MAGNOLIA BARK ACTIVES TO PREVENT INFLAMM'AGING OF THE SKIN

INFLAMMATION IS AN IMPORTANT WAY FOR OUR BODIES TO REACT TO INFECTION AND FOREIGN PATHOGENS. PARADOXICALLY, THE SAME PROCESS THAT OUR IMMUNE SYSTEM USES TO PROTECT OUR BODIES FROM INFECTION CAN ALSO LEAD TO VISIBLE SIGNS OF AGEING. IN THE PROCESS OF AGEING, THE IMMUNE SYSTEM BECOMES LESS EFFECTIVE AND ITS CAPACITY TO MANAGE THE INFLAMMATORY RESPONSE IS REDUCED. THIS CAN LEAD TO CHRONIC INFLAMMATION. THIS PROCESS IS CHARACTERIZED BY A SLOW BUT CONTINUOUS PRODUCTION OF FREE RADICALS THAT AGGRAVATES WRINKLES, FINE LINES AND SAGGING SKIN. BESIDES, AS WE GROW OLDER, WE BECOME MORE SUSCEPTIBLE TO CHRONIC INFLAMMATION. LET'S EXPLORE HOW CHRONIC INFLAMMATION IS ASSOCIATED WITH SKIN AGEING.

ACUTE AND CHRONIC INFLAMMATION

Acute inflammation is the shortterm immune response that our body mounts in cases of trauma, infection and allergy. Without inflammation, we would not be able to survive in a hostile world infested with hazardous microorganisms. In fact, people with a compromised inflammatory response capacity — from drugs or an immune system malfunction could develop a life-threatening infection even from ordinarily harmless micro-organisms.1 Inflammation involves a number of responses that destroy or, at least, slow down invading pathogens. When foreign pathogens are identified by the immune system,

a number of physiological events occur in an effort to eliminate those pathogens. The inflammatory response represents a complex network of events designed to facilitate a return to physiological homeostasis and tissue repair. Acute inflammation is characterized by a number of phenomena, including an increase in local blood flow, the migration and activation of immune cells in the affected area. the release of large amounts of free radicals in a short period of time, the destruction of normal tissue, scar tissue deposition and so on.²

In a perfect world, this response takes place just as it should, releasing proinflammatory compounds when needed and then turning them off with antiinflammatory compounds when the threat has been sufficiently addressed. If infection remains, inflammation may become chronic and continue for weeks or even years. Sometimes, chronic inflammation may persist even without significant infection, either because the inflammation response has become too sensitive or because the immune system begins to perceive some of the body's own tissues as being foreign. Chronic inflammation continues to stimulate proinflammatory components when they may not be needed. As such, ageing is associated with an increase

in chronic inflammation.¹ As we age, we tend to develop autoimmune conditions as well as chronic inflammation. It is no wonder that chronic inflammation contributes to the ageing process because it overwhelms tissues with free radicals and promotes the destruction of normal cells. During chronic inflammation, the immune system produces low levels of the key molecular players, such as prostaglandins, cytokines and nuclear factorkappa B (NF-κB).² Like most ageing mechanisms, chronic inflammation creates a vicious cycle. The ageing process tends to increase the level of chronic inflammation and that, in turn, accelerates ageing. 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.

FIGHTING INFLAMM'AGING

NF- κ B) is an important transcription factor in the



regulation of inflammation; many proinflammatory stimuli can activate it. NF-KB exists in a latent state in the cytoplasm, bound to specific inhibitory proteins ($I\kappa Bs$ or Inhibitors of κB). The degradation of IkB proteins initiates a signal that ultimately activates NF-ĸB. This takes place via the activation of a kinase named IkB kinase (IKK). When activated, often by extracellular signals, IKK phosphorylates two serine residues in IkB that trigger its degradation by the proteasome. NF- κ B is then free to enter into the nucleus to regulate the transcription of multiple proinflammatory mediator genes and matrix-metalloproteinases (MMPs). Finally, NF-KB is turned off by itself. In the skin, an excess of reactive oxygen species (ROS) can make NF-κB chronically active, leading to a continued release of inflammatory mediators and, thus, to chronic inflammation. ROS can be overgenerated by ageing, external stresses (such as UV, pollution, toxins, chemical irritants) and internal ones (lifestyle, diet, lack of sleep).

Magnolia officinalis is a natural Inhibitor of NF-ĸB. It is a medicinal plant belonging to the Chinese 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 - saiboku-to and hangekobuku-to — contain magnolia bark and have been used to treat disorders from bronchial asthma to depression to anxiety. Magnolol and honokiol are the two pharmacologically active substances present in Magnolia bark. These two low molecular weight lignans synergistically reduce inflammation by inhibiting NF-ĸB activation and activity through IKK (IKB kinase) enzyme inactivation.3 As a result, the production of inducible-nitric oxide synthase (iNOS), interleukin 8 (IL-8), tumour necrosis factor alpha (TNF-a) and COX-2 is inhibited.⁴ In addition, they have antioxidant, antibacterial and antiangiogenic 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 Magnolol also has antidepressive, antiallergic and antiasthma effects whereas honokiol is anxiolytic.

