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# Impact of Dietary Phytochemicals on Gut Microbiota and Intestinal Barrier Integrity – Nutritional Interventions and Their Role in Chronic Diseases Prevention

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## ABSTRACT

**Introduction:** In recent decades, the development of chronic diseases has become a global problem burdening health care resources. The intestinal microbiota is a complex community of microbes involved in maintaining host homeostasis, and nutritional interventions affecting its functioning are the subject of many scientific studies. Phytochemicals are bioactive components of plants that have multiple actions in the metabolic pathways of human cells. There are many studies describing their diverse activities, including anti-inflammatory, anti-cancer, anti-allergic, and antioxidant. In this review, we described the effects of resveratrol, quercetin, curcumin, fisetin, berberine on the gut microbiota and intestinal barrier integrity through various metabolic pathways and the effects of their consumption on the development of chronic diseases.

**Materials and Methods:** The analysis was conducted based on data available in studies found in the PubMed database. The research concerned the impact of phytochemicals on the gut microbiota and intestinal barrier integrity and their relationship with the development of chronic diseases.

**Conclusions:** Studies indicate that diet has a direct impact on the state of the gut microbiota. A link between the consumption of products rich in phytochemicals and the reduction of the development of chronic diseases through the modulation of the gut microbiota has been described. Dietary interventions are an interesting and promising research subject, and development in this field should continue to be implemented in clinical practice.

**Keywords**: gut microbiota, phytochemicals, chronic diseases, nutrition

## Introduction

In the last decades chronic diseases, such as type 2 diabetes, obesity, chronic kidney disease, hypertension, coronary heart disease and arthritis, have become one of the main problems in healthcare and remain a significant cause of mortality and morbidity around the world. Due to the increasing costs of treatment, public health experts are drawing attention to the importance of preventive strategies [1]. The occurrence of chronic diseases is the result of lifestyle, genetics, environmental influences and daily habits, including nutrition. Therefore, chronic diseases are - at least partially - preventable in many cases [2]. In recent years, due to the great interest in the topic of chronic diseases prevention, dietary choices and their impact on the functioning of the gut microbiota and the intestinal barrier integrity, are the subject of an increasing number of studies. It is known that chemical compounds supplied with food affect the environment of the gut microbiome, therefore providing compounds that have a beneficial effect on gut bacteria may be a promising strategy for treating or preventing many diseases [3].

The human gastrointestinal tract is a habitat for a dynamic community of microorganisms (bacteria, fungi, viruses, parasites) that collectively form the gut microbiome. It is estimated that about 100 trillion bacteria participate in this mutually beneficial relationship. The interconnection is the result of years of co-evolution and crosstalk between human and bacterial cells [4]. It is well known the gut microbiota has multiple important roles in human physiology, and its composition can be influenced by many factors including pH of gastrointestinal tract, production of digestive enzymes and bile acids, oxygen concentration, mucus production, and peristalsis [5,6]. The proportion of bacterial phyla varies depending on the part of the gastrointestinal tract (Table 1.). In healthy subjects, the stomach is colonized by five major bacterial phyla: Pseudomonadota, Bacteroidota, Actinomycetota, Bacillota and Fusobacteriota. Bacillota and Pseudomonadota constitute the main phyla colonizing the small intestine, while in the large intestine, the most common phyla are Bacillota, Bacteroidota, Actinomycetota, Pseudomonadota and Verrucomicrobiota. Each perturbation in the gut microbiome profile may lead to dysbiosis and can have a key role in human disease progression [6,7]. In addition to supporting the processes of fermentation, food digestion and synthesis of vitamins, the intestinal microbiome performs many functions essential for maintaining the homeostasis of the host organism. Its participation in metabolic processes and immune mechanisms seems to be the most significant [7]. The interactions between the microbiome, intestinal mucosa and immune cells are crucial in creating the gut barrier (GB) and maintaining its integrity. A normal GB is composed of many layers and functions not only as a physical

barrier, but also as a functional one. The outer part of the GB is composed of a layer of mucus, proteins involved in defense mechanisms (such as secretory immunoglobulin A) and intestinal microbiota. The middle part is formed by a single layer of intestinal epithelial cells, and the inner part is composed of immune system cells. The intestinal epithelial cells are tightly connected to each other by the apical junctional complex, which includes tight junctional proteins, desmosomes and adherens junctions [8,9]. Factors damaging the GB may cause disruption of its integrity, which results in easier penetration of bacteria and small molecules into the systemic circulation of the host. The malfunctions eventually trigger an immune system response and the development of inflammation [9]. Daily dietary choices and maintaining diversity in the food consumed, significantly influence the functioning of GB and microbiota from the first days of life. In newborns, when solid foods are introduced to the diet, an increase in the number and diversity of gastrointestinal bacteria is observed, whereas the reduced diversity of foods in the older population results in a depletion of intestinal bacterial species [3]. Therefore, diet seems to be an extremely important modifiable factor influencing the condition of the intestinal microbiota and the proper functioning of the GB. In recent years, dietary modulation has become the subject of numerous scientific studies describing the influence of different nutrients on the dynamic microbiota environment.

| | Estimated total abundance of bacteria | Dominant phyla |
|---|---|---|
| Oral cavity | $10^{11} – 10^{12}$ | Actinomycetota, Bacteroidota, Bacillota, Fusobacteriota, Pseudomonadota, Saccharibacteria, Spirochaetota |
| Stomach | $10^{7}$ | Pseudomonadota, Bacteroidota, Actinomycetota, Bacillota, Fusobacteriota |

| | | |
|---|---|---|
| Duodenum<br>Jejunum<br>Ileum | $10^7$ - $10^{11}$ | Bacillota, Bacteroidota, Pseudomonadota, Fusobacteriota, Actinomycetota |
| Colon | $10^{14}$ | Bacillota, Bacteroidota, Actinomycetota, Pseudomonadota, Verrucomicrobiota |

**Table 1. Total abundance and dominant phyla of bacteria colonizing human gastrointestinal tract [6,10,11].**

Phytochemicals are a group of chemical compounds (such as polyphenols, carotenoids, saponins, isoprenoids) with many biological activities necessary for the physiological processes of plants. They are bioactive compounds found in plant foods – vegetables, fruit, nuts, whole grains, teas [12]. So far, scientists have discovered over 1000 phytochemicals, and their participation in many metabolic pathways important in human cells have been described. They possess antioxidant, anti-inflammatory and antimicrobial activities. There are dozens of studies describing their participation in the regulation of immunological processes, anti-cancer, analgesic and anti-allergic mechanisms [13,14,15]. This suggests a beneficial effect of phytochemicals in maintaining general homeostasis, which makes them a promising target for further scientific research. The constantly growing interest in the issue of human microbiota results in the search for new solutions to improve its functioning. Recent research indicates the beneficial effect of phytochemicals on maintaining the homeostasis of the intestinal microbiome [16]. This review aims to summarize current knowledge on the role of consuming foods rich in selected phytochemicals (Table 2.), its influence on the composition and functioning of the gut microbiome and the importance of nutritional interventions in prevention of chronic diseases.

| | |
|---|---|
| Resveratrol | Dark grapes, peanuts, raisins, blueberries, cranberries |
| Quercetin | Grapes, apples, berries, onions, broccoli, peppers, nuts, wine |
| Curcumin | Curcuma longa (root) |
| Fisetin | Apples, persimmons, grapes, onions, kiwi, kale, strawberries, cucumbers |
| Berberine | Coptidis rhizoma |

**Table 2. Food sources of phytochemicals [17,18,19].**

## Materials and Methods

A literature search was conducted across multiple databases, including PubMed and Google Scholar. Keywords, and their combinations, such as "gut microbiota," "gut barrier," "phytochemicals," "nutrition," and "chronic diseases" were used to identify relevant studies. Analysis included findings from clinical trials, reviews and meta-analyses examining interconnections between gut microbiota, food rich in phytochemicals and development of chronic diseases. Additional data was sourced through reference lists of chosen studies to capture relevant research missed by the initial search.

