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(54) Title: CELLULOSE ACETATE 1,2-BENZENEDICARBOXYLATE COSMECEUTICAL

(57) Abstract: A pharmaceutical composition for topical administration to a human comprising 10 to 20 weight % of micronized cellulose acetate 1, 2-benzenedicarboxylate, 10 to 15 weight % polyethylene-polypropylene glycol, 2 to 3 weight % hydroxypropyl-methyl cellulose and the balance being water. The composition is useful to treat acne, blackheads, skin inflammation, eczema, insect bites, psoriasis, shingles, dermatitis, diaper rash, hives, pityriasis rosea, ringworm, athlete's foot, jock itch, rosacea and sunburn.

# CELLULOSE ACETATE 1,2-BENZENEDICARBOXYLATE COSMECEUTICAL

## Cross-Reference to Related Application

This application claims the benefit of priority under 35 USC 119(e) for provisional application Serial No. 60/904,233 filed March 1, 2007, the entire contents of which are incorporated by reference herein.

## Background of the Invention

### Field of the Invention

The present invention concerns compositions and methods for treating topical inflammatory conditions, including several skin conditions, such as acne, blackheads, skin inflammation, eczema, insect bits, psoriasis, shingles, dermatitis, diaper rash, hives, pityriasis rosea, ringworm, athlete's foot, jock itch, rosacea and sunburn, and for the promotion of clear skin.

### The State of the Art

Acne (such as acne vulgaris) is the most common pustular condition of the skin, disfiguring afflicted persons with inflammatory and noninflammatory lesions (including pustules, papules and comedones) during the active phase, and with atrophic scars afterwards. It occurs most commonly in teenagers, but is not confined to adolescents, as increasing numbers of people over 20 years of age are seeking advice on treatment for acne. Although acne is generally considered to be self-limiting, its social effects can be substantial, and it may have its most severe effects on the psyche. In about 60% of teenagers, disease severity and embarrassment are sufficient for them to self-medicate with proprietary preparations and/or seek medical advice.

Acne is a multifactorial disease affecting the pilosebaceous units of the skin. Each unit consists of a large, multilobed sebaceous gland, a rudimentary hair and a wide follicular canal lined with stratefied squamous epithelium. They are found over most of the body surface, but

are largest and most numerous on the face, chest, and upper back. Normally, desquamated follicular cells are carried to the surface by the flow of sebum. Under the abnormal circumstances of acne vulgaris, an abnormal desquamination process provokes increased sloughing of the epithelium, which becomes more cohesive because of defective keratinization. This process causes blockage of the follicular orifice with accumulation of dead cells. Androgen stimulates the undifferentiated hormonally responsive cells making up the outer layer of the sebaceous gland lobule to divide and differentiate. Sebum production favors proliferation of the anaerobe *Propionibacterium acnes*, which is a normal commensal to the pilosebaceous unit, which can elicit hypersensitivity responses in acne.

The basic lesion of acne is the microcomedo. Accumulation of sebum and keratinous debris results in a visible closed comedo, or whitehead, and its continued distension causes an open comedo, or blackhead. The dark color of blackheads is due to oxidized melanin. Blackheads and microcysts are noninflammatory lesions of acne, but some comedones evolve into inflammatory papules, pustules, or nodules, and can become chronic granulomatous lesions. The initial inflammatory cell in an acute acne papule is the CD4+T lumphocyte. Duct rupture is not a prerequisite for inflammation, which is due to the release of pro-inflammatory substances from the duct. When inflammation develops, neutrophil chemotaxis occurs. These neutrophils secrete hydrolytic enzymes that cause further damage and increased permeability of the follicular wall. In pustules, neutrophils are present much earlier. More persistent lesions exhibit granulomatous histology that can lead to scarring.

