PERSONAL CARE INGREDIENTS - FORMULATION - MANUFACTURE

Nore than morning coffee for your eyes



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More than morning coffee for your eyes

Emina Besic Gyenge, Stefan Hettwer, Brigit Suter, Sandra Breitenbach, Barbara Obermayer – Rahn, Switzerland

The eyes are the window to the soul and are the most sincere part of our face. Youthful, bright and energetic eye appearance is therefore our most prominent flagship. Dark circles and eye bags can make you look tired, dull and older than your years. Before you spend time and money buying concealers, you should understand why we have those pesky problems.

Puffy eyes and dark circles around the eyes generally result from a variety of factors such as lack of sleep, physical or emotional exhaustion, stress, allergies or inherited facial features. This condition affects individuals of all ages, genders and ethnicities. Additionally, our appearance worsens due to the ageing process of the skin, involving sagging skin, skin thinning and subcutaneous fat distribution. Although it is a not healththreatening condition it can influence quality of life and well being. Temporarily relief may be achieved through such home remedies as cold cucumber slices, but a longer-lasting solution requires identification of the underlying cause and specific treatment. As mentioned above, there are different factors that cause, or to be more precise, make periorbital dark circles visible.

Firstly, skin around the eyelids, so called periorbital skin, is on average about 0.5 mm thick and compared to the rest of the body (average 2 mm) is the thinnest skin. This region contains many small blood vessels, which appear bluish through the pale skin. The reason is not that the veins and blood inside them are blue, but rather that subcutaneous tissue only reflects blue/violet wavelengths of light. If skin is darker or lighter, veins do not appear bluish. Rather, they are brown or greenish and for humans with albinism they are even dark purple or dark red, resembling the actual colour.

Secondly, some red blood cells constantly leak into the surrounding skin. If the blood vessel walls are weakened or damaged, or if the circulation slows down, more red blood cells leak into the surrounding tissue where, just as in the case of a bruise, haemoglobin (the protein which transports oxygen and gives blood cells their red colour) gradually breaks down. It is the diversely coloured

Abstract

The most delicate skin on our body is found around the eyes, so-called periorbital skin. Regardless of what skin type one has, you may assume that everyone has more or less sensitive skin in that area. This part of our body is always exposed to environmental conditions and is a mirror of how we feel. Therefore, it deserves special attention and intensive care. Rahn has developed a natural product with an ingenious combination of different xanthines, artichoke extract and the fructan polysaccharide (levan) addressing the problem of dark circles and puffy eyes. It successfully reduces eye bag volume and any associated skin discolouration, and rejuvenates the eye area.

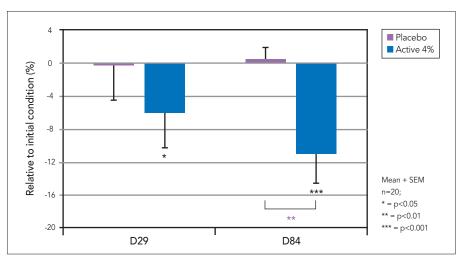


Figure 1: Application of an emulsion with 4% active significantly reduces eye bag volume. Eye bag volume was reduced by 6% after 29 days and 11.1% after 84 days of treatment. The effect was significantly over the baseline and placebo. Placebo treatment did not have any measurable effects. The statistical values in blue relate to the comparison of active with the placebo, whereas the black values relate to the comparison with the initial condition. Wilcoxon signed-rank test.

degradation products of the blood cells that cause dark discoloration under the eyes. The same effect is responsible for bruises, which heal within two to three weeks, going from blue-violet over green and finally to yellow.

Thirdly, another problem that goes handin-hand with periorbital dark circles is puffiness. Swelling occurs in the eye area when the lymphatic circulation is delayed and fluid builds up increasingly due to fatigue or ageing (oedema). Puffiness of the skin tissue is a consequence of the delayed natural drainage of fluids below the eyes. Increased fragility in the smallest blood vessels can also lead to swelling around the eyes, since more vessel fluid can escape into the surrounding tissue. However, swelling in the eye region can also arise due to age-related processes such as the storage of excess fatty tissue and sagging skin. Basically, the ligaments that support fat pads under the eyes weaken and cause the fat to slip and bulge forward. Bulging lower eyelids add a shadow effect and are detrimental to the appearance.

