MINI-REVIEW

Research Trends in Plant-Derived Oligomers for Health Applications

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Abstract: Objective: Epidemiological data illustrates that there is a strong relationship between dietary intake of natural bioactive compounds and their beneficial properties against various diseases, and this stimulates academic and industrial interest in using plant-derived compounds for health and making medicines. For this reason, recent health related studies in the literature have focused on a variety of many plant-derived bioactive compounds. Even though the bioactivities of such compounds have widely been investigated, there are few studies about oligomeric species and their activities.

Methods: In this review, extraction and isolation methods of the plant-derived oligomers and the use of such oligomers in health applications are summarised.

Results: In the literature, many studies state that oligomeric compounds have benefits to human health. To maximize these beneficial properties, various ways to use oligomeric compounds have been examined and summarised.

Conclusion: A better understanding of the specific activities of distinct components of plant-derived oligomers is expected to open new avenues for drug discovery. This review gives an overview of oligomers with health beneficial properties and their possible applications in healthcare.

Keywords: Plant-derived oligomers, oligopeptides, oligosaccharides, probiotics, prebiotics, drugs delivery systems, health applications, functional foods.

1. INTRODUCTION

The importance of functional foods, nutraceuticals, and other natural health products has generated interest in connection with disease risk reduction and the promotion of health in general [1]. Recent developments in functional foods have resulted in many studies that investigate their beneficial properties for human health [2].

There is a significant interest in using natural compounds as potential cancer therapeutics or cancer preventive agents for different cancer types [3-6]. Oligomeric compounds and their beneficial properties are important constituents of functional foods for health applications.

Oligomers are low molecular weight polymers consisting of a small number of repeated units (dimers, trimers, and tetramers are oligomers with two, three, and four monomers, respectively) whose physicochemical properties are dependent on the length of the chain [7]. Plant-derived oligomers are observed in various classes of compounds, including carbohydrates, proteins, melanins, and lipids.

Oligosaccharides are a group of carbohydrates that comprise 2–10 monosaccharides linked together in a linear or branched fashion [8]. Oligosaccharides can be produced naturally, or derived from polysaccharides after chemical, physical, or biochemical degradations; and they can be produced chemical/ enzymatic synthesis [9].

The most abundant oligosaccharides are disaccharides, such as sucrose, maltose, and lactose [10]. The functional oligosaccharides are intermediate between simple sugars and polysaccharides and claimed as dietary fibers and prebiotics. These compounds, as non-absorbable food ingredients, are microbial food supplements and may benefit the host by selectively stimulating salutary bacteria in the large intestine [11]. Functional oligosaccharides are non-digestible by human microbiota, the most known of which are fructo-oligosaccharides, galacto-oligosaccharides, cyclodextrins,
and soy-oligosaccharides [8]. Oligosaccharides are commonly bound to lipids and amino acids via O-glycosidic and N-glycosidic bonds yielding glycolipids and glycoproteins [12]. Due to their chemical structure, the functional oligosaccharides are substrates that can only be consumed by a limited number of bacteria, thus stimulating their growth [13]. Cyclodextrins, which are a member of a family of cyclic oligosaccharides, consist of a macrocyclic ring of glucose subunits joined by α-1,4 glycosidic bonds. They are widely used in food, pharmaceutical, chemical, agricultural and environmental applications. Complexation of beta-cyclodextrin with various different food colorants or natural compounds has been shown to enhance water solubilities and improve the light stabilities of those compounds. The structure β-cyclodextrin is shown in Fig. (1).

Fig. (1). Structure of β-cyclodextrin.

While carbohydrates are well known to be dietary staples, it is only recently recognized that oligosaccharides have become the subject of significant interest due to their resistance to digestion in the upper gastrointestinal tract and fermentation in the large bowel in addition to their fat replacement and sweetening ability. These properties lead to the usage of oligosaccharides for functional effects such as for a healthy gastrointestinal tract, improvement of glucose absorption in the microbiota [17]. Nutritional studies suggest that the physicochemical properties of oligopeptides play an important role in their absorption in the microbiota [17].

Essential oils found in the roots, leaves, and flowers of plants often contain lipids with oligomeric structures, consisting of terpenoids (two or more isoprene [2-methyl-1,3-butadiene] units), that possess antimicrobial and antioxidant activity [18].

For plant-derived oligomers, the peanut is a very important source for both academic and industrial teams because it contains all the oligomeric groups, thereby offering opportunities for fundamental and applied research; honey also consists of various oligomers like oligosaccharides, proteins, and polyphenols [19], however, it is important to note that some plants are rich in one oligomer group.