## Resveratrol

Resveratrol (3,5,4’-trihydroxy-trans-stilbene) is a natural polyphenol, first found in the roots of Veratrum grandiflorum and then isolated from the root of Polygonum cupsidatum. Its production in plants increases under stress conditions, such as exposure to pathogens or physical injury, making it a vital component of the plant's defense mechanisms. Many natural food products have been described as sources of resveratrol, including blueberries, grapes, cranberries, peanuts, and red wine [20]. In recent years, many scientific studies have appeared describing the impact of resveratrol on biochemical processes in animal and human cells and the potential benefits of its use in the treatment and prevention of chronic diseases. It has been

demonstrated to have antimicrobial, anti-diabetic, anti-obesity, anti-cancer and anti-atherosclerosis properties [21,22]. Despite the extensive studies highlighting significant interactions between dietary resveratrol and gut microbiota, the exact mechanisms connecting bacteria, dietary changes, and the onset of chronic diseases remain under investigation. In individuals with type 2 diabetes, a relationship has been observed between dysbiosis, increased insulin resistance, and the onset of complications such as neuropathy, retinopathy, and nephropathy [23]. Jung et al. [24] conducted a study analyzing the composition of the microbiota in normal and diet-induced obese mice. For 8 weeks, mice were fed a standard (12.41% kcal from fat) or high-fat diet (60% kcal from fat). In both groups, 200 mg/kg/day of resveratrol was administered or not. Resveratrol treatment decreased the abundance of Clostridium cluster XI, Lactococcus, Oscillibacter and Hydrogenoanaerobacterium in mice fed the high-fat diet. The authors concluded that these alterations were linked to mTOR (mammalian target of rapamycin), a tyrosine protein kinase involved in activating insulin-like growth factor 1 receptors and insulin receptors. In mice, changes in intestinal inflammation and insulin resistance associated with resveratrol treatment were observed, and mTOR signaling played a key role in altering the composition of the intestinal microbiota.

Several studies have highlighted the impact of resveratrol intake on the Bacillota/Bacteroidota ratio within gut microbiota, showing that an increased ratio is linked to obesity. In both humans and the mice model, a reduction in the ratio of Bacillota to Bacteroidota and a reduction in the abundance of Clostridium strains and the frequency of occurrence in the Lachnospiraceae family were observed [25]. Chen et al. [26] conducted a study using male rats that developed nonalcoholic fatty liver disease (NAFLD) when fed a high-fat diet. After six weeks of resveratrol supplementation, there was a notable increase in the abundance of Ruminococcaceae, Akkermansia muciniphila, and Lachnospiraceae. Resveratrol supplementation resulted in upregulation in the expression of tight junctions in the intestinal barrier and reduced intestinal permeability. In rats, inhibition of the development of NASH and colon inflammation was observed. Thus, leveraging resveratrol's effects on gut microbiota and gut barrier emerges as a promising strategy for preventing chronic diseases. However, it should be taken into consideration that the use of resveratrol may be difficult due to its phase II metabolism in the liver. Research suggests that, in comparison to other polyphenols, resveratrol has low bioavailability and limited ability to penetrate the blood-brain barrier after oral administration [27]. Further research describing metabolic pathways linking resveratrol and GB is necessary.

**Quercetin**

Quercetin is a natural flavonoid widely present in vegetables, fruits, cereals, nuts [28]. It has been described to possess many beneficial health properties (antioxidant, antiapoptotic, anti inflammatory, anti-diabetic) and plays an important role in treatment of aging-related diseases [29]. It is engaged in intestinal barrier repairing and remodeling the intestinal microbiota [30]. A mice study with Citrobacter rodentium-induced colitis, conducted by Lin et. al. [31] has shown that dietary quercetin supplementation (30mg/kg) resulted in suppression of production of pro-inflammatory cytokines (IL-17, TNFα, IL-6) while promoting the production of IL-10 in colon tissues. IL-10 is crucial for maintaining cellular homeostasis and modulating inflammation, acting as an anti-inflammatory cytokine that protects against uncontrolled immune response [32.] Another study [33] has demonstrated that quercetin enhanced Bacteroides, Bifidobacterium, Lactobacillus, Clostridia population and reduced Fusobacterium and Enterococcus populations. Animal studies have also shown that glycoside forms of quercetin can suppress the translocation of gut-invasive bacteria such as Escherichia coli, Enterococcus spp., Proteus spp., and Klebsiella pneumoniae. In the mice model quercetin was able to alleviate intestinal oxidative damage ($H_2O_2$-induced colitis) [34]. This protective effect was attributed to the upregulation of glutamate-cysteine ligase catalytic subunit, an enzyme involved in glutathione synthesis, as well as increased transcription of glutathione reductase, leading to higher intracellular glutathione levels and the elimination of excessive reactive oxygen species (ROS) produced by $H_2O_2$.

Several studies have indicated that quercetin can enhance the expression of tight junctions, improve gut barrier function [35,36] promote intestinal cell proliferation, and support the regenerative capacity of intestinal mesenchymal stem cells [34,37]. The impact on quercetin-mediated assembly and expression of tight junctions proteins was possible due to the change in phosphorylation status [35]. In addition, quercetin by the PKC$\alpha$/ERK1-2 signaling pathway activation could upregulate intestinal goblet cells secretory capacity and mucin level in gut lumen, which provided positive effects on integrity of GB [38]. Immune regulatory function of quercetin has been widely described [38]. Decreased infiltration of macrophages, neutrophils, Th17 cells and increased regulatory T cell proportion were observed in mice study during quercetin treatment [36]. Those findings indicate that dietary quercetin can exert therapeutic effects and may be an effective strategy in controlling colitis caused by various etiology via modifying gut microbiota or different pleiotropic effects. Given this information,

further research into quercetin's role in gut microbiota modulation presents a promising avenue for the therapy of inflammatory bowel disease [39].

**Curcumin**

Curcumin is a natural phytochemical found in the rhizome of Curcuma longa, widely used as a dietary spice. Many studies have confirmed its anti-inflammatory and anti-oxidant mechanisms impacting the management of various diseases - including type 2 diabetes mellitus, neurological disorders, gastrointestinal diseases, and several types of cancer [40,41]. Furthermore, curcumin and its metabolites have been shown to positively influence gut microbiota [42]. Curcumin was described to normalize the gut microbiota dysbiosis to a certain extent. The diversity of gut microbiota of mice has been increased during oral administration of curcumin. The relative abundances of several bacterial species associated with Alzheimer's Disease development (Bacteroidaceae, Prevotellaceae, and Lactobacillaceae) could be modulated by curcumin [43]. Studies have indicated that curcumin administration can significantly alter the ratio between beneficial and harmful bacterial strains, favoring the growth of beneficial types, such as Lactobacilli, Bifidobacteria, and butyrate-producing bacteria, while simultaneously reducing pathogenic bacteria such as Enterobacteria, Prevotellaceae, Coriobacterales, and Rikenellaceae, which are often associated with chronic diseases development. [44,45,46]. In ovariectomized rats with induced estrogen deficiency, change in abundance and distribution of intestinal microflora has been observed. Oral administration of curcumin (100mg/kg/day per 12 weeks) was able to partially reverse changes in the diversity of gut microbiota [53].

