

The effect of cannabis on inflammatory skin diseases

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Introduction

"Cannabis" contains cannabinoids that can be used to treat diseases. The active substance is the psychoactive Delta-9-Tetrahydrocannabinol (THC) and non-addictive cannabidiol (CBD). In the United States, of all marijuana users, about 10% are used for medical purposes. The use of cannabis to relieve skin symptoms has been studied to suppress itching, swelling, inflammation and skin cancer. Studies on the use of cannabis to treat skin itching have found that it has an effect in treating itching in 86.4% of patients. It is also speculated that cannabis may have anti-inflammatory properties. It is useful for use in the treatment of atopic dermatitis and allergic contact dermatitis. It has been found that cannabis reduces allergic reactions, swelling and inflammation in laboratory animals. Based on research on cannabis, there is generally an assumption that cannabis is likely to be beneficial for the treatment of psoriasis and skin cancer, as it has the ability to inhibit the formation of skin cells from building too much. Studies on the use of cannabis seed extract to treat acne and dandruff inflammation (Seborrheic dermatitis) have found that cannabis reduces redness and oily skin.

Cannabis

Cannabis contains more than 450 chemicals, which more than 60 types are cannabinoids. The main component is delta-9-tetrahydrocannabinol (THC) and other substances in the same group such as Cannabinol (CBN), Cannabidiol (CBD), Cannabichtomme (CBC), Cannabigerol (CBG), etc. Based on the most studied data and related to the benefits or harms of cannabis extracted as an active ingredient, delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) are believed to have therapeutic properties. CBD extract has important effects that are believed to be beneficial, including anti-seizure, anti-vomiting, appetite stimulating, analgesic, restlessness, and sleep. When CBD is administered in combination with THC, adverse

reactions to THC can be reduced. THC extract acts on the nervous system, resulting in an acute effect on the body, feeling relaxed and having fun. However, there are negative psychotropic side effects, including nervousness, depression, and impairment in concentration, memory and learning as well as the operation of the motion system, speech, vocabulary and affect heartbeat and blood pressure. The benefits of THC extract from cannabis have an effect on cancer patients, and there are research results to support. It was found that THC was better at preventing nausea and vomiting in patients receiving chemotherapy than many anti-nausea and vomiting drugs. As a result, Thailand is urgently amending the Narcotics Penalty Act No. 7 B.E. 2562 (2019) to unlock the use of medical marijuana.

Cannabis is a family of 3 common plants: *Cannabis sativa*, *Cannabis Indica*, and *Cannabis ruderalis*. Cannabis contains many cannabinoids and has pharmacological effects and medicinal properties. The function of cannabinoid in the skin is associated with maintaining skin homeostasis, skin strength, as well as skin self-repair.

Important active ingredients in cannabis

Delta-9-Tetrahydrocannabinol (THC), the THC in cannabis has psychotropic effects, making it addictive but also has anti-inflammatory effects. It reduces nausea, vomiting, and stimulates appetite. Cannabidiol (CBD), CBD in Cannabis has an effect on reducing inflammation. It reduces spasms, helps calm, relaxing, and has the ability to inhibit the growth of many tumor cells in vitro. And it has no addictive effect. The terpenes in cannabis give it a specific smell and taste of cannabis. It has therapeutic properties and is also a synergist by working with cannabinoids.

The skin area has cannabinoid receptors, CB1 and CB2, which are the most abundant and densest in the body compared to other organs. This makes it possible to use cannabis extracts, especially CBD and terpenes, in the treatment of certain skin diseases and can be used as a component of cosmeceuticals. Anti-inflammatory properties in cannabis can treat diseases related to inflammation of the skin, such as dermatitis, psoriasis, acne, some skin cancers, skin allergies, some types of hair loss, etc.