Van Laere and Wissing patented the use of oligosaccharides for nutritional composition with health-promoting action, in particular, having a bifidogenic effect and an anti-adhesive effect on pathogenic microorganisms to the intestinal wall [20].

The exciting potential of plant-derived oligomers has motivated fundamental studies of structure-activity relationships, and more applied studies of the structures and compositions of oligomers produced by various plant sources (variety, environmental conditions, etc.), and extraction and isolation methodologies with a view to generating industrially viable processes and products utilising these oligomers.

2. EXTRACTION AND ISOLATION METHODS

An overview of popular methods for the extraction and isolation of plant-derived oligomers is given in the following section.

2.1. Extraction Processes of Oligosaccharides from Different Sources

Various extraction methods and sources for plant-derived oligosaccharides have been reported in the literature. Guo and coworkers investigated ultrasound-microwave synergistic extraction of prebiotic oligosaccharides from sweet potatoes (Ipomoea batatas L.). In the study, dried and ground sweet potatoes were mixed with distilled water at 1:15 (w/v) solid to liquid ratio, the starch was removed as explained in their earlier work with ultra-high pressure treatment [21], and the starch-depleted sample was subjected to ultrasound-microwave-assisted-extraction (UMAE). After rotary evaporation, the concentrated liquid was precipitated with three volumes of 95% ethanol (v/v) and stored overnight at 4 °C to precipitate polysaccharides and proteins. After removal of the precipitate by using a macroporous resin, the supernatant was purified via size exclusion chromatography, yielding oligosaccharides. Optimum extraction yields of prebiotic oligosaccharides from sweet potatoes (PPOS4 and PPOS5) were obtained at 100 s extraction time, 300W ultrasonic power, and 200W microwave power. Under these conditions, the experimental yields of PPOS4 and PPOS5 were 1.472, and 5.476%, respectively [22].
Liang and coworkers extracted crude oligosaccharides from pumpkins (Cucurbita moschata Duch.). Pumpkins were pulped and mixed with distilled water at a 1:3 solid to liquid ratio and heated at 90 °C for 3 h. Isolation of the supernatant fractions after centrifugation and concentration by rotary evaporation followed by the addition of three times the volume of ethanol resulted in the precipitation of proteins and oligosaccharides. The supernatant fraction was separated by the membrane filter method yielding oligosaccharides. The pumpkin oligosaccharide recovery ratio of 81.3% was reported at optimum conditions [23].

Sanchez Lopes and coworkers used Stevia rebaudiana (Bertoni) roots to obtain fructo-oligosaccharides to enable studies of their prebiotic activity. The roots of S. rebaudiana were placed in a liquid medium with 33.3% strength Murashige and Skoog (MS/3) medium that was supplemented with 30 g/L D-sucrose and 2.0 mg/L α-naphthaleneacetic acid, and the roots were then dried. The oligosaccharides were extracted from the roots with water under reflux conditions at 80 °C for 5 h followed by filtration, concentration by rotary evaporation, and mixing with ethanol at a ratio of 1:3 (v/v) to precipitate crude aqueous extract. The ethanolic supernatant was collected and lyophilized to yield the dry extract of the soluble fructan fraction (SFF). The oligosaccharides isolated from S. rebaudiana roots were observed to enhance the growth of both bifidobacteria and lactobacilli, with strain specificity in their fermentation ability. The FOS yield from the SFF that was obtained from S. rebaudiana roots was 24%, [24].

Lu and coworkers extracted oligosaccharides from lotus (Nelumbo nucifera Gaertn.) seeds simultaneously employing ultrasonication and microwaves to assist the extraction process. By using the response surface methodology, optimum extraction parameters were determined to be: extraction time 325 s, liquid-solid ratio 10 mL/g (L/S ratio), ultrasonic power 300 W, and microwave power 250 W. Moreover, the yield of total oligosaccharides increased by 76% compared with traditional methods like hot water extraction, ultrasonic or microwave-assisted extraction. Their findings showed that ultrasonic-microwave-assisted extraction was efficient for the extraction of oligosaccharides. The yield of lotus seed oligosaccharides achieved using traditional warm water backflow method with 82 °C for 66.05 min and liquid-solid ratio 70.00 mL/g, was 6.228 ± 0.06%. By adopting ultrasonic-assisted extraction with 320 W, liquid-solid ratio 15.00 mL/g and 65 °C for 48.32 min, the yield of lotus seed oligosaccharides was 9.362 ± 0.07%, yet by adopting the microwave-assisted extraction, ultrasonic/microwave-assisted extraction with microwave power of 320.00 W and liquid-solid ratio of 20.00 mL/g for 6.27 min, the yield was found to be 8.645 ± 0.04%. While the yield of lotus seed oligosaccharides was 11.009 ± 0.019% though ultrasonic-microwave synergy extraction for 5.42 min resulted in enhanced extraction yields with shortened extraction time compared to the independent extraction process through the traditional warm water soaking, ultrasonic-assisted, and microwave-assisted method [25].