Various studies report that curcumine affects intestinal barrier. Additionally, research suggests that curcumin positively influences the intestinal barrier. It is a compound potentially able to restore disrupted intestinal permeability on in vitro models [47]. In human colon carcinoma cell lines (Caco-2) curcumin attenuated the disruption of intestinal barrier function by counteracting LPS-induced IL-1β secretion and preventing tight junction protein disruption [48]. Hou et. al. [49] conducted a study in which rats with NAFLD fed a high-fat diet for 16 weeks developed impairments in function of GB. However, treatment with curcumin (200 mg/kg daily) improved the structure of intestinal tight junctions, reduced serum concentrations of TNF-α and LPS, and upregulated occludin expression in the intestinal mucosa. The group with curcumin intervention showed a decrease in inflammatory cell infiltration and hepatocyte steatosis. In mice study, after 16 weeks of high fat high cholesterol containing diet (Western diet, WD) and 100 mg/kg daily oral curcumin supplementation observed its protective effects

against WD-induced disruption of GB function, restoring activity of alkaline phosphatase (IAP) activity and the expression of tight junction proteins ZO-1 and claudin-1 [50]. Notably, a decrease in IAP levels has been observed in patients with inflammatory bowel disease. Chimeric human IAP was evaluated in gut dysbiosis, inflammatory bowel disease and acute kidney injury as therapeutic protein [51,52]. Collectively, these findings suggest that curcumin plays a vital role in maintaining intestinal barrier integrity and could serve as a promising therapeutic strategy to prevent the development of metabolic diseases.

**Fisetin**

Fisetin, a flavonol found naturally in a variety of fruits and vegetables, is classified as a bioactive phytochemical with significant effects on cell division, angiogenesis, carcinogenesis, oxidative stress, and inflammation [54]. Research has shown that fisetin provides neuroprotective benefits against neurodegeneration by influencing the composition and diversity of gut microbiota. In mouse models, fisetin significantly reduces dopaminergic neurodegeneration caused by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) [55]. Research has indicated that fisetin offers neuroprotective benefits in cases of neurodegeneration by influencing the composition and diversity of gut microbiota. For instance, a study by Hill-Burns et al. found that patients with Parkinson's Disease displayed a reduced abundance of Lachnospiraceae compared to healthy individuals [57]. Srivastav et al. demonstrated that the application of probiotics could significantly increase the metabolite BHP of butyrate and confirmed that butyrate is able to protect against MPTP- induced neurotoxicity by preventing the loss of dopaminergic neurons and dopamine depletion. Additionally, it reduces gliosis proliferation in Substantia Nigra and upregulates neurotrophic factors [58]. This study suggests that fisetin may enhance neuroprotection by increasing the population of Lachnospiraceae bacteria. This increase helps to mitigate gut inflammation and decrease the production of toxic substances that can impact brain health and function. Dysbiosis has been noted in individuals with Alzheimer's disease (AS), where the gut microbiota may generate potentially harmful and pro-inflammatory substances. This, in turn, can initiate chronic systemic inflammation, which plays a role in both neuroinflammation and neurodegeneration [61,62]. Fisetin is able to modulate gut microbiota, reducing potentially pathogenic gram-negative bacteria without affecting probiotic microflora. Bactericidal activity against E. coli, P. aeruginosa, and C. albicans has been observed. The author's investiogation into the gut-brain axis and the modulation of the microbiome has revealed fistein's potential in Alzheimer's disease therapy.

By influencing the gut microbiome, fisetin presents a promising strategy for restoring a healthy microbial community and mitigating neuroinflammatory processes [63].

Study conducted by Qian Ren et al. [59] indicated that fisetin protected against hyperuricemia-induced chronic kidney disease (CKD), this protective effect was achieved through modulation of gut microbiota-mediated tryptophan metabolism and aryl hydrocarbon receptor (AHR) activation. Following fisetin treatment, significant restoration of dysregulated gut bacteria, improvement in kidney function, and a reduction in renal fibrosis were observed in mice experiencing CKD. L-kynurenine, one of gut microbiota-derived tryptophans' metabolites was found to correlate with fisetin's nephroprotective effects. AHR and an endogenous L-kynurenine receptor were increased in hyperuricemic mice, afterwards decreased in mice treated with fisetin. In vitro studies have shown that inhibition of AHR activation reduced L-kynurenine-induced fibrosis. Furthermore, the accumulation of uremic toxins in the bodily fluids of CKD patients can trigger AHR activation, influencing the progression of the disease. Notably, AHR can be activated by ligands, specifically tryptophan metabolites [60].

Lin et al. [56] conducted a study where mice with fisetin treatment exhibited a significantly higher abundance of Lachnospiraceae, a beneficial butyrate-producing bacterium that is associated with gut health. Butyrate serves as an energy source for the gut epithelium. It also inhibits the activation of NF-κB, helping to reduce gut inflammation. Lachnospiraceae, a bacteria known for its antiinflammatory properties, has been observed as a decrease in dextran sulfate sodium induced colitis [64]. After fisetin treatment notable increase in the abundance of Lachnospiraceae was increased. In addition, fisetin was able to improve microbial imbalance by increasing relative abundance of Bacillota and Verrucomicrobiota. It should be mentioned that Bacillota possess anti-inflammatory properties and play an important role in colitis management [65]. Verrucomicrobiota by its ability to generate mucin-degrading enzymes helps to maintain a healthy gut barrier function. By breaking down mucus, these bacteria create an environment that enables other bacteria to accesss essential nutrients and establish a balanced microbial community within the gut [66].

**Berberine**

Berberine is an active alkaloid predominantly found in all parts of Berberis vulgaris, particularly in its fruit, known as barberry. The berberine content in the fruit ranges from 5.2% to 7.7% [67]. This compound is recognized for its various pharmacological properties and diverse therapeutic applications. Its lipid-lowering, insulin-resistance improving action has been widely described

and it was the main purpose of various clinical trials associated with its influence on cardiovascular, gastrointestinal, endocrine, central nervous system and anticancer properties [68]. Berberine operates through multiple mechanisms, including the modulation of gastrointestinal microbiota composition, leading to a reduction in blood lipid and glucose levels. This suggests a potential role in preventing obesity and combating insulin resistance [69]. Studies have shown that treatment with berberine enriches the abundance of Bacteroides in the colon and terminal ileum of mice, while decreasing populations of Lactobacillus acidophilus, Lactobacillus murinus, Lactococcus lactis, Ruminococcus gnavu, and Ruminococcus schinkii [70]. Acting on so many strains of bacteria obviously has an impact on health. Mice studies have described that berberine (given orally) modified intestinal bacterial composition by increasing the abundance of butyrate-producing bacteria, then butyrate enters the blood and reduces blood lipid and glucose levels [71]. Glucagon-like peptide 1 (GLP-1) and Peptide YY (PYY) upregulation induced by butyrate may be important in preventing or treating obesity and insulin resistance [72]. PYY and neuropeptide YY have a key role, closely related to appetite regulation and obesity formation [73].

