



Health benefits of a polyphenols-rich diet in patients with irritable bowel syndrome – a narrative review

Dieta bogata w polifenole – jakie korzyści może przynieść pacjentom z zespołem jelita nadwrażliwego? Przegląd narracyjny

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■ Abstract

Introduction and Objective. Irritable bowel syndrome (IBS) is a compound, functional disorder of the digestive system. It is characterized by abdominal pain and change of the rhythm of bowel movements. Despite many studies, the pathophysiological cause of IBS has not been found. Nevertheless, it is suspected that inflammatory processes can play a huge part in the development of the disease. Currently, there is no effective treatment which could cure IBS. Many methods, including change in diet are recommended to IBS patients to help decrease the symptoms. Polyphenols which can be found, among others, in green tea, turmeric and red wine, show anti-inflammatory and anti-cancer action, prebiotic properties and immunomodulate action. Benefits from their use are seen in many different diseases. The aim of the review was to find articles published in 2004–2022 concerning the influence of a polyphenols rich diet on IBS symptoms.

Review Methods. A systemic review was carried out according to the PRISMA protocol (Preferred Reporting Items for Systemic Reviews and Meta-Analysis). Databases such as *Pubmed* and *Scopus* were screened systematically. Of the 72 articles found, 50 articles were left after the removal of duplicates. Finally, 7 studies were included in the review.

Brief description of the state of knowledge. Currently, there is no single factor which could be defined as the cause of IBS; therefore, IBS is considered a multifactorial disease. Researchers postulate many possible reasons: dysbiosis, gut-brain axis disorders or gastrointestinal barrier dysfunction. Possible treatments include low FODMAP diet or the Mediterranean diet. Some studies have shown the beneficial influence of a polyphenols rich diet.

Summary. On the basis of the screened articles, the conclusion may be drawn that a polyphenols rich diet can be beneficial for IBS patients. However, due to the small amount of data, further studies are needed to clearly recommend a polyphenols rich diet as an additional treatment in IBS.

■ Key words

Resveratrol, Polyphenols, Irritable Bowel Syndrome

■ Streszczenie

Wprowadzenie i cel pracy. Zespół jelita nadwrażliwego (IBS) jest złożonym, funkcjonalnym zaburzeniem układu pokarmowego. Mimo licznych przeprowadzanych badań nie udało się dotąd określić patofizjologicznej przyczyny zespołu. Niemniej jednak podejrzewa się, iż jedną z głównych przyczyn rozwoju choroby są procesy zapalne. Obecnie nie istnieje terapia, która pozwoliłaby na wyleczenie IBS; jednym z głównych zaleceń dla chorego jest zmiana stylu życia (w tym diety). Polifenole to związki występujące np. w herbacie, kurkumie czy też czerwonym winie. Wykazują one aktywność przeciwzapalną, przeciwnowotworową, immunomodulującą oraz są prebiotykami. W wielu chorobach odnotowano znaczne korzyści z ich stosowania.

Metody przeglądu. Przeszukano bazy danych Pubmed i Scopus. Odnaleziono 72 artykułów naukowych, przeczytano abstrakty 50 prac, które pozostały po usunięciu duplikatów. Finalnie do przeglądu włączono 7 prac.

Opis stanu wiedzy. Naukowcy wskazują na wiele możliwych przyczyn IBS, takich jak dysbioza, zaburzenia osi mózg–jelita, dysfunkcja bariery jelitowej etc. Leczenie polega głównie na zmianie stylu życia pacjenta, w tym zmianie diety. Polecane diety w IBS obejmują np. dietę low FODMAP czy też dietę śródziemnomorską. Niektóre badania pokazują, że dieta bogata w polifenole także mogłaby przynieść znaczne korzyści osobom chorującym na IBS.

Podsumowanie. Biorąc pod uwagę korzyści zdrowotne płynące ze zmiany diety na dietę bogatą w polifenole, takie jak: zmniejszenie ilości szkodliwych bakterii jelitowych, działanie antybakteryjne etc., autorzy pracy doszli do wniosku, iż dieta bogata w polifenole może być rozważona u pacjentów z IBS jako terapia dodatkowa. Ponieważ niewiele jest danych na ten temat, niezbędne jest przeprowadzenie kolejnych badań w celu potwierdzenia tej tezy.

