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# Synbiotics – a promising approach for the primary prevention and dietary management of cow's milk allergy

Nutricia presents the final installment in a three-part series of discussions around allergies in early life. This article focuses on synbiotics, a promising approach for primary prevention and dietary management of cow's milk allergy (CMA).

## The global rise of allergy

The prevalence of allergic diseases, such as food allergy, atopic eczema, allergic rhinitis and asthma, is rising dramatically worldwide.<sup>1</sup> CMA is one of the most common allergies in infants and young children, affecting up to 5% of the world population.<sup>2</sup>

## The importance of the gut microbiota in early life

The immune system develops quickly during the first 1000 days of life; it is well known that both the establishment and maintenance of an optimal microbial community is important for the development of the immune system and essential to maintain health, especially in infants and children.<sup>3</sup>

Environmental factors such as mode of delivery, diet and use of antibiotics influence the infant gut and immune system. These factors can cause an imbalance of the gut microbiota known as dysbiosis, which impairs the development of the immune system, resulting in a state of inflammation and

potentially giving rise to allergic diseases.<sup>4</sup> For this reason, targeting the gut microbiota is suggested to be important in reducing the risk or persistence of allergic diseases like CMA.<sup>5</sup>

## The synbiotic concept

Synbiotics are a combination of pre- and probiotics.<sup>6</sup> Pre- and probiotics can influence the immune system directly, or indirectly, via the gut microbiota, and therefore they may play a role in preventing the onset of an allergic disease.<sup>7</sup> The objective of combining pre- and probiotics is to achieve stronger positive effects than with either component alone (synergy).<sup>8</sup>

The gut microbiota of infants with allergic conditions is characterized by low levels of *Bifidobacteria* and *Lactobacilli* compared with

healthy infants.<sup>9</sup> Human milk contains human milk oligosaccharides (HMOs) and live bacteria that are provided at a critical stage in the early development of the gut microbiota.<sup>10</sup>

Given the presence and important role of these naturally occurring pre- and probiotics, and recognising that breast feeding is not always possible, there is a compelling rationale to combine pre- and probiotic ingredients (synbiotics) in infant formula so that functionally it more closely resembles human breast milk.

## Synbiotics as a promising approach for CMA

A growing amount of clinical evidence shows that pre- and probiotics can have beneficial effects in infants at risk of, or living with food allergies.<sup>11-14</sup>

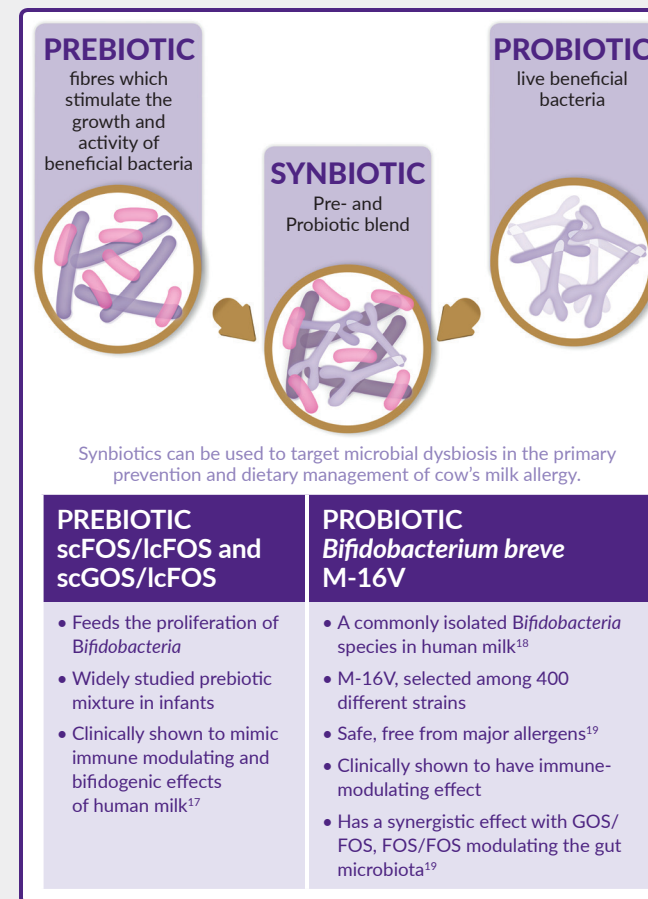
Traditional strategies for the dietary management of food allergies such as extensively hydrolysed formula (EHF) or amino acid formula (AAF) have been successful, with most subjects having symptom resolution and achieving oral tolerance with time. However, rising allergy prevalence in the world has led to research on the possibility to further develop effective tolerance to allergens in prevention and dietary management strategies.<sup>15</sup>

Supplementation with specific prebiotic mixtures and probiotic bacteria has been a logical next step in promoting immune system development and balanced gut microbiota as part of strategies for the nutritional management of CMA.

