FACTSHEET

THE REASONING BEHIND THE BIO-KULT DOSAGE

Bio-Kult is a unique multi-species, multi-strain probiotic with 14 strains of beneficial bacteria. All our strains have shown *in vitro* that they are able to work synergistically together. We believe that it is the greater number of strains in a product that are more important than the dosage.

BIO-KULT LIVE PROBIOTIC STRAINS ARE MANUFACTURED TO THE LATEST HIGH QUALITY STANDARDS

All our products are manufactured to an extremely high standard (cGMP accredited) in our purpose built facility in Somerset, enabling us to stay in complete control of our quality standards. The beneficial bacteria themselves are encapsulated (with a protective coating) during a freeze drying process (lyophilisation). No refrigeration is therefore required and stability is guaranteed for up to 2 years. The Bio-Kult blister packs offer further high protection against moisture and extremes of temperature, thus ensuring the stability, integrity and quality of the product is kept for every individual capsule until the end of shelf life.

THE FULL BIO-KULT COUNT IS GUARANTEED UNTIL THE END OF THE 2 YEAR SHELF LIFE

An independent UKAS accredited laboratory continuously carries out strict humidity and temperature controlled 2 year stability testing for our Bio-Kult range. Each test has so far yielded results to support the stability of the stated live bacterial count for the full 2 year shelf life of the product when kept at room temperature of below 25°C (opposed to only at the time of manufacture). A higher start count is therefore not necessary to counteract instability in shelf life.

A HIGH PROPORTION OF THE BIO-KULT DOSE WILL ARRIVE IN THE SMALL INTESTINE INTACT

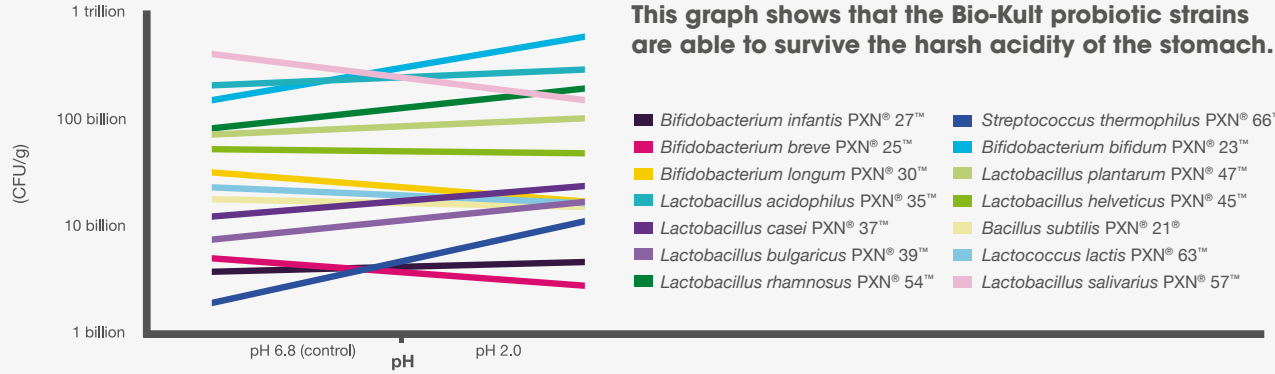
In order to produce beneficial effects within the gastrointestinal tract (GIT), probiotic microorganisms must have the capacity to survive and metabolise in the gut. They must therefore be resistant to stomach acidity. During an *in vitro* study Bio-Kult probiotics held at a pH of 2.0 for a 2 hour period showed no significant loss in viability of any of the bacterial strains. A higher original count is therefore not necessary to counter balance a measureable loss in concentration.

BIO-KULT STRAINS HAVE SHOWN ANTIMICROBIAL EFFECTS AND THE ABILITY TO COLONISE

Tejero-Sarinena[1], found that 13 out of 14 Bio-Kult strains had inhibition activity against pathogens *Salmonella typhimurium, Streptococcus aureus, Escherichia coli, Enterococcus faecalis* and *Clostridium difficile* largely due to the production of varying levels of lactic acid. Many strains showed good adhesive properties to intestinal epithelial cells indicating their ability to temporary colonise the GIT. One strain, the *Bacillus subtilis* PXN 21 has been shown to stimulate the immune system and colonise in the gut for up to 21 days after consumption[2].

MULTI-STRAIN PROBIOTICS APPEAR TO BE BETTER THAN SINGLE STRAINS

Each human being carries trillions of different bacteria, consisting of hundreds of different individual bacterial strains in their gut with each strain having unique properties and health benefits. It could therefore be suggested that a multi-strain probiotic should exert more positive benefits on a wider range of gastrointestinal complaints. A review by Chapman *et al* in 2010[3] concluded that probiotic mixtures appear to be effective against a wider range of symptoms and conditions. The studies reviewed included those looking at irritable bowel syndrome and gut function, diarrhoea, atopic disease, immune function and respiratory tract infections, gut microbiota modulation, inflammatory bowel disease and treatment of Helicobacter pylori infection. The conclusion of this review was that based on all the studies examined, multi-strain products appeared to show greater benefit than single strains, including strains that are components of mixtures themselves.



This graph shows that the Bio-Kult probiotic strains are able to survive the harsh acidity of the stomach.

