

## Caveat emptor

### *“Probiotics” might not be what they seem*

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#### ABSTRACT

**OBJECTIVE** To assess whether commercially prepared probiotic products contain viable organisms, as claimed by their manufacturers, particularly whether products labeled as containing *Lactobacillus* did so. To identify and quantify as many species as feasible and to compare them with the contents listed on labels.

**DESIGN** Randomized, double-blind trial.

**SETTING** Community hospital in Chilliwack, BC.

**MAIN OUTCOME MEASURES** Trial of 10 randomly chosen brands of probiotic preparations bought over-the-counter in British Columbia's lower mainland. Only products claiming to contain *Lactobacillus* were included in this study. Viable organisms in each probiotic brand and quantities of *Lactobacillus* in each product.

**RESULTS** None of the 10 products tested matched their labeled microbiologic specifications. Two brands grew nothing aerobically or anaerobically. No *Lactobacillus* grew in five brands, although their labels stated that this was the main species. Eight brands contained viable cells, but only 10% of the number stated by their manufacturers.

**CONCLUSION** Most product labels did not adequately identify or quantify microbes. Use of probiotics should not be recommended at this time.

#### RÉSUMÉ

**OBJECTIF** Vérifier si le contenu des produits probiotiques commerciaux renfermant des organismes vivants est conforme aux prétentions des fabricants, notamment si les produits étiquetés comme renfermant du lactobacille en contiennent vraiment. Identifier et quantifier le plus de produits possible et comparer les résultats obtenus au contenu indiqué sur l'étiquette.

**TYPE D'ÉTUDE** Essai randomisé à double insu.

**CONTEXTE** L'hôpital municipal de Chilliwack, C.-B.

**PRINCIPAUX PARAMÈTRES ÉTUDIÉS** Choix au hasard de 10 marques de produits probiotiques en vente libre dans le plateau continental de Colombie-Britannique. Seuls les produits censés contenir du lactobacille ont été inclus. Présence d'organismes viables et quantité de lactobacilles dans chaque produit.

**RÉSULTATS** Aucun des produits étudiés ne correspondait aux spécifications microbiologiques de l'étiquette. Dans deux cas, les cultures aérobiques et anaérobiques ont été stériles. Cinq autres n'ont donné aucune croissance de lactobacille, même si ce devait être l'espèce principale selon l'étiquette. Les huit marques avec des cellules viables contenaient seulement 10% des quantités annoncées par le fabricant.

**CONCLUSION** La plupart des étiquettes n'indiquaient pas adéquatement l'identité et la quantité des microbes. À l'heure actuelle, on ne devrait pas promouvoir l'usage des probiotiques.

This article has been peer reviewed.

Cet article a fait l'objet d'une évaluation externe.

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Probiotics is a broad term that refers to the concept of feeding live microbial organisms to human beings with the goal of preventing and treating disease. The word probiotic is derived from a Greek term and means “for life.” The first reference to health benefit dates back to the early 1900s when the Nobel prize–winning Russian physician Elie Metchnikoff hypothesized that Bulgarian peasants lived long, healthy lives because they consumed fermented milk products.<sup>1</sup>

In the last century, many proponents of probiotic treatment have cited various benefits: “maintains healthy digestion,” “assists in general well-being,” “builds immunity, adding years to your life.” Much of the enthusiasm for probiotic treatment is among proponents of what might be termed alternative medicine. With any commonly used Internet search engine you will get more than 16 000 sites referencing the word. It is hardly a surprise that sales are soaring.<sup>2</sup>

Although probiotic preparations have been available commercially for years, data on their benefits and mechanism of action remain scarce.<sup>3</sup> Possible mechanisms include the synthesis of antimicrobial substances, competition for nutrients required for growth of pathogens, modification of toxins or toxin receptors, and stimulation of nonspecific immune responses to pathogens.<sup>4</sup>

In recent decades, *Bifidobacterium*, *Saccharomyces boulardii*, and *Lactobacillus* have been investigated for their probiotic potential. One of the most commonly studied probiotic organisms is *Lactobacillus casei* subsp *rhamnosus* (LGG).<sup>5</sup> Studies attempt to show benefit in prevention and treatment of various illnesses (such as diarrhea, urinary tract infections, irritable bowel syndrome, yeast infections, cancer, and hypertension) but fail to demonstrate sound evidence.<sup>6</sup>

A few rigorously controlled scientific trials have been conducted. Recently, a systematic review of published, randomized, double-blind, placebo-controlled trials demonstrated clinically significant evidence that probiotic organisms (in particular LGG) are beneficial in reducing the duration of acute infectious diarrhea in children.<sup>7</sup> Other trials have demonstrated benefit

from probiotic treatment in ameliorating symptoms of antibiotic-associated diarrhea among children.<sup>8</sup> In these studies meticulous care was taken to keep the probiotic organisms in their “live” form. Statistical heterogeneity was noted across the studies. There were differences in both the dosage and duration of treatment. Importantly, products cited in these particular studies contained at least 10 times more probiotic organisms than commercially available products do.<sup>9</sup>

While no obvious adverse effects from these products have been reported in any study, information is limited.<sup>10</sup> Geralk Tannock in Horizon Scientific Press says “the pathogenicity of lactobacilli is generally low; one case has been reported in which a probiotic lactobacillus was found associated with a liver abscess.”<sup>11</sup>

So what are physicians’ attitudes toward their patients’ use of probiotic products? A recent survey, published in the *Canadian Medical Association Journal* asked whether physicians recommend probiotic treatments to their patients to prevent antibiotic-associated diarrhea.<sup>12</sup> Of the 68% who responded, 32% reported that they recommend probiotic products to their patients when prescribing antibiotics.

