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(54) **COMPOSITIONS FOR THE TREATMENT OF INFLAMMATION OF THE GASTROINTESTINAL TRACT**

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(57) **ABSTRACT**

Provided herein are methods for preventing or alleviating the symptoms of and inflammation associated with inflammatory diseases and conditions of the gastrointestinal tract, for example, those involving the esophagus. Also provided herein are pharmaceutical compositions useful for the methods of the present invention.

COMPOSITIONS FOR THE TREATMENT OF INFLAMMATION OF THE GASTROINTESTINAL TRACT

CROSS-REFERENCE

[0001] This application claims the benefit of U.S. Provisional Application No. 60/987,720, filed Nov. 13, 2007; U.S. Provisional Application No. 61/012,012, filed Dec. 6, 2007; U.S. Provisional Application No. 61/015,998, filed Dec. 21, 2007; U.S. Provisional Application No. 61/019,818, filed Jan. 8, 2008; U.S. Provisional Application No. 61/034,941, filed Mar. 7, 2008; U.S. Provisional Application No. 61/035,348, filed Mar. 10, 2008; U.S. Provisional Application No. 61/054,103, filed May 16, 2008; U.S. Provisional Application No. 61/054,104, filed May 16, 2008; U.S. Provisional Application No. 61/054,105, filed May 16, 2008; U.S. Provisional Application No. 61/054,106, filed May 16, 2008; U.S. Provisional Application No. 61/054,107, filed May 16, 2008; and U.S. Provisional Application No. 61/090,658, filed Aug. 20, 2008, which applications are incorporated herein by reference.

BACKGROUND OF THE INVENTION

[0002] Esophageal inflammation disorders are gaining increased recognition in both adults and children. One example is eosinophilic esophagitis (EE or EoE), which is an emerging, and fast-growing disorder characterized by high levels of eosinophils in the esophagus, as well as basal zone hyperplasia. EoE is thought to be provoked, in at least a subset of patients, by food allergies or airborne allergen exposure (1-5, 44). EoE diagnosis is often associated with other hypersensitivity disorders, including asthma, rhinitis, and other food and aeroallergen inhalant sensitivities (39-40). Diagnosis is often made, e.g., in young children and depends on the finding of 15 to 20 or more to 24 or more eosinophils per high power field (eos/hpf) within esophageal mucosal biopsies (6-12).

[0003] In parallel with other atopic disorders, the incidence of EoE appears to be increasing (15, 35). The disorder may present with reflux-like symptoms, pain and dysphagia, clinical symptoms similar to the presentation of gastroesophageal reflux disease ("GERD") (42). Symptoms of EoE include, for example, abdominal pain, chest pain, choking, difficulty swallowing, failure to thrive, nausea, reflux not relieved by standard anti-flux therapy, skin rash or hives, vomiting, and weight loss. In one series, 15% of EoE patients had concurrent developmental delay (45).

[0004] Although EoE is becoming more frequently diagnosed throughout developing countries (7, 8, 13-16) many aspects of the disease remain unclear including its etiology, natural history and optimal therapy. Symptoms of EoE often mimic those of GERD and include vomiting, dysphagia, pain and food impaction (8, 14, 17-20). However, treatment of EoE and GERD differ and it is important to distinguish between them, particularly as untreated EoE may be associated with esophageal narrowing in 10-30% of cases (14, 18, 20, 21). The overlap of GERD and EoE symptoms is common; failure to respond to high PPI GERD treatment may be one diagnostic guideline for EoE (42). The common occurrence regarding misdiagnosis of EoE for GERD often results in delayed treatment for patients with EoE. (42).

[0005] Long term systemic steroid therapy can result in significant secondary side effects on growth and bone development. Although treatment with anti-IL-5 monoclonal antibody has been reported to be successful in EE or EoE, this therapy is currently not approved for use in children (36).

[0006] Current treatments include elimination diets (22, 23), and elemental formulas (2, 24). Identifying true inciting food allergens can be difficult and elemental formulas are often unpalatable, thereby making dietary interventions complicated (1, 22). Improvised puff and swallow techniques may be difficult for patients, especially smaller children, and especially children with developmental delays, to perform efficiently. This may result in a less than effective dose of a topical steroid being delivered to the esophagus.

SUMMARY OF THE INVENTION

[0007] Certain embodiments of the present invention provide for a method of treating, preventing or alleviating inflammation of the gastrointestinal tract comprising orally administering to an individual in need thereof a composition comprising a corticosteroid, a preservative, an isotonic agent, a surfactant, and an excipient.

[0008] In certain embodiments, the corticosteroid is, by way of non-limiting example, fluticasone propionate. In some embodiments, the corticosteroid is present in the composition in an amount of about 0.01 mg to about 1.0 mg of corticosteroid per gram of composition.

[0009] In some embodiments, the preservative is, by way of non-limiting example, benzalkonium chloride. In certain embodiments, the preservative is present in the composition in an amount of about 0.0002% to about 0.03% w/w of the composition.

[0010] In some embodiments, the isotonic agent is, by way of non-limiting example, dextrose. In certain embodiments, the surfactant is, by way of non-limiting example, polysorbate 80. In some embodiments, the excipient is an excipient that increases the interaction of the composition with a surface of the gastrointestinal tract (e.g., the mucosa and/or epithelium of the gastrointestinal tract or of a specific site of the gastrointestinal tract, such as the esophagus). In certain embodiments, the excipient that increases the interaction of the composition with a surface of the gastrointestinal tract (e.g., the mucosa and/or epithelium of the gastrointestinal tract or of a specific site of the gastrointestinal tract, such as the esophagus) is a viscosity enhancing agent. In some embodiments, the viscosity enhancing agent is selected from, by way of non-limiting example, microcrystalline cellulose, carboxymethyl cellulose sodium and a combination thereof. In certain specific embodiments, the viscosity enhancing agent is a combination of microcrystalline cellulose and carboxymethyl cellulose sodium. In other specific embodiments, the viscosity enhancing agent is carboxymethyl cellulose sodium. In some embodiments, a corticosteroid containing composition of the present invention comprises a second excipient. In certain embodiments, the second excipient is selected from, by way of non-limiting example, an excipient that increases the interaction of the composition with a surface of the gastrointestinal tract (e.g., the mucosa and/or epithelium of the gastrointestinal tract or of a specific site of the gastrointestinal tract, such as the esophagus), a binder, a filler, a disintegrant, a diluent, a carrier a vehicle and combinations thereof. In certain specific embodiments, the second excipient that increases the interaction of the composition with a surface of the gastrointestinal tract (e.g., the mucosa and/or epithelium of the gastrointestinal tract or of a specific site of the gastrointestinal tract, such as the esophagus) is a second viscosity enhancing agent.

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[0011] In some embodiments, the composition further comprises a fragrance. In specific embodiments, the fragrance is, by way of non-limiting example, phenylethyl alcohol. In some embodiments, the fragrance is present in the composition in an amount of about 0.0005 to about 0.4% w/w of the composition.

[0012] In certain embodiments, the vehicle is present in the composition in an amount of about 50% to about 99.5% w/w of the composition. In some embodiments, the vehicle is selected from a liquid vehicle, a solid vehicle and combinations thereof. In certain embodiments, the solid vehicle is selected from, by way of non-limiting example, talc, bentonite, kaolin calcium carbonate, and combinations thereof. In some embodiments, the liquid vehicle is selected from, by way of non-limiting example, water, ethanol, an organic solvent, an oil and combinations thereof.

[0013] In some embodiments, the composition is formulated as a suspension of microfine corticosteroid particles suspended in an aqueous vehicle. In certain embodiments, the composition has a pH of about 5 to about 7.

[0014] In some embodiments, the composition further comprising a sweetener, a flavoring agent or a combination thereof.

[0015] In specific embodiments, the corticosteroid is microfine fluticasone propionate, the preservative is benzalkonium chloride, the isotonic agent is dextrose, the surfactant is polysorbate 80, the fragrance is phenylethyl alcohol, and the excipient that increases the interaction of the composition with a surface of the gastrointestinal tract (e.g., the mucosa and/or epithelium of the gastrointestinal tract or of a specific site of the gastrointestinal tract, such as the esophagus) is a combination of microcrystalline cellulose and carboxymethyl cellulose sodium. In some specific embodiments, the corticosteroid is microfine fluticasone propionate, the preservative is a combination of benzalkonium chloride and phenylethyl alcohol, the isotonic agent is dextrose, the surfactant is polysorbate 80, and the excipient that increases the interaction of the composition with a surface of the gastrointestinal tract (e.g., the mucosa and/or epithelium of the gastrointestinal tract or of a specific site of the gastrointestinal tract, such as the esophagus) is a combination of microcrystalline cellulose and carboxymethyl cellulose sodium. In more specific embodiments, the composition further comprises an aqueous vehicle. In even more specific embodiments, the composition is formulated as a suspension of microfine corticosteroid particles suspended in the aqueous vehicle. In some specific embodiments, the composition has a pH of about 5 to about 7. In certain embodiments, the composition further comprises a second excipient that increases the interaction of the composition with a surface of the gastrointestinal tract (e.g., the mucosa and/or epithelium of the gastrointestinal tract or of a specific site of the gastrointestinal tract, such as the esophagus).

[0016] In some embodiments, the benzalkonium chloride is present in the composition in an amount of about 0.0002% to about 0.03% w/w of the composition and the phenylethyl alcohol is present in the composition in an amount of about 0.0005 to about 0.4% w/w of the composition.

[0017] In certain embodiments, the present invention provides for methods of administering about 0.25 mg to about 3 mg of corticosteroid per day.

[0018] In some embodiments, the present invention provides for methods of treating inflammation of the esophagus. In certain embodiments, the present invention provides for methods of treating, preventing or alleviating and/or methods of treating, preventing or alleviating individuals diagnosed with eosinophilic esophagitis, an inflammatory bowel disease involving the esophagus, Crohn's disease, coeliac disease, eosinophilic duodenitis, functional dyspepsia, esophageal inflammation secondary to caustic/irritant ingestion, persistent/recurrent esophageal strictures of any cause and including caustic/irritant ingestion, pill-induced esophagitis, systemic diseases, congenital diseases, epithelial hyperplasia, basal cell hyperplasia, elongated papillae, dilated vessels in papillae, fungal esophagitis (e.g., Candida, turolopsis, histoplasma *Aspergillus*, etc.), viral esophagitis (e.g., HSV, CMV, V2V), bacterial esophagitis (e.g., tuberculosis, actinomycosis, syphlis), corrosive esophagitis, radiation esophagitis, chemotherapy esophagitis, graft vs. host disease, a skin disease with esophageal involvement (e.g., bullous pemphigoid, pemphigus vulgaris, epidermolysis bollosa, Stevens-Johnson syndrome), Behçet's disease, sarcoidosis, idiopathic esophagitis, eosinophilic gastritis, Ménétrier's disease, parasitic gastritis, lymphocytic esophagitis, inflammatory bowel disease-associated esophagitis, parasitic gastritis, or post-surgery inflammation. In specific embodiments, the present invention provides for methods of treating, preventing or alleviating and/or methods of treating, preventing or alleviating gastrointestinal disorders in individuals diagnosed with eosinophilic esophagitis. In some embodiments, the present invention provides for methods of treating, preventing or alleviating and/or methods of treating, preventing or alleviating individuals diagnosed with gastroesophageal reflux disease (GERD), nonerosive reflux disease (NERD), or erosive esophagitis.

[0019] In some embodiments, the present invention provides for methods of treating, preventing or alleviating individuals that are adults, children or infants. In some embodiments, the individual is a child less than 19 years old, less than 16 years old, less than 12 years old, less than 8 years old, less than 6 years old, less than 4 years old, or an infant less than 2 years old.

INCORPORATION BY REFERENCE

[0020] All publications and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication or patent application was specifically and individually indicated to be incorporated by reference.

DETAILED DESCRIPTION OF THE INVENTION

[0021] In certain embodiments, the present invention is directed to methods and pharmaceutical compositions for treating, preventing or alleviating the symptoms of and inflammation associated with inflammatory diseases involving the gastrointestinal tract, including the upper-gastrointestinal tract (e.g., inflammatory diseases involving pre-colonic gastrointestinal inflammation), esophagus, stomach and/or digestive tract. Provided herein are methods of treating, preventing or alleviating, for example, esophageal inflammation in an individual. In certain embodiments, these methods comprise orally administering to said individual a corticosteroid in association with at least one excipient that increases the interaction of the composition with a surface of the gastrointestinal tract (e.g., the mucosa and/or epithelium of the gastrointestinal tract or of a specific site of the gastrointestinal tract, such as the esophagus). In some embodiments, the

increased viscosity of the composition allows the composition to be in contact with the in esophagus for an extended period of time following administration.

