Nutritional Approach to Chronic Constipation1

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Chronic constipation (CC) is one of the most common gastroenterological diagnoses in clinical practice. Treatment includes several steps, depending on the severity of symptoms. Lifestyle modifications and increased intake of fiber and water are suggested by most health professionals. Unfortunately, the recommendations in this regard are the most varied, often conflicting with each other and not always based on solid scientific arguments.

Keywords: chronic constipation ; food ; fiber ; water ; diet ; nutrition

1. Mineral Water

The first line treatment for CC involves an adequate intake of water (1.5–2 L/day), even though this is not based on strong scientific evidence. Despite the colon’s high capacity for absorption of ingested water, the laxative action of waters, especially those rich in magnesium and sulfates, has been known for a long time [1].

Waters rich in magnesium sulfate owe their laxative effectiveness mainly to the magnesium compounds they contain. Magnesium hydroxide ($Mg(OH)_2$) is commonly used as an osmotic laxative at doses greater than 2 g/day. In the stomach, this reacts with the protons (H^+) of the gastric acid, producing Mg^{2+} and water. However, if taken in high doses, $Mg(OH)_2$ is converted in the gut to magnesium carbonate ($MgCO_3$), absorbing water from the intestinal walls and hydrating and softening the stool [2][3]. Excessive use of this type of water is not recommended in elderly patients with renal insufficiency because the risk of hypermagnesemia could be higher[3].

The main effect of magnesium is the osmotic effect due to its incomplete absorption. However, other mechanisms are being hypothesized, such as an increased secretion of cholecystokinin (CCK) and Peptide YY (PYY), which in turn modulate intestinal motility, of nitric oxide synthase (NOS), which acts on smooth muscle, and of aquaporin-3 (AQP-3), which regulates the secretion of water in the lumen [4][5]. Moreover, a further mechanism of action could be due to sulfates, which can have a prebiotic action, i.e., they act as a substrate selectively utilized by host microorganisms, thereby conferring a benefit on sulfate-reducing bacteria, as defined by ISAPP in 2016 [2][6].

Bicarbonate-alkaline waters probably act through the serotoninergic system, as suggested by Fornai et al. Indeed, the laxative effect of a bicarbonate alkaline water in mice was antagonized by alosetron (5-HT3 antagonist), even if the increase in colonic reflexes due to the stimulation of duodenal osmoreceptors, together with an action on gastrin and CCK secretion, cannot be ruled out [7][8].

See **Table 2** for the characteristics of the waters examined by clinical studies.

Table 2. Description of the specific waters studied for treatment of constipation, their chemical composition, doses used, and outcomes.

Water	Chemical Composition	Doses	Outcomes
Calcium/magnesium sulfate-rich mineral water	**573 mg/L calcium, 105 mg/L magnesium, 1.535 mg/L sulfate, and other 2.650 mg/L carbon dioxide**	**1 L/day**	**Bowel frequency improved**
Magnesium-sulfate mineral water	**549 mg/L calcium, 119 mg/L magnesium, 1.530 mg/L sulfate, 14.2 mg/L sodium, 4.1 mg/L potassium, 383.7 mg/L bicarbonate, 4.3 mg/L nitrate**	**1 L/day**	**Bowel frequency improved**
Bicarbonate-alkaline water	**113.7 mg/L sodium, 11.6 mg/L potassium, 30.5 mg/L magnesium, 206.1 calcium, 689.3 mg/L bicarbonate.**	**2 L/day**	**Bowel frequency improved**

2. Dietary Fiber

Guidelines for chronic constipation are generic, recommending that patients “increase fiber intake” [1][9].

Dietary fiber, defined as “the remnant of plant components that are resistant to hydrolysis by human alimentary enzymes” is a class of non-digestible carbohydrates resistant to gastric acids and hydrolysis by digestive enzymes, while “functional” fiber is defined as isolated, non-digestible carbohydrates that have beneficial physiological effects in humans [10][11][12][13]. The fiber group also includes lignin, a highly branched non-polysaccharide polymer, which complies with the definition of dietary fiber, although it cannot be classified as a carbohydrate. Finally, some digestible polysaccharides are still classified as dietary fibers because, when inside the food matrix, they are not reached by the digestive enzymes, such as resistant starch type 1 [14].

In the colon, fiber may be fermented by the microbiota, with production of gas (CO_2, CH_4, H_2) and short chain fatty acids (SCFAs), i.e., butyrate, acetate, and propionate, which create osmotic load, accelerating intestinal transit [15][16][17][18]. Moreover, butyrate, which is an important source of energy for the colonic mucosa, also acts at the level of the neurons of the myenteric plexus, increasing gut motility [19][20].

