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(54) Title: CANNABIDIOL FOR REDUCING A STEROID DOSE AND TREATING INFLAMMATORY AND AUTOIMMUNE DISEASES

(57) Abstract: The invention provides methods for preventing, ameliorating and treating the steroid side effects, steroid refractory conditions, autoimmune diseases and liver inflammation by using Cannabidiol and a steroid composition.

CANNABIDIOL FOR REDUCING A STEROID DOSE AND TREATING INFLAMMATORY AND AUTOIMMUNE DISEASES

[001] This application claims the benefit of priority from U.S. Patent Application No. 15/143,694, filed on May 2, 2016. The content of the above document is incorporated by reference in its entirety as if fully set forth herein.

FIELD OF INVENTION

[002] The present invention relates to methods and uses of Cannabidiol compositions in reducing a steroid dose and treating inflammatory and autoimmune diseases and conditions.

BACKGROUND OF THE INVENTION

[003] Steroids such as corticosteroids are useful in the management of many inflammatory diseases such as asthma for more than 50 years. Regardless of the route used, it is advisable to limit the use of these agents to patients who clearly require them and to take all precautions to minimize side effects.

[004] There is ample evidence that the HPA axis function is suppressed by exogenous corticosteroids.

[005] Several investigators have found that some patients receiving daily doses >5 mg prednisone (or of other corticosteroids in equivalent pharmacologic doses) for months to years have evidence of suppression of HPA function. This inhibition of adrenal function in the presence of stress, e.g., surgery, severe trauma, or a serious illness, may cause circulatory collapse and death if not promptly treated with supplemental hydrocortisone. As in status asthmaticus, the precise amount of hydrocortisone has not been clearly delineated and various regimens have been proposed.

[006] Intravenous supra-pharmacological doses of corticosteroids are used in various inflammatory and autoimmune conditions because they are cumulatively less toxic than sustained steroid treatment at lower quantitative dosage. Their action is supposed to be mediated through non-genomic actions within the cell. Common indications for use in children include steroid resistant and steroid dependent nephrotic syndrome, rapidly progressive glomerulonephritis, systemic vasculitis, systemic lupus erythematosus, acute renal allograft rejection, juvenile rheumatoid arthritis, juvenile dermatomyositis, pemphigus, optic neuritis, multiple sclerosis and acute disseminated encephalomyelitis. Methylprednisolone and dexamethasone show similar efficacy in most conditions. Therapy is associated with significant side effects including worsening of hypertension, infections, dyselectrolytemia and behavioral effects. Adequate monitoring is essential during usage.

[007] Glucocorticoids exert a variety of immunosuppressive, anti-inflammatory and anti-allergic effects on primary and secondary immune cells and tissues. Studies have shown that the cellular effects of glucocorticoids are mediated by genomic and various nongenomic mechanisms.

[008] Within the cell, glucocorticoids form complexes with specific cytosolic glucocorticoid receptors (cGCR) which is a multiprotein complex containing several heat-shock proteins (hsp70 and hsp90), and has a zincfinger motif needed for transcription function. The cGCR also interacts with immunophilins, cochaperones such as p23 and src, and several kinases of the mitogen-activated protein kinase (MAPK) signaling system. The activated glucocorticoid receptor complex moves to the nucleus, binds as a homodimer to a specific DNA sequences in the promoters of the genes that it will affect (glucocorticoid responsive elements, GRE), and activates transcription factors, thus causing inhibition or induction of transcription, translation and finally the synthesis of specific regulator proteins.

[009] Induction of transcription via positive GRE is termed "transact vation". Inhibition of transcription can occur via direct interaction between the GCR and negative GRE, or, transcription factors can be displaced from the positive GRE through direct protein-protein interaction between transcription factors and the GCR. These direct positive and negative gene modulations affect proteins like cytokines, chemokines, inflammatory enzymes and adhesion molecules, resulting in modification of inflammation and immune response mechanisms.

[010] In another genomic mechanism termed "transrepression", monomers of the glucocorticoid/GCR complex directly or indirectly interact with transcription factors. One example is the induction of synthesis of IkB, which decreases the amount of the pro-inflammatory transcription factor NF-κB that could translocate to the nucleus and activate transcription of genes for IL-1, IL- 6, and TNF-a.

[011] At high concentrations, glucocorticoid molecules intercalate into cell membrane, which alters cellular functions by influencing cation transport via the plasma membrane and by increasing the proton leak of the mitochondria. These result in reduced calcium and sodium cycling across plasma membranes of immune cells, which is thought to contribute to rapid immunosuppression and a subsequent reduction of the inflammatory process. Glucocorticoid receptors have been found to be expressed on cell membranes of human cells (mGCR); mGCR-mediated mechanism may be involved in the rapid induction of apoptosis, and induction of lipomodulin, which inhibits production of prostaglandins and leukotrienes.

[012] The immunosuppressive clinical effects observed when high dose glucocorticoids are administered intravenously occur too rapidly to be explained by the classic (genomic) mechanism of action alone. Evidence suggests that high in vivo levels of steroids obtained by pulse corticosteroid therapy have qualitatively different pharmacologic effects than those produced at lower doses. High doses of glucocorticoids have been shown to inhibit NFkappaB

action (transrepression) only at concentrations within the cell obtainable by the highest oral or intravenous doses.30 Buttgereit et al have postulated 3 "modules" of glucocorticoid effect on cells resulting from different concentrations: (i) low concentrations mediate effects via genomic events; (ii) medium concentrations bind as well to cell surface receptors, which activate cross membrane signal transmission for genomic and nongenomic intracellular events; and (iii) at very large concentrations steroids dissolve in the cell membrane resulting in greater membrane stability and reduced non-genomic cell function generally.

[013] A single glucocorticoid application at a high dose has a strong effect due to 100% saturation of cytosolic receptors; however, the effect would last only for a short period because receptor occupation rapidly reverts to the original value unless a new dose is given. Therefore, a single high dose is unlikely to have sustained effect. Overall, the effects of corticosteroid pulses appear to include downregulation of activation of immune cells and proinflammatory cytokine production, leading to reduced expression of adhesion molecules and reduced movement of neutrophils into sites of inflammation. These effects are qualitatively like those seen with anti-TNF-alpha therapy.

SUMMARY OF THE INVENTION

[014] In one embodiment, provided a method for treating a subject afflicted with an autoimmune disease or liver inflammation, comprising administering to the subject a therapeutically effective amount of a composition comprising a cannabidiol (CBD) or a functional derivative thereof, thereby treating a subject afflicted with an autoimmune disease or liver inflammation. In one embodiment, autoimmune hepatitis is treated by the present methods. In some embodiments, a method for treating a subject afflicted with an autoimmune disease or liver inflammation may further comprise the step of administering to the subject a therapeutically effective amount of a composition comprising a steroid.

[015] According to the present invention, a composition comprising a CBD or a functional derivative thereof can be substantially devoid of Tetrahydrocannabinol (THC).

[016] The invention further provides, in some embodiments, a method for enhancing the therapeutic effect of a steroid in a subject afflicted with an autoimmune disease or liver inflammation, comprising administering to the subject: (1) a steroid and (2) a cannabidiol (CBD) or a functional derivative thereof, thereby enhancing the therapeutic effect of a steroid in a subject afflicted with an autoimmune disease or liver inflammation. According to some embodiments, enhancing the therapeutic effect of a steroid is rendering a refractory steroid dose of a steroid a therapeutic effective dose of the steroid. According to some embodiments, enhancing the therapeutic effect of a steroid is reducing the effective dose of the steroid. According to some embodiments, enhancing the therapeutic effect of a steroid is reducing side effects associated with the steroid.

[017] The invention further provides, in some embodiments, a method for reducing the dose of a steroid in a subject afflicted with an autoimmune disease or liver inflammation, comprising administering to the subject: (1) a steroid and (2) a cannabidiol (CBD) or a functional derivative thereof, thereby reducing the dose of a steroid in a subject afflicted with an autoimmune disease or liver inflammation.

DETAILED DESCRIPTION OF THE INVENTION

[018] In one embodiment, provided herein methods for preventing, ameliorating and treating a steroid side effect, a steroid refractory condition, an autoimmune disease and/or a liver inflammation by administering Cannabidiol. In one embodiment, provided herein methods for preventing, ameliorating and treating a steroid side effect, a steroid refractory condition, an autoimmune disease and/or a liver inflammation by administering Cannabidiol and a steroid composition. In one embodiment, treating a steroid side effect is administering CBD or a functional derivative thereof to a subject treated with a steroid

and suffering from a steroid side-effect. In one embodiment, treating a steroid side effect is administering CBD or a functional derivative thereof to a subject chronically treated with a steroid and suffering from a steroid side-effect. In one embodiment, treating a steroid side effect is reducing the required therapeutically effective amount/daily-dose of the steroid by at least 20%, 30%, 40%, 50%, or 60%.

[019] In one embodiment, provided herein a method for treating a subject afflicted with an immunological disease or disorder (such as an autoimmune disease) or inflammation, comprising administering to the subject a therapeutically effective amount of a composition comprising a cannabidiol (CBD) or a functional derivative thereof, thereby treating a subject afflicted with an autoimmune disease or liver inflammation.

[020] In one embodiment, inflammation is an inflammatory disease. In one embodiment, inflammation is chronic inflammation or a chronic inflammatory disease. In one embodiment, inflammation is a liver inflammatory disease.

[021] In one embodiment, provided herein a method for treating a subject afflicted with an autoimmune disease or a liver inflammation, comprising administering to the subject a therapeutically effective amount of: (1) a composition comprising a cannabidiol (CBD) or a functional derivative thereof; and (2) a therapeutically effective amount of a composition comprising a steroid, thereby treating a subject afflicted with an autoimmune disease or liver inflammation. In one embodiment, provided herein a method for treating a subject afflicted with an autoimmune disease or a liver inflammation, comprising administering to the subject a therapeutically effective amount of single composition or at least 2 compositions comprising: a cannabidiol (CBD) or a functional derivative thereof and a steroid, thereby treating a subject afflicted with an autoimmune disease or liver inflammation.

[022] In one embodiment, provided herein a method for treating an immune disease or an inflammatory disease comprising the steps of (A): assessing the required steroid dose, wherein a required dose beyond the recommended dose (recommended steroid dose range for a given disease is provided within the product insert of the steroid, the Merck Index, the Merck manual, the MSD manual, or the PDR) or within the upper 20%, 30% or 40% of the recommended dose range, further requires: (B) administering: (a) the required steroid dose or a steroid dose lower by 20 to 80% from the required steroid dose; and (b) CBD or a functional derivative thereof.

[023] In one embodiment, provided herein a method for chronically treating a chronic immune disease or a chronic inflammatory disease comprising the steps of (A): assessing the required steroid dose, wherein a required dose beyond the recommended dose (recommended steroid dose range or required steroid dose for a given disease is within the product insert of the steroid, the Merck Index, the Merck manual, the MSD manual, or the PDR) or within the upper 20%, 30%, 40%, 50%, or 60% of the recommended dose range, further requires: (B) administering: (a) the required steroid dose or a steroid dose lower by 20 to 80% from the required steroid dose; and (b) CBD or a functional derivative thereof. In one embodiment, a chronic immune disease or a chronic inflammatory disease is a disease requiring a steroid treatment lasting for more than 45 days, 60 days, 90 days, 6 months, 9 months, or a year.

[024] In one embodiment, provided herein a method for chronically treating a chronic immune disease or a chronic inflammatory disease comprising the steps of (A): diagnosing a subject at risk of being afflicted with an immune or an inflammatory condition or disease for having a chronic immune or chronic inflammatory condition or disease, wherein a diagnosis of a chronic immune or chronic inflammatory condition or disease, requires: (B)

administering: (a) a required steroid dose or a steroid dose lower by 20 to 70% from the required steroid dose; and (b) CBD or a functional derivative thereof.

[025] In one embodiment, provided herein CBD or a functional derivative thereof for lowering a steroid dose in a subject in need thereof. In one embodiment, provided herein CBD or a functional derivative thereof for reducing and/or lowering by at least 20%, 30%, 40%, 50%, 60% or 70% a steroid dose in a subject in need thereof. In one embodiment, provided herein CBD or a functional derivative thereof for inhibiting or decreasing a side effect associated with a steroid. In one embodiment, provided herein CBD or a functional derivative thereof for treating a chronic inflammatory disease and/or a chronic immune disease. In one embodiment, provided herein: (a) a steroid and (b) CBD or a functional derivative thereof for treating a chronic inflammatory disease and/or chronic immune disease. In one embodiment, "a subject in needed thereof" is a subject afflicted with any one or more of the diseases and conditions as described herein. In one embodiment, a chronic immune disease is a chronic autoimmune disease.

