*Jordan Journal of Pharmaceutical Sciences, Volume 18, No. 3, 2025*

# Effect of Lignin and other Biopolymers on Hyperlipidemia and Gut Microbiota

***Amira Abu-Omar[1], Eliza Hasan[1], Joana Gil-Chávez[2], Tamara Athamneh[3], Husam Abazid[4], Pavel Gurikov[5], Mohammad A. A. Al-Najjar[1*]***

[1] Department of Pharmaceutical Sciences and Pharmaceutics, Faculty of Pharmacy Applied Science Private University, Jordan
[2] Institute of Thermal Separation Processes, Hamburg University of Technology, Hamburg, Germany
[3] Nanotechnology center, Jordan University of Science and Technology, Irbid, Jordan
[4] Department of Clinical Pharmacy the Therapeutic, Faculty of Pharmacy Applied Science Private University, Amman, Jordan
[5] Laboratory for Development and Modelling of Novel Nanoporous Materials, Hamburg University of Technology, Hamburg, Germany.

## ABSTRACT

So far, dietary fibers such as lignin, cellulose, pectin, guar gum, and psyllium have been well-studied for their preventive and therapeutical potential using animal and human models, especially for their beneficial effects on chronic metabolic conditions like dyslipidemia and related disorders. Dyslipidemia is a dangerous metabolic disorder related to hypercholesterolemia, coronary artery disease, and coronary heart disease. Earlier research has demonstrated that these dietary fibers can lower high serum lipid levels through different mechanisms. One of the most important mechanisms is the modification of gut microbiota. Increasing the abundance of lactic acid bacteria (LAB), which can metabolize different dietary fibers like lignin, may potentially reduce the cholesterol level. This review aims to provide useful insights and comprehensive discussions about current knowledge related to the properties, and the effects of dietary fibers mainly lignin in controlling hyperlipidemia and their effects on gut microbiota. Google Scholar, Research Gate, and Scopus are the search engines exploited to collect data by using lignin, biopolymers, gut microbiota, and hyperlipidemia as search terms.

**Keywords:** Lignin, biopolymers, gut microbiota, hyperlipidemia.

## 1. INTRODUCTION

Dietary fibers are the general term for lignin and polysaccharides (e.g. cellulose, mucus, and gums) [1]. These fibers can alter gastrointestinal function from the mouth to the anus [2] because a large amount of them are non-digested and non-absorbed plant carbohydrates by endogenous enzymes in the human small intestine [2]. But they undergo bacterial fermentation in the large intestine which affects the amount and species composition of the microbiota [1-3]. This fermentation process improves the health of the gut and different organs via the production of bioactive metabolites such as short-chain fatty acids that lead to changes in the immune system responses, reduction of intracolonic pH, and modulations of blood lipid levels [2].

Hyperlipidemia is described by extreme levels of lipids (low-density lipoprotein (LDL), triglycerides (TGs), and total cholesterol (TC)) in the blood. High plasma concentrations of lipid and lipoprotein fractions are related to the development and progression of various diseases, such as cardiovascular disease (CVD) and acute myocardial infarction (AMI) [4, 5]. Many studies on humans and animals have demonstrated the ability of dietary fiber such as lignin to reduce cholesterol levels by binding to bile acids in the intestine [6, 7]. The purpose of the present review is to highlight recent findings related to the chemical structure, the properties,

[*] ***Corresponding author: Mohammad A. A. Al-Najjar***
moh_alnajjar@asu.edu.jo
Received: 10/12/2023 Accepted: 31/10/2024.
DOI: https://doi.org/10.35516/jjps.v18i3.2077

and the effects of dietary fibers mainly lignin in controlling hyperlipidemia and their effects on gut microbiota.

## 2. METHODOLOGY

The information in this review paper was collected from 113 eligible papers that appeared on Google Scholar, Research Gate, and Scopus after searching on lignin, biopolymers, gut microbiota, and hyperlipidemia terms.

## 3. DIETARY FIBERS

### 3.1. Biopolymers

The definition of dietary fibers has been changed by the scientific community throughout the decades. Dietary fibers are comprised of the remnants of plant material that resist digestion by human gastrointestinal enzymes. The definition includes all indigestible polysaccharides such as celluloses, hemicelluloses, oligosaccharides, pectin, gums, waxes and lignin [1, 2]. Dietary fibers are categorized into two groups depending on their solubility in water; the first group is the insoluble fibers that are abundant in lignin, cellulose, and hemicelluloses, and the second group is the soluble fibers like pectin, guar gums, oat bran, and psyllium [3].

The irregular properties of polymer surfaces have been utilized since ancient times [4]. In fact, unique interfacial dynamics and high porosity of polysaccharides make them feasible candidates for pharmaceutical lipid adsorption applications [4, 5]. Pectin has been extensively evaluated for oil capsulation capacity in the digestive tract multiple times and after a multitude of clinical trials, was approved by the EFSA for the treatment of hypercholesterolemia and obesity [4]. The positive effect of dietary fibers on human's cholesterol levels and oil absorption/adsorption has been reported in numerous studies [6-10]; however, the individual effect and contribution of the lignin to this effect have been practically neglected so far.

### 3.2. Lignin

*3.2.1. Lignin as the Necessary Polyphenolic Polymer in the Plant Structure*

Lignin is the second most abundant natural polymer, the largest source of polyphenols and phenolic compounds, and the second largest biopolymer available on Earth, following cellulose [11, 12], being present in plant biomass composition in about 20–35% [13]. The term "lignin" comes from the Latin word 'lignum', which means wood [14]. Many kinds of wood constitute different percentages of lignin for example, the fraction of lignin varies widely between hardwood 32% and softwood 25%.

Lignin has a molecular weight that ranges between 700 and 100.000 Da and has a complex structure because of aromatic alcohols that are derived from phenylpropanoids [15]. These alcohols or monolignols are represented as H (p-hydroxyphenyl), G (guaiacyl), and S (syringyl) [15]. However, aromatic rings consist of different numbers of the methoxy groups [15]. It is characterized by complex cross-linked phenyl propane polymer, dark-colored, hydrophobic, insoluble in water and 72% sulfuric acid but soluble in both strong concentrated acids and concentrated bases [15-20].

Lignin is responsible for providing rigidity to the plant cell wall through the lignification process [21], the process includes holding the cellulose and hemicellulose fiber together which allows plants to expand significantly in size and height [15, 16]. Lignification also protects plant cells against environmental stress conditions by inhibiting the enzymatic hydrolysis of microorganisms and enhancing water movement in plants [16, 22-24].

*3.2.2. Lignin extraction challenges and as its industrial by-product*

It is almost difficult to extract lignin from plant material because of its complex structure that holds cellulose and hemicellulose together. Even the typical isolation methods such as alkali extraction, extensive milling, or enzymatic isolation can't achieve typical degradation, high purity, or less contamination of lignin [17]. Nowadays, technical lignin (also called native lignin) can be generated as a by-product of the industrial process (e.g., cellulose pulp from paper production and lignocellulose biomass from ethanol production).

Industries that use plants as a starting material for their processes generate an enormous amount of waste products and lignin is considered one of these bio-based waste materials, the reason for this, is that the major components of interest are still cellulose and hemicellulose, as these biomolecules have a clear application pathway [16, 25]. The industrial-scale production of technical lignin as the scum of the pulp and paper industry occurs after the delignification process, being sulfite, kraft, and soda [26, 27]. Technical lignin can also be obtained from emerging biorefining processes, including organosolv (OS), steam explosion (SE), ammonia fiber expansion (AFEX), and hydrothermal pretreatment (AS) [26, 28-31]. Unsurprisingly, the chemical, physical, and technical properties of these lignins strongly depend on their origin, extraction, and purification processes. The products of these methods will differ based on the type of linkage that every process aims to cleave. For instance, harsh acidic and alkaline conditions will result in the splitting of C-O bonds that interrelate the monolignols, cleavage of lignin-carbohydrate linkage, and sulphonation of the lignin aliphatic chain [26, 28-31].

