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Winclove probiotics

Medical background

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: nonspecific AAD which is usually mild, and Clostridium difficile associated diarrhea (CDAD), which can lead to severe and life threatening pseudomembranous colitis[1]. 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 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 peturbations[5,6].

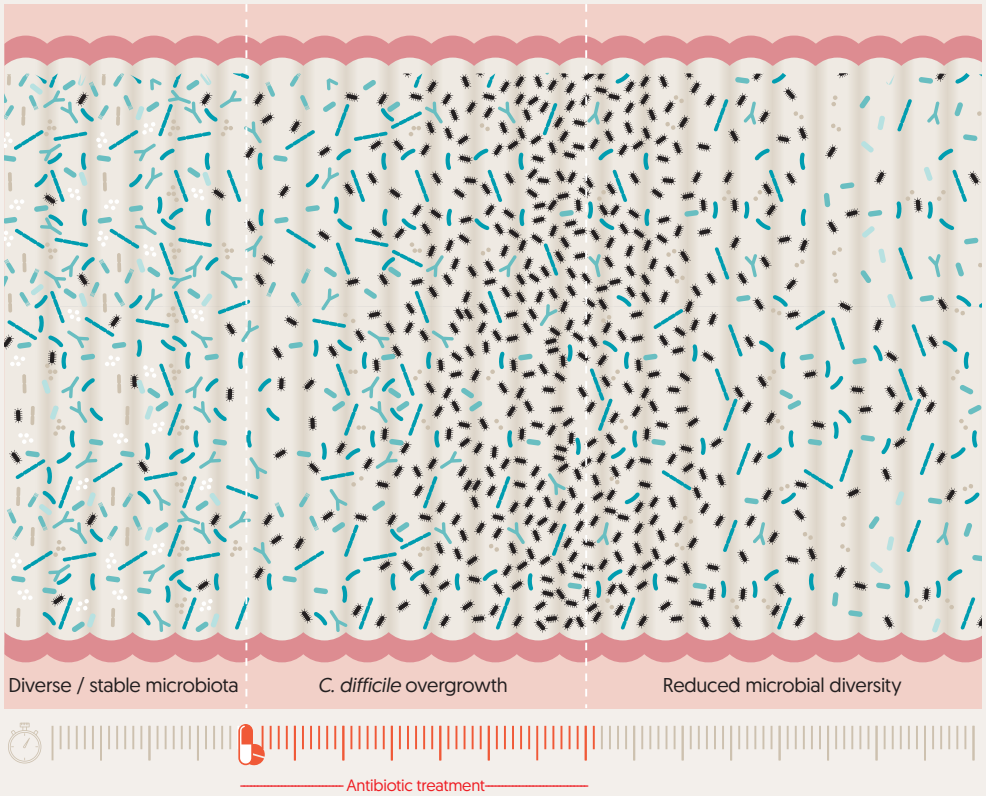

Figure 1: Antibiotics have a profound impact on the intestinal microbiota. They cause a temporary decrease in microbial diversity leading to loss of colonization resistance and overgrowth of potential pathogens such as *C. difficile*.

Product development

Ecologic® AAD is a multispecies probiotic formulation, developed to prevent and restore antibiotic-induced disturbances of the microbiota and subsequently the risk of antibioticassociated side effects, such as AAD. The formulation consists of 9 specifically 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*
- *Entercoccus faecalis*
- *Escheria coli*
- *Bacillus subtilus.*