Khuituan and coworkers extracted oligosaccharides from fresh dragon fruits. Washed fruits were separated as peel and flesh; both parts were ground and extracted using pectinase, the resultant low molecular weight fraction without prebiotic properties was removed by yeast cultivation, after which the yeast cells were removed by filtration, yielding an oligosaccharide fraction [26].

Desai and coworkers extracted oligosaccharides from green coffee beans. Hot water extraction, pressure hydrolysis, and viscozyme methods were used; the hot water infusion was carried out using distilled water at 60 °C for 2 h. The insoluble fraction in the extracts was treated with chloroform/methanol (2:1) solutions, yielding glycolipids in the chloroform fraction and oligosaccharides in the extraction solvent. The oligosaccharides extracted from green coffee were used as a carbon source for the cultivation of three probiotic LAB strains. It was observed that the oligosaccharides stimulated the growth of Lactobacillus plantarum (MTCC 5422), by increasing their number from 8.09×10⁷ to 5.4×10⁹ cells/ml within 48 h. The enzymatic (Viscozyme), thermal (roasting) and aqueous (hot water infusion) extraction yielded 19.92 ± 2.1% of Mono-oligosaccharides with mannose (6.90 ± 0.9 µg/Mg) and galactose (8.35 ± 1.0 µg/Mg) as major components. The study showed that coffee and coffee by-products can be a promising source for novel functional food rich in bioactive oligomers [27].

2.2. Extraction Processes of Oligopeptides from Different Sources

In the literature, there are various extraction methods and sources for plant-derived oligopeptides.

Marsegla and coworkers extracted oligopeptides from cocoa beans. Finely ground cocoa beans were suspended in 0.1 N HCl. With the addition of (L, L)-phenylalanlyphenylalanine, the suspension was homogenized and centrifuged, then filtered and extracted 4 times with diethyl ether, and filtered again. The resulting aqueous solution was acidified with a formic acid solution (0.1%), filtered through Sartorius Vivaspin 2 filters (nominal molecular cut-off 10,000 Da) using an Amicon Micropartition system MPS-1. The filtrate was dried under nitrogen, and re-dissolved in acidified water (0.1% formic acid). Analysis by High-Pressure Liquid Chromatography (HPLC) and mass spectrometry (MS) showed 44 oligopeptides. The data obtained for roasted products showed that thermal treatments reduced the total content of peptides by almost 30% [28].

Another study using cocoa beans as a source of oligopeptides employed Dichloromethane to de-fat ground cocoa beans in a Soxhlet extraction apparatus for 18 h. The defatted powder was dried under vacuum, and then extracted using an acidified methanolic solution (MeOH:H₂O:CH₃COOH::70:28:2). The extraction solution was subjected to ultrasonication for 10 min, stirred for 30 mins at room temperature, filtered, and analyzed with HPLC. Oligopeptides were extracted from the dried defatted cocoa powder with a single step process [29].

Ren and coworkers isolated two novel α-glucosidase inhibitory oligopeptides from hemp (Cannabis sativa L.) seed protein (HSP). The extraction process involved defatting and drying hemp seed meal, followed by sieving with a 120 mesh screen. The obtained powder was dispersed...
in distilled water at a ratio of 1:20 (w/v). The pH of the extraction solution was adjusted to 8.5 with 1 M NaOH. The solution was stirred for an hour at 37 °C, and after centrifugation, the supernatant was collected and the pH was adjusted to 4.5 with 1 M HCl solution. The resultant precipitate was washed and re-dispersed in distilled water. The mixture was dialyzed, homogenized, and freeze-dried prior to enzymatic hydrolysis. The hydrolysates with high α-glucosidase inhibitory activity could successfully be prepared by treatment with an Alcalase-catalysed process [30].

Rojas and coworkers isolated low molecular weight oligopeptides from soybean hulls (which are also used as animal feed). The soybean hulls were found to be a rich source of both proteins and cellulose, and therefore also potentially an ethanol source, which is a much-needed commodity for processes and oligopeptides [31].

In 1994, Cheng and coworkers used Aster Tataricus as a source for oligopeptides. Three novel oligopeptides, aterinin A-C have been isolated from the roots of A. tataricus and their structures were elucidated by chemical, enzymatic, and spectral methods [32].