Berberine's influence on gastrointestinal barrier remains the subject of many studies. Research by Chen et al. demonstrated that berberine administration increased the number of colonic glands and mucus secretion from goblet cells, enhancing intestinal barrier function and reducing serum glycolipid levels in hamsters with glucolipid metabolism disorders [74]. This study has proven berberine via modulating gut microbiota and gut-microbiota-related tryptophan metabolites could alleviate intestinal barrier dysfunction. In another study by Min Tang et al. [75], the influence of the trichothecene deoxynivalenol (DON) on piglets has been investigated. Trichothecenes, produced by the fungus Fusarium, contaminate food crops and can cause significant public health issues, leading to adverse reactions such as vomiting, abdominal pain, loss of appetite, nausea, growth inhibition, diarrhea, and immunotoxicity [76]. Piglets were assigned to groups with a basal diet, basal diet with 4mg/kg DON, basal diet with 4 mg/kg DON and 40 mg/kg of Berberine for 21 days. In groups with added berberine to diet multiple beneficial actions were observed. Berberine was able to inhibit intestinal injury induced by DON through increasing serum antioxidant enzymes expression and T cell surface antigens and reducing proinflammatory cytokines release in the small intestine. Notable upregulation of the protein levels as zonula occludens 1 (ZO-1), Occludin, Claudin-1, increased morphological parameters of the jejunum have been observed. The multidirectional effect of berberine related to the modulation of intestinal microbiota and GB should therefore be the

subject of further scientific research so that in the future its properties can be used to prevent the development of chronic diseases.

## Conclusions

An unbalanced diet, bad eating habits, low food quality, exposure to stress, use of antibiotics and low physical activity affect the composition and functioning of the intestinal microbiota environment [77,78,79]. Although the composition of the human microbiota is unique to each individual and remains relatively constant throughout most of life, the type and variety of foods consumed is known to cause some alterations in the complex community of microbes [80,81]. Chronic diseases remain an important health care problem therefore it is necessary to look for effective, and at the same time relatively easy to apply methods of prevention. In this review, we described the importance of the gut microbiome and gut barrier in maintaining overall homeostasis and the dietary interventions that could potentially benefit their functioning. Dietary phytochemicals have been shown to have the ability to modulate many metabolic processes in human cells. Resveratrol, quercetin, curcumin, fisetin, berberine belong to the group of phytochemicals and have a potential effect on preventing the development of chronic diseases such as type 2 diabetes, metabolic syndrome, obesity, atherosclerosis, and chronic kidney disease. It should be taken into consideration that the phytochemical content of natural products may be difficult to determine. Therefore, it is necessary to establish the amount of natural sources of phytochemicals consumed through food that will provide a beneficial effect on the gut microbiome and gut barrier. Recent population-based studies suggest the use of the PI (Phytochemical Index) indicator to determine the health effects of products rich in phytochemicals. The method is based on a comparison of energy in a diet derived from foods rich in phytochemicals to total energy intake per day [82]. It has been demonstrated that the use of a high PI diet is correlated with a reduction in risk factors for diseases such as obesity, NAFLD and breast cancer [83,84,85]. The wide variety and availability of phytochemical sources makes them an interesting subject for further research. However, in order to use them in clinical practice, a thorough analysis of the mechanisms involved in crosstalk between human gut microbiota and intestinal epithelium is necessary.

**Author's contribution**

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**References**


1. Greenberg H, Pi-Sunyer FX. Preventing preventable chronic disease: An essential goal. Prog Cardiovasc Dis. 2019 Jul-Aug;62(4):303-305. doi: 10.1016/j.pcad.2019.08.002. Epub 2019 Aug 14. PMID: 31421079.
2. Airhihenbuwa CO, Tseng TS, Sutton VD, Price L. Global Perspectives on Improving Chronic Disease Prevention and Management in Diverse Settings. Prev Chronic Dis. 2021 Apr 8;18:E33. doi: 10.5888/pcd18.210055. PMID: 33830913; PMCID: PMC8051856.
3. Zmora N, Suez J, Elinav E. You are what you eat: diet, health and the gut microbiota. Nat Rev Gastroenterol Hepatol. 2019 Jan;16(1):35-56. doi: 10.1038/s41575-018-0061-2. PMID: 30262901.
4. Takiishi T, Fenero CIM, Câmara NOS. Intestinal barrier and gut microbiota: Shaping our immune responses throughout life. Tissue Barriers. 2017 Oct 2;5(4):e1373208. doi: 10.1080/21688370.2017.1373208. Epub 2017 Sep 28. PMID: 28956703; PMCID: PMC5788425.
5. Flandroy L, Poutahidis T, Berg G, Clarke G, Dao MC, Decaestecker E, Furman E, Haahtela T, Massart S, Plovier H, Sanz Y, Rook G. The impact of human activities and lifestyles on the interlinked microbiota and health of humans and of ecosystems. Sci Total Environ. 2018 Jun 15;627:1018-1038. doi: 10.1016/j.scitotenv.2018.01.288. Epub 2018 Feb 3. PMID: 29426121.
6. de Vos WM, Tilg H, Van Hul M, Cani PD. Gut microbiome and health: mechanistic insights. Gut. 2022 May;71(5):1020-1032. doi: 10.1136/gutjnl-2021-326789. Epub 2022 Feb 1. PMID: 35105664; PMCID: PMC8995832.
7. Adak A, Khan MR. An insight into gut microbiota and its functionalities. Cell Mol Life Sci. 2019 Feb;76(3):473-493. doi: 10.1007/s00018-018-2943-4. Epub 2018 Oct 13. PMID: 30317530; PMCID: PMC11105460.
8. Di Tommaso N, Gasbarrini A, Ponziani FR. Intestinal Barrier in Human Health and Disease. Int J Environ Res Public Health. 2021 Dec 6;18(23):12836. doi: 10.3390/ijerph182312836. PMID: 34886561; PMCID: PMC8657205.
9. Li Q, von Ehrlich-Treuenstätt V, Schardey J, Wirth U, Zimmermann P, Andrassy J, Bazhin AV, Werner J, Kühn F. Gut Barrier Dysfunction and Bacterial Lipopolysaccharides in Colorectal Cancer. J Gastrointest Surg. 2023 Jul;27(7):1466-1472. doi: 10.1007/s11605-023-05654-4. Epub 2023 Mar 27. PMID: 36973501; PMCID: PMC10366024.