[026] In one embodiment, provided herein CBD or a functional derivative thereof for decreasing the daily amount and/or daily dose of a steroid in a subject in need thereof. In one embodiment, provided herein CBD or a functional derivative thereof for decreasing the daily amount and/or daily dose of a steroid in a subject afflicted with autoimmune hepatitis. In one embodiment, provided herein CBD or a functional derivative thereof for rendering a refractory daily amount and/or daily dose of a steroid in a subject afflicted with a disease as described herein - a therapeutically effective dose.

[027] In one embodiment, provided herein CBD or a functional derivative thereof for reducing, inhibiting and/or eliminating a steroid side effect in a subject treated with steroid therapy. In one embodiment, provided herein CBD or a functional derivative thereof for reducing, inhibiting and/or eliminating a steroid side effect in a subject chronically treated

with a steroid therapy. In one embodiment, provided herein CBD or a functional derivative thereof for decreasing the daily amount and/or daily dose of a steroid in a subject chronically treated with a steroid therapy.

[028] a refractory daily amount and/or daily dose of a steroid in a subject afflicted with a disease as described herein - a therapeutically effective dose.

[029] In one embodiment, "reducing" or "lowering" a steroid dose is "reducing" or "lowering" a required steroid dose which is beyond the recommended steroid dose. In one embodiment, recommended steroid dose range or required steroid dose for a given disease and/or a given steroid is provided within the product insert of the steroid, the Merck Index, the Merck manual, the MSD manual, or the PDR.

[030] In one embodiment, "reducing" or "lowering" a steroid dose is "reducing" or "lowering" a required steroid dose within the upper 20%, 30%, 40%, 50%, or 60% of the recommended dose range (the recommended dose range as provided within the product insert of the steroid, the Merck Index, the Merck manual, the MSD manual, or the PDR). In one embodiment, "reducing" or "lowering" a steroid dose is rendering a previously refractory daily dose - a therapeutically effective daily dose.

[03 1] In one embodiment, provided herein a method for reducing the amount of a steroid in the treatment of a subject afflicted with an autoimmune disease or an inflammation, comprising administering to the subject a therapeutically effective amount of a composition comprising a cannabidiol (CBD) or a functional derivative thereof and a therapeutically effective amount of a composition comprising a steroid.

[032] In one embodiment, provided herein a method for reducing the amount of a steroid in the treatment of a subject afflicted with an autoimmune disease or an inflammation, comprising administering to the subject a therapeutically effective amount of a

composition comprising a cannabidiol (CBD) or a functional derivative thereof and a reduced amount of a composition comprising a steroid.

[033] In one embodiment, combination therapy of cannabidiol (CBD) or a functional derivative thereof with a steroid enables reduction in the therapeutic effective amount or dose of the steroid. In one embodiment, combining CBD or a functional derivative thereof with a steroid enables reduction in the necessary amount of the steroid to be administered. In one embodiment, combining CBD or a functional derivative thereof with a steroid enables reduction in the dose of a steroid (referring to the dose of a monotherapy) while maintaining or increasing the therapeutic effect. In one embodiment, combining CBD or a functional derivative thereof with a steroid enables reduction in the dose of a steroid (referring to the dose of a monotherapy) while decreasing steroid side effects. In one embodiment, combining CBD or a functional derivative thereof with a steroid enables reduction in the dose of a steroid (referring to the dose of a monotherapy) while maintaining or increasing the therapeutic effect and decreasing steroid side effects.

[034] In one embodiment, combining CBD or a functional derivative thereof with a steroid is administering each of CBD or a functional derivative thereof and the steroid, separately and/or in separate compositions. In one embodiment, combining CBD or a functional derivative thereof with a steroid is daily administering each of CBD or a functional derivative thereof and the steroid, separately or together. In one embodiment, separately is in two distinct compositions. In one embodiment, separately is in distinct time points during the day. In one embodiment, together is within a single composition. In one embodiment, together is at the same time.

[035] In one embodiment, "reduction" refers to reducing the steroid monotherapy dose. In one embodiment, "reduction" refers to reducing a steroid side effect. In one embodiment, reduction is at least 10% reduction in the daily or weekly steroid dose. In one

embodiment, reduction is at least 20% reduction in the daily or weekly steroid dose. In one embodiment, reduction is at least 30% reduction in the daily or weekly steroid dose. In one embodiment, reduction is at least 40% reduction in the daily or weekly steroid dose. In one embodiment, reduction is at least 50% reduction in the daily or weekly steroid dose. In one embodiment, reduction is at least 60% reduction in the daily or weekly steroid dose. In one embodiment, reduction is at least 70% reduction in the daily or weekly steroid dose.

[036] In one embodiment, provided herein a method for enhancing the therapeutic effect of a steroid in a subject treated with a steroid, comprising administering to the subject a steroid and a cannabidiol (CBD) or a functional derivative thereof, thereby enhancing the therapeutic effect of a steroid in a subject treated with a steroid. In one embodiment, a method for enhancing the therapeutic effect of a steroid in a subject treated with a steroid, further comprises evaluation of the steroid's side-effect and/or steroid treatment efficacy within the subject. In one embodiment, a subject as described herein is first evaluated as a subject at risk of a given steroid dose (side effects etc.). In one embodiment, a subject as described herein is suffering from a steroid side effect. In one embodiment, a subject as described herein is treated with a steroid in an amount within the upper 10%, 20%, 30%, 40%, or 50% of the daily recommended dose range of a steroid. In one embodiment, a subject as described herein is in need of a chronic steroid treatment.

[037] In one embodiment, provided herein a method for reducing the weekly or daily dose of a steroid in a subject treated with a steroid, comprising administering to the subject a steroid and a cannabidiol (CBD) or a functional derivative thereof, thereby reducing the weekly or daily dose of a steroid in a subject treated with a steroid.

[038] In one embodiment, provided herein a method for enhancing the therapeutic effect of a steroid in a subject afflicted with an autoimmune disease or liver inflammation, comprising administering to the subject a steroid and a cannabidiol (CBD) or a functional

derivative thereof, thereby enhancing the therapeutic effect of a steroid in a subject afflicted with an autoimmune disease or liver inflammation.

[039] In one embodiment, provided herein a "chronic treatment" to a chronic inflammatory disease and/or a chronic immune disease as described herein. In one embodiment, "chronic treatment" is a medical treatment that continuously lasts for more than 2, 4, 6, 10, 12, 15, 18, or 24 months. In one embodiment, "chronic treatment" is a medicinal daily treatment that continuously lasts for more than 6 months. In one embodiment, "chronic treatment" is a medicinal daily treatment that continuously lasts for more than 12 months. In one embodiment, "chronic treatment" is a medicinal daily treatment that continuously lasts for more than 18 months. In one embodiment, "chronic treatment" is a medicinal daily treatment that continuously lasts for more than 24 months.

[040] In one embodiment, inflammation or an inflammatory disease treatable by the methods and composition as described herein is a chronic inflammation. In one embodiment, inflammation or an inflammatory disease treatable by the methods and composition as described herein is: rheumatoid arthritis, atherosclerosis, heart disease, Alzheimer, asthma, acquired immunodeficiency disorder(AIDS), cancer, congestive heart failure (CHF), multiple sclerosis (MS), diabetes, infections (bacteria, fungi, parasites), gout, IBD-inflammatory bowel disease, aging and any other neurodegenerative CNS disease.

[041] In one embodiment, provided herein a method for using a steroid in a "chronic treatment" or chronically administering a steroid. In one embodiment, provided herein a method for chronically administering a steroid to a subject in need thereof, comprising administering to the subject a cannabidiol (CBD) or a functional derivative thereof, daily, for at least 2, 3, 6, 10, 12, 18, 24, or 30 months, thereby chronically administering a steroid to a subject in need thereof. In one embodiment, provided herein a method for chronically

administering a steroid to a subject in need thereof, comprising administering to the subject a steroid and a cannabidiol (CBD) or a functional derivative thereof, daily, for at least 2, 3, 6, 10, 12, 18, 24, or 30 months, thereby chronically administering a steroid to a subject in need thereof.

[042] In one embodiment, chronically administering or chronical administration is a daily administration for a period of at least 2, 3, 6, 10, 12, 18, 24, or 30 months. In one embodiment, chronically administering or chronical administration is weekly administration for a period of at least 2, 3, 6, 10, 12, 18, 24, or 30 months. In one embodiment, chronically administering or chronical administration is bi-weekly administration for a period of at least 2, 3, 6, 10, 12, 18, 24, or 30 months.

[043] In one embodiment, provided herein a method that substantially reduces risks and side effect associated with using steroids chronically and daily (for a period of more than 6 months, 12 months, 18 months, 24 months, or 30 months). In one embodiment, provided herein a method for reducing the therapeutic effective amount of a steroid in a chronic steroid treatment. In one embodiment, provided herein a method for reducing the dose and the therapeutic effective daily amount of a steroid in a subject consuming a steroid in an amount within the upper 30% of the daily recommended dose range of a steroid. In one embodiment, provided herein a method for reducing the dose and the therapeutic effective daily amount of a steroid in a subject consuming a steroid in an amount beyond the daily recommended dose range of a steroid.

[044] In one embodiment, a steroid side effect comprises: indigestion or heartburn, increased appetite, sleeping difficulties, changes in mood and behavior, increased risk of infections, pain, high blood sugar or diabetes, Cushing's syndrome, thin skin, glaucoma or cataract, a sore mouth or throat, a cough, oral thrush, nosebleeds, folliculitis, contact

dermatitis, acne, changes in skin colour, excessive hair growth, depression, or any combination thereof.

[045] In one embodiment, provided herein a method for treating a disease such as an inflammatory disease or an immune disease by administering to a patient a reduced therapeutic effective amount of a steroid and 50 to 500 mg of CBD. In one embodiment, the combination or dual therapy as described herein permits daily, prolonged and effective utilization of a steroid while minimizing the harmful side-effects associated with a steroid.

[046] In one embodiment, a steroid or corticosteroid side effect that is reduced or inhibited by the current methods is a: cosmetic change, facial rounding, dorsal hump formation, striae, weight gain, acne, alopecia, facial hirsutism, osteopenia with vertebral compression, brittle diabetes, psychosis, pancreatitis, opportunistic infection, labile, hypertension, infection, heart-rate disturbances, and malignancy. In one embodiment, CBD provides means for substantially reducing an initial high dose of steroid. In one embodiment, CBD provides means for masking the adverse effect of a given dose of a steroid.

[047] In one embodiment, a composition as described herein comprises at least 50% v/v and/or w/w CBD. In one embodiment, a composition as described herein comprises at least 60% v/v and/or w/w CBD. In one embodiment, a composition as described herein comprises at least 70% v/v and/or w/w CBD. In one embodiment, a composition as described herein comprises at least 80% v/v and/or w/w CBD. In one embodiment, a composition as described herein comprises at least 90% v/v and/or w/w CBD.

[048] In one embodiment, a composition as described herein is devoid of THC. In one embodiment, a composition as described herein is substantially devoid of THC. In one embodiment, a composition as described herein comprises less than 20% v/v and/or w/w THC. In one embodiment, a composition as described herein comprises less than 15% v/v

and/or w/w THC. In one embodiment, a composition as described herein comprises less than 10% v/v and/or w/w THC. In one embodiment, a composition as described herein comprises less than 7.5% v/v and/or w/w THC. In one embodiment, a composition as described herein comprises less than 5% v/v and/or w/w THC. In one embodiment, a composition as described herein comprises less than 2% v/v and/or w/w THC. In one embodiment, a composition as described herein comprises less than 1% v/v and/or w/w THC. In one embodiment, a composition as described herein comprises less than 0.5% v/v and/or w/w THC. In one embodiment, a composition as described herein comprises less than 0.1% v/v and/or w/w THC.

[049] In another embodiment, a CBD derivative is a synthetic isomer of CBD. In another embodiment a CBD derivative is (+)CBD. In another embodiment, a CBD derivative is (-) and/or (+) CBD-DMH. In another embodiment, a CBD derivative is (+) 70H-CBD. In another embodiment, a CBD derivative is (-) and/or (+) 70H-CBD-DMH. In another embodiment, a CBD derivative is (-) and/or (+) COOH-CBD. In another embodiment, a CBD derivative is and (-) and/or (+) COOH-CBD-DMH. In another embodiment, a CBD derivative is a (+) and/or a (-)CBD analogue such as disclosed in Bisogno et al., Br. J. Pharm. 2001;134:845-852 which is hereby incorporated by reference in its entirety. In another embodiment, a derivative is a functional derivative.