*3.2.3. A Novel Technique to produce Highly Pure Lignin*

A number of novel biorefining technologies focus on the separation and valorization of the three main biomass components: lignin, cellulose, and hemicellulose; considering that lignin is no longer a residue but a source of potential added value [29, 30]. With today´s society's demand for environmentally friendly processes and products, hydrothermal pretreatment (AS) and hydrothermal processing (HP) can be considered promising methods to obtain high-value lignin, which ideally should be sulfur-free, solvent-free, and sustainable. A highly pure lignin can be produced using the OS process in, which it is separated from the biomass using organic solvent (mostly ethanol or methanol) at high temperatures (100-250°C) and pressure. OS lignin is soluble in organic solvents, has low molecular weights, and contains insignificant amounts of carbohydrates and ash [32, 33]. Aquasolv lignin is separated from the biomass by treatment with compressed water under a pressure ranging from 30 to 50 bar, at 180–230 °C for 10–40 min [34-36].

*3.2.4. Lignin in the Commercial and Medical Industries*

Lignin has found its way in producing certain economic value for biorefineries, where it is mainly used for energy production and the literature shows promising results for lignin to be applied in chemical synthesis and plastic and material applications, however, the efforts to valorize this material into goods and to bring these applications to the market are yet to be improved. Several technical lignins (kraft, soda, lignosulfonates) are already being applied in low-value applications such as cement admixtures and viscosity modifiers [32, 33]. In addition, it can be found in dyes, paints, emulsifiers, binding, thermosets, synthetic floorings, and sequestering and dispersal agents. OS lignin can be used in formulations of resins (i.e., epoxy and phenol-formaldehyde), stabilizers, and filler in polyurethane foams, adhesives, and dispersants with biocidal properties [32, 33]. Aquasolv has been used in aerogels for biomedical applications, antioxidant filler in adhesives for human consumption, and alternative to activated charcoal [34-36]. Lignin offers the stability and mechanical impact as an active filler for natural rubber [20]. However, due to the natural properties that lignin exerts in nature, the possibility to enter high-value markets where biobased materials are required is endless, for instance, lignin can be used in cosmetic formulations, as a natural ingredient and it can be used as antioxidant, antifungal, antiparasitic and anticarcinogenic activity [16]. Furthermore, lignin produced by novel bio-refinery processes such as OS is known to be non-cytotoxic, cheap to produce, and has no interaction with the human intestine due to its branched fractions. This has led to the evaluation of such lignins as potential oil adsorbents and, consequentially, anti-hypercholesterolemic agents. They can be used against

hypercholesterolemia and obesity, also to decrease the incidence of chronic degenerative disease [25]. Generally, near-nature structured lignins are reported as indigestible biopolymers, however, some authors report that small parts can be broken down and fermented in the small intestine. Others report that only 10 % of lignin is mainly digested in the stomach and the rest is indigestible and is excreted completely in the stool [19]. Many studies reported that lignin can adsorb hydrocarbons and toxins [18, 19], and resist bacterial disintegration in the gastrointestinal tract more than any other natural polymers [15, 16].

*3.2.5. Nano-sized Lignin Applications and Benefits*

A recent study has reported that the incorporation of OS lignin into nanoscale zero-valent iron boosts its hexavalent chromium detoxification performance in the aquatic environment [37]. In recent years, lignin has gained considerable attention in synthesizing nanoparticles for manufacturing lignin-based nanomaterials to take advantage of unexplored lignin in high-value-added applications. For example, nano-sized lignin has added numerous values to industrial products by improving the durability of items such as rubber and textiles [38]. Also, enhanced UV shielding, besides, the quality, chemical and physical properties. Furthermore, lignin nanosized has a wide application in sterile biomedical devices, food packing materials, cosmetics industrial and tissue engineering [38, 39]. Lignin is the most suitable choice in medical research. According to the biodegradability, absorption capacity, non-toxic properties, antibacterial, antioxidant, and anti-parasite activity, lignin nanoparticles with various dosage forms have significant potential for drug delivery [40, 41]. Lignin nanoparticles as drug delivery are capable of loading hydrophobic drugs such as coumarin-6 and hexadecane, and hydrophilic drugs such as rhodamine 6G and doxorubicin hydrochloride (DOX) for cancer treatment. [39]. A recent study has evaluated the efficacy of the anticancer drug doxorubicin hydrochloride (DOX) and demonstrated the higher efficacy of DOX-loaded folic magnetic-functionalized lignin nanoparticles. In another study, when lignin was combined with microcrystalline cellulose as an excipient in tablets, the results showed a significantly enhanced tetracycline release. Also, aspirin tablets including lignin showed a higher release rate of the active ingredient compared to the tablets without [40].

**4. Lignin and hyperlipidemia**

*4.1. The Potential Effects of Natural Polymers on Lowering Cholesterol Level*

In general, natural polymers are known to decrease the risk of coronary heart disease by lowering cholesterol level in the blood, mainly due to their physical properties, such as dispersibility in water, viscosity, binding ability, absorptive and gelling capacity as well as fecal bulking capacity [42, 43]. Furthermore**,** soluble and insoluble fibers increase the movement of food through the intestine. These are associated with a high water-holding capacity, which results in an increased viscosity in the gastrointestinal tract and promoted the binding ability of bile acids in the small intestine. This consequently leads to reduce the absorption of cholesterol by bile acids and lowers its blood levels [44]. Another benefit is that soluble fibers interfere with sugar absorption to reduce the blood sugar concentration and provide short-chain fatty acids as by-products of fermentation in the colon. While insoluble fibers produce bulk effects on feces and the fermentation process occurs in the large intestine [6]. The gelling capacity of some biopolymers is also used to increase the sensation of satiety in consumers, resulting in lowering ingestion of potentially high-fat diets. Due to these properties, natural polymers such as chitosan, pectin, guar gum, and lignin are considered to be interesting candidates for the treatment of lipids high blood levels.

*4.2. Overview of Hyperlipidemia*

Hyperlipidemia is a disorder of lipid metabolism characterized by excessive accumulation of one or more of the lipids in the plasma, such as high serum cholesterol level in the bloodstream (>240 mg/dl) [45, 46]. Also, it can

be defined as a lipoprotein metabolic disorder associated with high (>159 mg/dl) serum low-density lipoprotein cholesterol (LDL-C) [47]. Hyperlipidemia is one of the most dangerous risk factors for cardiovascular disease (CVD), such as coronary heart disease (CHD) atherosclerosis, and stroke [48, 49]. A study reported that 12 million people die because of cardiovascular disease each year worldwide and according to the World Health Organization (WHO), by 2030, CVD will affect approximately 23.6 million people globally [49-51].

Published studies reported an inverse correlation between the low blood level of high-density lipoprotein cholesterol (HDL-C) (which is below 40 mg/dl) and coronary heart disease. [52, 53]. Accumulation of cholesterol and other lipids in the atrial wall is the major cause of atherosclerosis, which is considered a key complication of cardiovascular diseases, such as acute infarction and hypertension [50, 54]. Lifestyle, dietary, and genetic disorders (e.g., familial hypercholesterolemia) are recognized as contributory risk elements for the development of hypercholesterolemia. Clinical trials demonstrated that a reduction in low-density lipoprotein cholesterol (LDL-C) levels could lower the incidence of atherosclerosis and CVD [46]. Another study indicated that a 1 % reduction in cholesterol level could decrease the risk of coronary heart disease by 2-3 % [51, 55].

*4.3. Statins medications: Action Mechanisms and Side Effects*

Statins medications -which are hydroxy-methyl-glutaryl-coenzyme-A (HMGCoA) reductase inhibitors- are the most widely used for the treatment of hyperlipidemia and cardiovascular disease (CVD) in many countries [56, 57]. They target hepatocytes and prevent HMG-CoA reductase enzyme that converts HMG-CoA into mevalonate, mevalonic acid is a precursor for cholesterol and non-steroidal compounds, therefore, the inhibition of mevalonate production reduces the level of cholesterol. Other action mechanisms of statins include: the improved uptake and degradation of low-density lipoproteins-cholesterol (LDL-C), prevention of the lipoproteins, and inhibition of the scavenger receptors expression [58]. Statins are efficient in the treatment of that condition; however, their intake has been positively correlated with various adverse effects like liver failure and muscle pain, which may lead to dose reduction or discontinuation of the treatment [57]. The most important side effect is muscle symptoms which reported about 25% of symptoms, including mild myalgia that may affect around 10% of statin users [57]. Another side effect is liver toxicity, generally, 2 - 3% of reported cases stated an increase in the serum liver enzymes [59], and few reports are associated with liver failure among statin users [57].