10. Baker JL, Mark Welch JL, Kauffman KM, McLean JS, He X. The oral microbiome: diversity, biogeography and human health. Nat Rev Microbiol. 2024 Feb;22(2):89-104. doi: 10.1038/s41579-023-00963-6. Epub 2023 Sep 12. PMID: 37700024; PMCID: PMC11084736.
11. Yersin S, Vonaesch P. Small intestinal microbiota: from taxonomic composition to metabolism. Trends Microbiol. 2024 Oct;32(10):970-983. doi: 10.1016/j.tim.2024.02.013. Epub 2024 Mar 19. PMID: 38503579.
12. Guan R, Van Le Q, Yang H, Zhang D, Gu H, Yang Y, Sonne C, Lam SS, Zhong J, Jianguang Z, Liu R, Peng W. A review of dietary phytochemicals and their relation to oxidative stress and human diseases. Chemosphere. 2021 May;271:129499. doi: 10.1016/j.chemosphere.2020.129499. Epub 2021 Jan 4. PMID: 33445014.
13. Park, K. The Role of Dietary Phytochemicals: Evidence from Epidemiological Studies. Nutrients 2023, 15, 1371. https://doi.org/ 10.3390/nu15061371
14. Kumar A, P N, Kumar M, Jose A, Tomer V, Oz E, Proestos C, Zeng M, Elobeid T, K S, Oz F. Major Phytochemicals: Recent Advances in Health Benefits and Extraction Method. Molecules. 2023 Jan 16;28(2):887. doi: 10.3390/molecules28020887. PMID: 36677944; PMCID: PMC9862941.
15. Shen J, Shan J, Zhong L, Liang B, Zhang D, Li M, Tang H. Dietary Phytochemicals that Can Extend Longevity by Regulation of Metabolism. Plant Foods Hum Nutr. 2022 Mar;77(1):12-19. doi: 10.1007/s11130-021-00946-z. Epub 2022 Jan 13. PMID: 35025006; PMCID: PMC8756168.
16. Yin R, Kuo HC, Hudlikar R, Sargsyan D, Li S, Wang L, Wu R, Kong AN. Gut microbiota, dietary phytochemicals and benefits to human health. Curr Pharmacol Rep. 2019;5:332-344. doi: 10.1007/s40495-019-00196-3. Epub 2019 Aug 19. PMID: 33224717; PMCID: PMC7678755.
17. Karaman Mayack B, Sippl W, Ntie-Kang F. Natural Products as Modulators of Sirtuins. Molecules. 2020 Jul 20;25(14):3287. doi: 10.3390/molecules25143287. PMID: 32698385; PMCID: PMC7397027.
18. Iside C, Scafuro M, Nebbioso A, Altucci L. SIRT1 Activation by Natural Phytochemicals: An Overview. Front Pharmacol. 2020 Aug 7;11:1225. doi: 10.3389/fphar.2020.01225. PMID: 32848804; PMCID: PMC7426493.

19. Akter R, Afrose A, Rahman MR, Chowdhury R, Nirzhor SSR, Khan RI, Kabir MT. A Comprehensive Analysis into the Therapeutic Application of Natural Products as SIRT6 Modulators in Alzheimer's Disease, Aging, Cancer, Inflammation, and Diabetes. Int J Mol Sci. 2021 Apr 17;22(8):4180. doi: 10.3390/ijms22084180. PMID: 33920726; PMCID: PMC8073883.
20. Tian B, Liu J. Resveratrol: a review of plant sources, synthesis, stability, modification and food application. J Sci Food Agric. 2020 Mar 15;100(4):1392-1404. doi: 10.1002/jsfa.10152. Epub 2019 Dec 14. PMID: 31756276.
21. Hou CY, Tain YL, Yu HR, Huang LT. The Effects of Resveratrol in the Treatment of Metabolic Syndrome. Int J Mol Sci. 2019 Jan 28;20(3):535. doi: 10.3390/ijms20030535. PMID: 30695995; PMCID: PMC6387422.
22. Rauf A, Imran M, Butt MS, Nadeem M, Peters DG, Mubarak MS. Resveratrol as an anti-cancer agent: A review. Crit Rev Food Sci Nutr. 2018 Jun 13;58(9):1428-1447. doi: 10.1080/10408398.2016.1263597. Epub 2017 Jul 21. PMID: 28001084.
23. Iatcu CO, Steen A, Covasa M. Gut Microbiota and Complications of Type-2 Diabetes. Nutrients. 2021 Dec 30;14(1):166. doi: 10.3390/nu14010166. PMID: 35011044; PMCID: PMC8747253.
24. Jung MJ, Lee J, Shin NR, Kim MS, Hyun DW, Yun JH, Kim PS, Whon TW, Bae JW. Chronic Repression of mTOR Complex 2 Induces Changes in the Gut Microbiota of Diet-induced Obese Mice. Sci Rep. 2016 Jul 29;6:30887. doi: 10.1038/srep30887. PMID: 27471110; PMCID: PMC4965768.
25. Inchingolo AD, Malcangi G, Inchingolo AM, Piras F, Settanni V, Garofoli G, Palmieri G, Ceci S, Patano A, De Leonardis N, Di Pede C, Montenegro V, Azzollini D, Garibaldi MG, Kruti Z, Tarullo A, Coloccia G, Mancini A, Rapone B, Semjonova A, Hazballa D, D'Oria MT, Jones M, Macchia L, Bordea IR, Scarano A, Lorusso F, Tartaglia GM, Maspero C, Del Fabbro M, Nucci L, Ferati K, Ferati AB, Brienza N, Corriero A, Inchingolo F, Dipalma G. Benefits and Implications of Resveratrol Supplementation on Microbiota Modulations: A Systematic Review of the Literature. Int J Mol Sci. 2022 Apr 5;23(7):4027. doi: 10.3390/ijms23074027. PMID: 35409389; PMCID: PMC8999966.
26. Chen M, Hou P, Zhou M, Ren Q, Wang X, Huang L, Hui S, Yi L, Mi M. Resveratrol attenuates high-fat diet-induced non-alcoholic steatohepatitis by maintaining gut barrier integrity and inhibiting gut inflammation through regulation of the endocannabinoid

system. Clin Nutr. 2020 Apr;39(4):1264-1275. doi: 10.1016/j.clnu.2019.05.020. Epub 2019 May 30. PMID: 31189495.

27. Robertson I, Wai Hau T, Sami F, Sajid Ali M, Badgujar V, Murtuja S, Saquib Hasnain M, Khan A, Majeed S, Tahir Ansari M. The science of resveratrol, formulation, pharmacokinetic barriers and its chemotherapeutic potential. Int J Pharm. 2022 Apr 25;618:121605. doi: 10.1016/j.ijpharm.2022.121605. Epub 2022 Feb 26. PMID: 35227804.
28. Nabavi, Seyed & Nabavi, Seyed & Eslami, Shahram & Moghaddam, Akbar. (2012). In vivo protective effects of quercetin against sodium fluoride-induced oxidative stress in the hepatic tissue. Food Chemistry. 132. 931–935. 10.1016/j.foodchem.2011.11.070.
29. Cui, Zhifu et al. “Therapeutic application of quercetin in aging-related diseases: SIRT1 as a potential mechanism.” *Frontiers in immunology* vol. 13 943321. 22 Jul. 2022, doi:10.3389/fimmu.2022.943321
30. Yuan M, Sun T, Zhang Y, Guo C, Wang F, Yao Z, Yu L. Quercetin Alleviates Insulin Resistance and Repairs Intestinal Barrier in *db*/*db* Mice by Modulating Gut Microbiota. Nutrients. 2024 Jun 14;16(12):1870. doi: 10.3390/nu16121870. PMID: 38931226; PMCID: PMC11206920.
31. Lin R, Piao M, Song Y. Dietary Quercetin Increases Colonic Microbial Diversity and Attenuates Colitis Severity in *Citrobacter rodentium*-Infected Mice. Front Microbiol. 2019 May 16;10:1092. doi: 10.3389/fmicb.2019.01092. PMID: 31156598; PMCID: PMC6531918.
32. Carlini V, Noonan DM, Abdalalem E, Goletti D, Sansone C, Calabrone L, Albini A. The multifaceted nature of IL-10: regulation, role in immunological homeostasis and its relevance to cancer, COVID-19 and post-COVID conditions. Front Immunol. 2023 Jun 8;14:1161067. doi: 10.3389/fimmu.2023.1161067. PMID: 37359549; PMCID: PMC10287165.
33. Dönder Y, Arikan TB, Baykan M, Akyüz M, Öz AB. Effects of quercitrin on bacterial translocation in a rat model of experimental colitis. Asian J Surg. 2018 Nov;41(6):543-550. doi: 10.1016/j.asjsur.2017.12.002. Epub 2018 Jan 20. PMID: 29371051.
34. [Dong Y, Hou Q, Lei J, Wolf PG, Ayansola H, Zhang B. Quercetin Alleviates Intestinal Oxidative Damage Induced by H2O2 via Modulation of GSH: In Vitro Screening and In Vivo Evaluation in a Colitis Model of Mice. ACS Omega. 2020 Apr 2;5(14):8334-8346. doi: 10.1021/acsomega.0c00804. PMID: 32309744; PMCID: PMC7161027.]