[0022] An individual suitable for treatment with the compositions disclosed herein may, for example, have been diagnosed with a disease or condition including, but not limited to, eosinophilic esophagitis, inflammatory bowel diseases involving the esophagus, Crohn's disease, coeliac disease, eosinophilic duodenitis, functional dyspepsia, esophageal inflammation secondary to caustic/irritant ingestion, persistent/recurrent esophageal strictures of any cause and including caustic/irritant ingestion, pill-induced esophagitis, systemic diseases, congenital diseases, epithelial hyperplasia, basal cell hyperplasia, elongated papillae, dilated vessels in papillae, fungal esophagitis (e.g., Candida, turolopsis, histoplasma *Aspergillus*, etc.), viral esophagitis (e.g., HSV, CMV, V2V), bacterial esophagitis (e.g., tuberculosis, actinomycosis, syphlis), corrosive esophagitis, radiation esophagitis, chemotherapy esophagitis, graft vs. host disease, a skin disease with esophageal involvement (e.g., bullous pemphigoid, pemphigus vulgaris, epidermolysis bollosa, Stevens-Johnson syndrome), Behçet's disease, sarcoidosis, idiopathic esophagitis, eosinophilic gastritis, Ménétrier's disease, parasitic gastritis, lymphocytic esophagitis, inflammatory bowel disease-associated esophagitis, parasitic gastritis, or post-surgery inflammation. The composition may also be used in treating other gastrointestinal disorders, including stomach and duodenal ulcers, hyperactive acidic discharge disorders, such as Zollinger-Ellison syndrome and laryngeal disorders. Further, the compositions may also be used in treating other gastrointestinal disorders, including, by way of non-limiting example, gastroesophageal reflux disease (GERD), nonerosive reflux disease (NERD), or erosive esophagitis.

[0023] Provided herein are methods for treating, preventing and alleviating any chronic inflammatory or malignant state that involves the gastrointestinal tract, such as the esophagus, and responds to steroid therapy. The methods of the present invention are useful, for example, for treating, preventing and alleviating inflammation and/or symptoms and associated with eosinophilic esophagitis, inflammatory bowel diseases involving the esophagus, Crohn's disease, coeliac disease, eosinophilic duodenitis, functional dyspepsia, esophageal inflammation secondary to caustic/irritant ingestion, persistent/recurrent esophageal strictures of any cause and including caustic/irritant ingestion, pill-induced esophagitis, systemic diseases, congenital diseases, Epidermolysis bullosa, epithelial hyperplasia, basal cell hyperplasia, elongated papillae, dilated vessels in papillae, fungal esophagitis (e.g., Candida, turolopsis, histoplasma *Aspergillus*, etc.), viral esophagitis (e.g., HSV, CMV, V2V), bacterial esophagitis (e.g., tuberculosis, actinomycosis, syphlis), corrosive esophagitis, radiation esophagitis, chemotherapy esophagitis, eosinophilic gastric outlet obstruction and related inflammation, graft vs. host disease, a skin disease with esophageal involvement (e.g., bullous pemphigoid, pemphigus vulgaris, epidermolysis bollosa, Stevens-Johnson syndrome), Behçet's disease, sarcoidosis, idiopathic esophagitis, eosinophilic gastritis, Ménétrier's disease, parasitic gastritis, lymphocytic esophagitis, inflammatory bowel disease-associated esophagitis, parasitic gastritis, and post-surgery inflammation. The present methods are also useful for treating, preventing or alleviating symptoms and/or inflammation associated with other diseases or conditions of the gastrointestinal tract, for example, the upper gastrointestinal tract, where it is beneficial to target a particular target site, rather than provide systemic therapy. Also provided herein are pharmaceutical compositions useful in the methods of the present application. As used herein, inflammation and/or symptoms associated with a disorder or disease disclosed herein includes inflammation and/or symptoms associated with, caused by and/or resulting from the disorder or disease.

[0024] As used herein, unless otherwise stated, the use of the terms "a", "an" and "the" include both singular and multiple embodiments. As used herein, the term "individual" includes any animal. In some embodiments, the animal is a mammal. In certain embodiments, the mammal is a human. In specific embodiments, the human is an adult. In other embodiments, the human is a child. In yet other embodiments, the human is an infant. As used herein, the phrase "method of treating" or "method for treating" encompasses methods of preventing, reducing the incidences of, providing prophylactic treatment, treating and alleviating. As used herein, the phrase "an effective amount" and "a therapeutically effective amount" is an amount sufficient to elicit a change in the symptoms of or inflammation associated with gastrointestinal disorders, including but not limited to esophageal inflammation. As used herein, the term "or" includes "and" and "or".

[0025] As used herein, the phrase "treating inflammatory diseases involving the esophagus" includes treating symptoms of such diseases and treating inflammation associated with the diseases.

[0026] Methods and Compositions

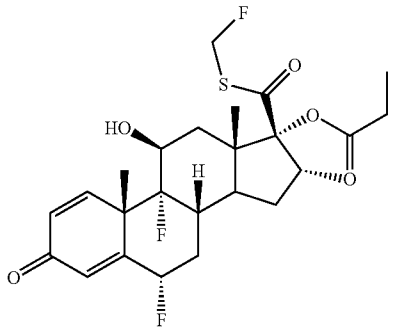
[0027] In certain embodiments, the corticosteroids used in the present invention include topical steroids including, for example, fluticasone. In some embodiments, corticosteroids are selected from, by way of non-limiting example, aclometasone, amcinomide, beclometasone, betamethasone, budesonide, ciclesonide, clobetasol, clobetasone, clocortolone, cloprednol, cortivazol, deflazacort, deoxycorticosterone, desonide desoximetasone, dexamethasone, diflorasone, diflucortolone, difluprednate, fluclorolone, fludrocortisone, fludroxycortide, flumetasone, flunisolide, fluocinolone acetonide, fluocinonide, fluocortin, fluocortolone, fluorometholone, fluperolone, fluticasone, fuprednidene, formocortal, halcinonide, halometasone, hydrocortisone aceponate, hydrocortisone buteprate, hydrocortisone butyrate, loteprednol, medrysone, meprednisone, methylprednisolone, methylpiednisolone aceponate, mometasone furoate, paramethasone, prednicarbate, prednisone, prednisolone, prednylidene, remexolone, tixocortol, triamcinolone and ulobetasol, combinations and pharmaceutically acceptable salts and esters thereof. In a specific embodiment, the corticosteroid is fluticasone (e.g., the fluticasone ester fluticasone propionate).

[0028] Provided herein are methods and pharmaceutical compositions for treating, preventing or alleviating the symptoms of, and inflammation associated with, inflammatory diseases of the gastrointestinal tract, including but not limited to the esophagus.

[0029] In certain embodiments, a corticosteroid (e.g., fluticasone propionate) that is administered in oral form, in a formulation with increased fluid viscosity, is delivered to the esophagus in an effective dose to reduce the inflammation of the esophagus.

[0030] In one aspect, an exemplary corticosteroid is fluticasone propionate. Fluticasone propionate (S-(fluoromethyl) 6α,9-difluoro-11β-17-dihydroxy-16α-methyl-3-oxoan-

drosta-1,4-diene-17β-carbothioate, 17 propionate or (6α, 11β,16α,17β)-6,9-Difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)androsta-1,4-diene-17-carbothioic acid S-(fluoromethyl) ester), is a corticosteroid sometimes used in inhaled form to treat pulmonary conditions.



Fluticasone Propionate

[0031] In certain embodiments, the pharmaceutical composition described herein includes one or more excipients. Excipients useful herein include, by way of non-limiting example, binders, fillers, lubricants, isotonic agents, surfactants, antioxidants, chelating agents, preservatives, buffers, pH adjusting agents (e.g., hydrochloric acid and/or sodium hydroxide), solvents, flavoring agents, coloring agents, sweeteners, fragrances, excipients that increase the interaction of the composition with a surface of the gastrointestinal tract (e.g., the mucosa and/or epithelium of the gastrointestinal tract or of a specific site of the gastrointestinal tract, such as the esophagus) and combinations thereof. Excipients that increase the interaction of the composition with the surface of the gastrointestinal tract (e.g., the mucosa and/or epithelium of the gastrointestinal tract or of a specific site of the gastrointestinal tract, such as the esophagus) include excipients that enhance the viscosity of the composition, excipients that impart a mucoadhesive characteristic to the composition, and excipients that enhance the absorption of the composition through a surface of the gastrointestinal tract (e.g., the mucosa and/or epithelium of the gastrointestinal tract or of a specific site of the gastrointestinal tract, such as the esophagus). In some embodiments wherein the composition is a suspension, surfactants are utilized in order to obtain an efficient dispersion of corticosteroid (e.g., fluticasone propionate) particles in the suspension.

[0032] Sweeteners include, by way of non-limiting example, sucrose, lactose, glucose, fructose, arabinose, xylose, ribose, mannose, galactose, dextrose, sorbose, sorbitol, mannitol, maltose, cellobiose, xylitol and the like. Flavoring agent include, by way of non-limiting example, peppermint, wintergreen, grape and cherry. Fragrances include, by way of non-limiting example, phenylethyl alcohol.

[0033] In some embodiments, surfactants include, by way of non-limiting example, polysorbates (e.g., polysorbate 80), Tween®, poloxamers, polyoxyethylene alkyl ethers, polyoxyethylene castor oil derivatives and combinations thereof. In a specific embodiment, the surfactant is polysorbate 80.

[0034] In certain embodiments, an isotonic agent includes, by way of non-limiting example, dextrose, glycerin, mannitol, sodium chloride, potassium chloride and combinations thereof. In specific embodiments, the isotonic agent is dextrose (e.g., dextrose anhydrous).

[0035] Preservatives include, by way of non-limiting example, benzalkonium chloride, methylparaben, propylparaben, potassium sorbate, phenylethyl alcohol and sodium benzoate. In specific embodiments, the preservative is benzalkonium chloride.

[0036] In some embodiments, the compositions comprise an excipient that increases the interaction of the composition with a surface of the gastrointestinal tract (e.g., the mucosa and/or epithelium of the gastrointestinal tract or of a specific site of the gastrointestinal tract, such as the esophagus). In certain embodiments, the excipient or excipients chosen increase the interaction of the composition with the surface of the gastrointestinal tract (e.g., the mucosa and/or epithelium of the gastrointestinal tract or of a specific site of the gastrointestinal tract, such as the esophagus) by at least 1.02 fold, by at least 1.05-fold, by at least 1.1 fold, by at least 1.2 fold, by at least 1.25-fold, by at least 1.5-fold, by at least 2-fold, by at least 3-fold, by at least 4-fold, by at least 5-fold, by at least 10 fold, or by at least 20 fold. In certain embodiments, the increased interaction of the composition is an at least 1.02 fold, by at least 1.05-fold, by at least 1.1 fold, by at least 1.2 fold, by at least 1.25-fold, by at least 1.5-fold, by at least 2-fold, by at least 3-fold, by at least 4-fold or by at least 5-fold of interaction of the composition with the esophagus that occurs following passing of the bolus of the composition being swallowed. In certain embodiments, these increases are measured and compared to the measure of an otherwise similar composition lacking the excipient or excipients that increase the interaction of the composition with the surface of the gastrointestinal tract. In certain instances, increased interaction of the composition is measured as a function of the amount of composition present in the esophagus (e.g., after the bolus has passed through the esophagus). In specific instances, the amount of composition present in the esophagus is measured in any suitable manner, e.g., by radiolabeling the composition and measuring the amount of the composition in the esophagus utilizing gamma scintigraphy. An increase in the interaction of the composition with the surface of the gastrointestinal tract (e.g., the mucosa and/or epithelium of the gastrointestinal tract or of a specific site of the gastrointestinal tract, such as the esophagus) may be measured by measuring the retention time of the material along a length of a surface of the gastrointestinal tract (e.g., the mucosa and/or epithelium of the gastrointestinal tract or of a specific site of the gastrointestinal tract, such as the esophagus), wherein the retention time is increased in the presence of the excipient as compared to its absence. In some embodiments, a portion composition is retained on the esophagus after oral administration (e.g., after initial swallowing) for at least 5 seconds, for at least 6 seconds at least 10 seconds, for at least 12 seconds, for at least 15 seconds, for at least 30 seconds, for at least 60 seconds, for at least 2 minutes, for at least 4 minutes, for at least 10 minutes, for at least 15 minutes, for at least 30 minutes, or the like. In certain embodiments, the portion of the composition that is retained on or within the esophagus is at least 1%, at least 2%, at least 3%, at least 4%, at least 5%, at least 6%, at least 7%, at least 8%, at least 9%, at least 10%, at least 15%, at least 20%, at least 30%, at least 40%, at least 50%, or the like. In certain embodiments, the composition is retained on the esophagus after oral administration for about 15 seconds to about 120 seconds, or for about 30 to about 90 seconds. In another embodiment, an increased

interaction may be measured by the decrease in physiological manifestations or symptoms of the disease or ailment to be treated, including a decrease in total eosinophil counts in a target sample.

