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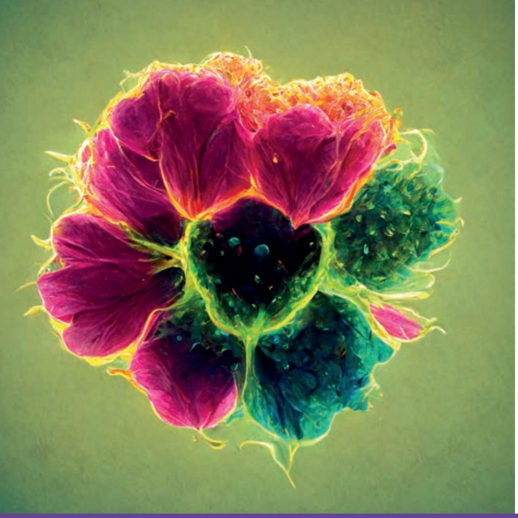

Image created by Provital through an independent research lab that uses Artificial Intelligence to expand the human imaginative power (Midjourney).

Dermohacking Senescence with a New AI-proven & Biotech Ingredient

C. Vigo Xancó, S. Bouhrir E. Escudero, D. Manzano

Modern science has opened a variety of new ways to improve survival and quality of life. Meanwhile, the recent movement towards preventative health among the ever-increasing mature segment of the population, has boosted the emerged success of new healthcare concepts such as biohacking. This one-health movement goes hand in hand with unprecedented scientific advances appearing in the anti-aging field, particularly for cellular senescence.

As these new advances on cellular senescence take ground in the scientific community, the beauty industry can better tap into the opportunities that this longevity era can offer.

In this regard, Provital is taking the lead in a new type of cosmetics that will leverage technology, science, natural and holistic preferences to push the boundaries on efficacy and selectivity, while still supporting an environmentally friendly brand positioning: Dermohacking cosmetics.

Altheostem™ is Provital's first ***dermohacker***. An *Althaea rosea* stem cell active that has proven its ability to selectively eliminate cellular senescence.

This lab-grown active ingredient leverages biotechnology for a selective biological action on aged skin. In this article, Provital describes how the positive effects of its senolytic activity are thoroughly tested *in vitro* and *in vivo*, using both instrumental and Artificial Intelligence analysis, thus unveiling its well-aging power.

Welcome to DERMOHACKING COSMETICS

Humans have long harboured an obsession with living forever, but not at any price. Ever since some of humanity's oldest tales, one of its deepest desires has been to attain everlasting life [1]. Now, modern science has opened up a variety of new ways to improve survival and quality of life, and members of the technology-driven ultra-rich are adopting these new approaches in an attempt to extend and enjoy their own lives for longer.

That longstanding appetite for life intensifies along with a worldwide population ageing phenomenon. As this is a large, growing and relatively affluent demographic, older consumers offer a great chance for innovation to cater to their special demands, where health takes a central stage and the approach to well-aging is holistic, seeking balance in body and mind with wider lifestyle choices that include supplementation, exercise, diet, beauty products and therapy. In response to the increased interest in this type of "healthy fix" for ageing among older consumers, manufacturers across consumer health have taken different approaches to leverage preventative health.

With this recent trend in preventative health, new terms and movements are leading innovations in healthcare. Biohacking, for example, is a term that is getting more and more popular amongst healthcare. It basically refers to the reasoning behind the health benefits one can achieve by employing certain changes in daily habits. It details how these little "hacks" to our own physiology can affect our aging process, and how technology can make them feasible.

The emerged success of the biohacking concept in healthcare goes hand in hand with the unprecedented scientific advances that are occurring in the anti-ageing field, particularly with the discovery that the rate of ageing is controlled by genetic pathways and biochemical processes conserved in evolution – such as cellular senescence [2]. As this relation between ageing and cellular senescence becomes established in the scientific community, the beauty industry can better tap into the opportunities that the longevity era and the innovation-eager consumer offer.

In this regard, Provital is taking the lead in a new type of cosmetics that will leverage technology, science and natural preferences to push the boundaries on efficacy and personalisation, while still supporting an environmentally friendly brand positioning: Welcome to ***Dermohacking*** **cosmetics**.

· Dermo-like Science ·

When further analysing the current proactive approach to health, we see that the consumer is looking for efficacy and results. This aligns with the notable growth that dermocosmetics segment has experienced in the last years, where brands leverage science-backed claims, which subsequently gives them a greater perception of safety, efficacy and transparency. Now that the dermocosmetic user tends to be younger, digitally-savvy and have more natural preferences; clean beauty, plant-based, traditional medicine-based, and doctor-founded brands can overlap with dermocosmetic consumers' demands by combining the perceived safety of their natural origin with new powerful science-backed claims.

· Technological Hacking ·

At present, personalisation is only about using technologies like AI, AR, and VR to guide consumers to personalised advice or product matching. However, it is through selective mechanisms of action that a beauty product will be able to address the specific needs of each person's skin by selectively 'hacking' the damaged cells. Plus, through a specifically designed biotechnological obtention, an ingredient can tackle both sustainability and technological advances to achieve the desired specific effect.

Altheostem™ (*Althaea rosea* stem cells active) appears as a new kind of well-aging ingredient that blends both dermocosmetic and biohacking concepts: A new plant stem cell-based active that selectively eliminates skin cellular senescence.

1. Sustainable lab-grown ingredient: *Althaea rosea* petal stem cells

As introduced above, the new ingredient launched by Provital is sustainably obtained from lab-grown stem cells derived from the flower petals of *Althaea rosea*. This eco-responsible biotechnological obtention method allows the preservation of the flower's environment in nature, a full traceability of the raw material, and a production process that consumes less water; thus, providing this active ingredient with superlative ecological standards such as Vegan-compliance, COSMOS-Approved and 100% Natural Origin (ISO16128).

2. Selective mechanism of action: Leading-edge senolytic activity

Cellular senescence is a stress response to damaging inputs such as genotoxic or oxidative stress, telomere shortening, DNA injury or mitochondrial dysfunction, which results in irreversible resistance to apoptosis. Although it is a normal and healthy cellular response in young tissues, the accumulation of senescent cells over time has deleterious consequences in some critical physiological processes [3,4]. In fact, senescence is considered one of the most important hallmarks of ageing, and one of the reasons why human skin develops certain age-related alterations in elastic fibre morphology, facial wrinkles, and perceived age [5,6]. So, senescent cells are occupying a spot while not participating positively in the maintenance of the healthy skin tissue; they are a hindrance for a young skin tissue.

It is not surprising then that cell senescence, and the inflammatory factors that follow it – known as the senescence-associated secretory phenotype (SASP) – are widely studied in pharmacology as treatment targets. In the anti-ageing field, the strategies followed when attempting to block the negative effects of senescent cells can be classified as *Senomorphic* (when the objective is to supress the SASP phenotype) and *Senolytic* (when the target is the selective elimination of senescent cells).

Although senolysis is an emerging anti-ageing pharmacological strategy, its use in the cosmetic field is still very limited; yet the skin was one of the first organs in which senescent cells were identified [8]. In fact, it may contain up to 55% of senescent fibroblasts [9], whose specific type of SASP has shown unique features related to various skin ageing and homeostatic processes other than the common features such as pro-inflammatory and matrix-degradation phenotypes [10].

Provital saw the scientific opportunity that this represented and embarked upon the development of a new biotechnological plant ingredient that displayed senolytic activity in dermal fibroblasts to ultimately provide a cosmetic formula with an effective way of prolonging the skin's youthful and healthy state.

2.1 *In vitro* methods

To evaluate the leading-edge senolytic activity of the ingredient, Provital performed various assays that demonstrate how the active selectively reduces the viability and the number of senescent Human Dermal Fibroblasts (HDFs) by inducing their apoptosis, and how such activity is transferred into certain biological pathways of the skin.

These experiments allowed the quantification and double-substantiation of the senolytic activity thanks to the use of two different HDF senescent models.

- First, HDFs were induced with H_2O_2 to cause extrinsic cell senescence. Then, these chemically induced senescent cells were treated with different concentrations of Altheostem™. Their viability was then analysed by quantifying the ATP levels. On the other hand, the number of senescent cells was quantified by the proportion of β-galactosidase-positive cells.
- Furthermore, a second type of senescent model was used to quantify the selective induction of apoptosis on senescent HDFs. In this case, the replicative model of cellular senescence was used, where HDFs from a young donor were continuously subcultured, until they lost their division capacity and showed a previously defined senescent marker [9]. Then, these naturally induced senescent cells were treated with different concentrations of Altheostem™ and two different apoptotic markers were quantified.

2.2 *In vitro* results

All the measurements of Senescent HDFs were compared to Normal HDFs, which were the same cell lines that had not been induced for any kind of senescence.

The resulting *in vitro* analysis is featured in the poster "*Senolysis, a cutting-edge strategy for healthy skin ageing, is activated by Althaea rosea stem cells*" [5], which was ranked among the Top 10 best posters at the IFSCC Congress 2020 in Yokohama (out of a total of 367 exhibited); and could be summarized as:

2.2.1 Dose-dependent senolytic activity:

β-galactosidase is a known and specific biomarker for senescent cells [8]. So, it is no surprise to see how senescent HDFs show a dramatic increase in the proportion of β-galactosidase-positive cells **(Figure 1)**. The interesting part of this graph is that this proportion decreases as the concentration of the active increases, thus indicating a dose-dependent reduction in the number of senescent cells.

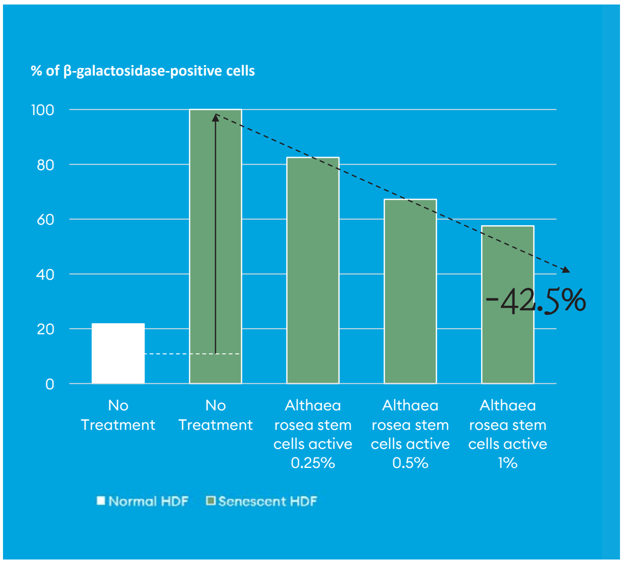

Fig. 1 The proportion of β-galactosidase-positive senescent cells diminishes proportionally to the increasing dose (%) of *Althaea rosea* stem cells active.

2.2.2 Selective elimination of senescent cells:

The other viability evaluation performed with the *Althaea rosea* stem cells active was the quantification of the ATP levels of the senescent and normal HDFs. To this end, **Figure 2** shows how it significantly reduces the viability of senescent cells at any of the assayed concentrations (ranging from 0.5 to 1%); and, even more importantly, the differences in the reduction detected in the viability of senescent and normal HDFs were statistically significant at all the assayed concentrations and go down to 44.5% when treating with the active at a dose of 1%. This not only proves that such effect is selective to senescent cells, but also shows a dose-dependent activity.

2.2.3 Selective apoptotic effect on senescent cells:

One of the identifying phenotypes of senescent cells is their resistance to apoptosis. In fact, a proposed mechanism to evaluate the activity of the senolytic compounds is their capacity to induce the apoptosis of senescent cells, often by upregulating pro-apoptotic molecular pathways.

In the case of the analysed active, the analysis of the apoptosis was first performed through the quantification of the levels of phosphatidylserine exposure (a biomarker of apoptotic early events) on the surface of the senescent HDFs treated with different concentrations of the active. The results were compared with those obtained in normal HDFs and showed that, while normal HDFs remained the same, the treatment of senescent HDFs with the active increased the apoptosis levels by 36% at highest concentrations, thus indicating a selective induction of apoptosis for those formerly resistant to it.

Such selectivity was also observable thanks to the evaluation of a second marker of apoptosis, the activation of Caspase-3/7 analysed by high-throughput automated imaging acquisition and high-content screening **(Figure 3)**.

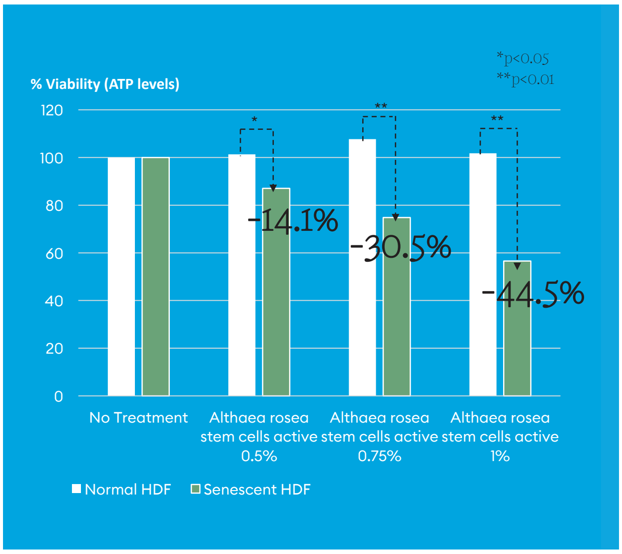

Fig. 2 The viability of senescent cells is significantly and selectively reduced by treatment with the *Althaea rosea* stem cells active.