Inflammation

Inflammation is a defense mechanism against a foreign body that occurs on injured cells or tissues and promotes cell and tissue repair. However, more inflammation goes from inflammatory substance and free radicals. This causes the tissue function in the injured area to malfunction. Moreover, inflammatory processes occurring in the body are associated with the development of diseases such as cardiovascular diseases, Alzheimer's disease, Parkinson's disease, diabetes, cancer, infectious shock, inflammatory gastrointestinal diseases, Rheumatoid arthritis and various inflammatory diseases.¹

There are two types of inflammation: 1) acute inflammation, which occurs rapidly within seconds or minutes; After receiving the stimulus and persisting about 2 to 3 days, but usually no more than a week. Acute inflammation helps to eliminate pathogens, which is good for the body and 2) chronic inflammation, which is a reaction in which the body has inflammation for weeks or months. The main characteristic of chronic inflammation is that there are fibrosis tissue is formed. Many blood vessels are formed, and macrophages and lymphocytes are found. These cells play an important role in the inflammatory process and are involved in the release of important chemical mediators, including nitric oxide, prostaglandins, and cytokines. If the body develops chronic inflammatory processes, it can lead to heart disease, diabetes, overweight, or cancer.²

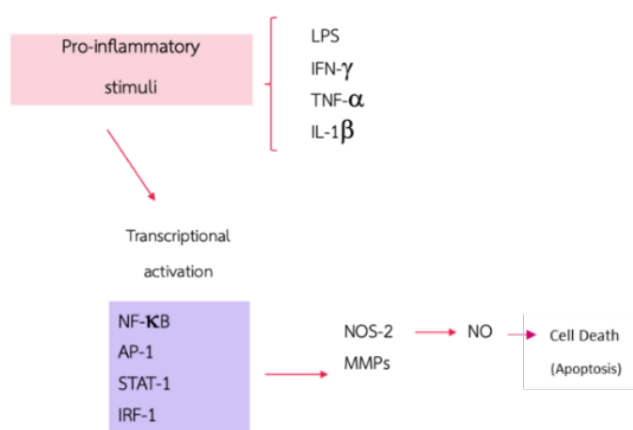


Figure 1: Nitric oxide activation mechanism³

Inhibition of inflammation

At present, efforts have been made to find natural substances that can be anti-inflammatory, as natural substances are safe and have fewer side effects than synthetic ones. Scientists have discovered phytochemicals such as phenolic compounds, flavonoids, iridoids or anthocyanins in many plants, vegetables, fruits, and herbs with anti-inflammatory abilities.

Substances that inhibit excessive nitric oxide production and prostaglandin can be used to treat inflammatory diseases, such as using iNOS inhibitors or inhibition of iNOS enzyme expression, non-steroidal types (NSAIDs) such as aspirin and ibuprofen, which are good painkillers. However, the use of these drugs causes side effects such as stomach ulcers.⁴

Psoriasis and Chronic Dermatitis

Psoriasis and Chronic Dermatitis are chronic skin diseases with the main signs being redness, bulges, clear boundaries. It is covered with silvery thick flakes. Some have pustules spreading all over the body, scalp, with abnormal nails as well. The rash may be accompanied by itching and arthritis deformities. Skin rashes are caused by keratinocyte skin cells dividing rapidly for unknown reasons, but are believed to be caused by immune system disorders. T skin lymphocyte in combination with genetic factors and external stimuli. In addition to psoriasis showing skin symptoms, it may also be found in conjunction with other diseases such as coronary artery disease, diabetes, high cholesterol, paresis, paralysis, etc.

The exact cause is still unknown. Based on current evidence, it is known that this is likely due to a combination of factors, including genetics, immune system and external triggers.

Genetic factors in monozygotic twins, the incidence of psoriasis is two to three times higher compared to dizygotic twins. This will help support that genetic factors play an important part. In the occurrence of psoriasis, psoriasis patients have a family history of the disease with 35% to 90%. A study in Germany found that if both parents had psoriasis, they would have psoriasis. The children are 41% more likely to get the disease. If both parents have psoriasis, the child has a 14% chance of developing it. But if they have a relative with psoriasis, the chance of getting psoriasis is only 6%.

Psoriasis is also associated with HLA - CW6. It was found that whites and Japanese people with HLA- Cw6 had a relative risk of developing the disease 13 times and 25 times, respectively. HLA-Cw6 is also associated with age at which symptoms begin with HLA-Cw6. In 90% of patients with early-onset symptoms and 50% with late-onset symptoms but HLA-Cw was found in 67% of the normal population. This causes psoriasis to be divided into type I, which has HLA-Cw6 expression, early-onset expression and a family history of psoriasis. The rash spreads all over the body and recurs frequently. Type II does not have HLA-Cw6 expression, late-onset symptoms, and no family history of psoriasis.