The aims of treating acne are to minimize the number and severity of lesions, prevent scarring, limit disease duration,

and reduce the social and psychological stress that affects many patients, particularly teenagers. Conventional treatment is directed to correcting the following three major factors that seem to cause acne: (1) androgenic stimulation of the sebaceous glands and increased sebum production; (2) abnormal keratinization and impaction in the pilosebaceous canal causing obstruction to sebum flow; and (3) proliferation of *P. acnes*. Thus, topical agents that remove comedones, such as topical retinoids are particularly effective because they normalize desquamination within the follicular orifice, which allows the sebum to flow freely onto the surface of the skin. Adalpalene, tretinoin, and tazarotene have been shown to have efficacy in treating mild to moderate acne, but all three have reported to have skin-irritating side effects including erythema, pruritis, burning/stinging, and scaling/flaking (Physicians' Desk Reference®, 56th ed., 2002, p. 2523). The side effects of retinoid use are so extreme that many individuals cannot tolerate topical application of these agents at all.

Isotretinoin ("ACCUTANE") is a powerful drug in the treatment of acne, but is known to cause significant side effects, such as liver damage, birth defects, chapped lips, dry skin, irritation of the eyes, joint and muscle pain, rash, intestinal symptoms, urinary symptoms, headache, increased sensitivity to sunburn, decreased night vision, increase in the level of blood fats and depression.

Salicylic acid and benzoyl peroxide have been used to treat acne for some time. Both agents dry the skin, which helps in acne management, but they cause some skin irritation in perilesional skin areas of acne patients, especially patients with sensitive skin, and in some cases the erythema is extreme. Moreover, it has been recently reported that benzoyl peroxide seems to induce free radical production that

can produce skin changes that qualitatively resemble ultraviolet B damage, e.g., increases in epidermal thickness, and deleterious changes in elastin and glycosaminoglycan content. Topical and oral antibiotics (especially tetracycline, erythromycin, and clindamycin) are sometimes prescribed for patients with inflammatory papules and pustules. However, in addition to the undesirability of antibiotic overuse in general, which can lead to enhanced susceptibility to infection, disadvantages to such treatments include phototoxicity and interactions with other medications.

Other factors that play a role in exacerbating acne, including oil-based cosmetics and some drugs (e.g., androgenic hormones, high progestin birth control pills, systemic corticosteroids, and iodide- and bromide-containing agents) are often minimized during acne treatment.

Treatments for acne are disclosed in USP 7,125,882 to Perricone, USP 7,129,275 to Lee et al. and USP 7,018,396 to Sierra et al.

Eczema is a form of dermatitis, or inflammation of the upper layers of the skin. The term eczema is broadly applied to a range of persistent or recurring skin rashes characterized by redness, skin edema, itching and dryness, with possible crusting, flaking, blistering, cracking, oozing or bleeding. Areas of temporary skin discoloration sometimes characterize healed lesions, though scarring is rare.

The term eczema refers to a set of clinical characteristics. Classification of the underlying diseases has been haphazard and unsystematic, with many synonyms used to describe the same condition. A type of eczema may be described by location (e.g., hand eczema), by specific appearance (eczema craquele or discoid), or by possible cause

(varicose eczema). Further adding to the confusion, many sources use the term eczema and the term for the most common type of eczema (atopic eczema) interchangeably.

More common eczemas include the following:

Atopic eczema is believed to have a hereditary component, and often runs in families whose members also have hay fever and asthma. An itchy rash is particularly noticeable on the face, scalp, neck, inside of elbows, behind knees, and buttocks. Experts are urging doctors to be more vigilant in weeding out cases that are in actuality irritant contact dermatitis. It is very common in developed countries, and rising.

Contact dermatitis is of two types: allergic (resulting from a delayed reaction to some allergen, such as poison ivy or nickel), and irritant (resulting from direct reaction to, say, a solvent). Some substances act both as an allergen and an irritant (e.g., wet cement). Other substances cause a problem after sunlight exposure, bringing on phototoxic dermatitis. About three quarters of cases of contact eczema are of the irritant type, which is the most common occupational skin disease. Contact eczema may be curable provided the offending substance can be avoided, and its traces removed from one's environment.

Xerotic eczema is dry skin that becomes so serious it turns into eczema. It worsens in dry winter weather, and the limbs and trunk are most often affected. The itchy, tender skin resembles a dry, cracked, river bed. This disorder is very common among the older population. Itchthyosis is a related disorder.

