The effect of probiotic fermented milk that includes *Bifidobacterium lactis* CNCM I-2494 on the reduction of gastrointestinal discomfort and symptoms in adults: a narrative review

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Abstract

**Aim:** determine the effectiveness of fermented milk that included *Bifidobacterium lactis* CNCM I-2429 for reducing gastrointestinal (GI) discomfort in healthy adults.

**Methods:** we conducted a systematic literature search to identify studies reporting the use of *B. animalis* spp. *lactis* for GI discomfort/confort in healthy adults. A total of 5,329 records were identified, of these 99 full-text articles were assessed. Searches for additional trials were conducted using the names of authors of each identified study and several relevant databases. The study selection was carried out according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Studies were included if they were randomized controlled trials; the included subjects were healthy adults; and the intervention group received *B. lactis* CNCM I-2494. Studies were excluded if they were non-randomized trials, if they included subjects who were not healthy, if they included the use of any other intervention, or if they compared different products without a placebo group. The methodological quality of the studies was evaluated using the Oxford Quality Scale and the Cochrane Concealment Assessment. A meta-analysis was not possible.

**Results:** the search strategy identified two studies that included a total of 538 healthy women, aged 18–60 years, normal weight or overweight (BMI 18–30 kg/m²). GI well-being was significantly improved in the Probiotic group vs. the Control group in one study, with no differences in the other. The percentage of responders for GI well-being was higher in the Probiotic group vs. the Control group in the first study but not in the second.

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**Resumen**

**Objetivo:** determinar la eficacia de la leche fermentada con *Bifidobacterium lactis* CNCM I-2429 en la reducción de molestias GI en adultos sanos.

**Métodos:** se realizó una búsqueda sistemática en la literatura para identificar estudios que informaron del uso de *B. animalis* spp. *lactis* para molestias/confort GI en adultos sanos. Se identificaron un total de 5,329 registros, de estos se evaluaron 99 artículos de texto completo. Las búsquedas de ensayos adicionales se realizaron utilizando los nombres de los autores de cada estudio identificado y varias bases de datos relevantes. La selección de los estudios se llevó a cabo de acuerdo con las guías de Artículos de Información Preferidos para Revisiones Sistémicas y Meta-Análisis (PRISMA). Los estudios eran incluidos si eran ensayos randomizados con placebo, si los sujetos de estudio eran adultos sanos y si el grupo de intervención recibió *B. lactis* CNCM I-2494. Se excluyeron los estudios que no eran randomizados, que incluían adultos que no estaban sanos, que incluían el uso de cualquier otra intervención o si comparaban diferentes productos sin un grupo placebo. La calidad metodológica de los estudios se evaluó utilizando la Escala de Calidad de Oxford y la Evaluación Cochrane de ocultamiento. No fue posible un metaanálisis.

**Resultados:** la estrategia de búsqueda identificó dos estudios que incluyeron un total de 538 mujeres sanas, con edades entre 18 a 60 años, de peso normal o sobrepeso (IMC de 18-30 kg/m²). En uno de los estudios las molestias GI disminuyeron significativamente en el grupo de probiótico frente al grupo control en el primer estudio, pero no en el segundo. Las síntomas GI se redujeron significativamente en el grupo probiótico frente al grupo control en ambos estudios.
GI symptoms were significantly decreased in the Probiotic group vs. the Control group in both studies. Bowel function was assessed by one study; the stool frequency did not differ between the groups, but a decrease in stool consistency was observed in the Probiotic group but not in the Control group. Possible mechanisms of action (gut motility, hypersensitivity, gut permeability, and gut microbiota) were also described.

**Conclusion:** probiotic fermented milk containing *B. lactis* CNCM I-2494 by healthy women may improve GI well-being and decrease the frequency of GI symptoms.

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Key words: Probiotic. Gastrointestinal discomfort. Healthy subjects. Women.

