



Irene Montaña

Fighting the effects of chronic inflammation in the skin

IRENE MONTAÑO, PhD

Mibelle Biochemistry, Bolimattstrasse 1
Buchs, 5033, Switzerland

ABSTRACT: The immune system becomes less effective with ageing and its capacity to manage the inflammatory response is reduced. This can lead to chronic inflammation, a process characterized by a slow but continuous production of free radicals which aggravates wrinkles, fine lines and sagging skin. During this process, the Nuclear Factor Kappa B (NF-κB) remains active instead of self-regulating its level. Magnolol and honokiol are the main component of the Magnolia bark extract and are known to block NF-κB as well as having anti-oxidants and anti-bacterial properties. In a commercial available ingredient these low soluble substances were incorporated into lecithin liposomes for an optimal skin uptake. In clinical studies, the Magnolia based ingredient was shown to reduce redness in facial skin, to restore moisture and to prevent loss of skin elasticity.

INTRODUCTION

Without inflammation we will not be able to survive in a hostile world contaminated with hazardous microorganisms. In fact, people whose capacity for inflammatory response is compromised (by drugs or due to immune system malfunction) could develop life-threatening infection even from ordinarily undamaging microorganisms (1). Acute inflammation is the short-term immune response our bodies mount in cases of trauma, infection, and allergy. Inflammation engages a number of responses intended to demolish or at least slow down invading pathogens.

When foreign pathogens are recognized by the immune system, a number of physiological events take place in the effort to eliminate those pathogens. Inflammation induces inflammatory cells like macrophages, neutrophils, monocytes, to invade at the site of infection. This leads to the release of large amounts of free radicals and the death and degradation of the organism, agent or affected cells. After that, inflammation resolves, the healing step initiates and tissue homeostasis is re-established (2).

If infection remnants, inflammation may turn into chronic and go on for weeks or even years (Figure 1). Occasionally, chronic inflammation may persist even without major infection, either because the inflammation response has become too sensitive or because the immune system begins to notice some of the body's own tissues as foreign. Chronic inflammation continue to stimulate pro-inflammatory components cells when they may not be needed.

As it turns out, aging is associated with the increase in such form of chronic inflammation (1). In addition, as we age, we tend to develop autoimmune conditions as well as chronic inflammation. During chronic inflammation, the immune system persists to produce low levels of the key molecular players such as prostaglandins, cytokines and Nuclear Factor-kappa B (NF-κB) (2). Like most mechanisms of aging, chronic inflammation creates a vicious cycle. The aging process tends to increase the level of chronic inflammation and that, in turn, accelerates aging. When the skin is involved, it can accelerate fine lines, wrinkles and enlarged pores, as well as puffiness, sagging, blotchiness or reddening of the skin. The ultimate cause being the breakdown of collagen and elastin fibres.

KEY PLAYER IN THE PROCESS OF CHRONIC INFLAMMATION

An important transcription factor involved in the regulation of inflammation is the Nuclear Factor-kappa B (NF-κB). It exists in a latent state in the cytoplasm bound to specific inhibitory proteins, IκBs (Inhibitor of κB). The degradation of IκB proteins provides the signal to ultimately activate NF-κB. This takes place via activation of a kinase named the

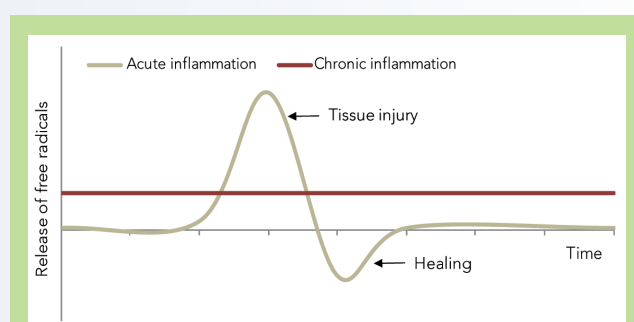


Figure 1. Inflammatory responses: Acute vs. Chronic. The release of free radicals in acute inflammation is large but punctual. In contrast, in chronic inflammation it is small but continuous.

IκB kinase (IKK). When activated, generally by signals coming from the outside of the cell, two serine residues in IκB are phosphorylated by IKK which will conduct to its degradation by the proteasome. NF-κB is now free to enter into the nucleus to regulate the transcription of multiple pro-inflammatory mediators genes and Matrix-Metalloproteinases (MMP). Ultimately, NF-κB is turned off by itself.

In the skin, an excess of reactive oxygen species (ROS) can make NF-κB chronically active leading to a continuous release of inflammatory mediators and thus to chronic inflammation. These ROS can be over-generated by aging, external stresses (such as UV, pollution, toxins, chemical irritants) and internal ones (lifestyle, diet, lack of sleep).