Seborrhoeic dermatitis causes dry or greasy scaling of the scalp and eyebrows. Scaly pimples and red patches sometimes appear in various adjacent places. In newborns, it causes a thick, yellow crusty scalp rash called cradle cap, which seems related to lack of biotin, and is often curable.

Less common eczemas include the following:

Dyshidrosis occurs only on palms, soles and sides of fingers and toes. Tiny opaque bumps called vesicles, thickening, and cracks are accompanied by itching which gets worse at night. A common type of hand eczema, it worsens in warm weather.

Discoid eczema is characterized by round spots of oozing or dry rash, with clear boundaries, often on the lower legs. It is usually worse in winter. The cause is unknown, and the condition tends to come and go.

Venous eczema occurs in people with impaired circulation, varicose veins and edema, and is particularly common in the ankle area of people over 50. This is a redness, scaling, darkening of the skin and itching. The disorder predisposes to leg ulcers.

Dermatitis herpetiformis (Duhring's disease) causes intensely itchy and typically symmetrical rash on the arms, thighs, knees and back. It is directly related to celiac disease, and can often be put into remission with appropriate diet.

Neurodermatitis is an itchy area of thickened, pigmented eczema patch that results from habitual rubbing and scratching. Usually there is only one spot. It is often curable through behavior modification and anti-inflammatory

medication. Prurigo nodularis is a related disorder showing multiple lumps.

Heretofore, the treatment of eczema involved the use of emollients, corticosteroids (which can cause the skin to thin and become fragile or cause bone demineralization (osteoporosis)), immunomodulators (pimecrolimus) and tacrolimus (which may cause lymph node or skin cancer) and antibiotics.

Psoriasis is an immune-mediated disease which affects the skin and joints. It commonly causes red scaly patches to appear on the skin. The scaly patches caused by psoriasis, called psoriatic plaques or lesions, are areas of excessive skin production and inflammation. Skin rapidly accumulates at these sites and takes a silvery-white appearance. Plaques frequently occur on the skin of the elbows and knees, but can affect any area including the scalp or genitals.

Types of psoriasis include the following:

Plaque psoriasis (psoriasis vulgaris) is the most common form of psoriasis. It affects 80 to 90% of people with psoriasis. Plaque psoriasis typically appears as raised areas of inflamed skin covered with silvery white scaly skin. These areas are called plaques.

Flexural psoriasis (inverse psoriasis) appears as smooth inflamed patches of skin. It occurs in skin folds, particularly around the genitals, the armpits, and under the breasts. It is aggravated by friction and sweat and is vulnerable to fungal infections.

Guttate psoriasis is characterized by numerous small oval (teardrop-shaped) spots. These numerous spots of psoriasis

appear over large areas of the body, such as the trunk, limbs and scalp. Guttate psoriasis is associated with streptococcal throat infection.

Pustular psoriasis appears as raised bumps that are filled with non-infectious pus (pustules). The skin under and surrounding pustules is red and tender. Pustular psoriasis can be localized, commonly to the hands and feet (palmoplantar pustulosis), or generalized with widespread patches occurring randomly on any part of the body.

Erythrodermic psoriasis involves the widespread inflammation and exfoliation of the skin over most of the body surface. It may be accompanied by severe itching, swelling and pain. It is often the result of an exacerbation of unstable plaque psoriasis, particularly following the abrupt withdrawal of systemic treatment. This form of psoriasis can be fatal, as the extreme inflammation and exfoliation disrupt the body's ability to regulate temperature and for the skin to perform barrier functions.

Ointment and creams containing coal tar, dithranol (anthralin), corticosteroids, vitamin $D_3$ analogues (for example, calcipotroil), and retinoids have been routinely used to treat psoriasis. Such creams often result in irritation of normal skin.

Psoriasis which is resistant to topical and phototherapy is treated by medications that are taken internally by pill or injection. This is called systemic treatment. Patients undergoing systemic treatment are required to have regular blood and liver function tests because of the toxicity of the medication.

Herpes zoster, colloquially known as shingles, is the reactivation of varicella zoster virus (one of the *Herpesviridae* group), leading to a crop of painful blisters over the area of a dermatome.

The treatment of shingles is generally with antiviral drugs such as aciclovir (Zovirax), famciclovir (Famvir) or valaciclovir (Valtrex). For the antiviral drugs to be effective, patients typically need to begin taking them within 2 to 3 days of the appearance of the rash.

