthesis from cholesterol and decreases levels of circulating cholesterol[128].

Six studies measured blood pressure in relation to pectin intake. However, only one of the studies demonstrated a decrease in blood pressure after 16 g/d of sugarbeet pectin for 84 d[85], whereas the others evaluated lower doses (0.1–15 g/d) of supplementation and did not show any changes to blood pressure[51,54,110–112].

Summary for bioavailability of micronutrients

Twenty human intervention studies (reported in twenty-two publications) investigating the effect of pectin on the bioavailability of micronutrients were included in this review. Most of these studies evaluated citrus pectin ($n = 10$), apple pectin ($n = 6$) or pectin from a non-defined origin ($n = 4$) (Figure 5). The doses of pectin tested in studies ranged from 0.1 g/d to 36 g/d (Figure 6), with an average and median tested dose of 14.2 g/d and 11.5 g/d, respectively. The average duration of pectin intervention was 12.4 d, though the median was 1 d, as eleven of the twenty-two studies were 1-d, single-intake studies (Figure 7). Most frequently evaluated outcomes were iron bioavailability ($n = 9$; ten publications)[49,112,129–136], calcium bioavailability ($n = 4$)[23,49,133,136] (Figure 8) and other minerals bioavailability: copper ($n = 4$ non-randomised studies)[109,130,133,136]; zinc ($n = 4$ non-randomised studies)[49,109,130,137]; magnesium ($n = 3$ non-randomised and $n = 1$ RCT crossover studies)[49,109,136,137]; sodium ($n = 2$ non-randomised studies)[49,136]. Fifteen studies were conducted with healthy adults and five with non-healthy adults: idiopathic hemochromatosis ($n = 1$)[129,131], ileostomy subjects ($n = 1$)[49], diabetes ($n = 1$)[109] and hypercholesterolaemia/hyperlipoproteinaemia ($n = 2$)[112,136].

One study found lower apparent iron absorption from the small intestine in six subjects with ileostomy[49], and one single-intake study in patients with idiopathic haemochromatosis exhibited a significant drop in fractional absorption of inorganic iron compared with cellulose[129,131]. On the contrary, seven other studies conducted in healthy or hypercholesterolaemic/lipoproteinaemic subjects found no effect on iron balance at daily doses between 0.25 and 15 g/d and up to 84 d of supplementation[112,130,132–136]. Similarly, no significant effect on calcium balance was reported by the four studies that investigated it with a daily dose of pectin between 15 and 36 g/d and up to 84 d of supplementation[23,49,133,136]. There was also no effect on the balance of the other evaluated minerals mentioned above. In general, pectin dietary supplementation had no impact on mineral balance in humans. There is a possibility that pectin might bind with some minerals in foods (e.g. Ca^{2+}) or in the small intestine and limit their local absorption, with a possible influence of the degree of methylation on this phenomenon[138], but this is not confirmed by human intervention studies[49,135,137], even at high doses such as 36 g/d of HM pectin (72%) for 42 d[23] or in sensitive population like preterm infants (0.085% in human milk fortifier for 28 d)[139]. As pectin is completely fermented in the large intestine and metabolised into SCFA, this can enhance the absorption of minerals from the colon, as it has been demonstrated for other non-digestible fermentable carbohydrates and prebiotics[140]. The potential of colonic absorption estimated at approximately 10% for calcium in humans might fully compensate for the potential reduction in the small intestine and explain the neutral impact on mineral balance.