35. Suzuki T, Hara H. Role of flavonoids in intestinal tight junction regulation. J Nutr Biochem. 2011 May;22(5):401-8. doi: 10.1016/j.jnutbio.2010.08.001. Epub 2010 Dec 16. PMID: 21167699.

36. Riemschneider S, Hoffmann M, Slanina U, Weber K, Hauschildt S, Lehmann J. Indol-3-Carbinol and Quercetin Ameliorate Chronic DSS-Induced Colitis in C57BL/6 Mice by AhR-Mediated Anti-Inflammatory Mechanisms. Int J Environ Res Public Health. 2021 Feb 25;18(5):2262. doi: 10.3390/ijerph18052262. PMID: 33668818; PMCID: PMC7956562.

37. Regmi S, Seo Y, Ahn JS, Pathak S, Acharya S, Nguyen TT, Yook S, Sung JH, Park JB, Kim JO, Young CS, Kim HS, Jeong JH. Heterospheroid formation improves therapeutic efficacy of mesenchymal stem cells in murine colitis through immunomodulation and epithelial regeneration. Biomaterials. 2021 Apr;271:120752. doi: 10.1016/j.biomaterials.2021.120752. Epub 2021 Mar 5. PMID: 33730631.

38. Damiano S, Sasso A, De Felice B, Di Gregorio I, La Rosa G, Lupoli GA, Belfiore A, Mondola P, Santillo M. Quercetin Increases MUC2 and MUC5AC Gene Expression and Secretion in Intestinal Goblet Cell-Like LS174T via PLC/PKCα/ERK1-2 Pathway. Front Physiol. 2018 Apr 6;9:357. doi: 10.3389/fphys.2018.00357. PMID: 29681865; PMCID: PMC5897515.

39. Ju S, Ge Y, Li P, Tian X, Wang H, Zheng X, Ju S. Dietary quercetin ameliorates experimental colitis in mouse by remodeling the function of colonic macrophages via a heme oxygenase-1-dependent pathway. Cell Cycle. 2018;17(1):53-63. doi: 10.1080/15384101.2017.1387701. Epub 2018 Jan 2. PMID: 28976231; PMCID: PMC5815442.

40. Ayati Z, Ramezani M, Amiri MS, Moghadam AT, Rahimi H, Abdollahzade A, Sahebkar A, Emami SA. Ethnobotany, Phytochemistry and Traditional Uses of Curcuma spp. and Pharmacological Profile of Two Important Species (C. longa and C. zedoaria): A Review. Curr Pharm Des. 2019;25(8):871-935. doi: 10.2174/1381612825666190402163940. PMID: 30947655

41. Esatbeyoglu T, Huebbe P, Ernst IM, Chin D, Wagner AE, Rimbach G. Curcumin--from molecule to biological function. Angew Chem Int Ed Engl. 2012 May 29;51(22):5308-32. doi: 10.1002/anie.201107724. Epub 2012 May 4. PMID: 22566109.

42. Feng W, Wang H, Zhang P, Gao C, Tao J, Ge Z, Zhu D, Bi Y. Modulation of gut microbiota contributes to curcumin-mediated attenuation of hepatic steatosis in rats. Biochim Biophys Acta Gen Subj. 2017 Jul;1861(7):1801-1812. doi: 10.1016/j.bbagen.2017.03.017. Epub 2017 Mar 21. PMID: 28341485.

43. Sun ZZ, Li XY, Wang S, Shen L, Ji HF. Bidirectional interactions between curcumin and gut microbiota in transgenic mice with Alzheimer's disease. Appl Microbiol Biotechnol. 2020 Apr;104(8):3507-3515. doi: 10.1007/s00253-020-10461-x. Epub 2020 Feb 24. PMID: 32095862.

44. Le Chatelier E, Nielsen T, Qin J, Prifti E, Hildebrand F, Falony G, Almeida M, Arumugam M, Batto JM, Kennedy S, Leonard P, Li J, Burgdorf K, Grarup N, Jørgensen T, Brandslund I, Nielsen HB, Juncker AS, Bertalan M, Levenez F, Pons N, Rasmussen S, Sunagawa S, Tap J, Tims S, Zoetendal EG, Brunak S, Clément K, Doré J, Kleerebezem M, Kristiansen K, Renault P, Sicheritz-Ponten T, de Vos WM, Zucker JD, Raes J, Hansen T; MetaHIT consortium; Bork P, Wang J, Ehrlich SD, Pedersen O. Richness of human gut microbiome correlates with metabolic markers. Nature. 2013 Aug 29;500(7464):541-6. doi: 10.1038/nature12506. PMID: 23985870.

45. McFadden RM, Larmonier CB, Shehab KW, Midura-Kiela M, Ramalingam R, Harrison CA, Besselsen DG, Chase JH, Caporaso JG, Jobin C, Ghishan FK, Kiela PR. The Role of Curcumin in Modulating Colonic Microbiota During Colitis and Colon Cancer Prevention. Inflamm Bowel Dis. 2015 Nov;21(11):2483-94. doi: 10.1097/MIB.0000000000000522. PMID: 26218141; PMCID: PMC4615313.

46. Shen L, Liu L, Ji HF. Regulative effects of curcumin spice administration on gut microbiota and its pharmacological implications. Food Nutr Res. 2017 Aug 9;61(1):1361780. doi: 10.1080/16546628.2017.1361780. PMID: 28814952; PMCID: PMC5553098.

47. Faralli A, Shekarforoush E, Ajalloueian F, Mendes AC, Chronakis IS. In vitro permeability enhancement of curcumin across Caco-2 cells monolayers using electrospun xanthan-chitosan nanofibers. Carbohydr Polym. 2019 Feb 15;206:38-47. doi: 10.1016/j.carbpol.2018.10.073. Epub 2018 Oct 29. PMID: 30553335.

48. Wang J, Ghosh SS, Ghosh S. Curcumin improves intestinal barrier function: modulation of intracellular signaling, and organization of tight junctions. Am J Physiol Cell Physiol. 2017 Apr 1;312(4):C438-C445. doi: 10.1152/ajpcell.00235.2016. Epub 2017 Mar 1. PMID: 28249988; PMCID: PMC5407015.