Jiang and coworkers used peanuts for the aqueous extraction of peanut oil and oligopeptides. The optimum extraction conditions were reported to be hydrolysis at 60 °C, a pH of 9.5, and the ratio of material to water 1:5 (w/w), for 90 min, followed by Alcalase enzyme treatment 1.5% (w/w) and hydrolysis for 5h, resulting in a yield of 71% (w/w) of protein hydrolysates which include %80 oligopeptides. The addition of the alkaline extraction before the enzymatic hydrolysis was observed to improve the yield of both peanut oil and oligopeptides [33, 34].

Soto-Sierra and coworkers provided an interesting review of the extraction and fractionation of protein products from microalgae [35].

2.3. Extraction Processes of Phenolic Oligomers from Different Sources

Plant-derived phenolics are produced by a variety of plants.

Jia and coworkers extracted polyphenolic oligomers from Cinnamomum parthenoxylon bark to investigate the hypoglycemic activity of the oligomers against streptozotocin-induced diabetes. 2 kg dried and powdered cinnamon barks were suspended in acetone/water (1:1, v/v) solution for 2 hours, filtered and the residue was subjected to the same process once again. The combined extracts were concentrated under vacuum, partitioned with ether, and a macro resin column was used to isolate the oligomers. The obtained extracts were freeze-dried. 86 g extract was obtained. The results suggested that from HPLC fingerprint data, the molecular weights of the oligomers in the extract were mostly B-type procyanidins. Results showed a significant reduction in blood glucose levels in normal and STZ-induced rats after 2 weeks of treatment with polyphenolic oligomer-rich extract of C. parthenoxylon barks [36].

Sugiyama and coworkers extracted oligomeric procyanidins from apples and studied their ability to inhibit pancreatic lipase [37]. Their extraction process was adapted from a method reported by Yanagida and coworkers, where unripe apples were homogenized in 0.1% (w/w) potassium pyrosulfite solution and kept at 4 °C for 24 h. The supernatant was centrifuged and filtered, the filtrate was subjected to column chromatography to remove monomeric structures in the crude apple polyphenol isolate, after which it was freeze-dried [38]. To investigate the relationship between the degree of polymerization and the inhibitory effects on pancreatic lipase activity, the procyanidins were fractionated. The procyanidins were the main contributor to the effect of apple polyphenol extract on inhibiting triglyceride absorption [37].

Strandas and coworkers studied phenolic oligomers isolate from flaxseeds. Dried and ground flaxseeds were defatted with hexane twice, then mixed with ethanol, water, and 2 M NaOH for 16h at room temperature. The solution pH was adjusted to pH 3 with 2 M H2SO4. After the centrifugation, the supernatant was collected and concentrated under vacuum until it was dried. The dried extract was dissolved in 10% methanol solution and separated via silica column chromatography. The flaxseed oligomer fractions were separated according to their hydrophobicity [39].

Bors and coworkers isolated caffeic acid oligomers from Salvia officinalis by adaptation of the method reported by Lu and coworkers [40, 41], which enabled them to investigate the antioxidant mechanisms of the isolated caffeic acid oligomers [42].

Gonzalez Sarrias and coworkers extracted resveratrol oligomers from ground Carex gynandra leaves that were sequentially extracted with hexane, acetone, and methanol at room temperature. The combined extracts for each solvent were concentrated under vacuum, subjected to column chromatography, and analysed by NMR, proving that the oligomers obtained were pallidol, α-viniferin, trans-miyabenol C, kobophenol A and kobophenol B [43]. For example, α-viniferin, which is a trimer of resveratrol, can be isolated from various plant resources. It shows an inhibitory effect towards the enzyme acetylcholinesterase (EC 3.1.1.7), which has an important role as an anti-inflammatory agent. In Fig. (2), the structure of α-viniferin is shown.

![Fig. (2). Structure of α-viniferin.](image-url)
3. HEALTH BENEFITS AND APPLICATIONS

The potential beneficial health properties in addition to their nutritional values of plant-derived oligomers are increasingly studied.

Shankar and coworkers studied the application of amyloid-β protein (Aβ) natural oligomers to treat the effects on Alzheimer’s by reducing the progressive loss of the hippocampal synapses. To treat slices with Aβ, the equivalent of 75 µl pooled, and lyophilized size exclusion chromatography fractions of 7PA2 cells conditioned medium were reconstituted in slice culture medium (SCM) and applied to each insert. The study shows that physiological concentrations of naturally secreted dimers and trimers, but not monomers, are effective in reducing the loss of hippocampal synapses [45].