**Introduction**

Probiotics are defined as live microorganisms that, when administered in adequate amounts, confer health benefits to the host. We are gaining an increased understanding of the importance of having an adequate gut microbiome for optimal health and especially for a healthy gut. The intestinal microbiota comprise a complex and dynamic bacterial community that plays an important role in human health. Changes in microbiota composition (dysbiosis) or function, or altered microbiota/host interactions, directly correlate with several diseases, and, conversely, the beneficial effects of specific probiotic strains may be associated with specific health claims. There are often alterations in intestinal *Bifidobacteria* levels, or in the species composition, in patients with intestinal microbiota dysbiosis. According to the rationale for using microorganisms of the genus *Bifidobacterium* as probiotics is to modulate the intestinal *Bifidobacteria* population to elicit specific responses. For example, *B. longum* strains exhibit differential immunomodulatory properties.

There is growing consumer interest in the potential therapeutic and preventive health benefits of probiotics, and there is a steady stream of commercially available products that contain probiotics. It is worth noting that beneficial microorganisms have long been a part of the human diet, and Elie Metchnikoff who was awarded a Nobel Prize in 1907 for his studies of phagocytosis and the prolongation of life, was an early pioneer of the enteric use of probiotics. Metchnikoff believed that lactic acid bacteria could improve health, and he recommended daily consumption of fermented milk (yogurt) in enhancing human health and longevity.

For a microorganism to be considered a probiotic, it must be genetically defined; have defined phenotypic, morphologic, and biochemical characteristics; be deposited in an internationally recognized culture collection; be non-pathogenic; grow and adhere in the bowel mucosa; compete and prevail over enteropathogenic microorganisms; produce beneficial metabolites for the host (like vitamins and short chain fatty acids); and remain alive through the manufacturing and storage processes. Probiotics may be delivered in different forms, with fermented milk being one such form.

Many disorders affect the digestive tract. Colonic transit disturbances (such as constipation and irritable bowel syndrome, IBS) are common and represent an important target for the probiotic industry. Changes in gut microbiota composition (dysbiosis) or function, or altered microbiota/host interactions, directly correlate with several diseases, and, conversely, the beneficial effects of specific probiotic strains may be associated with specific health claims. There are often alterations in intestinal *Bifidobacteria* levels, or in the species composition, in patients with intestinal microbiota dysbiosis. According to the rationale for using microorganisms of the genus *Bifidobacterium* as probiotics is to modulate the intestinal *Bifidobacteria* population to elicit specific responses. For example, *B. longum* strains exhibit differential immunomodulatory properties.

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Independent studies have confirmed that the connection between emotional and physical health involves multiple bidirectional neurocircuitry and endocrine signaling mechanisms. In particular, anxiety can influence gut microbiota. Recent advances have provided more detailed insights into the important role of microbiota in human health and disease and in particular into the interactions of gut microbiota and emotional stress and diet. A review of pre-clinical studies note that the disruptive impact of emotional stress on the gut can be prevented, and even partially reversed, by probiotic administration. The authors suggest that pre- and probiotic formulations and fermented food can be used to influence mental health and to control GI symptoms. GI pain can be a good way to characterize dysregulation of the brain-gut axis and, in IBS, the use of a probiotic fermented product may mitigate suffering.

Several systematic reviews have looked at the potential beneficial effects of probiotics for IBS, colon transit time, or constipation due to high interest in the use of products that may manipulate gut microbiota that affect these GI conditions. Pooling data from several studies (eg more than 20) but with different strains and in different patients groups (eg IBS-C, IBS-D, IBS-M) does not allow researchers to determine the efficacy of a single strain or of a specific combination of strains, which is the main limitation of such a global approach. Indeed, no systematic review has been performed to date in non-disease patients despite the interest of using functional probiotic foods in this population.

Here we performed a systematic review of a clearly defined probiotic food that is commercially available (Activia®: Danone), a fermented milk product enriched with B. lactis CNCM I-2494 (called B. animalis or lactis DN-173 010 in some studies), which is associated with two classical yogurt starters, S. thermophilus (CNCM strain number 1-1630) and L. bulgaricus (CNCM strains number 1-1632 and 1-1519), and with Lactococcus lactis ssp. lactis (CNCM strain number 1-1631) 1. B. lactis DN-173 010 has a high survival capacity in the human GI tract and exhibits probiotic properties in the colon. The effect of this specific probiotic fermented milk product on bowel function and on IBS has been described in the literature. The objective of this review was to narrow the research question and to determine the effectiveness of this commercially-available probiotic food for a specific GI condition, GI discomfort, in a well-defined target population of healthy adults.