Pityriasis rosea is a skin disease marked by patches of pink, oval rash. Pityriasis rosea can affect members of either sex or any age. However it is most common in females and those between the ages of 8 and 35.

Ultraviolet light treatment or phototherapy may shorten the duration of the condition and may be prescribed for extensive and persistent cases of pityriasis. Corticosteroid creams may also be prescribed to relieve the itching associated with pityriasis rosea.

Athlete's foot, jock itch and ringworm are tinea infections. Tinea is a fungus that can grow on the skin, hair or nails. As it grows, it spreads out in a circle, leaving normal-looking skin in the middle. This makes it look like a ring. At the edge of the ring, the skin is lifted up by the irritation and looks red and scaly. These infections are usually treated with anti-fungal creams, sprays or ointments.

Rosacea is a common chronic skin condition characterized by a spectrum of clinical indications including flushing episodes, erythema, telangiectasia, inflammatory papulopustular eruptions resembling acne, and ocular symptoms. Although accurate incidence data for the United States are not

available, data obtained in Sweden suggest that some form of rosacea may be present in up to 10% of the average population. Sufferers are mostly of European origin, generally with fair skin and blue eyes. Women are more prone to develop rosacea than men, with flushing episodes and erythema being the most common symptoms found.

The etiology of rosacea is unknown, but it is presumed to be a genetically determined anamalous vascular response that develops in the third to sixth decades of life. The hypothesis that the basis pathogenesis of the disease is a flushing disorder is based on several findings. The disease appears to be more prevalent in northern climates where cold exposure is experienced more often, and in light-skinned persons in whom flushing is common and sensitivity to sunlight is particularly high. Accordingly, rosacea may represent a type of hypersensitivity reaction disease in which vascular sensitivity is a central mechanism in its etiology. The correlation between sensitive blood vessels and sensitive skin has, however, not yet been determined. Epidemiological studies suggest that the regulatory mechanism of blood vessels may be of importance in the onset and development of rosacea. Studies show that 27% of rosacea patients were found to suffer from migraine and 42% from a tendency to flush, both of which represent about twice the level that would typically be found in a control group.

An etiological role has also been proposed for the Demodex species, mites that normally inhabit human hair follicles and are reported to appear in a greater number of rosacea patients. A number of dietary factors, for example, hot drinks, alcohol, spicy foods and environmental conditions (e.g., temperature changes), are well-recognized triggers of the disease. In literature, there are also reports of possible involvement of altered immune function and

anomalously low skin surface lipids in the pathogenesis of rosacea.

The key to successful management of rosacea is early diagnosis and treatment. Treatment is generally aimed at controlling the symptoms and making the skin look better. At the present time, rosacea cannot be cured, though the frequency of its flare-ups may be diminished and their severity alleviated. Most cases of rosacea can be controlled with anti-inflammatory medications, combined with the avoidance of lifestyle and environmental factors that may aggravate the disorder in individual cases. Treatment generally works best at improving the pimples and bumps of rosacea; the redness of the skin is harder to treat. Therapeutic agents for inflammatory rosacea conditions are generally classified in the following two groups: (1) systemic and topical antibiotics; and (2) retinoids. Systemic and topical antibiotics include tetracycline, metronidazole, erythromycin, minocycline and clindamycin, but the use of these agents is often accompanied by drug side effects, the development of resistance, and changes in the normal microbial flora. Retinoids include tretinoin (vitamin A or retinoic acid), which is applied topically to inhibit follicular keratinization, and isotretinoin (13-cis-retinoic acid) ("ACCUTANE"), which is administered systemically to suppress activity of the sebaceous glands. Retinoids are often irritants and are not advised for individuals with sensitive skin. Retinoids can also be phototoxic and they can induce thin and easily bruisable, fragile skin.

Metronidazole (5-methyl-5-nitromidazole-1-ethanol), an antibacterial, is currently one of the more frequently prescribed treatments for rosacea in the United States. It is available as a topical cream under the name Metrogel™ from Galderma. Metronidazole is structurally similar to some

materials which are believed to be carcinogens and is, in fact, listed by the U.S. Environmental Protection Agency as reasonably anticipated to be a human carcinogen. See the Merck Index, 1996, page 1051.