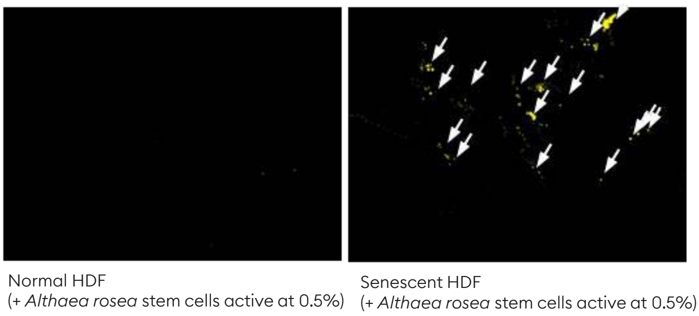

Fig. 3 Images showing Caspase-3/7 activation events (Apoptosis biomarker) thus proving that induction of apoptosis is only observable and quantifiable on formerly resistant-to-apoptosis senescent HDFs.

2.2.4 Positive anti-ageing outcomes resulting from Senolytic activity on the skin

To further evaluate the biological relevance of the recently discovered senolytic activity of the active in the context of its potential anti-ageing application [7], a gene expression analysis of relevant genes involved in Extracellular Matrix (ECM) remodelling was performed. For this purpose, the expression levels of certain genes on natural aged HDFs (from an old donor) treated or not treated with the active were compared.

The results in **Figure 4** show a clear induction of the genes involved in the formation of the extracellular matrix, including COL1A2, ADAMTS2 (both involved in collagen formation), HAS3 and FBN2 (involved in hyaluronic acid and fibrillin biosynthesis, respectively). Conversely, genes involved in extracellular matrix degradation such as the metalloproteinases MMP7 and MMP9 and the pro-inflammatory factor GM-CFS are strongly repressed [11].

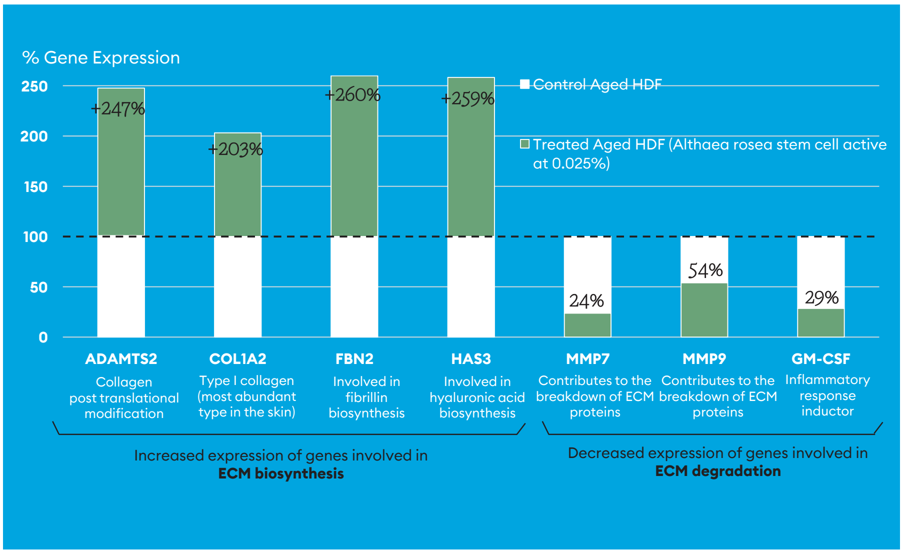

Fig. 4 The activation of senolysis promotes the right modulation of the expression of genes involved in the ECM remodelling of senescent HDFs

Altogether, these *in vitro* results strongly suggest the positive outcomes that the senolytic activity of the *Althaea rosea* stem cells active exerts on ageing skin cells.

3. Quantifiable well-aging power: Clinical study strengthened by Artificial Intelligence

3.1 Clinical methods

- Instrumental analysis:
  A panel of 70 healthy female subjects, aged between 45 and 65 years were studied in a double-blind *in vivo* study. A formulation with 2% Altheostem™ was applied by 35 volunteers, and 35 applied the placebo, (according to a previously defined randomisation list) and efficacy tests were performed after 28 and 56 days of treatment.

  The methods and instruments used for the different parameters studied in this part of the study were:
  – Spectrophotometer/Colorimeter CM-700D
  – Cutometer®
  – Ultrasound analysis
  – Skin Profilometry (Primos 3D analysis)

- Artificial Intelligence analysis:
  The Visual Apparent Age of the same panel of 70 healthy female subjects was thoroughly studied *in vivo* thanks to a cutting-edge and highly reliable system based on Artificial Intelligence. This age estimation module consists of a Machine Learning system that, based on Image Data, predicts the age of subjects in a controlled environment. To create an efficient system for apparent age estimation, an ensemble of different convolutional neural networks (CNNs) was used. The latter works together to extract information from each of the analysed pictures. The age detection model was initially trained using 55,134 images from 13,617 subjects with ages ranging from 16 to 77 years old. The source data in Provital's study consists of 207 videos showing the evolution of the subjects during different stages of treatment (D0-D28-D56). These videos were recorded in Full HD at 30 frames per second (FPS) and have an average duration of 36 seconds, with a total of 223,560 images analysed. These CNNs firstly isolate and crop the subject's face from the image to eliminate possible background noise with a face detector, and then that portion of the image containing the subject's face is fed to 3 different models that estimate the age of the subject **(Figure 5)**.

3.2 Clinical results & discussion

3.2.1 Instrumental Analysis:

The results at day 56 of the various instrumental tests performed prove that the active significantly promotes:

- +8.5%* Healthy glow
  The active provides 7.4% more skin radiance than the placebo after only 28 days, a difference that keeps on increasing until the last day of this clinical assay, providing the significant improvement expressed above in the glowing appearance compared to the placebo.
- +16.8%* Elastic recovery (ability to recover the skin's original position after deformation)
- -18.6%* Skin sagging (uplifting and moisturising properties)
- +17.9%* Biological elasticity (balanced composition of the skin's elastin fibre network)
  The active showed a statistically significant effect in all three elasticity parameters after 56 days of treatment and compared to the placebo. However, it already provided a better elastic recovery (12.19%), a significant lifting effect (18.87%*) and improved skin elastic composition (7.98%) after only 28 days of treatment.
- +7.8%*** Skin redensification
  The resulting increase in total skin thickness was impressive: after only 28 days, the ingredient increased dermal and epidermal thickness by 6.4%, which represents a statistically significant difference of 4.8%***vs placebo in that same period. Nonetheless, these numbers almost doubled after 56 days, suggesting that the active reverses the loss of skin thickness associated with age in both

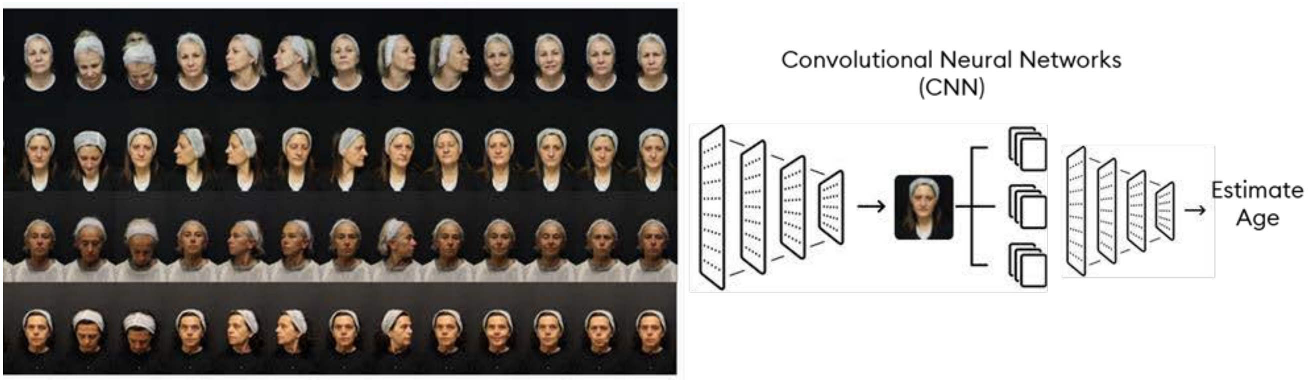

Fig. 5 Age estimation module used for the AI-test. The images in this representation are real examples of some volunteer's cropped faces (extracted and isolated from the videos). Then, each portion of the image containing the subject's face is fed to 3 different models that estimate the age of the subject.

the dermis and the epidermis in a significant and cumulative fashion.

- -13.8%*** Wrinkle depth
  The active significantly decreases wrinkle depth both after 28 and 56 days of treatment, by -8.01% and -13.86%, respectively.
- -6.7%* Wrinkle volume
  It also markedly decreases wrinkle volume down to -2.55% at day 28 and -6.76%

  *[*p<0.05; ***p<0.001; all results expressed as a difference vs the variation of each parameter in the placebo.]*

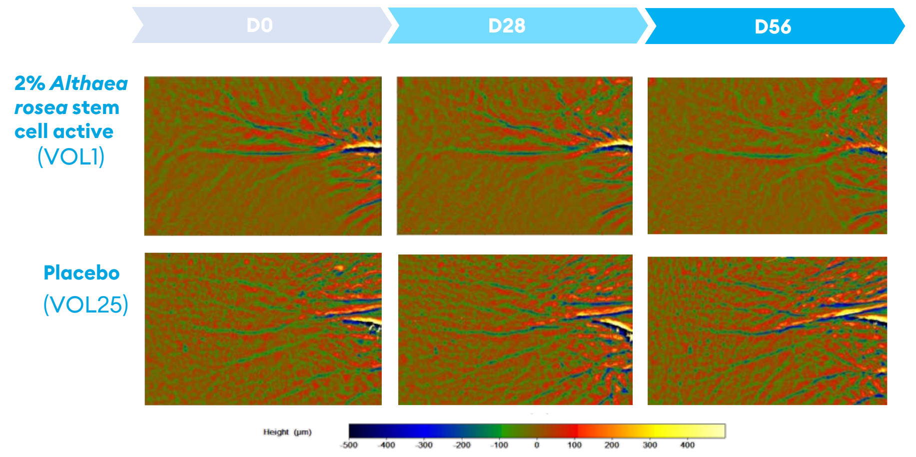

Fig. 6 The active's anti-wrinkle effect is significant and visible (Primos 3D images of two volunteers' periocular area).

- -5.7 years less in the periocular area
  This "X-year less" effect is evaluated by fitting the periocular wrinkle depth data obtained in this study into a reference curve constructed from a large database that links the biological age of female volunteers with wrinkle depth. This estimation shows how the active decreases the average estimated age of the volunteers by 2.8 years and 5.7 years after 28 and 56 days of treatment, respectively, and as always, compared with the placebo.

This remarkable and cumulative anti-wrinkle effect is also visible in the 3D Primos images of the volunteers' crow's-feet area, as can be observed in **Figure 6**.

3.2.2 Visual apparent age based on Artificial Intelligence:

The results obtained from this AI-analysis show how the apparent age decreased by approximately 3.26 years in the group treated with the active at the end of treatment (56 days) vs the group treated with placebo. In fact, the difference was already of 1.04 years less in the treated group than in the placebo group after only 28 days.

It is thanks to this last calculation that Provital could estimate the change in the Visual Apparent Age of all volunteers, thus proving the well-aging power of the *Althaea rosea* stem cells active through Artificial Intelligence.

4. Dermohacking senescence through the eternal power of plant stem cells

In summary, Provital anticipated the effect of the current fervour for life in the ever-increasing mature segment of the population, and combined nature and science to capture the essence of immortality in a brand-new approach to well-aging: Dermohacking Cosmetics.

Altheostem™ (Provital's *Althaea rosea* stem cells active) appears as the first of its kind, blending both dermocosmetic and biohacking concepts in this new plant stem cell-based active that selectively eliminates skin cellular senescence, thus providing the next-level efficacy, selectivity, and sustainability aspects that the global well-aging market demands.

As demonstrated in this article, this active ingredient displays senolytic activity on senescent HDF. This is demonstrated in different cellular senescent HDF models, as well as and using various molecular and cellular techniques (including cell viability, β-galactosidase staining and apoptosis quantification). Such senolytic effect on dermal fibroblasts leads to a series of positive biological consequences for ageing skin.

So, it is by selectively triggering this senolytic mechanism, that Altheostem™ appears as an undeniable 'dermohacker', with such a significant improvement on ageing skin that the apparent age – ultimately calculated for all volunteers using an AI-system – decreases over 3 years on average vs placebo.

References:

[1] *Horton JS, Priest NK*. No Title. The Conversation UK (University of Bath) [Internet]. 2018;(Silicon Valley's quest for immortality – and its worrying sacrifices). Available from: https://theconversation.com/silicon-valleys-quest-for-immortality-and-its-worrying-sacrifices-101405

[2] *López-Otín C, Blasco MA, Partridge L, Serrano M, Kroemer G*. The Hallmarks of Aging Europe PMC Funders Group. Cell [Internet]. 2013;153(6):1194–217. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3836174/pdf/emss-55354.pdf

[3] *Campisi J*. Aging, cellular senescence, and cancer. Annu Rev Physiol. 2013;75:685–705.

[4] *Serrano M*. Ageing: Tools to eliminate senescent cells. Nature. 2017;545(7654):294–6.