Contrary to the studies that have evaluated mineral balances, intervention studies aiming to evaluate the potential impact of pectin-derived ingredients on vitamins and one type of flavonoid (i.e. quercetin), are all single-intake studies, except one that was short-term (7 d), and all were randomised crossover (Figure 8). Two single-intake studies found no significant impact of pectin on the mean serum concentration of α-tocopherol (vitamin E) when it was consumed with pectin (0.1 g of apple pectin or 8.9 g of HM citrus pectin)[122,141,142]. One study reported a reduction of urinary excretion of ascorbic acid (vitamin C) in healthy subjects with intake of citrus pectin for 7 d, and the reduction tended to be more important with 14.2 g/d than 4.2 g/d[143]. Another study demonstrated that a single intake of 15 g of apple pectin could increase serum vitamin A levels versus an intake of vitamin A without fibre[144]. On the contrary, the mean plasma increase of β-carotene for the next 48 h after a single intake of 12 g of citrus pectin mixed with food was lower than with the same meal without pectin[145]. Another single-intake study in six healthy adults showed a lower relative increase in plasma concentrations (24-h area under the curve) of β-carotene, lycopene, and lutein with almost 9 g of HM citrus pectin or other fibres such as guar gum, alginate, cellulose and wheat bran than without dietary fibre[142]. The possible interaction between pectin and bile salts may create a transient physical barrier that limits lipase to access the lipid surface and interferes with the formation of micelles that are needed for the absorption of hydrophobic compounds such

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as β-carotenes[146], but interestingly, this does not seem to happen for the vitamins A and E, which are also hydrophobic. Pectin seemed to impact vitamin A bioavailability positively and had no effect on vitamin E, as mentioned above.

In an experiment, LM citrus pectin was used to coat folic acid-fortified rice and, thus, protect the folic acid during the washing and cooking of the rice. Despite a lower bioavailability of the folic acid with the pectin coating (5% w/w, equivalent to 10 g), the coating helped to protect folic acid during washing and cooking, still providing a slightly higher folic acid intake than without coating[147]. Finally, one study in nineteen healthy adults reported higher 24-h urinary excretion of quercetin and its metabolites after a single intake taken via a drink containing 2 g of HM apple pectin versus the same drink without added pectin. In another study reported in the same publication and conducted in a subgroup of six subjects, a dose–effect relationship (between 0.6 and 2 g) was suggested, and a greater effect of HM than LM apple pectin was found[148]. It is difficult to conclude the effects of pectin on various vitamins and polyphenols from human studies, but the structure–function relationship is also thought to play a role there, as suggested by *in vitro* studies[146]. In addition, it is important to consider that the composition of food matrices and the conditions of intake will also influence the role of pectin on the bioavailability of micronutrients. A recent *in vitro* study with Caco-2 cells showed that the reduced bioaccessibility of ferulic acid and naringenin (a citrus flavonoid) seen with an HM apple pectin was completely counteracted by the concomitant intake of sucrose or olive oil[149].

Summary for immune health

In total, eight studies (reported in nine publications) were included in the scoping review related to immune health outcomes. Studies that evaluated immune health-related outcomes were the recent studies ranging from 2008 to 2022 (Figure 4). Three of the studies used RG-I from carrots[150–152] and one RG-I from peels of Korean citrus hallabong[111] and were performed with very low doses (0.1–1.5 g/d, Figures 5 and 6). The maximum tested dose was generally lower (mean 6.5 g/d, median 5.4 g/d) than for other health outcomes, and the duration of dietary supplementation had a mean of 31 d and a median of 28 d of intervention (Figures 6 and 7). All studies were RCT parallel studies[44,45,63,67,110,111,150–152] (Figure 8). Four studies related to enteral feeding evaluated the frequency of infections and general health status with pectin (5–16 g/d)[45,68,150,152]. Major immune-related health outcomes studies included immunostimulatory markers such as IL-6, soluble intracellular cell adhesion molecule-1 (siCAM), high-sensitivity C-reactive protein (Hs-CRP), IL-10, IL-1β and TNF-α ($n = 3$)[110,111,151]; lymphocyte count ($n = 1$)[44]; and cases of gastroesophageal reflux disease (GERD) in children with cerebral palsy ($n = 1$)[63]. General outcomes found pectin related to enhanced immune response and reduced disease symptoms. For instance, carrot-derived RG-I accelerated an innate immune response and reduced symptoms of an acute viral infection with rhinovirus[150]. In another study, pectin was used in a therapy for children with cerebral palsy to test effectiveness in decreasing vomiting and chronic respiratory symptoms[63]. Here, it was observed that children on the high-pectin diet (2:1 enteral formula to pectin liquid) had significantly decreased reflux episodes and vomiting and decreased cough and respiratory symptoms.