Due to the negative side effects of statins and the overall negative perception by the population in use, many research and development activities focus on finding new methods to control hyperlipidemia such as dietary intervention and natural/herbal products (e.g., biopolymers) [47]. This is because, the current hypolipidemic medicines are expensive and have serious side effects and the natural products show multi-action activity among various medical conditions, such as, CVD, inflammatory disease, and cancer [49, 51].

*4.4. Lignin as Alternative Choice to Manage Hyperlipidemia*

Diets rich in fiber were found to lower the total blood cholesterol levels by 26% plus LDL-C levels by 29% in normal and hyperlipidemic adults [60]. Moreover, studies have shown a decreased risk of hyperlipidemia when consuming food rich in antioxidants and biopolymers. Lignin is one of the biopolymers with the most potential effect to decrease cholesterol level, not only due to their functionality and abundance but also due to its low price [4, 7-9].

Generally, the lignin effect and chemical composition depend on several factors such as its plant source, the extraction process, and biomass used. A new oral formulation which includes lignin admixed with methylcellulose was investigated for hyperlipidemia

treatment. The combination with methylcellulose facilitates lignin dispersion in the gastrointestinal tract. Therefore, treating hyperlipidemia patients by administering lignin results in about a 20% reduction in blood cholesterol levels. Lignophenols (LPs) are high-purity lignin derivatives with ahigh phenolic content, and are described as stable molecules, although their physiological role is still unclear. Treatment with LPs markedly decreased oleate-induced apo-B secretion from HepG2 cells in a dose-dependent manner [25]. In general, dietary fibers have exhibited several actions on the intestine by increasing peristaltic movement, stimulating intestinal food passage, increasing feces volume andweight, and transit time [43]. Researchers studied the impacts of the indigestible residue of foods on the bulk of the stool, especially the impacts of cellulose, hemicellulose, and lignin on laxation. By analysis of the stool, it was found that lignin is digested faster than cellulose and hemicellulose and it was found in high percentages in the residue that recovered in the stool, while cellulose and hemicellulose went through the human gut in smaller amounts. Therefore, the number of residues disappearing from the gut influences the volume of the stool more than the number of residues fed or the amount recovered in the stool [61].

For over five years, Hillman and his coworkers [62] focused on the dietary fiber components and their various actions on the human body. They conducted many studies to determine the impact of daily dietary supplementation with pure pharmaceutical citrus pectin 12 g/d, pure alpha-cellulose 15 g/d, and pure auto-hydrolysis lignin 12 g/d on the human body. It was found that cellulose decreased stool pH from 6.38 to 6.12, decreased stool pass time by 27%, and increased in stool weight by 57%. In comparison with pectin and lignin, cellulose showed a significant change in stool characteristics while pectin and lignin did not. On the other side, neither cellulose, pectin, and hydrolysis lignin significantly changed serum cholesterol levels in healthy subjects over eight weeks [63]. However, a study was conducted in diet-induced obese mice, while using a lignin-rich fraction of brewer's spent grain. In the animal model, body weight gain was significantly reduced with all fibers tested, but only the lignin-rich fraction and lignin-rich fraction cellulose decreased fasting plasma low-density lipoprotein cholesterol and total cholesterol compared to the high-fat diet group. The results suggest that the consumption of lignin-rich fraction induced beneficial systemic changes in mice via gut microbiota, bile acids, and gene expression in the liver. More studies in the future should focus on through assessments of the effect of different types of lignin on the organism's physiology and targeted physiological effects. The establishment of a structure-function relationship is crucial to unravel the true potential of lignin for high-value applications like the case of food, nutraceuticals, and pharmaceuticals.

## 5. MISCELLANEOUS BIOPOLYMERS AND TREATMENT OF HYPERLIPIDEMIA

Polymers synthesized by living organisms are considered to be interesting candidates for industry and pharmaceutical lipid adsorption.

### *5.1. Chitosan in the Previous Studies*

Chitosan is a natural polymer that has been evaluated for oil capsulation proficiency in the digestive tract, and it is available in the market as a counter (OTC) drug for fat adsorbents and hypercholesterolemia treatment [19, 64].

### *5.2. Cellulose in the Previous Studies*

Another example of a biopolymer that is used to improve lipid profile is cellulose, a polysaccharide that is the most prominent component of plant cell walls [6]. The effect of cellulose didn't exert any significant change on serum lipids of high-fat diet rats models for six weeks [65]. On the other hand, the effect of cellulose was examined in healthy volunteers, after three weeks of treatment with cellulose, there was no significant change in serum cholesterol levels but the weight of the feces was changed [66]. In other studies, doses of 15-20 g/dL of cellulose

were given to adult volunteers for four weeks and it was observed that a small increase in stool output can be achieved [66]. Evaluation of hypolipidemic impacts of dietary insoluble fibers has been extensively investigated in mice, for instance, a study in which mice were fed a high-fat diet over three weeks found that serum cholesterol levels can be decreased when using three types of fiber (cholestyramine, chitosan, and cellulose). In particular, cholestyramine, which resulted in decreased lipid absorption and increased fecal bile acid output. In contrast, cellulose did not affect cholesterol absorption or fat excretion in mice [67]. In a similar study, the effect of cellulose on lipid metabolism in rats was compared with that of other soluble dietary fibers such as pectin and guar gum. Cellulose-feeding mice showed the highest blood cholesterol levels and body weight gain compared to pectin and guar gum-feeding mice. Moreover, pectin and guar gum with high molecular weight were more effective in fecal fat excretion and bile acids than cellulose [44]. The viscosity of the guar gum in the stomach is one of the important reasons for its ability to reduce total cholesterol in humans and animal models. The high viscosity can influence the absorption and the digestion of food. Guar gum has been found to prolong the retention of chyme in the intestine slowing down the food digestion process, thus, resulting in lower total cholesterol levels. The mechanisms of action for pectin have been well-studied in the literature.

*5.3. Pectins in the Previous Studies*

Pectins are natural polymers composed of groups of polysaccharides and are mainly obtained from fruits and vegetables. Currently, they are commercially extracted (citrus peel or apple pomades) by chemical or enzymatic methods [68]. The mucilaginous fibers such as pectin, guar gum, and oat bran form gel in the small intestine which interferes with the absorption of total cholesterol and bile acids [69]. Different gelling fibers might achieve approximately a 7% reduction in total cholesterol levels. Pectin showed an effective decrease in plasma cholesterol levels and liver cholesterol synthesis among animal models such as rats, hamsters, chickens, and rabbits, where dosages of 6-15 g/day for 4 weeks [70]. Many studies conducted on rats and healthy adults recommended pectin with a high methoxyl group as an effective hypo-cholesterolemic agent [71, 72]. Thereafter, low-methoxyl pectin presented the most hypolipidemic effects when the low-fat diet was given to rats, but regarding the high-fat diet, pectin had no impact on serum lipids [65, 73]. Although, using high methoxyl pectin in young healthy adults showed a significant alleviation in blood cholesterol, there was no difference in using high methoxyl pectin on fecal lipids compared to pectin with less methoxyl content [71]. This result could be understood from the capacity of pectin in forming gel, which is required in lowering the cholesterol levels rather than differences in bile acid binding due to different methoxyl contents [71].

*5.4. Guar Gum in the Previous Studies*

Guar gum is derived from the endosperm of *Cyamopsis tetragonoloba*. Chemically, guar gum is a mixture of polysaccharide consisted of galactose and mannose [68]. It forms a highly viscous gel when dissolved in water. Studies showed that guar gum has a strong influence on reducing cholesterol levels and body weight in hyperlipidemic rats [43]. Also, the impact of guar gum on healthy rats was investigated for 28 days, the results revealed that guar gum markedly decreased total cholesterol levels (TC), triglyceride (TG), low-density lipoprotein (LDL) as well as high-density lipoprotein (HDL). These results concluded that guar gum had hypolipidemic effects in both hyperlipidemic and normal rats which may prevent atherosclerosis [74]. The effect of guar gum was also studied in patients with primary hyperlipidemia over six weeks. The results showed that the blood cholesterol and LDL levels decreased as compared to the control group. Clinically, guar gum has been used in treating patients with type two hyperlipidemia to reduce total cholesterol levels [69, 75]. It was noticed that the

stool volume and output frequency in humans given partially hydrolyzed guar gum were high, which might be related to the ability of guar gum to lower serum cholesterol levels by increasing cholesterol elimination as fecal bile acids [75-77].