[0037] In specific embodiments, following oral administration of a composition described herein to the esophagus (e.g., following initial swallowing or drinking of the composition), at least 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 15%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or 95% by weight of the corticosteroid or composition administered is present within the esophagus (e.g., as measured by gamma scintigraphy) after at least 5 seconds, 10 seconds, 15 seconds, 20 seconds, 25 seconds, 30 seconds, 40 seconds, 45 seconds, 50 seconds, or 1, 1.5, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55 or 60 minutes following application of the composition to the esophagus. In certain instances, even small differences (e.g., increases) in adherence times (e.g., residence times) between formulations can result in therapeutically significant or clinically significant results or improvements.

[0038] In one aspect of the invention, the use of the excipients may act to decrease the quantity of active agents needed to elicit a response in the absence of the excipients. In some embodiments, the excipients may decrease the amount of corticosteroid used, for example, from about 1 to about 3 mg of fluticasone propionate in the absence of excipient to about 500 μg to about 2 mg of fluticasone propionate in the presence thereof. Accordingly, the compositions provided herein may provide an additional advantage of decreasing the amount of active agent needed to treat subjects afflicted with inflammatory diseases involving the gastrointestinal tract, including the esophagus, stomach and/or digestive tract.

[0039] In certain embodiments, the corticosteroid is administered in combination with an excipient that enhances the viscosity of the composition. It is to be understood that in various embodiments of the present invention, the viscosity of the oral dosage form is at a level that is sufficient to deliver an effective amount of the composition to the site of gastrointestinal inflammation, e.g., the esophagus. In some embodiments, the effective amount of the composition delivered to the esophagus is an amount sufficient to coat the esophagus, and thereafter deliver the composition to the affected areas, including by way of example only, the lower esophagus, the esophageal-stomach juncture, the stomach and/or the duodenum. In certain embodiments, the viscosity of the oral dosage form is such that when administered orally, it is not so thick as to cause difficulty in swallowing, cause gagging, or be unpalatable. Those of ordinary skill in the art can determine the viscosity of the compositions provided herein, and may thus determine appropriate ranges. In certain embodiments, the viscosity of the oral dosage form is a viscosity that is sufficient to provide exposure of the corticosteroid to the esophagus for a sufficient period of time such that the symptoms of and/or inflammation associated with inflammatory diseases involving the gastrointestinal tract, including the esophagus, are reduced following administration of the corticosteroid containing oral dosage form.

[0040] One method for determining sufficient viscosity may include monitoring changes in the interaction of the composition with a surface of the gastrointestinal tract (e.g., the mucosa and/or epithelium of the gastrointestinal tract or of a specific site of the gastrointestinal tract, such as the esophagus), including but not limited to measuring changes in residence or retention time of the composition in the absence and presence of the excipient. Another method for determining whether the composition is sufficiently viscous is by determining whether the inflammation of the esophagus is reduced after treatment with the composition.

[0041] Viscosity may be, for example, measured at room temperature, at about 20-25 degrees Celsius, or at about 37 degrees Celsius to mimic body temperature. The viscosity of a liquid generally decreases as the temperature is raised. In various embodiments of the present invention, the viscosity of the composition described herein is any viscosity suitable for delivery of the corticosteroid to the inflamed portion of the gastrointestinal tract. In some embodiments, the viscosity of the composition is at least about 2 centipoise (cP), or at least about 25 cP, or at least about 50 cP. In some embodiments, the viscosity of the composition is at least about 100 cP. In one aspect, the viscosity of the composition is from about 25 centipoise (cP) to about 800 cP, as measured with a Brookfield viscometer at 25 degrees Celsius, more preferably at about 50 cP to about 800, or about 300 cP to about 800 cP. In another aspect, the viscosity of the composition may range from about 250 cP to about 600 cP or about 400 cP to about 600 cP. In specific embodiments, the viscosity of the formulation is about 100 cP, or about 200 cP, or about 300 cP, or about 400 cP or about 500 cP, e.g., as measured with a Brookfield viscometer at 25 degrees Celsius (e.g., equipped with an ultra low adapter).

[0042] Viscosity can also be determined by any method that will measure the resistance to shear offered by the substance or preparation. Many viscometers are available to those in the pharmaceutical Field, and include those built by, for example, Brookfield.

[0043] In some embodiments, the viscosity of the composition is measured at room temperature (about 25 degrees C.) with a shear rate of about 13.2 sec^{-1}. In certain embodiments, provided herein is a composition having a viscosity under such conditions that is at least about 2 centipoise (cP), at least about 25 cP, at least about 30 cP, at least about 35 cP, about 35 cP, at least about 40 cP, about 40 cP, at least about 50 cP, at least about 200 cP, at least about 225 cP, at least about 250 cP, at least about 300 cP, or at least about 400 cP. In some embodiments, the viscosity of the composition under such conditions is about 50 cP to about 250,000 cP, about 50 cP to about 70,000 cP, about 50 cP to about 25,000 cP, about 50 cP to about 10,000 cP, about 50 cP to about 3,000 cP, about 50 cP to about 2,000 cP, about 250 cP to about 250,000 cP, about 250 cP to about 70,000 cP, about 250 cP to about 25,000 cP, about 250 cP to about 10,000 cP, about 250 cP to about 3,000 cP, or about 250 cP to about 2,000 cP. In one aspect, the viscosity of the composition, as measured at 25 degrees Celsius, is from about 25 centipoise (cP) to about 800 cP, about 50 cP to about 800, or about 300 cP to about 800 cP (e.g., measured by a Brookfield viscometer). In another aspect, the viscosity of the composition under such conditions may range from about 100 cP to about 200 cP, about 200 cP to about 300 cP, about 250 cP to about 600 cP or about 400 cP to about 600 cP. In specific embodiments, the viscosity of the formulation measured under such conditions is about 30 cP, about 40 cP, about 100 cP, about 200 cP, about 300 cP, about 400 cP, about 500 cP, or about 250,000 cP.

[0044] In some embodiments, the viscosity of the composition is measured at room temperature (about 25 degrees C.) with a shear rate of about 15 sec^{-1} (e.g., with a gap between the spindle and the sample chamber wall of about 6 mm or greater). In certain embodiments, provided herein is a com-

position having a viscosity under such conditions that is at least about 150 centipoise (cP), at least about 160 cP, at least about 170 cP, at least about 180 cP, at least about 190 cP, or at least about 200 cP. In some embodiments, the viscosity of the composition under such conditions is about 150 cP to about 250,000 cP, 160 cP to about 250,000 cP, 170 cP to about 250,000 cP, 180 cP to about 250,000 cP, or 190 cP to about 250,000 cP.

[0045] Viscosity-enhancing excipients that may be used in pharmaceutical compositions described herein include, but are not limited to, acacia (gum arabic), agar, aluminum magnesium silicate, sodium alginate, sodium stearate, bladderwrack, bentonite, carbomer, carrageenan, Carbopol, xanthan, cellulose, microcrystalline cellulose (MCC), ceratonia, chondrus, dextrose, furcellaran, gelatin, Ghatti gum, guar gum, hectorite, lactose, sucrose, maltodextrin, mannitol, sorbitol, honey, maize starch, wheat starch, rice starch, potato starch, gelatin, sterculia gum, xanthum gum, polyethylene glycol (e.g. PEG 200-4500), gum tragacanth, ethyl cellulose, ethylhydroxyethyl cellulose, ethylmethyl cellulose, methyl cellulose, hydroxyethyl cellulose, hydroxyethylmethyl cellulose, hydroxypropyl cellulose, poly(hydroxyethyl methacrylate), oxypolygelatin, pectin, polygeline, povidone, propylene carbonate, methyl vinyl ether/maleic anhydride copolymer (PVM/MA), poly(methoxyethyl methacrylate), poly(methoxyethoxyethyl methacrylate), hydroxypropyl cellulose, hydroxypropylmethyl-cellulose (HPMC), sodium carboxymethyl-cellulose (CMC), silicon dioxide, polyvinylpyrrolidone (PVP: povidone), Splenda® (distributed by McNeil Nutritionals, LLC Fort Washington, Pa. 19034-2299; comprising 1 g of dextrose, maltodextrin and sucralose) or combinations thereof. In one non-limiting example, the viscosity-enhancing excipient is Splenda®. In specific embodiments, the viscosity-enhancing excipient is a combination of MCC and CMC (e.g., Avicel® RC-591 (manufactured by FMC Corporation; colloid forming attrited mixture of microcrystalline cellulose and carboxymethylcellulose sodium, NF, BP; Avicel® RC-591 product brochure, RC-591 (5/99) is hereby incorporated by reference in its entirety)). In more specific embodiments, a composition described herein comprises a first viscosity enhancing agent (e.g., Avicel® RC-591) and a second viscosity enhancing agent (e.g., Splenda®). In another non-limiting example, the viscosity-enhancing excipient is CMC.

[0046] Mucoadhesive agents including, but not limited to, at least one soluble polyvinylpyrrolidone polymer (PVP); a water-swellable, but water-insoluble, fibrous, cross-linked carboxy-functional polymer; a crosslinked poly(acrylic acid) (e.g. Carbopol 947P); a carbomer homopolymer; a carbomer copolymer; a hydrophilic polysaccharide gum, maltodextrin, a cross-linked alignate gum gel, a water-dispersible polycarboxylated vinyl polymer, at least two particulate components selected from the group consisting of titanium dioxide, silicon dioxide, and clay, or a mixture thereof. The mucoadhesive agent may be used in combination with a viscosity increasing excipient, or may be used alone to increase the interaction of the composition with the esophagus. In one non-limiting example, the mucoadhesive agent is maltodextrin. Those of ordinary skill in the art will recognize that the mucoadhesive character imparted to the composition should be at a level that is sufficient to deliver an effective amount of the composition to, for example, the esophagus in an amount that may coat the esophagus, and thereafter deliver the composition to the affected areas, including by way of example only, the lower esophagus, the esophageal-stomach juncture, the stomach and/or the duodenum. Also, the mucoadhesiveness should be at a level that may be given orally, i.e. allows a patient to swallow, limits a gagging reaction, and is palatable. Those of ordinary skill in the art can determine the mucoadhesive characteristics of the compositions provided herein, and may thus determine appropriate ranges. One method for determining sufficient mucoadhesiveness may include monitoring changes in the interaction of the composition with a surface of the gastrointestinal tract (e.g., the mucosa and/or epithelium of the gastrointestinal tract or of a specific site of the gastrointestinal tract, such as the esophagus), including but not limited to measuring changes in residence or retention time of the composition in the absence and presence of the excipient. Another method for determining whether the composition is sufficiently mucoadhesive is by determining whether the inflammation of the esophagus is reduced after treatment with the corticosteroid. As used herein, a mucoadhesive agent is an agent that adheres to a gastrointestinal surface (e.g., either or both of a gastrointestinal epithelia or mucosa).

[0047] Mucoadhesive agents have been described, for example, in U.S. Pat. Nos. 6,638,521, 6,562,363, 6,509,028, 6,348,502, 6,319,513, 6,306,789, 5,814,330, and 4,900,552, each of which is hereby incorporated by reference in its entirety.

[0048] In one non-limiting example, the mucoadhesive agent is maltodextrin. Maltodextrin is a carbohydrate produced by the hydrolysis of starch that may be derived from corn, potato, wheat or other plant products. Maltodextrin may be used either alone or in combination with other mucoadhesive agents to impart mucoadhesive characteristics on the compositions disclosed herein. In one embodiment, a combination of maltodextrin and a carbopol polymer are used to increase the mucoadhesive characteristics of the compositions disclosed herein. In some embodiments, any composition or formulation described herein comprises greater than about 7% w/w, greater than about 8% w/w, greater than about 9% w/w, greater than about 10% w/w, greater than about 11% w/w, greater than about 12% w/w, greater than about 13% w/w, greater than about 14% w/w, greater than about 15% w/w, greater than about 16% w/w, greater than about 17% w/w, greater than about 18% w/w, greater than about 19% w/w, greater than about 20% w/w, greater than about 21% w/w, greater than about 22% w/w, greater than about 23% w/w, greater than about 24% w/w, greater than about 25% w/w, greater than about 26% w/w, greater than about 27% w/w, greater than about 28% w/w, greater than about 29% w/w or greater than about 30% w/w of maltodextrin. In specific embodiments, the maltodextrin is substantially dissolved in a liquid vehicle of the composition or formulation. In certain embodiments, the maltodextrin has a dextrose equivalents (DE) of greater than 4, greater than 5, greater than 10, greater than 11, greater than 12, greater than 13, greater than 14, greater than 15, about 15, about 4 to about 10, about 4 to about 9, about 4 to about 8, about 11 to about 20, about 12 to about 19, about 13 to about 18, or about 14 to about 16. In specific embodiments, the first maltodextrin has a DE of about 4 to about 10, about 4 to about 9, or about 4 to about 8 and the second maltodextrin has a DE of about 10 to about 20, about 12 to about 19, or about 13 to about 18. In some embodiments, at least one maltodextrin utilized in a composition described herein has a molecular weight high enough to

increase the solubility of a corticosteroid, or to increase the suspendability of a corticosteroid particle.