Regarding pathogenesis psoriasis and chronic inflammatory skin disease, it is believed to start with triggers such as infection, stress, injury, and others that are not yet known. It innates immune cells such as plasmacytoid, dendritic cells, natural killer cells, keratinocytes. These cells secrete cytokines (Interferon α , Tumor necrosis factor α , Interleukin -1 β , Interleukin-6) to activate myeloid dendritic cells. These cells stimulate the naive T cells (T-naive) in the lymph nodes to differentiate into T helper type 17 (TH17) / Tcytotoxic type 17 (Tc17), and T helper type 1 (TH1) / T cytotoxic type 1 (Tc1) in the skin using IL-12 and IL-23, respectively.

TH17 and TH1 where the skin secretes IL-17A,IL-17F, IL-22 from TH17/ Tc17 and IFN - γ , TNF - α from TH1/Tc1, respectively, stimulate keratinocyte cells to divide more. The activated keratinocyte cells secrete various cytokines and chemokines to stimulate the same cycle.

According to the study, inflammation is an innate immune response to any type of injury. While acute inflammation is vital for survival, abnormal regulation of innate immune responses causes chronic inflammation. Many synthetic anti-inflammatory drugs have side effects. Therefore, natural anti-inflammatory agents are needed. Cannabis sativa L. may be a good source of anti-inflammatory molecules. Here we have tested the anti-inflammatory properties of cannabis extract and pure cannabinoids in lipopolysaccharide induced inflammation (LPS) in human THP-1 macrophages. We found that prior treatment with cannabidiol (CBD), delta-9-tetrahydrocannabinol (THC) or extracts containing high levels of CBD or THC reduced the induction levels of various cytokines. CBD is more effective than THC, and its extracts are ultimately more effective than pure cannabinoids. The cytokines of IL-6, IL-10, and MCP-1 are

most sensitive before CBD and THC treatment whereas IL-1 β , IL-8 and TNF- α are less responsive. Our work therefore demonstrates the potential of using cannabinoids or/and cannabis extracts to reduce inflammation and designates IL-6 and MCP-1 as sensitive markers for analyzing the effects of the substance. Cannabinoids against inflammation in macrophages.⁵

Conclusion and recommendations

Cannabis is a genus of cannabis, contains cannabinoids (Cannabinoids), which have pharmacological effects and medicinal properties. Functional system of cannabinoid in the skin is associated with maintaining skin homeostasis, skin strength, as well as skin self-repair. The main active ingredients in cannabis are: 1. Delta-9-Tetrahydrocannabinol (THC) THC in cannabis has psychotropic effects, but it also has anti-inflammatory effects, causing relaxation, sleep, reducing nausea and vomiting, and stimulating appetite. 2. Cannabidiol (CBD) CBD in cannabis has the effect of reducing inflammation. It reduces spasms, helps calm, relax, and has properties to inhibit the growth of many types of tumor cells in vitro. 3. The terpenes in cannabis give it a specific smell and taste of cannabis. It has therapeutic properties and is also a synergist by working with cannabinoids.

Psoriasis and chronic inflammatory skin diseases are found 1-2% of the population. They are mostly found in both males and females in people aged 20-30 years and 50-60 years old. People with these diseases have an impact on their daily lives, including socialization and lack of confidence, whether it's in terms of dressing, dealing with the symptoms of the disease. Therefore, getting to know the disease, taking care of oneself, managing stress are therefore crucial.

Due to the anti-inflammatory properties of the compounds in cannabis, there has been an interest in using cannabis to treat diseases related to inflammation of the skin, such as dermatitis, psoriasis, skin allergies, acne, some skin cancers, some hair losses, etc. It has been discovered that the function of cannabinoid in the skin is heavily involved in maintaining skin homeostasis, skin strength, as well as skin self-repair. It has a balancing effect on the immune system, immunomodulatory effects as well as anti-oxidant properties. There is also evidence to support that the compounds in cannabis can activate CB1 and CB2 receptors located in the

sensory nerve regions of the skin and at the skin cells can help reduce itching as well. For the reasons mentioned above, Institute of Dermatology Thailand recognizes the importance of studying and developing cannabis as an alternative for the treatment of various skin diseases. It uses only cannabidiol (CBD) and terpenes because it has no psychotropic effect and is therefore safer to use than THC. Treatment methods depend on the symptoms of each disease. It is mainly used as a topical medication and may be taken orally or drops of CBD oil as a treatment. Hemp extract, in addition to being useful in the treatment of skin diseases, it can also be used as a component of cosmeceutical products.

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