

## REVIEW ARTICLE

# Review of Constipation Treatment Methods with Emphasis on Laxative Foods

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**Abstract: Background:** Constipation is a common public health concern experienced by all individuals during their life affecting the quality of life. In this paper, we aimed to provide an overview of the existing evidence regarding the role of food ingredients, including bran, prune, fig, kiwifruit, and flax-seed in constipation treatment.

**Scope and Approach:** We searched Scopus, Pub Med, and Science Direct by using the keywords, “laxative foods” and “constipation”, for searching studies assessing laxative food ingredients and their beneficial effects on constipation treatment and/or control.

**Key Finding and Conclusion:** Lifestyle modifications such as increasing dietary fiber and fluid intake and daily exercise are the proposed first line treatments for constipation. Optimizing ‘diet’ as an efficient lifestyle factor may contribute to the well-being of patients. The use of laxative food ingredients including bran, prune, fig, kiwifruit, flax-seed, probiotics, and prebiotics is a convenient alternative to cope with constipation. According to previous findings, laxative food ingredients could be considered as effective treatments for subjects suffering from constipation. Many studies have assessed the pharmacological and non-pharmacological roles of these ingredients in treating constipation, however, their importance has not been thoroughly investigated.

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## 1. INTRODUCTION

According to the ROME III criteria [1], constipation is diagnosed when at least 2 of the following items are included: straining during defecation, lumpy or hard stools, a sensation of incomplete evacuation or anorectal obstruction, manual maneuvers to facilitate defecation, and/or less than three defecations per week [2]. Generally, constipation is defined as the infrequent or difficult passage of stool and is the most prevalent functional gastrointestinal disorder [3].

Constipation dramatically affects health-related quality of life due to a wide range of signs and symptoms including discomfort, restlessness, vomiting, abdominal distension, gut obstruction and perforation. An association between constipation and fatal pulmonary embolism has also been reported [3-6]. Pulmonary embolization results from the performance of the Valsalva maneuver and its effects on peripheral blood flow and intrathoracic pressures, contributing to constipation [7]. The frequency rate of constipation is crucial. However, a prevalence of 50% has been reported among adults [8]. In the British population, the prevalence of constipation was reported between 2%-51.5% [9-12]. In Western societies, the prevalence of functional constipation among the elderly population was reported to be about 24%, which was more common among women [13]. Chronic functional constipation is affected by demographic characteristics (age and gen-

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der), physical activity, dietary habits, psychosocial and behavioral factors, and socioeconomic status [14]. Additionally, it may be primary or secondary to other medical problems such as endocrine and metabolic disorders, myopathic, psychological conditions and structural abnormalities of the intestinal tract. For instance, individuals with neurological disorders are at higher risk for constipation with a prevalence of 27-62% [15, 16].

Treatment of constipation still remains a clinical challenge. In a recent study on over 5000 patients receiving medications for constipation, about 50% of them were dissatisfied with their current therapy [17]. On the other hand, only about one-third of constipated patients seek medical care and many of them self-treat their symptoms either by increasing their fiber intake or by using over-the-counter (OTC) laxatives [2, 18]. Initial therapeutic measures in disease management include recommendations for modifying lifestyle such as adequate fluid intake and non-strenuous exercise, increasing natural fiber intake, and sparing time for bowel movements (BMs) [19]. However, evidence supporting these measures is rather weak [20]. There are several traditional therapeutic methods for constipation including bulking agents (psyllium), stool softeners (apricots, peaches, plums, grapes, prunes), stimulant laxatives (senna), osmotic laxatives (foods high in fiber), *etc.* [21, 22]. However, it should be kept in mind that repeated administration of purgative medicines may result in diarrhea, enteritis, colorectal dysfunction, and may also be considered as a risk factor for colorectal neoplasm [23]. In mild functional constipation, general treatment measures such as increased intake of water and dietary fiber, and the use of simple laxatives have been suggested. A diet with enough fiber (20-35 g each day) helps form a soft and bulky stool. Sufficient dietary fiber is also needed to promote normality in bowel movement frequency over the long term [24]. Colonic transit has been shown to be related to stool weight and dietary fiber intake [24]. However, to the best of our knowledge, there are only few studies assessing dietary fiber intake by patients with chronic constipation [24]. Thus, the present study was conducted with the aim of reviewing laxative food ingredients used for treating and/or controlling constipation.

## 2. METHODS

A comprehensive literature review was conducted with the use of the Scopus, PubMed, and Science Direct scientific databases, without the limit of the year of publication. Key search words included laxative food ingredients, bran, prune, fig, kiwifruit, flax-seed, probiotics, prebiotics, and constipation treatment. Published clinical studies were identified and reviewed for summarizing their findings in the present paper. The reference section of each identified publication was also searched for any studies that might have been missed in the database search.

## 3. FINDINGS

### 3.1. Classification of Constipation

According to the pathophysiology of constipation, it can be divided into three groups: slow transit (ST), normal-

transit (NT) or obstructed defecation (OD) constipation. Paré *et al.* (2007) in a study on North American population reported that 59%, 13%, and 25% of patients suffered from NT, ST and OD forms of constipation, respectively. Additionally, 3% of them had a mixed ST/OD condition [16]. Likewise, in a study on Thai population, the prevalence of NT, ST and OD conditions was reported to be 47%, 13%, 29%, respectively, along with 11% with a mixed ST/OD condition [25]. However, this classification has some overlaps and on the other hand, constipation may be associated with Irritable Bowel Syndrome (IBS). In general, there is about a 50% overlap between IBS and ST constipation. Furthermore, it has been shown that 10% to 13% overlap exists between ST and OD forms of constipation [26].

#### 3.1.1. Slow Transit Constipation

There are some pieces of evidence on the possibility that ST constipation may be due to global motor abnormality. Abnormalities in the ST form of constipation are not limited to the colon and rectum but motility changes in the stomach and jejunum have also been documented. Scott *et al.* (2003) reported evidence of jejunal motility disorders in about one-third of patients with the ST condition [27]. Delayed gastric emptying and abnormal gastric accommodation have also been reported by other authors [28-30]. A loss of coordination between contractile activity in the rectum and sigmoid colon as well as reduced rectal sensory threshold have been implicated in ST constipation [30-33]. In fact, ST constipation is more prevalent in young women who have less bowel movement [34]. In these patients, a high-fiber diet may increase stool weight, decrease colon-transit time, and eventually relieve constipation. Patients with severe ST conditions show poor response to dietary fiber and laxatives [34-39].

#### 3.1.2. Normal-Transit Constipation

Normal-Transit or functional constipation is the most prevalent form of constipation. In patients with this form of illness, stool transition and frequency are normal [40]. These patients feel difficulty in defecation or hard stools. Furthermore, patients may experience bloated and abdominal cramping and pain as well as psychological distress [40], and some of them may have reduced rectal sensation [41]. Dietary fiber alone or in combination with osmotic laxatives could relieve the symptoms of this type of constipation [39]. Failure to respond to these interventions suggests an impaired disturbance of evacuation or transit. However, this condition needs further management [42].

#### 3.1.3. Obstructed Defecation

This syndrome is relatively common, which is characterized by a difficult and often painful evacuation, a sense of incomplete evacuation, perineal support or finger insertion into the vagina or anus to defecate, frequent enemas, and laxative abuse. Half of the constipated patients suffer from OD, occurring more frequently in females (II). The pathophysiology of OD is poorly understood. Recent studies have suggested that this syndrome develops because of multiple and/or difficult labors and is the cause of obstruction. It may result from rectoanal intussusception, rectocele, pelvic organ

prolapse, enterocele, sigmoidocele, or solitary rectal ulcer syndrome. Furthermore, rectal hyposensitivity (blunted rectum), idiopathic megarectum, hereditary internal sphincter myopathy and nutcracker anus are the rare causes of OD [43, 44]. Osmotic agents are useful for patients who suffer from OD and in whom first-line bulk-forming agents or stool softeners do not work. Some recent evidence suggested that low dosage of polyethylene glycol (PEG), lactulose, and sorbitol as osmotic agents enhances stool passage in these patients [45, 46].

### 3.2. Defecation Disorders

Defecation disorders are common due to the dysfunction of the pelvic floor or anal sphincter. Some other terms used to describe defecation disorders include anismus, pelvic-floor dyssynergia, obstructed constipation and functional fecal retention in childhood [36]. Behavioral issues such as sexual abuse play an important role in this type of constipation [47], as well as conscious frequent suppression and postponement of the urge to defecate [37].

### 3.3. Pregnancy Constipation

As mentioned before, constipation could be experienced at all periods of life such as childhood, adulthood or old age. Constipation is also a common problem among pregnant women.

About 11-38% of pregnant women suffer from constipation, especially in the third trimester. Physiologic and anatomic changes in the gastrointestinal tract predispose pregnant women to develop constipation. Continuously rising progesterone and estrogen concentration and reduction in the motilin hormone level have been suggested as the causes of constipation during pregnancy [48, 49]. Also, water absorption increases in the intestine, which causes the stool to dry out. Low fluid and fiber intake, decreased maternal activity, and increased vitamin supplementation (e.g. iron and calcium) may also be the contributing factors [48, 49].

### 3.4. Treatment of Constipation

Chronic constipation is a hard-to-treat condition, thus prevention is considered as the best solution [50]. There is a wide range of treatment measures. Pharmacological (over-the-counter) laxatives are the most common treatments for constipation. However, these drugs are not ideal for clinical practice due to their potential adverse side effects [51] and thus, patients should be informed of their side effects. Therefore, alternative treatment measures are required. Although there is limited data on the effectiveness of lifestyle and behavioral modification, it could be considered as the recommended first-line treatment [52]. Increasing fiber intake through dietary or medicinal intervention (laxative foods) has been well accepted as a method of choice in modality treatment in order to relieve symptoms, especially complaints of infrequent or hard stools [51].