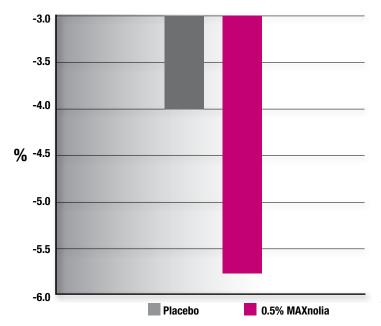
PREPARING MAGNOLIA BARK FOR COSMETIC USE

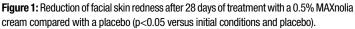
Owing to the low solubility of magnolol and honokiol in water, it has been necessary to develop a proprietary procedure to extract the active substances for use in a water-soluble ingredient. Ethanol and

water are used to obtain an extract of Magnolia bark. This solution is then spraved onto a carrier of maltodextrin and phospholipids. The result is an alcohol-free powder that contains preliposomes (MAXnolia). When MAXnolia is formulated in a cream, these preliposomes turn immediately into liposomes in the water phase and the active ingredients are incorporated into the lecithin bilayer membranes. The process has a number of advantages, including the fact that the resulting ingredient is

preservative-free and alcoholfree, with good skin delivery because of the liposomes.

ACTIVE INGREDIENTS





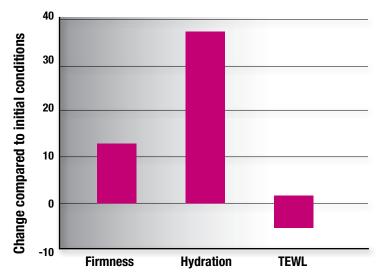


Figure 2: Improvement in skin firmness and hydration after applying a cream containing MAXnolia (0.5%) for 4 weeks (p<0.05 versus initial conditions and placebo).

Ageing of the skin is a process with very direct effects on the daily life and psychological and social well-being of an individual. The skin is a major sensory organ; it is the body's first line of defence against infectious organisms and physical harm, and it plays a very important role in controlling body temperature. Slowing down the skin's ageing process will, therefore, not only help us to keep a more youthful appearance but will most likely have beneficial effects for the whole organism. Inflammation is an essential part of the body's healing process: it occurs at the cellular level when the immune system tries to fight off diseasecausing germs and repair injured tissue. This normal, healthy process of tissue repair leads inevitably to the production of large quantities of inflammatory factors while the body gets rid of the damaged or infected tissue before repairs can start. However, if this process is left unfinished (more likely in older individuals), chronic inflammation can occur. The inhibition of NF- κB activity by magnolol and honokiol helps to stop the chronic inflammatory process, which is linked 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, restores moisture and reduces redness in facial skin. An overall improvement was achieved in the skin quality where the antiinflamm'aging ingredient was applied.

CLINICAL STUDY RESULTS

Determination of the anti-redness effect: A clinical study was done for 4 weeks with 20 women who had visible facial skin redness. A cosmetic product containing 0.5% MAXnolia was applied, twice a day, on one side of the face and a placebo cream was applied to 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 colour intensity from areen to red — and an increase of a* indicates an increase in the red constituent of the skin. Results showed that the Magnolia-based ingredient significantly reduced half-side facial skin redness compared with the placebo (Figure 1).

Evaluation of the antiageing effect on the eye contour area: A cream containing 0.5% of the active was applied twice a day on the eye contour area to evaluate its antiwrinkle effect. The clinical trial was done for 2 months with 21 volunteers aged from 35 to 58. Two parameters were assessed using a Cutometer SEM 575 (Courage and Khazaka GmbH, Cologne, Germany): skin elasticity and skin fatique, which indicate the loss of elasticity caused by repetitive mechanical stresses (skin elasticity tends to decrease with age whereas skin fatigue increases). Results showed that a Magnolia extractbased cream increased the skin elasticity of the crow's feet and decreased skin fatigue compared with the placebo.

ENHANCING SKIN OUALITY

A general improvement of the skin was determined on volunteers aged from 54 to 78 after 28 days in vivo. A cream containing 0.5% MAXnolia was applied to both the face and the inner side of the forearms. Skin hydration and firmness were measured on the inner side of the forearms using a Corneometer MPA 5 CPU

(Courage and Khazaka) and a Cutometer MPA 580, respectively. Trans Epidermal Water Loss (TEWL) was determined on the face using an 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 with the placebo (Figure 2). PHM

REFERENCES

- 1. F. Licastro, et al., "Innate Immunity and Inflammation in Ageing: A Key for Understanding Age-Related Diseases," Immun. Ageing 2, 8 (2005).
- 2. R.N. Mitchel and R.S. Cotran, "Acute and Chronic Inflammation," in V. Kumar, et al. (Eds.), Robbins Basic Pathology (Saunders, Elsevier BV, Amsterdam, the Netherlands, 2003).
- 3. A.K-W. Tse, *et al.*, "Magnolol Suppresses NF-kB Activation and NF-KB Regulated Gene Expression Through Inhibition of the IKK Enzyme Activation," Mol. Immunol. 44, 2647-2658 (2007).
- 4. J.S. Lee, et al., "Anti-Inflammatory Effects of Magnolol and Honokiol are Mediated Through Inhibition of the Downstream Pathway of MEKK-1 in NF-kB Activation Signalling," Planta Medica 71(4), 338-343 (2005).
- 5. Y.C. Lo, et al., "Magnolol and Honokiol Isolated from Magnolia officinalis Protect Rat Heart Mitochondria Against Lipid Peroxidation," Biochem. Pharmacol. 47(3), 549-553 (1994).

FOR MORE INFORMATION

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