- *Bifidobacterium infantis* PXN® 27™
- *Bifidobacterium breve* PXN® 25™
- *Bifidobacterium longum* PXN® 30™
- *Lactobacillus acidophilus* PXN® 35™
- *Lactobacillus casei* PXN® 37™
- *Lactobacillus bulgaricus* PXN® 39™
- *Lactobacillus rhamnosus* PXN® 54™
- *Streptococcus thermophilus* PXN® 66™
- *Bifidobacterium bifidum* PXN® 23™
- *Lactobacillus plantarum* PXN® 47™
- *Lactobacillus helveticus* PXN® 45™
- *Bacillus subtilis* PXN® 21®
- *Lactococcus lactis* PXN® 63™
- *Lactobacillus salivarius* PXN® 57™

PROBIOTICS MULTIPLY QUICKLY ONCE IN THE GUT

Multiplication of bacteria in the correct environment of the gut will be rapid. Some say with numbers possibly doubling every 20 minutes to eight hours.

NUMEROUS STUDIES SHOWN BENEFIT WITH DOSAGES BETWEEN 5 x 10^8 (500 MILLION) AND 5-10 x 10^9 (5-10 BILLION) CFU PER DAY

The study of the human GIT is a fascinating area, and one where there is still so much to be explored and understood. The GIT contains a complex mix of beneficial, harmless and potentially pathogenic microorganisms and this mix varies greatly between individuals. The use of probiotics to modulate this balance is also still an area of much on-going research and debate.

In 2009 McFarland[4] stated that there is still no consensus on the most effective dose of a probiotic. She highlights that the range of daily doses in clinical trials has ranged from 1 x 10^7 (10 million) to 1 x 10^{11} (100 billion) a day and that a dose that is found to be effective for one probiotic strain may not be effective for another[5].

We understand that effective dosage will differ between individuals, be dependent on their level of dysbiosis and the condition or imbalance being addressed. Whilst eradicating pathogenic overgrowth from the body, one may experience a side effect known as 'die off' which could be more severe when commencing probiotic intake with a higher dose. We regularly receive positive feedback on Bio-Kult from our customers, practitioners, health food stores etc. Bio-Kult gives the practitioner flexibility to work with their client, varying the dosage as required.

The following table highlights a handful of published successful studies:

Author & Year	Dosage	Probiotic	Study methods
Fateh *et al*, 2011[6]	1 x 10^8 CFU/ capsule (200 million CFU/day) for 4 weeks	*Streptococcus thermophilus* PXN® 66™, *B. breve* PXN® 25™, *B. longum* PXN® 30™, *L. acidophilus* PXN® 35™, *L. bulgaricus* PXN® 39™, *L. rhamnosus* PXN® 54™ and *L. casei* PXN® 37™ and prebiotic	In 60 men the synbiotic mixture was significantly more effective in **increasing stool frequency** by up to 1.58 times a week and improving consistency compared to placebo.
Coccorullo *et al*, 2010[7]	1 x 10^8 CFU/day (100 million) for 8 weeks	*Lactobacillus reuteri*	In 44 **infants** at least 6 months old the probiotic significantly **increased frequency of bowel movements** compared to placebo.
Lamiki *et al*, 2010[8]	2 x 10^9 CFU/day (2 billion) for 6 months	*Lactobacillus acidophilus, L. helveticus* and *Bifidobacterium* spp.	In 46 patients previously affected by symptomatic uncomplicated **diverticular disease**, of those who received the multi-strain probiotic, **68% were still symptom free** at the end of the study.
Kotani *et al*, 2010[9]	4 x 10^9 CFU/day (4 billion) for 12 weeks	*Lactobacillus pentosus*	In 80 healthy **elderly** individuals salivary SIgA secretion was significantly accelerated, indicating potential to **improve mucosal immunity**.
Kajander *et al*, 2008[10]	4.8 x 10^9 CFU/day (4.8 billion) for 5 months	*Lactobacillus rhamnosus, Propionibacterium freudenreichii* ssp. *shermanii* JS and *Bifidobacterium animalis* ssp. *Lactis*	In 86 patients the **IBS score significantly decreased** 14 points vs. 3 points with placebo, especially for distension and abdominal pain. Microbiota was stabilised, increased with probiotic (1.9), decreased with placebo (-2.9).
Bekkali *et al*, 2007[11]	4 x 10^9 CFU/day (4 billion) for 4 weeks	*Bifidobacteria bifidum, B. infantis, B. longum, Lactobacilli casei, L. plantarum* and *L. rhamnosus*	In 20 **children** aged 4-16 the probiotic **increased bowel movements** from twice a week to 4.2 times, and significantly **reduced abdominal pain** from 45% to 25%.
Reid *et al*, 2001[12]	Over 10^8 CFU/day (100 million) for 28 weeks	*Lactobacillus rhamnosus* and *Lactobacillus fermentum*	In 42 healthy women the orally administered lactobacilli were able to restore and maintain a **normal urogenital flora.**
Oksanen *et al*, 1990[13]	2 x 10^9 CFU/day (2 billion) for 2 weeks	*Lactobacillus rhamnosus*	In 756 tourists travelling to southern Turkey, maximum **protection against travellers' diarrhoea** was reported as 40% in 1 destination.

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