■ Słowa kluczowe

resveratrol, polifenole, zespół jelita drażliwego

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INTRODUCTION

IBS is compound, functional disorder of the digestive system, characterized by chronic abdominal pain and uncomfortable change in the rhythm of bowel movements. Despite many studies, no pathophysiological cause of IBS has been found. Nevertheless, it is suspected that inflammatory processes can play a large part in the development of the disease, which is partially confirmed by the fact that IBS appears just after infection in some patients. Other factors which can lead to IBS development include mast cells increase, changes in microbiota, and dysfunction of the gut-brains axis [1]. According to the Rome IV Diagnosis Criteria for Irritable Bowel Syndrome, patients who have had recurrent abdominal pain on average for at least one day per week during the previous three months which are associated with two or more of the following: related to defecation (may be increased or unchanged by defecation), change in stool frequency, change in stool form (appearance) [2]. However, there is no test to definitively diagnose IBS. Nevertheless, procedures such as colonoscopy, CT scan or upper endoscopy are helpful in eliminating different causes of symptoms. Recommended laboratory tests among patients with IBS include lactose intolerance test, breath test for bacterial overgrowth and stool test [3]. Currently, although as much as 11% of the population worldwide are suffering from IBS, there is no effective treatment which could cure the disease. The holistic approach towards the IBS patients is significant and accounts for many different recommended methods which can help decrease the symptoms, and include physical activity, low FODMAP diet, the Mediterranean diet, use of probiotics, or physical activity, including practicing yoga [4]. Psychobiotics therapy has also been shown to decrease depression in patients with chronic gastrointestinal symptoms [5]. Based on the symptoms, medications may be also recommended, including: fibre supplements, laxatives, anti-diarrheal medications, anticholinergic medications, tricyclic/ SSRI anti-depressants and pain relief medications. There are also drugs approved specifically for IBS patients, such as: alosetron, eluxadoline, rifaximin, lubiprostone and linaclotide [3].

One of the main factors which could trigger IBS symptoms is wrong diet. However, the principles of nutrition cannot be unequivocally defined since there is a large variability of sensitivity to certain products among individuals with IBS. Proper diet is very important in IBS which is the reason for the many studies being conducted with the aim of assessing the optimum method of providing nutrition for these patients. In this respect, polyphenols are considered to be such highly essential functional foods in the diet. The three main families of polyphenols include: lignans, stilbenes, and phenolic acids. Currently, several studies are being conducted to properly evaluate their health consequences. Polyphenols serve a vital function in the protection of the organism from external stimuli and in eliminating reactive oxygen species (ROS), which are instigators of several illnesses [6].

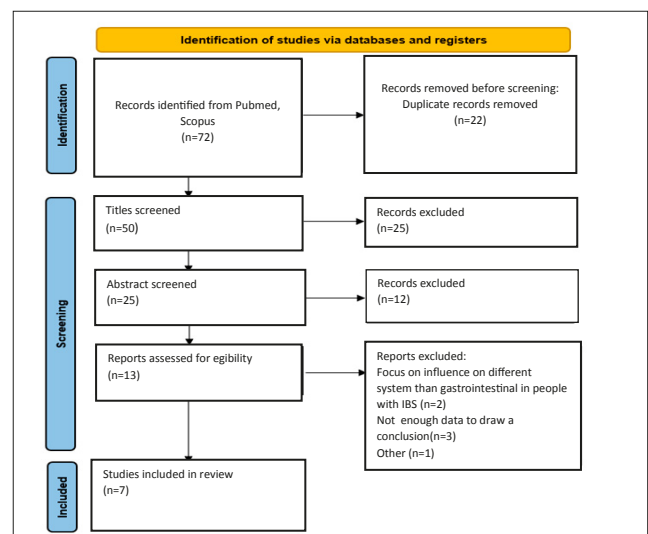
Resveratrol is one of the polyphenols – organic compounds which show many biological functions, and can be found, among others, in green tea or turmeric. Research has shown that people who consume large amounts of polyphenols products have a decrease in harmful microbiota, such as clostridium spp, and an increase in such good microbiota as bifidobacterium and lactobactillus, compared to people who do not consume these products. [7]. Polyphenols also

have anti-inflammatory and anti-cancer action, prebiotic properties and immunomodulate action, and the benefits from their use have been observed in such diseases as Crohn's disease – a chronic inflammation of the digestive tract, colitis ulcerosa (ulcerative colitis) – inflammation and ulceration of the colon and rectum, and irritable bowel syndrome [8].