Nutricia believes that optimal prevention and management strategies combine milk hydrolysate- or amino acid-based formulas with additional ingredients (such as pre- and probiotics). These promote environmental conditions in the gut to train the immune system, supporting the natural development of oral tolerance. Protein

hydrolysates may contribute to the induction of oral tolerance via controlled exposure to specific peptides of the allergenic protein.<sup>16</sup>

Recognizing the importance of a balanced gut microbiota, and building on the increasing evidence of bacterial presence in human milk, Nutricia is supporting a comprehensive research programme to investigate the efficacy of a specific synbiotic mixture of prebiotics (short chain galacto-oligosaccharides (scGOS) or short chain fructo-oligosaccharides (scFOS) + long chain fructo-oligosaccharides (lcFOS)) in a 9:1 ratio- and probiotic strain *B. breve* M-16V.



## Scientific substantiation of the synbiotic concept for allergy management

Nutricia has undertaken an extensive clinical research programme to support the safety, tolerability and efficacy of the synbiotic concept:

### Future of allergy management for CMA patients

The dramatic increase in allergic disease requires a new focus on strategies for the primary prevention and dietary management of food allergy. Increasing insights have highlighted the importance of the gut microbiota for overall health and targeting the gut microbiota appears to

be a new way to reduce the incidence and persistence of allergic diseases like CMA.

Nutricia believes that there is a strong rationale to include pre-, pro- and synbiotics in the diet of these infants and has an extensive clinical trial programme

underway investigating the role of these ingredients in the primary prevention and dietary management of CMA.

Nutricia continues to collaborate with global experts to further its understanding of the impact of nutrition on food allergy.

## Synbiotics may rebalance the gut microbiota in Caesarian-section infants and reduce severity of atopic dermatitis in infants

The results of the JULIUS Study showed that a formula supplemented with synbiotics (scGOS/lcFOS/*B. breve* M-16V) re-established the delayed colonisation of *Bifidobacterium* in Caesarian-section delivered infants, from the first days of life and provided the physiological conditions for a healthy gut, as observed in vaginally born infants. Exploratory data suggested a potential protective effect on adverse events related to skin disorders and atopic dermatitis (AD) early in life.<sup>21</sup>

The SYNBAD Study confirmed the bifidogenic capacity of this synbiotic blend in infants with AD. In addition, the synbiotic (EHF) reduced AD severity within the subgroup of infants with IgE associated AD, and improved diaper/nappy dermatitis symptoms.<sup>12</sup> The 1 year follow-up data also showed reduced prevalence of asthma-like symptoms and medication use in infants with AD.<sup>13</sup>

## Synbiotics are safe, hypoallergenic and improve the microbiota of infants with CMA

Clinical studies have shown that an AAF with synbiotics is hypoallergenic, well tolerated and supports normal growth in both healthy and CMA infants.<sup>22-24</sup> The ASSIGN study investigated the effects of an AAF including synbiotics (scFOS/lcFOS/*B. breve* M-16V) on percentages of *Bifidobacteria* and *Eubacterium rectale/Clostridium coccoides* (ER/CC) in feces from infants with suspected non-IgE mediated CMA. Feces from age matched healthy breastfed reference group were also collected. An eight week intervention with an AAF with these specific synbiotics was shown to lead to increased levels of "infant like" *Bifidobacteria* and decreased "adult like" ER/CC compared to an AAF without synbiotics. These bacterial changes approximated the levels in the healthy breastfed group. This supports the hypothesis that an AAF with synbiotics improves the fecal microbiota of infants with suspected non-IgE mediated CMA.<sup>14</sup>

The ongoing PRESTO study includes infants with confirmed IgE-mediated CMA, randomly allocated to receive the same AAF with or without synbiotics for 12 months and will assess cow's milk tolerance acquisition over 12, 24 and 36 months. This trial will inform future studies primarily focusing on the clinical outcomes in the specific CMA populations.

For more information visit [www.nutriciaresearch.com/allergy/](http://www.nutriciaresearch.com/allergy/)

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