Fiber can retain water, increasing the hydration of the stool. In this context, it is important to point out that the consistency of the stool is closely related to its water content, and even minimal variations can lead to changes in fecal consistency [21]. A normal stool contains 74% of water, whereas a hard stool has less than 72% and a soft stool at least 76%. Therefore, a percentage of as little as 2% in water content can make a difference to stool form [22]. This small variation in consistency allows the stool to be more rapidly moved distally by the peristaltic waves of the colon and more easily evacuated. The peristaltic waves differ according to their amplitude and frequency. The hardest stools are mainly propelled by high amplitude waves, whereas low amplitude waves, which are more frequent during the day, are mainly linked to gas or soft stool movement. Therefore, a small variation in water content also allows better exploitation of the propulsive activity of low amplitude waves, thus resulting in an increase in daily bowel movements (BMs) [22].

The various kinds of fiber are often considered as a homogenous group with the same characteristics, but they are quite different in terms of solubility, fermentability, and viscosity, having different effects at the gastrointestinal level [17]. According to their structure, they can be divided into short- and long-chain carbohydrates.

The short-chain carbohydrates include fructo-oligosaccharides (FOS) and galacto-oligosaccharides (GOS). These favor the growth of Bifidobacteria and, consequently, the production of large quantities of SCFAs, as well as gas. This can contribute to the onset of the most important side effect of fiber, i.e., bloating [23].

Fiber-types can be further classified according to their:

- solubility, which depends on their hydrophilicity (physical property of molecules to bind with water), and varies according to the degree of polymerization of the molecule;
- viscosity (degree of resistance to flow);
- fermentability (ability to be metabolized by bacteria in the absence of oxygen) [24].

Solubility also has an impact on fermentability as it increases both the distribution of the molecule along the intestine and its metabolism by gut microbiota.

Fiber can therefore be further divided into:

- Soluble, viscous, fermentable (e.g., Guargum)

-Soluble, viscous, unfermentable (e.g., Psyllium, HPMC—Hydroxypropyl methylcellulose)

-Soluble, non-viscous, fermentable (e.g., Inulin, FOS, GOS, Pectin)

-Soluble, non-viscous, unfermentable (e.g., PHGG—Partially Hydrolyzed Guar Gum)

-Insoluble and slowly fermentable (e.g., Wheat bran, Resistant starch)

- Insoluble and unfermentable (e.g., Cellulose, Lignin)

Rapidly fermented soluble fiber is found in legumes, wheat, potatoes, rice, barley and rye. It acts as a prebiotic, thereby increasing biomass (and indirectly fecal mass), with consequent production of SCFAs and gas.

Soluble fiber that is only moderately fermented acts by retaining large quantities of water, forming gels, normalizing fecal consistency, and it is the most widely studied fiber as regards its action on FC and IBS-C [22].

Insoluble types of fiber, such as wheat bran, act on intestinal transit by means of an irritative stimulus on the mucosa, which, in turn, induces secretion of water and mucus. However, this is achieved only by the larger and coarse bran particles, while the finer and smooth ones have not been shown to share this laxative property [22][25][26].

3. The Role of Food

Food could play a key role in the pathophysiology and treatment of CC. Its beneficial effect is due not only to the fiber content, but also to the presence of other substances (i.e., polyphenols, sorbitol, etc.) synergistically acting and enhancing their beneficial effect. Furthermore, the presence of fiber within food, and not isolated in a pharmaceutical formulation, greatly influences its effect on the bowel, because some intrinsic food features, such as particle size and matrix porosity, can modify the fiber availability for the action of digestive enzymes [14].

For obvious reasons, it is impossible to analyze the mechanisms linked to all kinds of foods, so we only focused on some foods frequently recommended to constipated patients due to their laxative properties.

A randomized clinical trial compared the effects of dried plums and psyllium in patients with CC [27]. Forty subjects were enrolled in an 8 week, single-blind, randomized cross-over study. Subjects received either dried plums (50 g b.d., fiber = 6 g/day) or psyllium (11 g b.d., fiber = 6 g/day) for 3 weeks each, with a 1 week washout period. The number of complete spontaneous BMs per week (primary outcome measure) and stool consistency scores improved significantly with dried plums when compared to psyllium. The authors hypothesize that the most powerful laxative effect of dried plums is due to the presence of sorbitol (14.7 g/100 g) and polyphenols (184 mg/100 g), in addition to the fiber. Indeed, sorbitol acts as an osmotic laxative and holds onto water.