Treatment for rosacea is disclosed in USP 6,723,755 to Chomczynski and USP 7,078,048 to Kang et al.

It would be desirable to treat and prevent acne vulgaris manifested by the symptoms of pustule, papule, and comedone formation described above, minimizing the number and severity of lesions. It would also be desirable to provide a homogeneous skin complexion, while simultaneously reducing pore size, evening out skin texture, minimizing scar formation, treating acneform scars left after resolution of the active phase, promoting clear and firm skin tone, and providing a healthier look. It would also be desirable to have topical compositions that are effective in ameliorating skin irritation caused by conventional acne formulations so that more efficacious therapies can be devised for individual patients based on their different medical needs.

There is a need for an effective topical treatment for treating the skin conditions discussed hereinabove, especially by applying a safe substance, such as micronized cellulose acetate phthalate (cellulose acetate 1,2-benzenedicarboxylate or "CAP").

United States patent application Serial No. 11/494,722 filed July 27, 2006 discloses a method for treating topical inflammatory conditions, such as eczema, psoriasis, acne, shingles and insect bites, comprising topically administering a composition comprising micronized hydroxypropyl methylcellulose acetate succinate.

R.N. Fichorova, F. Zhou, V. Ratnam, V. Atanasiova, S. Jiang, N. Strick and A.R. Neurath, Antimicrobial Agent and Chemotherapy, Jan. 2005, Vol. 29, No. 1, pp. 323-335 disclose anti-HIV-1 microbicide cellulose acetate 1,2-benzendicarboxylate ("CAP") in a human *in vitro* model of vaginal inflammation. Fichorova et al. employ soluble CAP, but not micronized CAP.

The soluble CAP in the Fichorova et al. publication is not very stable and, when it is refrigerated, it is stable for only a month. The substance described in the Fichorova et al. publication has a maximum of only 3 weight % CAP.

Cellulose acetate phthalate has heretofore been disclosed for a method for decreasing the frequency of transmission of viral infections (USP 5,985,313); decreasing the frequency of transmission of human cytomegalovirus, human immunodeficiency virus or herpesvirus, or preventing the transmission or for treating a sexually transmitted bacterial infection (USP 6,165,493); and treating or preventing bacterial vaginosis (USP 6,462,030).

USP 6,572,875 and USP 6,596,297 disclose a biodegradable microbicidal vaginal barrier device comprising micronized cellulose acetate phthalate.

US 2005/0070501 discloses a water dispersible film comprising cellulose acetate phthalate for preventing HIV infection, treating bacterial vaginosis or preventing a non-viral sexually transmitted disease such as *Chlamydia trachomatis, Neisseria gonnorrhoeae, Haemophilus ducreyi* and *Trepunema pallidum*.

Summary of the Invention

It is an object of the present invention to provide safe and effective compositions and methods for the treatment of topical inflammatory conditions, including various skin conditions, such as acne, blackheads, skin inflammation, eczema, insect bites, psoriasis, shingles, dermatitis, diaper rash, hives, pityriasis rosea, ringworm, athlete's foot, jock itch, rosacea and sunburn.

It is a corresponding objective to alleviate the negative social and psychological impacts frequently suffered by persons afflicted with skin conditions, such as acne. Facial lesions and scars are one of the strongest forces driving the cosmetic industry. It would be desirable to have new and improved methods for treating acne, as it is so widely observed in the population, particularly among teenagers who are especially sensitive about their appearance and embarrassed with acne lesions and their disfiguring scars.

These objectives and advantages, as well as other objectives and advantages, are satisfied by the present invention.

In one aspect of the invention, there is provided a pharmaceutical composition for topical administration to a human, which includes micronized cellulose acetate 1,2-benzenedicarboxylate in a water suspension. The composition containing 10 to 20 weight % cellulose acetate 1,2-benzenedicarboxylate, 10 to 15 weight % polyethylene-polypropylene glycol and 2 to 3 weight % hydroxypropylmethyl cellulose, with the remainder being water.