[050] In one embodiment, the autoimmune disease is: Addison's disease, Agammaglobulinemia, Alopecia areata, Amyloidosis, Ankylosing spondylitis, Anti-GBM/Anti-TBM nephritis, Antiphospholipid syndrome, Autoimmune hepatitis, Autoimmune inner ear disease, Axonal & neuronal neuropathy, Behcet's disease, Bullous pemphigoid, Castleman disease, Celiac disease, Chagas disease, Chronic inflammatory demyelinating polyneuropathy, Chronic recurrent multifocal osteomyelitis, Cicatricial pemphigoid/benign mucosal pemphigoid, Churg-Strauss, Cogan's syndrome, Cold

agglutinin disease, Congenital heart block, Coxsackie myocarditis, CREST syndrome, Crohn's disease, Dermatitis herpetiformis, Dermatomyositis, Devic's disease, Discoid lupus, Dressier' s syndrome, Endometriosis, Eosinophilic esophagitis, Eosinophilic fasciitis, Erythema nodosum, Essential mixed cryoglobulinemia, Evans syndrome, Fibromyalgia, Fibrosing alveolitis, Giant cell arteritis, Giant cell myocarditis, Glomerulonephritis, Goodpasture's syndrome, Granulomatosis with Polyangiitis, Graves' disease, Guillain-Barre syndrome, Hashimoto's thyroiditis, Hemolytic anemia, Henoch-Schonlein purpura, Herpes gestationis or pemphigoid gestationis, Hypogammalglobulinemia, IgA Nephropathy, IgG4-related sclerosing disease, Inclusion body myositis, Interstitial cystitis, Juvenile arthritis, Juvenile diabetes, Juvenile myositis, Kawasaki disease, Lambert-Eaton syndrome, Leukocytoclastic vasculitis, Lichen planus, Lichen sclerosus, Ligneous conjunctivitis, Linear IgA disease, Lupus, chronic Lyme disease, Meniere's disease, Microscopic polyangiitis, Mixed connective tissue disease, Mooren's ulcer, Mucha-Habermann disease, Multiple sclerosis, Myasthenia gravis, Myositis, Narcolepsy, Neuromyelitis optica, Neutropenia, Ocular cicatricial pemphigoid, Optic neuritis, Palindromic rheumatism, PANDAS, Paraneoplastic cerebellar degeneration, Paroxysmal nocturnal hemoglobinuria, Parry Romberg syndrome, Pars planitis, Parsonnage-Turner syndrome, Pemphigus, Peripheral neuropathy, Perivenous encephalomyelitis, Pernicious anemia, POEMS syndrome, Polyarteritis nodosa, Polymyalgia rheumatic, Postmyocardial infarction syndrome, Postpericardiotomy syndrome, Polymyositis, Primary biliary cirrhosis, Primary sclerosing cholangitis, Progesterone dermatitis, Psoriasis, Psoriatic arthritis, Pure red cell aplasia, Pyoderma gangrenosum, Raynaud's phenomenon, Reactive Arthritis, Reflex sympathetic dystrophy, Reiter's syndrome, Relapsing polychondritis, Restless legs syndrome, Retroperitoneal fibrosis, Rheumatic fever, Rheumatoid arthritis, Sarcoidosis, Schmidt syndrome, Scleritis, Scleroderma, Sjogren's syndrome, Sperm & testicular autoimmunity, Stiff person

syndrome, Subacute bacterial endocarditis, Susac's syndrome, Sympathetic ophthalmia, Takayasu's arteritis, Temporal arteritis/Giant cell arteritis, Thrombocytopenic purpura, Tolosa-Hunt syndrome, Transverse myelitis, Type 1 diabetes, Ulcerative colitis, Undifferentiated connective tissue disease, Uveitis, Vasculitis, Vitiligo, and/or Wegener's granulomatosis. In one embodiment, the autoimmune disease is autoimmune hepatitis.

[051] In one embodiment, liver inflammation is Cirrhosis. In one embodiment, liver inflammation is hepatitis. In one embodiment, liver inflammation is hepatitis resulting from a viral infection. In one embodiment, a method as described herein provides treating a subject in need of a steroid or a corticosteroid treatment with: (a) steroid or a corticosteroid; and (b) CBD or a derivative thereof. In one embodiment, the steroid is methylprednisolone (MP). In one embodiment, treating a subject in need of a steroid or a corticosteroid treatment is treating a subject in need of a daily steroid or a corticosteroid treatment. In one embodiment, the steroid is any corticosteroid such as but not limited to: Betamethasone, Budesonide, Cortisone Dexamethasone, Hydrocortisone, Methylprednisolone, Prednisolone, and/or Prednisone.

[052] In one embodiment, the steroid is administered at steroid doses of 0.2 to 10 mg/kg body weight of the subject. In one embodiment, the steroid is administered at steroid doses of 0.5 to 10 mg/kg body weight of the subject. In one embodiment, the steroid is administered at steroid doses of 0.5 to 8 mg/kg body weight of the subject. In one embodiment, the steroid is administered at steroid doses of 0.5 to 5 mg/kg body weight of the subject. In one embodiment, the steroid is administered at steroid doses of 1 to 8 mg/kg body weight of the subject. In one embodiment, the steroid is administered at steroid doses of 1 to 5 mg/kg body weight of the subject. In one embodiment, the steroid is administered at steroid doses of 2 to 6 mg/kg body weight of the subject. In one embodiment, the steroid is administered at steroid doses of 1 to 2 mg/kg body weight of the subject.

[053] In one embodiment, a subject as described herein does not respond to a steroid or a corticosteroid treatment. In one embodiment, steroid or corticosteroid treatment is ineffective and/or required in high dose in a subject as described herein. In one embodiment, steroid or corticosteroid treatment causes undesired side effects in a subject as described herein. In one embodiment, a subject as described herein requires a steroid or a corticosteroid treatment for at least a month. In one embodiment, a subject as described herein needs a steroid or corticosteroid treatment for at least two months. In one embodiment, a subject as described herein needs a steroid or corticosteroid treatment for at least three months. In one embodiment, a subject as described herein needs a steroid or corticosteroid treatment for at least six months. In one embodiment, a subject as described herein is afflicted with a chronic disease or condition which requires a steroid or a corticosteroid treatment of at least a month. In one embodiment, a subject as described herein is afflicted with a chronic disease or condition which requires a steroid or a corticosteroid treatment of at least two months. In one embodiment, a subject as described herein is afflicted with a chronic disease or condition which requires a steroid or a corticosteroid treatment of at least three months. In one embodiment, a subject as described herein is afflicted with a chronic disease or condition which requires a steroid or a corticosteroid treatment of at least a month every year, for at least 3 years. In one embodiment, a subject as described herein is afflicted with a chronic disease or condition which requires a steroid or a corticosteroid treatment of at least two months every year, for at least 3 years.

[054] In one embodiment, a subject suffering a disease such as described herein is a subject requiring a steroid or a corticosteroid therapy. In one embodiment, a subject suffering a disease such as described herein will not respond to a steroid treatment of 0.5 to 25 mg/kg per day for at least 2 to 30 days. In one embodiment, steroid therapy in a

subject suffering a disease such as described herein results in unwanted steroidal side effects. In one embodiment, steroid therapy in a subject suffering a disease such as described herein does not inhibit at least on side effect associated with the disease. In one embodiment, steroid therapy is 0.2 to 80 mg/kg steroid per day for at least 2 to 30 days. In one embodiment, steroid therapy is 0.2 to 50 mg/kg steroid per day for at least 2 to 50 days. In one embodiment, steroid therapy is 0.2 to 30 mg/kg steroid per day for at least 2 to 50 days. In one embodiment, steroid therapy is 0.2 to 30 mg/kg steroid per day for at least 2 to 50 days. In one embodiment, steroid therapy is 0.2 to 20 mg/kg steroid per day for at least 2 to 50 days. In one embodiment, steroid therapy is 0.2 to 15 mg/kg steroid per day for at least 2 to 50 days.

[055] In one embodiment, a subject nonresponsive (or refractoriness) to a steroid or a corticosteroid treatment, to be treated per the methods as described herein, does not exhibit clinical progression after 3 days of steroid treatment. In one embodiment, a subject nonresponsive (or refractoriness) to a steroid or a corticosteroid treatment, to be treated per the methods as described herein, does not exhibit clinical progression after 5 days of steroid treatment. In one embodiment, a subject nonresponsive (or refractoriness) to a steroid or a corticosteroid treatment, to be treated per the methods as described herein, does not exhibit clinical progression after 7 days of steroid treatment. In one embodiment, a subject nonresponsive (or refractoriness) to a steroid or a corticosteroid treatment, to be treated according to the methods as described herein, does not exhibit clinical progression after 10 days of steroid treatment.

[056] In one embodiment, a subject to be treated according to the methods as described herein does not show any clinical improvement after 2 days of a steroid or a corticosteroid treatment. In one embodiment, a subject to be treated according to the methods as described herein does not show any clinical improvement after 5 days of a steroid or a corticosteroid

treatment. In one embodiment, a subject to be treated according to the methods as described herein does not show any clinical improvement after 3 days of a steroid or a corticosteroid treatment. In one embodiment, a subject to be treated according to the methods as described herein does not show any clinical improvement after 7 days of a steroid or a corticosteroid treatment. In one embodiment, a subject to be treated according to the methods as described herein does not show any clinical improvement after 9 days of a steroid or a corticosteroid treatment.

[057] In one embodiment, "clinical improvement" comprises incomplete response to a steroid or a corticosteroid treatment as defined in acceptable medical literature. In one embodiment, "clinical improvement" comprises incomplete response to a steroid or a corticosteroid treatment as defined by one of skill in the art. In one embodiment, a subject per the invention is a subject in need of a steroid or a corticosteroid treatment. In one embodiment, a subject per the invention is a subject treated with a steroid or a corticosteroid.

[058] In one embodiment, a subject per the invention is a subject treated with a steroid or a corticosteroid for at least a week. In one embodiment, a subject per the invention is a subject treated with a steroid or a corticosteroid for at least two weeks. In one embodiment, a subject per the invention is a subject treated with a steroid or a corticosteroid for at least a month. In one embodiment, a subject per the invention is a subject treated with a steroid or a corticosteroid for at least 3 months. In one embodiment, a subject per the invention is a subject treated with a steroid or a corticosteroid for at least 6 months.

[059] In one embodiment, a subject per the invention is a subject treated with a steroid or a corticosteroid showing a deterioration in at least one symptom or a condition associated with an autoimmune disease/autoimmune hepatitis/liver inflammation, after 3 days of a steroid treatment. In one embodiment, a subject per the invention is a subject

treated with a steroid or a corticosteroid showing a deterioration in at least one symptom or a condition associated with an autoimmune disease/autoimmune hepatitis/liver inflammation, after 5 days of a steroid treatment. In one embodiment, a subject per the invention is a subject treated with a steroid or a corticosteroid showing a deterioration in at least one symptom or a condition associated with an autoimmune disease/autoimmune hepatitis/liver inflammation, after 7 days of a steroid treatment. In one embodiment, a subject per the invention is a subject treated with a steroid or a corticosteroid showing a deterioration in at least one symptom or a condition associated with an autoimmune disease/autoimmune hepatitis/liver inflammation, after 14 days of a steroid treatment. In one embodiment, a subject per the invention is a subject treated with a steroid or a corticosteroid showing a deterioration in at least one symptom or a condition associated with an autoimmune disease/autoimmune hepatitis/liver inflammation, after 30 days of a steroid treatment.

[060] The compositions described herein, comprise Cannabidiol (CBD), or any functional derivative thereof *(i.e.* a CBD derivative possessing similar, equivalent, or increased efficacy). In some embodiments, the described compositions optionally further comprise at least one pharmaceutically acceptable carrier, diluent, excipient and/or additive.

[061] The phrase "CBD or any functional derivative thereof", according to some embodiments, refers to compounds and/or compositions that are substantially and/or essentially devoid of THC. In one embodiment, a composition comprising CBD or any functional derivative thereof, as described herein is substantially and/or essentially devoid of THC.

[062] The phrase "CBD or any functional derivative thereof", according to some embodiments, refers to compounds and/or compositions that comprise at least 80% CBD

or any functional derivative thereof. The phrase "CBD or any functional derivative thereof", according to some embodiments, refers to compounds and/or compositions that comprise at least 90% CBD or any functional derivative thereof. The phrase "CBD or any functional derivative thereof", according to some embodiments, refers to compounds and/or compositions that comprise at least 92% CBD or any functional derivative thereof. The phrase "CBD or any functional derivative thereof", according to some embodiments, refers to compounds and/or compositions that comprise at least 95% CBD or any functional derivative thereof. The phrase "CBD or any functional derivative thereof", according to some embodiments, refers to compounds and/or compositions that comprise at least 97% CBD or any functional derivative thereof. The phrase "CBD or any functional derivative thereof", according to some embodiments, refers to compounds and/or compositions that comprise at least 99% CBD or any functional derivative thereof.

[063] Cannabidiol is insoluble in water but soluble in organic solvents, such as oil. In one embodiment, a composition of the invention comprises a vehicle such as an organic solvent or oil. Accordingly, CBD can be formulated for use in the described methods through use of any organic solvent known to the pharmaceutical arts, including, but not limited to edible oils. When formulated for oral administration, any edible oil can be used in the CBD formulation, including olive oil.