[0049] In another non-limiting example, a mucoadhesive agent can be, for example, at least two particulate components selected from titanium dioxide, silicon dioxide, and clay, wherein the composition is not further diluted with any liquid prior to administration and the level of silicon dioxide, if present, is from about 3% to about 15%, by weight of the composition. Silicon dioxide, if present, may be selected from the group consisting of fumed silicon dioxide, precipitated silicon dioxide, coacervated silicon dioxide, gel silicon dioxide, and mixtures thereof. Clay, if present, may be kaolin minerals, serpentine minerals, smectites, illite or a mixture thereof. For example, clay can be laponite, bentonite, hectorite, saponite, montmorillonites or a mixture thereof.

[0050] In specific embodiments, provided herein are compositions comprising a viscosity enhancing agent and a mucoadhesive agent. In specific embodiments, the composition comprises about 0.005% (w/w) to about 3% (w/w) of a viscosity enhancing excipient (e.g., a CMC/MCC combination having a ratio as described herein), and about 1% (w/w) to about 30% (w/w) of a mucoadhesive agent (e.g., maltodextrin).

[0051] Examples of absorption enhancing include, but are not limited to, acylcamitines, surfactants, sodium lauryl sulfate, saponins, bile salts or bile acids including but not limited to cholanic acid, chilic acid, deoxycholic acid, glycocholic acid, tautocholic acid, chenodeoxycholic acid, lithocholic acid, ursocholic acid, ursodeoxycholic acid, isourosde oxycholic acid, lagodeoxycholic acid, glycodeoxycholic acid, glycochenodeoxycholic acid, dehydrocholic acid, hyocholic acid, hyodeoxycholic acid, or combinations thereof, dihydrofusidates, fatty acid derivatives, chitosan, carbopol, cellulosic agents, sterols, including but not limited to alcohols structurally related to steroids, including but not limited to cholestanol, coprostanol, cholesterol, epicholesterol, ergosterol, ergocalciferol, or combinations thereof, starch, dextran, cyclodextrin, or combinations thereof. Absorption enhancing agents may act by increasing absorption of the active agent, including corticosteroids and acid inhibitors, through a surface of the gastrointestinal tract (e.g., the mucosa and/or epithelium of the gastrointestinal tract or of a specific site of the gastrointestinal tract, such as the esophagus). Examples of absorption enhancing agents are disclosed in WO 2005/113008, which is hereby incorporated by reference in its entirety.

[0052] The compositions contemplated herein may also include a combination of excipients that are viscosity enhancing agents, mucoadhesive agents and/or absorption enhancing agents. Moreover, an excipient may exhibit multiple characteristics, i.e., may be both a viscosity enhancing agent and a mucoadhesive agent. The composition may also include excipients that do not impart characteristics of viscosity enhancing, mucoadhesive agents or absorption enhancing activity.

[0053] In certain embodiments, the pharmaceutical compositions provided herein are used to treat, prevent or alleviate inflammatory diseases involving the gastrointestinal tract, including the esophagus, stomach and/or digestive tract. In specific embodiments, the pharmaceutical composition is in liquid form Liquid forms include, by way of non-limiting example, solutions, suspensions, syrups, slurries, dispersions, colloids and the like. In specific embodiments, the liquid is a suspension.

[0054] The methods and compositions of the present invention are used by individuals of any age. By "individual" is meant any animal, for example, a mammal, or, for example, a human, including, for example, patients in need of treatment. In some embodiments, the individual is a human adult. In other embodiments, the individual is a human child or infant. In certain embodiments, the human child or infant is less than 16 years old, less than 12 years old, less than 8 years old, less than 6 years old, less than 4 years old or less than 2 years old.

[0055] Formulations

[0056] While the compositions of the present invention will typically be used in therapy for human patients, in certain embodiments, they are used in veterinary medicine to treat similar or identical diseases. In some embodiments, the compositions are used, for example, to treat mammals, including, but not limited to, primates and domesticated mammals. In some embodiments, the compositions are used, for example, to treat herbivores. The compositions of the present invention include geometric and optical isomers.

[0057] Pharmaceutical compositions suitable for use in the present invention include compositions wherein the active ingredient or ingredients are contained in an effective amount to achieve its intended purpose. In light of the detailed disclosure provided herein, determination of the effective amounts is well within the capability of those skilled in the art. It is expected that a skilled pharmacologist may adjust the amount of drug in a pharmaceutical composition or administered to a patient based upon standard techniques well known in the art.

[0058] The exact dosage will depend upon the route of administration, the form in which the composition is administered, the subject to be treated, the age, body weight/height of the subject to be treated, and the preference and experience of the attending physician. In certain embodiments, the optimal concentration of the corticosteroid in the composition depends upon the specific corticosteroid used, the characteristics of the patient, and the nature of the inflammation for which the treatment is sought. In various embodiments, these factors are determined by those of skill in the medical and pharmaceutical arts in view of the present disclosure.

[0059] Generally, a therapeutically effective dose is desired. A therapeutically effective dose refers to the amount of the corticosteroid that results in a degree of amelioration of symptoms and inflammation relative to the status of such symptoms prior to treatment. The dosage forms containing effective amounts are within the scope of the instant invention. In various embodiments, the amount of corticosteroid (e.g., fluticasone propionate) used in a method or in a composition described herein is from about 2.5 to 400 μg/kg of body weight per day, or for example, in the range of 5 to 300 μg/kg per day, or for example in the range of 5 to 200 μg/kg per day, or for example in the range of 5 to 100 μg/kg per day, or for example in the range of 10 to 100 μg/kg per day, or for example in the range of 10-50 μg/kg per day, or for example in the range of 10-100 μg/kg/day, or for example in the range of 5-50 μg/kg/day, or in an illustrative embodiment in the range of 10-60 μg/kg/day. In some embodiments, the amount of corticosteroid (e.g., fluticasone propionate) used in a method or in a combination disclosed herein includes, by way of non-limiting example, about 100 μg to about 20 mg, 300 μg to about 4 mg, about 50 μg to about 500 mg, about 50 μg to about 200 mg, about 50 μg to about 100 mg, about 50 μg to about 50 mg, about 250 μg to about 20 mg, about 250 μg to about 15 mg, about 250 μg to about 10 mg, about 250 μg to

about 5 mg, 250 μg to 3 mg, or 500 μg to 3 mg, or 500 μg to 2 mg, or 1 mg to 3 mg. In an illustrative embodiment, the dosage is provided in a sufficient volume to allow the composition to reach the esophagus in an effective amount.

[0060] In an illustrative embodiment, a dosage or amount (including a divided dose) of corticosteroid is provided in a composition of sufficient volume to allow any of the compositions disclosed herein to reach the targeted and/or inflamed portion of the gastrointestinal tract, including, e.g., the esophagus, in an effective amount. In some embodiments, the effective amount of the composition delivered to the esophagus is an amount sufficient to coat or at least partially coat the esophagus, and deliver the composition to the affected areas, including by way of example only, the lower esophagus, the esophageal-stomach juncture, the stomach and/or the duodenum. In certain embodiments, a composition described herein as a volume of, for example about 1-20 mL, or for example about 1-50 mL, or for example about 1-40 mL, or for example about 1-30 mL, or for example about 1-25 mL, or for example about 5-25 mL, or for example about 10-20 mL, or for example about 10 mL, or for example, about 15 mL, or for example, about 20 mL, or for example about 1-15 mL, or for example about 1-10 mL, or for example about 2-8 mL, or for example about 3-7 mL, or for example, about 4-6 mL, or for example, about 5 mL, or for example about 6-14 mL, or for example about 8-12 mL, or for example, about 9-11 mL, or for example, about 10 mL. In more specific embodiments, about 0.25 mg to about 6 mg, about 0.375 mg, about 0.5 mg, about 0.75 mg, about 1 mg, about 1.25 mg, about 1.5 mg, or about 2 mg of corticosteroid (e.g., fluticasone propionate) is formulated into a single or unit dose of a pharmaceutical composition described herein, the single or unit dose having a total volume of about 1-20 mL, or for example about 10-20 mL, or for example about 10 mL, or for example, about 15 mL, or for example, about 20 mL, or for example about 1-15 mL, or for example about 1-10 mL, or for example about 2-8 mL, or for example about 3-7 mL, or for example, about 4-6 mL, or for example, about 5 mL, or for example about 6-14 mL, or for example about 8-12 mL, or for example, about 9-11 mL, or for example, about 10 mL. As discussed herein, "liquid" encompasses slurries, solutions, suspensions, dispersions or any combination thereof, depending on the solubilities and amounts of the individual components and the vehicles and solvents used. In some embodiments, an appropriate palatable dosage is in a volume sufficient to coat or at least partially coat the esophagus, and in an illustrative embodiment, the volume is sufficient to coat or at least partially coat the esophagus and deliver the corticosteroid to the affected areas, including by way of example only, the lower esophagus, the esophageal-stomach juncture, the stomach, the duodenum and/or within 3 cm of the Z-line. The composition may be delivered, for example, four times a day, three times a day, twice a day, once a day, every other day, three times a week, twice a week, or once a week. The dosage may, for example, be divided into multiple doses throughout the day, or be provided, for example, in four, three, two, or one dose a day. In certain instances, administration more frequent administration (e.g., b.i.d. versus once a day) provides for a shorter overall therapy or a quicker onset of symptom resolution. In one illustrative example, the dose is provided once a day.

[0061] In certain embodiments, the volume of a liquid dosage is sufficient so as to at least partially reach the esophagus, but not so great so as to reach the stomach upon initial administration. In certain embodiments, the volume of the formulation is selected in an amount such that after at least 5 seconds, 10 seconds, 15 seconds, 30 seconds, 45 seconds, or 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55 or 60 minutes following oral administration, less than 99%, 98%, 97%, 96%, 95%, 94%, 93%, 92%, 91%, 90%, 85%, 80%, 70%, 60%, 50%, 40%, 30%, 20%, 10% or 5% of the formulation has reached the stomach. It is to be understood that the disclosure herein includes the disclosure of each time with each percentage. By way of non-limiting example, in various specific embodiments, formulation and/or the volume of the formulation is selected in an amount such that after at least 15 seconds, less than 98% of the formulation has reached the stomach; after at least 15 seconds, less than 95% of the formulation has reached the stomach; after at least 1 minute, after at least 1 minute, less than 95% of the formulation has reached the stomach; after at least 2 minutes, less than 95% of the formulation has reached the stomach; after at least 1 minute, less than 90% of the formulation has reached the stomach; or after at least 2 minutes, less than 90% of the formulation has reached the stomach. In some embodiments, the volume of the formulation is selected in an amount such that after at least 5 seconds, 10 seconds, 15 seconds, 30 seconds, 45 seconds, or 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55 or 60 minutes following oral administration, less than 99%, 98%, 97%, 96%, 95%, 94%, 93%, 92%, 91%, 90%, 85%, 80%, 70%, 60%, 50%, 40%, 30%, 20%, 10% or 5% of the corticosteroid has reached the stomach. It is to be understood that the disclosure herein includes the disclosure of each time with each percentage. By way of non-limiting example, in various specific embodiments, the volume of the formulation is selected in an amount such that after at least 15 seconds, less than 98% of the corticosteroid has reached the stomach; after at least 15 seconds, less than 95% of the corticosteroid has reached the stomach; after at least 1 minute, less than 95% of the corticosteroid has reached the stomach; after at least 2 minutes, less than 95% of the corticosteroid has reached the stomach; after at least 1 minute, less than 90% of the corticosteroid has reached the stomach; or after at least 2 minutes, less than 90% of the corticosteroid has reached the stomach. It is to be understood that in certain embodiments, the volume of the formulation suitable to achieve the above depends on the nature of the formulation, including, by way of non-limiting example, the identity of the excipient or excipients used, the amount of the excipient or excipients used (if any), the identity and amount of the corticosteroid used, and the identity and amounts of the any other components present in the formulation.