There are different ways to solve the problem and regain a youthful and brighteyed appearance. Using special makeup techniques to camouflage or neutralise darkness produce immediate effects but only cover up the symptoms. Beneath the makeup layers and colour correcting concealers, dark circles lie in wait for the makeup remover to reveal the naked truth.

A better solution is to fight the problem at its roots. Slimexir® with its sophisticated active ingredients directly fights the cause of dark circles and puffiness, the result of fat bulging. For most of us, starting the day with coffee or tea is part of our daily mantra. Xanthines such as caffeine serve as mild stimulants increasing alertness in the central nervous system and warding off sleepiness. These molecules have been found to act as nonselective adenosine receptor agonists¹ and as competitive nonselective phosphodiesterase inhibitors² leading to the activation of lipolysis. Consequently, with the idea of perking up the tissue and triggering fat decomposition, Rahn has, in X-Melt® (INCI: Xanthine), combined different xanthines in the best possible manner to achieve the optimal synergistic effect, outperforming the effect of caffeine alone. Furthermore, artichoke extract (INCI: Cynara Scolymus Leaf Extract) supports X-Melt's lipolysis effect and stimulates the circulation and drainage,³ successfully removing the products of fat breakdown. Sagging skin caused by volume reduction is effectively prevented by levan (INCI: Fructan). Its exceptional cosmetic properties firm and strengthen the skin surface, resulting in irregularities appearing less often.⁴ Applying Slimexir improves the appearance of the skin tremendously. It acts on all three levels, namely: fat decomposition, lymphatic drainage and skin firmness.

Material and methods

The *in vivo* study has been performed in accordance with the principles of good laboratory practice (GLP), good clinical practice (GCP), and in compliance with the quality assurance system requirements. The study was in accordance with the World Medical Association's Declaration of Helsinki. All study participants signed a written

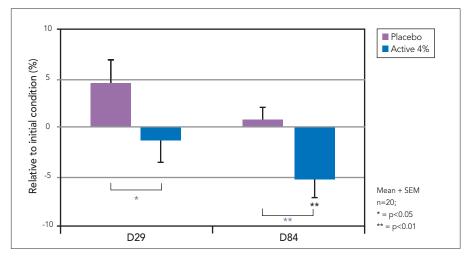


Figure 2: Application of an emulsion with 4% active significantly reduces skin roughness. The arithmetical mean deviation of the roughness profile (Ra) after 29 and 84 days of treatment was significantly improved (1.3% and 5.3%) in comparison to the initial state and against placebo. Placebo treatment did not have any positive effects. The statistical values in blue relate to the comparison of active with the placebo, whereas the black values relate to the comparison with the initial condition. Wilcoxon signed-rank test.

informed consent at the beginning of the study.

In a double-blind, placebo-controlled study 40 female subjects (20 per treatment group), between the ages of 35 and 65, with healthy, Caucasian skin and ageing signs, dark circles and eye bags were tested. The volunteers applied either placebo or verum emulsions containing 0 % or 4 % active twice daily for 84 days.

Primos was used to obtain 3D images of the skin topography, measuring eye bag volume and skin smoothness. Changes in the brightness and colour of the skin directly below the eye were determined using a Minolta Chromameter CR 400 as per the L*a*b colour system. An increase in the L* measurement value represents brighter skin. A decrease in the a* measurement value reduces skin reddening and an increase in the b* measurement value reduces blueness. Standardised photographic images obtained with normal, cross polarised and UV lamp of both hemi-faces and the front are obtained before, during and after the treatment (D0, D29 and D84) with the VISIA-CR system (Canfield, US), in order to quantify the evolution of the anti-ageing and brightening effect.

