

## Ingredients in infant milks

### Protein content of infant milks

Proteins are composed of amino acids, eight of which are essential (cannot be synthesised by the human body), and these must be provided in adequate proportions in the diet. Protein requirements for infants are based on the concentrations of amino acids in mature human milk. Regulations require infant formula to contain an available quantity of each amino acid at least equal to that found in human breastmilk.

Whey and casein are the two major proteins of human milk. Whey, the predominant protein source, contains many different proteins and non-protein nitrogen. Colostrum is predominantly whey, and early breastmilk is whey-dominant (60:40), but the proportions of casein and whey become approximately equal later in lactation (Jensen, 1995). Whey and casein are present in cows' milk and goats' milk in different proportions to those found in breastmilk.

#### Cows' milk protein

The majority of infant formulas are based on highly modified cows' (bovine) milk. Both the protein quantity and protein composition differ between cows' milk and mature human milk. The total protein content of cows' milk is higher than that of mature human milk (3.3g/100ml vs 1.3g/100ml respectively) (Poskitt and Morgan, 2005).

Whey and casein are present in cows' milk in different proportions to those found in breastmilk, with casein the predominant protein source (whey:casein ratio typically 20:80). First cows' milk based infant formula generally has an altered whey:casein ratio (60:40) to bring it closer to that found in breastmilk which is whey-dominant, however some products use whey:casein ratios of 50:50 or 70:30. Infant milk marketed for 'hungrier babies' has a whey:casein ratio of 20:80.

The concentrations of some essential amino acids in cows' milk are lower than in human milk, and the concentrations of tryptophan and cysteine in cows' milk are approximately half of those in mature human milk (Heine et al, 1991). Therefore, in order for infant formula based on cows' milk to meet the amino acid requirements of infants, the total protein content of most infant milks has historically been higher than that of breastmilk.

#### Goats' milk protein

Several products on the UK market are based on goats' milk protein. Goats' milk is casein dominant and the whey:casein ratio may be altered in infant milk to bring it closer to the ratio found in breastmilk, which is whey dominant. Similarly to cows' milk, the concentrations of some essential amino acids in goats' milk are lower than in human milk and therefore, in order for infant formula based on goats' milk to meet the amino acid requirements of infants, the total protein content has historically been higher than that of breastmilk.

The protein in goats' milk is very similar to that found in cows' milk and most babies who react to cows' milk protein will also react to goats' milk protein. The Department of Health recommends that infants with proven cows' milk protein intolerance who require a formula, can be prescribed an extensively hydrolysed infant formula. Goats' milk based infant milk is

also unsuitable for babies who are lactose-intolerant, as it contains similar levels of lactose to cows' milk based infant formulas (Department of Health, 2007).

In their 2012 report on the suitability of goats' milk as a protein source for infant and follow-on formula milks, EFSA clearly state that there is no evidence of any difference in 'digestibility' between formula made from goat's milk or cows' milk protein, and insufficient data to support the belief that the incidence of allergic reactions is lower when feeding goats' milk based infant milks compared with cows' milk based infant formula (EFSA, 2012).

### **Partially hydrolysed protein**

Partially hydrolysed proteins are permitted for use as the protein source in infant milks. EFSA (2014) has recommended a higher protein content when protein hydrolysates are used in infant milks but acknowledges that adequacy still needs to be established based on clinical evaluation.

Partially hydrolysed proteins are created using enzymatic processes to break proteins naturally found in a food into smaller fragments. The hydrolysis of proteins can produce either partially or extensively hydrolysed proteins. Extensively hydrolysed proteins are used in products available on prescription only and for use under medical supervision for the dietary management of mild to moderate cows' milk protein allergy (CMPA), multiple allergies, gastroenterological disorders and cystic fibrosis.

Infant milks containing partially hydrolysed proteins are not suitable for infants diagnosed with CMPA, however they were originally added to the market by manufacturers claiming that they could prevent allergies in atopic infants. Much of the evidence used to support this hypothesis is based on industry funded studies with a high risk of bias, as highlighted in a recent Cochrane review (Osborn, Sinn & Jones, 2018). A systematic review, commissioned by the Food Standards Agency, into the evidence on diet and allergy in the first year of life also found no evidence that use of partially hydrolysed formula reduced the risk of allergy or autoimmune outcomes in infants at high risk (Boyle, 2016). A recent study has also raised the possibility of adverse effects from the use of partially hydrolysed whey protein based infant formula, although their clinical significance is unknown (Davoine-Paturet et al., 2019).

