TITLE: Anti-inflammatory and skin soothing composition for cosmetics and therapeutic treatment

BACKGROUND

1. Field

[0001] The present invention is a mineral-rich microorganism-driven composition comprising Lactobacillus Ferment Lysate, Lactobacillus Ferment, and Smithsonite Extract for inhibition of inflammation. Inflammation can be involved in multiple systemic diseases as well as skin problems such as atopic dermatitis (eczema), hives, or psoriasis.

2. Description of the Related Art

[0002] Lactobacillus Ferment Lysate is obtained from the extraction of *Lactobacillus brevis* which is a gram-positive bacteria. Lactobacillus Ferment is the collection from the fermentation of *Lactobacillus brevis*. Smithsonite Extract is obtained from Smithsonite stone. It is highly rich in zinc minerals. The combination of those components may help prevent and treat inflammatory skin disorders.

[0003] Millions of people suffer from skin disorders resulting from exposure to UV radiation, environmental factors, and lifestyle. Inflammation is a hallmark of many acute and chronic skin disorders, including psoriasis, atopic dermatitis, and skin cancer. Inflammation involves a cascade of molecular reactions and cellular activities aimed at tissue regeneration after a simple skin incision or multiple burns. It includes dilation of venules and arterioles, increased vascular permeability, and increased blood flow with tissue penetration of leukocytes. Besides, typical inflammatory responses can also be observed during tissue dysfunction due to proteolytic activity and regeneration of new humoral production for cell proliferation, formation of new functional, and connective tissues. If inflammatory cascades do not reach a resolution, they may contribute to organ dysfunction and death (Arulselvan P et al. 2016).

[0004] Inflammation has five major signs: redness, swelling, heat, pain, and loss of function. There might be also other less common signs depending on the type of inflammation and severity. There are two types of inflammation: acute inflammation and chronic inflammation. Platelets and granulocytic cells such as neutrophils, eosinophils, basophils, and mast cells, are activated during the acute phase of inflammation. They produce and release a variety of soluble mediators that promote and control the inflammatory response. In chronic inflammation, lymphocytic infiltration often occurs. T and B lymphocytes can serve as specific cytotoxic effectors or secrete antibodies or cytokines that contribute to

tissue damage or inflammatory cell recruitment. Following lymphocytic infiltration, macrophages tend to aggregate at the site of damage. They can be the initial response to chronic illnesses by releasing several pro-inflammatory lymphocyte-stimulating cytokines and chemokines (Germolec DR et al. 2018).

[0005] IL-6, IL-1, IL-2, TNF-α, IFN-γ, and transforming growth factor (TGF)-β are the most well-known cytokines for stimulating and maintaining inflammatory responses. They are majorly regulated by transcription factors such as nuclear factor kappa B (NF-κB) and the signal transducers and activators of transcription (STAT) family. There are two major groups of chemokines: CXC and CC chemokines. CC group chemokines are involved in the recruitment of monocytes, eosinophils, basophils, and lymphocytes. CXC group chemokines attract other polymorphonuclear leukocytes.

[0006] Anti-inflammatory treatment is a type of treatment that is used to reduce inflammation in the body or affected areas on the skin. There are several different types of medications that can be used to treat inflammation, including nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and immunosuppressants. NSAIDs work by inhibiting the activity of enzymes called cyclooxygenases (COX), which play a key role in the production of prostaglandins. Prostaglandins are chemicals that are involved in the inflammation process. Corticosteroids work by inhibiting the production of inflammation-promoting chemicals such as cytokines and leukotrienes (Vane JR and Botting RM, 1998).

[0007] The existing anti-inflammatory formulation in medications may not sufficiently prevent and treat the skin condition. There might be multiple reasons why they fail. Firstly, the underlying cause of the inflammation is not being properly addressed. Secondly, the individual is experiencing side effects from the medication. The individual has an intolerance or allergy to the medication. Lastly, the individual's condition is resistant to the medication.

[0008] The present invention provides a composition that has the anti-inflammatory feature. All components in the invention are naturally occurring sustainable actives. They are easily accessible, have excellent processing properties, and can be effectively used in humans.

[0009] The present inventors have searched for components in the invention. The benefits of the invention’s components are listed below.