#### 3.4.1. Lifestyle and Dietary Modification

The gentlest remedies for constipation include increased physical activities, certain yoga postures, an increase of fluid

intake and dietary changes including increased fiber and fruit intake. The adequate intake (AI) values of 21 and 38 g/d were established for women and men 19 years or older [53]. It is well known that fibers have an important role in the occurrence and development of constipation, however, the total dietary fiber intake in adults appears to be much less than the AI levels [54]. Therefore, although some drugs and other modalities (e.g. biofeedback, surgery) have been used to treat constipation, intake of sufficient amount of dietary fibers is still a cornerstone in the prevention and treatment of this disorder [55].

#### 3.4.2. Pharmacological Treatments

##### 3.4.2.1. Bulking Laxatives

These organic polysaccharides are effective in the treatment of constipation via retaining fluid in the stool and increasing stool weight and consistency [16, 18, 56, 57]. Examples of organic polysaccharides are bran, psyllium (natural agents), methylcellulose and calcium polycarbophil (synthetic agents). Fiber has no major adverse effects and is usually well tolerated. However, flatulence, abdominal bloating, pain and stool impaction are reported as the side-effects of such treatments [58, 59].

##### 3.4.2.2. Stool Softeners

Stool softeners mainly act as detergents and lubricate stool by enhancing interaction between water and solid stool, thereby these agents lead to soft and consistent stool and ease evacuation of hard stool. This category involves docusate sodium and docusate calcium. There is insufficient data to support their effectiveness on chronic constipation [58, 60].

##### 3.4.2.3. Osmotic Laxatives

Lactulose, PEG, sorbitol, Magnesium hydroxide (milk of magnesia), and magnesium citrate have been considered as osmotic agents. Poorly absorbed ions or molecules draw water into the lumen and therefore cause softer stool and ease clone propulsion [61]. Abdominal cramping, bloating, and flatulence may be the side effects of these agents but seldom they lead to electrolyte imbalance [50]. In recent years, several new pharmacological classes have appeared or have been studied for the treatment of chronic constipation such as 5-HT<sub>4</sub> receptor agonists, colonic secretagogues and opioid antagonists [62].

##### 3.4.2.4. HT<sub>4</sub> Receptor Agonists

Serotonin (5-hydroxytryptamine, 5-HT) regulates gastrointestinal motility and sensitivity and also secretion through the activation of the 5-HT receptor located in the gastrointestinal enteric nervous system [62, 63]. Cisapride and Tegaserod are used in the treatment of constipation but these drugs increase the risk of cardiovascular events and subsequently have been withdrawn from the market [62]. Prucalopride, a full 5-HT<sub>4</sub> receptor agonist from the benzofuran carboxamide chemical class (a), improves colonic transit in humans [64, 65]. The data of a majority of clinical trials do not indicate any significant cardiovascular toxicities of Prucalopride

[66]. A number of other 5-HT<sub>4</sub> agonists such as velusetrag (TD-5108) and naronapride (ATI-7505) are under consideration. These drugs enhance transit time [67].

#### ***3.4.2.5. Colonic Secretagogues***

Lubiprostone is one of the novel therapies identified as an effective agent in the management of chronic constipation by promoting the secretion of intestinal fluid, but few patients have claimed nausea during treatment [68, 69]. Another new drug presented in the market is Linaclotide which acts as a luminal guanylin receptor and enhances intestinal chloride and fluid secretion [70].

#### ***3.4.2.6. Opioid Antagonists***

In order to treat opiate-induced constipation, a number of opioid antagonists are recently being investigated. Since these agents do not cross the blood-brain barrier, they have been used for reducing peripheral adverse effects of opioids such as constipation, nausea and vomiting without any interruption with analgesic efficacy. A meta-analysis assesses the efficacy of methylnaltrexone and alvimopan, while there is

not enough evidence for other antagonists such as naloxone and nalbuphine [71]. However, the use of opioid antagonists in non-opiate-induced constipation treatment protocols has not been completely assessed [72].

#### ***3.4.3. Laxative Foods***

As mentioned above, most patients do not consider the order of treatment according to the guidelines and immediately use OTC laxatives and other related medicines without trying natural laxatives present in food ingredients like fruit, dried fruit, seeds, etc. Since medications have shown some side effects and usually patients are not satisfied with their treatments, food-based, natural alternatives are needed to substitute the current on the market OTC laxatives and fiber supplements as the first line treatment. Several studies have been conducted to evaluate the effect of laxative food ingredients on constipation treatment (Table 1). Some foods such as prunes, pears, figs, kiwifruit, bran cereals, flax-seed, and other fiber-rich agents produce bulky stool and help in frequent intestinal movements and contractions and consequently result in the prevention and treatment of constipation [15].

**Table 1. Selected publications on Laxative food ingredients for constipation prevention and treatment.**

Food Ingredients	Dose	Period	Health Condition	Effect	Ref.
Wheat bran	10g	4 wk	Elderly patients	Improved stool weight and consistency and reduced the number of days without stools compared with control phase	[113]
Disivit™ (mixed of oats, corn, wheat and soybean)	12.5g dietary fiber	2 wk	Constipated patients	Improved bowel movement frequency and stool consistency and reduced laxative intake compared with basal phase	[137]
Wheat bran	21g	2 wk	Patients with irritable bowel syndrome constipation	Improved stool frequency, consistency and abdominal pain compared with basal phase but abdominal distension increased	[138]
Bran	20g/d	4 wk	Patients with chronic constipation	Intestinal transit time decreased and bowel frequency and stool weight increased in comparison to their two-week basal period	[139]
Bran	20g/d	4 day	Orthopedic surgical patients	Bowel movement increased and incidence of constipation reduced compared with control group	[140]
Wheat bran	40g	6 d	Healthy volunteers	Stool output, bowel movement frequency increased, mean stool water content increased compared with placebo-controlled group	[141]
Wheat bran	20g	6 d	Healthy volunteers	Stool output, bowel movement frequency and mean stool water content increased compared with placebo-controlled group	[141]
Rye bread	8 ×40 g fibre rich rye bread	3 wk	Free-living subjects	Total intestinal transit time decreased, fecal frequency increased and gastrointestinal symptoms increased compared with subjects who intake yoghurt containing Lactobacillus or control group	[142]

(Table 1) contd...

Food Ingredients	Dose	Period	Health Condition	Effect	Ref.
Wheat bran+ psyllium	69g	3 wk	Free-living participants	Increases in fecal bulk, less intestinal transit time, greater bowel movement frequency, increase in activity of the bowel compared with control diet	[143]
Rye bread	240 g/d	3 wk	Adults with self-reported constipation and using laxatives	Total intestinal transit time reduced, the number of bowel movements increased, Feces was more frequently softened and defecation was eased compared with other groups	[144]
Dietary fiber (Glucomannan)	100 mg/kg per d up to 5 g/d	4 wk	Chronically constipated children	Defecation frequency and abdominal pain improved	[145]
Cocoa husk supplement (fiber)	10.4 g/d (3-6 y) or 20.8 g/d (7-10 y)	4 wk	Children with chronic idiopathic constipation	Total transit time decreased, number of bowel movements increased, reports of hard stools reduced, stool consistency and pain improved	[146]
Dietary fiber	10 g fiber in 125-mL yogurt drink	8 wk	Children with constipation	No difference in defecation frequency and fecal incontinence frequency compared with subjects who intake lactulose	[147]
Dietary fiber (Glucomannan)	100 mg/kg two times a day	12 wk	Children with severe brain damage and chronic constipation	Stool frequency increased, Laxative use and painful defecation was reduced in comparison to placebo group	[148]
Inulin enriched yogurt (1.23 g inulin in 100g yogurt)	125 ml enriched yogurt twice a day	2 wk	IBS patients with constipation (IBS-C)	Stool frequency increased, Bowel transit time decreased, emptying, Bloating and Abdominal pain improved compared with placebo group	[149]
Prunes	100 g	12 wk	Healthy postmenopausal women	No difference in bowl movement compared with subjects who intake 75 g of dried apples daily	[74]
prune juice	125 mL of the test prune juice, twice a day	2 wk	Volunteers with certain gastrointestinal symptoms	Difficulty of defecation decreased but flatulence increased compared with baseline	[77]
Yoghurt containing galacto-oligosaccharides (GOS), prunes and linseed	GOS (12 g/day), prunes (12 g/day) and linseed (6 g/day)	3 wk	Elderly subjects with self-reported constipation	Defecation frequency increased, defecation was easier, constipation relieved compared with baseline and control group	[150]
Prune	at least 50 g of prune and 200 ml of prune juice per day	4 wk	Adults with self-reported constipation	Bowel movements increased, defecation time decreased, stool consistency increased, and abdominal pain during defecation decreased compared with placebo group	[151]
Prunes/psyllium	100 g/11g	3 wk	Patients with chronic constipation	Bowel movements and stool consistency increased compared to psyllium	[152]
Kiwifruit	One kiwifruit per 30 kg bodyweight	3 wk	Healthy volunteers	Bulkier and softer stool, as well as more frequent stool production compared with baseline	[104]
Kiwifruit	Kiwi fruit twice daily	4 wk	Constipated patients	Transit time, rectal sensation and score for annoyance of constipation decreased and satisfaction of bowel habit improved, decrease in days of laxative use compared with baseline	[24]
Kiwifruit	Two Hayward green kiwifruits per day	4 wk	Patients diagnosed with IBS/C	Colon transit time decreased, defecation frequency increased and bowel function improved compared with control group	[97]

(Table 1) contd...