Summary of other health-related outcomes

Twenty-one studies were categorised as 'other topics'. Of these studies, the dose of pectin under investigation ranged from 0.6 g/d to 36 g/d (Figure 6), with an average and median tested dose of 12.4 g/d and 10 g/d, respectively. The average duration of pectin intervention was 35 d, and the median was 21 d (Figure 7). The following health-related outcomes in this category include detoxification from radioactivity ($n = 4$)[153–156], heavy metals ($n = 3$)[133,157,158], cancer-related physiological markers ($n = 2$)[33,159], bioavailability of drugs ($n = 2$)[160,161], and infant growth parameters ($n = 2$)[139,162] and another eight studies investigated various markers related to metabolic and cardiovascular health[22,23,34,118,163–166] (Figure 8).

Three out of four studies showed a reduction of ^{137}Cs in populations previously exposed to radioactivity (Figure 8) when they were given apple pectin (3–10 g/d) for 14–28 d[153–156]. The authors hypothesised that pectin, by binding caesium in the gastrointestinal (GI) tract, can prevent its absorption into the systemic circulation and increase its faecal excretion[154]; thus, it might be more efficient in case of exposure to contaminated foods than to reduce the contamination level of people exposed via other means[155]. Similarly, three single-arm studies also showed the potential of citrus-derived pectin (15 g/d of hydrolysed pectin or 3.6 g/d of HM pectin) to reduce blood levels of toxic elements such as heavy metals in less than 20 d[132,157,158]. Authors proposed that the RG-II part of pectic polysaccharides can chelate very specifically some cations like Pb^{2+} but not essential ones like Mg^{2+}, Zn^{2+}, Fe^{2+} and Fe^{3+}[133,167]. However, there is still debate whether this mechanism can only happen in the gut and contribute to preventing exposure from contaminated foods[167] or if it can also help in case of previous exposure that would require a partial absorption of pectin molecule before its fermentation by the gut microbiota[133].

Two single-arm studies suggested that approximately 15 g/d of hydrolysed citrus pectin could improve quality of life in patients with cancer and might limit progression of prostate-specific antigen level in blood[33,159]. Two single-intake, cross-over studies evaluated the bioavailability of drugs (digoxin and valproic acid) given with pectin (5 g of non-defined pectin and 14 g of HM citrus pectin, respectively) and did not find a reduced appearance of the molecules in the blood, but possibly a delayed arrival[160,161].

Two RCT parallel trials have evaluated the use of pectin in nutritional solutions dedicated to preterm infants[139] or severely malnourished young children in India[162]. While the first one showed no effect or slight improvement of the growth parameters after 28 d, the second showed that using pectin at 10 g/kg/d in replacement of arachis oil was not relevant to accelerate weight gain in these conditions.

The possible protection of dietary fibres in the context of cardiovascular health does not seem to be related to platelet function or haemostasis, as suggested by a study where HM

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pectin was given at a daily dose of 36 g for 42 d (wheat bran was also tested with no significant effect)[22]. Similarly, in an RCT parallel study, dietary supplementation with 9.6 g hydrolysed citrus pectin for 168 d did not influence various collagen markers possibly involved in cardiac fibrosis[34]. An RCT parallel study did not show any additional benefit of 0.6 g/d pectin for 56 d to reduce further serum level of trimethylamine-*N*-oxide (TMAO) compared with grape pomace polyphenols alone[118]. Another RCT parallel study evaluated a 12-week supplementation with 8 g hydrolysed citrus pectin without showing any significant effect on knee osteoarthritis severity and pain management[163]. Another three single-intake studies have evaluated the intake of 2 g of apple pectin on flushing symptoms after niacin intake[165] and on the release of pancreatic GI hormones and endogenous methanol production after the consumption of 10–15 g of pectin (non-described)[164,166].