Some concerns, especially in a UK study published in the *British Medical Journal*,<sup>13</sup> have been noted about the contents of commercial probiotic preparations. The microbial content of 13 different brands bought over-the-counter in Britain was investigated. This study revealed species that were not listed on their labels and numbers of viable cells far lower than those stated by their manufacturers.

Many people are buying probiotic products off the shelf, and some physicians are, at least in part, recommending these products to their patients. This project was undertaken to answer the following questions. Are North American commercial probiotic preparations viable? Do they contain *Lactobacillus* as stated on their labels? What is the quantity of lactobacilli in each product? Do these products contain species not listed on their labels?

## METHODS

I purchased, at random, 10 different brands of probiotics from six different retail stores in BC’s lower

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mainland. Most medical studies used *Lactobacillus* species; therefore I chose only products claiming to contain this bacterium. I complied with instructions on the containers and refrigerated as directed.

The preparations were aseptically transferred from their original containers to sterile screw-topped tubes. A microbiologist then took the specimens to the laboratory to be cultured. Both the person transferring the powder and the microbiologist were blinded to the contents of the preparations (Table 1).

The objective was to determine whether the products did, in fact, contain viable bacteria. Each product was cultured twice under appropriate conditions. The cultures were examined to determine whether *Lactobacillus* species grew as stated on each container.

Colonies on each Petri dish were quantified. I compared my results with the quantity labeled on each product. Species other than those listed on the product containers were identified and recorded. Due to the limitations of this study, I was unable to

identify all species contained in each sample. All products were manufactured in North America.

## RESULTS

None of the products matched their labeled microbiologic specifications qualitatively or quantitatively (Table 2). Two of the 10 probiotic products cultured (specimens A and D) grew nothing. Four brands (A, D, E, and I) did not grow the *Lactobacillus* species listed on their labels. Four brands (B, C, E, and G) contained species not listed on the label (*Enterococcus faecium*, *Bifidobacterium*, *Streptococcus oralis*). Some of the species not listed on the label were found to be resistant to ciprofloxacin. This was an incidental finding of unclear importance.

Each brand quantified the bacterial species listed on its label differently. Specimen E did not quantify at all. Some products quantified per capsule, others quantified all species into one number, and yet others used percentages. The number of probiotic organisms per capsule, as claimed by manufacturers, ranged from 2 to 20 billion. My results ranged from 20 to 80 million.

## DISCUSSION

Using lactic bacteria to treat human disease is not a new concept. Recent studies report evidence in favour of probiotic products for treating specific conditions. Standardized scientific analysis precisely defining and quantifying each probiotic strain is still required. In theory, if probiotic treatment is proven beneficial in reducing illness, the cost of medical care will be reduced, stays in hospital will be shorter, and fewer days will be lost from work.

This study found that commercially available over-the-counter products were inaccurately labeled. Some products tested contained only dead bacteria. Most labels did not adequately identify the microbes in their products. *Lactobacillus* was listed among the contents of each product but was found in only half the samples and in numbers one tenth their stated concentration. There were inconsistencies in the nomenclature and quantification of these products.

**Table 1. Standardized culture procedure**

<b>Method for culture test</b>
<ul style="list-style-type: none"> <li>Aseptically transfer two capsules from original containers to sterile screw-topped tubes. Obtain specimen by cutting capsule with sterile scalpel</li> <li>Label specimens by sequential number</li> <li>Use Biological Safety Cabinet for specimen preparation and planting</li> <li>Dispense 6 mL of 0.45% saline into sterile screw-topped tubes</li> <li>Suspend or dissolve two loopfuls of the specimen into the saline solution</li> <li>Replace top and blend with the Vortex mixer for 30 s. Allow tube to stand for 30 min</li> </ul>
<b>Method for set-up</b>
<ul style="list-style-type: none"> <li>Put 1 loopful of solution on glass slide for Gram stain</li> <li>Put 1 drop onto the following culture media: BAP, Choc, Mac, Bruc, CNA</li> <li>Streak for isolation</li> <li>Put 1 drop into a thio broth (thioglycollate with indicator, vitamin K1, and hemin)</li> <li>Use 1:1000 loop and streak to a BAP for rough quantitation</li> </ul>
Incubate for 48 hours at 37°C
Incubate plates both aerobically and anaerobically
Perform Gram stain on the initial specimen
Count and identify as many colony types as possible on each medium
Identify and test for susceptibility as required
<b>Record results</b>
BAP—bacterial alkaline phosphatase, CNA—calcium nutrient agar.