How to treat inflamm'aging

Magnolia officinalis is a natural Inhibitor of NF-κB. It is a medicinal plant belonging to the China pharmacopoeia and its bark has been used for thousands of years in Asia to treat the stagnation of qi (lack of energy) and more precisely digestive disorders, anxiety and allergic diseases. In Japan, two of the most popular herbal medicines used, one called saiboku-to and another called hange-kobuku-to, contain magnolia bark and have been used for treating disorders from bronchial asthma to depression to anxiety.

The Magnolia bark extract contains two pharmacologically active substances named Magnolol and honokiol. These two low molecular weight lignans synergistically reduce inflammation by inhibiting NF-κB activation and activity through IKK (IκB kinase) enzyme inactivation (3). As a result, the production of inducible-nitric oxide synthase (iNOS), interleukine 8 (IL-8), tumour necrosis factor α (TNF-α) and COX-2 (4) is inhibited. In addition, they have antioxidant, anti-bacterial and anti-angiogenic effects and can relieve spasms. Japanese researchers have determined that the magnolol and honokiol components of Magnolia officinalis are one thousand times more potent than alpha-tocopherol (vitamin E) in their antioxidant activity (5).

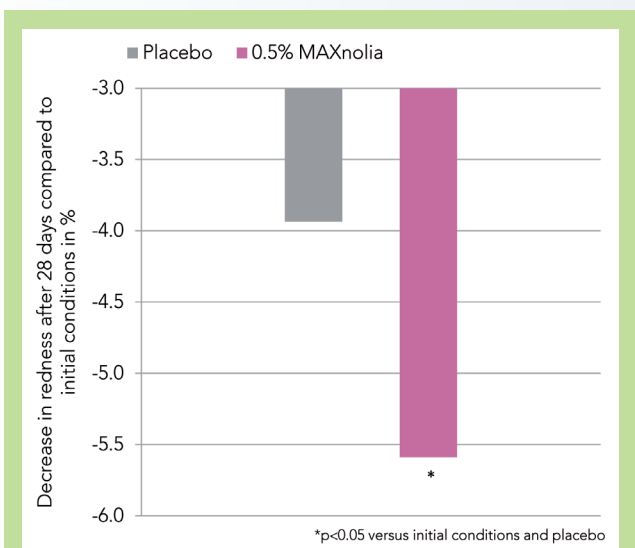


Figure 2. Reduction of facial skin redness after 28 days of treatment with a 0.5 percent MAXnolia cream in comparison to placebo.

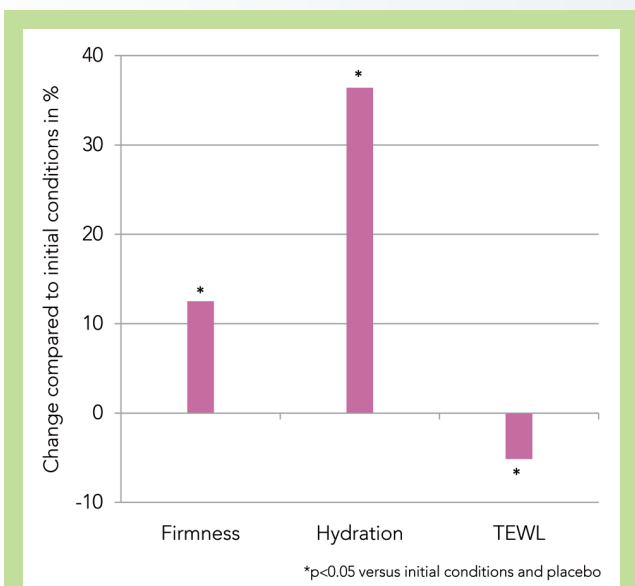


Figure 3. Improvement of the crow's feet area. After 28 days application of a cream with 0.5 percent MAXnolia, skin elasticity increased and skin fatigue was reduced.

Development of a cosmetic ingredient based on Magnolia bark

Due to the low solubility of Magnolol and honokiol in water it has been necessary to develop a proprietary system to extract the active substances for use in a water soluble ingredient. Ethanol and water are used to obtain an extract of the Magnolia bark. This solution is then sprayed onto a carrier of maltodextrin and phospholipids. The result is a powder free of alcohol that contains pre-liposomes (MAXnolia). When MAXnolia is formulated in a cream, these pre-liposomes turn immediately into liposomes in the water phase and the active ingredients are incorporated into the lecithin bi-layer membranes. The ingredient that results is preservative free and alcohol free, with good skin delivery due to the liposomes.