Structure–function relationships

A remaining gap throughout this review of the literature was evident regarding the structure–function relationship of pectin. Pectin structural characteristics such as DE, MW and other structural regions (homogalacturonan, xylogalacturonan, RG-I, RG-II) largely influence the functional properties of pectin after ingestion. These compositions dictate the health-related outcomes of pectin consumption. For instance, gut microbiota access and ability to metabolise these pectin structures depends on traits such as DE, the composition of neutral sugars and the degree of structure branching (i.e. the ratio between the linear homogalacturonan and the branched RG-I and -II). Therefore, gut microbiome composition changes, production of SCFA and other metabolite production is dependent on these structural characteristics[11].

Furthermore, while many current studies of pectin demonstrate post-prandial glucose reduction and maintenance of normal blood cholesterol, there is little investigation into the structure of pectin exuding these effects. Much of this gap is due to the lack of pectin type reported in publications. In this review, for instance, the majority of pectin botanical sources was 'non-defined'. Such dependencies on pectin structure with health outcomes were demonstrated in a compelling study by Wanders *et al.* (2014), when comparing non-fibre control with gelled, bulking and viscous forms of pectin, which found that only gelled pectin (with high viscosity and water holding capacity) significantly improved satiety, as well as reduced glucose and insulin peaks[95]. Such findings demonstrate the important physico-chemical properties of pectin when examining health outcomes.

Similarly, many of the studies discussed here related to fat metabolism did not specify pectin structure. A better understanding of how MW and DE influence gastric emptying times and gut viscosity could, therefore, allow for a more precise pectin structure target in terms of capability to lower total and LDL-cholesterol and triacylglycerol. For example, in previous animal studies, higher DE pectin had greater effects on decreasing triacylglycerol and increased bile acid secretion[168,169]. Much has come to light on the role of the structure of pectin and its ability to lower blood cholesterol. For instance, a study by Brouns *et al.* (2012) found that pectin of high MW and high DE (from citrus or apple) was more effective in terms of cholesterol reduction[9]. Such results have been documented in animal studies demonstrating the relationship between the molecular structure of pectin and blood cholesterol[170,171]. As found in this scoping review, human clinical studies have limited documentation on the types of pectin used, and therefore, results are less consistent.

While pectin has been demonstrated to have various immunomodulatory effects in *in vitro* and animal studies, including RG bioactivity and the ability to suppress inflammatory markers such as IL-1β and IL-6[172,173], only recently has this work been studied in humans. Interestingly, many of the immune studies *in vitro* do take into account the structure and source of pectin, as well as DE[174]. Other structural characteristics such as RG-I regions also influence the functional properties of pectin. For example, McKay *et al.* (2021), analysed RG-I extracted from bell peppers and carrots and classified the composition and structure before testing in humans[151]. This prior analysis determined that the immunostimulatory effects were due to this specific type of RG-I backbone more so than the type of side chain and also confirmed safety and acceptability in humans. Lutter *et al.* (2021) and McKay *et al.* (2022) then tested this carrot-derived RG-I in a clinical trial and found that consumption of this pectin accelerated innate immune responses and decreased common cold symptoms[150,152]. Lee *et al.* (2016) similarly tested RG though derived from citrus pectin and also found improved immune function[111]. However, four of the nine studies in the immune response category listed the pectin source as 'non-defined'. This illustrates the structure–function relationship of pectin being largely unexplored in humans, though extremely important in determining bioactivity potential. There is, therefore, a need for further investigation into pectin molecular weights, DE, RG-I, side chains and monosaccharide components in relation to health outcomes under controlled experiments in humans[10].