In another aspect of the invention, there is provided a method for treating a topical inflammatory condition by

topically administering to a human in need thereof a pharmaceutically effective amount of the aforesaid composition, which includes micronized cellulose acetate 1,2-benzenedicarboxylate in a water suspension.

In a further aspect of the invention, there is provided a method for treating acne, blackheads, eczema, insect bites, psoriasis, shingles, dermatitis, diaper rash, hives, pityriasis rosea, ringworm, athlete's foot, jock itch, ringworm, rosacea and sunburn by topically administering to a human in need thereof a pharmaceutically effective amount of the aforesaid composition, which includes micronized cellulose acetate 1,2-benzenedicarboxylate in a water suspension.

In still another aspect of the invention, there is provided a method for producing micronized cellulose acetate 1,2-benzenedicarboxylate suspension involving the following steps:

(a) mixing cellulose acetate 1,2-benzenedicarboxylate and polyethylene-polypropylene glycol ("POLOXAMER 188") in at least one pharmacologically acceptable organic solvent which is capable of dissolving the cellulose acetate 1,2-benzenedicarboxylate and the polyethylene-polypropylene glycol to form a first solution,

(b) mixing in water, hydroxypropylmethyl cellulose ("HPMC") and polyethylene-polypropylene glycol to form a second solution,

(c) mixing the second solution into the first solution while stirring to form a third solution,

(d) adding water to the third solution while mixing to form a fourth solution,

(e) centrifuging the fourth solution and discarding the resultant supernatant to form a fifth solution,

(f) resuspending the fifth solution in water containing hydroxypropylmethyl cellulose to form a sixth solution,

(g) centrifuging the sixth solution and discarding the resultant supernatant to form a seventh solution, and

(h) resuspending the seventh solution in water containing hydroxypropylmethyl cellulose.

Detailed Description of the Invention

The present invention is based on the discovery of a composition including micronized cellulose acetate 1,2-benzenedicarboxylate in a water suspension (such as "AQUACOAT", FMC BioPolymer, Philadelphia, PA, USA), is a remarkable promoter of skin health. Without wishing to be bound by any particular theory of operability, it is considered that such composition has the ability to control skin inflammation caused by some internal bodily function by interacting with the surface of the skin.

The composition of the invention comprises:

(a) 10 to 20 weight % micronized cellulose acetate 1,2-benzenedicarboxylate,

(b) 10 to 15 weight % polyethylene-polypropylene glycol ("POLOXAMER 188"),

(c) 2 to 3 weight % hydroxypropylmethyl cellulose (3,800 to 4,500 cps), and

(d) with the balance being water (such as distilled water).

Preferably the composition comprises:

(a) 15 to 18 weight % cellulose acetate 1,2-benzenedicarboxylate,

(b) 10 to 12 weight % polyethylene-polypropylene glycol,

(c) 8 to 12 weight % glycerol,

(d) 2 to 2.5 weight % hydroxypropylmethyl cellulose (4,000 to 4,200 cps),

(e) 0.05 to 0.3 weight % of one or more preservatives, and

(f) with the balance being water.

Non-limiting examples of preservatives that can be used in the aforesaid composition include ascorbic acid, methyl paraben, ethylparaben, propylparaben, benzoic acid, sorbic acid, sodium benzoate, and potassium sorbate. The total amount of preservatives ranges from 0.05 to 0.3 weight %, preferably 0.1 to 0.3 weight %.

The topical compositions of the present invention can comprise additional ingredients found in skin care compositions, such as tinting (coloring) agents, fragrances and antioxidants, such as vitamin C or vitamin C derivatives, such as fatty acid esters of ascorbic acid, such as ascorbyl palmitate, butylated hydroxyanisole (BHA) and propyl gallate.

The cellulose acetate 1,2-benzenedicarboxylate in the composition is micronized so as to be less than 10 microns in size, and preferably approximately 1 micron in size (i.e., slightly larger than the size of bacteria). Thus, the cellulose acetate 1,2-benzenedicarboxylate is micronized to a size of 1 to 10 microns.

The pH of the topical composition (suspension) is approximately 2.5 to 3.

The topical composition has no known toxicity problems and has a mild odor, which lasts only for a short time. Such odor can be reduced or eliminated by the use of a fragrance.