Methods

Literature search

York Health Economic Consortium conducted a systematic literature search to identify studies reporting the use of B. animalis spp. lactis for GI discomfort/comfort that are indexed in the Ovid MEDLINE database. The following search terms were used: “bifidobacterium”, “lactis or animalis”, “bifidus”, “digestivum or regularis or actiregularis or essensis or danregularis”, “yogurt or yoghurt or yoghourt or milk or probiotic”, “activia or activiaTM or activiaR”, “dn173010 or dn-173010”, “CNM12494 or CNMC I-2494”, “colon or colons or colonic”, “intestine or intestinal or gastrointestinal”, “bowel or gut or digestive or digestion”, “blot or distend or distension or fullness or satiety or wellbeing”, “gas or gaseous or flatulence or flatulent or flatus or belch or burp or eructate”, “borborygm or rumble or rumbling or gurgle or gurgling”, “pain or painful or discomfort or unconfort or comfort or cramp”, “stool or defecate or fecal or faeces or constipation or constipated or hypomotility or diarrhea or incontinent”, “gastrointestinal tract or intestine or lower gastrointestinal tract”, “gastrointestinal diseases or gastrointestinal motility or colonic disease or functional/or irritable bowel syndrome”.

Searches for additional trials were conducted using the names of authors of each identified study and several relevant databases: MEDLINE In-process, EMBASE, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, Database of Abstracts of Reviews of Effects, Health Technology Assessment Database, Science Citation Index, Conference Proceeding Citation Index – Science, OAIITES, OpenGrey, National Technical Information Service, BIOSIS Citation Index, CAB Abstracts, Food Science and Technology Abstracts, Clinical Trials.gov, International Clinical Trials Registry Portal. In addition to searches of bibliographic databases, we searched selected major conference proceedings from the last three years (2012–2014). There was no language restriction for the searches that we performed.

Study selection (Figure 1)

The study selection and the construction of the flow diagram was carried out using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. We selected trials that reported the use of B. lactis CNCM I-2494 for GI discomfort/comfort. A total of 5329 records were identified through database searching, and 15 records were identified through other sources; 2219 of these were duplicates. After removing duplicates, 3125 records were screened and assessed for relevance based on their titles and abstracts. Of these, 99 full-text articles were assessed to see if they met the eligibility criteria. Studies were included if they met these criteria: they were randomized controlled trials; the included subjects were healthy adults; and the intervention group received B. lactis CNCM I-2494. Studies were excluded if they were non-randomized trials, if they included adults who were not healthy; if they included the use of any other intervention, or if they compared different products without a placebo group. At the end of this process, just two human trials met the inclusion criteria for this systematic review. We
also looked at preclinical studies in animal models and at other human studies to gain insights into the possible mechanisms of action of this probiotic dairy food.

Study quality

The data from the two studies were extracted, and the design quality was evaluated individually by one researcher and confirmed by a second researcher. Discrepancies were resolved through discussion or by consulting a third researcher.

The risk of bias was appraised using criteria for assessing the risk of bias specifically for randomized trials. The methodological quality of the studies was evaluated using the Oxford Quality Scale, with a score of "1" indicating low quality and a score of "5" indicating high quality. The Cochrane Concelmation Assessment was also applied: (A=adequate concealment, B=uncertain, C=clearly inadequate). This includes a criteria evaluation of the randomization procedure, blinding, and individual attrition. A meta-analysis was not possible; pooled analysis of the two selected trials was conducted previously.