*5.5. Psyllium in the Previous Studies*

Psyllium is derived from the psyllium seed husk (PSH) of *Plantago ovate.* Studies on PSH showed that its gel-forming carbohydrate is not able to be fermented, this non-fermentation is responsible for the laxative and hypolipidemic activity [78]. This laxative effect alleviates constipation through absorbing water from the gastrointestinal contents and consequently increasing stool volume [78]. As a hypolipidemic, the impact of psyllium was studied in subjects that were administrated 9.6 g of psyllium per day into their usual diets for over five weeks. The results showed that there was a decrease in blood lipid levels by 9% [60]. Another study demonstrated a reduction in total cholesterol and LDL concentration of about 5-17%, and 8-20% respectively. This reduction was observed in mild to moderate hypercholesterolemic patients when psyllium was incorporated as 3.4–10.2 g three times daily for 12 weeks [60, 69]. Moreover, a meta-analysis study was performed on hypercholesterolemia patients consuming psyllium-enriched cereal as a part of the low-fat diet, results also showed lowered cholesterol levels and LDL concentrations [6].

*5.6. Oat and Wheat Bran Fibers in the Previous Studies*

Oat bran dietary fiber has a lower density than wheat bran dietary fiber, it contains 50% of water-soluble fiber, whereas wheat bran contains 8% of water-soluble fiber. However, oat and wheat brans influence lipid metabolism differently. A study that evaluates the impacts of oat and wheat brans on lipid profile in healthy adults showed that oat bran significantly lowers cholesterol and LDL blood levels, but, no significant change was noted with wheat bran [79]. In an *in vivo* study, wheat bran demonstrated no hypolipidemic effect in rats fed on both the low and high-fat diet but showed decreased VLDL and lowered serum TG with the high-fat diet [65]. *Borel et. al* (1989) reported in their study that wheat bran had no impact on human lipid profile whereas in rats it decreases total cholesterol and triglyceride in the liver [80]. In another study, the effects of oat and wheat brans on human large bowel were determined. The results showed that oat bran increases fat excretion and stool weight by fermentation of soluble fiber in the colon [81]. In hyperlipidemic men, oat bran demonstrated a reduction in total cholesterol levels through decreasing bile acid and cholesterol absorption and stimulating fecal bile acid excretion [82].

## 6. GUT MICROBIOTA

Microbes live on all human body surfaces, but a significant number of these microbes habitat in the gastrointestinal tract. The human gut contains more than 10000 microbial species that form a complex ecological community called gut microbiota. Bacteria are classified into aerobic and anaerobic organisms, the latter is the most bountiful of gut microbiota such as members of the phyla *Firmicutes*, *Bacteroidetes*, *Bifidobacterium*, *Clostridium*, *Eubacterium*, *Ruminococcus*, *Peptococcus*, and *Peptostreptococcus*. The main facultative anaerobic bacteria are *Escherichia*, *Enterobacter*, *Enterococcus*, *Klebsiella*, *Lactobacillus*, and *Proteus* [83, 84]. The gut microbiota has important benefits on host metabolism, immune system, vitamin synthesis, protection against different diseases, improving angiogenesis, and regulation of lipid storage. For example, some bacteria ferment the undigested food to produce short-chain fatty acids such as acetic, propionic, and butyric acid which are rapidly absorbed from the colonic mucosa to supply energy to the epithelial cells [85]. Due to this, the gut microbiota has lately been defined as a "vital organ" because of its multi-interactional with other organs through several pathways such as the immunological, and metabolic paths. Any imbalance in the gut microbial diversity not only leads to gut-related problems but also affects other organ-related diseases such as gastrointestinal disease, obesity,

colorectal cancer, and hyperlipidemia [83, 84]. Gut microbiota diversity depends on several host factors such as diet, age, and environmental factors [86]. However, diet is now considered one of the main factors in changing the gut microbiota; thus, this manipulation of the microbiota could be used as a therapeutic approach to inhibit or treat several diseases. Diet, probiotics, antimicrobials, and fecal microbiota transplant are considered potential strategies for microbiota manipulation [84].

**6.1. Lignin and gut microbiota**

The resistance of lignin to breakdown both in the environment and the gastrointestinal tract is higher than cellulose and hemicellulose. For this reason, lignin is one of the materials that is harder to valorize as the conditions for depolymerization and further use are expensive and use harsh chemical conditions. Bacteria are known to degrade lignin belong to actinomycetes, some Firmicutes, α-proteobacteria, and γ-proteobacteria [23]. These are responsible for lignin biodegradation through producing three enzymes, lignin peroxidases (LiPs), manganese peroxidases (MnPs), and laccases. These enzymes are responsible for the breakdown of lignin bonds by depolymerization processes, such as catalytic reduction, hydrolysis reaction, and catalytic oxidation [14, 23]. The expression of these enzymes differs based on the microorganism, many strains with the best-known degrading ability of lignin were identified in γ – proteobacteria, specifically, *Pseudomonas fluorescens* (produce lignin peroxidase), *Pseudomonas putida* (produce manganese peroxidase), and *Escherichia coli* (produce laccase). Moreover, lignin-degrading enzymes were identified in wood-degrading fungi, which mostly live as saprotrophs or parasites in ecosystems [14, 23]. All types of fungi, particularly white-rot fungi can degrade lignin totally to $CO_2$ and $H_2O$. For example, *Marasmius quercophilus* producing laccase, and *Agaricus bisporus* producing laccase and manganese peroxidase [14, 23, 87].

**6.1.1 lignin degradation by human gut microbiota**

In general, maintaining a good and healthy gut microbiota plays a key role in our health, gut microbiota helps control the digestive and benefit the immune system, thus having an impact on several health aspects. An imbalance or unhealthy population of microbes in the intestine can significantly contribute to weight gain, high blood sugar, and high cholesterol as well as other disorders. The effect of lignin, especially alkali lignin from brewer's spent grain, was studied on the gut microbiota [88]. The soluble fraction of lignin obtained after enzymatic hydrolysis was found to be altered in the *in vitro* colon fermentation. Conversely, the insoluble lignin fraction remained unaltered. Another important finding of this study is that none of the fractions evaluated inhibited the growth of *Lactobacillus* and *Bifidobacterium* bacteria, concluding this as a very positive outcome [88]. For the soluble fraction of the alkali lignin, if metabolites are formed during its fermentation, it will be important to assess the health- effects of these, thus opening new research fields and applications for lignins.

**6.1.2 lignin degradation by animals' gut microbiota**

A very limited range of organisms can decompose lignin more than cellulose. For example, some bacteria and white-rot basidiomycetes are considered as the primary degraders of lignin by producing oxidative enzymes [89]. Terrestrial animals such as termites use lignin as a nutrient resource. The role of gut microbiota in cellulose degradation in termites has been well documented, but lignin degradation in termites remains unclear. Several bacteria have been isolated from termites that exhibit degradation capabilities of lignin such as *Acinetobacter calcoaceticus* from *Mastotermes darwiniensis* termite, *Bacillus firrnus* from *Reticulitermes santonensis*, *Comamonas acidotvorans* from *Nasutitermes nigriceps*, and *Rhodococus erythropolis* [90-92]. Moreover, the degradation of lignin and lignin-derived aromatic compounds by the gut microbes was studied in termites-feeding guilds such as wood, soil feeders, and fungus cultivators [91]. Recent results demonstrated that bacterial degradation of lignin in the guts of wood-feeding termites such as *Nasutitermes lujae* and *Reticulitermes flavipes* have a profound impact on aromatic

compounds only in the presence of oxygen [91].