OBJECTIVE

The aim of thereview was to revise views on the role of polyphenols in IBS

MATERIALS AND METHOD



Reports excluded:
Focus on the influence of systems other than gastro-intestinal in people with IBS (n=2).
Insufficient data to draw a Conclusion (n=3).
Other (n=1).

A systemic review was conducted in databases such as *Pubmed* and *Scopus* according to the

PRISMA protocol with the aim of finding articles published in 2004–2022 concerning the influence of polyphenols-rich diet on IBS symptoms. A total of 72 studies were found, of which 50 were left after the removal of duplicates. Finally, seven studies were selected for inclusion in the review.

RESULTS

Resveratrol can affect intestinal response on stressogenic factors. Resveratrol is a polyphenolic nutraceutical that exhibits pleiotropic activities in human subjects. It is reported that this compound can potentially improve the therapeutic outcome in patients suffering from many different conditions, including diabetes mellitus, obesity, colorectal cancer, etc. [6]. Some studies show that resveratrol can also be beneficial in IBS. Currently, many supplements are available which contain resveratrol in different doses. Although the majority

contain up to 100mg/capsule, even higher doses of 5 g/day of resveratrol are strongly encouraged and considered to be safe for one month, and are well tolerated [9].

In one of the studies analyzed for this review, three groups of mice were tested, two of which were subjected to chronic-acute combined stress (CACS) for the duration of 19 days. Three weeks before commencement of the experiment, one of them was additionally supplemented with resveratrol. The remaining group was neither exposed to any stress factor nor administered with resveratrol. In behavioural tests conducted on day 20 in mice exposed to stressors, they showed a significant decrease in the sucrose preference test. This did not occur in the other two groups of mice, nor in the mice treated with resveratrol before exposition, nor in the mice which did not undergo CACS (chronic-acute combined stress). This indicates the possible antidepressant action of resveratrol.

On day 22, the Abdominal Withdrawal Reflex (AWR) test was conducted. A disposable silicon balloon was inserted into the rectum of each mouse. After the mice had recovered from the anaesthetic and acclimatised for at least 30 minutes, the AWR test was conducted. The AWR score was assigned as follows: 0 = no behavioural response to distension, 1 = brief head movements followed by immobility, 2 = contraction of abdominal muscle without lifting of the abdomen, 3 = lifting of abdomen, 4 = body arching and lifting of pelvic structure. There were no significant differences in catheter distention up to 0.25 ml between groups in the AWR test. However, in 0.35ml, 0.50ml and 0.65 distention in the mice not exposed to stress, and those which underwent resveratrol treatment, a significant decrease in AWR score was noted, compared to CACS exposed non-resveratrol group.

On day 23, the Intestinal Motility Assay (IMA) was carried out. The mice were administered with a blue-labeled 10% dextrose solution by gavage. 30 minutes after injection of the blue dye the mice were euthanized. The ratio of the dye migration distance/total intestinal length was calculated. In the previously resveratrol treated group and non-stress exposed mice the ratio was significantly higher, compared to the mice which did not receive resveratrol and were exposed to stress factors.

The conclusion that can be drawn from the study is that resveratrol can help retain proper intestinal motility despite long-term exposure to stressogenic circumstances, and can also be effective as an antidepressant [10].

The gut-brain axis relies on intestinal function monitoring and connecting the emotional brain centrum (cortex and hippocampus) with intestinal function as motility. The most recent research shows that visceral hypersensitivity can influence the central nervous system and lead to anxiety and depression – which acts like a vicious circle worsening the visceral hypersensitivity and intestinal motility dysfunction. In the experiment, the rats were exposed to chronic-acute combined stress (CACS) for the duration of 22 days with the aim of inducing depression/anxiety behaviours, motility dysfunction and visceral hypersensitivity. The mice were divided into two groups with Group 1 administered with resveratrol 50 minutes before each CACS. Behavioural tests were conducted on days 23–26; the results were as follows: rats exposed to CACS with no resveratrol treatment showed less mobility in the forced swimming test, a twice as big increase in the amount of faecal output (which were used as an indirect measure of intestinal tract motility), and a significant

increase in Abdominal Withdrawal Reflex Test (AWR). This outcome was not observed in mice treated with resveratrol nor in the group which did not undergo CACS. These results may indicate the antidepressant effect of resveratrol, and shows that it can also work protectively against motility dysfunction and visceral hypersensitivity which can occur as results of stress exposure in IBS patients [11].