**Table 2. Culturing results**

SPECIMEN CHARACTERISTICS	A	B	C	D	E (CHILDREN'S FORMULA)	F	G	H	I	J
Viable organisms in sample	No growth	Lactobacillus species and Bifidobacterium species	Lactobacillus species and Enterococcus faecium	No growth	E faecium	Lactobacillus species	Streptococcus oralis and Lactobacillus species	Lactobacillus species, possibly 2 types	E faecium	Lactobacillus species
Lactobacillus cultured in samples	No	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes
Species identified not listed on label	None	Bifidobacterium	E faecium	None	E faecium	None	S oralis	None	E faecium	None
Quantity per capsule as stated on label	2 billion	4 billion viable cells	1.5 billion live cells	4 billion active cells	Not listed	10 billion active cells	6 billion active cells	6 billion active cells <sup>†</sup>	6 billion live cells (enteric coated)	3 billion viable cells
Actual quantity per capsule	No growth	50 million	20 million	No growth	20 million	80 million	50 million	50 million	20 million	30 million
Microorganisms manufacturers claimed to be in product	L acidophilus	• L rhamnosus • L acidophilus • E faecium	• L acidophilus • B bifidum • B longum	• L rhamnosus • L acidophilus	• L acidophilus • B bifidum • B infantis	• L rhamnosus • L acidophilus • B bifidum	• L rhamnosus • S thermophilus • L acidophilus • B longum • L casei • Bulgariars	• L rhamnosus • L casei • L acidophilus • B longum	• L acidophilus • L rhamnosus • Bifidobacterium • E faecium	L rhamnosus
Manufacturer	UAS Laboratories in Minnetonka, Minn	SISU enterprises in Burnaby, BC	Kyo-Dophilus, "The Friendly Trio"—for optimal friendly bacteria for balanced intestinal flora" in Vancouver, BC	Swiss Herbal Remedies Ltd, "Probiotic culture anti-cholesterol Plus Fos" in Richmond Hill, Ont	Nutrition Now Children's PB8 in Vancouver, BC	Natural Factors Probiotic Formula in Burnaby, BC	Trophic Canada Ltd in Toronto, Ont	Natural Factors in Burnaby, BC	Swiss Natural Sources in Toronto, Ont	Swiss in Burnaby, BC

\*Per mL of initial dilution.

<sup>†</sup>No expiry date.


Extra species not listed on the label were identified. It was impossible to identify all organisms in each product due to lack of funding.

No current government regulations apply to over-the-counter probiotic products.<sup>14</sup> The public has no guarantee that these products contain viable organisms or that they contain the species listed on their labels. Many of the products tested contained species other than those listed, none of which are known to be harmful. Without government regulation, however, products that contain harmful bacteria could be on the market.

Growing public interest in wellness has fueled demand for more probiotic products. In an attempt to support our patients, and in light of the low toxic effects, many physicians do not advise against using these products.

This study has some limitations. It is possible that mostly unsuitable brands were chosen, although the choice was random. The testing was carried out in only one laboratory, although the method was explicit and standardized.

## CONCLUSION

This study indicates that many commercial probiotic preparations do not contain the active ingredients listed on their labels. Consumers essentially are buying products that have no proven benefit and are not what they claim. 

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### Competing interests

*None declared*

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### EDITOR'S KEY POINTS

- Probiotic preparations contain live microbial organisms used to prevent and treat disease. Some evidence suggests they reduce the duration of diarrhea. Although sales have soared, there are some concerns about the accuracy of manufacturers' claims for commercial preparations.
- This study was designed to determine whether commercially available probiotic products with *Lactobacillus* contained the amount alleged on the packaging.
- Ten randomly chosen examples of probiotic preparations were cultured in the laboratory; several grew no colonies at all, some had very small colony counts, and some capsules contained bacilli not listed on the label.
- Family physicians should make their patients aware that commercial probiotic preparations probably do not contain what their labels say they do. Caveat emptor.

### POINTS DE REPÈRE DU RÉDACTEUR

- Les préparations probiotiques contiennent des micro-organismes vivants censés prévenir et traiter des maladies. Certaines observations suggèrent qu'elles réduisent la durée des diarrhées. Malgré une forte progression des ventes, des doutes ont été émis concernant les précisions fournies par les fabricants.
- Cette étude avait pour but de vérifier si des préparations commerciales de probiotiques avec *lactobacille* contenaient les quantités annoncées sur l'emballage.
- Dix préparations probiotiques choisies au hasard ont été cultivées en laboratoire; plusieurs sont demeurées stériles, d'autres ont donné un très petit nombre de colonies et certaines capsules renfermaient des bacilles non indiqués sur l'étiquette.
- Le médecin de famille devrait avertir ses patients que le contenu des préparations commerciales de probiotiques ne correspond probablement pas à ce qu'annoncent les étiquettes. Aux risques de l'acheteur.

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