49. Hou HT, Qiu YM, Zhao HW, Li DH, Liu YT, Wang YZ, Su SH. [Effect of curcumin on intestinal mucosal mechanical barrier in rats with non-alcoholic fatty liver disease]. Zhonghua Gan Zang Bing Za Zhi. 2017 Feb 20;25(2):134-138. Chinese. doi: 10.3760/cma.j.issn.1007-3418.2017.02.011. PMID: 28297801.

50. Ghosh SS, Bie J, Wang J, Ghosh S. Oral supplementation with non-absorbable antibiotics or curcumin attenuates western diet-induced atherosclerosis and glucose intolerance in LDLR-/- mice--role of intestinal permeability and macrophage activation. PLoS One. 2014 Sep 24;9(9):e108577. doi: 10.1371/journal.pone.0108577. PMID: 25251395; PMCID: PMC4177397.

51. Tuin A, Poelstra K, de Jager-Krikken A, Bok L, Raaben W, Velders MP, Dijkstra G. Role of alkaline phosphatase in colitis in man and rats. Gut. 2009 Mar;58(3):379-87. doi: 10.1136/gut.2007.128868. Epub 2008 Oct 13. PMID: 18852260.

52. Kiffer-Moreira T, Sheen CR, Gasque KC, Bolean M, Ciancaglini P, van Elsas A, Hoylaerts MF, Millán JL. Catalytic signature of a heat-stable, chimeric human alkaline phosphatase with therapeutic potential. PLoS One. 2014 Feb 24;9(2):e89374. doi: 10.1371/journal.pone.0089374. PMID: 24586729; PMCID: PMC3933536.

53. Zhang Z, Chen Y, Xiang L, Wang Z, Xiao GG, Hu J. Effect of Curcumin on the Diversity of Gut Microbiota in Ovariectomized Rats. Nutrients. 2017 Oct 19;9(10):1146. doi: 10.3390/nu9101146. PMID: 29048369; PMCID: PMC5691762.

54. Kashyap D, Sharma A, Sak K, Tuli HS, Buttar HS, Bishayee A. Fisetin: A bioactive phytochemical with potential for cancer prevention and pharmacotherapy. Life Sci. 2018 Feb 1;194:75-87. doi: 10.1016/j.lfs.2017.12.005. Epub 2017 Dec 7. PMID: 29225112.

55. Chen TJ, Feng Y, Liu T, Wu TT, Chen YJ, Li X, Li Q, Wu YC. Fisetin Regulates Gut Microbiota and Exerts Neuroprotective Effect on Mouse Model of Parkinson's Disease. Front Neurosci. 2020 Dec 14;14:549037. doi: 10.3389/fnins.2020.549037. PMID: 33381005; PMCID: PMC7768012.

56. Lin A, Zheng W, He Y, Tang W, Wei X, He R, Huang W, Su Y, Huang Y, Zhou H, Xie H. Gut microbiota in patients with Parkinson's disease in southern China. Parkinsonism Relat Disord. 2018 Aug;53:82-88. doi: 10.1016/j.parkreldis.2018.05.007. PMID: 29776865.

57. Hill-Burns EM, Debelius JW, Morton JT, Wissemann WT, Lewis MR, Wallen ZD, Peddada SD, Factor SA, Molho E, Zabetian CP, Knight R, Payami H. Parkinson's disease and Parkinson's diseafse medications have distinct signatures of the gut microbiome. Mov

Disord. 2017 May;32(5):739-749. doi: 10.1002/mds.26942. Epub 2017 Feb 14. PMID: 28195358; PMCID: PMC5469442.

58. Srivastav S, Neupane S, Bhurtel S, Katila N, Maharjan S, Choi H, Hong JT, Choi DY. Probiotics mixture increases butyrate, and subsequently rescues the nigral dopaminergic neurons from MPTP and rotenone-induced neurotoxicity. J Nutr Biochem. 2019 Jul;69:73-86. doi: 10.1016/j.jnutbio.2019.03.021. Epub 2019 Apr 6. PMID: 31063918

59. Ren Q, Cheng L, Guo F, Tao S, Zhang C, Ma L, Fu P. Fisetin Improves Hyperuricemia-Induced Chronic Kidney Disease via Regulating Gut Microbiota-Mediated Tryptophan Metabolism and Aryl Hydrocarbon Receptor Activation. J Agric Food Chem. 2021 Sep 22;69(37):10932-10942. doi: 10.1021/acs.jafc.1c03449. Epub 2021 Sep 10. PMID: 34505780.

60. Liu JR, Miao H, Deng DQ, Vaziri ND, Li P, Zhao YY. Gut microbiota-derived tryptophan metabolism mediates renal fibrosis by aryl hydrocarbon receptor signaling activation. Cell Mol Life Sci. 2021 Feb;78(3):909-922. doi: 10.1007/s00018-020-03645-1. Epub 2020 Sep 23. PMID: 32965514; PMCID: PMC11073292.

61. Mou Y, Du Y, Zhou L, Yue J, Hu X, Liu Y, Chen S, Lin X, Zhang G, Xiao H, Dong B. Gut Microbiota Interact With the Brain Through Systemic Chronic Inflammation: Implications on Neuroinflammation, Neurodegeneration, and Aging. Front Immunol. 2022 Apr 7;13:796288. doi: 10.3389/fimmu.2022.796288. PMID: 35464431; PMCID: PMC9021448

62. Sochocka M, Donskow-Łysoniewska K, Diniz BS, Kurpas D, Brzozowska E, Leszek J. The Gut Microbiome Alterations and Inflammation-Driven Pathogenesis of Alzheimer's Disease-a Critical Review. Mol Neurobiol. 2019 Mar;56(3):1841-1851. doi: 10.1007/s12035-018-1188-4. Epub 2018 Jun 23. PMID: 29936690; PMCID: PMC6394610

63. Sip S, Rosiak N, Sip A, Żarowski M, Hojan K, Cielecka-Piontek J. A Fisetin Delivery System for Neuroprotection: A Co-Amorphous Dispersion Prepared in Supercritical Carbon Dioxide. Antioxidants (Basel). 2023 Dec 21;13(1):24. doi: 10.3390/antiox13010024. PMID: 38275644; PMCID: PMC10812833

64. Ashiqueali SA, Chaudhari D, Zhu X, Noureddine S, Siddiqi S, Garcia DN, Gostynska A, Stawny M, Rubis B, Zanini BM, Mansoor MAM, Schneider A, Naser SA, Yadav H, Masternak MM. Fisetin modulates the gut microbiota alongside biomarkers of senescence and inflammation in a DSS-induced murine model of colitis. Geroscience. 2024

Jun;46(3):3085-3103. doi: 10.1007/s11357-024-01060-z. Epub 2024 Jan 8. PMID: 38191834; PMCID: PMC11009197.

65. Stojanov S, Berlec A, Štrukelj B. The Influence of Probiotics on the Firmicutes/Bacteroidetes Ratio in the Treatment of Obesity and Inflammatory Bowel disease. Microorganisms. 2020 Nov 1;8(11):1715. doi: 10.3390/microorganisms8111715. PMID: 33139627; PMCID: PMC7692443.