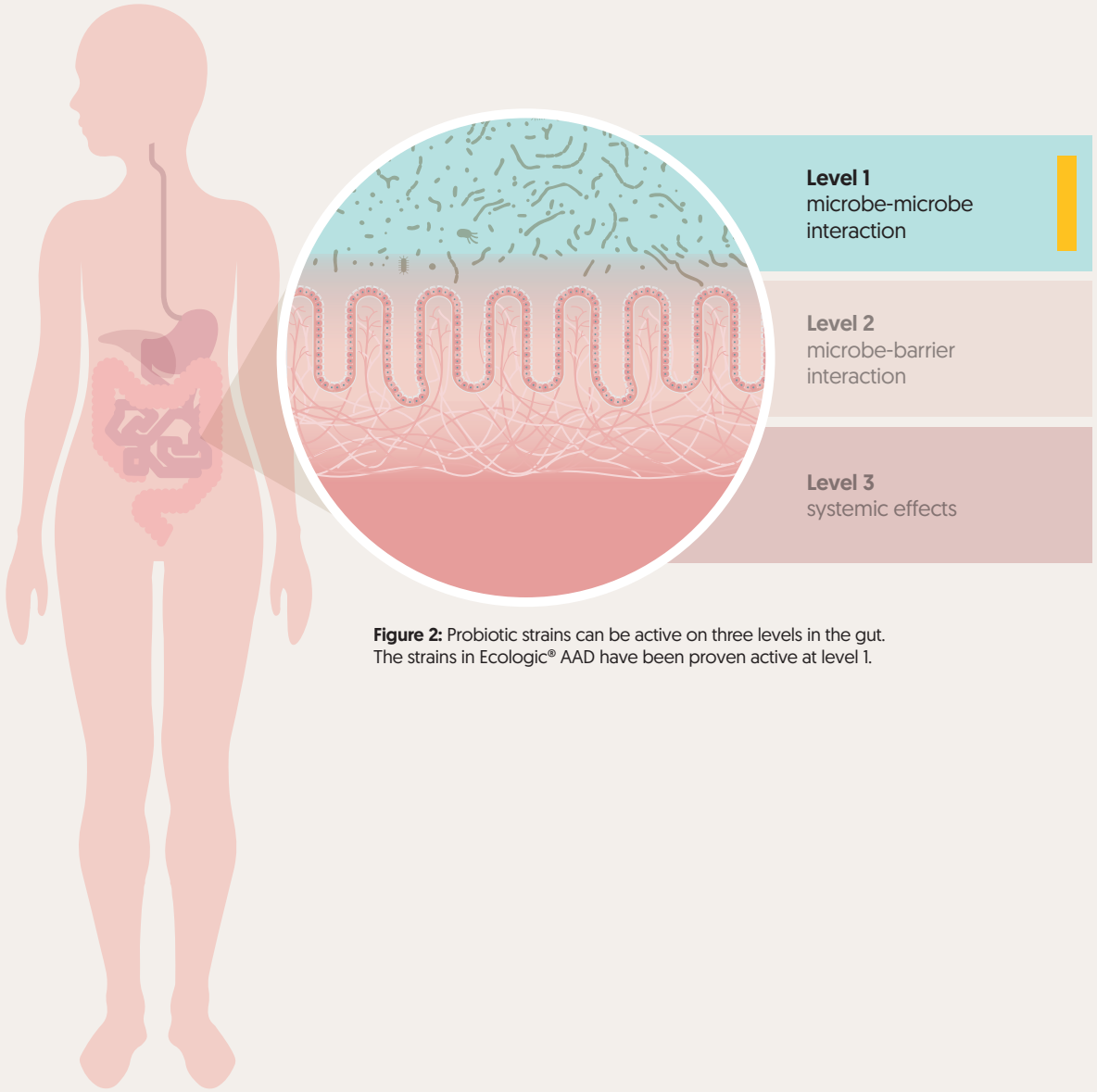

Figure 2: Probiotic strains can be active on three levels in the gut. The strains in Ecologic® AAD have been proven active at level 1.

Clinical evidence

Winclove's premium probiotic formulation Ecologic® AAD has been tested in multiple clinical trials, children, adults and the elderly taking antibiotics.

The first study was performed in collaboration with Maastricht University Medical Center+ (NL), and showed that Ecologic® AAD significantly reduced the risk of diarrhoea-like defecation with 39% (see figure 3)[5]. Furthermore, 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 group[6]. The results therefore suggest that restoration of the intestinal microbiota is one of the important mechanisms determining the efficacy of probiotics in AAD.
This result was confirmed in an open label study performed at the Department of Surgery Country Clinic in Austria. One hundred and ninety nine patients on antibiotics after surgical intervention received Ecologic® AAD which resulted in a significantly lower incidence of AAD. Less than 1% in the entire study group developed AAD[7], which normally ranges between 5-39%.