[5] *Manzano D, Perez-Aso M, Bosch J, Martínez-Teipel B*. Senolysis, a cutting-edge strategy for healthy skin ageing , is activated by *Althaea rosea* stem cells. Poster presented on IFSCC Congress.2020;1–12.

[6] *Waaijer MEC, Gunn DA, Adams PD, Pawlikowski JS, Griffiths CEM, van Heemst D, et al*. P16INK4a Positive Cells in Human Skin Are Indicative of Local Elastic Fiber Morphology, Facial Wrinkling, and Perceived Age. Journals of Gerontology – Series A Biological Sciences and Medical Sciences. 2016;71(8):1022–8.

[7] *Dimri GP, Lee X, Basile G, Acosta M, Scott G, Roskelley C, et al*. A biomarker that identifies senescent human cells in culture and in aging skin *in vivo*. Proc Natl Acad Sci U S A. 1995;92(20):9363–7.

[8] *Waldera Lupa DM, Kalfalah F, Safferling K, Boukamp P, Poschmann G, Volpi E, et al*. Characterization of Skin Aging-Associated Secreted Proteins (SAASP) Produced by Dermal Fibroblasts Isolated from Intrinsically Aged Human Skin. Journal of Investigative Dermatology [Internet]. 2015;135(8):1954–68. Available from: http://dx.doi.org/10.1038/jid.2015.120

[9] *Lewis DA, Travers JB, Machado C, Somani AK, Spandau DF*. Reversing the aging stromal phenotype prevents carcinoma initiation. Aging. 2011;3(4):407–16

[10] Aging Cell – 2013 – Kim - Implications of time-series gene expression profiles of replicative senescence.pdf.

[11] *Mylonas A, O'Loghlen A*. Cellular Senescence and Ageing: Mechanisms and Interventions. Frontiers in Aging. 2022;3(March):1–10.

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IN & OUT Routine to Prevent Skin Aging

G. Fattorini, S. Zanzottera

abstract

Hyaluronic acid is a very well-known ingredient in the cosmetic market thanks to its beneficial effects on the skin. Usually linked to the specific molecular weight, the biological effectiveness can be reached by different stimulations related to a wide range of molecular weights, able to mimic the biology and the skin tissues requirements ensuring a targeted and broad-spectrum action. The present paper aims to demonstrate the efficacy of a specific sodium hyaluronate, based on Full Spectrum Technology, in counteracting skin aging signs when administered in an IN&OUT beauty routine: as an ingredient of a cosmetic product and as the main constituent of a food supplement.

Introduction

The "Nutricosmetics" word [1] is becoming more and more popular among both consumers and in the scientific community. It can be defined as "any ingredient or product for oral intake (food supplements or functional drinks) with known benefits for skin, hair and nails and with the aim of improving their appearance from the inside, integrating any physical deficiencies". One of the most important purpose is to delay aging, helping to protect the skin from the physiological aging activity and exposome.

In addition, this market segment turnover is constantly growing, with a global forecast over 12 billion dollars by 2030, recording a CAGR over 8% in the period 2022-2030 [2]. Despite the slowdown in the cosmetic market, linked to the emergency situation from COVID-19, the period we witnessed gave a boost to the segment of Nutricosmetics thanks to a growing interest due to the change in lifestyles.

Constituting a relevant category, among the wider sector of food supplements, nutricosmetics belong to the holistic concept where a state of inner well-being is closely linked to the aesthetic appearance. More than ever, consumers are looking for solutions to slow the signs of aging with less invasive tools, such as plastic surgery, requiring treatments that are easy to integrate into the daily personal care routine and to achieve results within a short-time.

Despite being a discipline dating back only to the last twenty years, there are numerous studies in the literature that show a significant correlation between the adequate intake of special dietary supplements and the improvement of skin quality [3].

The effectiveness of these benefits increases considerably if, in a combined treatment, specific active cosmetics are used to act on the skin in some "IN&OUT" treatments; that combine the oral intake of food supplements (IN) and the topical application of cosmetic products (OUT) to reduce imperfections and skin damages caused by several factors.

Complementary treatment between cosmetic and nutraceutical products - the IN&OUT approach - represents one of the most valuable aids for the skin, and now it is considered the future trend in the beauty market. Many consumers are inserting beauty supplements into their personal care routine, acting on the same skin condition, through mechanisms of action with a complementary activity, able to achieve the same beauty goals.

The combined activity of cosmetic and topical nutrition treatments can be a valid alternative in all those skin imperfections and pre-pathological situations, in which often invasive pharmacological treatments are used with potential major adverse effects.

The IN&OUT approach dedicated to specific targets, through different mechanisms of action, complementary and sometimes even synergistic, allows an enhanced activity of nutraceutical and cosmetic ingredients, going even beyond the plateau of individual treatments and, achieving high-level results without contraindications.

The evolution in hyaluronans technology

The cosmetic hyaluronans industrial production has been going under many changes in the past decades, from the animal extraction of rooster combs to the supervised biofermentation by bacteria such as *streptococcus* or *bacillus species*. The control of biotechnological production parameters allows to obtain a specific quite narrow range of molecular weights.

Usually, hyaluronans have different biological activities, linked to the specific molecular weight, but for a biological effectiveness, it is therefore important to ensure the availability of a coexistence of molecular weights – a wide range of molecular weights – able to mimic the physiology and the requirements of skin tissues and to ensure the exercise of a targeted and broad-spectrum action.

In effect, it has been observed that a cell submitted to LMW HA can react in a complete opposite manner of a HMW HA. Studies on mesenchymal cells showed that an inflammatory reaction induced by LMW HA could be opposed to an anti-inflammatory reaction linked to the presence of HMW HA [4].

ROELMI HPC has confirmed these observations with the development of the *Full Spectrum technology* (HA Tech 2.0®) which allows to obtain a spectrum of sodium hyaluronate molecular weights for specific and effective applications through a fine modulation of fermentation parameters: the PrincipHYAL® Line, biotechnological ingredients that reproduce a specific spectrum of molecular efficacy, with a targeted focus on the skin:

- PrincipHYAL® Difference: a wide spectrum of molecular weights studied to get long-term anti-aging effect on the skin. It helps to decrease skin wrinkles volume, to improve skin elasticity, smoothness, by diminishing roughness, scaliness & number of wrinkles. Skin complexion is improved, with a good moisturization and skin barrier strength.
- PrincipHYAL® Cube³: a wide spectrum of molecular weights studied to get short-term lifting effect with a proved efficacy of carrier for both lipo- and water-soluble ingredients;
- PrincipHYAL® Aurora: a proved regenerating and wound-healing effect for a completely new skin;
- PrincipHYAL® Signal-10: quicker permeation than classic form of hyaluronans for an immediate effect of moisturization and elasticity

These actives, based on determined spectrum of molecular weights (instead of just one molecular weight), are obtained through the control of different parameters during the biofermentation process. Selected from a screening of several *in-vitro* and *in-vivo* data, they target an accurate cosmetic performance, with surprisingly higher results.

The technology has then shifted to the nutraceutical market with the development of ExceptionHYAL® line to fully integrate in tissues physiology and match biological needs, effectively supporting health, and improving life quality. The members of the ExceptionHYAL® line are:

- **ExceptionHYAL® Star:** targeting skin beauty and anti-aging from within, its rejuvenating effect is quick and visible in 14 days only, with significantly less marked and deep wrinkles. Further, it effectively improves healthy skin parameters, providing hydration, tone and elasticity. It does not only prevent and support skin ageing, but can also help in case of dryer and sensitive skins due to sun/cold exposure.
- **ExceptionHYAL® Blossom:** realized to counteract menopause discomforts.
- **ExceptionHYAL® Wink:** meant to truly support ocular well-being.
- **ExceptionHYAL® Jump:** designed for joint pain reduction and enhanced mobility.
- **ExceptionHYAL® Relief:** created to effectively alleviate unpleasant digestive issues as heartburn and acid reflux.

Efficacy dossier

Skin moisturization

Skin moisturization was measured on the face according to the Corneometer® method, using the Corneometer® CM 825 (Courage + Khazaka, electronic GmbH). Data are reported as mean percentage variation with respect to T0.

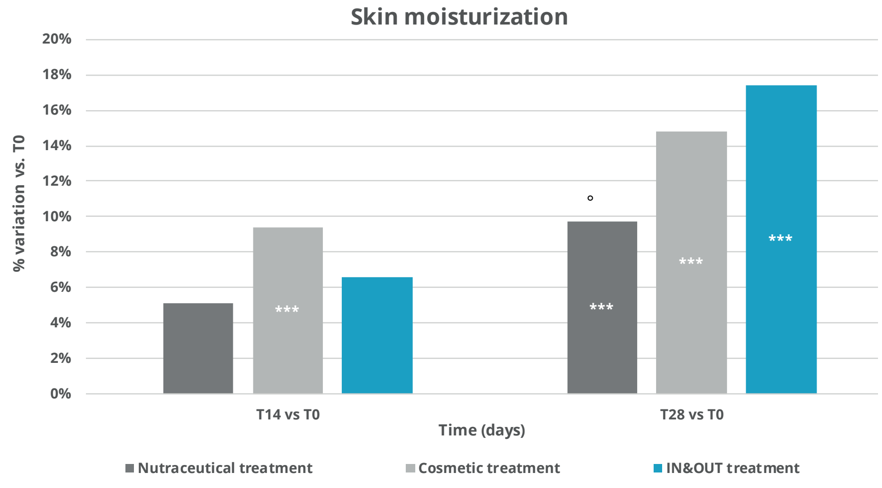

Fig. 1 Skin hydration *(*** p < 0.001 vs. T0, * p < 0.05 vs. T0, ° p<0.05 vs Group 3).*

Topical application and oral intake to improve skin antiaging efficacy [5]

A clinical study aims to evaluate the combined effect of a treatment consisting in: a cosmetic product containing 0.5% PrincipHYAL® Difference and a food supplement containing 200mg of ExceptionHYAL® Star. The study has been performed on the skin anti-aging effect. The evaluated parameters are: skin hydration, skin tonicity/elasticity and skin profilometry.

The two ingredients were administered, alone and in combination, to healthy adult Caucasian female subjects for a period of 4 weeks of products' use, with a 14-day follow-up period using only a placebo cosmetic product. According to a predisposed randomization list, eligible subjects are divided in 3 groups:

- **Nutraceutical treatment:** 25 subjects used placebo cosmetic product + ExceptionHYAL® Star active food supplement
- **Cosmetic treatment:** 25 subjects used PrincipHYAL® Difference active cosmetic product + food supplement placebo
- **IN&OUT treatment:** 25 subjects used the complete active treatment (PrincipHYAL® Difference active cosmetic product + ExceptionHYAL® Star active food supplement)

The results indicated a progressive increment in the skin moisturization, that resulted significant at T14 for Cosmetic treatment ($p < 0.001$) and at T28 for all three groups ($p < 0.001$) with respect to T0. Increased moisturization is perceived also in the 14-day follow-up period **(Figure 1)**.

Skin elasticity and skin firmness

Skin elasticity and skin firmness were evaluated with the Cutometer® MPA 580 (Courage + Khazaka Electronic, Köln, Germany). Skin elasticity was calculated as the R2 ratio (Ua/Uf), that is the ratio between the final deformation (Uf) and the total deformation recovery of the skin (Ua) and indicates the ability of the skin to return to its original state after a stressing event: the closer the value is to 1, the more elastic the skin.

Parameter R0 = Uf, is related to skin firmness: a reduction of such parameter indicates an improvement of the skin ability to oppose to the deformation imposed by the probe during the suction phase.

Skin looks firmer during the treatment and maintained in time in the 14-day follow-up period (data not shown).

Skin profilometry

Skin profilometry was assessed using Primos 3D (Canfield Scientific Europe, BV, Utrecht, Netherlands) and evaluated in terms of wrinkle depth and skin smoothness (expressed as the Ra value). A progressive and significant decrease in the mean

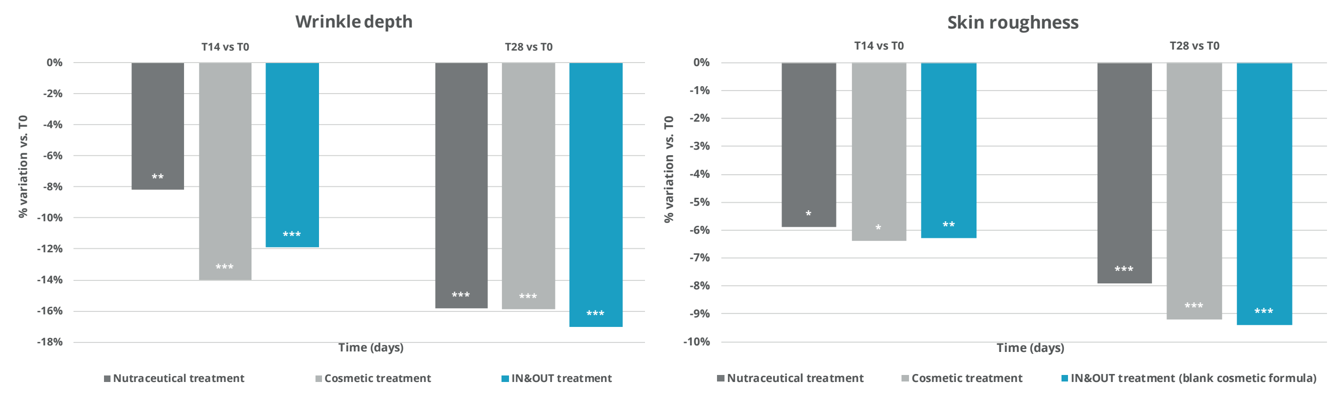

Fig. 2 Skin profilometry *(* p<0.05 vs T0; ** p<0.01 vs T0; *** p<0.001 vs T0).*

wrinkle depth and in the Ra value was observed throughout the treatment period for all three groups, showing a peak at T28.