CLINICAL STUDIES

Determination of the anti-redness effect and improvement of the Skin Quality

A clinical study was carried out over 4 weeks with 20 women aged from 54 to 78 having visible facial skin redness. A cosmetic product containing 0.5 percent MAXnolia was applied twice per day on one side of the face and the placebo cream on the other side (vehicle-controlled half side comparison). Skin redness was determined by measuring the parameter a* in the L*a*b* colour system using a Chromameter. a* characterizes the colour intensity from green to red and an increase of a* indicates an increase of the red constituent of the skin. Results showed that the Magnolia based ingredient significantly reduced half-side facial skin redness compared to the placebo (Figure 2). In parallel, a cream containing 0.5 percent MAXnolia was applied to the inner side of the forearms. Skin hydration and firmness were measured using respectively a Corneometer MPA 5 CPU (Courage+Khazaka GmbH, Cologne) and a Cutometer MPA 580 (Courage+Khazaka GmbH, Cologne). Trans Epidermal Water Loss (TEWL) was determined on the face by means of AquaFlux Model AF200 (Biox Systems Ltd, London, UK). At day 0 the parameters were determined in the test areas under standardized conditions and the first application of the products was done. From day 1 to 28 the test products were applied twice a day and at day 28 the parameters were measured again. Results showed that the cream containing MAXnolia significantly increased skin hydration and firmness and decreased TEWL compared to the placebo (Figure 3).

Evaluation of the anti-ageing effect on the eye contour area

To evaluate the anti-wrinkle effect a cream containing 0.5 percent of the active was applied twice per day on the eye contour area. The clinical trial was carried out over 2 months on 21 volunteers aged from 35 to 58. Two parameters were assessed using a Cutometer SEM 575 (Courage & Khazaka): the skin elasticity and the skin fatigue which indicates the loss of elasticity due to repetitive mechanical stresses (skin elasticity tends to decrease with age whereas skin fatigue increases). Results showed that Magnolia extract based cream increased the skin elasticity of the crow's feet and decreased the skin fatigue compared to the placebo (Figure 4).

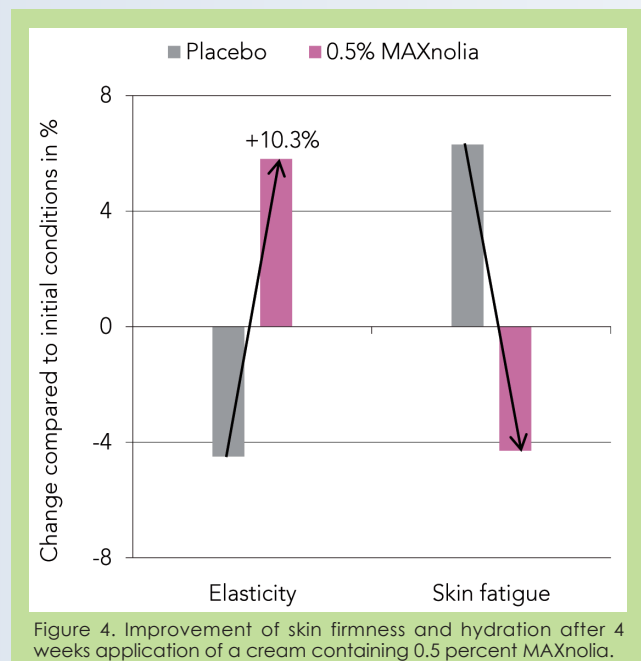


Figure 4. Improvement of skin firmness and hydration after 4 weeks application of a cream containing 0.5 percent MAXnolia.

CONCLUSIONS

The skin is a major sensory organ, it is the first defence line of the body against infectious organisms and corporal injury. Besides, it plays a very important role in controlling body temperature. Aging of the skin is a process with very direct effects on the daily life and psychological and social well-being of an individual. Slowing down the aging processes of the skin will then not only help us to maintain a more youthful appearance but will most likely have favourable effects for the whole organism. Inflammation is a vital part of the body's healing process: It occurs at the cellular level when the immune system tries to fight off disease-causing germs and repair injured tissue. This normal, healthy process of tissue repair guides inevitably to the production of big amounts of inflammatory factors while the body gets rid of the injured or infected tissue before repair can start. Nevertheless, if this process is left incomplete (most probable to take place in older individuals), chronic inflammation can arise. The inhibition of NF- κ B activity by magnolol and honokiol helps to stop the chronic inflammatory process which is correlated to the skin's ageing process and the development of lines, wrinkles, blotchiness and reddening of the skin. The results presented in this article show that the Magnolia based ingredient prevents loss of skin elasticity, re-establishes moisture and diminishes redness in facial skin. An overall improvement was accomplished in the skin quality where the anti-inflammatory ingredient was applied.

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