In the UK, 'Comfort' milks are based on partially hydrolysed whey protein and more recently manufacturers have introduced several standard infant milk products to the market which are based on partially hydrolysed whey proteins. There is no evidence to suggest any benefit for infants from using these infant milks over those based on cows' or goats' milk protein.

### **Soya protein**

Soya protein-based infant formula combine protein from soya beans with water, vegetable oils, maltodextrins, vitamins and minerals. The amino acid profile of soya protein is deficient in sulphur-containing amino acids, and soya protein-based milks must therefore be fortified with the sulphur-containing amino acid L-methionine. Soya protein based infant formula (supplemented with methionine) support normal growth and development in healthy term infants during the first year of life (Mendez et al, 2002),

The required composition of soya protein based infant formula is different to that of cows' or goats' milk based infant formula for a number of micronutrients including iron and phosphorus due to differences in bioavailability. Soya protein-based infant formula is suitable for vegetarians, but not for vegans, as the Vitamin D is sourced from sheep's wool lanolin.

Soya based infant formula has sometimes been used for children who require an alternative to cows' milk based infant formula because they have an allergy or intolerance to cows' milk, or because they have a specific condition such as galactosaemia or galactokinase deficiency, however, its use for children aged under 6 months is controversial. Concerns have been raised over the potential allergenic effect of soya protein-based infant formula in infants at high risk of atopy and the potential role of phyto-oestrogens on infant development.

Soya protein-based infant formula has been used as an alternative to cows' milk protein-based infant formula in children with cows' milk protein allergy (CMPA). In a review of trials comparing the effect of prolonged feeding of either soya or cows' milk protein-based infant formula, meta-analysis found no significant difference between feeding groups in the incidence of childhood asthma, eczema or rhinitis. The authors concluded that soya protein-based infant formula cannot be recommended for allergy prevention or food intolerance in infants at high risk of atopy (Osborn and Sinn, 2006).

It is recognised that a proportion of children with CMPA are also allergic to soya protein. The Chief Medical Officer has recommended that soya protein-based infant formula should not be used as the first line of treatment for infants under 6 months of age who have CMPA or cows' milk protein intolerance, as this is the period when they are most likely to become sensitised to soya protein (Chief Medical Officer, 2004). ESPGHAN recommends that soya protein-based infant formula should not be used for infants under 6 months of age and that the use of therapeutic milks based on extensively hydrolysed proteins (or amino acid preparations if hydrolysates are not tolerated) should be preferred to the use of soya protein formula in the treatment of cows' milk protein allergy (Agostoni et al, 2006).

### **$\alpha$ -lactalbumin**

Several first infant milks and follow-on milks currently on the market in the UK contain  $\alpha$ -lactalbumin enriched whey.  $\alpha$ -lactalbumin is the predominant protein fraction of human milk whey and is particularly high in tryptophan, it accounts for 28% of the total protein in human milk and only 3% of the total protein in cows' milk. Infant formula based on cows' milk therefore generally have a lower concentration of  $\alpha$ -lactalbumin than human milk. Goats' milk is similar to cows' milk in its composition with respect to whey protein fractions (Haenlein, 2004).

It has been reported that a higher protein content in infant formula is associated with higher weight in the first two years of life (Koletzko et al, 2016). The protein content of most formula is now at the lower end of EU regulations, with infant formula typically providing a protein content of 1.2g - 1.3g/100ml. The primary limiting factor in reducing the total protein concentration in infant formula is the ability to provide sufficient quantities of essential amino acids. Enriching whey protein fractions in formula with substantially higher concentrations of  $\alpha$ -lactalbumin, which contains the limiting amino acids tryptophan and cysteine in higher amounts, has been one way in which formula manufacturers have achieved lower protein intakes in formula and these have not shown any impact on normal growth and development (Lien et al, 2004; Trabulsi et al, 2011). There are manufacturers selling bovine  $\alpha$ -lactalbumin whey products and making considerable claims about their efficacy that are yet to be substantiated and agreed by scientific committees.

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