IN&OUT combination program provided better results than single treatments (cosmetic use or nutraceutical supplementation only) in ameliorating aging-related clinical signs **(Figure 2)**.

Conclusions

The mechanisms of action involved concern the skin well-being, by preventing the natural aging process.

Groups of volunteers treated with either the cosmetic product alone or the nutraceutical alone showed good results compared to the placebo or the initial test time, demonstrating the efficacy of the administered active ingredients. In addition, the groups enrolled with combined treatments (IN&OUT) showed higher improvements, effectively demonstrating that the topical application together with the oral intake represents a high performance, which could open up new market opportunities and innovation.

2.0 Full Spectrum Hyaluronans are the ultimate approach to skin health and anti-aging from both topical applications and oral intake. The combined synergy of Hyaluronans-based actives is the advanced solutions for quick, positive and permanent results.

Designed to mimic skin natural biology, 2.0 Full Spectrum Hyaluronans fully integrate in tissues cellular processes, enhancing skin properties. The IN&OUT approach extends improvement over time, empowering beauty from within, thanks to the renewed biological memory built by orally taken Hyaluronans.

The active cosmetic product is exclusive distributed in Germany by S. GOLDMANN GMBH & CO.

References:

[1] *Dini I, Laneri S.* Nutricosmetics: A brief overview. Phytother Res. 2019 Dec; 33(12):3054-3063. doi: 10.1002/ptr.6494. Epub 2019 Sep 3. PMID: 31478301.

[2] Nutricosmetics Market Outlook 2022-2030, Future Markets Insights (FMI)

[3] *Sun Q, Wu J, Qian G, Cheng H.* Effectiveness of Dietary Supplement for Skin Moisturizing in Healthy Adults: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Frontiers in Nutrition (9) 2022

[4] *Kothapalli D, Zhao L, Hawthorne EA, Cheng Y, Lee E, Puré E, Assoian RK.* "Hyaluronan and CD44 antagonize mitogendependent cyclin D1 expression in mesenchymal cells"; J. Cell Biol. (2007); (176): 535.

[5] *Carlomagno, F.; Roveda, G.; Michelotti, A.; Ruggeri, F.; Tursi, F.* Anti-Skin-Aging Effect of a Treatment with a Cosmetic Product and a Food Supplement Based on a New Hyaluronan: A Randomized Clinical Study in Healthy Women. Cosmetics 2022, 9, 54. https://doi.org/10.3390/cosmetics9030054

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Austrian Natural Astaxanthin – a Unique Active Ingredient for Biological Cell Protection

E. Willeit

abstract

As life expectancy continues to rise, healthy ageing is on everyone's lips. We strive for eternal youth by maintaining general physical health, wellbeing and the natural functionality of our skin to avoid visible signs of age. A Sisyphean task because we cannot stop the ageing process of our body and skin, but we can positively influence and delay it through preventive strategies. Antioxidants play a very important role to inhibit ageing. The most effective antioxidant is astaxanthin which, due to its biological potential of cell protection, is considered the strongest natural antioxidant. Therefore, it is the perfect choice as anti-ageing ingredient since it acts as a protective shield to reduce environmental stress and skin ageing. Numerous clinical studies have already revealed its positive effects on skin ageing processes due to its unique molecular structure. BDI-BioLife Science can prove the effects of astaxanthin with in-house human clinical studies in the field of cosmetics with its branded active ingredient, an oleoresin with an astaxanthin content of 5%.

As protective shield, the skin is constantly exposed to external environmental influences and stress caused by internal factors such as athletic exertion and external factors such as UV rays. To maintain and support the skin as a protective barrier, numerous active ingredients are used in cosmetics. As part of these active ingredients, antioxidants can neutralise stress factors in the skin and can offer protection against those toxic substances. There is a variety of antioxidants such as vitamin C and coenzyme Q10, but natural astaxanthin has proven to be nature's most powerful antioxidant yet discovered, with properties that by far surpass all its peers. In direct comparison, astaxanthin is 6,000 times more powerful than vitamin C and 100 times more powerful than vitamin E by neutralising singlet oxygen [1].

Astaxanthin is not only an incredibly powerful antioxidant, but also unique in terms of how it works in our bodies because it spans the cell membrane to protect the entire cell. The length and shape of an astaxanthin molecule allows it to span the cell membrane, having one end of the molecule in the lipid-soluble part of the cell and the other end in the water-soluble part **(Figure 1)**. This makes astaxanthin distinctively characteristic of being able to protect the entire cell. Astaxanthin has been found capable of flowing throughout the entire body into the bloodstream, to the muscle tissue and skin as well as into various critical organs. This double feature of running through the body and being able to protect the entire cell makes astaxanthin a super-effective antioxidant and an anti-inflammatory agent for humans [3].

Astaxanthin – the red diamond among antioxidants

Astaxanthin belongs to the carotenoid family, more precisely to the xanthophylls. In nature, the red pigment can be found in photosynthetic organisms such as bacteria, algae and yeasts. The highest concentrations of natural astaxanthin can be obtained from the freshwater microalga *Haematococcus pluvialis*. Due to its enormous antioxidant power, astaxanthin is considered the red diamond among radical scavengers and has been proven to be significantly more efficient at counteracting reactive oxygen species (ROS) compared to other antioxidants. Thanks to its unique molecular structure, it is non-pro-oxidative [2].

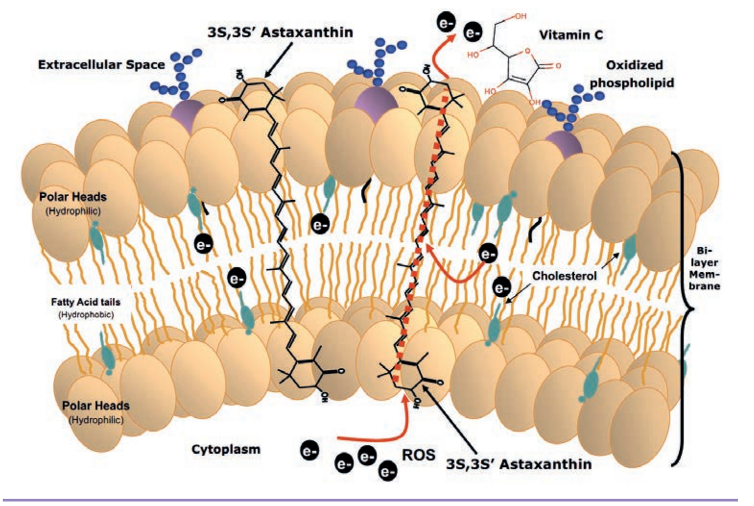

Fig. 1 Astaxanthin spans the cell membrane in a transmembran orientation.

In several human studies, astaxanthin has improved overall skin health and counteracted skin ageing by providing comprehensive protection against ROS-related damage. Positive effects on the human skin have been shown particularly regarding wrinkle depth, elasticity, moisture, age spots and skin texture. Astaxanthin improves skin elasticity by strengthening the collagen layer and revitalises photoaged skin by getting rid of free radicals in all skin layers. Moreover, it positively affects skin health both through supplemental nutrition and topical applications in cosmetics. To increase efficacy, these applications can also be combined [4].

Skin ageing – Principle of cause and effect

Our skin is the outermost barrier against environmental impacts. Whenever the skin is exposed to reactive oxygen species (ROS) and free radicals, oxidative stress is occurring subsequently. Oxidative stress plays a crucial role in human skin damage. When singlet oxygen attacks cell membranes, it activates enzymes that lead to cell death, changes of skin appearance and the onset of active skin ageing processes. Singlet oxygen can also interfere with the DNA, triggering a series of cell processes that ultimately lead to inflammation [5]. Many age-related conditions are caused by increased levels of proinflammatory cytokines and cellular senescence. Due to increased environmental influences in the 21st century, a continuous low level of chronic inflammation increases leading to a gradual erosion of normal cell structure and functioning, which results in enhancing a slow but progressive ageing process also known as inflammageing. When skin structure and function decline, the skin becomes more sensitive and highly vulnerable to oxidative damage [6].

A healthy individual normally has a certain level of antioxidants as natural defence mechanism to prevent free radical formation, maintain oxidative balance and protect the skin against oxidative damage and associated inflammations. However, through ongoing high exposure to ROS in our daily life, not only the barrier function of the skin deteriorates, but also the metabolic activity of cells and the intrinsic antioxidant level decrease, favouring intracellular oxidative stress and subsequent inflammatory reactions.

High daily exposure to free radicals and the decreasing ability to protect ourselves from the formation and effects of these toxic reactive substances create a need to support our bodies in counteracting oxidative stress and subsequent cellular damage. The use of antioxidants in cosmetic formulations is one way to counteract the environmental effects on our skin.

Astaxanthin and its biological cell protection properties

Reactive oxygen species, responsible for extrinsic premature skin ageing, have increasingly aroused interest by the cosmetic industry as the human skin is permanently exposed to a pro-oxidative environment. These ROS are considered toxic derivatives of oxygen and cause skin damage as soon as the organism's defence system is no longer capable of inactivating most ROS.

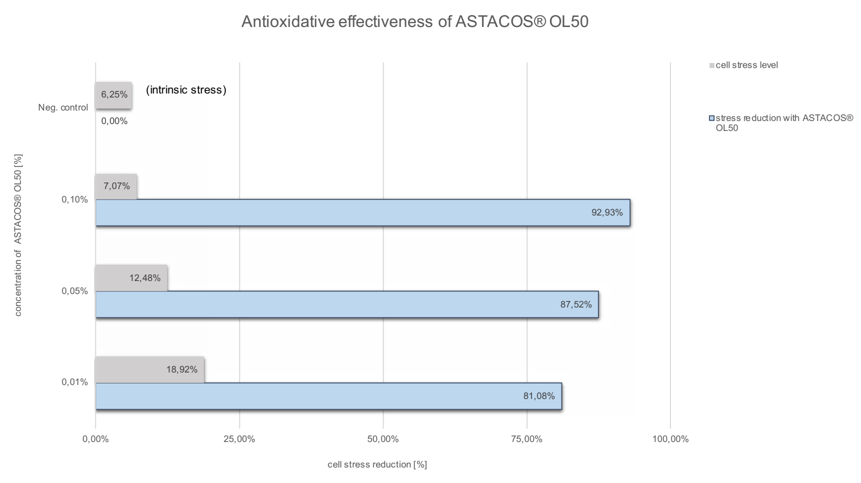

Fig. 2 Cell stress reduction by oleoresin with a content of 5% astaxanthin in different concentrations dissolved in olive oil 24 hours after ROS induction by H_2O_2.

Cells have a natural stress level (6.25% neg. control in **Figure 2**) that increases with exposure to ROS. Enhanced intracellular stress accelerates cellular ageing and promotes age-related skin changes such as wrinkles and age spots. In an *in vitro* study, the influence of oleoresin with a content of 5% astaxanthin regarding antioxidant efficacy against ROS was investigated. To determine the potential antioxidant effect, primary human keratinocytes were treated with 0.01%, 0.05% and 0.1% oleoresin with a content of 5% astaxanthin for 24 hours. After incubation time, 10µM of DCFH-DA (chemical used to detect the presence of oxidative molecules) were applied for one hour. Subsequently, 500µM H_2O_2 were added to induce oxygen radicals (ROS). As a check, untreated cells without induced ROS (negative reference) and unprotected ROS-induced (positive) cells were used. As shown in **Figure 2**, the active ingredient is able to strongly reduce oxidative stress in a dose-dependent manner [7].

Astaxanthin and its anti-ageing properties

Skin dryness, deep wrinkling, laxity, increasing transepidermal water loss (TEWL) and epidermal barrier disorders are typical characteristics of aged skin. Astaxanthin, derived from the microalga *Haematococcus pluvialis*, has proven several positive effects on the human skin, especially on wrinkle depth, elasticity, moisture, age spots and skin texture.

For an *in vivo* study, 20 healthy female test subjects between 24 and 56 years of age (Ø 34) with normal skin were recruited. All tests were performed within one day and conducted on the inner side of the forearms. Test substances 0.05% ASTACOS® OL50 diluted in organic jojoba oil and 100% organic jojoba oil were tested.

To determine skin hydration, the Corneometer MPA 5 CPU was used. The skin roughness (firmness) was measured using the Frictiometer MPA 5 CPU. The results were evaluated using descriptive statistics and the Wilcoxon Rank Test (statistical model to ensure reliable results). The test subjects were instructed not to use any topical preparations on the test areas within a period of seven days before the study until the completion of the study. When the study started, the parameters were determined in the relevant test areas as a negative control sample. Then the test products, 0.05% ASTACOS® OL50 diluted in jojoba oil and 100% jojoba oil, were applied to the corresponding test areas. After 2 hours of incubation time, the parameters of skin hydration and skin roughness (firmness) were measured again in the test zones. Even after a single application of 0.05% ASTACOS® OL50 diluted in jojoba oil, the skin roughness (firmness) and the hydration level of the skin had improved, as shown in **Figure 3** [8].