[064] In one embodiment, substantially and/or essentially devoid of THC is less than 15% by weight or weight/weight THC. In one embodiment, substantially and/or essentially devoid of THC is less than 10% by weight or weight/weight THC. In one embodiment, substantially and/or essentially devoid of THC is less than 7% by weight or weight/weight THC. In one embodiment, substantially and/or essentially devoid of THC is less than 5% by weight or weight/weight THC. In one embodiment, substantially and/or essentially devoid of THC is less than 3% by weight or weight/weight THC. In one embodiment,

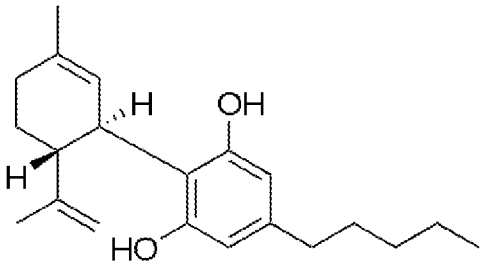
substantially and/or essentially devoid of THC is less than 1% by weight or weight/weight THC. In one embodiment, substantially and/or essentially devoid of THC is less than 0.5% by weight or weight/weight THC. In one embodiment, substantially and/or essentially devoid of THC is less than 0.3% by weight or weight/weight THC. In one embodiment, substantially and/or essentially devoid of THC is less than 0.1% by weight or weight/weight THC. In one embodiment, substantially and/or essentially devoid of THC is less than 0.05% by weight or weight/weight THC. In one embodiment, substantially and/or essentially devoid of THC is less than 0.01% by weight or weight/weight THC.

[065] In one embodiment, a composition comprising CBD is a composition essentially devoid of THC and consisting: (1) CBD or any functional derivative thereof; and (2) a pharmaceutically acceptable excipient such as but not limited to: a CBD carrier, an emulsifier, a preservative, a buffer or any combination thereof. In one embodiment, a composition comprising CBD is a composition essentially devoid of THC and consisting: (1) CBD or any functional derivative thereof; (2) a pharmaceutically acceptable excipient such as but not limited to: a CBD carrier, an emulsifier, a preservative, a buffer or any combination thereof; and (3) less than 1% by weight or weight/weight THC. In one embodiment, a composition comprising CBD is a composition essentially devoid of THC and consisting: (1) CBD or any functional derivative thereof; (2) a pharmaceutically acceptable excipient such as but not limited to: a CBD carrier, an emulsifier, a preservative, a buffer or any combination thereof; and (3) less than 0.5% by weight or weight/weight THC. In one embodiment, a composition comprising CBD is a composition essentially devoid of THC and consisting: (1) CBD or any functional derivative thereof; (2) a pharmaceutically acceptable excipient such as but not limited to: a CBD carrier, an emulsifier, a preservative, a buffer or any combination thereof; and (3) less than 0.1% by weight or weight/weight THC. In one embodiment, a composition comprising CBD is a

composition essentially devoid of THC and consisting: (1) CBD or any functional derivative thereof; (2) a pharmaceutically acceptable excipient such as but not limited to: a CBD carrier, an emulsifier, a preservative, a buffer or any combination thereof; and (3) less than 0.05% by weight or weight/weight THC. In one embodiment, a composition comprising CBD is a composition essentially devoid of THC and consisting: (1) CBD or any functional derivative thereof; (2) a pharmaceutically acceptable excipient such as but not limited to: a CBD carrier, an emulsifier, a preservative, a buffer or any combination thereof; and (3) less than 0.01% by weight or weight/weight THC.

[066] In one embodiment, "% by weight or weight/weight" is from the entire weight of the composition. In one embodiment, "% by weight or weight/weight" is from the weight of CBD or any functional derivative thereof within the composition. In one embodiment, "% by weight or weight/weight" is from the weight of THC and CBD or any functional derivative thereof within the composition.

[067] In the methods described herein, cannabidiol, or a functional variant thereof, free or substantially free of THC, is administered to a subject treated with a steroid or a corticosteroid. In the methods described herein, purified or substantially purified (greater than 80% w/w, 85% w/w, 90%, w/w 95% w/w or 97% w/w) cannabidiol, or a functional variant thereof, is administered to a subject suffering from a disease such as described herein. Cannabidiol constitutes up to 40% of *Cannabis sativa* extracts, and is recognized as a major non-psychoactive cannabinoid, with a remarkable lack of any cognitive and psychoactive actions. CBD, also termed 2-[(6R)-3-Methyl-6-prop-l-en-2-yl-lcyclohex-2-envyl]-5pentylbenzene-l,3-diol, has the molecular formula of $C_{21}H_{30}O_2$. The chemical structure of CBD is shown in Formula I:



[068] A CBD derivative, is in some embodiments, a metabolite of CBD such as but not limited to: (-)-7-hydroxy-CBD and (-)-CBD-7-oic acid and their dimethylheptyl (DMH) homologs, as well as of the corresponding compounds in the enantiomeric (+)-CBD series. A CBD derivative is characterized, in some embodiments, by a structure wherein at least one of the hydroxyl substituent groups is converted to a stable form thereof. In one embodiment, a CBD derivative is cannabinol comprising a quinone ring. In one embodiment, a CBD derivative is an endocannabinoid derivative. In some embodiments, a CBD derivative is described in Frank D King; G Lawton; A W Oxford Progress in medicinal chemistry. Vol. 44. Pages 207-331, Elsevier Science, 2006 ISBN: 0080462103 9780080462103 which is hereby incorporated by reference in its entirety.

[069] In some embodiment, the dose, dosage, or daily dose or daily dosage of Cannbidiol or a functional derivative thereof is 50 to 2500 mg. In some embodiment, the dose, dosage, or daily dose or daily dosage of Cannbidiol or a functional derivative thereof is 150 to 1500 mg. In some embodiment, the dose, dosage, or daily dose or daily dosage of Cannbidiol or a functional derivative thereof is 100 to 1000 mg. In some embodiment, the dose, dosage, or daily dose or dosage of Cannbidiol or a functional derivative thereof is 200 to 1000 mg. In some embodiment, the dose, dosage, or daily dose or daily dosage of Cannbidiol or a functional derivative thereof is the therapeutically effective dose.

[070] The methods of the present invention provide long desired therapy for autoimmune disease/autoimmune hepatitis/liver inflammation by inhibiting the destructive inflammatory/immunologic process, alleviate symptoms associated with autoimmune disease/autoimmune hepatitis/liver inflammation and/or steroidal therapy, and prevent disease progression. The methods for treating autoimmune disease/autoimmune hepatitis/liver inflammation of the present invention provide, in some embodiments, treatment with Cannbidiol or a functional derivative thereof combined with systemic treatment of a steroid or a corticosteroid, optionally combined with additional medications. In some embodiments, Cannbidiol or a functional derivative thereof inhibit and/or decrease side-effects of a steroid. In some embodiments, CBD as described herein alleviates symptoms associated with autoimmune disease/autoimmune hepatitis/liver inflammation.

[071] The present invention now demonstrates the beneficial effects of treatment with Cannbidiol or a functional derivative thereof for the treatment of autoimmune disease/autoimmune hepatitis/liver inflammation. More specifically, the present invention demonstrates that treatment with the Cannabidiol or a functional derivative thereof compositions of the invention significantly reduces the severity, as well as other complications associated with autoimmune disease/autoimmune hepatitis/liver inflammation.

In some embodiments, CBD enhances the therapeutic effect of a steroid or a corticosteroid. In some embodiments, CBD reduces a side effect associated with the steroid or the corticosteroid. In some embodiments, CBD combined with a steroid or a corticosteroid provides a synergistic steroidal treatment. In some embodiments, CBD combined with a steroid or a corticosteroid provides a synergistic anti-inflammatory treatment to a subject as described herein. In some embodiments, CBD combined with a steroid or a corticosteroid provides a synergistic immune-modulating treatment to a subject as

described herein. In some embodiments, CBD renders a refractory steroid dose an effective therapeutic dose. In some embodiments, CBD enables the reduction of a steroid or a corticosteroid dose without compromising its therapeutic benefit, thereby reducing undesired side effects associated with a steroid or a corticosteroid. In one embodiment, autoimmune disease/autoimmune hepatitis/liver inflammation is steroid-refractory autoimmune disease/autoimmune hepatitis/liver inflammation.

In one embodiment, a steroid is a corticosteroid and/or glucocorticoid or a combination of glucocorticoids and/or corticosteroids. In one embodiment, a steroid is a synthetic steroid. In one embodiment, a corticosteroid and/or glucocorticoid is a synthetic corticosteroid and/or synthetic glucocorticoid. In one embodiment, the steroid is methylprednisolone, prednisolone, Prednisone, hydrocortisone, dexamethasone, beclomethasone, budesonide, clobetasol, triamcinolone, fluticasone, mometasone, Diflorasone Desoximetasone, aclometasone, fluocinonide, halobetasol, flurandrenolide, betamethasone, cortisone, prednisone or any equivalents thereof and/or a combination thereof.

[072] In one embodiment, steroid daily dose is a single dose per day. In one embodiment, steroid daily dose is divided to 2 to 8 portions/doses per day. In one embodiment, steroid treatment includes 0.2 to 25 mg/kg (body weight) per day steroid, for 2 to 30 days. In one embodiment, administering to the subject a therapeutically effective amount of a composition comprising the CBD or a functional derivative thereof is daily administering 5 to 1000 mg CBD. In one embodiment, administering to the subject a therapeutically effective amount of a composition comprising said CBD or a functional derivative thereof is daily administering 20 to 500 mg CBD. In one embodiment, mg/kg is mg per body weight in kg. In one embodiment, administering CBD or a functional derivative thereof is administering a composition comprising a therapeutically effective amount of CBD or a functional derivative thereof.

[073] In one embodiment, a therapeutically effective amount of CBD or a functional derivative thereof according to the invention is capable of reducing the daily therapeutic effective dose of a steroid by at least 20%. In one embodiment, a therapeutically effective amount of CBD or a functional derivative thereof according to the invention is capable of reducing the daily therapeutic effective dose of a steroid by at least 30%. In one embodiment, a therapeutically effective amount of CBD or a functional derivative thereof according to the invention is capable of reducing the daily therapeutic effective dose of a steroid by at least 40%. In one embodiment, a therapeutically effective amount of CBD or a functional derivative thereof according to the invention is capable of reducing the daily therapeutic effective dose of a steroid by at least 50%. In one embodiment, a therapeutically effective amount of CBD or a functional derivative thereof according to the invention is capable of reducing and/or eliminating a steroid side effect.

[074] In one embodiment, a method as described herein requires a step of determining that the given steroid dose is refractory. In one embodiment, a method as described herein further requires a step of gradually reducing the daily/weekly dose of a steroid by at least 10% per week up to 40% total dose reduction (the reduction in the weekly/daily dose is calculated from the initial steroid monotherapy daily/weekly dose). In one embodiment, a method as described herein further requires a step of gradually reducing the daily/weekly dose of a steroid by at least 20% per week up to 50% total dose reduction (the reduction in the weekly/daily dose is calculated from the initial steroid monotherapy daily/weekly dose). In one embodiment, a method as described herein further requires a step of gradually reducing the daily/weekly dose of a steroid by 10% to 50% per week up to 80% total dose reduction (the reduction in the weekly/daily dose is calculated from the initial steroid monotherapy daily/weekly dose).

[075] In one embodiment, a method as described herein requires a step of evaluating the required dose of a steroid, wherein a required dose beyond the recommended therapeutic effective and safe range of a steroid dose requires the dual or combined therapy as described herein. In one embodiment, a method as described herein requires a step of evaluating the required dose of a steroid, wherein a required dose of a steroid beyond the recommended therapeutic effective and safe range of a steroid dose requires obtaining an equivalent steroid therapeutic effect but with at least 20%, 30%, 40, or 50% lower steroid dose. In one embodiment, obtaining "an equivalent steroid therapeutic effect" but with a lower steroid dose as described herein required administering CBD or a derivative thereof together with the steroid therapy.

[076] In one embodiment, the combined or dual therapy includes a single composition comprising a steroid and CBD or a derivative thereof. In one embodiment, the combined or dual therapy includes a single composition comprising CBD or a functional derivative thereof. In one embodiment, the combined or dual therapy includes two separate compositions: the first composition comprising CBD or a functional derivative thereof and the second composition comprising a steroid. In one embodiment, provided herein is a kit comprising two separate compositions: the first composition comprising CBD or a functional derivative thereof and the second composition comprising a steroid. In one embodiment, provided herein is a kit comprising two separate compositions: the first composition comprising 50 to 500 mg CBD or a functional derivative thereof and the second composition comprising a steroid in a dose or an amount equal to or less than the required steroid dose/amount without treatment with CBD or a functional derivative thereof.

[077] In one embodiment, a functional derivative of CBD is a compound disclosed in Mechoulam R. and Lumi'r H. Cannabidiol: an overview of some chemical and

pharmacological aspects. Part I: chemical aspects. Chemistry and Physics of Lipids 121 (2002) 35/43 which is hereby incorporated by reference in its entirety. In one embodiment, a functional derivative of CBD is a compound disclosed in Handbook of Cannabis and Related Pathologies 1st Edition. Biology, Pharmacology, Diagnosis, and Treatment. Editors: Victor Preedy. eBook ISBN: 9780128008270. Hardcover ISBN: 9780128007563. Academic Press.