Phan and coworkers reported that plant-derived transient expression is an alternative platform to produce hemagglutinin-based subunit vaccines. The advantages of the subunit vaccines from plants are that they can be produced for a low price and plant production systems can be scaled up easily. They used stable trimeric H5 haemagglutinins in the endoplasmic reticulum of Nicotiana benthamiana leaf cells. As a result, they showed that H5 oligomers more effectively induce neutralizing antibodies in mice than H5Strep-tag trimers [46].

A review from Ji and coworkers examined the use of functional oligopeptides as a novel strategy for drug delivery. Various studies preferred oligopeptides for their properties such as specific targeting, cell penetration, self-assembled capacity, and responsiveness to the environment. Moreover, methods to target tumor neovasculature, cells, and organelles were summarized [47].

Peanut skin is a rich source of procyanidins, which are oligomers of catechin units and their derivatives. Bansode and coworkers reviewed peanut skin oligomers and its lipid-lowering function, concluding that with peanut skin extract supplementation, a reduction in total lipid levels can be achieved [48]. In Fig. (3), the structure of procyanidin A2 that is one of the oligomers identified in the extract, is given.

Fig. (3). Structure of procyanidin A2.

Their study revealed the bioavailability of Peanut skin extract (PSE) in rat plasma, especially procyanidin A2. The reduction in plasma lipid and fatty acid profiles of the rats, given a Western-type diet for 5 weeks, was observed. The supplementation of 300 mg/kg PSE in groups on a Western diet for five weeks also resulted in significantly lower triglyceride levels.

Yang and coworkers extracted oligosaccharides from flaxseed gum via enzymatic hydrolysis to determine their antioxidant and antitumor activities. The antioxidant activity of the extract was determined with DPPH and ABTS methods. The antitumor effect was tested against HeLa, HepG2, and MRC-5 cells. Their results showed that flaxseed gum oligosaccharides (FGOS) had better antioxidant activities than flaxseed gum (FG) on DPPH and ABTS radicals. Besides, 0.4 mg/ml FGOS displayed significant activities against HepG2 and HeLa cancer cells [49].

Özdemir and coworkers aimed to use ε-viniferin with cisplatin for its apoptotic effects in Glioma cell lines (C6). Cisplatin is a chemotherapy medication used to treat various cancer types. However, the major problem faced with treating glioblastoma is the inability of drugs to pass through the blood-brain barrier. With a combination of natural bioactive compounds and chemotherapy, agents can improve the sensitivity and cytotoxicity of the drugs. Their study showed a strong apoptotic effect with a combination of cisplatin and ε-viniferin. The combined 13.25 µM/cisplatin and 95 µM ε-viniferin treatment caused maximum caspase-3 activation in C6 cells (15.5%) at the end of the 72 h incubation. Their conclusion was the combined use of CDDP and e-VNF in C6 cells has the potential to treat glioblastoma [50].

Pai and coworkers used oligosaccharides to increase the binding properties of the nanostructured lipid carriers (NLC) to ocular mucins. In comparison with commercially available chitosan itself, chitosan oligosaccharides (COs) are more suitable for drug delivery applications due to lower molecular weight. Moreover, COs have better solubility in aqueous media at neutral pH, where it carries a net positive charge. These properties allow the nanocarriers to have a higher availability at the eye surface. In the study, the surface coating of the prepared NLC was done with the dripping method. The mucoadhesive behavior of COS-coated NLC changed drastically when compared to the uncoated NLC, resulting in higher amounts available at the ocular surface [51].

Chi and coworkers studied the effect of fructo-oligosaccharides (FOS) from Morinda officinal on mild to moderate depression. To investigate microbiota-gut-brain used in the study, FOS was introduced via intragastric gavage to rats subjected to mild stress conditions. The antidepressive effects were investigated through behavioral tests, intestinal morphology, and corticosterone levels. The results showed that FOS eased depression-like behaviors and repaired intestinal epithelial damages. In addition to that, FOS treatment decreased the corticosterone levels in the plasma and urine of the model rats. They concluded that the antidepressive efficacy of the FOS depends on the modulation of the gut microbiota [52].

The importance of gut microbiota has recently become a priority for biomedicine, with studies showing that both the immune system and metabolism are affected by gut microbiota.

Gong and coworkers studied the effects of wheat bran feruloylated oligosaccharides (FOs) on the gut microbiota.
The study was performed by in vitro fermentation with healthy human feces. They stated that FOs affect the overall community of the gut microbiota, and increased beneficial microorganisms such as *Bifidobacterium* and *Faecalibacterium* inhibit the growth of disease-related bacteria such as *Alstipes*, *Bilophila*, *Dorea*, *Enterobacteriaceae*, and *Oscillipora* [53].