Results

Eye bag volume / skin roughness The instrumental data (fringe projection) showed that application of verum emulsion with 4% active decreased eye bag volume significant over baseline by 6% after 29 days and by over 11% after 84 days on average. While the active produced a significant effect after 28 and 84 days, placebo did not show any effect at all. After 84 days, verum was significantly better than placebo (Fig 1). Furthermore, skin roughness improved remarkably. The arithmetical mean deviation of the roughness profile (Ra) was significantly better on day 29 and day 84 than at the

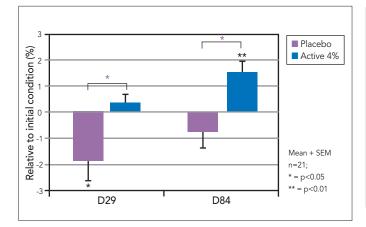


Figure 3: Application of an emulsion with 4% active has a significant lightening effect on the eye area. The brightness of the skin (L* value) was measured by conventional chroma meter measurement. The effect was significant over baseline and placebo. The statistical values in blue relate to the comparison of active with the placebo, whereas the black values relate to the comparison with the initial condition. Wilcoxon signed-rank test.

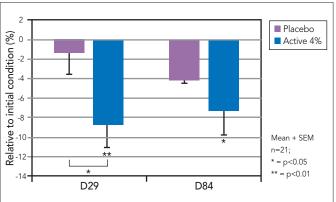


Figure 4: Application of an emulsion with 4% active significantly reduces skin redness. The a* value measurement revealed a significant reduction in skin redness after 29 and 84 days of treatment. Redness was reduced by 8.7% after 29 days and 7.3% after 84 days, respectively. The effect was significant over baseline and placebo. The statistical values in blue relate to the comparison of active with the placebo, whereas the black values relate to the comparison with the initial condition. Wilcoxon signed-rank test.

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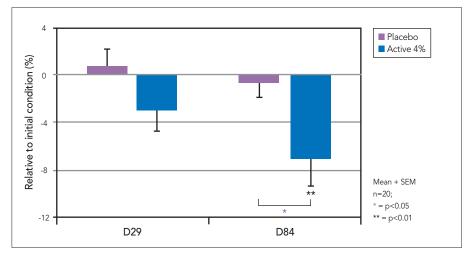


Figure 5: Application of an emulsion with 4% active significantly reduces skin blueness. The b* value measurement revealed a reduction in skin blueness of 3% after 29 days and 7.2% after 84 days. The effect after 84 days was significant over baseline and placebo. The statistical values in blue relate to the comparison of active with the placebo, whereas the black values relate to the comparison with the initial condition. Wilcoxon signed-rank test.

beginning of the study (improvement of 1.3 % and 5.3 % respectively; Fig 2). Additionally, the treatment after 84 days showed significantly better results even as compared to the placebo treatment, which did not produce a beneficial effect. The maximum height of the roughness profile (Rz) measurement showed an improvement of 1.3% after 29 days and 4.9% after 84 days respectively (data not shown), which is in agreement to the previously mentioned data.

Dark circles

The skin colour change was addressed by conventional chroma meter measurement. It revealed that application of 4% active had a significant lightening effect on the eye area, increasing over time (Fig 3). The results revealed a significant enhancement over baseline and placebo.

Additionally, skin redness was significantly reduced during treatment with 4% active. The results showed a reduction of 8.7% after 29 days and 7.3% after 84 days (Fig 4). In addition to this, skin blueness was reduced strikingly during treatment with 4% active. The results showed a reduction of 3% after 29 days and 7.2% after 84 days (Fig 5). In summary, the lightening effect combined with the reduction of the skin redness and blueness reveal an obvious improvement in the eye area appearance, which can be seen from Figure 6.

Photographic documentation

To underline the results obtained, macro photographs were taken. Figure 6 shows a representative image of subject number 21 at the beginning of the study and after 84 days of treatment with 4% active. The overall eye appearance was improved. Particularly noteworthy is the reduction of the visibility of capillary veins, which stand out through the delicate skin in the periorbital region (lower black arrows). Additionally, the dark skin regions are visibly lighter (upper black arrows).