[078] In one embodiment, a functional derivative of CBD is a compound which reduces psychotic symptoms. In one embodiment, a functional derivative of CBD is a compound which relieves convulsions and/or nausea. In one embodiment, a functional derivative of CBD is a compound which decreases anxiety. In one embodiment, a functional derivative of CBD is a compound which decreases inflammation. In one embodiment, a functional derivative of CBD is a compound which reduces depressive symptoms.

[079] In one embodiment, reducing a steroid effective dose is reducing a steroid monotherapy effective dose. In one embodiment, rendering an ineffective or refractory dose of a steroid - an effective dose, is providing a CBD-steroid combined therapy. In one embodiment, the ineffective or refractory dose of a steroid is a steroid dose provided in a monotherapy. In one embodiment, lowering a steroid dose is lowering the required steroid monotherapy dose.

[080] In one embodiment, the terms "monotherapy" or "single therapy" as used herein refer to treatment with steroid and without CBD. In one embodiment, the terms "monotherapy" or "single therapy" as used herein refer to treatment with steroid only. In one embodiment, the terms "monotherapy" or "single therapy" as used herein refer to treatment with steroid and any other composition which is devoid of CBD.

[08 1] In one embodiment, a subject as described herein is a human. In one embodiment, a subject as described cannot benefit from steroid treatment. In one embodiment, a steroid treatment is refractory to a subject such as described herein.

[082] Treating, according to some embodiments, includes inhibiting the progression or deterioration of autoimmune disease/autoimmune hepatitis/liver inflammation.

[083] In one embodiment, a therapeutically effective amount of a composition comprising a CBD or a functional derivative thereof comprises 0.5 mg to 1 g of a CBD or a functional derivative thereof. In one embodiment, a therapeutically effective daily dose of a CBD or a functional derivative thereof comprises 0.5 mg to 1 g of a CBD or a functional derivative thereof. In one embodiment, a therapeutically effective amount of a composition comprising a CBD or a functional derivative thereof comprises 5 mg to 750 mg of a CBD or a functional derivative thereof. In one embodiment, a therapeutically effective daily dose of a CBD or a functional derivative thereof comprises 5 mg to 750 mg of a CBD or a functional derivative thereof. In one embodiment, a therapeutically effective amount of a composition comprising a CBD or a functional derivative thereof comprises 5 mg to 600 mg of a CBD or a functional derivative thereof. In one embodiment, a therapeutically effective daily dose of a CBD or a functional derivative thereof comprises 5 mg to 600 mg of a CBD or a functional derivative thereof. In one embodiment, a therapeutically effective amount of a composition comprising a CBD or a functional derivative thereof comprises 50 mg to 500 mg of a CBD or a functional derivative thereof. In one embodiment, a therapeutically effective daily dose of a CBD or a functional derivative thereof comprises 50 mg to 500 mg of a CBD or a functional derivative thereof. In one embodiment, a therapeutically effective amount of a composition comprising a CBD or a functional derivative thereof comprises 80 mg to 400 mg of a CBD or a functional derivative thereof. In one embodiment, a therapeutically effective daily dose of a CBD or

a functional derivative thereof comprises 80 mg to 400 mg of a CBD or a functional derivative thereof. In one embodiment, a therapeutically effective daily dose of a CBD or a functional derivative thereof comprises 80 mg to 600 mg of a CBD or a functional derivative thereof. In one embodiment, a single therapeutically effective dosage of CBD or a functional derivative thereof comprises 30 mg to 400 mg of a CBD or a functional derivative thereof. In one embodiment, a single therapeutically effective dosage of CBD or a functional derivative thereof comprises 50 mg to 500 mg of a CBD or a functional derivative thereof. In one embodiment, a single therapeutically effective dosage of CBD or a functional derivative thereof comprises 80 mg to 300 mg of a CBD or a functional derivative thereof. In one embodiment, a single therapeutically effective dosage of CBD or a functional derivative thereof comprises 100 mg to 200 mg of a CBD or a functional derivative thereof.

[084] In one embodiment, a composition as described herein is a topical composition. In one embodiment, a composition as described herein is an oral composition. In one embodiment, a composition as described herein is a systemic composition. In one embodiment, a subject as described herein is treated with a combination of steroid compositions selected from: a topical composition, a systemic composition, and an oral composition.

[085] In one embodiment, provided a method for enhancing the therapeutic effect of a steroid in a subject in need of a steroid therapy, comprising administering to the subject the steroid and a cannabidiol (CBD) or a functional derivative thereof, thereby enhancing the therapeutic effect of a steroid in a subject in need of a steroid therapy. In one embodiment, provided a method for enhancing the therapeutic effect of a steroid dose or dosage in a subject in need of a steroid therapy, comprising administering to the subject the steroid dose or dosage and a cannabidiol (CBD) or a functional derivative thereof,

thereby enhancing the therapeutic effect of a steroid dose or dosage in a subject in need of a steroid therapy. In one embodiment, enhancing the therapeutic effect of a steroid is maintaining a fixed dose and combining it with a cannabidiol (CBD) or a functional derivative thereof. In one embodiment, enhancing the therapeutic effect of a steroid is rendering a refractory steroid dose and/or dosage, therapeutically effective. In one embodiment, enhancing the therapeutic effect of a steroid is rendering a sub-efficient steroid dose and/or dosage, therapeutically effective. In one embodiment, enhancing the therapeutic effect of a steroid is avoiding increase in steroid dose and/or dosage. In one embodiment, enhancing the therapeutic effect of a steroid is avoiding increase in steroid dose and/or dosage due to insufficient and/or poor clinical effect. In one embodiment, enhancing the therapeutic effect of a steroid is decreasing side-effects directly associated with a steroid treatment. In one embodiment, enhancing the therapeutic effect of a steroid is reducing the duration of steroid treatment. In one embodiment, a steroid is glucocorticosteroid, corticosteroid or any steroid known to one of skill in the art or described herein.

[086] In one embodiment, provided a pharmaceutical composition comprising a cannabidiol (CBD) or a functional derivative thereof for use in enhancing the therapeutic effect of a steroid. In one embodiment, provided a pharmaceutical composition comprising a cannabidiol (CBD) or a functional derivative thereof for use in reducing a dose or a dosage of a steroid. In one embodiment, provided a pharmaceutical composition comprising a cannabidiol (CBD) or a functional derivative thereof for use in reducing a dose or a dosage of a steroid while maintaining or enhancing the steroid's therapeutic effect. In one embodiment, provided a pharmaceutical composition comprising a cannabidiol (CBD) or a functional derivative thereof for use in maintaining or enhancing the therapeutic effect of a steroid therapy. In one embodiment, maintaining or enhancing

the therapeutic effect of a steroid therapy, according to the methods of the invention, include reducing the dosage or dose of a steroid in a subject treated with a cannabidiol (CBD) or a functional derivative thereof.

[087] In one embodiment, provided a pharmaceutical composition comprising a cannabidiol (CBD) or a functional derivative thereof for reducing the effective dose of a steroid. In one embodiment, provided a pharmaceutical composition comprising a cannabidiol (CBD) or a functional derivative thereof for reducing a side effect associated with steroid treatment. In one embodiment, provided a pharmaceutical composition comprising a cannabidiol (CBD) or a functional derivative thereof for reducing the effective dose of a steroid and thereby reducing a side effect associated with steroid treatment.

[088] In one embodiment, provided a pharmaceutical composition comprising a cannabidiol (CBD) or a functional derivative thereof for reducing the effective dose of a steroid in a subject afflicted with autoimmune disease/autoimmune hepatitis/liver inflammation. In one embodiment, provided a pharmaceutical composition comprising a cannabidiol (CBD) or a functional derivative thereof for reducing a side effect associated with steroid treatment in a subject afflicted with autoimmune disease/autoimmune hepatitis/liver inflammation. In one embodiment, provided a pharmaceutical composition comprising a cannabidiol (CBD) or a functional derivative thereof for reducing the effective dose of a steroid and thereby reducing a side effect associated with steroid treatment in a subject afflicted with autoimmune disease/autoimmune hepatitis/liver inflammation.

[089] In one embodiment, provided a pharmaceutical composition comprising a cannabidiol (CBD) or a functional derivative thereof for reducing the effective dose of a steroid in a subject afflicted with autoimmune disease/autoimmune hepatitis/liver

inflammation. In one embodiment, "effective dose" is the "therapeutically effective dose for a subject afflicted with autoimmune disease/autoimmune hepatitis/liver inflammation. In one embodiment, a pharmaceutical composition comprising a cannabidiol (CBD) or a functional derivative thereof reduces the effective dose of steroid by at least 10% and/or 10% w/w. In one embodiment, a pharmaceutical composition comprising a cannabidiol (CBD) or a functional derivative thereof reduces the effective dose of steroid by at least 20% and/or 20% w/w. In one embodiment, a pharmaceutical composition comprising a cannabidiol (CBD) or a functional derivative thereof reduces the effective dose of steroid by at least 30% and/or 30% w/w. In one embodiment, a pharmaceutical composition comprising a cannabidiol (CBD) or a functional derivative thereof reduces the effective dose of steroid by at least 50% and/or 50% w/w. In one embodiment, a pharmaceutical composition comprising a cannabidiol (CBD) or a functional derivative thereof reduces the effective dose of steroid by at least 75% and/or 75% w/w.

[090] In one embodiment, a pharmaceutical composition comprising a cannabidiol (CBD) or a functional derivative thereof reduces the effective dose of steroid by 10% to 70% w/w. In one embodiment, a pharmaceutical composition comprising a cannabidiol (CBD) or a functional derivative thereof reduces the effective dose of steroid by at least 30% w/w. In one embodiment, a pharmaceutical composition comprising a cannabidiol (CBD) or a functional derivative thereof reduces the effective dose of steroid by at least 40% w/w. In one embodiment, a pharmaceutical composition comprising a cannabidiol (CBD) or a functional derivative thereof reduces the effective dose of steroid by at least 50% w/w. In one embodiment, a pharmaceutical composition comprising a cannabidiol (CBD) or a functional derivative thereof reduces the effective dose of steroid by at least 60% w/w.

[091] In one embodiment, %w/w reflects the total amount of a steroid in a composition or a medicament administered to a given subject afflicted with a disease as described herein.

[092] In one embodiment, provided a method for enhancing the therapeutic effect of a steroid in a subject afflicted with autoimmune disease/autoimmune hepatitis/liver inflammation, comprising administering to the subject the steroid and a cannabidiol (CBD) or a functional derivative thereof, thereby enhancing the therapeutic effect of a steroid.

[093] In one embodiment, provided a method for reducing a side effect associated with a steroid in a subject afflicted with autoimmune disease/autoimmune hepatitis/liver inflammation and treated with a steroid, comprising administering to the subject the steroid and a cannabidiol (CBD) or a functional derivative thereof. In one embodiment, provided a method for reducing a side effect associated with a steroid in a subject afflicted with autoimmune disease/autoimmune hepatitis/liver inflammation and treated with a steroid, comprising administering to the subject the steroid and a cannabidiol (CBD) or a functional derivative thereof. In one embodiment, provided a method for reducing the effective dose of a steroid in a subject afflicted with autoimmune disease/autoimmune hepatitis/liver inflammation and treated with a steroid, comprising administering to the subject a reduced steroid dose and a cannabidiol (CBD) or a functional derivative thereof.

[094] In one embodiment, a steroid is an anabolic steroid. In one embodiment, a steroid is a corticosteroid. In one embodiment, a subject in need of a steroid therapy is afflicted with inflammation. In one embodiment, a subject in need of a steroid therapy is in need of reducing and/or inhibiting an immune response.

[095] In some embodiments, a reduced dose includes at least 15% (by weight) less steroid. In some embodiments, a reduced dose includes at least 20% (by weight) less steroid. In some embodiments, a reduced dose includes at least 25% (by weight) less

steroid. In some embodiments, a reduced dose includes at least 30% (by weight) less steroid. In some embodiments, a reduced dose includes at least 40% (by weight) less steroid. In some embodiments, a reduced dose includes at least 50% (by weight) less steroid.

[096] In some embodiments, the phrase "effective dose" is the dose effective for treating or ameliorating autoimmune disease/autoimmune hepatitis/liver inflammation as described herein. In some embodiments, the phrase "effective dose" is synonymous with the phrase "daily effective dose" as described herein. In some embodiments, the phrase "effective dose" is the dose effective for reducing bilirubin level in the blood of a subject afflicted with autoimmune disease/autoimmune hepatitis/liver inflammation. In some embodiments, the phrase "effective dose" is the dose effective for reducing and/or inhibiting a pathology and/or risk associated with autoimmune disease/autoimmune hepatitis/liver inflammation. In some embodiments, reducing the effective dose of a steroid results in minimizing or reducing at least one side effect associated with steroid treatment.