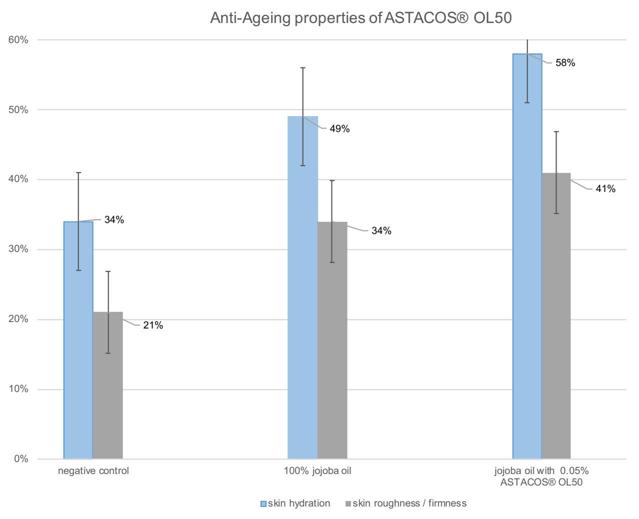

Fig. 3 Significant improvement of skin hydration and reduced skin roughness

In another *in vivo* efficacy study with a serum containing 0.05% of the active ingredient, the effectiveness of astaxanthin was confirmed in an application test that spanned over 4 weeks. A total of 25 female and male volunteers aged between 35 and 72 years (Ø 52.9 years; skin profile sensitive to atopic skin) participated in this *in vivo* study and were supervised and monitored by a dermatologist. All participating subjects were instructed to use only the investigational product once a day and to maintain their usual skincare routine. The subjects reported a significant reduction in wrinkles and lines as well as a reduction in age spots and pigmentation. It is also noteworthy that over 60% of the participants described their skin as finer after completion of the study [9][10].

Conclusions

Numerous research studies have led to the conclusion that astaxanthin can improve overall health of the skin and counteract skin ageing and inflammatory processes. Due to its multiple properties, astaxanthin acts exactly where it is needed and penetrates deep into the skin layers. In particular, protection against skin ageing as well as strong anti-ageing effects can be highlighted. Astaxanthin from microalgae is perfect for the use in leave-on products. When being extracted as oleoresin, the power antioxidant can be ideally incorporated into a wide variety of formulations such as facial applications, pretreatment and cell protection products, as it protects our skin against photoageing and supports anti-ageing.

Fig. 4 ASTACOS® OL50, oleoresin with an astaxanthin content of 5%; *Picture credits: Helmut Pierer*

BDI-BioLife Science GmbH has developed a special COSMOS-certified and NATRUE-approved active ingredient to bring this unique antioxidant into cosmetic formulations. ASTACOS® OL50 **(Figure 4)** is a vegan, animal testing-free ingredient, derived from the microalga *Haematococcus pluvialis*, containing 5% of natural astaxanthin. It has already shown its potential to neutralise free radicals in several *in vivo* and *in vitro* studies and has proven to be an efficient active ingredient for anti-ageing properties. With its in-house astaxanthin competence centre, BDI-BioLife Science supports its customers with expertise in processing and formulating ASTACOS® OL50, confirmed by various frame formulations and scientific dossiers.

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References:

[1] *Y. Nishida, E. Yamashita, and W. Miki*, "Quenching Activities of Common Hydrophilic and Lipophilic Antioxidants against Singlet Oxygen Using Chemiluminescence Detection System," Carotenoid Sci., vol. 11, no. December, pp. 16–20, 2007.

[2] *R. R. Ambati, P. S. Moi, S. Ravi, and R. G. Aswathanarayana*, "Astaxanthin: Sources, extraction, stability, biological activities and its commercial applications – A review," Mar. Drugs, vol. 12, pp. 128–152, 2014.

[3] *B. Capelli, S. Talbott, and L. Ding*, "Astaxanthin sources: Suitability for human health and nutrition," Funct. Foods Heal. Dis., vol. 9, no. 6, pp. 430–445, 2019.

[4] *K. Tominaga, N. Hongo, M. Karato, and E. Yamashita*, "Cosmetic benefits of astaxanthin on humans subjects," Acta Biochim. Pol., vol. 59, no. 1, pp. 43–47, 2012.

[5] *K. Scharffetter-Kochanek et al.*, "Photoaging of the skin from phenotype to mechanisms," Exp. Gerontol., vol. 35, no. 3, pp. 307–316, 2000.

[6] *S. M. Pilkington, S. Bulfone-Paus, C. E. M. Griffiths, and R. E. B. Watson*, "Inflammaging and the Skin," J. Invest. Dermatol., vol. 141, no. 4, pp. 1087–1095, 2021.

[7] D. G.-R. institute for reliable Results, "Physiological/Histological *in vitro* Expertise," no. March, 2021.

[8] Dr. Hauck R&D GmbH, "Efficacy Test *in vivo* conducted with ASTACOS® OL50 (Cosmetic Study)," 2021.

[9] D. G. K. (Institute for E. D. at Witten/Herdecke, "REPORT über einen Anwendungs- und Verträglichkeitstest des Prüfpräparates," 2021.

[10] *T. Seki, H. Sueki, H. Kohno, and K. Suganuma*, "Effects of astaxanthin from *Haematococcus pluvialis* on human skin," pp. 98–103, 2001.

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T(r)opical Retinol Alternative with Added Value

S. Hettwer

abstract

Retinol has a long tradition in cosmetics as an ingredient for acne-prone skin and in the anti-ageing field. Its effectiveness is undisputed. Retinol is well known and in demand among consumers. Since consumers are showing increasing interest in the ingredients of cosmetics and the trend is moving towards sustainability, more and more natural cosmetic active ingredients are in demand. For retinol, an active ingredient from the tropical plant *Maclura cochinchinensis* comes into question here, which has retinol-like effects and is very mild to the skin. In addition, Maclura extract has other positive properties for the skin that retinol does not have.

Introduction

If you suffered from acne vulgaris as a teenager, you know that you do a lot to at least get through this transition emotionally intact. Blemished skin has a huge impact on quality of life and psychosocial well-being. Getting this under control is not easy and is even associated with strong side effects.

A little over 50 years ago, the US FDA allowed the first topical use of a retinoid, namely tretinoin, for the treatment of acne vulgaris [1]. Tretinoin is the commercial name for retinoic acid (vitamin A acid, all-trans retinoic acid). Over the years, derivatives of retinoic acid have been developed to improve both the stability of the active ingredient and the tolerance of the skin to the active ingredient. In the meantime, the 4th generation of retinoid active substances is available. Strong skin irritations such as itching and redness still occur quite frequently. However, they disappear after a few weeks of consistent use or can be treated well with cortisone. The benefit in acne vulgaris is undisputed and typically the skin disease can be completely treated with retinoids.

Over the years of use, other dermatological applications became apparent, such as treatment of atrophic scars, post-inflammatory hyperpigmentation, photo-damaged skin and melasma. Furthermore, a general "skin rejuvenating" effect was observed.

Since retinoic acid is not permitted in cosmetics due to its high pharmacological effect and the strong side effects to be expected, a precursor of retinoic acid, retinol, is used instead. Retinol, together with retinaldehyde and retinoic acid, belongs to the vitamin A family, which is produced from pro-vitamin A (or beta-carotene) in our metabolism. Vitamin A is absorbed into the body through food, as are retinyl esters. The cleavage of the ester directly forms retinol, which is further converted to retinal and retinoic acid. To understand the effect of retinol on the skin, we need to look at the biological processes at the cellular level:

In cells, retinoic acid is considerably more effective than retinol [2]. Retinoic acid binds to and activates specific protein receptors on the DNA, the retinoic acid receptors (RAR) and retinoic X receptors (RXR). Eventually, hundreds of specific genes are activated [3]. Activation of these genes is important for reducing the state of acneic skin, but also provides a rejuvenated appearance of the skin. It is believed that for retinol to be biologically effective, it is first converted to retinoic acid. The binding of retinoic acid to its receptor activates numerous genes in keratinocytes, fibroblasts and sebocytes. They control the regulation of sebum, the quality of the horny layer and collagen synthesis. The uniqueness of retinol lies in the fact that it is an anti-ageing molecule with anti-acne properties.

As a versatile, effective concept for ageing and/or acne-prone skin, retinol has a long tradition in cosmetics. Modern consumers like to buy cosmetics with retinol. They are very sensitive to skin health, prefer multifunctional effects and look for substantial active concepts like retinol can offer.

Since the effectiveness of retinol is based at least in part on its conversion into retinoic acid, it is not surprising that undesirable side effects such as skin redness and itching or a disturbed skin barrier may occur during use. This is preferable during the day, as retinoic acid can be photosensitising. Retinol is therefore often preferred in cosmetics that are applied in the evening or together with a suitable sun protection factor. However, it must be clearly stated that the irritation potential of topically applied retinol is significantly lower compared to retinoic acid.

As consumers increasingly seek milder products that are gentle on the skin barrier, demand for retinol alternatives is on the rise.

For this purpose, we have to look for substances that on the one hand activate the RAR and RXR receptors, but on the other hand do not trigger skin irritations. After intensive research, RAHN-Cosmetic Actives has succeeded in isolating prenylated isoflavones from the tropical plant *Maclura cochinchinensis* as a valuable retinol alternative (SEBOCLEAR™-MP or Maclura extract, INCI: Propanediol, Bioflavonoids).

Results

At first glance, when looking at the molecular structures of retinol and the prenylated isoflavones, no similarities are apparent. Only, both have prenyl groups. In the case of the isoflavones, they are attached to the aromatic rings as functional groups **(Figure 1)**.

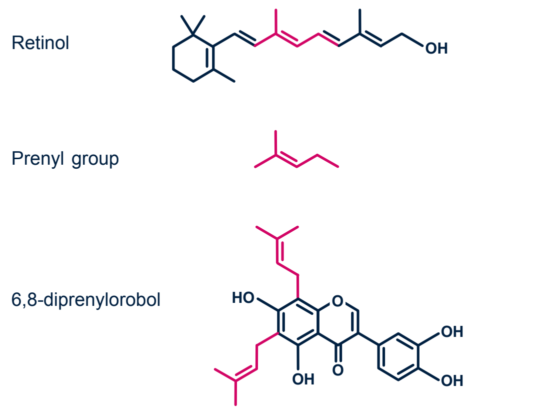

Fig. 1 Molecular structures of retinol and a prenylated isoflavone. Both contain prenyl groups.

Retinol, on the other hand, basically consists of a chain of prenyl residues. It is therefore not to be expected at first that prenylated isoflavones could activate genes with RARE. However, we were able to observe a concentration-dependent, agonistic binding of the prenylated isoflavones to RAR and RXR receptors, which suggests that the corresponding genes can also be activated **(Figure 2)**.

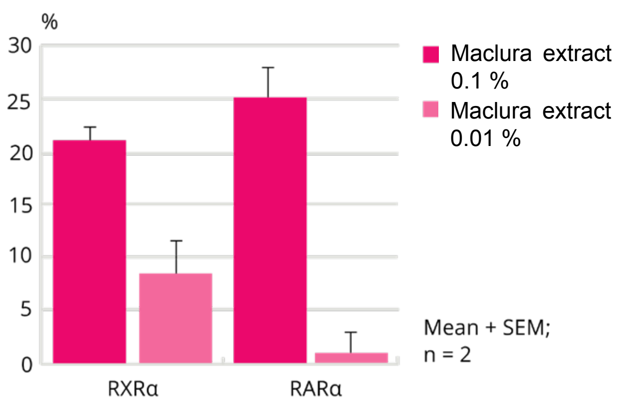

Fig. 2 Maclura extract binds to retinoic acid receptors in an agonistic way.

When investigating the biological efficacy, it became apparent that sebocytes do not develop to the stage of lipid synthesis when the active ingredient is applied. Instead, they remain stuck in a premature stage (not shown). As a consequence, a reduced sebum production of the sebaceous glands can be expected, which was also confirmed *in vivo* **(Figure 3)**. The study with participants having acne-prone skin showed that the application with 3% of Maclura extract led to a strong decrease in the number of active sebaceous glands already after 28 days.

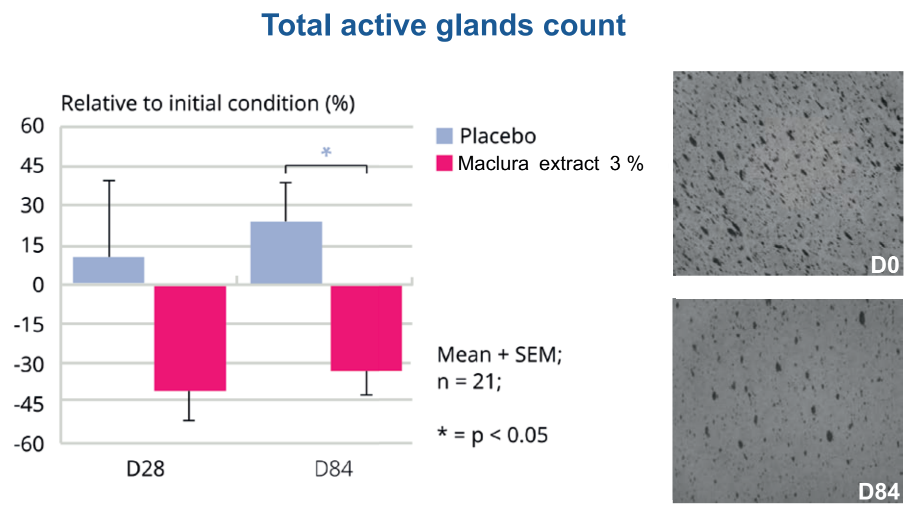

Fig. 3 Maclura extract reduces the number of sebum producing glands.