Trans-Resveratrol can probably affect CACS-induced IBS-like symptoms, including depression, anxiety and intestinal dysfunction. Low doses of antidepressant drugs are being used currently in IBS treatment, and it is therefore postulated that replacing them with resveratrol could be as beneficial or even more so for IBS patients.

Substances rich in polyphenols – olive oil. In traditional medicine the olive tree has been identified as a source of several botanical drugs. In addition to the fruit (olive), the leaves and by-products of the milling of olives also contain, specifically, phenolic derivatives, such as phenolic acids, phenolic alcohols (hydroxytyrosol), flavonoids, and secoiridoids (oleuropein). Recent studies have shown that olive leaf extract has anti-inflammatory properties and the extract also shows a spasmolytic effect on the ileum and proximal colitis. Due to the content of a high dose of polyphenols, it is considered that this extract can restore the integrity of the intestinal barrier and reduce the level of pro-inflammatory cytokines. This hypothesis was proved in experiments conducted on guinea pigs *ex vivo*. Cumulative concentration-response curves of extracts were constructed using Papaverine as the positive control. Depending on the type of polyphenols-rich product, there was spasmolytic effect which occurred either in the ileum and colitis, or only in the ileum. Therefore, the use of olive seems to be beneficial and should be considered as a possible treatment of IBS [12].

Acacia catechu, Camellia sinensis. In another study, the impact of a polyphenols-rich diet on signal pathways and cytokines were analyzed. The researchers focused on such polyphenols-rich substances as Acacia catechu and Camellia sinensis, which produce the relaxing effect of acacia on the ileum and colitis. Acacia extract can also reduce the tension of colitis and acts as an antibacterial agent against *C. jejuni*, *E.coli* and *Salmonella* Spp. While Camellia sinensis shows an antioxidant function and has an influence on the transcription of inflammatory-response genes, this in turn can decrease the inflammatory process. Olea europaea polyphenols-rich substances have direct contact with the gastric and intestinal mucosa, allowing a direct cellular exposure [13].

Turmeric. Turmeric is another polyphenols-rich substance which causes the inhibition of mast cell degranulation and a decrease in TNF α , IL-4 secretion. Mast cells are one of the main reasons for inflammatory reaction. Activated cells release such substances as histamine, heparin, and a nerve growth factor. A significant increase in mast cells has been observed in IBS patients; therefore, it is suspected that these cells can play a large part in the pathophysiological mechanism which leads to IBS development. [14]. Clinical studies have shown that curcumin is safe at doses of 12 g/day, but exhibits poor systemic bioavailability. Nevertheless, it can be enhanced by the addition of an adjuvant, such as piperine [24].

In a trial in which 500 volunteers with IBS participated and lasted for eight weeks, the participants were given 72 or 144 mg of turmeric daily. Reduction of IBS symptoms was observed in both groups. [15]. There are many products available on the market that contain different doses of turmeric in the form of pills, capsules, or even turmeric tea. One of the conducted studies shows that 500mg/day of turmeric was associated with greater improvements in digestive complaints and anxiety levels in adults with self-reported digestive complaints [16]. Summing-up, polyphenols work as mast cell regulators and can lead to a reduction in IBS symptoms and consequently improve the quality of a patient's life. The potential beneficial effects of turmeric use in IBS patients lead to the conclusion that turmeric supplements could be considered as an additional treatment.

Can polyphenols replace probiotics in IBS treatment?

Irritable bowel syndrome is a frequent functional gastrointestinal disorder, and alterations in the gut microbiota composition contributes to generation of the symptom. The exact mechanisms of probiotics in the human body are not fully understood, but probiotic supplements are thought to improve IBS symptoms through manipulation of the gut microbiota [17]. The most effective probiotics for IBS seem to be those containing *Bifidobacterium infantis* and other strains of bifida bacteria. Other common probiotic strains, such as *acidophilus* and *lactobilli*, have shown to be less effective in the treatment of symptoms, although they may still help in some cases[18].