[097] In one embodiment, provided a method for enhancing the therapeutic autoimmune disease/autoimmune hepatitis/liver inflammation effect of a given steroid dose in a subject afflicted with autoimmune disease/autoimmune hepatitis/liver inflammation and treated with a steroid, comprising administering to the subject the given steroid dose and a cannabidiol (CBD) or a functional derivative thereof.

[098] In some embodiments, enhancing the therapeutic effect of a steroid enables the reduction of the steroid dose administered and/or the reduction of dosing. In some embodiments, enhancing the therapeutic effect of a steroid is rendering a refractory steroid dose a therapeutic effective dose. In some embodiments, a refractory steroid dose is any steroid dose found to be refractory in a subject afflicted with autoimmune disease/autoimmune hepatitis/liver inflammation. In one embodiment, a refractory steroid

dose is a daily steroid dose of 0.2 to 20 mg/kg (body weight) per day found to be refractory in terms of therapeutic effect in a subject afflicted with autoimmune disease/autoimmune hepatitis/liver inflammation. In one embodiment, provided a method for treating a subject afflicted with steroid-refractory autoimmune disease/autoimmune hepatitis/liver inflammation, comprising administering to the subject: (a) a steroid; and (b) a cannabidiol (CBD) or a functional derivative thereof.

[099] In some embodiments, enhancing the therapeutic effect of a steroid is enhancing the therapeutic effect of a given or a fixed dose of a steroid. In some embodiments, enhancing the therapeutic effect of a steroid is enhancing steroid therapy which is reducing or gradually reducing (within a period of 3 days to 6 months) the administered dosage or dose of a steroid while maintain and/or improving/enhancing/maintaining: (a) the therapeutic effect of the reduced dose of a steroid; or (b) the efficacy of the steroid therapy. In some embodiments, enhancing the therapeutic effect of a steroid is rendering a refractory steroid therapy (treatment with a given steroid dose) - therapeutically effective and optionally further reducing or gradually reducing (within a period of 3 days to 6 months) the administered dosage or dose of a steroid (the dose or dosage found previously to be refractory) while continuously maintaining and/or improving/enhancing: (a) the therapeutic effect of the reduced dose of a steroid; or (b) the efficacy of the steroid therapy.

[0100] In some embodiments, enhancing the therapeutic effect of a given dose of a steroid or reducing the given dose of a steroid by maintain or improving the steroid's therapeutic effect can be a process wherein the steroid dose administered with CBD is gradually decreased over time. In some embodiments, enhancing the therapeutic effect of a given dose of a steroid or reducing the given dose of a steroid by maintain or improving the steroid's therapeutic effect can be a process wherein the steroid dose administered with CBD is gradually decreased over a period of 3 days to 6 months. In some embodiments,

enhancing the therapeutic effect of a given dose of a steroid or reducing the given dose of a steroid by maintain or improving the steroid's therapeutic effect can be a process wherein the steroid dose administered with CBD is gradually decreased over a period of 3 weeks to 3 months, over a period of 3 weeks to 2 months.

[0101] In some embodiments, the Cannabidiol or any functional derivative thereof according to the present invention is a natural product extracted and/or purified from *Cannabis sativa.* In other embodiments, the CBD or functional derivative thereof is a synthetic product. In still further embodiments, the CDB-containing composition is the Cannabis plant itself. Whenever reference is made herein to *"Cannabis sativa"* the same applies also to other Cannabis plants producing Cannabidiol, including *Cannabis indica* and *Cannabis ruderalis. Cannabis sativa* is referred to herein specifically, for the sake of brevity.

[0102] In some embodiments, the CBD, or a functional derivative thereof, is administered following onset of symptoms of inflammation, autoimmune disease/autoimmune hepatitis/liver inflammation as described herein. In other embodiments, the CBD, or a functional derivative thereof, is administered after a diagnosis is made of the form of autoimmune disease/autoimmune hepatitis/liver inflammation. In other embodiments, the CBD, or a functional derivative thereof, is administered with a steroid. In other embodiments, the CBD or a functional derivative thereof, is administered before and/or after a steroid. In one embodiment, inflammation is chronic inflammation and/or a chronic inflammatory disease. In one embodiment, a chronic inflammatory disease according to the invention, required steroidal treatment for at least a month. In one embodiment, a chronic inflammatory disease according to the invention, required steroidal treatment for at least 3 months. In one embodiment, a chronic inflammatory disease according to the invention, required steroidal treatment for at least 6 months.

[0103] Administration of the Cannabidiol or a functional derivative thereof compositions to a subject as described herein lasts for at least 20 days. Administration of the Cannabidiol or a functional derivative thereof compositions to a subject as described herein lasts for at least 30 days. Administration of the Cannabidiol or a functional derivative thereof compositions to a subject as described herein lasts for at least 40 days. Administration of the Cannabidiol or a functional derivative thereof compositions to a subject as described herein lasts for at least 50 days. Administration of the Cannabidiol or a functional derivative thereof compositions to a subject as described herein lasts for at least 60 days. Administration of the Cannabidiol or a functional derivative thereof compositions to a subject as described herein lasts for at least 70 days. Administration of the Cannabidiol or a functional derivative thereof compositions to a subject as described herein lasts for at least 80 days. Administration of the Cannabidiol or a functional derivative thereof compositions to a subject as described herein lasts for at least 90 days. Administration of the Cannabidiol or a functional derivative thereof compositions to a subject as described herein lasts for at least 100 days.

[0104] In some embodiments, the method of the invention may optionally further comprise the step of administering at least one additional therapeutic agent, including currently used drugs given to autoimmune disease/autoimmune hepatitis/liver inflammation patients. These additional therapeutic agents, specifically, any immunomodulatory agent or known medicament, may be either combined with Cannabidiol or may be administered separately in an additional separate step having an optional different mode of administration.

[0105] The pharmaceutical compositions containing Cannabidiol according to the present invention can be administered for prophylactic and/or therapeutic treatments. In therapeutic application, compositions are administered to a patient already suffering from

autoimmune disease/autoimmune hepatitis/liver inflammation in an amount sufficient to cure or at least partially arrest the condition and its complications. An amount adequate to accomplish this is defined as a "therapeutically effective dose." In prophylactic applications, compositions containing Cannabidiol are administered to a patient who is at risk of developing autoimmune disease/autoimmune hepatitis/liver inflammation. Such an amount is defined to be a "prophylactically effective dose". Amounts effective for both prophylactic and therapeutic purposes will depend upon the risk to develop autoimmune disease/autoimmune hepatitis/liver inflammation, the severity of autoimmune disease/autoimmune hepatitis/liver inflammation condition and the general state of the patient, but generally range from about 0.01 to about 10 mg/Kg body weight, specifically, about 0.5 to about 10 mg/Kg of Cannabidiol per day. Single or multiple administrations on a daily schedule can be carried out with dose levels being selected by the treating physician. It should be noted that doses of Cannabidiol can be elevated every day during the treatment period according to the clinical response of the patient, provided no significant drug related side effects present.

[0106] Additionally, the administration of Cannabidiol according to the invention, or pharmaceutical compositions comprising Cannabidiol, may be periodic, for example, the periodic administration may be effected twice daily, three times daily, or at least once daily for 2 days to 180 days, 90 to 180 days and 2 days to 12 months (or longer as needed) for the treatment of autoimmune disease/autoimmune hepatitis/liver inflammation following onset of symptoms or diagnosis.

[0107] In some embodiments, CBD is provided to a patient in once, twice, thrice or more doses per day. Specific embodiments of the invention relate to the use of typically two doses per day, each containing at least 10 mg Cannabidiol, but usually not more than a

daily dose of 600 mg. In one embodiment, a daily dose comprises 150 to 400 mg CBD administered in one or two dosages.

[0108] In some embodiments, the Cannabidiol compositions according to the present invention can be prepared in any type of oil, such as canola oil, olive oil, sunflower oil, soybean oil, corn oil, or paraffin oil.

[0109] In some embodiments, the administration of pharmaceutical compositions comprising Cannabidiol or any derivative thereof according to the invention for the prevention, treatment, amelioration of autoimmune disease/autoimmune hepatitis/liver inflammation, may be any one of oral, sublingual, buccal, rectal, vaginal, topical, parenteral, intravenous, intramuscular, subcutaneous, intra-peritoneal or via oral or nasal inhalation, such as in the form of purified vapors or by smoking of Cannabis.

[0110] Compositions and formulations for oral administration include powders or granules, suspensions or solutions in water or non-aqueous media, capsules, sachets, lozenges (including liquid-filled), chews, multi- and nano-particulates, gels, solid solution, liposome, films, ovules, sprays or tablets. Thickeners, flavoring agents, diluents, emulsifiers, dispersing aids or binders may be desirable.

[0111] Pharmaceutical compositions used to treat subjects in need thereof according to the invention, which may conveniently be presented in unit dosage form, may be prepared according to conventional techniques well known in the pharmaceutical industry. Such techniques include the step of bringing into association the active ingredients with the pharmaceutical carrier(s) or excipient(s). The compositions may be formulated into any of many possible dosage forms such as, but not limited to, tablets, capsules, liquid syrups, soft gels, suppositories, and enemas. The compositions of the present invention may also be formulated as suspensions in aqueous, non-aqueous or mixed media. The suspension

may also contain stabilizers. The pharmaceutical compositions of the present invention also include, but are not limited to, emulsions and liposome-containing formulations.

[0112] Addition to the ingredients particularly mentioned above, the formulations may also include other agents conventional in the art having regard to the type of formulation in question, for example those suitable for oral administration may include flavoring agents. Pharmaceutical formulations adapted for rectal administration may be presented as suppositories or enemas. Pharmaceutical formulations adapted for vaginal administration may be presented as pessaries, tampons, creams, gels, pastes, foams or spray formulations.

[0113] According to certain embodiments, pharmaceutical compositions comprising Cannabidiol, or any derivative thereof according to the present invention are also useful for parenteral administration, i.e., subcutaneously (s.c), intramuscularly (i.m.), and intravenously (i.v.). The compositions for parenteral administration commonly comprise a solution of Cannabidiol dissolved in an acceptable carrier.

[0114] In one embodiment, the compositions of the invention are suitable for oral administration. The Cannabidiol compositions can be administered from one or more times per day to one or more times per week, including once every other day. Dosing is dependent on the severity of the symptoms and on the responsiveness of the subject to the treatment. The skilled artisan will appreciate that certain factors may influence the dosage and timing required to effectively treat a subject, including but not limited to the severity of the disease, previous treatments, the general health and/or age of the subject, and other diseases present.

[0115] The present invention relates to the treatment of subjects, or patients, in need thereof. By "patient" or "subject in need" it is meant any mammal for which administration of the composition of the invention is desired, in order to prevent, overcome or slow down a medical condition. As described herein, the medical condition for treatment includes

autoimmune disease/autoimmune hepatitis/liver inflammation, or any of the conditions described herein that are associated with autoimmune disease/autoimmune hepatitis/liver inflammation.

[0116] The terms "treatment", "prevention" and "prophylaxis" refer to the complete range of therapeutically positive effects of administrating to a subject including inhibition, reduction of, alleviation of, and relief from, autoimmune disease/autoimmune hepatitis/liver inflammation. More specifically, treatment or prevention includes the prevention or postponement of development of the disease, prevention or postponement of development of symptoms and/or a reduction in the severity of such symptoms that will or are expected to develop. These further include ameliorating existing symptoms, preventing additional symptoms and ameliorating or preventing the underlying causes of symptoms.

[0117] To provide a "preventive treatment" or "prophylactic treatment" is acting in a protective manner, to defend against or prevent something, especially a condition or disease.

[0118] As used herein, "disease", "disorder", "condition" and the like, as they relate to a subject's health, are used interchangeably and have meanings ascribed to each and all of such terms.

[0119] The term "pharmaceutical composition" refers to an active compound in any form suitable for effective administration to a subject, *e.g.,* a mixture of the compound and at least one pharmaceutically acceptable carrier.

[0120] The term "therapeutically effective amount" is intended to mean that amount of a drug or pharmaceutical agent that will elicit the biological or medical response of a tissue or human that is being sought by a researcher, medical doctor, or other clinician, or by the subject himself.

[0121] As used herein, a "pharmaceutically acceptable carrier" means a carrier or diluent that does not cause significant irritation to a subject and does not abrogate the biological activity and properties of the administered compound.

[0122] A "pharmaceutically acceptable excipient" means an inert substance added to a pharmaceutical composition to further facilitate administration of the compound. Examples, without limitation, of excipients include calcium carbonate, calcium phosphate, various sugars and types of starch, cellulose derivatives, gelatin, vegetable oils and polyethylene glycols.

[0123] In one embodiment, a composition as described herein is formulated to a suitable route of administration, such as: topical, oral, rectal, transmucosal, transnasal, intestinal or parenteral delivery, including intramuscular, subcutaneous and intramedullary injections as well as intrathecal, direct intraventricular, intravenous, intraperitoneal, intranasal, or intraocular injections.