Ruminant animals consume lignin-including grasses but can only digest the polysaccharides, this happens with the microbial biodegradation of cellulose and hemicellulose in the rumens [17]. Ruminants can exploit fiber components such as lignin efficiently because their digestive system depends on microbial degradation in the stomach [93]. However, the microbial activity in the rumen showed a potential breakdown of benzyl ether bonds of lignin under anaerobic conditions. [94]. It has been found that fungi are capable of degrading the lignocellulose complex to its fractions e.g. cellulose, hemicellulose, and lignin. Twelve species of Cyathus were isolated from cattle dung to evaluate lignin biodegradation in kenaf by fermentation of the sum of $^{14}C$ released into solution and $^{14}C$ released into the gas phase over a month. Three species were able to remove lignin more rapidly than other species e.g. *Cyathus pallidus*, *C. africanus*, and *C. berkeleyanus*. While *Cyathus canna* has particularly the greatest degradation observed of lignin than other plant parts [95]. In wheat straw, *Cyathus stercoreus* showed great lignin degradation as matched with cellulose [96]. The extraction of lignin was using alkaline media, and the samples were taken from cow dung and other sources. The most collective positive results came from *Pseudomonas sp* which acts as a lignin-degrading bacteria by oxidative enzymes [97]. Further studies on the giant panda discovered that it lacks lignin-degrading enzymes, which are responsible for lignocellulose digestion. It was proven that *Pseudomonas putida* and the mangrove forest bacteria were integrated with lignin degradation by laccase enzyme. The microbial gut flora of giant panda indicated that lignolytic enzymes may facilitate lignin breakdown [98].

**6.2. The effect of other biopolymers on gut microbiota**

**6.2.1 Degradation of cellulose and hemicellulose by gut microbiota**

Although only soluble fibers can be fermented by colonic microbiota insoluble are poorly fermented by gut microbiota [99], the effect of insoluble fibers on gut microbiota was investigated. In a recent paper by *Kim et al.* (2020), it was found that small amounts of cellulose are fermented by mammalian gut microbe while the rest is poorly fermented by non-mammalian gut microbes [100]. Contrary to giant pandas, degradation of cellulose inside the rumen has been associated with bacterial phyla *Firmicutes* and *Fibrobacteres* [101], because the composition of their digestive system lacks the necessary enzymes, which are responsible for cellulose digestion [102]. One of the studies suggested a new alternative method for cellulose degradation by utilizing rumen *Bacteroidetes* and polysaccharide utilization locus-catalyzed conversion of cellulose [101]. The beneficial role of cellulose has been performed on the gut microbiota of mice for 3 months. *Akkermansia, Parabacteroides, Lactobacillus, Clostridium, Eisenbergiella, Marvinnbryantia,* and *Romboutsia* were moer abundant in a high cellulose diet than a low cellulose diet, these findings indicated that cellulose can play a prominent role in maintaining gut hemostasis [100]. Effects of cellulose on the gut microbiota of aquatic animals have been studied on Atlantic salmon, only *Staphylococcus equorum* reported high production of cellulase enzyme [103].

**6.2.2 Degradation of pectin by gut microbiota**

One of the studies on dietary fiber like pectin detected that the levels of *Lachnospira, Dorea, Clostridium,* and *Sutterella* were increased after pectin fermentation by the human fecal microbiome, as well as increased in short-chain fatty acids (acetate and butyrate) levels after incubation with pectin [104]. Different sources of pectin also modulated human fecal microbiota, for instance, soy pectin showed a positive impact on *Lactobacillus rumis* [99]. In rats, fecal microbiota composition was assessed before and after citrus pectin supplementation, which led to an increases in the members of *Prevotellaceae* and *Ruminococcaceae*with no considerable changes were associated with pectin supplement in the gut microbiota [105]. In comparison with high-fat diet, apple-derived pectin has restored the normal levels of *Bacteroides* and

*Lactococcus* in the gut microbiota of rats [106].

**6.2.3 Degradation of Guar gum and psyllium by gut microbiota**

Guar gum is considered one of the beneficial soluble fibers on gut microbiota. In an *in vivo* study, the intake of partially hydrolyzed guar gum increased the levels of fecal beneficial bacteria *Bifidobacterium* and *Lactobacillus* [85]. In another *in vivo* study, it has been reported that short-chain fatty acids such as butyric acid are stimulated by fecal fermentation of partially hydrolyzed guar gum [85]. Furthermore, the impacts of hydrolyzed guar gum on gut microbiota and bowel movements revealed that genus levels of *Bifidobacterium*, *Ruminococcus*, and *Megasphaera* were increased, and the bowel movements were improved by consumption of hydrolyzed guar gum [107]. Additionally, guar gum has proven to prevent inflammatory bowel disease such as colitis in mice by adjusting gut microbiota [108]. Moreover, guar gum increased the abundance of *Bifidobacterium* in Wister rats using different viscosity preparations [99].

One of the recent studies investigated the effect of psyllium on constipation and gut environmentand showed that psyllium supplementation to healthy volunteers had significantly increased *Veillonella* and decreased *Subdoligranulum* [109]. In contrast, in constipated patients, the abundance of *Lachnospira*, *Faecalibacterium*, *Phascolarctobacterium*, *Veillonella*, and *Sutterella* was increased, and the levels of acetate and propionate were different [109].

Recently, researchers have been paying attention to cereal fibers and their activity on gut microbiota. The majorities of research have explored the potential effect of wheat bran on the gut environment on healthy adults.*Bacteroidetes*, *Firmicutes*, and *Actinobacteria* increased after the consumption of wheat bran [110]. Furthermore, one of the studies reported an increase in *lactobacilli* and *bifidobacteria* in total fecal bacteria levels after taking wholegrain oat granola by hyperglycemic or hypercholesterolemic patients [110].

**Table 1. Quick Information in Brief**

| Dietary Fibers | Biological Mechanisms | Biological Effect on Lipid Profile | Biological Effect on Gut Microbiota |
|---|---|---|---|
| **Cellulose** | -Increases bowel movements and fecal output [66].<br>-Decreases stool pH [62]. | -No significant effect on serum lipids [65]. | -Increases beneficial bacteria like *Akkermansia, Parabacteroides, Lactobacillus, Clostridium, Eisenbergiella, Marvinnbryantia,* and *Romboutsia* [100]. |
| **Pectin** | -Forms gel in the small intestine which interferes with the absorption of total cholesterol and bile acids [69].<br>- The gelling capacity increases the sensation of satiety in consumers and reduces the ingestion of high-fat diets [6]. | -Lowers total cholesterol and liver cholesterol synthesis [70]. | -Increases beneficial bacteria like *Lachnospira, Dorea, Clostridium*, and *Sutterella* [104].<br>-Boosts SCFA production (acetate, butyrate) [104]. |
| **Guar Gum** | -Increases the stool volume and output which leads to eliminating the cholesterol as fecal bile acids [75-77].<br>- The gelling capacity increases the sensation of satiety in consumers and reduces the ingestion of high-fat diets [6]. | -Decreases total cholesterol levels (TC), triglyceride (TG), low-density lipoprotein (LDL), and body weight [43]. | -Increases beneficial bacteria like *Bifidobacterium, Lactobacillus*; *Ruminococcus,* and *Megasphaera* [85]. |

| Dietary Fibers | Biological Mechanisms | Biological Effect on Lipid Profile | Biological Effect on Gut Microbiota |
|---|---|---|---|
| **Psyllium** | -The laxative effect alleviates constipation by absorbing water from the gastrointestinal contents and consequently increasing stool volume [78]. | -Lowers cholesterol levels and LDL concentrations [6]. | -Increases beneficial bacteria ( *Veillonella)* and decreased harmful bacteria (*Subdoligranulum)* [109] |
| **Oat Bran** | - Increases fat excretion and stool weight [81].<br>-Decreases bile acid and cholesterol absorption [82].<br>-Stimulates fecal bile acid excretion [82]. | - Significantly lowers cholesterol and LDL levels [79]. | -Increases beneficial bacteria ( *lactobacilli* and *bifidobacteria)* [110][110]. |
| **Wheat Bran** | -Increases the movement of food through the intestine [44]. | -No impact on human lipid profile [79]. | -Increases beneficial bacteria ( *Bacteroidetes*, *Firmicutes*, and *Actinobacteria)* [110] |
| **Chitosan** | - The gelling capacity increases the sensation of satiety in consumers and reduces the ingestion of high-fat diets [6].<br>-Decreases the absorption of dietary fats [19, 64]. | - Decreases cholesterol level [6]. | |
| **Lignin** | Binds to bile acids in the intestine [6, 7].<br>- Increases peristaltic movement, stimulats intestinal food passage, increase feces volume and weight, and transit time [43].<br>- The gelling capacity increases the sensation of satiety in consumers and reduces the ingestion of high-fat diets [6]. | - Decreases cholesterol levels [4, 7-9]. | -Increases beneficial bacteria ( *Lactobacillus* and *Bifidobacteri)* [88]. |