Results

Figure 1 summarizes the two well-conducted studies that we identified in our literature search. These studies had common outcomes of interest, met the selection criteria, and provided data for 538 healthy subjects. These studies were conducted by the same research group, had the same experimental design, and overall showed low risk of bias and adequate concealment. Each study was a single-center (Munich, Germany and Caen, France), randomized, double-blind, and controlled study that aimed to assess the effect of probiotic...
fermented milk containing \textit{B. lactis} CNCM I-2494 and \textit{B. lactis} DN-173 010 (Probiotic group) compared to a non-fermented dairy product (Control group). All subjects were women aged 18–60 years who were normal weight or overweight (BMI 18–30 kg/m\(^2\)) without a diagnosis of any digestive disease and with bowel movement frequency within the normal range (3–21 per week) that complained of digestive symptoms. For inclusion, subjects had to experience a minimal level of digestive symptoms (discomfort or abdominal pain, bloating, flatulence/passage of gas, borborygmi/rumbling stomach) in the past month. The frequency of digestive symptoms and bowel function (movement and stool consistency) were obtained weekly for a 2-week period after inclusion (before intervention). The subjects were randomized to consume two units of product per day for 4 weeks and then underwent a 4-week wash-out period in which they did not consume a specific product\(^{21}\).

\textbf{Outcome of two randomized controlled trials (Table 1)}

\textit{GI well-being}

The main outcome was GI well-being in both studies, which was assessed using a 3-point Likert scale (improved, no change, worsened) on a weekly basis. Each subject was classified as a responder or as a non-responder to assess the magnitude of the effect\(^{21,27}\). Each subject was classified as a responder or as a non-responder to assess the magnitude of the effect\(^{21,27}\).

In the Guyonnet et al. (2009) study, the percentage of women who reported an improvement in GI well-being was higher (\(P=0.006; \text{OR}=1.69; 95\% \text{CI}=1.17, 2.45\)) for the Probiotic group vs. the Control group\(^{21}\), while in Marteau et al. 2013 there was no difference between these groups (\(P \geq 0.05; \text{OR}=1.38; 95\% \text{CI}=0.89, 2.14\))\(^{26}\). The pooled data analyses, conducted for Marteau et al. (2013), showed that the Probiotic group had a significantly greater improvement in GI well-being (\(\text{OR}=1.36; 95\% \text{CI}=1.07, 1.73\))\(^{26}\). Similarly, the percentage of responders for GI well-being was higher in the Probiotic group (52\%) vs. the Control group (36.1\%) (\(P=0.025; \text{OR}=1.92; 95\% \text{CI}=1.09, 3.40\)) in the first paper\(^{21}\), but did not differ in the second\(^{26}\). A positive effect was observed in the pooled analysis (\(P=0.015; \text{OR}=1.53; 95\% \text{CI}=1.09, 2.16\)), with a difference in the responder rate of 10.6\% (Probiotic group, 53.2\% vs. Control group, 42.6\%) and a Number Needed to Treat (NNT) of 9.5\(^{26}\).

\textbf{Frequency of digestive symptoms}

Individual digestive symptoms, including abdominal pain/discomfort, bloating, flatulence/passage of gas, and borborygmi/rumbling stomach was evaluated weekly using a five-point Likert scale that ranged from 0 (never) to 4 (every day of the week)\(^{26,21}\). The composite score for these 4 symptoms ranged from 0 (none of the symptoms) to 16 (all symptoms, every day).

The scores from the 4-week intervention period showed an overall significant decrease in individual digestive symptoms in the Probiotic group vs. the Control group in both studies (\(P=0.044\) and \(P=0.33\)), and