[0124] Oral administration of a composition as described herein, in one embodiment, comprises a unit dosage form comprising tablets, capsules, lozenges, chewable tablets, suspensions, emulsions and the like. Such unit dosage forms comprise a safe and effective amount of the desired compound, or compounds, each of which is in one embodiment, from about 0.7 mg to about 280 mg/70 kg, or in another embodiment, about 0.5 mg to about 210 mg/70 kg.

[0125] The pharmaceutically-acceptable carriers suitable for the preparation of unit dosage forms of a composition as described herein for peroral administration are well-known in the art. In some embodiments, tablets typically comprise conventional pharmaceutically-compatible adjuvants as inert diluents, such as calcium carbonate, sodium carbonate, mannitol, lactose and cellulose; binders such as starch, gelatin and sucrose; disintegrants such as starch, alginic acid and croscarmelose; lubricants such as

magnesium stearate, stearic acid and talc. In one embodiment, glidants such as silicon dioxide can be used to improve flow characteristics of the powder-mixture. In one embodiment, coloring agents, such as the FD&C dyes, can be added for appearance. Sweeteners and flavoring agents, such as aspartame, saccharin, menthol, peppermint, and fruit flavors, are useful adjuvants for chewable tablets. Capsules typically comprise one or more solid diluents. In some embodiments, the selection of carrier components depends on secondary considerations like taste, cost, and shelf stability, which are not critical for the purposes of this invention, and can be readily made by a person skilled in the art.

[0126] In one embodiment, the oral dosage form comprises predefined release profile. In one embodiment, the oral or topical dosage form of the present invention comprises a dosage form (composition) or dosage forms having different release profile for the compounds described herein.

[0127] Peroral compositions, in some embodiments, comprise liquid solutions, emulsions, suspensions, and the like. In some embodiments, pharmaceutically-acceptable carriers suitable for preparation of such compositions are well known in the art. In some embodiments, liquid oral compositions comprise from about 0.012% to about 0.933% w/w or w/v of the desired compound or compounds, or in another embodiment, from about 0.033% to about 0.7% w/v or w/w.

[0128] In some embodiments, compositions for use in the methods of this invention comprise solutions or emulsions, which in some embodiments are aqueous solutions or emulsions comprising a safe and effective amount of the compounds of the present invention and optionally, other compounds, intended for topical intranasal administration. In some embodiments, compositions comprise from about 0.01% to about 10.0% w/v or w/w of a subject compound. In some embodiments, compositions comprise from about

0.1% to about 2.0 w/w or w/v, which is used for systemic delivery of the compounds by the intranasal route.

[0129] In another embodiment, the pharmaceutical compositions are administered by intravenous, intra-arterial, or intramuscular injection of a liquid preparation. In some embodiments, liquid formulations include solutions, suspensions, dispersions, emulsions, oils and the like. In one embodiment, the pharmaceutical compositions are administered intravenously, and are thus formulated in a form suitable for intravenous administration. In another embodiment, the pharmaceutical compositions are administered intra-arterially, and are thus formulated in a form suitable for intra-arterial administration. In another embodiment, the pharmaceutical compositions are administered intramuscularly, and are thus formulated in a form suitable for intramuscular administration.

[0130] Further, in another embodiment, the pharmaceutical compositions are administered topically to body surfaces, and are thus formulated in a form suitable for topical administration. Suitable topical formulations include gels, ointments, creams, lotions, drops and the like. For topical administration, the compounds of the present invention are combined with an additional appropriate therapeutic agent or agents, prepared and applied as solutions, suspensions, or emulsions in a physiologically acceptable diluent with or without a pharmaceutical carrier.

[0131] In one embodiment, pharmaceutical compositions of the present invention are manufactured by processes well known in the art, e.g., by means of conventional mixing, dissolving, granulating, dragee-making, levigating, emulsifying, encapsulating, entrapping or lyophilizing processes.

[0132] In some embodiments, the compounds/ingredients described hereinabove are included in the pharmaceutical or cosmetic composition of the present invention at a concentration suitable for achieving an anti-inflammatory effect or skin disease

medication. In some embodiments, the pharmaceutical or cosmetic composition is buffered to a pH of 5.5-7.5 since. In another embodiment, a composition as described includes a dermatologically or topically acceptable carrier.

[0133] The phrase "dermatologically acceptable carrier", refers, in some embodiments, to a carrier which is suitable for topical application onto the skin, i.e., keratinous tissue, has good aesthetic properties, is compatible with the active agents of the present invention and any other components, and is safe and non-toxic for use in mammals. An effective amount of carrier is selected from a range of about 20% to about 99.99%, or from about 40% to about 99.9%, by weight, of the composition.

[0134] In another embodiment, a composition as described includes an emulsion carrier, including, but not limited to, oil-in-water, water-in-oil, water-in-oil-in-water, and oil-in-water-in-silicone emulsions, a cream, an ointment, an aqueous solution, a lotion or an aerosol.

[0135] In some embodiments, emulsions according to the present invention comprise a pharmaceutically effective amount of an agent disclosed herein and a lipid and/or an oil. Lipids and oils may be derived from animals, plants, or petroleum and may be natural or synthetic (i.e., man-made). In some embodiments, emulsions also comprise a humectant, such as but not limited to glycerin. In some embodiments, emulsions of the invention comprise from about 1% to about 10%, or from about 2% to about 5%, of an emulsifier, based on the weight of the carrier. Emulsifiers may be nonionic, anionic or cationic. Suitable emulsifiers are described in, for example, U.S. Pat. No. 3,755,560, issued to Dickert, et al. Aug. 28, 1973; U.S. Pat. No. 4,421,769, issued to Dixon, et al., Dec. 20, 1983; and McCutcheon's Detergents and Emulsifiers, North American Edition, pages 317-324 (1986). The term "about", in some embodiments, refers to +/- 10% of the recited value.

[0136] In some embodiments, the composition of the invention is a foam. In another embodiment, an emulsion comprises an anti-foaming agent to minimize foaming upon application to the keratinous tissue. In some embodiments, the composition of the invention comprises a water-in-silicone emulsion.

[0137] In some embodiments, a topical composition of the present invention comprises a surfactant. In some embodiments, a topical composition of the present invention comprises an anionic surfactant. In one embodiment, a composition as described herein comprises from about 0.05% to about 10% or from about 1% to about 6% or from about 1% to about 3% of at least one hydrophilic surfactant which can disperse the hydrophobic materials in the water phase (percentages by weight of the topical carrier). In some embodiments, surfactants include any of a wide variety of known cationic, anionic, zwitterionic, and amphoteric surfactants. See, McCutcheon's. Detergents and Emulsifiers, North American Edition (1986), published by Allured Publishing Corporation; U.S. Pat. No. 5,011,681 to Ciotti et al., issued Apr. 30, 1991; U.S. Pat. No. 4,421,769 to Dixon et al. issued to Dec. 20, 1983; and U.S. Pat. No. 3,755,560 all of which are hereby incorporated by reference in their entireties.

[0138] In some embodiments, a topical composition of the present invention comprises a cationic emulsifier such as but not limited to amino-amides. Nonlimiting examples of cationic emulsifiers include: stearamidopropyl PG-dimonium chloride phosphate, behenamidopropyl PG dimonium chloride, stearamidopropyl ethyldimonium ethosulfate, stearamidopropyl dimethyl (myristyl acetate) ammonium chloride, stearamidopropyl dimethyl cetearyl ammonium tosylate, stearamidopropyl dimethyl ammonium chloride, stearamidopropyl dimethyl ammonium lactate, and mixtures thereof.

[0139] In some embodiments, a topical composition of the present invention comprises from about 25% to about 98% or from about 65% to about 95% or from about 70% to

about 90% water by weight of the topical carrier. A pharmaceutical or a cosmetic composition of the present invention can be formulated in any of a variety of forms utilized by the pharmaceutical or cosmetic industry for skin application including solutions, lotions, sprays, creams, ointments, salves, gels, etc.

[0140] In one embodiment, pharmaceutical compositions for use in accordance with the present invention are formulated in conventional manner using one or more physiologically acceptable carriers comprising excipients and auxiliaries, which facilitate processing of the active ingredients into preparations which, can be used pharmaceutically. In one embodiment, formulation is dependent upon the route of administration chosen.

[0141] In one embodiment, injectables, of the invention are formulated in aqueous solutions. In one embodiment, injectables, of the invention are formulated in physiologically compatible buffers such as Hank's solution, Ringer's solution, or physiological salt buffer. In some embodiments, for transmucosal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art.

[0142] In one embodiment, the preparations described herein are formulated for parenteral administration, e.g., by bolus injection or continuous infusion. In some embodiments, formulations for injection are presented in unit dosage form, e.g., in ampoules or in multidose containers with optionally, an added preservative. In some embodiments, compositions are suspensions, solutions or emulsions in oily or aqueous vehicles, and contain formulatory agents such as suspending, stabilizing and/or dispersing agents.

[0143] The compositions also comprise, in some embodiments, preservatives, such as benzalkonium chloride and thimerosal and the like; chelating agents, such as edetate sodium and others; buffers such as phosphate, citrate and acetate; tonicity agents such as

sodium chloride, potassium chloride, glycerin, mannitol and others; antioxidants such as ascorbic acid, acetylcystine, sodium metabisulfote and others; aromatic agents; viscosity adjusters, such as polymers, including cellulose and derivatives thereof; and polyvinyl alcohol and acid and bases to adjust the pH of these aqueous compositions as needed. The compositions also comprise, in some embodiments, local anesthetics or other actives. The compositions can be used as sprays, mists, drops, and the like.

[0144] In some embodiments, pharmaceutical compositions for parenteral administration include aqueous solutions of the active preparation in water-soluble form. Additionally, suspensions of the active ingredients, in some embodiments, are prepared as appropriate oily or water based injection suspensions. Suitable lipophilic solvents or vehicles include, in some embodiments, fatty oils such as sesame oil, or synthetic fatty acid esters such as ethyl oleate, triglycerides or liposomes. Aqueous injection suspensions contain, in some embodiments, substances, which increase the viscosity of the suspension, such as sodium carboxymethyl cellulose, sorbitol or dextran. In another embodiment, the suspension also contain suitable stabilizers or agents which increase the solubility of the active ingredients to allow for the preparation of highly concentrated solutions.

[0145] In another embodiment, the active compounds can be delivered in a vesicle, in particular a liposome (see Langer, *Science* 249:1527-1533 (1990); Treat et al., in Liposomes in the Therapy of Infectious Disease and Cancer, Lopez- Berestein and Fidler (eds.), Liss, New York, pp. 353-365 (1989); Lopez-Berestein, ibid., pp. 317-327; see generally ibid).

[0146] In some embodiments, preparation of effective amount or dose can be estimated initially from in vitro assays. In one embodiment, a dose can be formulated in animal models and such information can be used to more accurately determine useful doses in humans.

[0147] In one embodiment, toxicity and therapeutic efficacy of the active ingredients described herein can be determined by standard pharmaceutical procedures *in vitro,* in cell cultures or experimental animals. In one embodiment, the data obtained from these *in vitro* and cell culture assays and animal studies can be used in formulating a range of dosage for use in human. In one embodiment, the dosages vary depending upon the dosage form employed and the route of administration utilized. In one embodiment, the exact formulation, route of administration and dosage can be chosen by the individual physician in view of the patient's condition. [See e.g., Fingl, et al., (1975) "The Pharmacological Basis of Therapeutics", Ch. 1p.1].

[0148] In one embodiment, depending on the severity and responsiveness of the condition to be treated, dosing can be of a single or a plurality of administrations, with course of treatment lasting from several days to several weeks or until cure is effected or diminution of the disease state is achieved.

[0149] In one embodiment, compositions of the present invention are presented in a pack or dispenser device, such as an FDA approved kit, which contain one or more unit dosage forms containing the active ingredient. In one embodiment, the pack, for example, comprise metal or plastic foil, such as a blister pack. In one embodiment, the pack or dispenser device is accompanied by instructions for administration. In one embodiment, the pack or dispenser is accommodated by a notice associated with the container in a form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals, which notice is reflective of approval by the agency of the form of the compositions or human or veterinary administration. Such notice, in one embodiment, is labeling approved by the U.S. Food and Drug Administration for prescription drugs or of an approved product insert.

EXAMPLES

Example 1: treating autoimmune Hepatitis with reduced steroid dose

[0150] Forty-one (41) patients over 18 years of age suffering from autoimmune Hepatitis with no signs of remission are recruited. Patients having history of psychosis or asthma, or consuming Cannabis during the last two months before the study are excluded from the study. 15 of the patients had Jaundice.

[0151] All patients are receiving standard treatment consisting of prednisolone in a daily dose of 40 to 60 mg/day.

[0152] On the first two weeks of trial all patients are receiving prednisolone monotherapy.