It is known that there are differences between use of Ecologic® AAD in children children, adults and elderly. However, the positive effect of Ecologic® AAD was also observed in a quadruple-blind, placebo-controlled multicentre study performed in collaboration with the internationally renowned researchers and paediatrician Hania Szajewska and Tim de Meij. In the study 350 children from the Netherlands and Poland, on antibiotics because of an infection, were randomized to receive Ecologic® AAD* or a placebo during antibiotics intake until one week after cessation. The study showed that the intake of Ecologic® AAD significantly reduced the development of AAD with 38% (see figure 4) and that no adverse effects were observed showing that Ecologic® AAD is both safe and effective.

** slightly modified version*

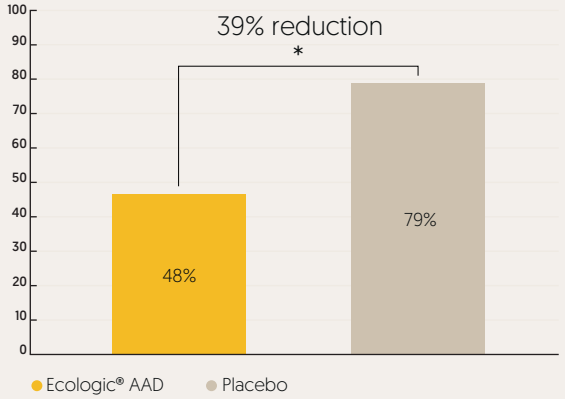

FIGURE 3: Diarrhea-like defecation occurred significantly less in the Ecologic® AAD group compared to the placebo group.

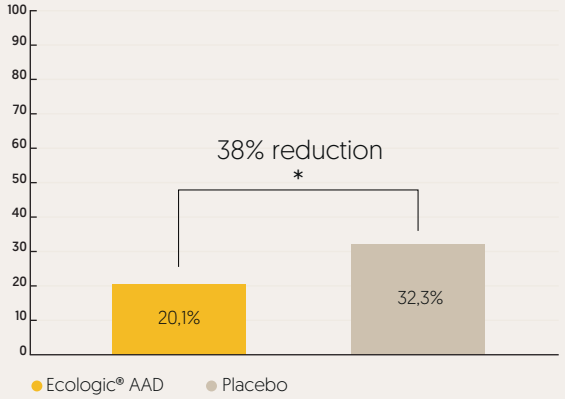

FIGURE 4: Significant reduction of AAD in in the Ecologic® AAD group compared to the placebo group

In addition, a study with a pragmatic participatory evaluation (PPE) design as conducted in a nursing home. In this study the incidence of AAD was significantly reduced with 44% in the period when Ecologic® AAD was used during antibiotic intake compared to when no probiotics were used[10]. In elderly with a known history of AAD this effect was even more pronounced (71% reduction).

In line with this are the results from a retrospective user trial which showed that intake of Ecologic® AAD reduced AAD during antibiotic intake and significantly reduced GI complaints (most notably nausea)[10]. Moreover 69% of participants indicate that they would like to continue the use of Ecologic® AAD (see figure 5).

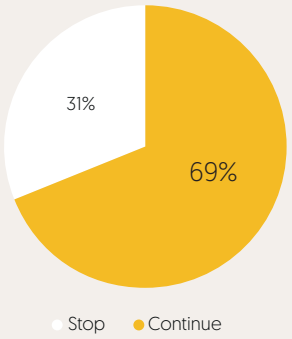

FIGURE 5: 69% of the study participants indicate they would like to continue the use of Ecologic® AAD

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[11].

Also, 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].

Formulation details

Indication	Prevention of antibiotic-associated side effects.
Colony forming units (CFU)	1 x 10^9 CFU/gram.
Bacterial strains	*B. bifidum* W23, *B. lactis* W51, *E. faecium* W54, *L. acidophilus* W37, *L. acidophilus* W55, *L. paracasei* W20, *L. plantarum* W62, *L. rhamnosus* W71, *L. salivarius* W57
PROBIOACT® Technology	Carefully selected ingredients that contribute to stability (shelf-life), GI-survival and metabolic activity of the probiotic strains.
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, sachets, or 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[13]. 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.

Contact us

We are deeply committed to your product's success and offer our scientific, commercial and broad knowledge bases to contribute in making this success a reality.
We are very much looking forward to explore this indication with you

Please reach out to us to discuss any questions and/or ideas that come to mind: **sales@winclove.com**

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Hulstweg 11
1032 LB Amsterdam
The Netherlands
T: +31 (0)20 435 02 35
www.wincloveprobiotics.com

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