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>(Guyonnet, Schlumberger, Mhamdi, Jakob, &amp; Chassany, 2009)</th>
<th>(Marteau, Guyonnet, Lafaye de Micheaux, &amp; Gelu, 2013)</th>
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<tbody>
<tr>
<td>Gastrointestinal Well-being</td>
<td>Percentage of women reporting an improvement was higher ((P=0.006) in Probiotic group vs. Control group. Percentage of responders was higher ((P=0.025) in Probiotic group vs. Control group.</td>
<td>Percentage of women reporting an improvement was not different between groups. Percentage of responders not different between groups.</td>
</tr>
<tr>
<td>Frequency of digestive symptoms</td>
<td>Observe more pronounced decrease ((P=0.044)) in overall score of 4-week period in Probiotic group vs. Control group. Borborygmi frequency showed higher decrease ((P=0.016)) in Probiotic group vs. Control group. Flatulence frequency showed higher decrease in Probiotic group vs. Control group in week 1 ((P=0.041), 2 ((P=0.028), 4((P=0.008). No difference in bloating score, abdominal pain or discomfort score.</td>
<td>Observe more pronounced decrease ((P=0.033)) in overall score of 4-week period in Probiotic group vs. Control group.</td>
</tr>
<tr>
<td>Bowel function</td>
<td>Stool frequency did not differ between groups. Stool consistency decrease ((P=0.02) in Probiotic group vs. Control group.</td>
<td>Results was not measured</td>
</tr>
<tr>
<td>Health-related quality of life</td>
<td>Digestive comfort dimension of Food and Benefits Assessment questionnaire increase ((P=0.027) in Probiotic group vs. Control group. Results of Psychological General Well-Being Index Questionnaire not differ between groups.</td>
<td>Results was not measured</td>
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this was also found in the pooled analysis ($P=0.003$). Guyonnet et al. (2009) reported all results for changes in each individual symptom over the 4-week period. Borborygmi frequency decreased more in the Probiotic group vs. the Control group over the 4-week period ($P=0.016$); the decrease in flatulence frequency was higher in the Probiotic group than in the Control group in the first ($P=0.041$), second ($P=0.028$), and fourth weeks ($P=0.008$). No significant differences were observed in the bloating score or in the abdominal pain or discomfort score$^{21}$.

**Bowel function**

Subjects reported daily bowel movements according to the Bristol stool scale$^{21}$. Only one study presented results for this secondary endpoint. Stool frequency did not differ between the Probiotic group and the Control group, but a decrease in stool consistency was observed in the Probiotic group vs. the Control group ($P=0.02$)$^{21}$.

**Health-related quality of life**

The Health-related quality of life (HRQoL) was assessed by self-administration of two questionnaires: the Food and Benefits Assessment (FBA) and the Psychological General Well-Being Index (PGWBI) at three time points: baseline, after 4 weeks, and after 8 weeks$^{21}$. Guyonnet et al. (2009) observed an increase ($P=0.027$) in digestive comfort as measured by the FBA questionnaire in the Probiotic group vs. the Control group after 4 weeks; however, the results of the PGWBI questionnaire were no different in the Probiotic vs. the Control groups$^{21}$.

**Discussion**

This review examined whether the consumption of probiotic fermented milk containing *B. lactis* CNCM I-2494/*B. lactis* DN-173 010, together with yogurt symbiosis strains and *L. lactis*, improved minor digestive symptoms in healthy women.

We only included randomized controlled studies that showed high quality methodology and a low risk of bias. These two studies showed that the inclusion of this specific probiotic in the everyday diet of healthy women could improve digestive comfort. Moreover, none of the studies we looked at reported a worse outcome for the interventional group, in agreement with findings of a recent meta-analysis$^{20}$. Ford et al. (2014) examined the efficacy and safety of this probiotic in idiopathic constipation and reported no adverse events in three identified RCTs$^{20}$. Our narrow and specific research question (the combination of 5 bacterial strains in fermented milk; a specific GI condition; and a specific target population) explains the limited number of studies (n=2) included in this review compared to other systematic reviews of probiotics and IBS.

GI well-being was the main outcome. Healthy women in the RTC conducted by Guyonnet et al. (2009) reported improvement in GI discomfort after just one week of probiotic ingestion$^{21}$. Guyonnet et al. (2009)$^{2}$ conducted another open-label study that assessed the effect of the same probiotic fermented milk in its commercially available form in real-life conditions i.e. in 371 men and women who consumed one or two portions of probiotics/day for 14 consecutive days$^{21}$. The results were obtained using a self-reported digestive comfort questionnaire. The percentage who reported improvement in digestive comfort was higher in volunteers who consumed this probiotic in low and higher doses (82.5% and 84.3% in the 1-portion and 2-portion groups, respectively) compared with the control group (2.9%)$^{21}$. These results indicate an overall positive effect for probiotics on the promotion of GI well-being.