## 7. CONCLUSION

It is obvious that each polymer has a unique feature or characterization that allows it to influence hyperlipidemia and the gut microbiota of both animals and humans. The type of dietary fiber whether soluble or insoluble (lignin, cellulose pectin, or guar gum, etc.) associated with different mechanisms of action, has demonstrated beneficial effects on high cholesterol levels in the blood accounting in several studies that are included in this review. Furthermore, many studies revealed that biopolymers could be used not only in prevention but also in the treatment of hyperlipidemia and its related complications. In addition, positive impacts were reported on the normal bacterial community by consuming biopolymers. Different biopolymers can support different useful groups of gut microbiota; thus, protecting the health of the gut. Taken together, it has been demonstrated that over the years the possibilities of using biopolymers in many applications aspects in the research fields have increased. The physicochemical and structural diversification of biopolymers such gel-forming, texturing, thickening, interfacial adsorption ability, and health-associated properties give them the potential use in the food and nutraceutical industry which is expected to

grow over the next years. But so far, there are limited studies on the bright aspects of dietary fibers, specifically lignin. Future research is still needed to investigate the effectiveness of lignin when combined with current anti-hyperlipidemia drugs, possibly using nanoparticle technology, for example.

## REFERENCES


1. Căpriţă A., et al. Dietary fiber: chemical and functional properties. *J. Agroaliment. Process. Technol*. 2010; 16:406-416.
2. Hillman L., et al. Effects of the fibre components pectin, cellulose, and lignin on bile salt metabolism and biliary lipid composition in man. *Gut*. 1986; 27:29-36.
3. Osfor M.M., et al. Effect of wheat bran consumption on serum lipid profile of hypercholesterolemia patients resident in Holly Makah. *Asian J. Nat. Appl. Sci*. 2016; 5:1.
4. Rodriguez-Gutierrez G., et al. Properties of lignin, cellulose, and hemicelluloses isolated from olive cake and olive stones: binding of water, oil, bile acids, and glucose. *J. Agric. Food Chem*. 2014; 62:8973-8981.
5. Boutlelis D.A., et al. The remedial effect of Ziziphus lotus extract against oxidative stress induced by deltamethrin pesticide in rats. *Jordan J. Pharm. Sci*. 2025; 18:483-495.
6. Madgulkar A.R., Rao M.R., Warrier D. Characterization of psyllium (Plantago ovata) polysaccharide and its uses. *Polysaccharides*. 2015; 871-890.
7. Al-Abd A.M., et al. Anti-angiogenic agents for the treatment of solid tumors: potential pathways, therapy and current strategies–a review. *J. Adv. Res*. 2017; 8:591-605.
8. Shanmugam M.K., et al. Potential role of natural compounds as anti-angiogenic agents in cancer. *Curr. Vasc. Pharmacol*. 2017; 15:503-519.
9. Moreyra A.E., Wilson A.C., Koraym A. Effect of combining psyllium fiber with simvastatin in lowering cholesterol. *Arch. Intern. Med*. 2005; 165:1161-1166.
10. Rajendhiran N., Bhattacharyya S. Preparation and evaluation of nanolipid carriers of bedaquiline: in vitro evaluation and in silico prediction. *Jordan J. Pharm. Sci*. 2024; 17:450-467.
11. Austin A.T., Ballaré C.L. Dual role of lignin in plant litter decomposition in terrestrial ecosystems. *Proc. Natl. Acad. Sci*. 2010; 107:4618-4622.
12. Brebu M., Vasile C. Thermal degradation of lignin—a review. *Cellulose Chem. Technol*. 2010; 44:353.
13. Norikura T., et al. Lignophenols decrease oleate-induced apolipoprotein-B secretion in HepG2 cells. *Basic Clin. Pharmacol. Toxicol*. 2010; 107:813-817.
14. Pollegioni L., Tonin F., Rosini E. Lignin-degrading enzymes. *FEBS J*. 2015; 282:1190-1213.
15. Samfira I., et al. Structural investigation of mistletoe plants from various hosts exhibiting diverse lignin phenotypes. *Digest J. Nanomater. Biostruct*. 2013; 8.
16. Espinoza-Acosta J.L., et al. Antioxidant, antimicrobial, and antimutagenic properties of technical lignins and their applications. *BioResources*. 2016; 11:5452-5481.
17. Leisola M., Pastinen O., Axe D.D. Lignin—designed randomness. *Bio-complexity*. 2012; 2012.
18. Rotstein O.D., et al. Prevention of cholesterol gallstones by lignin and lactulose in the hamster. *Gastroenterology*. 1981; 81:1098-1103.
19. Tolba R., Wu G., Chen A. Adsorption of dietary oils onto lignin for promising pharmaceutical and nutritional applications. *BioResources*. 2011; 6:1322-1335.
20. Watkins D., et al. Extraction and characterization of lignin from different biomass resources. *J. Mater. Res. Technol*. 2015; 4:26-32.

21. Moura J.C.M.S., et al. Abiotic and biotic stresses and changes in the lignin content and composition in plants. J. Integr. *Plant Biol*. 2010; 52:360-376.
22. Datta R., et al. Enzymatic degradation of lignin in soil: a review. *Sustainability*. 2017; 9:1163.
23. Janusz G., et al. Lignin degradation: microorganisms, enzymes involved, genomes analysis and evolution. *FEMS Microbiol. Rev.* 2017; 41:941-962.
24. Novaes E., et al. Lignin and biomass: a negative correlation for wood formation and lignin content in trees. *Plant Physiol.* 2010; 154:555-561.
25. Vinardell M.P., Mitjans M. Lignins and their derivatives with beneficial effects on human health. *Int. J. Mol. Sci.* 2017; 18:1219.
26. Berlin A., Balakshin M. Industrial lignins: analysis, properties, and applications. *Bioenergy Res.* 2014; 315-336.
27. Lora J. Industrial commercial lignins: sources, properties and applications. *Monomers Polym. Compos. from Renew. Resour*. 2008; 225-241.
28. Brodeur G., et al. Chemical and physicochemical pretreatment of lignocellulosic biomass: a review. *Enzyme Res.* 2011; 2011.
29. Laurichesse S., Avérous L. Chemical modification of lignins: towards biobased polymers. *Prog. Polym. Sci.* 2014; 39:1266-1290.
30. Perez-Cantu L., Liebner F., Smirnova I. Preparation of aerogels from wheat straw lignin by cross-linking with oligo (alkylene glycol)-α, ω-diglycidyl ethers. *Microporous Mesoporous Mater.* 2014; 195:303-310.
31. Prakash A., et al. Thermochemical valorization of lignin, in Recent advances in thermo-chemical conversion of biomass. *Elsevier.* 2015; 455-478.
32. El Hage R., et al. Characterization of milled wood lignin and ethanol organosolv lignin from miscanthus. *Polym. Degrad. Stab.* 2009; 94:1632-1638.
33. Zhao X., Cheng K., Liu D. Organosolv pretreatment of lignocellulosic biomass for enzymatic hydrolysis. *Appl. Microbiol. Biotechnol.* 2009; 82:815-827.
34. Ingram T., et al. Comparison of different pretreatment methods for lignocellulosic materials. Part I: conversion of rye straw to valuable products. *Bioresour. Technol.* 2011; 102:5221-5228.
35. Perez-Cantu L., et al. Comparison of pretreatment methods for rye straw in the second generation biorefinery: effect on cellulose, hemicellulose and lignin recovery. *Bioresour. Technol.* 2013; 142:428-435.
36. Zhuang X., et al. Liquid hot water pretreatment of lignocellulosic biomass for bioethanol production accompanying with high valuable products. *Bioresour. Technol.* 2016; 199:68-75.
37. Chi Z., et al. The innovative application of organosolv lignin for nanomaterial modification to boost its heavy metal detoxification performance in the aquatic environment. *Chem. Eng. J.* 2020; 382:122789.
38. Abraham B., et al. Lignin-based nanomaterials for food and pharmaceutical applications: recent trends and future outlook. *Sci. Total Environ.* 2023; 881:163316.
39. Vasile C., Baican M. Lignins as promising renewable biopolymers and bioactive compounds for high-performance materials. *Polymers (Basel).* 2023; 15:15.
40. Karagoz P., et al. Pharmaceutical applications of lignin-derived chemicals and lignin-based materials: linking lignin source and processing with clinical indication. *Biomass Convers. Biorefin.* 2023.
41. Kumar R., et al. Lignin: drug/gene delivery and tissue engineering applications. *Int. J. Nanomedicine.* 2021; 16:2419-2441.
42. Jiménez-Escrig A., Sánchez-Muniz F. Dietary fibre from edible seaweeds: chemical structure, physicochemical properties and effects on cholesterol metabolism. *Nutr. Res.* 2000; 20:585-598.
43. Samarghandian S., et al. Reduction of serum cholesterol in hypercholesterolemic rats by Guar gum. *Avicenna J. Phytomed.* 2011; 1:36-42.
44. Choi Y.-S., et al. Effects of soluble dietary fibers on lipid metabolism and activities of intestinal disaccharidases in rats. *J. Nutr. Sci. Vitaminol.* 1998; 44:591-600.

