

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Diet composition and immune status of the host are major contributors to the gut microbiome, nutrition, and the digestive and immune functions of the GI tract, including the digestion, absorption and utilization of nutrients. Proteins in the lumen are both ingested as well as secreted and contain a wide array of protein structures. Thus, luminal proteins vary widely in amino acid sequence and concentration, digestibility, as well as role(s) and function(s) in the digestive tract. Specially-formulated diets can take advantage of the compositional differences in protein sources to influence the luminal environment which can have an effect on nutritional status of a patient with enteropathy. While the etiology of various enteropathies is often not known, changes in the relationship between the microbiome, immune dysregulation, and malabsorption are often associated with the condition(s). In nonclinical studies, oral administration of the protein composition of ENTERAGAM helps to maintain normal intestinal cellular markers of immune activation (Th and Tc cell subsets) and intestinal cytokine expression, including tumor necrosis factor alpha (TNF α), interferon gamma (IFN γ), and interleukins (ILs; *e.g.*, IL-1 β , IL-6, IL-8, IL-17). The maintenance of cytokine expression and immune function is associated with normal nutrient absorption, barrier function, and intestinal permeability. Thus, plasma protein fractions containing immunoglobulins administered orally have been shown in numerous, nonclinical studies to support weight gain and nutritional status during the stressful weaning period. In clinical studies of IBS-D and HIV-associated enteropathy, nutritional intervention of SBI was shown to manage symptoms characteristic of both diseases associated with improvement in nutritional status. In support of the nonclinical results, HIV patients administered SBI, showed improvement in the clinical, functional (nutrient absorption with D-Xylose test), and immunological composition of the duodenal mucosal compartment.