[0062] In some embodiments, the volume of a composition or dose of a composition described herein is an amount sufficient to substantially coat (e.g., at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98% or at least 99% of) the length of the esophagus of an individual to whom the composition is administered. In certain embodiments, the volume of a composition or a dose of a composition described herein is about 0.05 mL/cm esophageal length to about 1 mL/cm esophageal length, about 0.1 mL/cm esophageal length to about 0.8 mL/cm esophageal length, about 0.2 mL/cm esophageal length to about 0.6 mL/cm esophageal length, or about 0.3 mL/cm esophageal length to about 0.5 mL/cm esophageal length, wherein the esophageal length is the esophageal length of the individual to whom the composition is administered. In some embodiments, the volume of a composition or dose of a composition

described herein is based on the esophageal length of an individual (e.g., male, female, or both) that is in the 50th percentile of height for their age. Therefore, in some embodiments, the volume of a composition or dose of a composition described herein is about 0.05 mL/cm esophageal length to about 1 mL/cm esophageal length, about 0.1 mL/cm esophageal length to about 0.8 mL/cm esophageal length, about 0.2 mL/cm esophageal length to about 0.6 mL/cm esophageal length, about 0.3 mL/cm esophageal length to about 0.5 mL/cm esophageal length, about 0.32 mL/cm esophageal length to about 0.41 mL/cm esophageal length, or about 0.3 mL/cm esophageal length to about 0.46 mL/cm esophageal length, wherein the esophageal length is the esophageal length of an individual having a height in the 50th percentile for the age of the individual to whom the composition is administered. In certain instances, esophageal length is the actual esophageal length of the individual or is calculated based on the equation: esophageal length= 1.048 (cm)+(0.167*height(cm)). In certain instances, for example, the 50th percentile height (CDC 2000) for male children age 2 is 87 cm, age 3 is 95 cm, age 4 is 102 cm, age 5 is 109 cm, age 6 is 115 cm, age 7 is 122 cm, age 8 is 128 cm, age 9 is 134 cm, age 10 is 139 cm, age 11 is 144 cm, age 12 is 149 cm, age 13 is 156 cm, age 14 is 164 cm, age 15 is 170 cm, age 16 is 174 cm, age 17 is 175 cm, and age 18 is 176 cm.

[0063] In some embodiments, any pharmaceutical composition or dose of a pharmaceutical composition described herein is provided or administered in a volume sufficient to provide a bolus when orally administered to an individual. In certain embodiments, the composition has a volume that does not systemically deliver excessive amounts of the active agent. In some embodiments, the pharmaceutical composition or dose is provided in a volume sufficient to provide a bolus when administered to an individual, wherein the size of the bolus at the distal end of the esophagus (e.g., the size of the bolus prior, e.g., immediately prior, to entering or passing the lower esophageal sphincter) is less than 90%, less than 85%, less than 80%, less than 75%, less than 70%, less than 65%, less than 60%, less than 55%, less than 50%, less than 45%, less than 40%, less than 35%, less than 30%, less than 25%, less than 20%, less than 15%, less than 10% or less than 5% of size of the bolus that entered the esophagus (e.g., the size of the bolus after, e.g., immediately after, passing the upper esophageal sphincter). In some embodiments, the size of the bolus is determined as a measure of diameter or of volume. In certain embodiments, diameter of the sphincter can be determined using gamma scintigraphy techniques. In specific embodiments, the volume of the composition or dose is adjusted given the length and/or diameter of the esophagus of the individual to whom the composition or dose is administered.

[0064] In some embodiments, the corticosteroid is present in a pharmaceutical composition described herein and/or administered to an individual according to a method described herein in any effective amount. In some embodiments, an effective amount is an amount sufficient to reduce inflammation or symptoms of inflammation associated with an inflammatory disease or condition of the gastrointestinal tract (e.g., the esophagus) as compared to the level of inflammation or symptoms of inflammation associated with an inflammatory disease prior to administration of the effective amount. In certain embodiments, effective amount is an amount sufficient to maintain a reduction in inflammation or symptoms of inflammation achieved in any manner including, but not limited to, by the administration of an effective amount sufficient to achieve such a reduction. In some embodiments, the effective amount is about 0.1 mg to about 20 mg, about 0.3 mg to about 4 mg, 0.05 mg to about 20 mg, about 0.05 mg to about 15 mg, about 0.05 mg to about 10 mg, about 0.05 mg to about 7.5 mg, about 0.05 mg to about 5 mg, about 0.25 mg to about 3 mg, about 0.25 mg to about 2.5 mg, about 0.5 mg to about 3 mg, about 0.5 mg to about 2 mg, about 0.5 mg to about 0.1 mg, about 0.5 mg to about 5 mg, about 0.5 mg to about 4 mg, about 1 mg to about 4 mg, about 1 mg to about 3 mg, about 2 mg to about 3 mg, or about 2 mg to about 4 mg. In specific embodiments, the effective amount of corticosteroid is about 0.1 mg to about 20 mg, about 0.3 mg to about 4 mg, 0.05 mg, about 0.1 mg., about 0.15 mg., about 0.25 mg., about 0.3 mg., about 0.35 mg, about 0.4 mg, about 0.37 mg, about 0.375 mg, about 0.7 mg, about 0.8 mg, about 0.75 mg, about 1 mg, about 1.2 mg, about 1.25 mg, about 1.3 mg, about 1.5 mg, about 2 mg, about 2.5 mg, about 3 mg, about 3.5 mg, about 4 mg, about 4.5 mg, about 5 mg, about 5.5 mg, about 6 mg, about 6.5 mg, about 7 mg, or about 7.5 mg or more.

[0065] Furthermore, in certain embodiments, the amount of a therapeutic agent (e.g., a corticosteroid such as fluticasone propionate) in a composition or a dose of a composition described herein is about 0.005 mg/cm esophageal length to about 0.3 mg/cm esophageal length, about 0.008 mg/cm esophageal length to about 0.2 mg/cm esophageal length, about 0.01 mg/cm esophageal length to about 0.15 mg/cm esophageal length, or about 0.015 mg/cm esophageal length to about 0.1 mg/cm esophageal length, wherein the esophageal length is the esophageal length of the individual to whom the composition is administered. In some embodiments, the volume of a composition or dose of a composition described herein is based on the esophageal length of an individual (e.g., male, female, or both) that is in the 50th percentile of height for their age. Therefore, in some embodiments, the amount of a therapeutic agent (e.g., a corticosteroid such as fluticasone propionate) in a composition or dose of a composition described herein is about 0.005 mg/cm esophageal length to about 0.3 mg/cm esophageal length, about 0.008 mg/cm esophageal length to about 0.2 mg/cm esophageal length, about 0.01 mg/cm esophageal length to about 0.15 mg/cm esophageal length, or about 0.015 mg/cm esophageal length to about 0.1 mg/cm esophageal length, wherein the esophageal length is the esophageal length of an individual having a height in the 50th percentile for the age of the individual to whom the composition is administered.

[0066] In certain embodiments, a dose or composition described herein is administered with food. In some embodiments, a dose or composition described herein is administered without food. In certain embodiments, a dose or composition described herein is administered in a fed or fasted state. In some embodiments, a dose or composition described herein is administered in the morning, in the afternoon, in the evening, at night, or a combination thereof. In some embodiments, the dose is administered at night. In another aspect, the dose is administered about 30 minutes prior to bed, with no food or water given after administration of the compositions herein. In yet another embodiment of the instant invention, the dose is administered prior to bedtime, wherein after administration of the composition, the patient or individual is in a substantially supine position for at least 30 minutes, at least 1 hour, at least 2 hours, at least 4 hours or at least 8 hours.

[0067] In some embodiments, provided herein are methods of treating, preventing, or alleviating inflammation or symptoms associated with inflammation of the gastrointestinal tract, e.g., the esophagus, comprising administering to an individual in need thereof a single unit dose of a pharmaceutical composition described herein from a multidose container. In specific embodiments, administering a single unit dose from a multi dose container comprises (1) shaking a multidose container, the multidose container comprising at least one unit dose of a pharmaceutical composition described herein; (2) pouring (or otherwise dispensing) a single unit dose from the multidose container into an administration device (e.g., a device suitable for administering to a human individual, such as a spoon, cup or syringe); and (3) administering the single unit dose to the individual in need thereof. In more specific embodiments, shaking of the multidose container occurs until the fluid therein has a viscosity suitable for pouring (e.g., easy pouring). In some specific embodiments, the process further comprises waiting after pouring the single unit dose and prior to administering the single unit dose to the individual in need thereof. In specific embodiments, the wait time is a time sufficient to allow the viscosity of composition to achieve a desired level, e.g., a viscosity to improve the coating capabilities of the composition. In some embodiments, the wait time is, e.g., about 3 seconds, or more; about 5 seconds, or more; about 10 seconds, or more; about 15 seconds, or more; about 20 seconds, or more; about 25 seconds, or more; about 30 seconds, or more; about 40 seconds, or more; about 45 seconds, or more; about 50 seconds, or more; or about 60 seconds, or more. In other specific embodiments, the composition is administered immediately following pouring the composition into the administration device. In some embodiments, the process comprises shaking the multidose container well.

[0068] In some embodiments, provided herein is a multiple unit container comprising about 2 to about 180, about 10 to about 60, about 14, or about 30 unit doses of any pharmaceutical composition described herein. In more specific embodiments, each dose comprises about 1 mL to about 20 mL, about 1 mL to about 25 mL, about 1 mL to about 20 mL, about 7 mL to about 25 mL, about 10 to about 20 mL, about 15 mL, about 20 mL, about 3 to about 7 mL, about 5 mL, about 8 mL to about 12 mL, or about 10 mL. In still more specific embodiments, each dose comprises about 0.1 to about 20 mg, about 0.1 to about 10 mg, about 0.1 to about 7.5 mg, about 0.1 to about 5 mg, about 0.3 to about 4 mg, about 0.25 to about 2.5 mg, about 0.3 mg to about 2 mg, about 0.5 mg to about 1 mg, about 0.7 mg to about 1.5 mg, about 0.375 mg, about 0.75 mg, about 1 mg, about 1.25 mg, about 1.5 mg or about 2 mg of corticosteroid. In certain embodiments, provided herein is a multiple unit container comprising about 10 mL to about 1500 mL, about 50 mL to about 600 mL, about 150 mL, about 300 mL, about 600 mL, or about 1,200 mL of any pharmaceutical composition described herein. In specific embodiments, the multidose container comprises about 330 mL or about 55 mL of a composition described herein. In some embodiments, a kit provided herein comprises any multidose container as described herein, a pharmaceutical composition as described herein (e.g., in a volume described), and a delivery or metered device (e.g., a syringe, a cup, a spoon, or the like). In specific embodiments, the delivery or metered device is incorporated into the container (e.g., a nebulizer, an aerosolizer, a pump, or the like), or is separate from the container. In certain embodiments, the pharmaceutical composition contained within any of the multiple unit containers described herein is physically and chemically stable.

[0069] In some embodiments, the corticosteroid is selected from, by way of non-limiting example, fluticasone propionate. In specific embodiments, corticosteroid is present in the composition in an amount of about 0.1 mg to about 20 mg, about 0.3 mg to about 4 mg, about 0.01 mg/mL to about 3 mg/mL, about 0.01 mg/mL to about 2 mg/mL, about 0.01 mg/mL to about 1.5 mg/mL, about 0.07 mg/mL to about 1.5 mg/mL, or about 0.07 mg/mL to about 1 mg/mL. In more specific embodiments, fluticasone propionate is present in an amount of about 0.01 mg/mL to about 3 mg/mL, about 0.01 mg/mL to about 1.5 mg/mL, or about 0.07 mg/mL to about 1 mg/mL. In other specific embodiments, fluticasone propionate is present in an amount of about 0.005 mg/mL to about 1.5 mg/mL, or about 0.01 mg/mL to about 1 mg/mL. In some embodiments, the corticosteroid is fluticasone propionate and the composition comprises about 0.01 mg to about 1.0 mg of fluticasone propionate/g of composition. In some embodiments, the composition comprises about 0.1 mg to about 1.0 mg of fluticasone propionate/g of composition. In certain embodiments, the composition comprises about 0.3 mg to about 0.6 mg of fluticasone propionate/g of composition. In specific embodiments, the composition comprises about 0.5 mg of fluticasone propionate/g of composition.

[0070] In certain embodiments, the present invention provides for an oral liquid formulation comprising corticosteroid particles. In certain embodiments, the particles are, e.g., microparticles or nanoparticles. In some embodiments, the particles are selected so as to increase or maximize the corticosteroid surface area per unit volume of the pharmaceutical formulation when compared to an otherwise identical pharmaceutical formulation comprising larger particles. In certain embodiments, a particle is selected so as to increase surface area of the corticosteroid per unit volume of pharmaceutical formulation, increased dissolution rate of the corticosteroid and increase the absorption in the gastrointestinal tissue of the corticosteroid.

[0071] In one embodiment, the corticosteroid containing composition comprises fluticasone propionate, a preservative, an isotonic agent, a surfactant, an aqueous vehicle, an excipient, an optional pH adjusting agent (e.g., hydrochloric acid and/or sodium hydroxide) and an optional sweetener and/or fragrance. In certain embodiments, the excipient is microcrystalline cellulose (MCC). In other embodiments, the excipient is carboxymethyl cellulose (CMC). In some embodiments, the corticosteroid containing composition contains two or more excipients. For example, in some embodiments, the two or more excipients are a combination of microcrystalline cellulose (MCC) and carboxymethyl cellulose (CMC). In some embodiments, the CMC/MCC combination (e.g., Avicel® RC-591) is present in the composition in an amount of about 1 mg/mL to about 150 mg/mL, 1 mg/mL to about 75 mg/mL, or about 5 mg/mL to about 40 mg/mL. In certain embodiments, the CMC/MCC mixed weight ratio is between about 1/99 and about 99/1, about 20/80 and about 5/95, or about 15/85 and about 10/90. In a specific embodiment, the CMC is NaCMC and the CMC/MCC mixed weight ratio is about 11/89. In some embodiments, the excipient is an excipient that increases the interaction of the composition with a surface of the gastrointestinal tract (e.g., the mucosa and/or epithelium of the gastrointestinal tract or of a specific site of the gastrointestinal tract, such as the esophagus) (e.g., a viscosity enhancing

agent). In certain embodiments, the composition is a liquid. In specific embodiments, the liquid composition is a suspension.