This resulted in a decrease in porhyrin-positive pores, i.e. *Cutibacterium acnes* infected sebaceous plugs (not shown). There was a clear clearing of the facial skin **(Figure 4)**.

Fig. 4 Maclura extract visibly reduces spots on acne-prone skin.

Sebum is produced by the sebocytes located in the sebaceous glands. The released sebum migrates to the surface of the skin. Excess sebum leads to impure and oily skin, promotes the proliferation of *Cutibacterium acnes* and triggers inflammation. Just like retinol, Maclura extract reduces sebum production, which is the first step in controlling oily skin. In addition, Maclura extract even counteracts inflammatory processes and rebalances the skin's disturbed microbiota **(Figure 5)**. It also inhibits the enzyme 5-α-reductase, which is also involved in excessive sebum production, especially in young men (not shown).

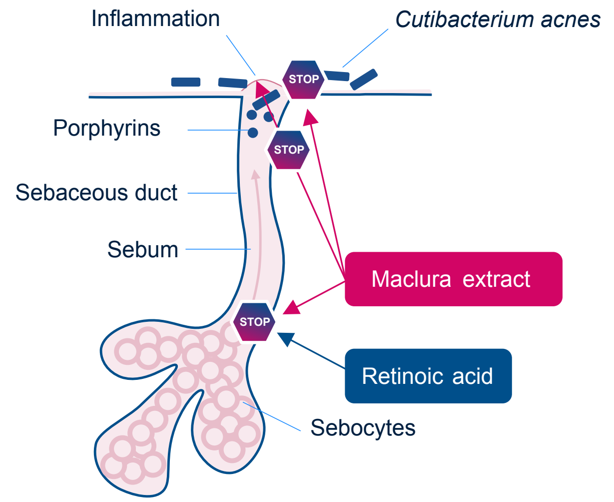

Fig. 5 While retinoic acid's activity is focused on sebum production, maclura extract can address inflammation and *Cutibacterium acnes* as well.

Like retinol, Maclura extract activates retinoic acid receptors and has anti-ageing effects. It increases skin firmness and elasticity, reduces wrinkles and improves skin flexibility, evenness and roughness **(Figure 6)**.

A similar application to effect relationship is shown here as with retinol / retinoic acid. Since the effect is based on a reprogramming of the keratinocytes (and sebocytes), a clearly and sustainably improved positive skin appearance only occurs after 4 weeks or later. When using retinoic acid, there is often even a so-called "burst" in the first few weeks, during which the acne worsens. Only after that, there is a visible improvement. This is not the case with Maclura extract. There is no strong "burst" reaction.

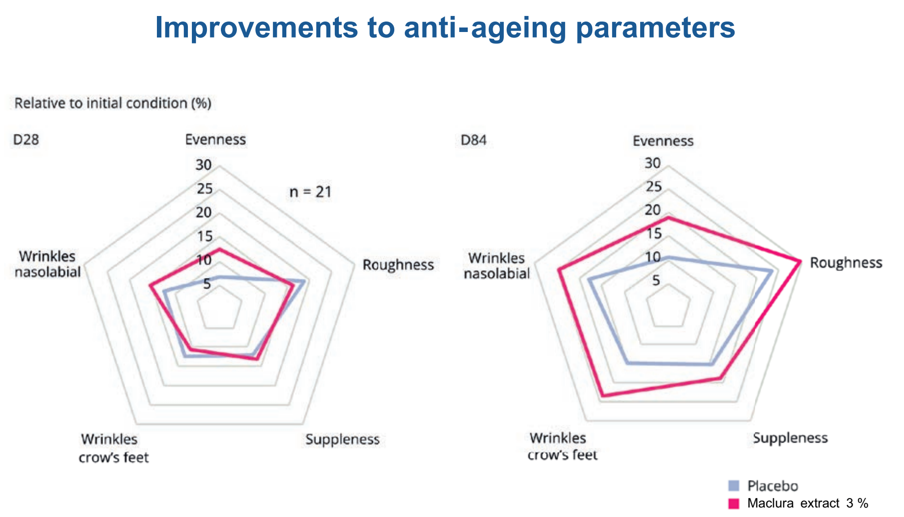

Fig. 6 Maclura extract clearly outperforms placebo in anti-ageing parameters.

Discussion

Maclura extract (SEBOCLEAR™-MP; INCI Propanediol, Bioflavonoids) is the propanediol-based extract from the leaves of the plant *Maclura cochinchinensis*. Only after intensive research, it was possible to specifically isolate three different prenylated isoflavones, including 6,8 diprenylorobol. After exclusion of undesired impurities, a clear, highly active plant extract could be presented. The extract has already been used successfully for several years for acne-prone skin and in the anti-ageing field. Advantages over retinol are as follows: It is a plant-based, water-soluble extract that does not dry out the skin or weaken the skin barrier. Therefore, there is no redness or itchiness with use, or the need to incorporate skin-soothing agents into the formulation to mitigate the irritating potential of retinol. The product is not photosensitive and can therefore be used in day and night cosmetics. Unlike retinol and retinyl esters, it does not have to be converted into an active form by the skin biology. In contrast, it is directly effective and very stable. Furthermore, Maclura extract possesses biological efficacies that retinol lacks: Besides attenuating inflammatory processes (i.e. Maclura extract is already skin-soothing), it acts on 5-α-reductase, a driver of sebum production, as well as *Cutibacterium acnes*, which promotes inflammatory skin processes and the typical acne pimples. Furthermore, it can even be used as a natural deodorant because it slows down the proliferation of corynebacteria in the armpit. The product has received numerous awards. Among others, it received the silver medal at in-cosmetics global 2018 and the bronze medal each at in-cosmetics Asia and Latin America, also in 2018. The product is thus versatile, shows retinol-like efficacy and is a real, natural alternative with the typical RAHN-Cosmetic Actives quality and efficacy.

Parameter	Retinol	Maclura extract
Activates RAR and RXR receptors	X	X
Delays maturation of sebocytes	X	X
Acts on acne prone skin	X	X
Has anti-ageing efficacy	X	X
Acts on the microbiota		X
Acts anti-inflammatory		X
Inhibits 5-alpha reductase		X
Natural origin	(X)[1]	X
Needs to be converted	X	
Can cause irritation	X	
Can cause "break outs"	X	
Photosensitive	X	
Usable in day and night cosmetics		X
Water soluble		X

[1] Recently, natural retinol qualities became available.

Table 1: Comparison of Retinol with Maclura extract

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References:

[1] *Baldwin H, Webster G, Stein Gold L, Callender V, Cook-Bolden FE, Guenin E.* 50 Years of Topical Retinoids for Acne: Evolution of Treatment. Am J Clin Dermatol 2021, 22: 315-327.

[2] *Repa JJ, Hanson KK, Clagett-Dame M.* All-trans-retinol is a ligand for the retinoic acid receptors. Proc Natl Acad Sci U S A 1993, 90: 7293-7297.

[3] *Balmer JE, Blomhoff R.* Gene expression regulation by retinoic acid. J Lipid Res 2002, 43: 1773-1808.

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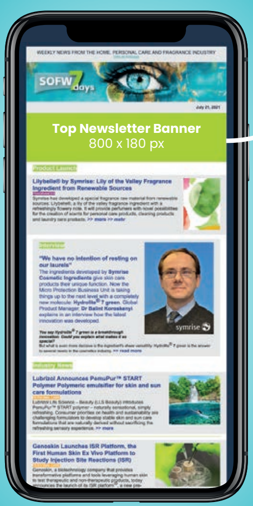


From Hygiene Ingredients to Soothing Solutions, How to Take Care of Acne-Prone Skin

L. Meunier , L. Schmidt , M. Herrmann

Acne-Prone skin is a common concern at any age. It typically manifests with pimples, blackheads, whiteheads, and skin sensitivity, and can appear on the face, back, and chest. In this article, we will discuss two solutions suitable for acne prone skin from different angles: SymClariol® [INCI: Decylene Glycol] which has been evaluated in a cosmetic gel showing improvement of both sebum and pimple; and SymControl® Care [INCI: Water (and) Glycerin (and) *Tetraselmis Suecica* Extract] that has been shown to normalize sebum and sensitivity levels of oily skin, as well as preventing pollution damage by strengthening the skin barrier, improving acne-prone skin comfort.

Introduction

Acne is one of the most common skin concerns at any age, affecting teenagers as well as young adults [1].

Acne prone skin typically manifests with pimples, blackheads, whiteheads, and skin sensitivity, and can appear on the face, back, and chest. One may ask why acne is more common for some subjects than others.

Acne develops when hair follicles get clogged with oils, dead skin cells, and bacteria. The oil, more commonly known as sebum, comes from sebaceous glands. This lipidic film usually helps to protect the skin from pollution and exterior aggression. But when there is too much sebum secretion, it can clog hair follicles and lead to inflammation [2]. In addition, with microorganisms living all over and, in our body, the higher prevalence of sebaceous glands on the face favors the overgrowth of lipophilic bacteria relevant in acne like *Cutibacterium acnes* but also *Staphylococcus aureus*, resulting in an imbalanced skin and leading to skin inflammation [3,4].

Excess of sebum in the hair follicles can form blackheads and whiteheads. With the overgrowth of bacteria, they can become red leading to pimples formation on the skin [5]. That is why manufacturers are looking to manage the sebum production increase of acne prone skin. One market example is Beiersdorf, Eucerin mattifying fluid, which contains salicylic acid and decylene glycol [6] and claims that "*Salicylic Acid has a comedolytic effect and addresses hyperkeratosis […] it also has antibacterial properties. Decanediol further prevents bacterial growth*" [7] that is controlling the oil, reducing redness, and soothing irritation.

In this article, we will discuss two solutions for formulators and manufacturers, that help in caring for acne prone skin from different angles.

Facial hygiene products are helping to limit the overgrowth of bacteria linked to acne formation. Like the bar soap Escudo from Kimberly Clark that claims on its packaging to contain SymClariol®, with an intention for the formulation "*to fight imperfections*" [8]. SymClariol® [INCI: Decylene Glycol], is a versatile cosmetic emollient that supports hygiene concepts by helping to limit the overgrowth of microorganisms from scalp to toe [9]. It balances sebum level and helps to limit the overgrowth of *C. acnes* [10] to maintain a clean and healthy skin.

SymControl® Care [INCI: Water (and) Glycerin (and) *Tetraselmis Suecica* Extract] is a natural and microbiome-friendly ingredient containing the extract of the marine microalgae *Tetraselmis suecica*, originally being isolated from the Mediterranean Sea, now sustainably cultivated under controlled conditions using outdoor solar energy. This ingredient is a sebum and sensitivity normalizer for oily skin, by helping to reduce COX-2 expression in sebocytes, a key enzyme at the origin of sebum production and skin sensitivity. It has previously shown to support the reduction of sebum levels in an *ex vivo* skin model of human sebaceous glands, as well as to prevent pollution damage by strengthening the skin barrier [12]. We will describe here how it contributes to a sebum reduction of all skin tones and balances pores activity of oily skin.

Materials and Methods

Pimple reduction – SymClariol®

The aim of this study is to evaluate the properties of a gel on oily skin. Two cosmetic carbomer gels were prepared, a placebo and a gel containing 2% SymClariol®. A panel of 20 male subjects (17-19 years of age) with oily skin condition was asked to apply the products on their foreheads with a half-side technique, meaning each subject applied both products in parallel.

The number of pimples and pustules was assessed by an expert and the sebum amount was measured using a SEBUMETER at the start of the evaluation (before the application of the product) and after 3 and 4 weeks.

Support of COX-2 expression reduction – SymControl® Care

In vitro modulation by the Tetraselmis suecica extract of prostaglandin-endoperoxide synthase 2 (PTGS2) - also known as cyclooxygenase 2 (COX-2), gene expression was investigated using human sebocytes. This enzyme plays an important role in sebum production but also in skin sensitivity. Primary human sebocytes were incubated with test products for 24 hours, followed by extraction, purification, and reverse-transcription of total RNA.

Sebum level reduction of all skin tones – SymControl® Care

In vivo trials were performed on 2 groups of 15 volunteers with light skin (female and male, phototypes I to III, 19 to 60 years old, with slight to pronounced oily skin), and on 1 group of 30 volunteers with darker skin (female and male, phototypes V to VI, 19 to 40 years old, with slight to pronounced oily skin), with twice daily application of the test products on semi-forehead.

Two hydrodispersion gels were used for each study, a placebo and gels containing 2% and 1% SymControl® Care, for the studies on volunteers with light and darker skin respectively. The products were applied topically twice daily on the semi-foreheads of the volunteers. The sebum level was measured with a Sebumeter® at the start of the study and after 4 weeks of product application. A color mapping of the sebum evolution has then been performed for the study on darker skin, using a scale ranging from 115 to 180 µg/cm^2.

Balances pores activity – SymControl® Care

A proof-of-concept *in vivo* study was performed on 2 groups of 21 subjects (female & male, phototypes I to V, 16 to 59 years old, with slight to pronounced oily skin).