Food Ingredients	Dose	Period	Health Condition	Effect	Ref.
Fermented milk (containing probiotics)	$2.6 \times 10^8$ CFU/g	11 d	Healthy volunteers	Improvement in colonic transit time	[122]
The Bifidus product (fermented milk containing yoghurt cultures plus probiotics)	Between $5 \times 10^7$ and $10^8$ CFU/g	10 d	Healthy female volunteers	Colonic transit time decreased	[153]
Probiotic	$10^9$ CFU/g	12 wk	Children with Constipation	No effects	[154]
Capsules containing probiotic	$8 \times 10^8$ CFU/g	4 wk	Children with chronic constipation	Defecation frequency increased, Abdominal pain and hard stool decreased	[13]
Fermented milk containing probiotic plus yoghurt strains	$1.25 \times 10^{10}$ CFU/g	2 wk	Patients with constipation	Stool frequency increased, defecation condition and stool consistency improved	[155]
Fermented milk containing probiotic with two classical yoghurt starters	$1.25 \times 10^{10}$ CFU/g	4 wk	Patient who fulfilled the Rome III criteria for IBS-C	Abdominal girth and gastrointestinal transit improved and symptomatology reduced	[156]
Buttermilk containing probiotic	$2 \times 10^{10}$ CFU/g	3 wk	Adults with self-reported constipation and using laxatives	Not effective in relieving constipation	[144]
Commercially drops containing probiotic	$10^8$ CFU/g	8 wk	Infants diagnosed with functional chronic constipation	Frequency of bowel movements increased, no significant difference in stool consistency	[157]
Capsules containing probiotic	$17.2 \times 10^9$ CFU/g	2 wk	Adults with self-reported constipation	Reduction in frequency of functional gastrointestinal symptoms in adults, decrease of Whole gut transit time	[158]
Capsules containing probiotic	$1.8 \times 10^9$ CFU/g	2 wk	Adults with self-reported constipation	Reduction in frequency of functional gastrointestinal symptoms in adults, decrease of Whole gut transit time	[158]
Probiotic milk drink	$6.5 \times 10^9$ CFU/g	4 wk	Patients with chronic constipation	Reduction of colonic transit time	[159]
Artichokes enriched with probiotics	$2 \times 10^{10}$ CFU/g	2 wk	Constipated patients	Satisfactory relief of symptoms, reduction in Gastrointestinal Symptom Rating Scale questionnaire and in its single items (frequency of evacuation, hard stools and feeling of incomplete evacuation)	[160]
Fermented milk containing probiotic	$3 \times 10^{10}$ CFU/g	4 wk	Subjects with functional constipation	No differences	[161]
Fermented milk drink containing probiotic	$6.5 \times 10^9$ CFU/g	8 wk	Subjects suffering from hard stools	Stool became softer, improvement of stool consistency	[162]
Probiotic	$10^8$ CFU/g	4 wk	Adult with functional constipation	Improvement of bowel movement frequency, no effect on stool consistency	[163]
Protexin (composed of seven probiotic)	$10^9$ CFU/g	4 wk	Children with chronic constipation	Improvement of stool frequency and consistency	[164]

### 3.4.3.1. Plum (Prune)

Garden plum (*Prunus domestica*) is being cultivated since the 12th century. It has different shapes, colors, sizes and fruit ripening date [73]. Plum has lower fat content and higher level of important nutrients including carbohydrates, vitamins and minerals and is considered as a healthy food. As a dietary component, plum has health-promoting features [74] and has an important role in clinical settings. The healing effects of plum have been observed in measles, and blood circulation and digestive problems [75]. Although dried plums and their juice are commonly used for constipation relief, other health benefits of them are less known among the general public [74]. Since it contains high contents of sorbitol and chlorogenic acids, plum is considered as a contact laxative [76]. Piirainen *et al.* (2007) observed the mild laxative effects of daily administration of prune juice in human volunteers [77]. Because of its beneficial nutritive value and relatively high amounts of biologically-active compounds, plum should be considered as a fixed element in human diet, whether as fresh fruit, traditional jam or prunes [73]. In addition to high contents of soluble and insoluble dietary fibers (about 6 g fiber/100 g including hemicellulose (3.0 g), pectin (2.1 g) and cellulose (0.9 g)), dried prunes contain other components that may contribute to the gastrointestinal function. These components include sugar alcohol sorbitol (14.7 g/100 g) and phenolic compounds (184 mg/100 g), predominantly chlorogenic and neochlorogenic acids, all of which are poorly absorbed by the small intestine and pass undigested into the colon [78]. Since sorbitol is not absorbed, in some healthy individuals it can act as an osmotic agent [79] and provide laxative effects [80]. The colonic microbiota ferments soluble fibers such as pectin and results in the proliferation of bacterial populations, generation of SCFA (short-chain fatty acid), and increase in stool weight [81]. On the other hand, insoluble fibers such as cellulose through mechanical intra-luminal stimulation induce the secretion and GI peristalsis resistant colonic fermentation and increase stool water and bulk [82]. *In vitro* studies demonstrated that chlorogenic acid is metabolised by specific colonic microbiota to form phenolic breakdown products such as caffeic acid, which stimulate bifidobacteria [83]. Bifidobacteria have been shown to have laxative effects when taken as a probiotic and after prebiotic supplementation [84].

### 3.4.3.2. Fig

Cultivated fig (*Ficus carica L.*) belongs to the Moraceae family and is considered as an important source of human food [85]. Figs contain cellulose, minerals, vitamins, and amino acids [86, 87] as well as high levels of fiber, minerals and water. Laxative activities of fig extract and paste have been reported previously. The cellulose content of fig *via* increasing water content and bulk and elevating viscosity could lead to an increase in fecal excretion [23]. Feeding fig paste increases fecal weight and reduces colonic transit time (CTT) in animals with diet-induced constipation [23]. It has been reported that oral administration of fig paste is safe and thus may be advised for constipated patients, especially those with diet-induced constipation [23].

### 3.4.3.3. Flax-seed

Flax (*Linum usitatissimum*), a member of the Linaceae family, is an annual herb with a crispy texture, nutty taste and blue flowers. Flax-seeds are small and flat and are found in various colors from golden yellow to reddish-brown [88, 89]. They are also known as linseed. Although these terms are used interchangeably in the literature, the term flax-seed denotes comestible flax while linseed refers to its industrial applicant [88]. Stem yields are good quality fiber with high strength and durability. The dietary fiber content of flax-seed has raised growing interest among nutritionists and medical researchers [90]. Both soluble and insoluble dietary fibers are found in flax-seed. Flax helps reduce the risk of various disorders such as heart, blood, joints, colon, aging and brain diseases [91]. For centuries, flax-seed has been used as a traditional medicine for constipation treatment. As a rich source of dietary fiber, flax-seed improves IBS symptoms such as constipation, abdominal pain and diarrhea [91]. Additionally, it softens the stool and increases its weight and size which results in easy passage of stool leading to decreased constipation and developing haemorrhoids. Although it has been indicated that flax-seed has similar laxative actions in both healthy [92, 93] and constipated individuals [55], few relevant controlled trials are available. For instance, in an animal study, Xu *et al.* (2012) showed that the administration of PDFM resulted in significant increments in stool frequency and weight and a marked decrement in the start time of defecation in both normal and constipated mice [93]. Although soluble fibers have wide effects on gastrointestinal transit [93], it was shown that the insoluble ones that inhibit digestive processes of the intestine lead to a reduction in the transit time within the stomach and the small intestine [94]. Furthermore, because of their swelling property, insoluble fibers cause larger bulk in the intestines. In fact, the laxative effects of dietary fibers (mixtures of soluble to insoluble) from natural food sources are entirely dependent on the luminal bulk [94].

### 3.4.3.4. Kiwifruit

*Actinidia deliciosa*, a genus of plants mostly cultivated for its fruit (kiwifruit), grows in various countries especially in Italy, New Zealand, Chile, and France [95]. These countries produce kiwifruit in large quantities. In a recent review of the potential health benefits of kiwifruit, its ability to improve gastrointestinal disorders, particularly constipation has been reported [96]. Because of its high dietary fiber capacity, as well as cysteine protease constituent and actinidin, a proteolytic enzyme of thiol-proteases, kiwifruit has been considered to have laxative effects [97, 98]. Kiwifruit is suggested to be a good dietary supplement, especially for the elderly who often experience constipation [98]. Kiwifruit is a good source of dietary fibers containing about 3.4 g /100 dietary fiber, which has high water-holding capacity which facilitates fecal bulking and improves laxation. The most important dietary fiber constituents in kiwifruit, in order of quantity, are in the form of pectic galactins [99, 100], hemicelluloses and cellulose [101-103]. Furthermore, actinidin, a proteolytic enzyme belonging to the class of thiol-proteases, can stimulate receptors in the colon, which increases colonic

motility, and finally facilitates laxation. To date, laxative effects of kiwifruit such as softening stool and increasing fecal bulking have been suggested in numerous anecdotal reports [104, 105]. Furthermore, other studies have investigated the ability of zyaactinase (the 100% natural ingredient derived from kiwifruit) to decrease constipation [95]. However, no controlled human trial data is available. The effectiveness of kiwifruit administration in constipated patients along with the improvement in their anorectal physiology has been reported [24, 98]. Additionally, Chan *et al.* (2010) indicated the treatment benefits of kiwifruit consumption only for 6 months or more in Chinese constipated subjects [97]. Furthermore, as a routine dietary constituent, kiwifruit appears to be an effective natural dietary intervention for IBS/C patients [97]. In constipated patients, consumption of kiwifruit resulted in significant decrements in CTT, improvements in stool form and volume, along with increased ease and satisfaction of defecation resulting in relief from constipation [98, 104, 105].

#### **3.4.3.5. Bran**

Bran is the coarse outer layer of cereal grain, such as wheat, rye and corn [106]. Bran is one of the most effective ingredients in increasing fecal weight [107]. Wheat bran has the best laxative potential among other bran such as cereals, partly because it is more resistant to fermentation than rye or oat bran [108]. On the other hand, few studies suggested corn bran as the most effective one [109]. Regular consumption of wheat bran decreases intestinal transit time [109, 110]. Some studies suggested that it is generally quite effective in decreasing transit time and increasing stool weight in healthy people but not for treating chronic constipation [111]. Wheat bran has been advocated to control constipation, and studies on its laxative effects go far back to 1930s [112, 113]. It has been suggested that intestinal transit is pathologically slow in individuals in industrialized societies due to the consumption of fiber-depleted foods [91]. Therefore, addition of low-cost bran to the diet has been suggested [114]. Currently it has been found that adding more wheat and bran fiber to the diet would be beneficial in alleviating pregnancy constipation *via* increasing the frequency of defecation and is preferable to stimulant laxatives, which may have side effects [115]. The effect of wheat bran on transit time has been studied in healthy subjects and in in-patients with constipation and irritable-colon syndrome [114]. In general, these studies showed that the administration of bran decreased the transit time in subjects with initially long (about 3 days or more) transit time, whereas it was slower among subjects with shorter (1 day or less) transit time [114]. In addition, in these studies, treatment with bran was followed by increased fecal volume. In addition to wheat, fiber-rich cereals such as rye and oats have much higher fecal-bulking potential than fruits and vegetables [116].