Interpreting the magnitude of the effect (responders’ rate difference = 10.6%; NNT = 9.5) is important for assessing the effect of this probiotic food on GI discomfort. There is a lack of guidelines for assessing the effects of functional foods on GI discomfort in the general population, and most of the thresholds/differences considered to be clinically relevant are defined for assessing drugs in diseased populations (e.g. a 10% difference in IBS for the rate of responders). Generally the magnitude of the anticipated effect for food is smaller than for drugs$^{28}$. A recent extensive systematic review of the effects of probiotics on IBS and chronic constipation$^{20}$ showed an NNT for the analysis of persistence of symptoms of 7–8, which differs slightly from the rate of responders observed for studies with the probiotic food containing *B. lactis* CNCM I-2494/*B. lactis* DN-173 010 in healthy subjects (NNT=9.5). Another recent meta-analysis assessed the effect of fiber supplementation on IBS$^{50}$, with fiber supplementation showing a significant benefit on a dichotomous outcome for IBS symptoms with an NNT of 10. The evidence for using rifaximin to treat IBS was reviewed recently$^{50}$ and showed a therapeutic gain of 9.8% for the responder’s rate, corresponding to an NNT of 10.2. The observed improvement in GI well-being with this probiotic food is in the lower spectrum of what is considered clinically relevant for a more severely affected population (i.e. patients with IBS) and therefore could be considered relevant.

Digestive symptom frequency was evaluated by both of the two included trials, and interventional probiotic study groups report decreased symptom severity$^{21,26}$. Although the relationship between the assessed digestive symptoms seems intuitively clear, in the Probiotic group there was a decrease in borborygmi and flatulence but no significant differences in bloating score or in the abdominal pain or discomfort score$^{21}$.
Bowel function was an important secondary outcome that was assessed based on decreases in stool consistency. Other studies have assessed effects on bowel function using alterations in colonic transit time to show the mechanism of action. In a double-blind cross-over study of healthy women who consumed three 125-g cups per day of fermented milk containing *Bifidobacteria animalis* DN-173 010 (Probiotic group) or fermented milk without bifidobacteria (Control group), x-ray analysis of the segmental colonic transit time showed that in the Probiotic group, the sigmoid transit time was shorter than for any other colon segment. Bouvier et al. (2001) conducted a double-blind study of healthy men and women that demonstrated that fermented milk containing *Bifidobacteria animalis* DN-173 010 improved colonic transit time and observed that the effect was more pronounced in women than in men. Miller et al. (2013) conducted a meta-analysis to study the short-term (10–28 days) effects of probiotic supplementation on intestinal transit time. They included 13 RCTs involving different probiotic strains and clinical conditions. The authors’ general conclusion was that probiotic supplementation was associated with reduced intestinal transit time, with consistent treatment effects in older adults. When a subgroup analysis of the Miller et al. meta-analysis was conducted, only two probiotic strains were associated with treatment effects: *B. lactis* HN019 and DN-173 010. Accordingly, it may be of interest to conduct an RCT with fermented milk containing *B. animalis* DN-173 010 in healthy subjects to assess colonic transit time as measured by radio-opaque markers.

In our investigation, only one of the two included studies assessed the HRQoL to ascertain the relevance of the observed improvement in symptoms and in the comfort dimension of GI well-being. Guyonnet et al. (2009) used two questionnaires, with one, considered by the authors to be the primary endpoint, showing an increased HRQoL score for women that ingested fermented milk containing *B. animalis* DN-173 010. The instrument was developed and validated for patient-reported outcomes to assess specifically the benefits of food or diet on HRQoL. Based on this study, we can conclude that results about probiotics leading to an improvement in digestive comfort dimension seem promising.

Product effects are dose-specific, and a recommendation about an adequate daily amount of probiotic intake should be based in its efficacy in clinical trials. The two included RCTs used two units of fermented milk containing *B. animalis* DN-173 010/daily, so the observed (related) effects are attributed to consuming this amount. Notably, the tested fermented milk product contained the same quantity of the different strains of bacteria. This reinforces the conclusion about the efficacy of this probiotic food, as the same product (matrix and type and quantity of bacterial strains) and same daily dosage (two 125-g servings per day) were tested in both independent RCTs. However, a previous study conducted by Guyonnet et al. (2009) compared groups consuming 1 or 2 portions of fermented milk product containing *B. animalis* DN-173 010 per day and did not find any significant difference between the low and high intake groups in terms of digestive comfort or digestive symptoms.