Li and coworkers examined the impact of oligosaccharides on the growth of four probiotic bacteria (*Lactobacillus plantarum*, *Leuconostoc mesenteroides*, *Lactobacillus casei*, and *Lactobacillus rhamnosus*). In the study, mulberry oligosaccharides were obtained from mulberry polysaccharides with three methods: physical hydrolysis, chemical hydrolysis, and enzymatic hydrolysis. Their findings were first showed that the oligosaccharides produced with enzymatic hydrolysis had the greatest effect on the growth of *L. rhamnosus*. Secondly, enzymatically prepared oligosaccharides were superior to the untreated mulberry polysaccharide and commercially available prebiotics [54].

An investigation of the effect of cellulose-derived oligomers on damage-associated molecular patterns and their responses was reported by de Azevedo Souza and coworkers. They showed that *Arabidopsis thaliana* could detect cellulose degradation products like cellulobiose and respond by activation of a signalling cascade leading to the increased expression of defense-related genes, with substantial overlap in Arabidopsis seedlings, an immune response that resulted in less cell damage following *P. syringae* infection [55].

Segun and coworkers used resveratrol derivatives from *Commiphora Africana* to investigate cytotoxicity against several human cancer cell lines. Cytotoxicity testing was carried out using the MTT assay on the breast (MCF7), liver (HepG2), lung (A549), and prostate (PC3) cancer cells. The obtained data validated the traditional use of *C. africana* in the treatment of cancer. They report the antiproliferative properties of the extracts and isolated compounds of *C. africana* on four human carcinoma cells [56].

Bose and coworkers used alginate oligosaccharides (AOs) to preserve fruit quality and increase storage life for strawberries. The ripening of the non-climacteric fruits mostly depends on the abscisic acid (ABA) amount. The use of AOs delayed the accumulation of ABA, which resulted in the prolonged storage life of strawberry. Strawberries were immersed into AOs solution for 60 seconds. The control group was immersed in distilled water. Then both treated and untreated fruits were kept at room temperature. With AOs treatment, the storage quality of the strawberry increased drastically. In AOs treated fruits, level of hardness, titratable acidity, pH, total soluble solids, vitamin C, anthocyanin, total phenol, and flavonoids increased and decay percentage found to decrease. Moreover, AOs treatment delayed the degradation of cell wall components and repressed the expression of cell wall degradation related genes [57].

Chen and coworkers used oligopeptide liposomes to deliver paclitaxel and anti-survivin siRNA for the synergistic treatment of breast cancer and metastasis. One of the problems faced during paclitaxel treatment is the drug resistance in cancer cells. Recent studies show that proteins like survivin cause the upregulation of the paclitaxel resistance. To downregulate the survivin expression has become the priority of the novel cancer treatments. For this purpose, Chen and coworkers preferred co-delivery of the paclitaxel and anti-survivin siRNA. Their results showed that the nano-carrier could successfully deliver two drugs into breast cancer cells. With the release of the anti-survivin siRNA, the survivin proteins were successfully blocked, allowing paclitaxel to work. They reported that the combination of paclitaxel and anti-survivin siRNA is a promising strategy to inhibit breast tumor growth and metastasis by using oligopeptide liposomes [58].

Noor and coworkers used stearic acid-chitosan oligomer coated nanostructured lipid carriers for topical delivery of dutasteride. Dutasteride promotes hair growth. To ease the delivery to the hair follicles, dutasteride-loaded nano lipid structures coated with chitosan oligomer-stearic acid were prepared. Dutasteride-loaded lipid particles prepared with the melt-dispersion ultrasonication method. Then, the prepared particles were dripped into chitosan oligomer-stearic acid solution. The characterization of the particles was done with NMR and FTIR analysis. They successfully prepared stearic acid-chitosan conjugates. The permeability studies revealed that with coating, the amount of dutasteride found in the skin was increased [59].

Ohara and coworkers investigated the beneficial properties of resveratrol dimer ε-viniferin against diet-induced obesity in mice. In the study to determine the anti-obesity effects of grape shoot extract (GSE) in vivo, mice were fed a high-fat diet with or without GSE for 4 weeks. Results showed that ε-viniferin exerted higher anti-adipogenesis activity in 3T3-L1 cells than t-resveratrol [60]. The obtained data suggested that GSE could be used to develop beverages or foods with health benefits against obesity.