#### **3.4.3.6. Probiotic and Prebiotic Foods**

According to the Food and Agriculture Organization/World Health Organization, probiotics are defined as “live microorganisms which when administered in adequate amounts confer health benefits on the host” [117, 118]. Pro-

biotics are reported to be useful in preventing a wide range of diseases as well as treating the existing symptoms [118, 119]. Many foods are rich in probiotics, including yogurt, kefir, fermented foods, such as sauerkraut and kimchi, kombucha, traditional fermented buttermilk, and fermented cheeses, such as Gouda [120]. The intestine, its microbiota, and the associated immune system have been the principal targets for consuming probiotics [121]. Currently, probiotics are used as effective agents in treating constipation. Studies have shown that imbalance of gut microbiota may result in constipation. Some probiotics, including Bifidobacteria and lactobacilli, decline colon pH by producing lactic, acetic and other acids and cause increased peristalsis of the colon and subsequently decrease CTT [122, 123]. There are no reports on the serious side effects of probiotics especially bifidobacteria and lactobacilli and studies showed good toleration in adults and children [124]. The diversity of probiotic strains used in clinical trials has complicated interpretation [124].

Prebiotics are non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon and thus improve the health of the host [125]. The stimulated bacteria of beneficial nature include bifidobacteria and lactobacilli [126]. The beneficial effects of prebiotics on constipation include enhancing biomass, stool weight, frequency and the health of the bowel mucosa [127]. In practice, prebiotics are non-digestible short-chain carbohydrates (SCCs) produced by human enzymes and sometimes categorized as non-digestible oligosaccharides (NDOs) [128]. Among these prebiotics, inulin and oligosaccharides are the most studied prebiotics and have been recognized as dietary fibers in most countries. Studies showed that inulin and oligosaccharides could enhance stool frequency and weight [129-133]. Similar to other fermented carbohydrates, prebiotics have mild laxative effects. Due to the small magnitude of laxation, it is difficult to demonstrate in human studies [134]. They are found in many high-fiber foods, including some fruits, vegetables, and whole grains. Some probiotic-rich foods may also contain prebiotics [135]. Human milk also has oligosaccharides that stimulate the growth of bifidobacteria in the infant's gut. Frequently occurring constipation in non-prebiotic formula-fed infants may be related to the absence of this substance [136].

## **CONCLUSION**

Constipation is a common health problem affecting people of all ages with undesirable effects on the quality of life. Most affected patients use over-the-counter laxatives which do not have side effects. It is logical to emphasize on lifestyle modification before taking any medication. These modifications include diet and physical activity, especially choosing beneficial food. Food ingredients such as fruits (plum, fig, kiwifruit) and seeds (flax-seed) naturally contain laxative materials which could be useful for chronic constipation by including them in the diet. All types of constipation may be successfully prevented and/or treated with laxative foods including wheat bran, prune, rye, inulin, kiwifruit, and pre/probiotic. Thus, it is suggested to use laxative foods



alone or in combination with each other to prevent or treat constipation.

### CONSENT FOR PUBLICATION

Not applicable.

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None.

### CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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### REFERENCES

- [1] Drossman DA, Corazziari E, Delvaux M, Spiller RC, Talley NJ, Thompson WG, *et al.* Rome III: the functional gastrointestinal disorders. VA: Degnon Associates McLean 2006; Vol. 1048.
- [2] Longstreth GF, Thompson WG, Chey WD, Houghton LA, Mearin F, Spiller RC. Functional bowel disorders. *Gastroenterology* 2006; 130(5): 1480-91. [http://dx.doi.org/10.1053/j.gastro.2005.11.061] [PMID: 16678561]
- [3] Mostafa SM, Bhandari S, Ritchie G, Gratton N, Wenstone R. Constipation and its implications in the critically ill patient. *Br J Anaesth* 2003; 91(6): 815-9. [http://dx.doi.org/10.1093/bja/aeg275] [PMID: 14633751]
- [4] Chu H, Zhong L, Li H, Zhang X, Zhang J, Hou X. Epidemiology characteristics of constipation for general population, pediatric population, and elderly population in China. *Gastroenterol Res Pract* 2014; 2014 [http://dx.doi.org/10.1155/2014/532734]
- [5] Higgins PDR, Johanson JF. Epidemiology of constipation in North America: a systematic review. *Am J Gastroenterol* 2004; 99(4): 750-9. [http://dx.doi.org/10.1111/j.1572-0241.2004.04114.x] [PMID: 15089911]
- [6] Schmidt FMQ, Santos VL. Prevalence of constipation in the general adult population: an integrative review. *J Wound Ostomy Continence Nurs* 2014; 41(1): 70-6. [http://dx.doi.org/10.1097/01.WON.0000438019.21229.b7] [PMID: 24378694]
- [7] Kollef MH, Neelon-Kollef RA. Pulmonary embolism associated with the act of defecation. *Heart Lung* 1991; 20(5 Pt 1): 451-4. [PMID: 1894524]
- [8] Smeltzer SC, Bare BG. Brunner & Suddarth's textbook of medical-surgical nursing. JB Lippincott Philadelphia 1992.
- [9] Heaton KW, Radvan J, Cripps H, Mountford RA, Braddon FE, Hughes AO. Defecation frequency and timing, and stool form in the general population: a prospective study. *Gut* 1992; 33(6): 818-24. [http://dx.doi.org/10.1136/gut.33.6.818] [PMID: 1624166]
- [10] Heaton KW, Cripps HA. Straining at stool and laxative taking in an English population. *Dig Dis Sci* 1993; 38(6): 1004-8. [http://dx.doi.org/10.1007/BF01295713] [PMID: 8508693]
- [11] Thompson WG, Heaton KW. Functional bowel disorders in apparently healthy people. *Gastroenterology* 1980; 79(2): 283-8. [http://dx.doi.org/10.1016/0016-5085(80)90142-0] [PMID: 7399231]
- [12] Connell AM, Hilton C, Irvine G, Lennard-Jones JE, Misiewicz JJ. Variation of bowel habit in two population samples. *BMJ* 1965; 2(5470): 1095-9. [http://dx.doi.org/10.1136/bmj.2.5470.1095] [PMID: 5838411]
- [13] Bu LN, Chang MH, Ni YH, Chen HL, Cheng CC. *Lactobacillus casei rhamnosus Lcr35* in children with chronic constipation. *Pediatr Int* 2007; 49(4): 485-90. [http://dx.doi.org/10.1111/j.1442-200X.2007.02397.x] [PMID: 17587273]
- [14] Peppas G, Alexiou VG, Mourtzoukou E, Falagas ME. Epidemiology of constipation in Europe and Oceania: a systematic review. *BMC Gastroenterol* 2008; 8(1): 5. [http://dx.doi.org/10.1186/1471-230X-8-5] [PMID: 18269746]
- [15] Kumar N, Kishore K. CHEMICAL AND HERBAL REMEDIES FOR CONSTIPATED PATIENTS: A. *Indian J Drugs* 2013; 1(2): 23-37.
- [16] Paré P, Bridges R, Champion MC, *et al.* Recommendations on chronic constipation (including constipation associated with irritable bowel syndrome) treatment. *Can J Gastroenterol* 2007; 21(Suppl. B): 3B-22B. [http://dx.doi.org/10.1155/2007/848706] [PMID: 17464377]
- [17] Johanson JF, Kralstein J. Chronic constipation: a survey of the patient perspective. *Aliment Pharmacol Ther* 2007; 25(5): 599-608. [http://dx.doi.org/10.1111/j.1365-2036.2006.03238.x] [PMID: 17305761]
- [18] Bharucha AE, Wald A, Enck P, Rao S. Functional anorectal disorders. *Gastroenterology* 2006; 130(5): 1510-8. [http://dx.doi.org/10.1053/j.gastro.2005.11.064] [PMID: 16678564]
- [19] Borody TJ. Laxative compositions and methods for treating constipation and related gastrointestinal diseases and conditions. Google Patents 2015.
- [20] Müller-Lissner SA, Kamm MA, Scarpignato C, Wald A. Myths and misconceptions about chronic constipation. *Am J Gastroenterol* 2005; 100(1): 232-42. [http://dx.doi.org/10.1111/j.1572-0241.2005.40885.x] [PMID: 15654804]
- [21] Brandt LJ, Prather CM, Quigley EMM, Schiller LR, Schoenfeld P, Talley NJ. Systematic review on the management of chronic constipation in North America. *Am J Gastroenterol* 2005; 100(s1)(Suppl. 1): S5-S21. [http://dx.doi.org/10.1111/j.1572-0241.2005.50613\_2.x] [PMID: 16008641]
- [22] Ramkumar D, Rao SSC. Efficacy and safety of traditional medical therapies for chronic constipation: systematic review. *Am J Gastroenterol* 2005; 100(4): 936-71. [http://dx.doi.org/10.1111/j.1572-0241.2005.40925.x] [PMID: 15784043]
- [23] Oh H-G, Lee H-Y, Seo M-Y, *et al.* Effects of *Ficus carica* paste on constipation induced by a high-protein feed and movement restriction in beagles. *Lab Anim Res* 2011; 27(4): 275-81. [http://dx.doi.org/10.5625/lar.2011.27.4.275] [PMID: 22232635]
- [24] Chan AOO, Leung G, Tong T, Wong NYH. Increasing dietary fiber intake in terms of kiwifruit improves constipation in Chinese patients. *World J Gastroenterol* 2007; 13(35): 4771-5. [http://dx.doi.org/10.3748/wjg.v13.i35.4771] [PMID: 17729399]
- [25] Bassotti G, Villanacci V, Maurer CA, *et al.* The role of glial cells and apoptosis of enteric neurones in the neuropathology of intractable slow transit constipation. *Gut* 2006; 55(1): 41-6. [http://dx.doi.org/10.1136/gut.2005.073197] [PMID: 16041063]
- [26] Prather CM. Pregnancy-related constipation. *Curr Gastroenterol Rep* 2004; 6(5): 402-4. [http://dx.doi.org/10.1007/s11894-004-0057-7] [PMID: 15341717]
- [27] Scott SM, Picon L, Knowles CH, *et al.* Automated quantitative analysis of nocturnal jejunal motor activity identifies abnormalities in individuals and subgroups of patients with slow transit constipation. *Am J Gastroenterol* 2003; 98(5): 1123-34. [http://dx.doi.org/10.1111/j.1572-0241.2003.07419.x] [PMID: 12809838]
- [28] Hemingway DM, Finlay IG. Effect of colectomy on gastric emptying in idiopathic slow-transit constipation. *Br J Surg* 2000; 87(9): 1193-6. [http://dx.doi.org/10.1046/j.1365-2168.2000.01505.x] [PMID: 10971427]
- [29] Mollen RMHG, Hopman WPM, Oyen WJG, Kuijpers HHC, Edelbroek MAL, Jansen JBMJ. Effect of subtotal colectomy on gastric emptying of a solid meal in slow-transit constipation. *Dis Colon Rectum* 2001; 44(8): 1189-95. [http://dx.doi.org/10.1007/BF02234643] [PMID: 11535861]