It is important to keep in mind that this review analyzed a specific probiotic that is included in a commercial fermented milk product in healthy volunteers. Thus, our results could help clinicians make evidence-based decisions about whether this probiotic should be recommended.

### Mechanisms of action

The effects of probiotic fermented milk product containing *B. lactis* CNCM 1-2494 could be mediated by several mechanisms of action that are involved in the control of GI functions and in interactions with gut microbiota.

### Effect on colonic transit time

Marteau et al. (2002) studied healthy women who ingested three 125-g cups per day of a fermented milk product containing *B. animalis* DN-173 010 (Activia®) vs. placebo. In one group containing *B. animalis* DN-173 010 vs. placebo. The protocol analysis was conducted with radio-opaque markers (three different types on three consecutive days, and a simple abdominal x-ray was taken on the fourth day). Colonic transit time was reduced by the probiotic test product (-12.2 h; \(P = 0.026\)).

### Effects on hypersensitivity and intestinal permeability

In everyday life, there are many stressful events that can exacerbate digestive symptoms, particularly in IBS patients, and there is evidence of an association between visceral hypersensitivity and some IBS symptoms. Moreover, there is frequently an increase in intestinal permeability in stressed patients, and this is associated with digestive disorders like bloating. Experimental results in an animal model of acute stress-induced visceral hyperalgesia and increased intestinal permeability show that fermented milk containing *B. lactis* CNCM 1-2494 is beneficial for symptoms control. Administration of a fermented milk probiotic at a concentration corresponding to 3.3 x 10^9...
Gut microbiota and probiotics could influence brain activity via signaling mechanisms and thus modulate behaviour. One interesting study measured the brain’s response to an ‘emotional faces attention task’ vs. the resting brain activity of women that consumed 2 units per day of fermented milk containing B. lactis CNCM I-2494 for 4 weeks and compared the data to that from controls and from a non-intervention group. The authors used functional magnetic resonance imaging before and after the intervention and found that probiotic ingestion modulated the responsiveness of an extensive brain network in healthy women, especially changes in midbrain connectivity.

Effects on gut microbiota

Gut microbiota includes both resident commensal bacteria and transient microbes introduced by the diet. Little is known about the role of diet on gut microbiota homeostasis. Veiga et al. (2014) used quantitative metagenomics, in silico genome reconstruction, and metabolic modeling to examine changes in the gut microbiome induced by a fermented milk product. In a subject with IBS, fermented milk containing B. animalis potentiates short chain fatty acid production, especially production of butyrate, and decreased the levels of the pathobiont Bilophila wadsworthia compared to a milk product. Another study reported that probiotic-containing food (B. lactis, L. lactis, L. bulgaricus, and S. thermophilus) reduces intestinal inflammation in a murine model of colitis. This was associated with an increase in lactate-consuming and butyrate-producing bacteria, a decrease in cecal pH, and an increase in select cecal short chain fatty acids.

An interesting study characterized the fecal human microbiomes of twin pairs after they consumed commercially fermented milk containing 5 bacterial fermented milk products and also studied the metatranscriptomes of gnotobiotic mice. The results show that consumption of fermented milk products was not associated with statistically significant changes in the resident community members within and between individuals. They also found that B. animalis subsp. Lactis CNCM I-2494 was the most prominent member in the microbiota during the 7-week period of fermented milk product consumption. More research is needed to understand how much influence such factors have on the well-being and digestive comfort (minor GI disturbance) of healthy subjects.

Conclusion

This review found evidence that probiotic fermented milk containing B. lactis CNCM I-2494, when consumed by healthy women, can improve GI well-being and decrease the frequency of GI symptoms.

Author contributions

Dan L. Waitzberg, Flávio A. Quilici, Sender Michzputen and Maria do Carmo Friche Passos contributed equally to this work; Dan L. Waitzberg and Maria do Carmo Friche Passos designed the research; Dan L. Waitzberg, Flávio A. Quilici, and Sender Michzputen performed the research; Dan L. Waitzberg and Maria do Carmo Friche Passos and Flávio A. Quilici analyzed the data; and Dan L. Waitzberg and Sender Michzputen wrote the paper.

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