Ose and coworkers investigated the ability of human intestinal anaerobes to metabolize different oligosaccharides. In the study, the metabolic properties of six oligosaccharides in 31 key gut anaerobes were investigated. The fermentation profiles indicated specific links between the microbial end-products and specific gut microbes. For instance, *bifidobacteria* readily metabolized fructooligosaccharide (FOSs) with a degree of polymerization (DP) 3, i.e. 1-kestose, but several strains used did not actively metabolize FOSs with DP4 and DP5, i.e. nystose and fructosylnystose. They stated that with the obtained data, it was possible to predict the impact of oligosaccharides in human intervention and gut microbiota modulation [61].

Zheng and coworkers reported that compressed food with added functional oligopeptides (CFMO) improved performance during military endurance training. When both the groups were compared, the recovery heart rates were significantly lower with the CFMO diet. CFMO led to better heart rate recovery, improved and maintained blood glucose, and increased removal of blood lactate. CFMO accelerated the removal of blood lactate during recovery, maintained oxygen supply, and increased fluid retention [62].

Li and coworkers regulated the lipid homeostasis with oligomer procyanidins from lotus seedpod. Regulating the lipid in the human body is crucial. Chronic accumulation of lipids can cause obesity, diabetes, and insulin resistance [63].
Oligomers were extracted with ethyl acetate to obtain lotus seedpod oligomeric procyanidin (LSOPC). LSOPC loaded emulsions were prepared with spontaneous emulsification method. In vivo studies showed that lotus seedpod oligomeric procyanidin (LSOPC) decreased total serum triglyceride and total cholesterol and elevated the high-density lipoprotein level in the hyperlipidemic rat model. They reported that the LSOPC-enriched emulsion showed increased antioxidant properties and suppressed fat hydrolysis in stimulated gastrointestinal medium through inhibition of lipase, which may contribute to the hypolipidemic effect. These results concluded that LSOPC could serve as a promising dietary supplement [64].

Shi and coworkers studied condensed tannin from rice straw and its inhibitory effect on Staphylococcus aureus. Rice straw is an agricultural waste, which can be used to utilize value-added products. In the study, rice straw was used as a source for tannins. For the extraction process, rice straw was treated as described in the literature [65]. Then, the treated rice straw was extracted with 70% ethanol solution at 60 °C for 2 hours. Then the inhibitory effect of extracted tannins was investigated. The tannins exhibited strong inhibitory effects on the growth of S. aureus. The fraction with 0.31g tannins/kg straw concentration showed the highest impact. In addition to that, the tannins inhibited biofilm formation by accelerating planktonic cell aggregation, and reduced the ability of cells to adhere to the surface [66].

Chen and coworkers used lotus seedpod proanthocyanidin (LSPC)-whey protein (WPI) complexes to enhance the physical and chemical stability of β-carotene-nanoemulsions. Lotus seedpod has been used for the extraction of proanthocyanidin in various studies [64, 67]. The results showed that LSPC-WPI complexes could be used as effective emulsifiers and antioxidants in nutraceutical-loaded nanoemulsions. The only drawback for the complexes was to obtain nanoemulsions stable in the pH above or below the isoelectric point of whey protein as pH 6.5 [68].

Another study used oligomeric proanthocyanidins to investigate its anti-cancer activity. Kawahara and coworkers extracted oligomeric proanthocyanidins from adzuki beans (Vigna angularis). Adzuki beans were soaked in water for 15 h. Then five fractions were obtained using Amberlite XAD-1180N, Toyopearl HW40F, and Sepacore C-18 reverse-phase flash column chromatography. Each fraction was characterized as (epi)catechin hexamer, heptamer, and octamer, epigallocatechin-(epi)catechin pentamer, and epigallocatechin-(epi)catechin hexamer using Mass Spectrometry. The anti-cancer activity was investigated against the human PC-3 prostate cancer cell line. The obtained data showed that each fraction showed significant anti-cancer activity. They also reported that fractions significantly suppressed the expression of the fatty acid-binding protein 5 gene, which plays critical roles in cell growth and metastasis in prostate cancer [69].

In Table 1, various oligomer sources and their application areas are summarized.

