INFANT FORMULA COMPOSITIONS AND NUTRITION CONTAINING GENETICALLY ENGINEERED HUMAN MILK PROTEINS

This application is a continuation of application Ser. No. 07/247,981, filed Sep. 22, 1988 now abandoned.

FIELD OF THE INVENTION

This invention relates to infant nutrition and in one embodiment it is particularly applicable to the enhancement or improvement of synthetic infant formulas. Another embodiment of this invention is concerned with improving the nutrition of very-low-birth-weight infants.

BACKGROUND OF THE INVENTION

It has been considered for a long time by nutritionists that the best food or nutrition supplied to an infant is its own mother's milk; i.e. fresh human milk. It is recognized, however, that many situations arise wherein the infant cannot be fed mother's milk and as a result synthetic infant milk formulas, predominantly based on cow's milk, have been prepared and used to nourish an infant. However, since it is generally believed that human milk provides superior nutrition for infants, much effort has been made to improve synthetic infant milk formulas to more closely similate mother's milk. For example, U.S. Pat. No. 4,303,692 (1981) discloses a synthetic infant milk formula which includes taurine at a level substantially equivalent to that found in human milk. In the manufacture of synthetic infant formula based on cow's milk, the taurine content of the cow's milk is low and may be diluted during the manufacture of the synthetic infant formula with the result that the produced synthetic infant formula contains a very low level of taurine. This was corrected, as disclosed in U.S. Pat. No. 4,303,692, by the addition of taurine to synthetic infant formula to bring its taurine content up to the level taurine is present in human milk. However, there are still many other components of fresh human milk which are not found in synthetic infant milk formulas, either cow milk-based formulas or soy protein-based formulas, which can and have usefully been added to synthetic infant formulas to provide an improved product for infant nutrition.

The protein and non-protein composition of the human milk and cow milk is described and set forth in the article by N.C.R. Raiha entitled "Nutritional Proteins in Milk and the Protein Requirement of Normal Infants", which appeared in the publication *Feeding the Normal Infant-Supplement, Pediatrics* pp. 136–141 (1985), published by the American Academy of Pediatrics. Among those proteins in human milk are listed alpha-lactalbumin, beta-lactoglobulin, lactoferrin, serum albumin, lysozyme, the immunoglobulins, mainly IgA and other proteins as well.

In the article by B. A. Friend et al. entitled "Newer Advances in Human Milk Substitutes for Infant Feeding" appearing in *Journal of Applied Nutrition*. Vol. 35. No. 2(1983), pp. 88–115, there is disclosed in some detail the composition of human milk compared with cow milk, evaporated milk formula, conventional synthetic infant milk formula based on cow milk and a synthetic protein milk-free formula. Additionally, there are comparisons made between the protein and non-protein nitrogen components in human milk and in cow milk including the various caseins which are to be found in human milk, viz. alpha-casein, beta-casein and kappa-casein. It is mentioned therein that human milk has a higher proportion of alpha-lactalbumin but no beta-lactoglobulin and that the host resistance factors or anti-

microbial proteins of human milk, viz, lactoferrin, lysozyme and secretory IgA, account for 75% of the protein in human colostrum as compared with 39% in mature human milk and less than 0.1% in cow's milk. This article also lists those host resistance factors present in human milk but absent in cow milk, viz. lymphocytes, macrophages, and secretory IgA.

Lactoferrin is present in a relatively high amount in human milk but in only a low amount in cow milk, whereas lactoperoxidase is present in a relatively low amount in human milk but in a high amount in cow milk. Lysozyme and bifidus-stimulating factors are to be found in a significant amount in human milk but only in trace amounts in cow milk. Similarly complement (C1–C9) is to be found in human milk but has not been positively identified in cow milk. The vitamin binding proteins are found in high amounts in human milk but in low amounts in cow milk.

It is seen, therefore, that if a synthetic infant milk formula is prepared based on cow's milk, it would be difficult, if not impossible, to more closely simulate the protein composition of human milk. To this end, i.e. more closely to simulate human milk, it is necessary that there be added to or incorporated in cow milk-based synthetic infant milk formulas, soy protein or meat-based synthetic infant formulas, those components which are present in human milk but are substantially absent from cow milk and the like.

Accordingly, it is an object of this invention to provide a synthetic infant milk formula which more closely simulates the composition of fresh human milk.

It is another object of this invention to provide protein components or compositions useful for enhancing or improving the nutritional value of synthetic infant milk formulas and also banked or pooled human milk.

It is yet another object of this invention to provide compositions useful for incorporation into the diet of an infant so as to enhance and improve the nutritional value of the diet.

Still another object of this invention is to provide techniques and routines for improving the diet and feeding of infants, particularly very-low-birth-weight infants.

How these and other objects of this invention are achieved will become apparent in the light of the accompanying disclosure. With respect to the disclosure of this invention, the disclosures of all the publications cited herein, including U.S. Pat. No. 4,303,692, are herein incorporated and made part of this disclosure.

SUMMARY OF THE INVENTION

Compositions containing human milk proteins, including the so-called host resistance factors (HRF) of human milk, are useful and are employed to enhance and improve the nutritional value of an infant's diet by including such compositions in the infant diet. These compositions can be incorporated in human milk, in synthetic infant milk formulas based on cow's milk or soy protein or can be supplied directly to the infant.

In the practices of this invention the human milk proteins, including the so-called host resistance factors (HRF) of human milk, are prepared by chemically synthesizing the same or by employing genetic engineering techniques for producing the human milk proteins including the host resistance factors, as recombinant human milk proteins or recombinant host resistance factors. The human milk proteins including the host resistance factors, because of their complexity, are preferably made by DNA genetic engineer-