[0072] In certain embodiments, the excipient that increases the interaction of the composition with a surface of the gastrointestinal tract (e.g., the mucosa and/or epithelium of the gastrointestinal tract or of a specific site of the gastrointestinal tract, such as the esophagus) is a viscosity enhancing agent. In some embodiments, the viscosity enhancing agent is present in about 0.01% to about 10% w/w of the composition. In certain embodiments, a viscosity enhancing agent is present in about 0.01% to about 5.0% w/w, about 0.01% to about 3.0% w/w, or about 0.1% to about 5.0% w/w, about 0.1% to about 3.0% w/w of the composition. In specific embodiments, a viscosity enhancing agent is a combination of microcrystalline cellulose and carboxymethyl cellulose (e.g., carboxymethyl cellulose sodium). In another specific embodiment, the viscosity enhancing agent is carboxymethyl cellulose. In some embodiments, one or more additional excipient that increases the interaction of the composition with a surface of the gastrointestinal tract (e.g., one or more viscosity enhancing agent) is added so as to provide a viscosity as described herein. Alternatively, the amount of the excipient that increases the interaction of the composition with a surface of the gastrointestinal tract (e.g., the mucosa and/or epithelium of the gastrointestinal tract or of a specific site of the gastrointestinal tract, such as the esophagus) present in the composition is increased so as to provide a viscosity as described herein.

[0073] In some embodiments, surfactants include, by way of non-limiting example, polysorbates (e.g., polysorbate 80), poloxamers, polyoxyethylene alkyl ethers, polyoxyethylene castor oil derivatives and combinations thereof. In certain embodiments, surfactants are present in an amount of about 0.0001% to about 5% w/w, about 0.0001% to about 2% w/w or about 0.001% to about 2% w/w of the composition. In a specific embodiment, the surfactant is polysorbate 80.

[0074] In certain embodiments, an isotonic agent includes, by way of non-limiting example, dextrose, glycerin, mannitol, sodium chloride, potassium chloride and combinations thereof. In specific embodiments, the isotonic agent is dextrose (e.g., dextrose anhydrous). In certain embodiments, the isotonic agent is included in any suitable amount, such as, by way of non-limiting example, between about 0.5 mg and about 0.5 g per gram of composition. In specific embodiments, the isotonic agent is included in an amount of about 10 mg and about 100 mg or about 40 mg to about 60 mg per gram of composition.

[0075] Preservatives include, by way of non-limiting example, benzalkonium chloride, methylparaben, propylparaben, potassium sorbate, phenylethyl alcohol and sodium benzoate. In specific embodiments, the preservative is potassium sorbate. In some embodiments, the preservative is present in an amount of about 0.0002% to about 0.5% w/w (or about 0.002% to about 0.5% w/w) of the composition. In specific embodiments, benzalkonium chloride is present in an amount of about 0.0002% to about 0.03% w/w, about 0.002% to about 0.03% w/w, or about 0.02% w/w of the composition. In some embodiments, phenylethyl alcohol is present in an amount of about 0.005% to about 0.4% w/w, about 0.05 to about 0.3% w/w, or about 0.25% w/w of the composition. In specific embodiments, both benzalkonium chloride and phenylethyl alcohol are present.

[0076] Sweeteners include, by way of non-limiting example, sucralose, sucrose, lactose, glucose, fructose, arabinose, xylose, ribose, mannose, galactose, dextrose, sorbose, sorbitol, mannitol, maltose, cellobiose, xylitol, honey and the like. In general, when utilized, the sweetener is utilized in an amount sufficient to at least partially mask the taste of the composition and/or the corticosteroid (e.g., fluticasone propionate).

[0077] Fragrances include, by way of non-limiting example, phenylethyl alcohol. The fragrance can be included in any suitable amount including, by way of non-limiting example, about 0.005% to about 0.4% w/w, about 0.05 to about 0.3% w/w, or about 0.25% w/w of the composition.

[0078] In some embodiments, the corticosteroid containing composition comprises microfine fluticasone propionate, microcrystalline cellulose, carboxymethyl cellulose sodium, dextrose anhydrous, polysorbate 80, potassium sorbate, water, optionally hydrochloric acid and optionally one or more additional excipient. In specific embodiments, the composition has a pH of about 5 to about 7. In a specific embodiment, at least one of the optional excipients is a sweetener, a flavoring agent, or a combination thereof.

[0079] In specific embodiments, the composition administered comprises a suspension of microfine fluticasone propionate in an aqueous medium. In some specific embodiments, microcrystalline cellulose and carboxymethyl cellulose sodium, dextrose anhydrous, polysorbate 80, phenylethyl alcohol, benzalkonium chloride, and water are contained in the aqueous medium. In more specific embodiments the composition is adjusted to a target pH of about 5 to about 7. In certain embodiments, the compositions provided herein are prepared utilizing any suitable source of active agents. In some embodiments, corticosteroid (e.g., fluticasone propionate) used in the compositions described herein are neat corticosteroid (e.g., fluticasone propionate). In some embodiments, the neat corticosteroid (e.g., fluticasone propionate) is neat, bulk corticosteroid. In certain embodiments, the neat corticosteroid (e.g., fluticasone propionate) is powder corticosteroid (e.g., fluticasone propionate). In specific embodiments, the neat corticosteroid (e.g., fluticasone propionate) is micronized corticosteroid (e.g., fluticasone propionate). In an exemplary embodiment, the composition comprises Flonase® (manufactured by GlaxoSmithKline; Flonase® Nasal Spray; 50 mcg of fluticasone propionate per spray and 120 metered sprays after initial priming; Prescribing Information dated August 2007, © 2007, FLN:1PI, is hereby incorporated by reference in its entirety), an optional diluent, and an optional sweetener. In some embodiments, the diluent is any carrier suitable for oral administration, including, by way of non-limiting example, water, ethanol, and combinations thereof. In a specific embodiment, the diluent is water. In some embodiments, the composition comprises Flonase®, an additional viscosity enhancing agent (e.g., Splenda®), an optional diluent, and an optional sweetener and/or flavoring agent. In some embodiments, the composition comprises Flonase® and a diluent wherein the Flonase® and diluent are present in a ratio between about 1:0.5 and about 1:100. In more specific embodiments, the diluted Flonase® composition further comprises an excipient that increases the interaction of the composition with a surface of the gastrointestinal tract (e.g., a viscosity enhancing agent).

[0080] In specific, non-limiting embodiments provided herein is a composition, or a method of administering a composition, comprising the components as set forth in either of Tables 1 or 2.

TABLE 1

Ingredient	Amount (% w/w)
Fluticasone propionate, microfine	0.05
Dextrose	5.0
Polysorbate 80	0.02
MCC and CMC	1.0-2.0
Benzalkonium chloride	0.02
Phenylethyl alcohol	0.25
Water	to 100

TABLE 2

Ingredient	Amount (% w/w)
Fluticasone propionate, microfine	0.01-0.1
Dextrose	4.0-6.0
Polysorbate 80	0.001-5
MCC and CMC	0.1-10
Benzalkonium chloride	0.002-0.5
Phenylethyl alcohol	0.05-0.4
Water	to 100

[0081] In some embodiments, initial treatment continues, for example, for about 3 days to 2 weeks for an acute condition, or about 4 weeks to about 16 weeks for a chronic condition, or about 8 weeks to about 12 weeks for a chronic condition. In various embodiments, longer therapy is needed, such as, for example, therapy similar to chronic therapy for persistent asthma. In some aspects of the present invention, patients are, for example, be treated for up to 6 months, or up to one year. In certain aspects, maintenance treatments last up to or longer than one year. In some embodiments, patients are treated on a maintenance basis or on an as needed basis during a problematic episode, depending on the severity of the condition. In certain embodiments, patients are treated on a rotating treatment basis, where treatment is provided for a period of time and then the patient is taken off of the drug for a period before treatment resumes again. When off the drug, the patient may be given no treatment, treatment with another medication, dietary therapy, or treatment with a reduced dosage. In certain embodiments, patients are given treatment with a higher dose of the composition until a desired reduced disease state is achieved, and then continued on a lower dose of the composition. In certain embodiments, a patient combines treatment with a composition described herein with a treatment with another medication, and/or dietary therapy. In certain embodiments, patients are given treatment with a higher dose of the composition until a desired reduced disease state is achieved, and then continued on a lower dose of the composition.

[0082] In various embodiments, the compositions of the present invention include pharmaceutically acceptable salts. Pharmaceutically acceptable salts are generally well known to those of ordinary skill in the art and include, by way of non-hmiting example, acetate, atosylate, benzenesulfonate, besylate, benzoate, bicarbonate, bitartrate, bromide, calcium edetate, camsylate, carbonate, citrate, edetate, edisylate, estolate, esylate, fumarate, gluceptate, gluconate, glutamate, glycollylarsanilate, hexylresorcinate, hydrabamine, hydrobromide, hydrochloride, hydroxynaphthoate, iodide, isethionate, lactate, lactobionate, malate, maleate, mandelate, mesylate, mucate, napsylate, nitrate, pamoate (embonate), pantothenate, phosphate/diphosphate, polygalacturonate, salicylate, stearate, subacetate, succinate, sulfate, tannate, tartrate, or teoclate. Other pharmaceutically acceptable salts may be found in, for example, Remington: The Science and Practice of Pharmacy (20th ed.) Lippincott, Williams & Wilkins (2000). In specific embodiments, pharmaceutically acceptable salts include, for example, acetate, benzoate, bromide, carbonate, citrate, gluconate, hydrobromide, hydrochloride, maleate, mesylate, napsylate, pamoate (embonate), phosphate, salicylate, succinate, sulfate, or tartrate. In certain embodiments, such salts are used for any of the corticosteroids described herein.

[0083] In certain embodiments, the compositions is formulated into liquid or solid dosage forms and administered systemically or locally. In some embodiments, the agents are delivered, for example, in a timed- or sustained-low release form as is known to those skilled in the art. Techniques for formulation and administration may be found in Remington: The Science and Practice of Pharmacy (20th ed.) Lippincott, Williams & Wilkins (2000). In specific embodiments, the composition is formulated as a liquid dosage form. In more specific embodiments, the liquid dosage form is an aqueous suspension of microfine corticosteroid (e.g., fluticasone propionate) particles.

[0084] In addition to the active or actives, various embodiments of the present invention provide for pharmaceutical compositions that contain suitable pharmaceutically acceptable excipients and auxiliaries. For example, in some embodiments, pharmaceutically acceptable excipients and/or auxiliaries are used to formulate the corticosteroids herein disclosed for the practice of the invention into dosages suitable for systemic administration is within the scope of the invention. In some embodiments, the corticosteroid is formulated readily using pharmaceutically acceptable excipients and/or auxiliaries well known in the art into dosages suitable for oral administration. Such excipients and/or auxiliaries enable the compositions of the invention to be formulated as tablets, pills, dragees, capsules, liquids, gels, syrups, slurries, suspensions and the like, for oral ingestion by a patient to be treated.

[0085] In certain embodiments, pharmaceutical preparations for oral use are obtained by combining an aqueous formulation of a corticosteroid (e.g., fluticasone propionate) with solid excipients, optionally grinding a resulting mixture, and processing the mixture of granules, after adding suitable auxiliaries, if desired, to obtain tablets or dragee cores. In certain embodiments, solid oral dosage forms (e.g., tablets, dragee cores, capsules, push-fit capsules, soft capsules, lozenges, etc.) are formulated such that the dosage forms substantially dissolve or disintegrate in the mouth and/or esophagus. In some embodiments, solid oral dosage forms are formulated such that the dosage forms substantially dissolve or disintegrate prior to reaching the stomach. In certain embodiments, an oral dosage form has substantially dissolved or disintegrated if at least 50%, by weight, of the dosage form has dissolved or disintegrated. In other embodiments, substantial dissolution or disintegration includes at least 60%, 70%, 80%, 90% or 95% by weight. Suitable excipients include, by way of non-limiting example, fillers such as sugars or starches, including dextrose, lactose, maltodextrin, sucrose, sucralose, mannitol, or sorbitol; cellulose preparations, for example, maize starch, wheat starch, rice starch, potato starch, or a combination thereof. In certain embodiments, the aqueous formulation comprises fluticasone propionate, a viscosity enhancing agent, a preservative, an

isotonic agent, a surfactant, an optional pH adjusting agent (e.g., hydrochloric acid and/or sodium hydroxide) and an optional sweetener and/or fragrance. In more specific embodiments, the aqueous formulation comprises fluticasone propionate, microcrystalline cellulose and carboxymethyl cellulose sodium, dextrose anhydrous, polysorbate 80, phenylethyl alcohol, and benzalkonium chloride, and has a target pH of about 5 to about 7. In some embodiments, prior to mixing the aqueous suspension with the solid excipients, the aqueous solvent is removed (e.g., by evaporation). Disintegrating agents are optionally added, such as the cross-linked polyvinylpyrrolidone, agar, or alginic acid or a salt thereof such as sodium alginate. In some embodiments, the pharmaceutical compositions used herein include excipients suitable for rendering the dissolving tablet palatable, such as sweeteners or flavoring agents.