Kiwi fruits are well known for their laxative properties. They are high in vitamin C and contain a wide range of other nutrients, such as fiber, potassium, vitamin E and folate, and various bioactive components. The latter include an array of antioxidants, phytonutrients, and enzymes, all able to provide functional and metabolic benefits [28]. It is hypothesized that the role of the kiwifruit for the treatment of CC is based on the content in dietary fiber, but also the potential role of actinidin. Actinidin is a cysteine protease with proteolytic activity enhancing protein digestion and decreasing gastrointestinal transit time [29]. The mechanism of action of Actinidin is still unclear. A recent hypothesis suggests that Actinidin cleaves the protein kiwellin into kissper and KiTH. Kissper is a small, anionic, cysteine-rich 39-residue peptide acting as an ion channel activator and as a modulator of GI motility. Both Kissper and KiTH display a range of beneficial activities, including an increase in anti-inflammatory response, a reduction in oxidative stress at the GI mucosal interface, and pH dependent and voltage-gated pore-forming activity, together with anion selectivity and channeling [30][31].

Other protease cysteines, apart from actinidine, which are potentially effective on CC, are found in pineapple, papaya, and figs (i.e., bromelain, papain, and ficin) [30][30].

In animal models, these enzymes prompt an improvement in protein digestion, decrease gastrointestinal transit time, and have an anti-inflammatory action [32][33][34].

Another study carried out by Eady et al. investigated whether daily consumption of three gold-fleshed kiwi fruit could alleviate constipation and improve gastrointestinal discomfort in mildly constipated individuals [35]. Thirty-two participants were enrolled in a 16-week randomized, single-blind, crossover study. Participants received either three kiwis (5 g of fiber/day) or 14.75 g Metamucil ® (5 g dietary fiber/day) for 4 weeks with a 4 week washout between treatments. The number of complete spontaneous BMs per week were significantly greater during daily consumption of three kiwis compared with the baseline and the Metamucil® treatment. Stool consistency also improved with the kiwi fruit producing softer stools and less straining. Gastrointestinal discomfort, abdominal pain, and constipation improved during the kiwi fruit consumption and constipation during the Metamucil® intervention. The authors conclude that daily consumption of three gold-fleshed kiwis is associated with a significant increase in bowel frequency and a reduction in pain and gastrointestinal discomfort.

Chey et al. report a partially randomized, comparative effectiveness trial evaluating kiwifruit, psyllium, and prunes in 79 patients with CC [36]. Eligible patients had <three complete spontaneous bowel movements (CSBMs) per week and were

partially randomized to green kiwifruit (2/d), prunes (100 g/d), or psyllium (12 g/d) for 4 weeks. There was a significant increase in weekly CSBM rate with all three treatments; stool consistency significantly improved with kiwifruit and prunes; straining significantly improved with kiwifruit, prunes, and psyllium. Patients randomized to the kiwifruit group reported significant improvement in bloating scores. The authors conclude that kiwifruit, prunes, and psyllium improve constipation symptoms in patients with CC.

Additionally, fig paste, in a study carried out on a constipation rat model, was able to improve constipation, increasing fecal output and water content, and decreasing transit time [37]. The results were confirmed by a randomized, double-blind, placebo-controlled study investigating 80 FC patients [38]. Ficus carica paste supplementation administered for 8 weeks showed a greater improvement in colon transit time, stool consistency, and abdominal discomfort compared with the placebo.

From a mechanistic point of view, the beneficial effects of F. carica paste on constipation are most likely related to its composition. F. carica contains high amounts of cellulose, phenols, flavonoids, and anthocyanins, which are reported to have laxative effects. These bioactive substances may stimulate the chloride channel and/or serotonergic signaling, which, in turn, stimulate colonic secretion of water, electrolytes, and mucin. In addition, fiber in F. carica can also decrease colonic mucinase activity so as to increase the mucin content and enhance the frequency of BMs [38].

Flaxseed (Linum usitatissimum) is an oil-based seed containing high amounts of alpha-linolenic acid, linoleic acid, lignans, fiber and many other bioactive components. Nowadays, flaxseed is known as a functional food with many health benefits for humans [39]. In particular, flaxseed could be a safe and effective treatment for constipation because it is a good source of soluble and insoluble fiber. Indeed, 50 g of flaxseed contain 13.3 g of dietary fiber, corresponding to about 50% of the recommended daily intake [40].

Moreover, due to its lipid content and mucilaginous component, flaxseed also has lubricating and stool-softening properties [41]. In a recent randomized controlled trial, 90 patients with FC were enrolled: 60 patients assumed flaxseed flour-enriched meals (50 g/day) and 30 patients lactulose (15 mL/day) for 4 weeks. Patients treated with flaxseed flour reported an improvement in bowel movement frequency and abdominal pain severity and less difficult defecation than those taking lactulose [41]. Furthermore, Hanif Palla et al., studying flaxseed in mice, showed that laxative effects were mediated primarily through a cholinergic pathway with weak histaminergic effects [42].

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