

## Probiotics and Cancer Therapy

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### What are probiotics?

Probiotics are considered to be live microorganisms. They are a mixture of beneficial live bacteria and/or yeasts that live in the body and play a significant role in the gut microbiome composition.<sup>1</sup> The microbiome consists of microbes that are both helpful and potentially harmful. Most are symbiotic (where both the human body and microbiota benefit) and some are pathogenic, but in small numbers are rarely harmful.

In a healthy body, pathogenic and symbiotic microbiota coexist without problems. If there is a disturbance in the balance, brought on by illness, cancer treatments, certain diets, or the prolonged use of antibiotics or other bacteria-destroying medications, dysbiosis can occur and the body may become more susceptible to disease.<sup>2</sup>

Probiotics have shown promise for a variety of health purposes. However, more research is needed to ascertain which probiotics are most helpful, the optimal dosing and the patient populations most likely to benefit.<sup>3</sup> A 2018 meta-analysis of 228 trials by Dr. LV McFarland et al., indicated strong evidence supporting the hypothesis that the efficacy of probiotics is both strain-specific and disease-specific.<sup>4</sup>

**Food products** containing probiotic microorganisms are generally classified as **food**.

**Pharmaceutical dosage forms** such as tablets and capsules containing probiotics are generally classified as **Natural Health Products (NHPs)**.<sup>5</sup>

### Which food products contain probiotics?

Probiotics in foods are primarily found in dairy products such as yogurts, cheeses and milk-based beverages such as kefir and buttermilk.

Probiotics can also be found in non-dairy foods and drinks such as miso, sauerkraut, pickled vegetables, kombucha and kimchi.

**Plant-based milks** such as soy, almond, cashew, coconut and rice milk often contain natural probiotics. Manufacturers may also add in active probiotic cultures and sugar.

**Kefir** is a tart and tangy cultured milk drink packed with various strains of beneficial probiotics and live cultures. Plain and flavored varieties of kefir are available however the flavored variety often contains added sugar.

**Miso soup** is fermented soy that contains healthy bacteria. Food sources of soy, including miso, tofu and soy milk are generally considered safe for people with and without hormone-sensitive cancers (such as breast, endometrial and prostate cancers).

**Kombucha** is a drink produced by fermenting sweet tea with a culture of yeast and bacteria. Commercial kombucha tea is labelled as non-alcoholic and contains less than 0.5% alcohol.<sup>6</sup> Kombucha may also contain high amounts of caffeine and sugar. The acidity of some kombucha teas may affect the absorption of drugs that are sensitive to gastric pH level, thereby reducing their effectiveness.<sup>7</sup>

**Commercially prepared probiotic food and drink are generally considered to be safe for people undergoing cancer treatment.** In addition, food sources of probiotics are composed of a complex variety of nutrients that work synergistically, thus providing an added benefit to the patient.

## **What are Natural Health Products (NHPs) probiotics?**

When probiotics are sold in a pharmaceutical dosage form (ie. capsules or tablets), they are considered to be Natural Health Products (NHPs) and regulated differently than foods containing probiotics.<sup>5</sup>

Probiotics as NHPs are regulated by Health Canada's Natural Health Products Directorate (NHPD).<sup>5</sup>

Although probiotic supplements are generally considered safe to use in healthy individuals, they can potentially become pathogenic and cause infections in immunocompromised patients. Many patients receiving chemotherapy drugs have weakened immune systems because of chemotherapy-induced leukopenias and as such, **NHP supplements (capsules and tablets) are generally NOT recommended for patients undergoing treatment with cancer medications.**

## **Can probiotics as NHPs be harmful?**

Cancer patients have compromised immunity caused by primary diseases, chemotherapy and radiotherapy. The effects of probiotics in this patient population may differ from those of healthy people and raise several critical concerns. The potential risks of probiotics in cancer patients and potential for serious invasive disease needs to be carefully weighed against their benefits.<sup>8</sup>

- Few studies have looked at the safety of probiotics in detail. There is a lack of solid information on the frequency and severity of side effects.
- Possible adverse effects of probiotics include systemic infections, gastrointestinal side effect, skin reactions, production of harmful substances by the probiotic microorganisms, transfer of antibiotic resistance genes from probiotic microorganisms to other microorganisms in the digestive tract, harmful effects of probiotic metabolites and abnormal stimulation of the immune system.<sup>8</sup>
- Some probiotic products have been reported to contain microorganisms other than those listed on the label. In some instances, these contaminants may pose serious health risks.<sup>3</sup>
- In a 2021 review conducted by Lu et al., case reports of oncology patients developing bacteremia following probiotic supplement use were documented.<sup>8</sup>
- A 2006 review conducted by Boyle et al. cited 12 cases of bacterial sepsis and 24 cases of fungal sepsis that were likely linked to probiotics.<sup>9</sup>
- Early observational data suggest that indiscriminate use of commercially available probiotics may be harmful in the setting of immune checkpoint blockade treatment in cancer patients.<sup>10</sup>

Although probiotic NHP supplements are generally safe to use in healthy individuals, many patients receiving cancer treatment have weakened immune systems and as such, NHP supplements **are generally NOT recommended for patients undergoing treatment with cancer medications.**

Probiotic NHPs supplements (capsules and tablets) have been promoted to prevent chemotherapy–induced diarrhea, however, few studies have looked at the safety of NHP probiotics in detail. The overall evidence to support their use is limited due to small sample size, poor methodology, variation in the species and strains of bacteria, and in the dosage and duration of administration.

Large scale, well designed clinical RCTs are needed to establish the efficacy and safety of NHP probiotics in the prevention of chemotherapy-induced diarrhea.

**A discussion should occur between the patient and oncologist or oncology pharmacist regarding the risks and benefits prior to taking a Natural Health Products/NHP probiotic supplement (capsules or tablets).**

**Commercially prepared probiotic food and drink are generally considered to be safe to consume for people undergoing cancer treatment.**

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