Possible side effects

The highest dose of pectin tested was 50 g/d for 14 d in adults[20], which did not report any adverse side effects. The longest studies evaluated pectin consumption at various doses for 168 d in adults who were healthy ($n = 1$) and non-healthy ($n = 2$ gut-related, $n = 1$ cancer and $n = 1$ hypertension), with no adverse side effects reported. In infants, the sustained consumption of 1 g/d of citrus pectin oligosaccharides for 127 d[30] also did not report any significant adverse reactions.

The most frequently reported side effects included GI symptoms such as flatulence or bloating, most classified as mild and stopped just after consumption or resolved by adaptation after a few days. These symptoms were typical for dietary fibre[25,27,39] and do not prevent the use of pectin in sensitive populations such as hospitalised patients with enteral feeding. Interestingly, digestive symptoms, such as diarrhoea, were generally improved with pectin[44,45,62,65,68].

Similarly to what occurs after the consumption of fruits, an endogenous production of methanol is produced when HM pectin (DE of 75% such as in apples) is fermented by bacteria inhabiting the large intestine[164]. However, the experimental model was very specific as study subjects had to consume

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ethanol to maintain a relatively high level of blood ethanol to annihilate methanol catabolism. As highlighted by EFSA[15], no sign of liver toxicity was noticed in the study of Cummings *et al.* (1979) in which five subjects consumed 36 g/d of HM pectin (DE 72%) for 42 d, and on the contrary, a recent review highlighted a promising role of pectin to limit the progression of liver damage in the context of alcoholic and non-alcoholic liver disease as currently illustrated by pre-clinical data[175].

Study limitations

As mentioned previously, many studies included in this scoping review neglected to include details of pectin botanical origin and structure. Without this information, it is difficult to draw conclusions between pectin intake and health-related functional outcomes, as many of these health effects are directly related to the physico-chemical properties and molecular composition of pectin. Also, some studies were performed with pure pectin products, whereas others used commercially available pectin solutions, which, most of the time, are standardised with sugar to provide a specific functionality in foods and beverages. This may lead to overestimating the tested doses as reported in the publications. Furthermore, due to the nature of a scoping review, the review presented here is an overview of the existing literature. Individual studies included were not subjected to critical quality assessment and risk of bias. A rigorous systemic review of specific health topics outlined here would make it possible to draw conclusions on the health effects of pectin in human intervention studies.

Conclusion

Pectin and pectin-derived ingredients appear to have potential benefits to improve human health that align with authorised health claims related to the consumption of dietary fibre. In addition to well-established effects recognised by health authorities for the regulation of blood glucose and cholesterol, this scoping review suggests evidence for pectin to improve gut health by reducing digestive symptoms in specific situations and may have a positive impact on the gut microbiome and gut microenvironment. Pectin composition related to improved immunomodulatory responses and overall immune health is also a growing topic. There is a substantial gap in the research on the structure–function relationship of pectin and human health outcomes. Further studies are needed to facilitate a deeper focus and understanding of pectin characteristics such as botanical origin, DE, MW and viscosity in relation to health outcomes. Detailed attention placed on these structure–function relationships will allow for a more targeted approach to the development of dietary pectin solutions to maintain health.

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Competing interests

All authors declare no competing interests.

Author contributions

Conceptualisation: F.R.; methodology: A.M.W., N.P., F.G., E.P.R., F.R.; systematic search and selection of studies: A.M.W., N.P., F.G., F.R.; data extraction: A.M.W., N.P., F.R.; writing – original draft: A.M.W., F.R.; writing – review and editing: A.M.W., N.P., F.G., E.P.R., F.R.; supervision: F.R. All authors have read and agreed to the published version of the manuscript.

Data availability

No new data were generated from this study. All citations are listed and are publicly available.

Supplementary material

To view supplementary material for this article, please visit https://doi.org/10.1017/S0954422424000180.

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