[0010] Lactobacillus Ferment Lysate (LFL) has been shown to have an anti-inflammatory effect. It reduces skin redness. It induces anti-microbial peptides (AMPs) expression. AMPs are broad-spectrum antibiotics against harmful invaders. LFL holds an anti-acne effect by killing *Propionibacterium acnes*. LFL helps improve the removal of dead skin cells. Moreover, LFL provides calming substances to the body through the delivery of GABA.

[0011] Lactobacillus Ferment (LF) has been shown to provide an anti-inflammatory effect by inhibiting the expression of pro-inflammatory cytokines. LF also provides wound healing and skin regeneration effects. It strengthens the skin barrier.

[0012] Smithsonite Extract protects against DNA damage by UV. It also reduces the formation of glycation end products (AGEs).

[0013] The object of the present invention is to provide a composition, a mixture of three components obtained from natural sources, that exhibits anti-inflammatory properties to prevent and treat inflammatory skin disorders.

3. Summary

[0014] The composition of this invention for preventing or treating inflammation in disorders comprises Lactobacillus Ferment Lysate, Lactobacillus Ferment, and Smithsonite Extract.

[0015] The present disclosure is also directed at providing a composition effective for the prevention and treatment of inflammatory skin disorders.

[0016] Compositions of the present invention may be in any form. Suitable forms include serum, emulsion, cream, essence, gels, sprays and ointments.

[0017] Sample formula using this invention per dose:
Lactobacillus Ferment Lysate – 10-90%
Lactobacillus Ferment – 10-90%
Smithsonite Extract – 10-90%

4. Detailed Description of the Embodiments

[0018] Lactobacillus ferment lysate is a fermented extract that is derived from the bacterium Lactobacillus. This type of bacteria is a common component of the human gut microbiome and is also found in fermented foods such as yogurt and sauerkraut. Lactobacillus ferment lysate is produced by cultivating Lactobacillus bacteria in a nutrient-rich medium and then breaking down the cells through a process called lysis, which releases the contents of the cells into the surrounding solution.

The resulting extract contains a variety of biomolecules, including proteins, enzymes, and small molecules, that are produced by the Lactobacillus cells during the fermentation

process. These biomolecules have a range of potential beneficial effects on the skin, including anti-inflammatory and antioxidant properties.

[0019] Lactobacillus ferment lysate has been shown to increase anti-microbial peptides (AMPs) such as LL-37 and hBD-2. It includes 1,800ppm more GABA and 3,500ppm more lactic acid compared to the only growth medium. It can inhibit nitric oxide production by 69% and 86% at concentrations of 50μg/ml and 100μg/ml, respectively. It has been also shown to significantly reduce the protein expression of Cox-2 at concentrations of 50μg/ml and 100μg/ml. It can inhibit 11β-HSD1 gene expression, which is involved in cortisol production. Halo test using Lactobacillus ferment lysate on *Propionibacterium acnes* exhibited 10mm of inhibition zone.

[0020] Clinical tests with a product including 3% Lactobacillus ferment lysate showed 46.7% improvement in the removal of dead skin cells according to the desquamation analysis. The same product reduced skin redness by 5.4% and 14.9% after 1 day and 2 days of usage, respectively.

[0021] Lactobacillus Ferment is obtained from the fermentation of the bacterium Lactobacillus. It includes only secreted extracellular biomolecules from Lactobacillus.

[0022] 1% Lactobacillus Ferment has been reported to induce cell proliferation by 20% as well as migration and wound healing. It enhanced skin barrier junction tightening by increasing gene expression of filaggrin, loricrin, and claudin-1. It suppressed gene expression of members of inflammation such as IL-6 by 60%, IL-1β by 50%, TNF-α by 30%, and COX-2 by 50%.

[0023] Smithsonite extract is a natural extract derived from the mineral smithsonite, which is a zinc carbonate mineral. Smithsonite extract is obtained by extracting the mineral from its natural source and processing it to produce a concentrated extract that contains various bioactive compounds found in smithsonite.

[0024] Smithsonite extract may have some antioxidant or anti-inflammatory properties, as zinc is known to have these effects on the skin. Smithsonite extract reduced Advanced Glycation End products (AGEs) by 62%. It increased intracellular metallothionein production by 37% and cellular growth by 48% upon UVB exposure. The results show that the Smithsonite extract, which is rich in zinc minerals, protects DNA and cells from toxic heavy metals and UV radiation.

[0025] A clinical study with an emollient including 0.25% zinc pyrithione showed improved psoriasis condition by 73.5% after twice-daily use for 3 months. Psoriasis is known as a chronic inflammatory skin disorder.