Discussion and conclusion

Today's insanely fast-paced world combined with unhealthy lifestyle choices leave their visible traces, in particular, around our eyes. Dark circles and puffy eyes can make even the most dynamic people look dull and tired. Sleep problems, allergies, exhaustion or inherited features are just some of the factors responsible for dark circles and swollen eyes. In general, in the advanced ageing process, the tissue and muscles surrounding the eyes weaken, and protruding fat tissue contributes to the swollen appearance. Sooner or later, time or better said long days and restless nights take their toll. Concealers may camouflage the darkness under your eyes but unfortunately, they cannot addresss the problem of a swollen eye area. For this, it is necessary to analyse and treat the problem at its roots. Rahn has developed Slimexir to tackle the problem of fat excess, fluid retention and sagging skin. Application of Slimexir may significantly reduce discolouration and puffiness in the eye area. The overall eye appearance is visibly rejuvenated after 84 days of treatment.

The mechanism behind Slimexir's mode of action is based on three different approaches (Fig 7). The sophisticated mix of xanthines in X-Melt inhibits maturation of pre-adipocytes into adipocytes probably via inhibition of the CCAAT / enhancer binding protein and the peroxisome proliferation active receptor PPARy.^{5.6} Additionally, it may be supported by inhibition of the AMPK/MAPK-signalling pathway during the early stage of adipogenesis.⁷ In this way, lipogenesis is reduced and less fat is stored in the adipocytes. Furthermore, lipolysis is activated via a cyclic adenosine monophosphate (cAMP)-dependent pathway.⁶ Here, we have been able to show that X-Melt and artichoke extract successfully trigger the fragmentation and decomposition of lipid droplets and activate the breakdown of any existing fat.⁶ The postulated mechanism works via phosphodiesterase inhibition and perilipin phosphorylation. Briefly, the decomposition of fat is controlled via the content of the messenger substance cAMP in adipocytes. Under normal conditions, the level of cAMP is kept low as the enzyme phosphodiesterase breaks down the cAMP into AMP, which prevents the activation of this process. An increased cAMP level leads to activation of the cAMP-dependent protein kinase A (PKA). Two PKA phosphorylates, namely perilipin, a protein envelops the fat vacuoles and prevents fat degradation, and hormone sensitive lipase (HSL), an enzyme, degrades triacylglycerols into free fatty acids. Phosphorylation induces two simultaneous effects. Firstly, perilipin



Figure 6: Application of emulsion with 4% active visibly brightens the eye area. Representative picture of test subject number 21 at the beginning of the study and after 84 days of treatment. The eye area appears brightened and rejuvenated. Black arrows indicate the lightening effect of the dark regions and reduction of the visibility of capillaries.

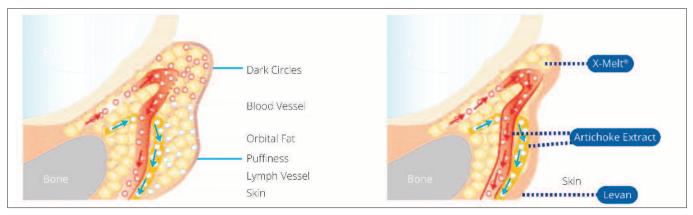


Figure 7: Slimexir's triple mode of activity. X-Melt reduces lipogenesis and induces the degradation of fat. The artichoke extract stimulates the cutaneous microcirculation and improves removal of the decomposed fat and excessive interstitial fluid, including degradation products of haemoglobin. The high molecular weight levan provides a firming film on the skin. It fights dark circles and swelling in the eye area.

changes its spatial structure and becomes a docking station for the activated HSL, leading to fat degradation. Secondly, the fat vacuole fragments into thousands of tiny lipid droplets. The enlarged surface area of the lipid droplets additionally facilitates the ability of HSL to gain access.⁸⁻¹⁰

The sophisticated mixture of xanthines in X-Melt outperforms the current reference substance, caffeine, in inhibiting lipogenesis and activating lipolysis. Furthermore, the artichoke extract promotes drainage and removal of haemoglobin degradation products via the lymphatic system and at the same time removes fatty acids via vascular system. The accumulation of interstitial fluid (oedema) is significantly reduced (data shown in Noticias de Cosmética y Perfumeria Issue 361, in press May/June). The large levan molecules with many lateral chains form a film on the skin ensuring surface firmness and preventing sagging skin induced by volume reduction. The eye area appears bright and rejuvenated.

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