

Your Guide to *Probiotics*

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BJN
British Journal of Nursing

**Gastrointestinal
Nursing**

What are probiotics?

Probiotics are ‘live microorganisms which, when administered in adequate amounts, confer a health benefit on the host’ (Food and Agriculture Organization (FAO) and World Health Organization (WHO), 2002).

Brief history of probiotics

- In the early 1900s, Professor Élie Metchnikoff advocated the intake of fermented dairy foods containing live lactic acid-producing bacteria, believing this would reduce the number of harmful gut microbes that produced toxins linked to ageing (Hamilton-Miller, 2008)
- In the 1930s in Japan, Dr Minoru Shirota applied Metchnikoff’s theory and produced a fermented milk drink containing high numbers of a live *Lactobacillus* strain, robust enough to survive passage through the gut (Levin, 2011).

Probiotics usually exert their effect on the human body via the gut. They often have more than one mechanism of activity, e.g. producing compounds that inhibit the growth of gut pathogens (Dobson et al, 2012), stimulating immune responses (van Baarlen et al, 2013) and positively influencing colonic metabolism (Dai et al, 2013). They can be used to treat gastrointestinal disorders ranging from diarrhoea, inflammatory bowel disease and cancer, to irritable bowel syndrome (IBS) and constipation. They may also help with extraintestinal problems owing to their influence on immune responses and because gut bacteria can colonise the urogenital area.

A health benefit reported with one probiotic, however, may not necessarily be seen with another. For example, some probiotics reduce the incidence of antibiotic-associated diarrhoea (Hickson et al, 2007; Wong et al, 2013), whereas others show no effect (Allen et al, 2013).

Probiotic products contain one or more strains (bacteria or yeasts) and sometimes vitamins, fibre or prebiotics. In general, they can be purchased in the form of fermented dairy products (drinks and yoghurts), other drinks, capsules, powders

or tablets. The FAO and WHO guidelines state that probiotics should be fully characterised to the level of the genus (e.g. *Lactobacillus*), species (e.g. *casei*) and strain (e.g. Shirota).

Quality control and product labels

The advertising and sale of probiotics have to abide by several UK regulations including those governing trading standards and commercial communications covering health or medical claims. It is best to pick a product from a trusted manufacturer (International Scientific Association for Probiotics and Prebiotics (ISAPP), 2013). When probiotics were first introduced in the UK, a survey raised concerns about poor and inaccurate labelling. Some contained lower-than-labelled microbial numbers and even the wrong strains (Hamilton-Miller et al, 1999). Most products have best by dates (BBDs). Even though the product may be safe to consume after this date, it will not be at optimum quality (i.e. the cell count may drop). Fermented dairy products normally have a shelf life of 4 weeks if stored correctly; the shelf life of tablets or capsules is usually much longer.

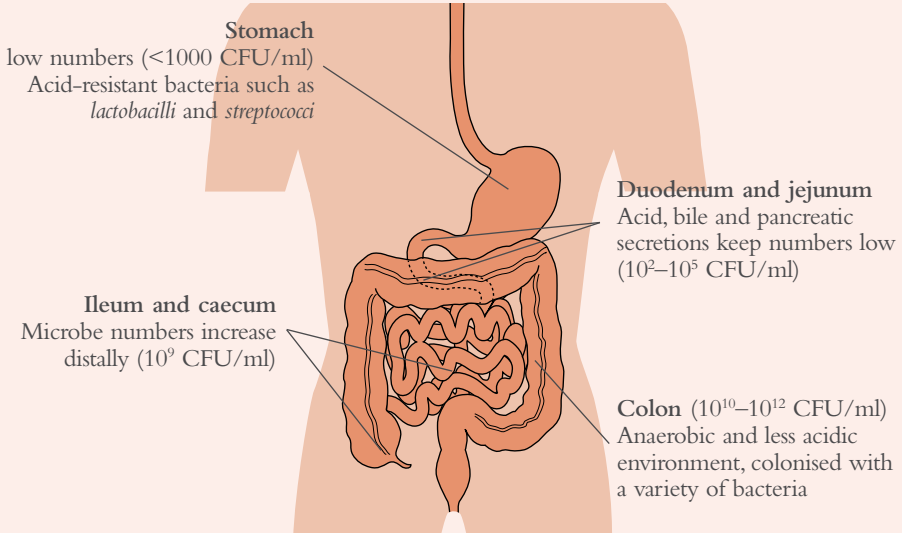
Scientific evidence

Over 9000 probiotic-related papers can be found on PubMed. Of these, over 900 are human trials, but studies may vary in quality. There is, however, strong evidence for several probiotic strains and products in different health areas. Systematic reviews and meta-analyses can be used to identify which strains have been found to be beneficial for particular disorders.

Probiotics that are administered orally should have scientific evidence to prove the strains survive alive in the gut temporarily. This is done by giving the strain(s) to volunteers and analysing their faeces to count the number of live probiotic bacteria. The probiotic bacteria are normally found at high counts during the intake period and for up to 1 week afterward.

Schematic of the human gut showing microbial density

Andrew Bezeal



Adapted from Holzapfel et al, 1998; CFU: colony-forming units—an indicator of the number of live microbial cells

Normally, probiotics do not permanently colonise the gut.