Hydrodispersion gels containing either 1% SymControl® Care or a combination of 2% niacinamide and 1% D-panthenol used as a positive control [12] were applied topically twice daily on the semi-foreheads of the volunteers. Measurement of the number of actives pores was performed at baseline and after 1 week, using a Visioscan® equipped with a Sebufix® foil.

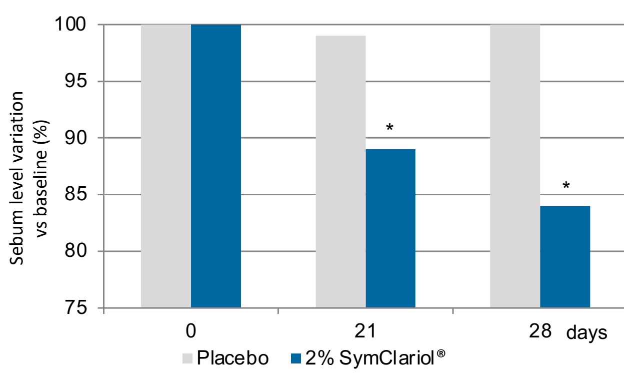


Fig. 1 Change in sebum content (compared to baseline), data normalized to $t_0 = 100\%$, * *significant difference vs placebo ($p<0.05$)*

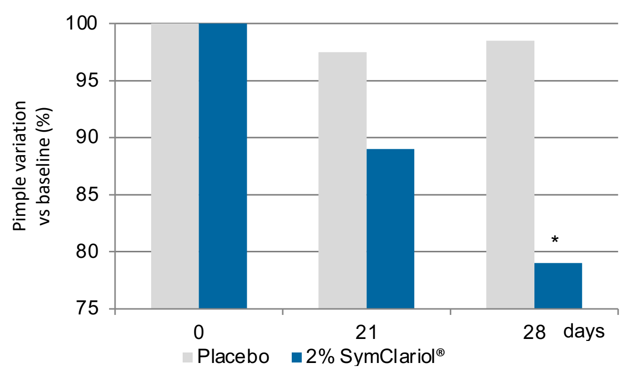


Fig. 2 Change in number of pimples/pustules (compared to baseline), data normalized to $t_0 = 100\%$, * *significant difference vs placebo ($p<0.05$)*

Results

Pimple reduction – SymClariol®

For the placebo cosmetic gel even after 28 days, no reduction of sebum was observed **(Figure 1)**, and the number of pimples was only reduced by 1.5% **(Figure 2)**.

For the cosmetic gel containing 2% SymClariol®, a significant ($p<0.05$) reduction of sebum **(Figure 1)** and pimples **(Figure 2)** was observed already after 21 days. Continuing this downward trend the amount of sebum reached a reduction of 16% after 28 days **(Figure 1)** and a reduction of more than 20% of the pimples after 28 days of use **(Figure 2)**, both representing a significant reduction vs initial value and placebo ($p<0.05$).

SymClariol® – A multifunctional with antimicrobial properties

Showing antimicrobial properties against fungi, yeast, gram-negative and gram-positive bacteria, SymClariol® has a mild broad-spectrum profile **(Figure 3)**. It has low MIC (minimum inhibitory concentration) against *S. aureus*, linked to skin inflammation. SymClariol® also shows efficacy against *C. acnes*, a bacteria that has been found in the pimples of subjects presenting acne [13].

Gram positives	*Cutibacterium acnes*	225 ppm
	Staphylococcus aureus	250 ppm
	Staphylococcus epidermidis	225 ppm
Gram negatives	*Pseudomonas aeruginosa*	450 ppm
Dermatophytes	*Epidermophyton floccosum*	112 ppm
Yeast	*Candida albicans*	112 ppm
	Malassezia furfur	28 ppm

Fig. 3 MIC of SymClariol® against different micro-organisms

Support of COX-2 expression reduction – SymControl® Care

The *Tetraselmis suecica* extract dose-dependently supports the reduction of PTGS2 (COX-2) expression by 56% and 80% for concentrations of 0.01% and 0.1% of the microalgae extract, respectively **(Figure 4)**, showing a positive influence on the enzyme at the origin of sebum production and skin sensitivity.

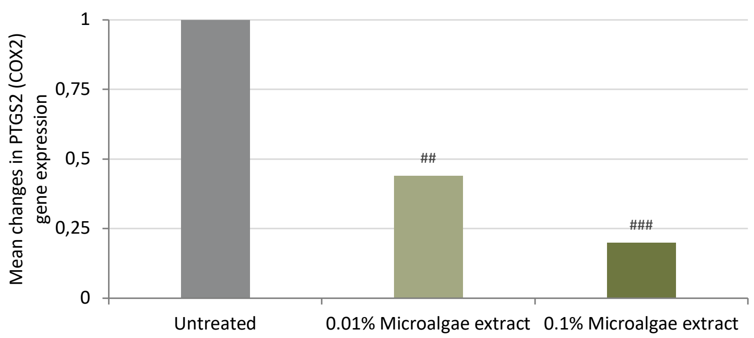


Fig. 4 Relative quantification measured changes in PTGS2 (COX2) gene expression relative to endogenous control GAPDH expression. COX-2 is encoded by the gene PTGS2. ## *significant difference vs untreated ($p<0.01$)*, ### *significant difference vs untreated ($p<0.001$)*

Sebum level reduction of all skin tones – SymControl® Care

A significant reduction of sebum is obtained after 4 weeks of product application in both studies **(Figure 5).** Reductions of 12% and 9% of sebum levels are shown for light skin (phototypes I to III) and darker skin (phototypes V to VI), respectively.

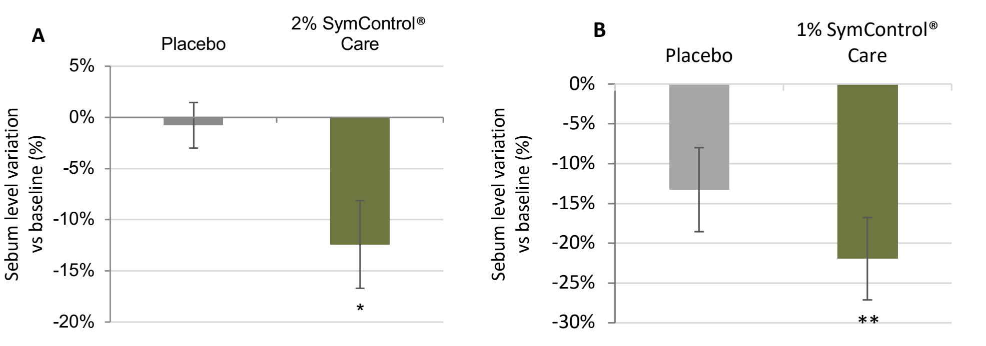
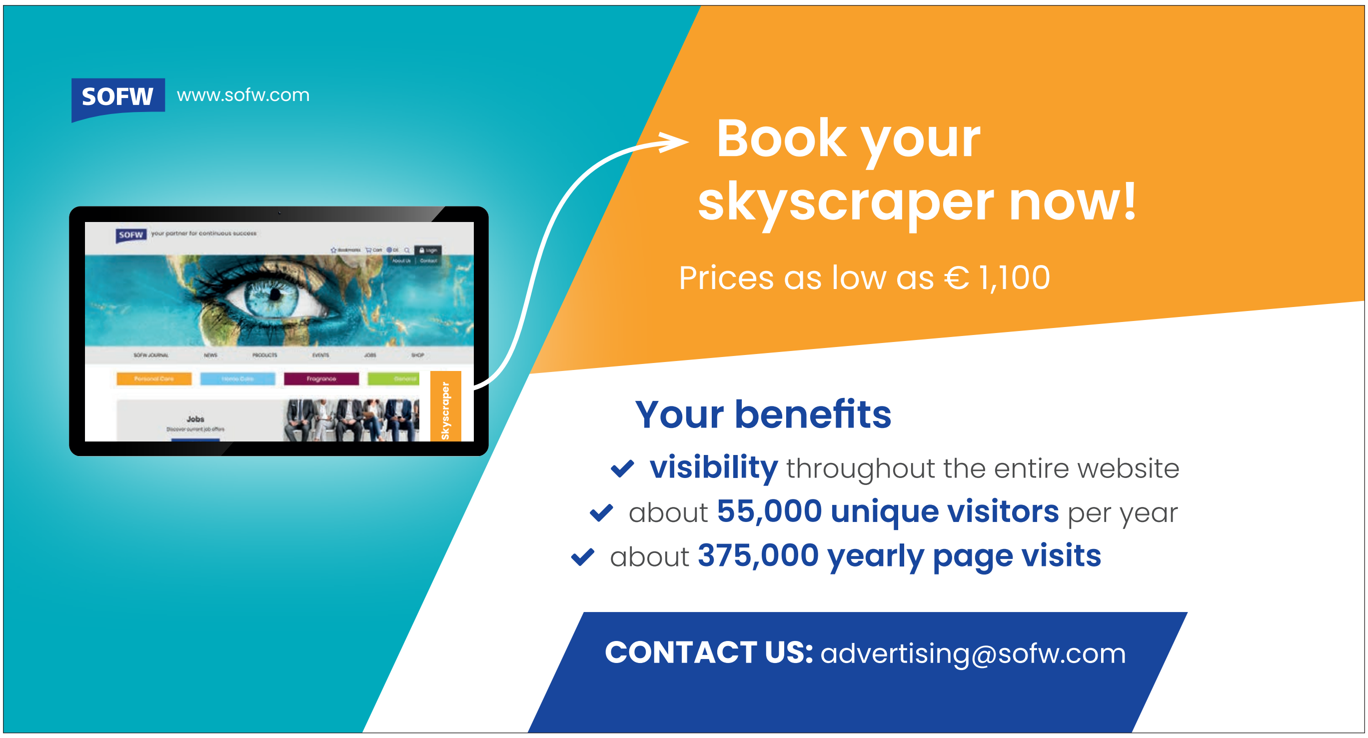


Fig. 5 Variation in sebum level after 4 weeks of product application (compared to baseline), **A**: Sebum reduction of light skin (phototypes I to III); **B**: sebum reduction of darker skin (phototypes V to VI), **significant difference vs placebo (p<0.05), **significant difference vs placebo (p<0.01)*

Fig. 6 Color mapping performed based on the sebum level evolution measured at the start of the study and after 4 weeks of product application, during the study on darker skin.

The color mapping performed for the study on darker skin visually highlights the reduction of sebum obtained with 1% SymControl® Care **(Figure 6)**.



Balances pores activity – SymControl® Care
A significant reduction of 49% in the number of active pores is obtained with SymControl® Care, which also shows a better efficacy than the positive control **(Figure 7)**.

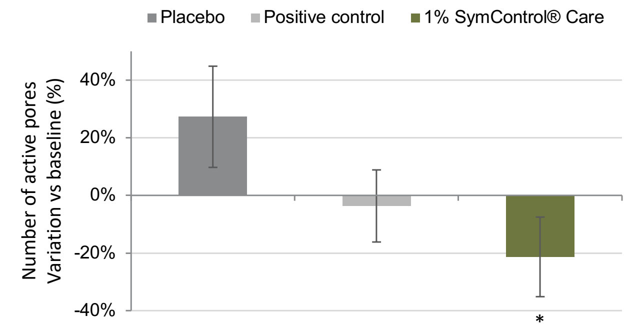


Fig. 7 Variation of the number of active pores after 1 week of product application (compared to baseline), **significant difference vs placebo ($p<0.05$)*

Conclusion

SymClariol® is a modern cosmetic hygiene ingredient that provides significant benefits for acne prone skin by helping to reduce sebum and pimples. It has an environmentally friendly profile which makes it a preferred ingredient in line with increasing legal and consumer requirements. In addition to being an emollient, SymClariol® shows good performance against specific facial microorganisms that are linked to acne-prone skin issues [14].

SymControl® Care supports a good reduction of the sebum level of all skin tones and balances pores activity of oily skin. It also helps to reduce the expression of one of the key enzymes at the origin of both sebum production and skin sensitivity. It is a microbiome-friendly and COSMOS approved ingredient, obtained thanks to blue biotechnology, and is based on a sustainably sourced Mediterranean microalgae.

A combination of both ingredients would help to maintain healthy skin and target an improved protection of acne prone skin against an increase of sebum production, pimple formation and sensitivity.

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- Sabine Lange

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References:

[1] *C. Bunick, J. Cohen*, Acne (*Acne Vulgaris*), Yale Medicine webpage, checked on June 26th, 2023, https://www.yalemedicine.org/conditions/acne#:~:text=Overview,common%20as%20time%20goes%20on.