45. Memon R.A., Gilani A.H. An update on hyperlipidemia and its management. 1995.
46. Otunola G.A., et al. Effects of diet-induced hypercholesterolemia on the lipid profile and some enzyme activities in female Wistar rats. *Afr. J. Biochem. Res.* 2010; 4:149-154.
47. Willey J.Z., et al. Lipid profile components and risk of ischemic stroke: the Northern Manhattan Study (NOMAS). *Arch. Neurol.* 2009; 66:1400-1406.
48. Wang J., et al. Selection of potential probiotic lactobacilli for cholesterol-lowering properties and their effect on cholesterol metabolism in rats fed a high-lipid diet. *J. Dairy Sci.* 2012; 95:1645-1654.
49. Yang X., Yang L., Zheng H. Hypolipidemic and antioxidant effects of mulberry (Morus alba L.) fruit in hyperlipidaemia rats. *Food Chem. Toxicol.* 2010; 48:2374-2379.
50. Matos S.L., et al. Dietary models for inducing hypercholesterolemia in rats. *Braz. Arch. Biol. Technol.* 2005; 48:203-209.
51. Xie N., et al. Effects of two Lactobacillus strains on lipid metabolism and intestinal microflora in rats fed a high-cholesterol diet. *BMC Complement. Altern. Med.* 2011; 11:1-11.
52. Hayek T., et al. Dietary fat increases high density lipoprotein (HDL) levels both by increasing the transport rates and decreasing the fractional catabolic rates of HDL cholesterol ester and apolipoprotein (Apo) AI: presentation of a new animal model and mechanistic studies in human Apo AI transgenic and control mice. *J. Clin. Invest.* 1993; 91:1665-1671.
53. Rader D.J. Molecular regulation of HDL metabolism and function: implications for novel therapies. *J. Clin. Invest.* 2006; 116:3090-3100.
54. Hexeberg S., et al. A study on lipid metabolism in heart and liver of cholesterol- and pectin-fed rats. *Br. J. Nutr.* 1994; 71:181-192.
55. Qanwil T., et al. Hypolipidemic and vasoprotective potential of *Caralluma edulis*: a histological and biochemical study. *Jordan J. Pharm. Sci.* 2025; 18:21-35.
56. Kiortsis D., et al. Statin-associated adverse effects beyond muscle and liver toxicity. *Atherosclerosis.* 2007; 195:7-16.
57. Thompson P.D., et al. Statin-associated side effects. *J. Am. Coll. Cardiol.* 2016; 67:2395-2410.
58. Stancu C., Sima A. Statins: mechanism of action and effects. *J. Cell. Mol. Med.* 2001; 5:378-387.
59. Famularo G., et al. Liver toxicity of rosuvastatin therapy. *World J. Gastroenterol.* 2007; 13:1286.
60. Olson B.H., et al. Psyllium-enriched cereals lower blood total cholesterol and LDL cholesterol, but not HDL cholesterol, in hypercholesterolemic adults: results of a meta-analysis. *J. Nutr.* 1997; 127:1973-1980.
61. Williams R.D., et al. The effect of cellulose, hemicellulose and lignin on the weight of the stool: a contribution to the study of laxation in man. *J. Nutr.* 1936; 11:433-449.
62. Hillman L., et al. Differing effects of pectin, cellulose and lignin on stool pH, transit time and weight. *Br. J. Nutr.* 1983; 50:189-195.
63. Hillman L.C., et al. The effects of the fiber components pectin, cellulose and lignin on serum cholesterol levels. *Am. J. Clin. Nutr.* 1985; 42:207-213.
64. Gades M.D., Stern J.S. Chitosan supplementation and fecal fat excretion in men. *Obes. Res.* 2003; 11:683-688.
65. Vigne J.L., et al. Effect of pectin, wheat bran and cellulose on serum lipids and lipoproteins in rats fed on a low- or high-fat diet. *Br. J. Nutr.* 1987; 58:405-413.
66. Eastwood M., et al. Effects of dietary supplements of wheat bran and cellulose on faeces and bowel function. *Br. Med. J.* 1973; 4:392-394.
67. van Bennekum A.M., et al. Mechanisms of cholesterol-lowering effects of dietary insoluble fibres: relationships with intestinal and hepatic cholesterol parameters. *Br. J. Nutr.* 2005; 94:331-337.

68. Kadajji V.G., Betageri G.V. Water soluble polymers for pharmaceutical applications. *Polymers.* 2011; 3:1972-2009.
69. Kay R.M. Effects of dietary fibre on serum lipid levels and fecal bile acid excretion. *Can. Med. Assoc. J.* 1980; 123:1213.
70. Brouns F., et al. Cholesterol-lowering properties of different pectin types in mildly hyper-cholesterolemic men and women. *Eur. J. Clin. Nutr.* 2012; 66:591-599.
71. Judd P.A., Truswell A. Comparison of the effects of high- and low-methoxyl pectins on blood and faecal lipids in man. *Br. J. Nutr.* 1982; 48:451-458.
72. Judd P.A., Truswell A. The hypocholesterolaemic effects of pectins in rats. *Br. J. Nutr.* 1985; 53:409-425.
73. Cara L., et al. Plasma lipid lowering effects of wheat germ in hypercholesterolemic subjects. *Plant Foods Hum. Nutr.* 1991; 41:135-150.
74. Mosa-Al-Reza H., Sadat D.A., Marziyeh A. Comparison of the beneficial effects of guar gum on lipid profile in hyperlipidemic and normal rats. *J. Med. Plants Res.* 2012; 6:1567-1575.
75. Shaikh T., Kumar S.S. Pharmaceutical and pharmacological profile of guar gum: an overview. *Int. J. Pharm. Pharm. Sci.* 2011; 3(suppl. 5):38-40.
76. Gee J.M., Blackburn N., Johnson I. The influence of guar gum on intestinal cholesterol transport in the rat. *Br. J. Nutr.* 1983; 50:215-224.
77. Overton P., et al. The effects of dietary sugar-beet fibre and guar gum on lipid metabolism in Wistar rats. *Br. J. Nutr.* 1994; 72:385-395.
78. Marlett J.A., Fischer M.H. The active fraction of psyllium seed husk. *Proc. Nutr. Soc.* 2003; 62:207-209.
79. Gold K.V., Davidson D.M. Oat bran as a cholesterol-reducing dietary adjunct in a young, healthy population. *West. J. Med.* 1988; 148:299.
80. Borel P., et al. Wheat bran and wheat germ: effect on digestion and intestinal absorption of dietary lipids in the rat. *Am. J. Clin. Nutr.* 1989; 49:1192-1202.
81. Chen H.-L., et al. Mechanisms by which wheat bran and oat bran increase stool weight in humans. *Am. J. Clin. Nutr.* 1998; 68:711-719.
82. Marlett J.A., et al. Mechanism of serum cholesterol reduction by oat bran. *Hepatology.* 1994; 20:1450-1457.
83. Prakash S., et al. The gut microbiota and human health with an emphasis on the use of microencapsulated bacterial cells. *J. Biomed. Biotechnol.* 2011; 2011:1-12.
84. Walsh C.J., et al. Beneficial modulation of the gut microbiota. *FEBS Lett.* 2014; 588:4120-4130.
85. Ohashi Y., et al. Faecal fermentation of partially hydrolyzed guar gum. *J. Funct. Foods.* 2012; 4:398-402.
86. Shatha A., et al. Changes in gut microbiota of alloxan-induced diabetic rats in response to orally administered combined aqueous extracts of olive leaves and ginger. *J. Appl. Pharm. Sci.* 2022; 12:1-10.
87. Fisher A.B., Fong S.S. Lignin biodegradation and industrial implications. *AIMS Bioeng.* 2014; 1:92-112.
88. Ohra-aho T., et al. Structure of brewer's spent grain lignin and its interactions with gut microbiota in vitro. *J. Agric. Food Chem.* 2016; 64:812-820.
89. Cragg S.M., et al. Lignocellulose degradation mechanisms across the Tree of Life. *Curr. Opin. Chem. Biol.* 2015; 29:108-119.
90. Varma A., et al. Lignocellulose degradation by microorganisms from termite hills and termite guts: a survey on the present state of art. *FEMS Microbiol. Rev.* 1994; 15:9-28.
91. Brune A., Miambi E., Breznak J.A. Roles of oxygen and the intestinal microflora in the metabolism of lignin-derived phenylpropanoids and other monoaromatic compounds by termites. *Appl. Environ. Microbiol.* 1995; 61:2688-2695.
92. Kudo T. Termite-microbe symbiotic system and its efficient degradation of lignocellulose. *Biosci. Biotechnol. Biochem.* 2009; 73:1-6.