[0153] On the third week of trial all patients are receiving CBD (STI Pharmaceuticals, Brentwood, Essex, UK) dissolved in olive oil at a concentration of 2.5% and (oral) at a dose of 75 mg CBD twice a day together with prednisolone at a dose reduced by 30%.

[0154] On the fourth week of trial all patients are receiving CBD (STI Pharmaceuticals, Brentwood, Essex, UK) dissolved in olive oil at a concentration of 2.5% and (oral) at a dose of 100 mg CBD twice a day together with prednisolone at a dose reduced by 50% from the initial dose of 40 to 60 mg/day.

[0155] On the fifth week of trial all patients are receiving CBD (STI Pharmaceuticals, Brentwood, Essex, UK) dissolved in olive oil at a concentration of 2.5% and (oral) at a dose of 150 mg CBD twice a day together with prednisolone at a dose reduced by 65% from the initial dose of 40 to 60 mg/day.

[0156] During the first two weeks 75% of the patients are suffering from at least one prednisolone specific side effects.

[0157] During the third week 62% of the patients are suffering from at least one prednisolone specific side effects. During the fourth and the fifth weeks there is a steady decline in the number of patients suffering from at least one prednisolone specific side effects to 53% and 36%, respectively.

[0158] Importantly, no side effects due to the use of CBD are reported. On the fifth week sign of remission are appearing in 68% of the patients with normalization of aminotransferases and immunoglobulin G. These signs of remission are attributed to the steroids and not to CBD.

[0159] After total remission, the present dual CBD and low-dose steroid therapy is continued as maintenance therapy for 18 to 30 months.

[0160] These results are indicating that administration of Cannabidiol reduces the severity of steroids' side effects due to a substantial increase in the potency of a lower dose of steroid once administered with Cannabidiol. Unlike dual therapy with Azathioprine, CBD is not showing any side-effects within the current daily doses. This finding is utmost important as CBD-steroid treatment unlike azathioprine-steroid treatment is free of side effects such as: cholestatic hepatitis, pancreatitis, arthralgias, fever, vomiting, nausea, emesis, rash, opportunistic infection bone marrow suppression and malignancy which are attributed to the use of azathioprine.

[0161] Moreover, CBD unlike Azathioprine unexpectedly and dramatically reduces steroidal side effects.

Example 2: Cannabidiol (CBD)/steroid for treatment of severe UC

[0162] A 42 years old male with severe relapse of Ulcerative colitis (UC) is refractory to both high-dose of oral prednisone and intravenous hydrocortisone cyclosporine for 14 days.

[0163] The patient is immediately starting dual daily treatment of 70 mg prednisone and 250 mg oral CBD. After 6 days of dual CBD/prednisone therapy the patient is in complete cessation of diarrhea, abdominal pain and fever.

Example 3: Cannabidiol (CBD/steroid for treatment of erythroderma)

[0164] A 35 years old female with is afflicted with severe erythroderma, confirmed by skin biopsy. The patient is now 10 days refractory to twice daily Triamcinolone topical treatment and complains of severe skin blistering and burning.

[0165] The patient is immediately starting dual daily treatment of once daily topical Triamcinolone and 300 mg oral CBD. After 5 days of dual CBD/ Triamcinolone therapy the patient is relieved of any steroidal side effects with dramatic remission in erythroderma.

Example 4: Cannabidiol (CBD) renders a refractory high dose of steroids and tacrolimus -effective

[0166] 63 years old female with hepatitis developed jaundice with bilirubin level of 4.2 mg%. She started tacrolimus and high-dose steroids- prednisone, and had a partial response for a short period of time. Two months later, while still given tacrolimus and steroids she developed pancreatitis and had an upsurge in bilirubin to 8.5 mg%.

[0167] She started oral CBD 150 mg BID. Jaundice resolved gradually and bilirubin dropped to normal levels. Steroids could be tapered off by 50% to a low dose of 7.5 mg QD with no CBD and or steroidal side-effects.

Example 5: Cannabidiol (CBD) renders an ineffective dose of Dexamethasone - effective

[0168] 68 years old female with Rheumatoid Arthritis (RA) developed pericarditis with sudden flares of joint pain. She is immediately treated for 14 days with Dexamethasone (4 mg orally every 12 hours) with only slight improvement of joint pain and developed anemia.

[0169] She's is immediately prescribed with oral CBD 150 mg BID and the daily dexamethasone dose is decreased to 3 mg orally every 12 hours. After 10 days from the beginning of treatment the patient is relived of burning joint pain and no signs of anemia are apparent, Dexamethasone is further reduced to 2 mg orally every 12 hours. After 14 days from the beginning of treatment the patient is still relived of burning joint pain and walks more comfortably, Dexamethasone is further reduced to 1.5 mg orally every 12 hours.

Example 6: Cannabidiol (CBD) renders a refractory high dose of Prednisone - effective

[0170] A 58 years old male with refractory follicular lymphoma underwent an allogeneic hematopoietic cell transplantation. One month later he was admitted with severe late onset acute skin inflammation and upper (nausea and vomiting) plus lower gastrointestinal

involvement (bloody diarrhea, crampy abdominal pain and severely inflamed and ulcerated mucosa).

[0171] He started high-dose steroids (Prednisone). Despite skin response, GIT inflammation was refractory to prolonged systemic treatment of steroids.

[0172] He started oral CBD 150 mg BID, symptoms improved gradually and a very good partial response (VGPR) was attained to the steroids. Prednisone was tapered off to 20 mg QD (40%)- found to be therapeutically effective.

[0173] The present CBD treatments, unexpectedly, rendered a dangerously high dose or a refractory dose of a steroid-therapeutically effective with minimal to no steroid side effects.

CLAIMS

What is claimed is:

1. A method for enhancing the therapeutic effect of a steroid, reducing a daily dose of a steroid, or a combination thereof in a subject afflicted with inflammation, an immune disease or a combination thereof, comprising administering to said subject a cannabidiol (CBD) or a functional derivative thereof, thereby enhancing the therapeutic effect of a steroid, reducing a daily dose of a steroid, or a combination thereof in a subject afflicted with inflammation, an immune disease or a combination thereof.

2. A method for chronically administering a steroid to a subject in need thereof, comprising administering to said subject a cannabidiol (CBD) or a functional derivative thereof, thereby chronically administering a steroid to a subject in need thereof.

3. The method of any one of claims 1 and 2, further comprising diagnosing said subject as a subject afflicted with a steroid side-effect.

4. The method of any one of claims 1 and 2, further comprising diagnosing said subject as a subject afflicted with chronic inflammatory and/or immune disease.

5. The method of claim 1, wherein said immune disease is an autoimmune disease.

6. The method of any one of claims 1 and 3 to 5, wherein said enhancing the therapeutic effect of a steroid is rendering a refractory steroid dose a therapeutic effective dose.

7. The method of any one of claims 1 to 6, wherein said CBD or said functional derivative thereof is daily dose of 20 to 500 mg said CBD or said functional derivative thereof.

8. The method of any one of claims 1 and 3 to 7, wherein said CBD or a functional derivative thereof is substantially devoid of Tetrahydrocannabinol (THC).

9. The method of claim 2, wherein said autoimmune disease is autoimmune hepatitis.

10. A method for treating a subject afflicted with an autoimmune disease or liver inflammation, comprising administering to said subject a therapeutically effective amount of a composition comprising a cannabidiol (CBD) or a functional derivative thereof, thereby treating a subject afflicted with an autoimmune disease or liver inflammation.

11. The method of claim 10, further comprising diagnosing said subject as a subject afflicted with a steroid side-effect.

12. The method of any one of claims 10 and 11 wherein said subject is treated with a steroid and suffers from a steroid side-effect.

13. The method of claim 10, further comprising the step of administering to said subject a therapeutically effective amount of a composition comprising a steroid.

14. The method any one of claims 10 to 13, wherein said composition comprising a CBD or a functional derivative thereof is substantially devoid of Tetrahydrocannabinol (THC).

15. The method any one of claims 10 to 14, wherein said autoimmune disease is autoimmune hepatitis.

16. The method any one of claims 10 to 15, wherein said liver inflammation is Cirrhosis.

17. The method any one of claims 10 to 16, wherein said administering to said subject a therapeutically effective amount of a composition comprising said CBD or said functional derivative thereof is daily administering 20 to 500 mg said CBD or said functional derivative thereof.

18. A cannabidiol (CBD) or a functional derivative thereof for use in: enhancing the therapeutic effect of a steroid, reducing a daily dose of a steroid, or a combination thereof.

19. The CBD or a functional derivative thereof for use according to claim 18, wherein said enhancing the therapeutic effect of a steroid, reducing a daily dose of a steroid, or a combination thereof is in a subject afflicted with inflammation, an immune disease or a combination thereof.

20. A cannabidiol (CBD) or a functional derivative thereof for use in treating a subject chronically treated with a steroid.

21. The CBD or a functional derivative thereof for use according to claim 19, wherein said immune disease is an autoimmune disease.

22. The CBD or a functional derivative thereof for use according to any one of claims 18, 19 and 21, wherein said enhancing the therapeutic effect of a steroid is rendering a refractory steroid dose a therapeutic effective dose.

23. The CBD or a functional derivative thereof for use according to any one of claims 18 to 22, wherein said CBD or said functional derivative thereof is a daily dose of 20 to 500 mg said CBD or said functional derivative thereof.

24. The CBD or a functional derivative thereof for use according to any one of claims 18 to 23, wherein said CBD or a functional derivative thereof is substantially devoid of Tetrahydrocannabinol (THC).

25. The CBD or a functional derivative thereof for use according to claim 21, wherein said autoimmune disease is autoimmune hepatitis.

26. A cannabidiol (CBD) or a functional derivative thereof for use in treating an autoimmune disease or liver inflammation.

27. The CBD or a functional derivative thereof for use according to claim 26, wherein said treating an autoimmune disease or liver inflammation is treating a subject afflicted: (a) with a steroid side effect; and (b) an autoimmune disease or a liver inflammation.

28. The CBD or a functional derivative thereof for use according to any one of claims 26 and 27, substantially devoid of Tetrahydrocannabinol (THC).

29. The CBD or a functional derivative thereof for use according to any one of claims 27 and 28, wherein said autoimmune disease is autoimmune hepatitis.

30. The CBD or a functional derivative thereof for use according to any one of claims 27 to 29, wherein said liver inflammation is Cirrhosis.

31. The CBD or a functional derivative thereof for use according to any one of claims 26 to 30, wherein said CBD or said functional derivative thereof is a daily dose of 20 to 500 mg said CBD or said functional derivative thereof.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL2017/050483

A. CLASSIFICATION OF SUBJECT MATTER
IPC (2017.01) A61K 31/56, A61K 31/352, A61K 31/573

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC (2017.01) A61K 31/56, A61K 31/352, A61K 31/573

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, **where** practicable, search terms used)
See extra sheet.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2011195096 A1 (Dekel Pharmaceuticals LTD [IL]; Kindler Seth [IL]; Shmulewitz Ascher PL]); 11 Aug 2011 (2011/08/11) abstract, paragraph 0039, 0054-0055, 0144	1-4,6,18-20,22
Y	abstract, paragraph 0039, 0054-0055, 0144	1-31
X	US 2009005461 A1 (University of South Carolina [US]; Nagarkatt Prakash S [US]); 01 Jan 2009 (2009/01/01) claims 1, 3, 8, paragraphs 0006, 0008-0009	10, 14, 15,17,26,28, 29,31
Y	claims 1, 3, 8, paragraphs 0006, 0008-0009	9,10, 14, 15,25,26,28, 29
X	US 6274635 B1 (Immugen Pharmaceuticals INC [US]; Travis Craig A [US]); 14 Aug 2001 (2001/08/14) column 3 line 42, column 21 line 20, column 20 line 12	2,4,5,7,10,13,17,20, 21,23,26,31
Y	column 3 line 42, column 21 line 20, column 20 line 12	1-31

☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the International search	Date of mailing of the international search report
03 Aug 2017	03 Aug 2017
Name and mailing address of the ISA: Israel Patent Office Technology Park, Bldg.5, Malcha, Jerusalem, 9695101, Israel Facsimile No. 972-2-5651616	Authorized officer SHAPIRA Elena Telephone No. 972-2-5657823

B. FIELDS SEARCHED:

* Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Databases consulted: BLAST, Esp@cenet, Google Patents, CAPLUS, BIOSIS, EMBASE, MEDLINE, MARPAT, Google Scholar, DWPI, Derwent Innovation

Search terms used: CBD, 24(6R)-3-Methyl-6-prop-l-en-2-yl-lcyclohex-2-envyl]-5pentylbenzene-l,3-diol, Cannabidiol, -)-7-hydroxy-CBD, (-)-CBD-7-oic acid, steroid, corticosteroid, glucocorticoid,Prednisolone, Prednisone, dexamethasone, triamcinolone,Hepatitis, liver inflammation, autoimmune disease, inflammatory

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IL2017/050483

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