- [30] Penning C, Vu MK, Delemarre JB, Masclee AA. Proximal gastric motor and sensory function in slow transit constipation. *Scand J Gastroenterol* 2001; 36(12): 1267-73. [http://dx.doi.org/10.1080/003655201317097100] [PMID: 11761015]
- [31] Gonlachanvit S, Patcharatrakul T. Causes of idiopathic constipation in Thai patients: associations between the causes and constipation symptoms as defined in the Rome II criteria. *J Med Assoc Thailand= Chotmaihet thangphaet* 2004; (6): S22-8.
- [32] Lundin E, Karlbom U, Westlin J-E, et al. Scintigraphic assessment of slow transit constipation with special reference to right- or left-sided colonic delay. *Colorectal Dis* 2004; 6(6): 499-505. [http://dx.doi.org/10.1111/j.1463-1318.2004.00694.x] [PMID: 15521943]
- [33] Rao SSC, Sadeghi P, Batterson K, Beatty J. Altered periodic rectal motor activity: a mechanism for slow transit constipation. *Neurogastroenterol Motil* 2001; 13(6): 591-8. [http://dx.doi.org/10.1046/j.1365-2982.2001.00292.x] [PMID: 11903920]
- [34] Preston DM, Lennard-Jones JE. Severe chronic constipation of young women: 'idiopathic slow transit constipation'. *Gut* 1986; 27(1): 41-8. [http://dx.doi.org/10.1136/gut.27.1.41] [PMID: 3949236]
- [35] Camilleri M, Thompson WG, Fleshman JW, Pemberton JH. Clinical management of intractable constipation. *Ann Intern Med* 1994; 121(7): 520-8. [http://dx.doi.org/10.7326/0003-4819-121-7-199410010-00008] [PMID: 8067650]
- [36] Doig CM. ABC of colorectal diseases. Paediatric problems--I. *BMJ* 1992; 305(6851): 462-4. [http://dx.doi.org/10.1136/bmj.305.6851.462] [PMID: 1392963]
- [37] Klauser AG, Schindlbeck NE, Müller-Lissner SA. Symptoms in gastro-oesophageal reflux disease. *Lancet* 1990; 335(8683): 205-8. [http://dx.doi.org/10.1016/0140-6736(90)90287-F] [PMID: 1967675]
- [38] Loening-Baucke V. Encopresis and soiling. *Pediatr Clin North Am* 1996; 43(1): 279-98. [http://dx.doi.org/10.1016/S0031-3955(05)70406-5] [PMID: 8596685]
- [39] Voderholzer WA, Schatke W, Mühldorfer BE, Klauser AG, Birkner B, Müller-Lissner SA. Clinical response to dietary fiber treatment of chronic constipation. *Am J Gastroenterol* 1997; 92(1): 95-8. [PMID: 8995945]
- [40] Ashraf W, Park F, Lof J, Quigley EMM. An examination of the reliability of reported stool frequency in the diagnosis of idiopathic constipation. *Am J Gastroenterol* 1996; 91(1): 26-32. [PMID: 8561138]
- [41] Mertz H, Naliboff B, Mayer E. Physiology of refractory chronic constipation. *Am J Gastroenterol* 1999; 94(3): 609-15. [http://dx.doi.org/10.1111/j.1572-0241.1999.922\_a.x] [PMID: 10086639]
- [42] Lembo A, Camilleri M. Chronic constipation. *N Engl J Med* 2003; 349(14): 1360-8. [http://dx.doi.org/10.1056/NEJMra020995] [PMID: 14523145]
- [43] Boccasanta P, Venturi M, Stuto A, et al. Stapled transanal rectal resection for outlet obstruction: a prospective, multicenter trial. *Dis Colon Rectum* 2004; 47(8): 1285-96. [http://dx.doi.org/10.1007/s10350-004-0582-3] [PMID: 15484341]
- [44] D'Hoore A, Penninckx F. Obstructed defecation. *Colorectal Dis* 2003; 5(4): 280-7. [http://dx.doi.org/10.1046/j.1463-1318.2003.00497.x] [PMID: 12814403]
- [45] Djalma JA, Cleveland MV, McGowan J, Herrera JL. A randomized, multicenter, placebo-controlled trial of polyethylene glycol laxative for chronic treatment of chronic constipation. *Am J Gastroenterol* 2007; 102(7): 1436-41. [http://dx.doi.org/10.1111/j.1572-0241.2007.01199.x] [PMID: 17403074]
- [46] Leung L, Riutta T, Kotecha J, Rosser W. Chronic constipation: an evidence-based review. *J Am Board Fam Med* 2011; 24(4): 436-51. [http://dx.doi.org/10.3122/jabfm.2011.04.100272] [PMID: 21737769]
- [47] Leroi A-M, Berkelmans I, Denis P, Hémond M, Devroede G. Anismus as a marker of sexual abuse. Consequences of abuse on anorectal motility. *Dig Dis Sci* 1995; 40(7): 1411-6. [http://dx.doi.org/10.1007/BF02285184] [PMID: 7628260]
- [48] Bonapace ES Jr, Fisher RS. Constipation and diarrhea in pregnancy. *Gastroenterol Clin North Am* 1998; 27(1): 197-211. [http://dx.doi.org/10.1016/S0889-8553(05)70353-8] [PMID: 9546090]
- [49] Trotter MD, Naaz A, Li Y, Fraker PJ. Enhancement of hematopoiesis and lymphopoiesis in diet-induced obese mice. *Proc Natl Acad Sci USA* 2012; 109(20): 7622-9. [http://dx.doi.org/10.1073/pnas.1205129109] [PMID: 22538809]
- [50] Ford AC, Suares NC. Effect of laxatives and pharmacological therapies in chronic idiopathic constipation: systematic review and meta-analysis. *Gut* 2011; 60(2): 209-18. [http://dx.doi.org/10.1136/gut.2010.227132] [PMID: 21205879]
- [51] Wald A. Chronic constipation: advances in management. *Neurogastroenterol Motil* 2007; 19(1): 4-10. [http://dx.doi.org/10.1111/j.1365-2982.2006.00835.x] [PMID: 17187583]
- [52] Bove A, Bellini M, Battaglia E, et al. Consensus statement AI-GO/SICCR diagnosis and treatment of chronic constipation and obstructed defecation (part II: treatment). *World J Gastroenterol* 2012; 18(36): 4994-5013. [http://dx.doi.org/10.3748/wjg.v18.i36.4994] [PMID: 23049207]
- [53] Electrolytes I of M (US). P on DRI for, Water DRI, dietary reference intakes for water, potassium, sodium, chloride, and sulfate. National Academy Press 2005.
- [54] O'Neil CE, Nicklas TA, Zanovec M, Cho S. Whole-grain consumption is associated with diet quality and nutrient intake in adults: the National Health and Nutrition Examination Survey, 1999-2004. *J Am Diet Assoc* 2010; 110(10): 1461-8. [http://dx.doi.org/10.1016/j.jada.2010.07.012] [PMID: 20869484]
- [55] Tarpila A, Wennberg T, Tarpila S. Flaxseed as a functional food. *Curr Top Nutraceutical Res* 2005; 3(3): 167.
- [56] Emmanuel AV, Tack J, Quigley EM, Talley NJ. Pharmacological management of constipation. *Neurogastroenterol Motil* 2009; 21(Suppl. 2): 41-54. [http://dx.doi.org/10.1111/j.1365-2982.2009.01403.x] [PMID: 19824937]
- [57] Singh KK, Mridula D, Rehal J, Barnwal P. Flaxseed: a potential source of food, feed and fiber. *Crit Rev Food Sci Nutr* 2011; 51(3): 210-22. [http://dx.doi.org/10.1080/10408390903537241] [PMID: 21390942]
- [58] Singh S, Rao SSC. Pharmacologic management of chronic constipation. *Gastroenterol Clin North Am* 2010; 39(3): 509-27. [http://dx.doi.org/10.1016/j.gtc.2010.08.001] [PMID: 20951915]
- [59] Spinzi G, Amato A, Imperiali G, et al. Constipation in the elderly: management strategies. *Drugs Aging* 2009; 26(6): 469-74. [http://dx.doi.org/10.2165/00002512-200926060-00003] [PMID: 19591521]
- [60] Klaschik E, Nauck F, Ostgathe C. Constipation--modern laxative therapy. *Support Care Cancer* 2003; 11(11): 679-85. [http://dx.doi.org/10.1007/s00520-003-0525-x] [PMID: 14505158]
- [61] Foxx-Orenstein AE, McNally MA, Odunsi ST. Update on constipation: one treatment does not fit all. *Cleve Clin J Med* 2008; 75(11): 813-24. [http://dx.doi.org/10.3949/ccjm.75.11.813] [PMID: 19068963]
- [62] Tack J. Current and future therapies for chronic constipation. *Best Pract Res Clin Gastroenterol* 2011; 25(1): 151-8. [http://dx.doi.org/10.1016/j.bpg.2011.01.005] [PMID: 21382586]
- [63] Costilla VC, Foxx-Orenstein AE. Constipation: understanding mechanisms and management. *Clin Geriatr Med* 2014; 30(1): 107-15. [http://dx.doi.org/10.1016/j.cger.2013.10.001] [PMID: 24267606]
- [64] De Maeyer JH, Lefebvre RA, Schuurkes JAJ. 5-HT4 receptor agonists: similar but not the same. *Neurogastroenterol Motil* 2008; 20(2): 99-112. [http://dx.doi.org/10.1111/j.1365-2982.2007.01059.x] [PMID: 18199093]
- [65] Liu LWC. Chronic constipation: current treatment options. *Can J Gastroenterol* 2011; 25(Suppl. B): 22B-8B. [http://dx.doi.org/10.1155/2011/360463] [PMID: 22114754]

