Ingredients in infant milks

Acidified infant milk and postbiotics

The term postbiotics refers to soluble products or metabolic by-products secreted by live bacteria (probiotics), or released after bacterial break down, such as enzymes, peptides, oligosaccharides, polysaccharides, cell surface proteins, and organic acids. It is being suggested that postbiotics may have anti-inflammatory, immunomodulatory, anti-obesogenic, antihypertensive, hypocholesterolemic, anti-proliferative, and antioxidant activities (Aguilar-Toalâ et al, 2018). These suggested properties could mean that postbiotics might contribute to the improvement of host health by improving specific physiological functions. Currently mechanisms of action for postbiotics have not been entirely elucidated.

The presence of postbiotics in infant milks is not a new development as 'acidified' infant milks produced by fermentation with lactic acid producing bacteria have been available in other European countries such as France and in African countries for many years. They contain postbiotics and have been described as:

"Infant and follow-on formulae that have been fermented with lactic acid-producing bacteria during the production process, but do not contain live bacteria in the final product due to inactivation of the fermenting bacteria by heat treatment or other means". (ESPGHAN, 2007).

They have typically been marketed as being useful in preventing a range of gastrointestinal symptoms and, in particular, in preventing diarrhoeal disease. Despite widespread use globally, there is little published data available to support their use.

There are a small number of studies that have investigated the effects of fermented infant milks on diarrhoeal disease amongst infants who are receiving complementary foods. Brunser et al,1989 showed a reduction in the incidence of diarrhoea as well as a lower proportion of days with diarrhoea and shorter duration of episodes in Chilean children fed acidified Nestlé Pelargon formula, compared to those receiving the same formula but non acidified. In a more recent controlled clinical trial that examined the effect of a fermented formula on the incidence of acute diarrhoea in healthy 4–6-months-old infants, reductions in the severity, but not in the incidence of diarrhoea were reported. The outcomes of this trial were based on parental report and 4 visits with a paediatrician. The trial was sponsored by Blédina (Nutricia). There was no breastfed reference group and the milk did not contain prebiotics. Neither the composition of the milk, nor the proportion of fermented milk used were disclosed (Thibault et al, 2004).

Recent additions to the formula milk market in the UK have included infant milks containing approximately a quarter of their whey component from milk fermented with the lactic acid producing bacteria Bifidobacterium breve and Streptococcus thermophiles. These milks therefore contain metabolites from the fermentation process but do not contain live bacteria. Despite this, the milks are not marketed as acidified or fermented milks but as containing postbiotics, a new ingredient. Infant milks that contain a proportion of fermented milk claim to also contain 3'-galactosyllactose, this HMO is produced as a result of the fermentation of the cows' milk used in the product mix.

A number of claims have been made about the use of postbiotics in combination with a prebiotic GOS:FOS mix including:

‘Gut and immune markers closer to breastfed infants' and 'This combination of prebiotics and postbiotics have been shown to support a healthy gut in infants, important for immune system development and functioning.'

In 2007 The ESPGHAN Committee on Nutrition carried out a systematic review of the literature to assess knowledge on the effects of fermented infant formula without live bacteria. They concluded that "*the published data on the effects of fermented infant formulae without live bacteria are limited and do not allow firm conclusions"* and that "*the effects of fermented infant formulae on infectious diarrhea and other relevant outcomes should be assessed in further randomized controlled trials"* (Agostoni et al, 2007).

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Probiotics

Probiotics are live micro-organisms that, when administered in adequate amounts, confer a health benefit on the host (FAO/WHO, 2001). The composition of the intestinal microflora is recognised as a major determinant of the well-being of the host (Vandenplas et al, 2011). Human breastmilk contains probiotics as well as hundreds of different types of prebiotic oligosaccharides. Cows’ milk contains virtually none (Teitelbaum and Walker, 2002). In their efforts to provide infant milks that mimic the bifidogenic activity of breastmilk, many manufacturers have supplemented their infant milk products with prebiotics and/or probiotics. The rationale for their use in infant milks is that they may be capable of modifying the balance of intestinal microflora in favour of commensal (beneficial) bacteria over pathogenic bacteria, which it is suggested may offer a protective effect against some common childhood infections. Studies available to support the use of probiotics alone, or in combination with prebiotics (synbiotics) in infant milks, vary greatly in respect of quality, the bacterial strains used, dose and outcomes measured.

There has generally been considered to be insufficient evidence to recommend the addition of probiotics to infant feeds for prevention of allergic disease, food hypersensitivity or diarrhoea (Osborn and Sinn, 2007; Szajewska and Mrukowicz, 2001). The most recent

research used to support the use of synbiotics in follow-on formula milks comes from a randomised control trial in healthy term infants aged 6 months to 1 year. This study reported that infants who consumed follow-on formula milk supplemented with prebiotic oligosaccharides and the probiotic bacteria *Lactobacillus fermentum* (CECT5716) had fewer incidences of gastrointestinal and upper respiratory tract infections and an overall reduction in incidences of infectious diseases compared to infants who consumed a formula containing only prebiotic oligosaccharides (Maldonado et al, 2012). A further study sponsored and co-written by Hipp Organic, designed to examine the safety and tolerance of this formula in infants from 1 to 6 months of age, found a reduction in incidence of gastrointestinal infections only (Gil-Campos et al, 2012).

In a systematic review of randomised control trials (RCTs) that compared the use of infant or follow-on formula milks supplemented with probiotics and/or prebiotics, the ESPGHAN Committee on Nutrition noted that, whilst there was some evidence available to suggest an association between the use of specific probiotics in infant milk and a reduction in the incidence of gastrointestinal infections and antibiotic use, there was too much uncertainty to draw reliable conclusions. Where infant milks were supplemented with synbiotics, the committee found that the quantity of data from RCTs was too sparse and again concluded that there was too much uncertainty to draw reliable conclusions. The routine use of probiotic supplements in infant milk for infants was not recommended. Whilst the committee found no evidence for adverse effects of probiotic use in products for infants, they did raise some specific concerns:

"First, timing, that is, the administration often begins in early infancy, sometimes at birth when the gut microbiota is not fully established, and factors that influence microbiota may permanently affect the development of the ecosystem. Second, duration, that is, the daily administration of such products is often prolonged (several weeks or months). Last but not least, delivery is in the form of a specific matrix (infant formula) that could be the only source of feeding of an infant." (Braegger et al, 2011)

Hipp Organic has been the only one of the market-leading infant milk companies to try and add probiotic bacterial strains to their infant milks. However, in spring 2013 the Department of Health informed Hipp that it did not approve of the addition of probiotic bacteria to their powdered formula. The Department of Health requested additional information on the suitability of the bacterial strain for nutritional use in infant foods and reiterated that the manufacturer's instruction for reconstitution at 40-50ºC was at variance with Department of Health recommendations that all standard infant formula powders should be reconstituted at 70ºC. Hipp Organic formula marketed in the UK make no claims for added probiotics and have labelling instructions in line with UK recommendations. The placing on the market and subsequent removal of milks supplemented with probiotics highlight the need for more stringent regulatory frameworks around the addition of optional ingredients to infant milks.

EFSA (2014) has reiterated in their *Scientific opinion on the essential composition of infant and follow-on formulae* that there is no benefit to infant health from adding probiotics or synbiotics (prebiotics and probiotics) to infant or follow-on formula.

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