### Table 1. Sources of oligomers and their application areas.

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<tr>
<th>Oligomer Source</th>
<th>Application Area</th>
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<td>Adzuki Beans</td>
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<td>Rice Straw</td>
<td>Antibacterial activity</td>
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<td>Grape shoot</td>
<td>Diet-induced obesity</td>
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<td>Lotus seedpod</td>
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<td>Carex Species</td>
<td>Against Colon Tumorigenic Cells</td>
<td>[43]</td>
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<tr>
<td>Salvia officinalis</td>
<td>Antioxidant properties</td>
<td>[42]</td>
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<td>Peanut Skin</td>
<td>Lipid-lowering activity</td>
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<td>Cyphostemma crotalariorides</td>
<td>Antifungal properties</td>
<td>[71]</td>
</tr>
</tbody>
</table>

CONCLUSION

In this review, we aimed to provide an overview of plant-derived oligomeric structures, their sources, and extraction methods, which are interesting in current research in both academic and industrial settings. Early studies about oligomers focused on their extraction and characterization, which led to studies of their potentially beneficial properties to health. The interesting functional properties, bioavailability, and bioactivity of oligomers motivate further study (e.g. for their potential to act as drugs or drug delivery systems).
From an economic point of view, the growing use of plant-derived materials will have environmental benefits, including waste reduction, lower greenhouse gas emissions,rewilding, and others. By utilizing the waste products of the agricultural and food industries it may be possible to obtain value-added products, promote rural investment, reduce the volume of harmful chemicals/pollutants, conserve ecosystems and biodiversity, and this will help transition to the circular economy; all of which support the United Nations Sustainable Development Goals (SDGs), specifically SDG 1, 2, 3, 8, 9, 12, 13 and 15. We believe that the findings and promising results of these studies reviewed here will be of interest to a broad readership and hopefully inspire collaborative research involving parties from both academic and industrial settings.

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CONFLICT OF INTEREST

Authors declare no conflict of interest, financial or otherwise.

CONSENT FOR PUBLICATION

Not applicable

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ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tbody>
<tr>
<td>ABA</td>
<td>Abscisic Acid (ABA) Amount.</td>
</tr>
<tr>
<td>ABTS</td>
<td>2, 2'-azinobis (3-ethylbenzothiazoline-6-sulfonic acid)</td>
</tr>
<tr>
<td>AOs</td>
<td>Alginate Oligosaccharides</td>
</tr>
<tr>
<td>Aβ</td>
<td>Amyloid β protein</td>
</tr>
<tr>
<td>CDDP</td>
<td>Cisplatin β protein</td>
</tr>
<tr>
<td>CFMO</td>
<td>Compressed Food with Added Functional Oligopeptides</td>
</tr>
<tr>
<td>CH₃COOH</td>
<td>Acetic Acid</td>
</tr>
<tr>
<td>COs</td>
<td>Chitosan Oligosaccharides</td>
</tr>
<tr>
<td>DPPH</td>
<td>2,2-diphenyl-1-picrylhydrazyl</td>
</tr>
<tr>
<td>DPs</td>
<td>Degree of Polymerization</td>
</tr>
<tr>
<td>e-VNF</td>
<td>ε-viniferin</td>
</tr>
<tr>
<td>FG</td>
<td>Flaxseed Gum</td>
</tr>
<tr>
<td>FGOS</td>
<td>Flaxseed Gum Oligosaccharides</td>
</tr>
<tr>
<td>FOs</td>
<td>Feruloylated Oligosaccharides</td>
</tr>
<tr>
<td>FOS</td>
<td>Fructo-Oligosaccharides</td>
</tr>
<tr>
<td>GSE</td>
<td>Grape Shoot Extract</td>
</tr>
<tr>
<td>H₂SO₄</td>
<td>Sulfuric Acid</td>
</tr>
<tr>
<td>HCl</td>
<td>Hydrochloric Acid</td>
</tr>
<tr>
<td>HPLC</td>
<td>High-Pressure Liquid Chromatography</td>
</tr>
<tr>
<td>HSP</td>
<td>Hemp Seed Protein</td>
</tr>
<tr>
<td>LSOPC</td>
<td>Lotus Seedpod Oligomeric Procyanidin</td>
</tr>
<tr>
<td>MeOH</td>
<td>Methanol</td>
</tr>
<tr>
<td>MS</td>
<td>Mass Spectrometry</td>
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<tr>
<td>NaOH</td>
<td>Sodium Hydroxide</td>
</tr>
<tr>
<td>NLC</td>
<td>Nanostructured Lipid Carriers</td>
</tr>
<tr>
<td>NMR</td>
<td>Nuclear Magnetic Resonance</td>
</tr>
<tr>
<td>PSE</td>
<td>Peanut Skin Extract</td>
</tr>
<tr>
<td>SCM</td>
<td>Slice Culture Medium</td>
</tr>
<tr>
<td>SFF</td>
<td>Soluble Fructan Fraction</td>
</tr>
<tr>
<td>STZ</td>
<td>Streptozocofin</td>
</tr>
<tr>
<td>UMAE</td>
<td>Ultrasound-Microwave-Assisted-Extraction</td>
</tr>
<tr>
<td>WPI</td>
<td>Whey Protein Complexes</td>
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</tbody>
</table>

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