To make the topical composition appear less white, a colorant or glycerine can be added.

The topical composition of the present invention serves to treat topical inflammatory conditions, such as the following skin conditions: acne, blackheads, eczema, insect bites, psoriasis, shingles, dermatitis, diaper rash, hives, pityriasis rosea, ringworm, athlete's foot, jock itch, rosacea and sunburn. The composition (cream) serves to smooth and even the complexion.

The following non-limiting examples of acne can be treated by the composition of the present invention: acne aggregata, bromide acne, common acne, congoblate acne, acne cosmetica, acne dtergicans, acne ephbica, acne fulminans, acne furunculoid, halogen acne, acne indurate, acne keloid, mechanical acne, acne medicamentosa, acne necrotica miliaris, acne neonatorum, acne oil, acne papulosa, pomade acne, premenstrual acne, acne rosacea, acne sycosiformis, tropical acne, acne venenata and acne vulgaris.

Non-limiting examples of dermatitis that can be treated by the topical composition of the present invention include atopic dermatitis, contact dermatitis, pemphigus dermatitis, seborrhic dermatitis, dermatitis herpetiformis and neurodermatitis.

Non-limiting examples of eczema that can be treated by the topical composition of the present invention include atopic eczema, xerotic eczema, dyshidrosis, discoid eczema and venous eczema.

Non-limiting examples of psoriasis that can be treated by the topical composition of the present invention include plaque psoriasis, flexural psoriasis, guttate psoriasis, pustular psoriasis and erythrodermic psoriasis.

Depending on the age of the patient, the symptoms and skin conditions, the topical composition according to the invention is applied in a pharmaceutically effective amount, for example, in an amount of 0.5 to 5 $mg/cm^2$.

Generally in the practice of the methods of the invention, the composition of the present invention is topically applied to the affected skin areas as needed, or at predetermined intervals. It is generally the case that improvement is noted with each successive application. The topical composition of the present invention is well-tolerated by the skin.

Insofar as has been determined to date, no adverse side-effects have been encountered with respect to the use of the topical composition of the present invention. It is an advantage of the present invention that the topical composition of this invention does not require a pharmaceutical prescription.

The use of the topical composition of the present invention on the face results in a clearer, smoother appearing complexion and a healthier look.

In step (a) of the method for producing a micronized cellulose acetate 1,2-benzenedicarboxylate suspension as discussed hereinabove, non-limiting examples of the at least one pharmacologically acceptable solvent include dimethylsulfoxide or a combination of ethyl acetate and ethanol. If a combination of ethyl acetate and ethanol are used, the ethyl acetate is preferably in an amount of 90 to 95 vol% and the ethanol is preferably in an amount of 5 to 10 vol%.

Examples

The following examples are presented to further illustrate and explain the present invention and should not be taken as limiting the invention in any regard.

Example 1: Preparation of Micronized Cellulose Acetate 1,2-Benzenecarboxylate ("CAP")

Mix in water, 10 wt% cellulose acetate 1,2-benzenecarboxylate and 1 wt% POLOXAMER 188 (Spectrum Chemicals) in 95 vol% ethyl acetate and 5 vol% ethanol to form a solution.

To 1 gram of the resultant solution, add 5 ml dropwise with vigorous vortexing of a second solution comprising 1 wt% HPMC (4,000 cps) and 1 wt% POLOXAMER 188 in water. Then add 5 ml water dropwise with vortexing.

Spin down (centrifuge) for 30 minutes at 5000 x g. Remove supernatant and resuspend in 10 ml of 0.1 wt% HPMC (4,000 cps) in water (wash step). Spin down (centrifuge) a second time and repeat the wash step.

This produces CAP having a purity of 99% in a water solution.

Example 2: Formulation of the Composition

Mix the following substances until homogeneous:
"AQUACOAT" (60 wt%)
glycerol (10 wt%)
HPMC 4,000 cps (2 wt%)
preservatives (about 0.2 wt%)
Water (to 100 wt%).

Example 3

This example illustrates the efficacy of using the topical composition of the present invention.