93. Krizsan S., Huhtanen P. Effect of diet composition and incubation time on feed indigestible neutral detergent fiber concentration in dairy cows. *J. Dairy Sci.* 2013; 96:1715-1726.
94. Kajikawa H., et al. Degradation of benzyl ether bonds of lignin by ruminal microbes. *FEMS Microbiol. Lett.* 2000; 187:15-20.
95. Abbott T.P., Wicklow D.T. Degradation of lignin by Cyathus species. *Appl. Environ. Microbiol.* 1984; 47:585-587.
96. Wicklow D.T., Detroy R.W., Jessee B. Decomposition of lignocellulose by Cyathus stercoreus (Schw.) de Toni NRRL 6473, a "white rot" fungus from cattle dung. *Appl. Environ. Microbiol.* 1980; 40:169-170.
97. Sasikumar V., et al. Isolation and preliminary screening of lignin degrading microbes. *J. Acad. Ind. Res.* 2014; 3:291-294.
98. Fang W., et al. Evidence for lignin oxidation by the giant panda fecal microbiome. *PLoS One.* 2012; 7:e50312.
99. Fåk F., et al. The physico-chemical properties of dietary fibre determine metabolic responses, short-chain fatty acid profiles and gut microbiota composition in rats fed low- and high-fat diets. *PLoS One.* 2015; 10:e0127252.
100. Kim Y., et al. Dietary cellulose prevents gut inflammation by modulating lipid metabolism and gut microbiota. *Gut Microbes.* 2020; 11:944-961.
101. Naas A.E., et al. Do rumen Bacteroidetes utilize an alternative mechanism for cellulose degradation? *mBio.* 2014; 5:e01401-14.
102. Zhu L., et al. Evidence of cellulose metabolism by the giant panda gut microbiome. *Proc. Natl. Acad. Sci. U.S.A.* 2011; 108:17714-17719.
103. Ringø E., et al. Effect of dietary components on the gut microbiota of aquatic animals. A never-ending story? *Aquac. Nutr.* 2016; 22:219-282.
104. Bang S.-J., et al. The influence of in vitro pectin fermentation on the human fecal microbiome. *AMB Express.* 2018; 8:1-9.
105. Ferrario C., et al. How to feed the mammalian gut microbiota: bacterial and metabolic modulation by dietary fibers. *Front. Microbiol.* 2017; 8:1749.
106. Jiang T., et al. Apple-derived pectin modulates gut microbiota, improves gut barrier function, and attenuates metabolic endotoxemia in rats with diet-induced obesity. *Nutrients.* 2016; 8:126.
107. Yasukawa Z., et al. Effect of repeated consumption of partially hydrolyzed guar gum on fecal characteristics and gut microbiota: A randomized, double-blind, placebo-controlled, and parallel-group clinical trial. *Nutrients.* 2019; 11:2170.
108. Takagi T., et al. Partially hydrolysed guar gum ameliorates murine intestinal inflammation in association with modulating luminal microbiota and SCFA. *Br. J. Nutr.* 2016; 116:1199-1205.
109. Jalanka J., et al. The effect of psyllium husk on intestinal microbiota in constipated patients and healthy controls. *Int. J. Mol. Sci.* 2019; 20:433.
110. Jefferson A., Adolphus K. The effects of intact cereal grain fibers, including wheat bran on the gut microbiota composition of healthy adults: a systematic review. *Front. Nutr.* 2019; 6:33.

# تأثير اللجنين والبوليمرات الحيوية الأخرى على فرط شحميات الدم وميكروبات الأمعاء

***أميرة أبو عمر[1] ، إليزا حسن[1]، جوانا جيل شافيز[2] ، تمارا عثمانة[3] ، حسام أبا زيد[4] ، بافيل غوريكوف[5]، محمد أ.أ. النجار[1]****

[1]قسم العلوم الصيدلانية والصيدلانيات، كلية الصيدلة، جامعة العلوم التطبيقية الخاصة، عمان، الأردن

[2]معهد عمليات الفصل الحراري، جامعة هامبورغ للتكنولوجيا، هامبورغ، ألمانيا

[3]مركز النانو تكنولوجي، جامعة العلوم والتكنولوجيا الأردنية، إربد، الأردن

[4] قسم الصيدلة السريرية العلاجية، كلية الصيدلة، جامعة العلوم التطبيقية الخاصة، عمان، الأردن

5 مختبر تطوير ونمذجة المواد النانوية المسامية الجديدة، جامعة هامبورغ للتكنولوجيا، هامبورغ، ألمانيا

## ملخص

حتى الآن، دُرست الألياف الغذائية، مثل اللجنين والسليلوز والبكتين وصمغ الغوار والسيليوم، بشكلٍ مُكثّف لإمكاناتها الوقائية والعلاجية باستخدام نماذج حيوانية وبشرية، وخاصةً لتأثيراتها الإيجابية على الحالات الأيضية المزمنة، مثل اضطراب شحميات الدم والاضطرابات المُرتبطة به. يُعدّ اضطراب شحميات الدم اضطرابًا أيضيًا خطيرًا يرتبط بارتفاع كوليسترول الدم، ومرض الشريان التاجي، وأمراض القلب التاجية. أظهرت أبحاث سابقة أن هذه الألياف الغذائية قادرة على خفض مستويات الدهون المرتفعة في المصل من خلال آليات مختلفة. ومن أهم هذه الآليات تعديل ميكروبات الأمعاء. فزيادة بكتيريا حمض اللاكتيك (LAB)، القادرة على استقلاب أنواع مختلفة من الألياف الغذائية مثل اللجنين، قد تُخفض مستوى الكوليسترول. تهدف هذه المراجعة إلى تقديم رؤى مفيدة ومناقشات شاملة حول المعارف الحالية المتعلقة بخصائص وتأثيرات الألياف الغذائية، وخاصةً اللجنين، في التحكم بفرط شحميات الدم وتأثيراتها على ميكروبات الأمعاء. تُستخدم محركات البحث جوجل سكولار، وبوابة الأبحاث، وسكوبس لجمع البيانات باستخدام اللجنين، والبوليمرات الحيوية، وميكروبات الأمعاء، وفرط شحميات الدم كمصطلحات بحث.

**الكلمات الدالة:** اللجنين، البوليمرات الحيوية، ميكروبات الأمعاء، فرط شحميات الدم.

* ***المؤلف المراسل: محمد أ.أ. النجار***

moh_alnajjar@asu.edu.jo

تاريخ استلام البحث 2023/12/10 وتاريخ قبوله للنشر 2024/10/31.