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(54) Title: THE USE OF 5-AMINOSALICYLIC ACID IN THE TREATMENT OF IRRITABLE BOWEL SYNDROME - DIARRHEAL PHASE OR TYPE (IBS-D)

(57) Abstract

Treatment for a human or other mammal afflicted with IBS-D, comprising the topical delivery to the intestinal tract of said human or other mammal, preferably the large intestine, of a safe and effective amount of a pharmaceutical composition consisting essentially of the 5-ASA active ingredient and pharmaceutically-acceptable excipients. Said topical delivery is preferably accomplished by the oral administration to said human or other mammal of a delayed-release composition consisting essentially of said 5-ASA active ingredient and a pharmaceutically-acceptable excipient.

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THE USE OF 5-AMINOSALICYLIC ACID IN THE TREATMENT OF IRRITABLE BOWEL SYNDROME - DIARRHEAL PHASE OR TYPE (IBS-D)

BACKGROUND OF THE INVENTION

The present invention relates to the novel method of treating a human or other mammal afflicted with Irritable Bowel Syndrome - Diarrheal Phase or Type (hereinafter referred to as IBS-D) comprising the topical delivery to the intestinal tract of said human or other mammal of a safe and effective amount of a pharmaceutical composition consisting essentially of the active ingredient 5-aminosalicylic acid (hereinafter referred to as "5-ASA"), and pharmaceutically-acceptable excipients. Said topical delivery is most preferably accomplished by the oral administration to said human or other mammal of a delayed-release composition consisting essentially of said 5-ASA active ingredient and a pharmaceutically-acceptable excipient.

Irritable bowel syndrome (hereinafter referred to as "IBS") is a poorly understood disorder for which there is presently no adequate treatment. IBS is usually the diagnosis given when an individual suffers from certain characteristic symptoms affecting the gastrointestinal tract and after the existence of other disorders have been eliminated. Accordingly, IBS sufferers exhibit altered bowel habits (characterized either by alternating diarrhea and constipation, solely constipation, or solely diarrhea), as well as abdominal pain and/or cramping, and various other symptoms including flatulence and abdominal distension, bloating, and rumbling. There is no detectable radiological or histological evidence of organic pathology, i.e. the presence of an infectious agent or observable inflammation or other pathology in the intestinal tract. IBS has been called functional bowel

disorder, mucomembraneous colitis, nervous diarrhea, colonic neurosis, colonic dyspepsia, colonic dysfunction, spastic colon, mucous colitis, irritable colon syndrome, unhappy colon, dissynergia of the colon, and disordered gastrocolonic reflex. It is estimated that about 10% of the adult population suffers from IBS and that this disorder accounts for from about 40% to about 70% of office visits to gastroenterologists. It has also been suggested that IBS is one of the leading causes of absenteeism from work due to illness.

As stated hereinabove, those suffering from IBS may experience diarrhea only, alternating diarrhea and constipation, or constipation only; accordingly, there has been a great deal of effort to categorize IBS patients based upon these symptoms. See Einar Krag, "Irritable Bowel Syndrome: Current Concepts and Future Trends," Scand. J. Gastroenteral, Vol. 20 (Suppl. 109), pp. 107-15, 1985; and Whitehead et al., "Irritable Bowel Syndrome - Physiological and Psychological Differences Between Diarrhea-Predominant and Constipation-Predominant Patients", Dig. Dis. Sci., Vol. 25, No. 6, pp. 404-13, June 1980 (hereinafter referred to as "Whitehead et al."). It has been estimated that about 50% of IBS sufferers experience IBS-Diarrheal phase or type (hereinafter referred to as IBS-D) and that 50% of IBS sufferers experience constipation only. Of the population which suffers from IBS-D, one-fifth experience only diarrhea (IBS-diarrheal type), and the remaining four-fifths experience alternating diarrhea and constipation (IBS-diarrheal phase).

The cause of IBS has been extremely difficult to determine, and there has been little success in differentiating possible causes with regard to symptomatic characterizations. It has been reported that IBS stems from the ingestion of certain foodstuffs (often wheat gluten or lactose); other theories as to the cause of IBS have implicated disorders of gut motility, while many gastroenterologists, however, have attributed IBS to psychological factors. See generally, V. Alun Jones, et al., "Food Intolerance: A Major Factor in the Pathogenesis of Irritable Bowel Syndrome", The Lancet, Vol. 2, No. 8308,

pp. 1115-17, November 20, 1982 (hereinafter referred to as "Jones et al."); Kumar et al., "The Irritable Bowel Syndrome: A Paroxysmal Motor Disorder", The Lancet, Vol. 2, No. 8462, pp. 973-77, November 1985 (hereinafter referred to as "Kumar et al."); Drossman et al., "Psychosocial Factors in the Irritable Bowel Syndrome," Gastroenterology, Vol. 95, (3), pp. 701-8, Sept. 1988; and Drossman et al., "The Irritable Bowel Syndrome," Gastroenterology, Vol. 73, p. 811-22, Oct. 1977.

In addition to confusion as to the cause of IBS-D, there is debate as to the precise site of the disorder in the intestinal tract; there is confusion as to whether the problematic region is the small intestine, the colon, or both, and whether the problematic site varies amongst individuals and/or depending on the symptoms. See, e.g. Kumar et al., op. cit., and Cann et al., "Irritable Bowel Syndrome: Relationship of Disorders in the Transit of a Single Meal to Symptom Patterns", Gut, Vol. 24, No. 5, pp. 405-11, May 1983.

Much of the early work on disorders of the gastrointestinal tract has involved ulcerative colitis and Crohn's disease, which are two of the most common Inflammatory Bowel Diseases (hereinafter referred to as "IBD"). In fact, patients with IBS-D present with symptoms which are markedly similar to those experienced with IBD, particularly ulcerative colitis and Crohn's disease and, therefore, the existence of IBD is generally investigated and ruled out before the diagnosis of IBS-D is given.

It has been reported that the administration of 5-ASA is effective in the treatment of ulcerative colitis and Crohn's disease. See U.S. Patent 4,496,552 to Halskov, issued January 29, 1985, and assigned to Farmaceutisk Laboratorium Ferring, hereby incorporated by reference herein.

It has further been stated that various gastrointestinal disorders including, in addition to IBS, Crohn's disease (regional ileitis), ulcerative colitis (proctitis, distal proctocolitis), atrophic gastritis, stump proctitis, coeliac disease, regional ileitis, peptic ulceration, and

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