The composition as described in Example 2 above was successful in treating acne (12 people), eczema (2 people), insect bites (5 people), and at a more extreme level of pain and discomfort psoriasis (1 person) and shingles (1 person). People treated for acne had all or most blackheads fall out or wash out easily, and had a general improvement in their complexions. The only complaint was a slight odor, which lasted for a short time.

It will be appreciated that the instant specification is set forth by way of illustration and not limitation, and that various modifications and changes may be made without departing from the spirit and scope of the present invention.

WHAT IS CLAIMED IS:

1. A pharmaceutical composition for topical administration to a human comprising micronized cellulose acetate 1,2-benzenedicarboxylate in a water suspension, the composition including 10 to 20 weight % of said micronized cellulose 1,2-benzenedicarboxylate, 10 to 15 weight % polyethylene-polypropylene glycol, 2 to 3 weight % hydroxypropylmethyl cellulose and the balance being water.

2. The pharmaceutical composition according to claim 1, which further comprises 8 to 12 weight % glycerol, 2 to 3 weight % hydroxypropylmethyl cellulose having a viscosity of 3800 to 4500 cps and 0.05 to 0.3 weight % of at least one preservative.

3. The pharmaceutical composition according to claim 1, wherein the cellulose acetate 1,2-benzenedicarboxylate is in an amount of 15 to 18 weight % and of a size of 1 to 10 microns, the polyethylene-polypropylene glycol is in an amount of 10 to 12 weight %, the hydroxypropylmethyl cellulose is in an amount of 2 to 2.5 weight % and has a viscosity of 4,000 to 4,200 cps.

4. The pharmaceutical composition according to claim 2, wherein the cellulose acetate 1,2-benzenedicarboxylate is in an amount of 15 to 18 weight % and of a size of 1 to 10 microns, the polyethylene-polypropylene glycol is in an amount of 10 to 12 weight %, the hydroxypropylmethyl cellulose is in an amount of 2 to 2.5 weight % and has a viscosity of 4,000 to 4,200 cps.

5. The pharmaceutical composition according to claim 4, wherein the at least one preservative is selected from the group consisting of ascorbic acid, methylparaben,

ethylparaben, propylparaben, benzoic acid, sorbic acid, sodium benzoate and potassium sorbate.

6. A method for treating a topical inflammatory condition in a human comprising topically administering to a human in need thereof a pharmaceutically effective amount of the composition according to claim 1.

7. The method according to claim 6, wherein the method is for treating acne, blackheads, skin inflammation, eczema, insect bites, psoriasis, shingles, dermatitis, diaper rash, hives, pityriasis rosea, ringworm, athlete's foot, jock itch, rosacea and sunburn.

8. The method according to claim 6, wherein the method is for treating acne.

9. The method according to claim 6, wherein the method is for treating eczema.

10. The method according to claim 6, wherein the method is for treating psoriasis.

11. The method according to claim 6, wherein the method is for treating shingles.

12. The method according to claim 6, wherein the method is for treating a blackhead.

13. The method according to claim 6, wherein the method is for treating dermatitis.

14. A method for preparing a micronized cellulose acetate 1,2-benzenedicarboxylate suspension comprising:

(a) mixing cellulose acetate 1,2-benzenedicarboxylate and polyethylene-polypropylene glycol in at least one pharmaceutically acceptable organic solvent which is capable of dissolving the cellulose acetate dicarboxylate and the polyethylene-polypropylene glycol to form a first solution;

(b) mixing in water, hydroxypropylmethyl cellulose and polyethylene-propylene glycol, to form a second solution;

(c) mixing the second solution into the first solution with stirring to form a third solution;

(d) adding water to the third solution while mixing to form a fourth solution;

(e) centrifuging the fourth solution and discarding the resultant supernatant to form a fifth solution,

(f) resuspending the fifth solution in water containing hydroxypropylmethyl cellulose to form a sixth solution;

(g) centrifuging the sixth solution and discarding the resultant supernatant to form a seventh solution; and

(h) resuspending the seventh solution in water containing hydroxypropylmethyl cellulose.

15. The method according to claim 14, wherein the organic solvent comprises ethyl acetate and ethanol.

16. The method according to claim 14, wherein the organic solvent is dimethylsulfoxide.