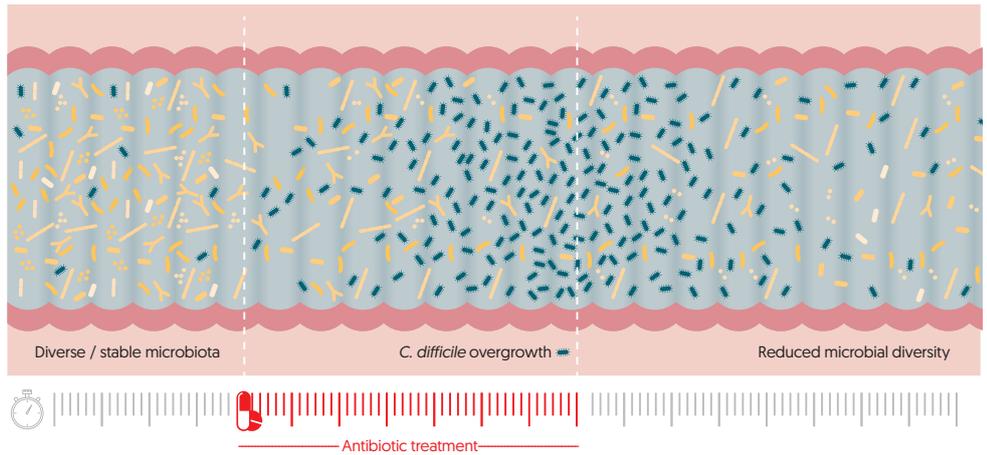


Reducing antibiotic-associated side-effects

Bacterial infections are often treated with antibiotics. It is generally known that antibiotic intake can cause a marked disturbance of the intestinal microbiota, as antibiotics do not only affect the targeted pathogens, but the indigenous microbiota as well.¹

A disturbance of the intestinal microbiota can lead to overgrowth of potential pathogens, which may result in the development of antibiotic-associated diarrhea [AAD] (figure 1). The incidence of AAD ranges from 5-39%.^{2,3} AAD can be divided into two types: non-specific AAD which is usually mild, and *Clostridium difficile* associated diarrhea [CDAD], which can lead to severe and life threatening pseudomembranous colitis¹. It was widely assumed that this disturbance of the intestinal microbiota was short-term, but nowadays it is accepted that antibiotics can profoundly affect the intestinal microbiota over a long period of time.⁴ Moreover, there

Figure 1: Antibiotics have a profound impact on the intestinal microbiota. They cause a temporary decrease in microbial diversity leading to loss of colonization resistance and overgrowth of potential pathogens such as *C. difficile*.



is growing evidence that these antibiotic induced disturbances of the microbiota play an important role in a multitude of disorders such as irritable bowel syndrome [IBS], inflammatory bowel disease [IBD], allergy, obesity and colorectal cancer.⁵ Therefore, preventing or restoring this disturbance is of great importance. The medical world is

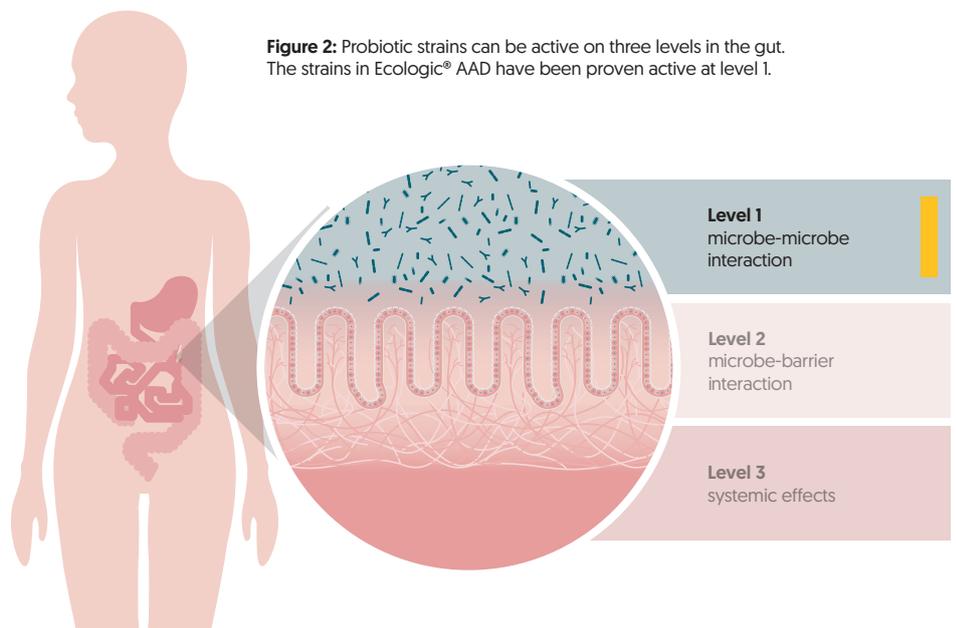
just now starting to accept that, even if AAD is not present, antibiotic treatment can cause a marked and prolonged disturbance of the microbiota leading to health issues in the long term. Ecologic[®] AAD has shown to be effective in preventing AAD and in restoring antibiotic-induced microbiota perturbations.^{5,6}

Strain selection

Ecologic[®] AAD is a multispecies probiotic formulation, developed to prevent and restore antibiotic-induced disturbances of the microbiota and subsequently the risk of antibiotic-associated side effects, such as AAD. The formulation consists of 9 specially selected probiotic strains. Probiotic strains can exert health effects at different levels in the gut (see figure 2). The bacterial strains of Ecologic[®] AAD have been selected for their capacity to inhibit AAD-related pathogens (level 1). The bacterial strains have been screened for their capacity to inhibit growth of the pathogens:

- *Clostridium difficile*
- *Clostridium perfringens*
- *Enterococcus faecalis*
- *Escheria coli*
- *Bacillus subtilis*.