66. Geerlings SY, Kostopoulos I, de Vos WM, Belzer C. Akkermansia muciniphila in the Human Gastrointestinal Tract: When, Where, and How? Microorganisms. 2018 Jul 23;6(3):75. doi: 10.3390/microorganisms6030075. PMID: 30041463; PMCID: PMC6163243.

67. Shidfar F, Ebrahimi SS, Hosseini S, Heydari I, Shidfar S, Hajhassani G. The Effects of Berberis vulgaris Fruit Extract on Serum Lipoproteins, apoB, apoA-I, Homocysteine, Glycemic Control and Total Antioxidant Capacity in Type 2 Diabetic Patients. Iran J Pharm Res. 2012 Spring;11(2):643-52. PMID: 24250489; PMCID: PMC3832145.

68. Imenshahidi M, Hosseinzadeh H. Berberine and barberry (Berberis vulgaris): A clinical review. Phytother Res. 2019 Mar;33(3):504-523. doi: 10.1002/ptr.6252. Epub 2019 Jan 13. PMID: 30637820.

69. Zhang X, Zhao Y, Zhang M, Pang X, Xu J, Kang C, Li M, Zhang C, Zhang Z, Zhang Y, Li X, Ning G, Zhao L. Structural changes of gut microbiota during berberine-mediated prevention of obesity and insulin resistance in high-fat diet-fed rats. PLoS One. 2012;7(8):e42529. doi: 10.1371/journal.pone.0042529. Epub 2012 Aug 3. PMID: 22880019; PMCID: PMC3411811.

70. Guo Y, Zhang Y, Huang W, Selwyn FP, Klaassen CD. Dose-response effect of berberine on bile acid profile and gut microbiota in mice. BMC Complement Altern Med. 2016 Oct 18;16(1):394. doi: 10.1186/s12906-016-1367-7. PMID: 27756364; PMCID: PMC5070223.

71. Wang Y, Shou JW, Li XY, Zhao ZX, Fu J, He CY, Feng R, Ma C, Wen BY, Guo F, Yang XY, Han YX, Wang LL, Tong Q, You XF, Lin Y, Kong WJ, Si SY, Jiang JD. Berberine-induced bioactive metabolites of the gut microbiota improve energy metabolism. Metabolism. 2017 May;70:72-84. doi: 10.1016/j.metabol.2017.02.003. Epub 2017 Feb 10. PMID: 28403947.

72. Vidrine K, Ye J, Martin RJ, McCutcheon KL, Raggio AM, Pelkman C, Durham HA, Zhou J, Senevirathne RN, Williams C, Greenway F, Finley J, Gao Z, Goldsmith F, Keenan MJ. Resistant starch from high amylose maize (HAM-RS2) and dietary butyrate reduce abdominal fat by a different apparent mechanism. Obesity (Silver Spring). 2014 Feb;22(2):344-8. doi: 10.1002/oby.20501. Epub 2013 Oct 15. PMID: 23630079.

73. Wu Y, He H, Cheng Z, Bai Y, Ma X. The Role of Neuropeptide Y and Peptide YY in the Development of Obesity via Gut-brain Axis. Curr Protein Pept Sci. 2019;20(7):750-758. doi: 10.2174/1389203720666190125105401. PMID: 30678628.

74. Chen Y, Hao Z, Zhao H, Duan X, Jia D, Li K, Yang Y, Cui H, Gao M, Zhao D. Berberine alleviates intestinal barrier dysfunction in glucolipid metabolism disorder hamsters by modulating gut microbiota and gut-microbiota-related tryptophan metabolites. J Sci Food Agric. 2023 Feb;103(3):1464-1473. doi: 10.1002/jsfa.12242. Epub 2022 Oct 10. PMID: 36168925.

75. Tang M, Yuan D, Liao P. Berberine improves intestinal barrier function and reduces inflammation, immunosuppression, and oxidative stress by regulating the NF-κB/MAPK signaling pathway in deoxynivalenol-challenged piglets. Environ Pollut. 2021 Nov 15;289:117865. doi: 10.1016/j.envpol.2021.117865. Epub 2021 Jul 31. PMID: 34358871.

76. Wei B, Xiao H, Xu B, Kuca K, Qin Z, Guo X, Wu W, Wu Q. Emesis to trichothecene deoxynivalenol and its congeners correspond to secretion of peptide YY and 5-HT. Food Chem Toxicol. 2023 Aug;178:113874. doi: 10.1016/j.fct.2023.113874. Epub 2023 Jun 5. PMID: 37286030.

77. Lange K, Buerger M, Stallmach A, Bruns T. Effects of Antibiotics on Gut Microbiota. Dig Dis. 2016;34(3):260-8. doi: 10.1159/000443360. Epub 2016 Mar 30. PMID: 27028893.

78. Molina-Torres G, Rodriguez-Arrastia M, Roman P, Sanchez-Labraca N, Cardona D. Stress and the gut microbiota-brain axis. Behav Pharmacol. 2019 Apr;30(2 and 3-Spec Issue):187-200. doi: 10.1097/FBP.0000000000000478. PMID: 30844962.

79. Campaniello D, Corbo MR, Sinigaglia M, Speranza B, Racioppo A, Altieri C, Bevilacqua A. How Diet and Physical Activity Modulate Gut Microbiota: Evidence, and Perspectives. Nutrients. 2022 Jun 14;14(12):2456. doi: 10.3390/nu14122456. PMID: 35745186; PMCID: PMC9227967.

80. Bibbò S, Ianiro G, Giorgio V, Scaldaferri F, Masucci L, Gasbarrini A, Cammarota G. The role of diet on gut microbiota composition. Eur Rev Med Pharmacol Sci. 2016 Nov;20(22):4742-4749. PMID: 27906427.

81. Ahmed H, Leyrolle Q, Koistinen V, Kärkkäinen O, Layé S, Delzenne N, Hanhineva K. Microbiota-derived metabolites as drivers of gut-brain communication. Gut Microbes. 2022 Jan-Dec;14(1):2102878. doi: 10.1080/19490976.2022.2102878. PMID: 35903003; PMCID: PMC9341364.

82. Rigi S, Mousavi SM, Shakeri F, Keshteli AH, Benisi-Kohansal S, Saadatnia M, Esmaillzadeh A. Dietary phytochemical index in relation to risk of stroke: a case-control study. Nutr Neurosci. 2022 Nov;25(11):2239-2246. doi: 10.1080/1028415X.2021.1954291. Epub 2021 Jul 26. PMID: 34311680.

83. Eslami O, Khoshgoo M, Shidfar F. Dietary phytochemical index and overweight/obesity in children: a cross-sectional study. BMC Res Notes. 2020 Mar 5;13(1):132. doi: 10.1186/s13104-020-04979-6. PMID: 32138761; PMCID: PMC7059655.

84. Ahmadi B, Ramezani Ahmadi A, Jafari M, Morshedzadeh N. The association of dietary phytochemical index and nonalcoholic fatty liver disease. Food Sci Nutr. 2023 May 3;11(7):4010-4019. doi: 10.1002/fsn3.3389. PMID: 37457157; PMCID: PMC10345673.

85. Acikgoz Pinar A, Yildiz E, Altundag K. Dietary Phytochemical Index and the Risk of Breast Cancer: A Case-Control Study. Nutr Cancer. 2023;75(2):482-487. doi: 10.1080/01635581.2022.2122518. Epub 2022 Sep 14. PMID: 36104945.