The majority of human microbiota are represented by such bacteria as Firmicutes and Bacterioides. These microbes can produce Short-Chain Fatty Acids (SCFA) which affect metabolic processes, such as, among others, lipogenesis, gluconeogenesis and the synthesis of proteins. They also show the ability to conduct detoxifying processes. Recent studies proved that polyphenols can act as prebiotics causing an increase in *Bifidobacterium* and *Lactobacillus*, good intestinal microbiota. They can also decrease the population of harmful intestinal bacteria. There are many factors which can contribute to the disturbance of microbiota: environmental, including diet, pollution and stress. Dysbiosis can secondarily lead to leaky gut syndrome, malabsorption, and intestinal metabolism disorders, disturbances which contribute to an increase in oxidative stress, and hence a higher level of free radicals which increase inflammatory processes. Ultimately, the effect of such disturbances as gastrointestinal diseases as gastritis, gastric cancer, inflammatory bowel diseases and irritable bowel syndrome, can occur. Because of polyphenols anti-inflammatory, anti-cancer and immunomodulate potentials they seem to be suitable substances for use against disturbances of the gastrointestinal system.

DISCUSSION

Undoubtedly a rich diet can bring many health benefits, not only for people struggling with IBS. Some studies show that olive oil, due to its high polyphenols content, exerts favourable effects on free radicals, gut microbiota, and carcinogenesis. The interaction between gut microbiota and

olive oil consumption could modulate colonic microbial composition or activity, with a possible role in cancer prevention[19]. Moreover, olive oil shows beneficial effects on cardiometabolic markers of health and act as neuroprotective agents through their anti-inflammatory and antioxidant activities[20]. Recent research shows that olive oil used as a primary source of fat can also be beneficial for patients struggling with non-alcoholic fatty liver disease (NAFLD), also known as non-alcoholic steatohepatitis (NASH) [21]. A high consumption of olive oil instead of different fats can also cause a decrease in the plasmatic levels of LDL-cholesterol, and an increase in HDL-cholesterol[22]

Turmeric consumption, because of its anti-inflammatory, antioxidant, antiapoptotic, antitumour, and antimetastatic activities, can bring many health benefits [23]. The results of one trial show that the participants who were supplemented with curcumin displayed reduced inflammation and oxidative stress, decreased pain and muscle damage, superior recovery and muscle performance, as well as better psychological and physiological responses [24]. Moreover, it is probable that curcumin can exert direct regulative effects, especially in the gastrointestinal tract; consequently, it might be hypothesized that curcumin directly exerts its regulatory effects on the gut microbiota [25].

Acacia catechu possesses a comprehensive variety of medicinal potentials, such as antimicrobial, anti-diarrheal, antinociceptive, anti-hyperlipidemic, anti-ulcer, antioxidant, anti-diabetic, anti-proliferative, haemolytic, and anti-inflammatory properties, due to the presence of bioactive compounds like polyphenols [26]

Camelia sinesis is known for its anticancer and anti-inflammatory properties [27], but there are still ongoing studies to unequivocally prove that theory.

SUMMARY

A large part of the human population (11%) suffering from irritable bowel syndrome [4]. As the cause of this disease is multi-factorial there is a need to find a therapy which can work against not only one, but many factors involved in IBS development. In this case, polyphenols are really promising because they can lead to a decrease in harmful intestinal bacteria, and increase the population of good intestinal bacteria. Polyphenols also act as anti-inflammatory substances, and can lead to a decrease in mast cells which are suspected to be one of the major causes of IBS. Resveratrol and different polyphenols contained in products such as turmeric can help reduce the symptoms of IBS and intestinal motility disorders or visceral sensitivity which often occur due to stressful situations.

CONCLUSIONS

On the basis of the screened articles, the conclusion can be drawn that a polyphenols-rich diet can be beneficial for IBS patients. However, due to the small amount of data, further studies are needed to clearly determine the recommendation of a polyphenols-rich diet as an additional treatment in Irritable Bowel Syndrome.

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