- [66] Portatalin M, Winstead N. Medical management of constipation. *Clin Colon Rectal Surg* 2012; 25(1): 12-9. [http://dx.doi.org/10.1055/s-0032-1301754] [PMID: 23449608]
- [67] Manini ML, Camilleri M, Goldberg M, *et al.* Effects of Velusetrag (TD-5108) on gastrointestinal transit and bowel function in health and pharmacokinetics in health and constipation. *Neurogastroenterol Motil* 2010; 22(1): 42-49, e7-e8. [PMID: 19691492]
- [68] Johanson JF, Morton D, Geenen J, Ueno R. Multicenter, 4-week, double-blind, randomized, placebo-controlled trial of lubiprostone, a locally-acting type-2 chloride channel activator, in patients with chronic constipation. *Am J Gastroenterol* 2008; 103(1): 170-7. [http://dx.doi.org/10.1111/j.1572-0241.2007.01524.x] [PMID: 17916109]
- [69] Lacy BE, Levy LC. Lubiprostone: a chloride channel activator. *J Clin Gastroenterol* 2007; 41(4): 345-51. [http://dx.doi.org/10.1097/01.mcg.0000225665.68920.df] [PMID: 17413599]
- [70] Bharucha AE, Waldman SA. Taking a lesson from microbial diarrheogenesis in the management of chronic constipation. *Gastroenterology* 2010; 138(3): 813-7. [http://dx.doi.org/10.1053/j.gastro.2010.01.022] [PMID: 20114092]
- [71] McNicol E, Boyce DB, Schumann R, Carr D. Efficacy and safety of mu-opioid antagonists in the treatment of opioid-induced bowel dysfunction: systematic review and meta-analysis of randomized controlled trials. *Pain Med* 2008; 9(6): 634-59. [http://dx.doi.org/10.1111/j.1526-4637.2007.00335.x] [PMID: 18828197]
- [72] Wong BS, Rao AS, Camilleri M, *et al.* The effects of methylnaltrexone alone and in combination with acutely administered codeine on gastrointestinal and colonic transit in health. *Aliment Pharmacol Ther* 2010; 32(7): 884-93. [http://dx.doi.org/10.1111/j.1365-2036.2010.04422.x] [PMID: 20839388]
- [73] Walkowiak-Tomczak D, Reguła J, Lysiak G. PHYSICO-CHEMICAL PROPERTIES AND ANTIOXIDANT ACTIVITY OF SELECTED PLUM CULTIVARS FRUIT. *Acta Sci Pol Technol Aliment* 2008; 7(4)
- [74] Lucas EA, Mocanu V, Smith BJ, Soung DY, Daggy BP. Daily consumption of dried plum by postmenopausal women does not cause undesirable changes in bowel function. *Energy* 2004; 25(9): 239. [kcal].
- [75] Li TSC. *Vegetables and fruits: nutritional and therapeutic values.* CRC Press 2008. [http://dx.doi.org/10.1201/9781420068733]
- [76] Jabeen Q, Aslam N. The pharmacological activities of prunes: The dried plums. *J Med Plants Res* 2011; 5(9): 1508-11.
- [77] Piirainen L, Peuhkuri K, Bäckström K, Korpela R, Salminen S. Prune juice has a mild laxative effect in adults with certain gastrointestinal symptoms. *Nutr Res* 2007; 27(8): 511-3. [http://dx.doi.org/10.1016/j.nutres.2007.06.008]
- [78] Stacewicz-Sapuntzakis M, Bowen PE, Hussain EA, Damayanti-Wood BI, Farnsworth NR. Chemical composition and potential health effects of prunes: a functional food? *Crit Rev Food Sci Nutr* 2001; 41(4): 251-86. [http://dx.doi.org/10.1080/20014091091814] [PMID: 11401245]
- [79] Corazza GR, Strocchi A, Rossi R, Sirolo D, Gasbarrini G. Sorbitol malabsorption in normal volunteers and in patients with coeliac disease. *Gut* 1988; 29(1): 44-8. [http://dx.doi.org/10.1136/gut.29.1.44] [PMID: 3343011]
- [80] Peters R, Lock RH. Laxative effect of sorbitol. *BMJ* 1958; 2(5097): 677-8. [http://dx.doi.org/10.1136/bmj.2.5097.677] [PMID: 13572866]
- [81] Buttriss JL, Stokes CS. Dietary fibre and health: an overview. *Nutr Bull* 2008; 33(3): 186-200. [http://dx.doi.org/10.1111/j.1467-3010.2008.00705.x]
- [82] Tomlin J, Read NW. Laxative properties of indigestible plastic particles. *BMJ* 1988; 297(6657): 1175-6. [http://dx.doi.org/10.1136/bmj.297.6657.1175] [PMID: 2849492]
- [83] Parkar SG, Trower TM, Stevenson DE. Fecal microbial metabolism of polyphenols and its effects on human gut microbiota. *Anaerobe* 2013; 23: 12-9. [http://dx.doi.org/10.1016/j.anaerobe.2013.07.009] [PMID: 23916722]
- [84] Tabbers MM, Chmielewska A, Roseboom MG, *et al.* Effect of the consumption of a fermented dairy product containing Bifidobacterium lactis DN-173 010 on constipation in childhood: a multicentre randomised controlled trial (NTRTC: 1571). *BMC Pediatr* 2009; 9(1): 22. [http://dx.doi.org/10.1186/1471-2431-9-22] [PMID: 19296845]
- [85] Mehraj H, Sikder RK, Haider MN, Hussain MS, Uddin AFMJ. Fig (*Ficus carica* L.): a new fruit crop in Bangladesh. *Int J Busin Soc Sci Res* 2013; 1(1): 1-5.
- [86] Solomon A, Golubowicz S, Yablowicz Z, *et al.* Antioxidant activities and anthocyanin content of fresh fruits of common fig (*Ficus carica* L.). *J Agric Food Chem* 2006; 54(20): 7717-23. [http://dx.doi.org/10.1021/jf060497h] [PMID: 17002444]
- [87] Veberic R, Colacic M, Stampar F. Phenolic acids and flavonoids of fig fruit (*Ficus carica* L.) in the northern Mediterranean region. *Food Chem* 2008; 106(1): 153-7. [http://dx.doi.org/10.1016/j.foodchem.2007.05.061]
- [88] Morris D. *Flax-A health and nutrition Primer.* Flax Council of Canada 2005.
- [89] Rubilar M, Gutiérrez C, Verdugo M, Shene C, Sineiro J. Flaxseed as a source of functional ingredients. *J Soil Sci Plant Nutr* 2010; 10(3): 373-7. [http://dx.doi.org/10.4067/S0718-95162010000100010]
- [90] Touré A, Xueming X. Flaxseed lignans: source, biosynthesis, metabolism, antioxidant activity, bio-active components, and health benefits. *Compr Rev Food Sci Food Saf* 2010; 9(3): 261-9. [http://dx.doi.org/10.1111/j.1541-4337.2009.00105.x]
- [91] Amin T, Thakur M. *Linum usitatissimum* L. (flaxseed)-a multifarious functional food. *Online Int Interdiscip Res J* 2014; 4(1): 220-38.
- [92] Dahl WJ, Lockert EA, Cammer AL, Whiting SJ. Effects of flax fiber on laxation and glycemic response in healthy volunteers. *J Med Food* 2005; 8(4): 508-11. [http://dx.doi.org/10.1089/jmf.2005.8.508] [PMID: 16379563]
- [93] Xu J, Zhou X, Chen C, *et al.* Laxative effects of partially defatted flaxseed meal on normal and experimental constipated mice. *BMC Complement Altern Med* 2012; 12(1): 14. [http://dx.doi.org/10.1186/1472-6882-12-14] [PMID: 22400899]
- [94] Brownlee IA. The physiological roles of dietary fibre. *Food Hydrocoll* 2011; 25(2): 238-50. [http://dx.doi.org/10.1016/j.foodhyd.2009.11.013]
- [95] Udani JK, Bloom DW. Effects of Kivia powder on gut health in patients with occasional constipation: a randomized, double-blind, placebo-controlled study. *Nutr J* 2013; 12(1): 78. [http://dx.doi.org/10.1186/1475-2891-12-78] [PMID: 23758673]
- [96] Singletary K. Kiwifruit: overview of potential health benefits. *Nutr Today* 2012; 47(3): 133-47. [http://dx.doi.org/10.1097/NT.0b013e31825744bc]
- [97] Chang C-C, Lin Y-T, Lu Y-T, Liu Y-S, Liu J-F. Kiwifruit improves bowel function in patients with irritable bowel syndrome with constipation. *Asia Pac J Clin Nutr* 2010; 19(4): 451-7. [PMID: 21147704]
- [98] Drummond L, Geary RB. Kiwifruit modulation of gastrointestinal motility. *Advances in food and nutrition research.* Elsevier 2013; pp. 219-32.
- [99] Dawson DM, Melton LD. Two pectic polysaccharides from kiwifruit cell walls. *Carbohydr Polym* 1991; 15(1): 1-11. [http://dx.doi.org/10.1016/0144-8617(91)90015-5]
- [100] Redgwell RJ, Melton LD, Brasch DJ, Coddington JM. Structures of the pectic polysaccharides from the cell walls of kiwifruit. *Carbohydr Res* 1992; 226(2): 287-302. [http://dx.doi.org/10.1016/0008-6215(92)84077-6]
- [101] Henare SJ, Rutherford SM. Digestion of kiwifruit fiber. *Advances in food and nutrition research.* Elsevier 2013; pp. 187-203.
- [102] Redgwell RJ, Melton LD, Brasch DJ. Cell-wall polysaccharides of kiwifruit (*Actinidia deliciosa*): effect of ripening on the structural features of cell-wall materials. *Carbohydr Res* 1991; 209: 191-202. [http://dx.doi.org/10.1016/0008-6215(91)80156-H]
- [103] Schröder R, Nicolas P, Vincent SJF, Fischer M, Reymond S, Redgwell RJ. Purification and characterisation of a galactoglucomannan from kiwifruit (*Actinidia deliciosa*). *Carbohydr Res* 2001; 331(3): 291-306. [http://dx.doi.org/10.1016/S0008-6215(01)00046-5] [PMID: 11383899]