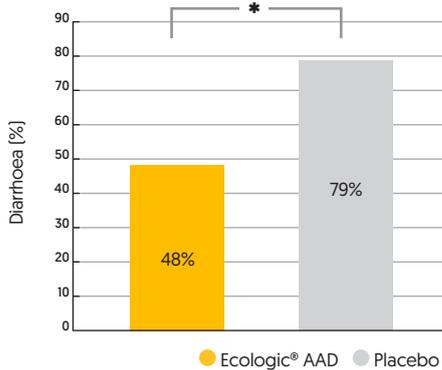
Figure 2: Probiotic strains can be active on three levels in the gut. The strains in Ecologic[®] AAD have been proven active at level 1.



Clinical evidence

Ecologic® AAD has been tested in a randomized, double-blind, placebo-controlled trial with healthy volunteers taking amoxicillin, performed by Maastricht University Medical Centre, The Netherlands⁵. The trial showed that **Ecologic® AAD significantly reduced the risk of diarrhoea-like defecation** (figure 3). It was also shown that the intestinal microbiota of participants in the probiotic group restored faster to the pre-antibiotic state than the intestinal microbiota of participants in the placebo group⁶. The results therefore suggest that restoration of the intestinal microbiota is

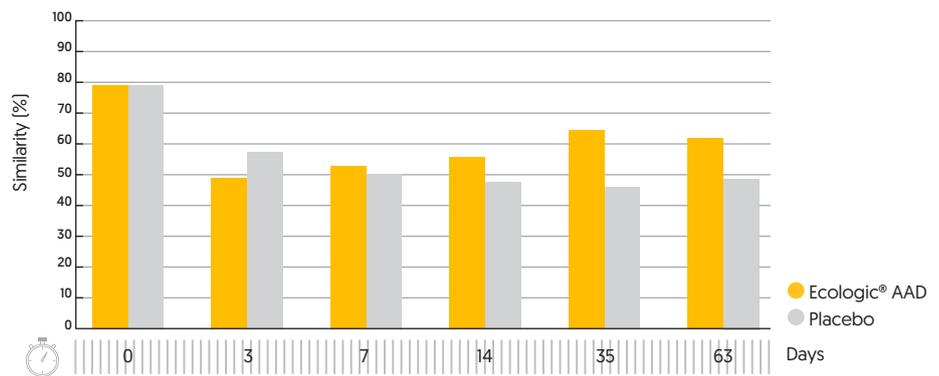
Figure 3: Diarrhea-like defecation occurred significantly less in the Ecologic® AAD group compared to the placebo group.



one of the important mechanisms determining the efficacy of probiotics in AAD (figure 4). Ecologic® AAD was also able to stimulate the production of cytokine secretory IgA (sIgA), an important immunoglobulin for the general defence against pathogens.

This result has been confirmed in a user trial in Austria with 199 participants. Hospitalised patients on antibiotics received Ecologic® AAD which resulted in **a significantly lower incidence of AAD**. Less than 1% in the entire study group developed AAD⁷, which normally ranges between 5-39%.

Figure 4: After day 35 there is a significantly faster recovery to the pre-antibiotic state of the microbiota in the Ecologic® AAD group compared to the placebo group.



Formulation details

Indication	Preventing antibiotic-associated side effects.		
Colony forming units (CFU)	1 x 10 ⁹ CFU/gram.		
Bacterial strains	<i>B. bifidum</i> W23 <i>B. lactis</i> W51 <i>E. faecium</i> W54	<i>L. acidophilus</i> W37 <i>L. acidophilus</i> W55 <i>L. paracasei</i> W20	<i>L. plantarum</i> W62 <i>L. rhamnosus</i> W71 <i>L. salivarius</i> W24
PROBIOACT® Technology		Protective and nutritional ingredients that improve the stability of the formulation, GI survival and metabolic activity of the bacteria.	
Recommended daily dosage	5 grams, twice daily.		
Treatment period	Start from the first day of antibiotic treatment until one week after cessation.		
Storage and stability	2 years stable at room temperature, no refrigeration needed.		
Available dosage forms	Dry powder which can be supplied as bulk or sachets, fully packed (with your design).		
Safety and Quality Profile	 	All probiotic strains have the Qualified Presumption of Safety (QPS) status or an extensive safety file. ¹⁰ Winclove is a NSF International Certified GMP Facility for manufacturing dietary supplements and is ISO 22000:2005 certified for the development and production of pre- and probiotics.	
Marketing		Medically endorsed under private label on a co-branding basis. Co-branding enables our business partners to use the scientific data in their marketing communication.	

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Furthermore, in a retrospective case report series of 10 patients with *C. difficile* infection (CDI), of whom 5 experienced recurrent CDI, twice-daily supplementation with Ecologic® AAD, besides antibiotics, resulted in complete recovery.⁸

Ecologic® AAD is recommended by the World Gastroenterology Organisation in their Global Guidelines (Feb 2017). The level of evidence on reducing antibiotic-associated diarrhoea is evaluated as level 2 evidence: Randomized trial or observational study with dramatic effect.⁹

This information is intended for business professionals only, not for consumers. The formulations contained herein are concepts, not commercially available and not intended to diagnose, cure or prevent any diseases.

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