CHAPTER 13

CURCUMIN

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Curcumin (diferuloylmethane), a principal polyphenol component of the dietary spice tumeric, has been used in Indian and Chinese medicine for the treatment of various systemic and skin diseases. The chemical structure of curcumin is shown in Figure 1. It is quite safe and has multiple biological activities, such as anti-inflammatory, anti-oxidant, anti-proliferative, wound-healing, anti-cancer, antiseptic, and antifibrotic activities. These effects are mediated through the regulation of various transcription factors, growth factors, inflammatory cytokines, protein kinases, and other enzymes. Recently, most of the preclinical and clinical studies determined the efficacy and safety of curcumin for various systemic diseases, such as cardiovascular, pulmonary, metabolic, neurodegenerative, autoimmune, and neoplastic disease. Additionally, curcumin has a protective effect on the skin by way of quenching free radicals and reducing inflammation through the inhibition of nuclear factor-kappa B (NF-kB). The many biological activities of curcumin have shown promise as an alternative treatment option for skin disease. However, its clinical use is limited because of poor bioavailability due to poor absorption, rapid metabolism, and rapid systemic elimination.[1-10] We reviewed the using of curcumin for some dermatological diseases.

1. PSORIASIS

Psorasis is one of the most common chronic inflammatory skin diseases. Worldwide prevalence is approximately 2-3%. Treatments for psoriasis are generally based on anti-proliferative actions, anti-inflammatory actions, or a combination of both. These treatment options are either time-consuming or have the potential for organ toxicity with chronic use. Thus, the need for alternative and less toxic therapies for psoriasis is clear.

Curcumin's anti-inflammatory activity occurs as a result of interaction with many molecules and cytokines. It down regulates various pro-inflammatory cytokine expressions, such as tumor necrosis factor (TNF-alfa), interleukins (IL-1, IL-2, IL-6, IL-8, IL-12), and chemokines, most likely through inactivation of the nuclear transcription factor, nuclear factor (NF)-kB. NF-κB, a ubiquitous eukaryotic transcription factor, is involved in the regulation of inflammation, cellular proliferation, transformation, and tumorigenesis. In addition, curcumin is a selective phosphorylase kinase (PhK) inhibitor, which has been shown to have anti-inflammatory and anti-proliferative effects. Also,curcumin has the ability to curtail keratinocyte proliferation.

Numerous studies suggest that curcumin may be an effective treatment for psorasis because it reduces the activity of PhK and has an inhibitory effect on NF-kB.

In a clinical phase 2 trial involving twelve patients with chronic plaque psoriasis, 4.5 g curcumin capsules were administered every day for 16 weeks. In this study, the response rate was low. Henge et al. reported that curcumin was more effective in reducing PhK levels when compared with calcipotriol, a vitamin D3 analogue in psoriasis. The resolution of psoriasis in the curcumin treated group was better than the others.This study investigated the anti-psoriatic activity of curcumin in patients is due to the suppression of PhK activity.[11-19]

2. MELANOMA

Malignant melanoma is the most aggressive and life-threatening skin cancer and is highly resistant to chemotherapy and radiotherapy. Thus, new treatment options for melanoma are needed. In vitro and animal studies have shown that curcumin has anti-oxidant, anti-mitotic, anti-metastatic, anti-inflammatuar, and anti-antigenic effects. In addition, curcumin has the ability to suppress UV irradiation-induced DNA mutagenesis. Curcumin's inhibitory effect on carcinogenesis has been demonstrated on multiple human carcinomas, such as breast, colon, prostate, melanoma, head and neck, cervical, oral, and pancreatic. It has the ability to inhibit carcinogenesis at three stages: tumor promotion, angiogenesis, and tumor growth. Some studies have shown the anti-tumor effect of curcumin in melanoma, but it is not widely known. Activation of NF-kB is associated with various steps in the development of malignancy, such as the expression of anti-apoptotic genes, angiogenesis, tumor promotion and metastasis. Curcumin has shown an anti-proliferative effect via inhibition of the transcription factor NF-kB and downstream gene products (including c-myc, Bcl-2, COX-2, NOS, Cyclin D1, Tnf-alfa, interleukins, and MMP-9).[20-27]

Jiang et al. investigated curcumin's role in apoptosis induction and proliferation inhibition in melanoma cells. They found that curcumin could induce apoptosis and inhibit proliferation in melanoma cells by affecting

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