Areas of good evidence of benefit

This is where numerous randomised controlled trials (RCTs) have been conducted:

- Gastrointestinal infections (treatment and/or risk reduction): infectious diarrhoea,

Clostridium difficile (Allen et al, 2010; Goldenberg et al, 2013)

- Gastrointestinal disorders: antibiotic-associated diarrhoea, IBS, constipation, necrotising enterocolitis, lactose maldigestion (Alfaleh et al, 2011; Hempel et al 2012; Hungin et al, 2013; Miller and Ouwehand, 2013; Whelan and Quigley, 2013)
- Extraintestinal infections (reduction of risk and/or duration): upper respiratory tract, urogenital (Hao et al, 2011; Grin et al, 2013)
- General reviews: Guarner et al, 2012; Sanders et al, 2013; Whelan and Quigley, 2013).

Did you know?

- We are born sterile (i.e. 100% human) but, within a few years, we become 90% bacterial
- In adults, microbial cells outnumber human cells by 10:1
- There are about 100 trillion bacteria in the human gut, weighing over 1 kg
- Many of the gut's bacteria perform useful functions, such as protecting against pathogens, supporting the immune system and producing beneficial by-products like vitamins and short-chain fatty acids.

Source: Ainsworth, 2011; Bims, 2013.

Areas of emerging evidence

This is where only a small number of RCTs have been conducted. They are often limited to a few strains and the results are not always strong:

- Gastrointestinal infections: *Helicobacter pylori*, norovirus (Nagata et al, 2011; O'Connor et al, 2013)
- Gastrointestinal disorders: colic, pouchitis, ulcerative colitis (Sung et al, 2013; Szajewska et al, 2013; Whelan and Quigley, 2013)
- Other areas: allergy, cancer, liver disease, obesity-related diseases, periodontal disease

(Fiocchi et al, 2012; da Silva et al, 2013; Gibson et al, 2013; Ma et al, 2013; Serban, 2013; Yanine et al, 2013).

Recommendations

Health professionals recommend that probiotics be taken during and for 1 week after antibiotic treatment, to reduce antibiotic-associated diarrhoea, and for IBS-type symptoms including constipation. If a patient with IBS wants to take a probiotic, the British Dietetic Association advises trying it for at least 4 weeks, and if there is no benefit, discontinuing it or trying another product (McKenzie et al, 2012).

Safety of probiotics

Lactobacilli have been consumed in fermented foods, such as yoghurts and milks, for centuries. Most of the strains used as probiotics have a good record of safe use. Reports even exist of certain strains being used for patients who are critically ill, immunocompromised or HIV-positive. A recent review of the probiotic effect on mortality in critically ill adult patients suggests that probiotics reduce the incidence of pneumonia and length of stay in the intensive care unit (ICU) (Barraud et al, 2013). Proceed with caution, however, before giving probiotics to such patients, as there are case reports (albeit rare) of associated infections. There is concern that the bacteria could translocate from the gut and cause sepsis (Hammerman et al, 2006; Whelan and Myers, 2010).

Cross-checking the evidence on a product's health benefit

- Contact the manufacturer, who may be able to send summaries and reprints of studies on their product or strains
- Check if there is a website for health professionals, where the research may be summarised
- Search PubMed or other databases, but remember that not all studies will contain the word 'probiotic'.

Many probiotics have been used in patients receiving enteral or parenteral nutrition (Whelan and Myers, 2010). Most trials showed either no effect or a positive effect on safety outcomes (e.g. mortality and infections). A health professional must weigh the risks and benefits because the patient may be at risk from his/her own gut bacteria or have poor immune function (Hammerman et al, 2006). The haematology subgroup of the British Dietetic Association Oncology group recently updated its dietary advice for patients with neutropenia, and still recommends the avoidance of probiotics (Beckerson et al, 2013). This advice, however, was based on uncertainty rather than robust evidence of harm. If considering a probiotic for a vulnerable patient, it might be prudent to first check the antibiotic sensitivity of the probiotic strain, so the correct treatment can

The label should state

Full strain name: The genus, species and strain designator, e.g. *Lactobacillus casei* Shirota. Sometimes, a commercial trademarked name may be used, e.g. Bifidus ActiRegularis (also known as *Bifidobacterium lactis* DN-173 010). Different strains of the same species may have differing effects; hence, always check the scientific evidence for a given strain

Number of live cells of the probiotic strain(s) it contains: This may be expressed simply—e.g. 6.5 billion—or more scientifically—e.g. 6.5×10^9 . The term colony-forming units (CFUs) may be used to indicate that the number is a count of live cells. Manufacturers have quality-control procedures to ensure the product contains the right strain and the stated number of live cells at the end of its shelf life

Suggested daily dosage: For instance, one bottle or one tablet per day. Dosage regimen and duration of use in clinical trials should be based on the manufacturer's recommendation

The benefits of a healthy lifestyle: Probiotics are not a substitute for this.

be given immediately if required. It should be noted that a trial with a mix of bacterial strains (Ecologic 641) delivered via nasojejunal tubes to patients with severe acute pancreatitis led to the recommendation that probiotics should not be given to these patients or those with multi-organ failure (Besselink et al, 2008).

Conclusion

Irrespective of a probiotic being a drink or a supplement, a nurse should first check that there is evidence of benefit for the patient concerned and whether there are any studies demonstrating its safe use. If in doubt, contact the manufacturer, who may be able to advise.

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Find the science behind *Lactobacillus casei* Shirota

Science has always been at the heart of the Yakult company. In the field of probiotics, the product has a long history of safe use and a reputation for quality.

A considerable body of research has been conducted with the Yakult strain, *Lactobacillus casei* Shirota. Healthcare professionals can find more information at:

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