[0086] In some embodiments, the pharmaceutical compositions described herein are in liquid form. Appropriate excipients for use in liquid form pharmaceutical compositions include, for example, those that increase the liquid viscosity of the liquid composition. Optional excipients also include, by way of non-limiting example, those that render the liquid composition palatable. Optional excipients include, by way of non-limiting example, sugars, including dextrose, lactose, sucrose, sucralose, maltodextrin, mannitol, or sorbitol; honey or combinations thereof.

[0087] Dragee cores are provided with suitable coatings. In some embodiments, concentrated sugar solutions are used for this purpose, which optionally contain gum arabic, talc, polyvinylpyrrolidone, carbopol gel, polyethylene glycol (PEG), and/or titanium dioxide, lacquer solutions, and suitable organic solvents or solvent mixtures. Dye-stuffs or pigments are optionally added to the tablets or dragee coatings for identification or to characterize different combinations of active corticosteroid doses.

[0088] In various embodiments, pharmaceutical preparations that are used orally include push-fit capsules made of gelatin, as well as soft, sealed capsules made of gelatin, and a plasticizer, such as glycerol or sorbitol. In some embodiments, the push-fit capsules contain the active ingredient or ingredients in admixture with a filler, binder, lubricant, stabilizer or a combination thereof. Fillers include, by way of non-limiting example, lactose. Binders include, by way of non-limiting example, starches. Lubricants include, by way of non-limiting example, talc and magnesium stearate. In soft capsules, the corticosteroids may be dissolved or suspended in suitable liquids, such as fatty oils, liquid paraffin, or liquid polyethylene glycols (PEGs). In addition, stabilizers are optionally added.

[0089] Diseases

[0090] In certain embodiments, diseases or conditions that are treated, prevented, or exhibit an alleviation of symptoms by administering a composition described herein include any disease or condition that involves inflammation of the gastrointestinal tract, including the esophagus, stomach and/or digestive tract. This includes, by way of non-limiting example, any chronic inflammatory or malignant state that involves the gastrointestinal tract (e.g., the esophagus, stomach and/or digestive tract) and responds to steroid therapy. The methods of the present invention are useful, for example, for treating, preventing and alleviating the symptoms of eosinophilic esophagitis, inflammatory bowel diseases involving the esophagus, Crohn's disease, coeliac disease, eosinophilic duodenitis, functional dyspepsia, acute esophageal inflammation secondary to caustic/irritant ingestion, persistent/recurrent esophageal strictures secondary to caustic/irritant, conditions due to ingestion, systemic diseases, congenital diseases, epithelial hyperplasia, basal cell hyperplasia, elongated papillae, dilated vessels in papillae, fungal esophagitis (e.g., Candida, turolopsis, histoplasma *Aspergillus*, etc.), viral esophagitis (e.g., HSV, CMV, V2V), bacterial esophagitis (e.g., tuberculosis, actinomycosis, syphlis), corrosive esophagitis, radiation esophagitis, chemotherapy esophagitis, graft vs. host disease, a skin disease with esophageal involvement (e.g., bullous pemphigoid, pemphigus vulgaris, epidermolysis bollosa, Stevens-Johnson syndrome), Behçet's disease, sarcoidosis, idiopathic esophagitis, eosinophilic gastritis, Ménétrier's disease, parasitic gastritis, lymphocytic esophagitis, inflammatory bowel disease-associated esophagitis, parasitic gastritis, and post-surgery inflammation. The methods of the present invention are also useful, for example, for treating, preventing and alleviating the symptoms of gastroesophageal reflux disease (GERD), nonerosive reflux disease (NERD) and/or erosive esophagitis.

[0091] It will be appreciated that reference herein to treatment extends to prophylaxis as well as the treatment of inflammation or other symptoms.

[0092] In certain embodiments, provided herein is a method of treating, preventing or alleviating inflammation of the gastrointestinal tract, including the esophagus, stomach and/or digestive tract, in an individual comprising orally administering to said individual any of the compositions described herein. In certain embodiments, oral administration includes the oral administration of a solid dosage form (e.g., tablets, dragee cores, capsules, push-fit capsules, soft capsules etc.) that is formulated such that the dosage form substantially dissolves or disintegrates in the mouth and/or esophagus. In some embodiments, solid oral dosage forms are formulated such that the dosage forms substantially dissolve or disintegrate prior to reaching the stomach. In certain embodiments, an oral dosage form has substantially dissolved or disintegrated if at least 50%, by weight, of the dosage form has dissolved or disintegrated. In other embodiments, substantial dissolution or disintegration includes at least 60%, 70%, 80%, 90% or 95% by weight. In certain embodiments, the oral dosage form is a liquid (e.g., a slurry, suspension, syrup, dispersion, solution, etc.)

[0093] In one aspect, a patient is administered a topical corticosteroid such as, for example, fluticasone propionate.

[0094] In some embodiments, the inflammation treated by the methods and compositions described herein is associated with eosinophilic inflammation and/or neutrophilic inflammation. In some embodiments, individuals (e.g., patients) to be treated with compositions described herein include those that have been diagnosed eosinophilic esophagitis, an inflammatory bowel disease involving the esophagus, Crohn's disease, coeliac disease, eosinophilic duodenitis, functional dyspepsia, esophageal inflammation secondary to caustic/irritant ingestion, persistent/recurrent esophageal strictures of any cause and including caustic/irritant ingestion, pill-induced esophagitis, systemic diseases, congenital diseases, epithelial hyperplasia, basal cell hyperplasia, elongated papillae, dilated vessels in papillae, fungal esophagitis (e.g., Candida, turolopsis, histoplasma *Aspergillus*, etc.), viral esophagitis (e.g., HSV, CMV, V2V), bacterial esophagitis (e.g., tuberculosis, actinomycosis, syphlis), corrosive esophagitis, radiation esophagitis, chemotherapy esophagitis, graft vs. host disease, a skin disease with esophageal involvement (e.g.,

bullous pemphigoid, pemphigus vulgaris, epidermolysis bollosa, Stevens-Johnson syndrome), Behçet's disease, sarcoidosis, idiopathic esophagitis, eosinophilic gastritis, Ménétrier's disease, parasitic gastritis, lymphocytic esophagitis, inflammatory bowel disease-associated esophagitis, parasitic gastritis, or post-surgery inflammation. In one non-limiting example, the patient has eosinophilic esophagitis. In some embodiments, individuals (e.g., patients) to be treated with the compositions described herein include those that have been diagnosed with gastroesophageal reflux disease (GERD), nonerosive reflux disease (NERD) and/or erosive esophagitis. In some embodiments, the patient is an adult. In other embodiments, the patient is a child or infant. In various aspects, a patient is a child or infant less than 16 years old, less than 12 years old, less man 8 years old, less than 6 years old, less than 4 years old or less than 2 years old.

[0095] In some embodiments, a composition is in a unit dose formulation for oral administration of a patient. In some embodiments, a unit dose of the corticosteroid is administered from a metered dose device, such as a metered dose inhaler. In certain aspects, from about 0.1 mg to about 20 mg, or about 0.25 mg to about 5 mg (e.g., about 1-2 mg/day or about 2-3 mg/day) corticosteroid per day is administered to the patient. In some embodiments, the corticosteroid is present in a unit dose in an amount of between about 0.1 mg to about 20 mg, or about 0.25 mg and about 5 mg. In some embodiments, the amount of corticosteroid administered daily or in a unit dose is between about 0.25 mg and about 3 mg. In other embodiments, the amount of corticosteroid present in a unit dose or administered daily is between about 1 and about 3 mg, or between about 1 and about 2 mg, or between about 2 and about 3 mg.

[0096] In some embodiments, the dose or volume of a composition administered herein is adjusted based on the efficacy of treatment. In certain embodiments, a diagnosis of eosinophilic esophagitis is achieved by administering a composition described herein and determining the efficacy of the treatment. In certain embodiments, a composition described herein and separately determined to be effective in treating eosinophilic esophagitis is utilized. Efficacy of treatment can be determined in any suitable manner including, e.g., symptom score assessment, gastrointestinoscopy (e.g., esophagogastroduodenoscopy), gastrointestinal (e.g., esophageal) biopsy, histological evaluation, or a combination thereof.

[0097] In some embodiments, a process for determining efficacy of a treatment (e.g., for eosinophilic esophagitis) described herein is a clinical symptom score assessment comprising (i) administering a composition described herein to an individual diagnosed with or suspected of having eosinophilic esophagitis; and (ii) evaluating one or more symptom of the individual. In certain embodiments, prior to administering the composition, the process comprises evaluating the one or more symptom of the individual. In specific embodiments, the symptom values determined following administration are compared to the symptom values determined prior to administration. In some embodiments, steps (i) and (ii) are repeated as desired. In some embodiments, such processes include the evaluation of one or more of the following categories of symptoms: (1) heartburn or regurgitation; abdominal pain or unexplained irritability in younger children; (3) nocturnal awakening with symptoms; (4) nausea or vomiting; (5) anorexia or early satiety; and/or (6) dysphagia, odynophagia, or food impaction. In some embodiments, the selected symptom categories are each scored; and the scores are optionally totaled. Total score or change in score is optionally utilized to diagnose a disorder and/or determine efficacy of treatment.

[0098] In certain embodiments, a process for determining efficacy of a treatment described herein comprises (i) administering a composition described herein to an individual diagnosed with or suspected of suffering from inflammation of the gastrointestinal tract (e.g., eosinophilic esophagitis); (ii) endoscoping the gastrointestinal surface of the individual; (iii) biopsying the gastrointestinal surface tissue; and (iv) evaluating the biopsied tissue and determining an endoscopy score of the tissues biopsied. In some embodiments, the process further comprises endoscoping additional gastrointestinal surface tissues. In specific embodiments, the process further comprises comparing the evaluated biopsied tissue and/or the endoscopy score obtained prior to administration of the composition to the biopsied tissue and/or endoscopy score subsequent to administration of the composition. In some embodiments, endoscopic findings are evaluated in any suitable manner including, by way of non-limiting example: (1) pallor and vascular markings (e.g., diminished vascular markings); (2) furrow with thickened mucosa; (3) presence of white mucosal plaques; and/or (4) concentric rings or strictures. In some embodiments, each category is scored and optionally totaled. Total scores and/or changes in scores are optionally utilized to diagnose a disorder and/or determine efficacy of treatment.

[0099] In some embodiments, provided herein is a process of diagnosing an individual with gastrointestinal inflammation by (i) detecting and/or measuring symptoms of the individual prior to administering to the individual a composition described herein; (ii) administering to the individual any composition described herein; (iii) detecting and/or measuring symptoms of the individual following administration of the composition; and (iv) comparing the symptoms measured or detected prior to and following administration of a composition described herein. If the symptoms exhibited by the individual are reduced (e.g., by a statistically significant or clinically relevant amount), a positive diagnosis occurs. In specific embodiments, the process of diagnosing an individual with gastrointestinal inflammation is diagnosing an individual with eosinophilic esophagitis.

[0100] The entirety of each patent, patent application, publication and document referenced herein is hereby incorporated by reference. Citation of the above patents, patent applications, publications and documents is not an admission that any of the foregoing is pertinent prior art, nor does it constitute any admission as to the contents or date of these publications or documents.

[0101] Unless defined otherwise, all technical and scientific terms used herein have the same meanings as commonly understood by one of ordinary skill in the art to which this invention belongs. Although any methods and systems similar or equivalent to those described herein can be used in the practice or testing of the present invention, the methods, devices, and materials are now described. All publications mentioned herein are incorporated herein by reference for the purpose of describing and disclosing the processes, systems, and methodologies which are reported in the publications which might be used in connection with the invention. Nothing herein is to be construed as an admission that the invention is not entitled to antedate such disclosure by virtue of prior invention.

[0102] Modifications may be made to the foregoing without departing from the basic aspects of the invention. Although the invention has been described in substantial detail with reference to one or more specific embodiments, those of ordinary skill in the art will recognize that changes may be made to the embodiments specifically disclosed in this application, and yet these modifications and improvements are within the scope and spirit of the invention. The invention illustratively described herein suitably may be practiced in the absence of any elements) not specifically disclosed herein. Thus, for example, in each instance herein any of the terms "comprising", "consisting essentially of", and "consisting of" may be replaced with either of the other two terms. Thus, the terms and expressions which have been employed are used as terms of description and not of limitation, equivalents of the features shown and described, or portions thereof, are not excluded, and it is recognized that various modifications are possible within the scope of the invention.