- [104] Rush EC, Patel M, Plank LD, Ferguson LR. Kiwifruit promotes laxation in the elderly. *Asia Pac J Clin Nutr* 2002; 11(2): 164-8. [http://dx.doi.org/10.1046/j.1440-6047.2002.00287.x] [PMID: 12074185]
- [105] Uebaba K, Urata T, Suzuki N, Arai T, Strong JM, Oono S, et al. Mild Laxative and QOL-improving Effects of Kiwi Fruit Extract in the Elderly-An Explanatory Study on Effectiveness and Safety. *Japanese J Complement Altern Med* 2009; 6(2): 97-103.
- [106] Jefferson A, Croton J. Using wheat bran fibre to improve bowel habits during pregnancy-a call to action. *Br J Midwifery* 2013; 21(5): 331-41. [http://dx.doi.org/10.12968/bjom.2013.21.5.331]
- [107] Burkitt DP. Dietary fiber: is it really helpful? *Geriatrics* 1982; 37(1): 119-26. [PMID: 6274739]
- [108] Karppinen S, Liukkonen K, Aura A, Forssell P, Poutanen K. *In vitro* fermentation of polysaccharides of rye, wheat and oat brans and inulin by human faecal bacteria. *J Sci Food Agric* 2000; 80(10): 1469-76. [http://dx.doi.org/10.1002/1097-0010(200008)80:10<1469::AID-JSFA675>3.0.CO;2-A]
- [109] Graham DY, Moser SE, Estes MK. The effect of bran on bowel function in constipation. *Am J Gastroenterol* 1982; 77(9): 599-603. [PMID: 6287838]
- [110] Harvey RF, Pomare EW, Heaton KW. Effects of increased dietary fibre on intestinal transit. *Lancet* 1973; 1(7815): 1278-80. [http://dx.doi.org/10.1016/S0140-6736(73)91294-4] [PMID: 4126073]
- [111] Müller-Lissner SA. Effect of wheat bran on weight of stool and gastrointestinal transit time: a meta analysis. *Br Med J (Clin Res Ed)* 1988; 296(6622): 615-7. [http://dx.doi.org/10.1136/bmj.296.6622.615] [PMID: 2832033]
- [112] Ansell J, Butts CA, Paturi G, et al. Kiwifruit-derived supplements increase stool frequency in healthy adults: a randomized, double-blind, placebo-controlled study. *Nutr Res* 2015; 35(5): 401-8. [http://dx.doi.org/10.1016/j.nutres.2015.04.005] [PMID: 25931419]
- [113] Ardron ME, Main AN. Management of constipation. *BMJ* 1990; 300(6736): 1400. [http://dx.doi.org/10.1136/bmj.300.6736.1400-d] [PMID: 2164852]
- [114] Andersson H, Bosaeus I, Falkheden T, Melkersson M. Transit time in constipated geriatric patients during treatment with a bulk laxative and bran: a comparison. *Scand J Gastroenterol* 1979; 14(7): 821-6. [http://dx.doi.org/10.3109/00365527909181410] [PMID: 395628]
- [115] Jewell D, Young G. Interventions for treating constipation in pregnancy. *Cochrane Database Syst Rev* 2001; 2 [http://dx.doi.org/10.1002/14651858.CD001142]
- [116] Monro JA. Faecal bulking index: A physiological basis for dietary management of bulk in the distal colon. *Asia Pac J Clin Nutr* 2000; 9(2): 74-81. [http://dx.doi.org/10.1046/j.1440-6047.2000.00155.x] [PMID: 24394391]
- [117] Homayouni A, Azizi A, Ehsani MR, Yarmand MS, Razavi SH. Effect of microencapsulation and resistant starch on the probiotic survival and sensory properties of synbiotic ice cream. *Food Chem* 2008; 111(1): 50-5. [http://dx.doi.org/10.1016/j.foodchem.2008.03.036]
- [118] Homayouni A, Bastani P, Ziyadi S, et al. Effects of probiotics on the recurrence of bacterial vaginosis: a review. *J Low Genit Tract Dis* 2014; 18(1): 79-86. [http://dx.doi.org/10.1097/LGT.0b013e31829156ec] [PMID: 24299970]
- [119] Ebrahimi B, Mohammadi R, Rouhi M, Mortazavian AM, Shojae-Aliabadi S, Koushki MR. Survival of probiotic bacteria in carboxymethyl cellulose-based edible film and assessment of quality parameters. *Lebensm Wiss Technol* 2018; 87. [http://dx.doi.org/10.1016/j.lwt.2017.08.066]
- [120] Sanders ME. Probiotics: definition, sources, selection, and uses. *Clin Infect Dis* 2008; 46(Supplement\_2): S58-61. [http://dx.doi.org/10.1086/523341]
- [121] Homayouni Rad A, Torab R, Mortazavian AM, Mehrabany EV, Mehrabany LV. Can probiotics prevent or improve common cold and influenza? *Nutrition* 2013; 29(5): 805-6. [http://dx.doi.org/10.1016/j.nut.2012.10.009] [PMID: 23306139]
- [122] Bouvier M, Meance S, Bouley C, Berta J-L, Grimaud J-C. Effects of consumption of a milk fermented by the probiotic strain bifidobacterium animalis DN-173 010 on colonic transit times in healthy humans. *Biosci Microflora* 2001; 20(2): 43-8. [http://dx.doi.org/10.12938/bifidus1996.20.43]
- [123] Picard C, Fioramonti J, Francois A, Robinson T, Neant F, Matuchansky C. Review article: bifidobacteria as probiotic agents -- physiological effects and clinical benefits. *Aliment Pharmacol Ther* 2005; 22(6): 495-512. [http://dx.doi.org/10.1111/j.1365-2036.2005.02615.x] [PMID: 16167966]
- [124] Bekkali NL, Bongers ME, Van den Berg MM, Liem O, Benninga MA. The role of a probiotics mixture in the treatment of childhood constipation: a pilot study. *Nutr J* 2007; 6(1): 17. [http://dx.doi.org/10.1186/1475-2891-6-17] [PMID: 17683583]
- [125] Homayoni Rad A, Akbarzadeh F, Mehrabany EV. Which are more important: prebiotics or probiotics? *Nutrition* 2012; 28(11-12): 1196-7. [http://dx.doi.org/10.1016/j.nut.2012.03.017] [PMID: 22840387]
- [126] Gibson GR, Probert HM, Loo JV, Rastall RA, Roberfroid MB. Dietary modulation of the human colonic microbiota: updating the concept of prebiotics. *Nutr Res Rev* 2004; 17(2): 259-75. [http://dx.doi.org/10.1079/NRR200479] [PMID: 19079930]
- [127] Malaguarnera M, Vacante M, Condorelli G, Leggio F, Di Rosa M, Motta M, et al. Probiotics and prebiotics in the management of constipation in the elderly. *Acta Med Mediter* 2013; 29(791)e798
- [128] Cummings JH, Macfarlane GT, Englyst HN. Prebiotic digestion and fermentation. *Am J Clin Nutr* 2001; 73(2)(Suppl.): 415S-20S. [http://dx.doi.org/10.1093/ajcn/73.2.415s] [PMID: 11157351]
- [129] Den Hond E, Geypens B, Ghooys Y. Effect of high performance chicory inulin on constipation. *Nutr Res* 2000; 20(5): 731-6. [http://dx.doi.org/10.1016/S0271-5317(00)00162-7]
- [130] Homayouni Rad A, Delshadian Z, Arefhosseini SR, Alipour B, Asghari Jafarabadi M. Effect of inulin and stevia on some physical properties of chocolate milk. *Health Promot Perspect* 2012; 2(1): 42-7. [PMID: 24688916]
- [131] Meksawan K, Chaotrakul C, Leeaphorn N, Gonlchanvit S, Eiam-Ong S, Kanjanabuch T. Effects of fructo-oligosaccharide supplementation on constipation in elderly continuous ambulatory peritoneal dialysis patients. *Perit Dial Int* 2016; 36(1): 60-6. [http://dx.doi.org/10.3747/pdi.2014.00015] [PMID: 25292404]
- [132] Meyer D, Stasse-Wolthuis M. The bifidogenic effect of inulin and oligofructose and its consequences for gut health. *Eur J Clin Nutr* 2009; 63(11): 1277-89. [http://dx.doi.org/10.1038/ejcn.2009.64] [PMID: 19690573]
- [133] Teuri U, Korpela R, Saxelin M, Montonen L, Salminen S. Increased fecal frequency and gastrointestinal symptoms following ingestion of galacto-oligosaccharide-containing yogurt. *J Nutr Sci Vitaminol (Tokyo)* 1998; 44(3): 465-71. [http://dx.doi.org/10.3177/jnsv.44.465] [PMID: 9742466]
- [134] Cummings JH, Macfarlane GT. Gastrointestinal effects of prebiotics. *Br J Nutr* 2002; 87(S2)(Suppl. 2): S145-51. [http://dx.doi.org/10.1079/BJN/2002530] [PMID: 12088511]
- [135] Al-Sheraji SH, Ismail A, Manap MY, Mustafa S, Yusof RM, Hassan FA. Prebiotics as functional foods: A review. *J Funct Foods* 2013; 5(4): 1542-53. [http://dx.doi.org/10.1016/j.jff.2013.08.009]
- [136] Coppa GV, Bruni S, Morelli L, Soldi S, Gabrielli O. The first prebiotics in humans: human milk oligosaccharides. *J Clin Gastroenterol* 2004; 38(6)(Suppl.): S80-3. [http://dx.doi.org/10.1097/01.mcg.0000128926.14285.25] [PMID: 15220665]
- [137] Odes HS, Lazovskii H, Stern I, Madar Z. Double-blind trial of a high dietary fiber, mixed grain cereal in patients with chronic constipation and hyperlipidemia. *Nutr Res* 1993; 13(9): 979-85. [http://dx.doi.org/10.1016/S0271-5317(05)80517-2]
- [138] Hotz J, Plein K. Effectiveness of plantago seed husks in comparison with wheat bran on stool frequency and manifestations of irritable colon syndrome with constipation. *Medizinische Klin (Munich, Ger)* 1983; 89(12): 645-51.
- [139] Badiali D, Corazziari E, Habib FI, et al. Effect of wheat bran in treatment of chronic nonorganic constipation. A double-blind controlled trial. *Dig Dis Sci* 1995; 40(2): 349-56.

