LOW BUFFER NUTRITIONAL COMPOSITION

FIELD OF THE INVENTION

The present invention concerns a liquid nutritional composition having low buffer strength.

BACKGROUND OF THE INVENTION

There are reports that indicate that breast fed infants experience fewer episodes of both gastrointestinal tract and respiratory tract infections than their bottle-fed counterparts (Jason et al., "Mortality and Infectious Disease Associated with Infant-Feeding Practices in Developing Countries," *Pediatrics,* 74(Suppl), 1984, 702–727; Kovar, et al, "Review of the Epidemiologic Evidence for an Association Between Infant Feeding and Infant Health," *Pediatrics,* 74(Suppl), 1984, 615–638). Accordingly, breast milk is considered to be the best food for newborn infants because of its nutritional value as well as its ability to provide protection against various infectious diseases. The greater protection associated with breast-feeding is believed to be due to the presence in human milk of a number of antimicrobial factors. Examples of anti-infective factors that are reportedly present in human milk but not conventional artificial formulas include lactoferrin, specific immunoglobulins, lysozyme, and lactoperoxidase. While the activity of anti-infective factors in human milk has been repeatedly demonstrated in vitro, the efficacy of individual factors has not been demonstrated in vivo.

Most intestinal pathogens are transmitted from human to human by the fecal-oral route. It is commonly believed that the acidic nature of gastric secretions provides a very effective host defense against intestinal pathogens by inactivating orally ingested pathogens before they reach the small or large intestine where they become established and cause disease. Indeed, numerous studies have described the germicidal role of gastric acid secretions in establishing a gastric barrier to infection (Drasar, et al., "Studies on the Intestinal Flora. I. The bacterial flora of the gastrointestinal tract in healthy and achlorhydric persons," *Gastroenterology,* 56, 1969, 71–79; Giannella, et al., "Influence of Gastric Acidity on Bacterial and Parasitic Enteric Infections," *Annals of Internal Medicine,* 78, 1973, 271–276).

For example, gastric contents from human subjects are virtually sterile when the pH is at a level of 4 or below. Secondly, studies with human volunteers have shown that the infective dose of *V. cholerae* is lowered from 10^8 to 10^4 bacteria by co-administration of sodium bicarbonate with the bacteria to neutralize gastric acid (Cash, et al., "Response of Man to Infection with *Vibrio cholerae.* I. Clinical, Serologic, and Bacteriologic Responses to a Known Inoculum," *The Journal of Infectious Diseases,* 129, 1974, 45–52). Such evidence collectively points to a major role for gastric acidity in the inactivation of orally ingested intestinal pathogens.

Studies with newborn infants, however, indicates minimal secretion of acid and pepsinogen in the stomach (Christie, D. L., "Development of Gastric Function During the First Month of Life," *Textbook of Gastroenterology and Nutrition in Infancy,* E. Lebenthal (ed), Raven Press, New York, 1981, pages 109–120; Deren, J. S., "Development of structure and function in the fetal and newborn stomach," *The American Journal of Clinical Nutrition,* 24, 1971, 144–159). Acid production rates on a body-weight basis are less than 50% of adult values for the first 3 months in infants. Adult production rates are not reached until 2 years of age (Agunod, et al., "Correlative Study of Hydrochloric Acid, Pepsin, and Intrinsic Factor in Newborns and Infants," *American Journal of Digestive Diseases,* 14, 1969, 400–414). This is in accordance with the observation that the pH of gastric contents is higher in infants (Gryboski, et al., *Gastrointestinal Problems in the Infant,* 2nd ed., W. B. Saunders and Co., Philadelphia, Pa., 1983, page 217; Usowicz, et al., "Does gastric acid protect the preterm infant from bacteria in unheated human milk?" *Early Human Development,* 16, 1988, 27–33) than in adults (Mayes, P. A., "Digestion/Absorption in the Gastrointestinal Tract," *Harper's Review of Biochemistry,* 19th ed., D. W. Martin, P. A. Mayes, and V. W. Rodwell (eds.), Lange Medical Publications, Los Altos, 1983, pages 546–558). Several studies have also shown that post-prandial gastric pH in bottle-fed infants is higher than the gastric pH in breast-fed infants. For example, Usowicz, et al. found that gastric pH in preterm infants tended to decrease with increasing age and was significantly lower in infants fed exclusively human milk (pH=2.7) when compared to formula-fed infants (pH=3.6). These investigators and others have found virtually sterile gastric contents when the pH was <3.5.

Human milk is known to have lower acid buffering properties than both cow milk and cow milk-based infant formulas (Bullen, et al., "The Effect of 'Humanised' Milks and Supplemented Breast Feeding on the Faecal Flora of Infants," *J. Med. Microbiol.,* 10(4), 1977, 403–413; Hentges, et al., "Influence of Infant Diets on the Ecology of the Intestinal Tract of Human Flora Associated mice," *Journal Pediatric Gastroenterology and Nutrition,* 14, 1992, 146–152).

It would be desirable to have an infant formula which more closely resembles human milk in its ability to allow the natural level of gastric acidity to be effective in inactivating orally ingested intestinal pathogens. It would also be desirable to provide such a product for maintaining the gastric barrier function in patients with compromised gastric acid secretory capacity such as the elderly or patients receiving treatments which reduce gastric acid output.

SUMMARY OF THE INVENTION

A liquid, nutritionally complete composition has been discovered which allows the natural level of gastric acidity to be more effective in inactivating orally ingested intestinal pathogens. The present invention is directed to a liquid, nutritionally complete composition, preferably an infant formula, having low buffer strength. As used herein, the term "buffer strength" means the volume of 0.1N HCl required to decrease the pH of a 50 milliliter (mL) volume of liquid composition from the starting pH to a pH of 3. As used herein, the term "low buffer strength" means a buffer strength of 18 or lower. A preferred buffer strength of the composition of the invention is about 9 to about 18, more preferred is about 11 to about 16, and most preferred is about 12 to about 15.

The present invention is also directed to a method for treating a subject in need of treatment by controlling orally ingested pathogenic organisms comprising administering to said subject an effective amount of the composition of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1—Buffer strength of human milk samples from 19 mothers.