[0103] While preferred embodiments of the present invention have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. Numerous variations, changes, and substitutions will now occur to those skilled in the art without departing from the invention. It should be understood that various alternatives to the embodiments of the invention described herein may be employed in practicing the invention. It is intended that the following claims define the scope of the invention and that methods and structures within the scope of these claims and their equivalents be covered thereby.

EXAMPLES

Example 1

Treatment of Gastrointestinal Inflammation

[0104] A 4 mL oral dosage formulation is prepared comprising the following ingredients:

Ingredient	Amount (% w/w)
Fluticasone propionate, microfine	0.05
Dextrose	5.0
Polysorbate 80	0.02
MCC and CMC	1.0-2.0
Benzalkonium chloride	0.02
Phenylethyl alcohol	0.25
Water	to 100

[0105] The fluticasone propionate containing dosage formulation is administered orally for the treatment of gastrointestinal inflammation.

Example 2

Treatment of Gastrointestinal Inflammation

[0106] A 2-4 mL oral dosage formulation is prepared comprising the following ingredients:

Ingredient	Amount (% w/w)
Fluticasone propionate, microfine	0.01-0.1
Dextrose	4.0-6.0
Polysorbate 80	0.001-5
MCC and CMC	0.1-10
Benzalkonium chloride	0.002-0.5
Phenylethyl alcohol	0.05-0.4
Water	to 100

[0107] The fluticasone propionate containing dosage formulation is administered orally for the treatment of gastrointestinal inflammation.

Example 3

[0108] This example details the efficacy and safety of once daily and twice daily use of fluticasone propionate formulations described herein in 5 mL, 7 mL, 10 mL, 12 mL, 15 mL, or 17.5 mL doses in inducing and maintaining remission of disease activity in children with EoE. A number of children (e.g., 20 per fluticasone propionate dose frequency, amount, and volume) are evaluated to determine the highest eosinophil count (eos/hpf) and the mean highest eosinophil count for the group. Evaluation of the highest eosinophil count (eos/hpf) and the mean highest eosinophil count for the group is also determined following therapy. Symptom scores and mean symptom scores are also determined before and after therapy.

[0109] In some instances, individuals who received previous therapy with proton pump inhibitor, elimination diet based upon skin or blood allergy testing, or elimination diet or refused elimination diet, but continued to have ≧24 eos/hpf on esophageal biopsy are included in the review. Patients are defined as having food or aeroallergen sensitization if RAST and/or skin prick testing are positive. No changes are made to longstanding therapy used for treating chronic conditions such as asthma or eczema and none of the children receive concurrent immune-modulatory treatment.

[0110] Endoscopy is performed using the Olympus P160 endoscope (by RD) and pan-esophageal, gastric and duodenal biopsies are taken. Eosinophilic esophagitis is diagnosed when ≧24 eos/hpf are found in at least one of the esophageal sites biopsied. Two mucosal biopsies re taken from the proximal esophagus (3 cm below the crycopharyngeus muscle), distal esophagus (3 cm above the gastroesophageal junction (GEJ), and mid-esophagus (midpoint between the crycopharyngeus muscle and the GEJ). Biopsies are processed routinely and evaluated by a pediatric pathologist (RN). The highest number of eosinophils per ×400 high power field are counted. Basal zone hyperplasia (BZH) is reported when basal zone cells extend towards the luminal surface of the epithelium (>25% of epithelial thickness).

[0111] Follow-up endoscopy with biopsies are taken after 3-4 months treatment. Counting the highest number of eos/hpf within biopsies determined the response to therapy and patients are categorized into responders (0-7 eos/hpf), partial-responders (8-23 eos/hpf) and non-responders (≧24 eos/hpf).

[0112] An EoE Endoscopy Score is devised to compare findings before and after treatment. It is calculated from procedure reports and photographs. Four categories, (1) pallor and diminished vascular markings; (2) furrowing with "thickened" mucosa; (3) white mucosal plaques; (4) concentric rings or strictures. For each category, one point is allocated if 1 or 2 esophageal sites are involved, and two points for pan-esophageal involvement. The maximum score is 8.

[0113] Patients receive a formulation described herein for between 0.25 and 2 mg daily and are instructed not to ingest any solids or liquids for 30 minutes afterwards. No dietary changes are made in patients already on dietary restrictions.

[0114] A modified symptom score based on children with acid-peptic disease is used routinely in the EoE clinic. The symptom categories include (1) heartburn or regurgitation; (2) abdominal pain or unexplained irritability in younger children; (3) nausea or vomiting; (4) anorexia or early satiety; (5) dysphagia or odynophagia, (6) nocturnal wakening with symptoms; (7) gastrointestinal bleeding (previous 4 months). Each category scored 0-2 points with a maximum of 14 points. Zero points are awarded if the symptom is absent; one point if the symptom is mild, did not interfere with daily activities; 2 points if the symptoms are severe enough to interrupt daily activities. Previous GI bleeding is considered mild (1 point) if there is no associated hemodynamic compromise or anemia, and severe (2 points) if bleeds are multiple, caused anemia, or required blood transfusion.

[0115] All statistical analysis is carried out using NCSS Statistical Softward Package. Two-tailed p values are calculated using paired t-tests to compare the means of patient values for eos/hpf, EoE Endoscopy Scores and Symptom Scores before and after fluticasone propionate therapy. Two-tailed unpaired t-tests are utilized in order to compare variables grouped by responders versus non-responders. Spearman's correlation coefficients are generated using GraphPad Prism software. Results with p values <0.05 are considered statistically significant. Both mean and median statistics re generated, both are equivalent and mean statistics are presented.

[0116] Subjects. Chart reviews are undertaken on a number of children. All children have >24 eos/hpf on repeat esophageal biopsy before starting therapy.

[0117] Treatment. Patients received formulations described herein for a designated amount of time (e.g., 1 week, 2 weeks, 1 month, 2 months, 3 months, 4 months, 6 months, or the like) before repeat endoscopy. Various patients received fluticasone propionate in amounts ranging from 0.25 to 2 mg/day.

[0118] Histology. Before treatment the mean highest eosinophil count is measured for all patients, including distal, mid and proximal esophageal sites. All sites are likewise evaluated aver the designated amount of time, and again if desired.

[0119] Upper Gastrointestinal Endoscopy. Before treatment, the mean EoE Endoscopy Score for all patients is determined. Following treatment the mean EoE Endoscopy Score is repeated. Decreases in endoscopy scores (e.g., of >95%, >90%, >85%, >75%, >50%, >25%, or the like) in an individual indicate successful treatment.

[0120] Symptom Score. Before treatment the mean symptom score for all patients is determined. It is again determined following treatment. Decreases in symptom scores (e.g., of >95%, >90%, >85%, >75%, >50%, >25%, or the like) in an individual indicate successful treatment (alone or in combination with the above referenced decreases in endoscopy scores).

[0121] Adults: these parameters are repeated in adults to determine efficacy and safety therein.

Example 4

[0122] This example details the efficacy and safety of once daily and twice daily use of fluticasone propionate in a formulation described herein in inducing and maintaining remission of disease activity in individuals (children and/or adults) with GERD. Doses of 0-1 mg, 1-2 mg, 2-3 mg, 3-4 mg, 4-5 mg, and 5-6 mg per daily dose are administered once a day, b.i.d. or t.i.d. in volumes of 3, 5, 7, 10, 12, 15, or 17.5 mL. A number of individuals (e.g., 20 per fluticasone propionate dose frequency, amount, and volume) are evaluated to determine the symptoms prior to therapy, during therapy and following therapy. Administration is conducted for 7 days, 14 days, and 28 days. Primary Outcome Measures include complete resolution of heartburn and regurgitation (e.g., no more than one day with either mild heartburn or regurgitation over the seven days prior to the assessment time-point). Secondary Outcome Measures include: Number of days with heartburn (daytime and night-time); Number of days with regurgitation (daytime and night-time); Number of heartburn and regurgitation-free days (24 hrs); Composite score of heartburn and regurgitation frequency and severity; Time to resolution of symptoms of heartburn/regurgitation; Severity of additional GERD symptoms; Quality of Life (assessed using PAGI-QOL to PGIC (Patient Global Impression of Change); Complete resolution of heartburn; Complete resolution of regurgitation; Average severity of heartburn (daytime and night-time); Average severity of regurgitation (daytime and night-time). These symptoms are scored (e.g., assigning a 3 to the most severe symptoms and a 0 to a lack of symptoms) and utilized to determine the efficacy of the treatment.

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What is claimed is:

1. A method of treating, preventing or alleviating inflammation of the gastrointestinal tract comprising orally administering to an individual in need thereof a composition comprising a corticosteroid, a preservative, an isotonic agent, a surfactant, and an excipient.

2. The method of claim **1**, wherein the corticosteroid is fluticasone propionate.

3. The method of claim **1**, wherein the corticosteroid is present in the composition in an amount of about 0.01 mg to about 1.0 mg of corticosteroid per gram of composition.

4. The method of claim **1**, wherein the preservative is benzalkonium chloride.

5. The method of claim **1**, wherein the preservative is present in the composition in an amount of about 0.0002% to about 0.03% w/w of the composition.

6. The method of claim **1**, wherein the isotonic agent is dextrose.

7. The method of claim **1**, wherein the surfactant is polysorbate 80.

8. The method of claim **1**, wherein the excipient is an excipient that increases the interaction of the composition with a surface of the gastrointestinal tract.

9. The method of claim **8**, wherein the excipient that increases the interaction of the composition with a surface of the gastrointestinal tract is a viscosity enhancing agent.

10. The method of claim **9**, wherein the viscosity enhancing agent is selected from microcrystalline cellulose, carboxymethyl cellulose sodium and a combination thereof.

11. The method of claim **10**, wherein the viscosity enhancing agent is a combination of microcrystalline cellulose and carboxymethyl cellulose sodium.

12. The method of claim **10**, wherein the viscosity enhancing agent is carboxymethyl cellulose sodium.

13. The method of claim **1**, wherein the composition further comprises a fragrance.

14. The method of claim **16**, wherein the fragrance is phenylethyl alcohol.

15. The method of claim **1**, wherein the fragrance is present in the composition in an amount of about 0.0005 to about 0.4% w/w of the composition.

16. The method of claim **1**, wherein the composition is a suspension of microfine corticosteroid particles suspended in an aqueous vehicle.

17. The method of claim **1**, wherein the composition has a pH of about 5 to about 7.

18. The method of claim **1**, wherein the composition further comprising a sweetener, a flavoring agent or a combination thereof.

19. The method of claim **1**, wherein:

a. the corticosteroid is microfine fluticasone propionate,

b. the preservative is a combination of benzalkonium chloride and phenylethyl alcohol,

c. the isotonic agent is dextrose,

d. the surfactant is polysorbate 80, and

e. the excipient that increases the interaction of the composition with a surface of the gastrointestinal tract is a combination of microcrystalline cellulose and carboxymethyl cellulose sodium.

20. The method of claim **19**, wherein the benzalkonium chloride is present in the composition in an amount of about 0.0002% to about 0.03% w/w of the composition and the phenylethyl alcohol is present in the composition in an amount of about 0.0005 to about 0.4% w/w of the composition.

21. The method of claim **1**, wherein the composition has a pH of about 5 to about 7.

22. The method of claim **1**, comprising administering about 0.1 mg to about 20 mg of corticosteroid per day.

23. The method of claim **1**, wherein the inflammation of the gastrointestinal tract is inflammation of the esophagus.

24. The method of claim **1**, wherein the individual has been diagnosed with eosinophilic esophagitis, an inflammatory bowel disease involving the esophagus, Crohn's disease, celiac disease, eosinophilic duodenitis, functional dyspepsia, esophageal inflammation secondary to caustic/irritant ingestion, persistent/recurrent esophageal strictures of any cause and including caustic/irritant ingestion, pill-induced esophagitis, systemic diseases, congenital diseases, intermediate esophagitis, epithelial hyperplasia, basal cell hyperplasia, elongated papillae, dilated vessels in papillae, fungal esophagitis, viral esophagitis, bacterial esophagitis, corrosive esophagitis, radiation esophagitis, chemotherapy esophagitis, graft vs. host disease, a skin disease with esophageal involvement, Behçet's disease, sarcoidosis, idiopathic esophagitis, eosinophilic gastritis, Ménétrier's disease, parasitic gastritis, lymphocytic esophagitis, inflammatory bowel disease-associated esophagitis, parasitic gastritis, or post-surgery inflammation.

25. The method of claim **23**, wherein the individual has eosinophilic esophagitis.

26. The method of claim **23**, wherein the individual has been diagnosed with gastroesophageal reflux disease (GERD), nonerosive reflux disease (NERD), or erosive esophagitis.

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