- [140] [http://dx.doi.org/10.1007/BF02065421] [PMID: 7851201]  
Ouellet LL, Turner TR, Pond S, McLaughlin H, Knorr S. Dietary fiber and laxation in postop orthopedic patients. *Clin Nurs Res* 1996; 5(4): 428-40.  
[http://dx.doi.org/10.1177/105477389600500405] [PMID: 8970280]
- [141] McRorie J, Kesler J, Bishop L, *et al.* Effects of wheat bran and Olestra on objective measures of stool and subjective reports of GI symptoms. *Am J Gastroenterol* 2000; 95(5): 1244-52.  
[http://dx.doi.org/10.1111/j.1572-0241.2000.02017.x] [PMID: 10811335]
- [142] Hongisto SM, Paajanen L, Saxelin M, Korpela R. A combination of fibre-rich rye bread and yoghurt containing *Lactobacillus GG* improves bowel function in women with self-reported constipation. *Eur J Clin Nutr* 2006; 60(3): 319-24.  
[http://dx.doi.org/10.1038/sj.ejcn.1602317] [PMID: 16251881]
- [143] Vuksan V, Jenkins AL, Jenkins DJA, Rogovik AL, Sievenpiper JL, Jovanovski E. Using cereal to increase dietary fiber intake to the recommended level and the effect of fiber on bowel function in healthy persons consuming North American diets. *Am J Clin Nutr* 2008; 88(5): 1256-62.  
[PMID: 18996860]
- [144] Holma R, Hongisto S-M, Saxelin M, Korpela R. Constipation is relieved more by rye bread than wheat bread or laxatives without increased adverse gastrointestinal effects. *J Nutr* 2010; 140(3): 534-41.  
[http://dx.doi.org/10.3945/jn.109.118570] [PMID: 20089780]
- [145] Loening-Baucke V, Miele E, Staiano A. Fiber (glucomannan) is beneficial in the treatment of childhood constipation. *Pediatrics* 2004; 113(3 Pt 1): e259-64.  
[http://dx.doi.org/10.1542/peds.113.3.e259] [PMID: 14993586]
- [146] Castillejo G, Bulló M, Anguera A, Escribano J, Salas-Salvadó J. A controlled, randomized, double-blind trial to evaluate the effect of a supplement of cocoa husk that is rich in dietary fiber on colonic transit in constipated pediatric patients. *Pediatrics* 2006; 118(3): e641-8.  
[http://dx.doi.org/10.1542/peds.2006-0090] [PMID: 16950955]
- [147] Kokke FTM, Scholtens PAMJ, Alles MS, *et al.* A dietary fiber mixture versus lactulose in the treatment of childhood constipation: a double-blind randomized controlled trial. *J Pediatr Gastroenterol Nutr* 2008; 47(5): 592-7.  
[http://dx.doi.org/10.1097/MPG.0b013e318162e43c] [PMID: 18979582]
- [148] Staiano A, Simeone D, Del Giudice E, Miele E, Tozzi A, Toraldo C. Effect of the dietary fiber glucomannan on chronic constipation in neurologically impaired children. *J Pediatr* 2000; 136(1): 41-5.  
[http://dx.doi.org/10.1016/S0022-3476(00)90047-7] [PMID: 10636972]
- [149] Isakov V, Pilipenko V, Shakhovskaya A, Tutelyan V. Efficacy of inulin enriched yogurt on bowel habits in patients with irritable bowel syndrome with constipation: a pilot study. *Federation of American Societies for Experimental Biology* 2013.
- [150] Sairanen U, Piirainen L, Nevala R, Korpela R. Yoghurt containing galacto-oligosaccharides, prunes and linseed reduces the severity of mild constipation in elderly subjects. *Eur J Clin Nutr* 2007; 61(12): 1423-8.  
[http://dx.doi.org/10.1038/sj.ejcn.1602670] [PMID: 17299467]
- [151] Han YH, Yon MY, Hyun TS. Effect of prune supplementation on dietary fiber intake and constipation relief. *Korean J Community Nutr* 2008; 13(3): 426-38.
- [152] Attaluri A, Donahoe R, Valestin J, Brown K, Rao SSC. Randomised clinical trial: dried plums (prunes) vs. psyllium for constipation. *Aliment Pharmacol Ther* 2011; 33(7): 822-8.  
[http://dx.doi.org/10.1111/j.1365-2036.2011.04594.x] [PMID: 21323688]
- [153] Marteau P, Cuillerier E, Meance S, *et al.* *Bifidobacterium animalis* strain DN-173 010 shortens the colonic transit time in healthy women: a double-blind, randomized, controlled study. *Aliment Pharmacol Ther* 2002; 16(3): 587-93.  
[http://dx.doi.org/10.1046/j.1365-2036.2002.01188.x] [PMID: 11876714]
- [154] Banaszkiwicz A, Szajewska H. Ineffectiveness of *Lactobacillus GG* as an adjunct to lactulose for the treatment of constipation in children: a double-blind, placebo-controlled randomized trial. *J Pediatr* 2005; 146(3): 364-9.  
[http://dx.doi.org/10.1016/j.jpeds.2004.10.022] [PMID: 15756221]
- [155] Yang Y-X, He M, Hu G, *et al.* Effect of a fermented milk containing *Bifidobacterium lactis* DN-173010 on Chinese constipated women. *World J Gastroenterol* 2008; 14(40): 6237-43.  
[http://dx.doi.org/10.3748/wjg.14.6237] [PMID: 18985817]
- [156] Agrawal A, Houghton LA, Morris J, *et al.* Clinical trial: the effects of a fermented milk product containing *Bifidobacterium lactis* DN-173 010 on abdominal distension and gastrointestinal transit in irritable bowel syndrome with constipation. *Aliment Pharmacol Ther* 2009; 29(1): 104-14.  
[http://dx.doi.org/10.1111/j.1365-2036.2008.03853.x] [PMID: 18801055]
- [157] Coccorullo P, Strisciuglio C, Martinelli M, Miele E, Greco L, Staiano A. *Lactobacillus reuteri* (DSM 17938) in infants with functional chronic constipation: a double-blind, randomized, placebo-controlled study. *J Pediatr* 2010; 157(4): 598-602.  
[http://dx.doi.org/10.1016/j.jpeds.2010.04.066] [PMID: 20542295]
- [158] Waller PA, Gopal PK, Leyer GJ, *et al.* Dose-response effect of *Bifidobacterium lactis* HN019 on whole gut transit time and functional gastrointestinal symptoms in adults. *Scand J Gastroenterol* 2011; 46(9): 1057-64.  
[http://dx.doi.org/10.3109/00365521.2011.584895] [PMID: 21663486]
- [159] Krammer H-J, Von Seggern H, Schaumburg J, Neumer F. Effect of *Lactobacillus casei* Shirota on colonic transit time in patients with chronic constipation. *Coloproctology* 2011; 33(2): 109-3.
- [160] Riezzo G, Orlando A, D'Attoma B, *et al.* Randomised clinical trial: efficacy of *Lactobacillus paracasei*-enriched artichokes in the treatment of patients with functional constipation--a double-blind, controlled, crossover study. *Aliment Pharmacol Ther* 2012; 35(4): 441-50.  
[http://dx.doi.org/10.1111/j.1365-2036.2011.04970.x] [PMID: 22225544]
- [161] Mazlyn MM, Nagarajah LH, Fatimah A, Norimah AK, Goh KL. Effects of a probiotic fermented milk on functional constipation: a randomized, double-blind, placebo-controlled study. *J Gastroenterol Hepatol* 2013; 28(7): 1141-7.  
[http://dx.doi.org/10.1111/jgh.12168] [PMID: 23432408]
- [162] Tilley L, Keppens K, Kushi A, Takada T, Sakai T, Vaneechoutte M, *et al.* A probiotic fermented milk drink containing *Lactobacillus casei* strain shirota improves stool consistency of subjects with hard stools. *Int J Probiotics Prebiotics* 2014; •••: 9.
- [163] Ojetti V, Ianiro G, Tortora A, *et al.* The effect of *Lactobacillus reuteri* supplementation in adults with chronic functional constipation: a randomized, double-blind, placebo-controlled trial. *J Gastrointest Liver Dis* 2014; 23(4): 387-91.  
[PMID: 25531996]
- [164] Sadeghzadeh M, Rabiiefar A, Khoshnevisasl P, Mousavinasab N, Eftekhari K. The effect of probiotics on childhood constipation: a randomized controlled double blind clinical trial. *Int J Pediatr* 2014; 2014  
[http://dx.doi.org/10.1155/2014/937212]