[2] *E. Makrantonaki, R. Ganceviciene, C.C. Zouboulis*, An update on the role of the sebaceous gland in the pathogenesis of acne, Dermato-Endocrinology, January 2011, 41-49 https://doi.org/10.4161/derm.3.1.13900

[3] *E.A.Grice and J.A.Segre*; Nature Reviews; Microbiology Vol.9, April 2011, p.245

[4] The Human Microbiome Project Consortium (2012) in Nature 486 (7402), 207-214 and 215-221

[5] *Zouboulis CC*, Acne and sebaceous gland function, Clinics in Dermatology (2011), 22 (5): 360–6, https://doi.org/10.1016/j.clindermatol.2004.03.004

[6] Mintel GNPD database: Record ID 10343450, Beiersdorf Eucerin Pro Acne Solution Acne-Oil Control A.I. Matt Fluid, published November 2022 in Poland

[7] Beiersdorf Eucerin DERMOPURE Mattifying Fluid, webpage, checked on July 06th, 2023, https://int.eucerin.com/products/dermo-pure/mattifying-fluid

[8] Mintel GNPD database: Record ID 7209427, Kimberly-Clark Escudo Antibacterial Anti-Acne Bar Soap, published January 2020 in Mexico

[9] *Makrantonaki, E., Ganceviciene, R., Zouboulis, C.C.* (2011, Jan). An update on the role of the sebaceous gland in the pathogenesis of acne, Dermato-Endocrinology,

[10] EP1598064B2, Combination of alkane diols and hydroxy acid for the treatment of acne

[11] *M. Herrmann et al.*, Sebum and skin barrier normalizer from blue technology (2018), 30th IFSCC congress

[12] *Z.D. Draelos et al.*, The effect of 2% niacinamide on facial sebum production, J. Cosmet Laser Ther (2006), 8(2), 96-101

[13] *C. Dessinioti, A.D. Katsambas*, The role of Propionibacterium acnes in acne pathogenesis: facts and controversies, Clinics in Dermatology, Volume 28, Issue 1, January–February 2010, 2-7, https://doi.org/10.1016/j.clindermatol.2009.03.012

[14] *F. Genrich*, From head to toe – Well cared for and protected with SymClariol®, Euro Cosmetics (2022, Oct.), 14-17.

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Wilhelm Haarmann – From Start-up to Billion-Dollar Company

Honoring the Pioneer of the Fragrance Industry on his 175th Birthday

K. Stanzl

Some scientific discoveries of previous centuries have become so commonplace today that the achievements of their discoverers are often forgotten. The 175th anniversary of Wilhelm Haarmann's birth (1847-1931) provides an opportunity to honor his position in the history of the chemical industry **(Figure 1)**.

On May 24, 2022 Gustav Ludwig Friedrich Wilhelm Haarmann would have turned 175 years old. It is a good opportunity to review his life and work, as he has largely been forgotten since his name disappeared from the company name Haarmann & Reimer, which has merged with Dragoco Gerberding & Co. AG and is called Symrise today. Haarmann's groundbreaking synthesis of vanillin was the starting point for an industry that has become an important part of the chemical industry over the last 150 years. The fragrance and flavor industry generates over 35 billion euros in revenue worldwide and has produced several Nobel laureates. It all began in a small shed in Altendorf am Holzmindebach, in what is now Lower Saxony.

Fig. 1 Wilhelm Haarmann around 1921

There are several works that deal with the life and work of Haarmann. Albert Ellmer (1883-1963) honored his life in an obituary [1]. Chemist Professor Georg Schwedt (*1943) writes about the origins of the fragrance industry in his book "Betörende Düfte, sinnliche Aromen" ("Enchanting Scents, Sensual Aromas") [2]. One chapter is dedicated to the products from Holzminden on the Weser River, the hometown of Haarmann. Margot Vogelmann looks at him and his time in the yearbook of the Holzminden district [3]. Björn Bernhard Kuhse (*1938) has written four additional works on Haarmann. The first work was his dissertation on chemical education [4], the second publication was a poorly written biography [5] with many errors, and as the third work, he published a fictional novel titled "Der Herr der Düfte" ("The Lord of Scents") [6], in which he doesn't pay too much attention to historical accuracy. His latest publication focuses on Haarmann's life and encounters with August Wilhelm Hofmann (1818-1892) based on historical data [7] Another publication on this topic comes from Schwedt again in 2017. This book mainly focuses on the initial phase of the discovery of vanillin and primarily cites sources without commenting on them [8]. The first comprehensive works on the emergence of the fragrance industry were written by the author [9].

Childhood, school years, studies, and doctorate

Wilhelm Haarmann was born in 1847 as the son of Heinrich Wilhelm Haarmann (1802–1884), the Chief Commissioner and administrator of the Sollinger quarries, in Holzminden. As Chief Commissioner, his father had served as a customs inspector in the service of the Duke of Brunswick and still lived in the customs house by the river. The half-timbered house still awaits residents today, who reach it by crossing the Weser Bridge from Höxter. However, back then, there was no bridge. After the wooden structure built in the 17th century quickly collapsed, the people of Holzminden relied on a ferry. Wilhelm's grandfather was Johann Christoph (1762-1842), who served as the chief forester in the Kingdom of Westphalia until 1813. After Holzminden became part of the Duchy of Brunswick in 1814, his grandfather lost his position and established a stoneware factory. In 1817, he was appointed Chamber Master Builder and passed the company on to his son Friedrich Ludwig (1798-1864), Heinrich Wilhelm's brother. Friedrich Ludwig had studied chemistry, mineralogy, and building construction at the University of Göttingen in preparation for taking over his father's factory. Soon, he handed over the company to his siblings and focused on his passion for construction. In 1831, he founded the Ducal School of Building Construction and became district master builder after his father's retirement in 1835. The forester also seemed to be responsible for the administration of the Sollinger quarries, which had been transformed from leasing to administration in 1828. Heinrich Wilhelm became the administrator of the quarries. The hard work provided an important source of income for many families in the area. In 1875, the stone trade was privatized and renamed "Administration der Sollinger Steinbrüche Haarmann & Comp." [10]. The railway line opened in 1865 between Holzminden via Kreiensen to Braunschweig, as well as the navigable Weser River, served as transport routes for the Sollinger sandstone, along with horse-drawn wagons. Particularly, the river was used to transport the splitable sandstone slabs to Bremen in the 18th and 19th centuries, from where they were sold worldwide. The harbor and quay facilities, built by Heinrich's brother, Friedrich Ludwig, served as the main loading point.

Life by the river was wild and exciting for Wilhelm, but also full of challenges. Floods would often cut off the house from the outside world, and the city could only be reached by boat. The river, rich in fish, provided fishermen with abundant catches that they would sell to the surrounding inns.

Wilhelm had four brothers and two sisters. He attended the gymnasium from 1858 to 1866, where the famous chemist Robert Wilhelm Bunsen (1811-1899) had already graduated in 1828.

Haarmann left school and began studying at the Clausthal University of Technology in 1866. This was a clear indication of his interest in his father's profession and a possible takeover of the Sollinger quarries. He spent a delightful year in Clausthal but decided to move to Göttingen in 1867 to pursue studies in chemistry. In May 1869, he transferred to Berlin to join August Wilhelm Hofmann (1818–1892), who had returned from England and established a new institute that was one of the most advanced chemical educational institutions of its time.

Meanwhile, in 1867, the German Chemical Society (Deutsche Chemische Gesellschaft, DChG) was founded in Berlin, following the example of the Royal Society of Chemistry in England. This made the capital of the North German Confederation the center of German chemical research. The 12-member committee tasked with revising the society's statutes included notable chemists such as the president, Hofmann, as well as Adolf Baeyer (1835–1917), Heinrich Gustav Magnus (1802–1870), Carl Alexander Martius (1838–1920), Eilhard Mitscherlich (1794–1863), Alphons Oppenheim (1833–1877), Carl Rammelsberg (1833–1899), Julius Rosenthal (1836–1915), Carl Scheibler (1827–1899), Ernst Schering (1824–1889), Hermann Wilhelm Vogel (1834–1898), and Hermann Wichelhaus (1842–1927), all renowned chemists, whether as researchers or entrepreneurs [11].

Just like with industrialization, Germany lagged behind in terms of scientific societies. The Chemical Society of London had already been founded in 1841, with Hofmann serving as its president in 1862, and in France, the Société Chimique de Paris was established in 1857. Until then, German chemists had come under the umbrella of the Gesellschaft Deutscher Naturforscher und Ärzte (Association of German Naturalists and Physicians), founded in 1822, as chemistry was seen as an auxiliary discipline of medicine. However, due to the specialization of various fields, separate societies began to form, starting with the Deutsche Physikalische Gesellschaft (German Physical Society) in Berlin in 1845. The statutes of the DChG were modeled after the great example of London, aiming to "promote the development of the entire field of chemistry" [12]. Haarmann was admitted as a student member to the society on June 13, 1870.

The war with France led to a temporary halt in many projects in German chemistry. Wilhelm interrupted his studies and volunteered for one year, joining the Royal Prussian Guard Fusilier Regiment. Haarmann described his enthusiasm for the war in a letter to his father on July 22, 1870:

"Dear Father!

I am delighted to inform you that August [his brother] has just arrived here to join immediately. It was about time, too, because with the great enthusiasm prevailing here, especially among the young people, our regiment had already received 600 to 700 one- and three-year volunteers, resulting in the last ones being turned away this afternoon due to overcrowding. Yesterday, I had already enlisted with my cousin Froböse but managed to ensure that we could join the same company together with August. Tomorrow, we will already have drill exercises, but it seems that we won't go to the field for at least another four weeks. So, dear Mother, and dear Father, you can rest assured, even though we are burning with impatience to finish the drill exercises as soon as possible." [13].

The war took him near Paris. However, even after Napoleon III (1769-1821) was captured on September 2, 1870, at Sedan, the war was not yet over. On September 4, the monarchy was overthrown in France, and a republican "government of national defense" took its place, continuing the war. Haarmann had to endure in Paris until the spring of 1871, even though Wilhelm I was proclaimed German Emperor in the Hall of Mirrors at Versailles on January 18, 1871. His initial enthusiasm had faded. He noted:

"Instead of giving us some rest after the hardships, hardly a day goes by without us engaging in exhausting drills with full gear or equally burdensome training marches in the surrounding area. [...] it's nothing more than one strain after another."[14].

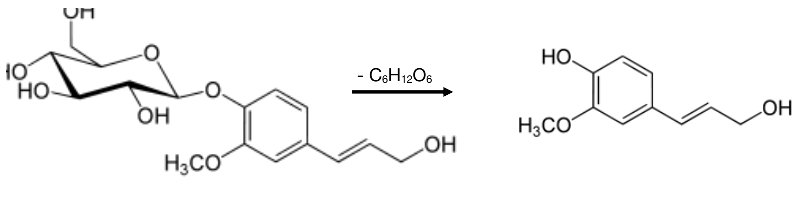
The Treaty of Frankfurt on May 10, 1871, imposed a reparation payment of five billion francs on France, and they had to cede Alsace and parts of Lorraine to Germany. The substantial amount of money led to an economic upswing in the German Empire, particularly in the chemical industry, which became the global leader. Disillusioned, Wilhelm returned from the war and was able to resume his work with Hofmann in Berlin in the autumn. He worked on reactions of salicylaldehyde and converted it with anhydrous hydrocyanic acid, resulting in the formation of salicylanilide, and determined its formula as $C_{14}H_{12}N_2O$ [15].

Haarmann was searching for a topic for his dissertation. He received support from his laboratory colleague Ferdinand Tiemann (1848-1899), who provided him with a substance that his former classmate Wilhelm Kubel (1832-1903) had noticed had a vanilla scent during its investigation. The idea of synthesizing a natural product intrigued Haarmann. However, in order to do so, he first needed to isolate and characterize the active ingredient.

Kubel had obtained the product from Theodor Hartig (1805-1880), a professor of forestry at Collegium Carolinum, who had discovered a crystallizing substance in the cambial sap of larch trees in 1861, later named coniferin. The cambial sap is "*the fluid obtained when trees are felled and debarked during the time of wood formation, and the remaining cambium on the surface of the wood is scraped off using glass shards and the scraped mass is squeezed out*"[16].

In 1866, Kubel had examined the substance and found that coniferin is a glucoside with a melting point of 185°C, which turned brownish and emitted a peculiar caramel odor at higher temperatures, eventually charring. He used dilute sulfuric acid to hydrolyze glucose from it and obtained a resinous substance that he couldn't identify but noticed the vanilla scent during this reaction. He analyzed coniferin and determined its composition as $C_{24}H_{32}O_{12} + 3H_2O$ [17]

For his doctoral thesis, Haarmann obtained cambial sap from tree trunks of coniferous trees that had been felled during wood formation from May to July, resulting in 20 grams of coniferin. He repeated Kubel's experiments. However, an attempt to extract coniferin from trees felled in December failed. The yield was extremely low, and he was unable to isolate the pure substance. Due to the limited amount, he could only conduct a few experiments. Haarmann burned the substance and obtained the same result as Kubel. He then hydrolyzed the coniferin with dilute sulfuric acid under heat and obtained, in addition to glucose, a substance that Kubel had already named coniferetin, now referred to as coniferyl alcohol. Haarmann formulated the reaction in his dissertation as follows: $C_{24}H_{32}O_{12} + H_2O = C_6H_{12}O_6 + C_{18}H_{22}O_7$ [18].



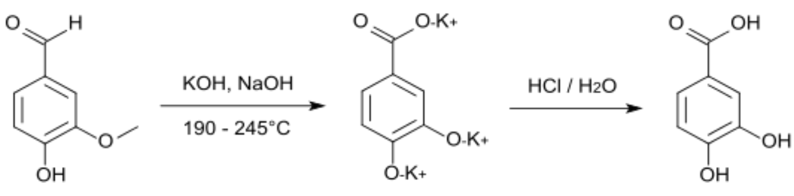
Coniferin $C_{16}H_{22}O_8$ Coniferylalkohol $C_{10}H_{12}O_3$

Reaction 1: Coniferin undergoes hydrolysis in dilute sulfuric acid at elevated temperature, leading to the formation of coniferyl alcohol with the liberation of glucose.

Later, he simplified Kubel's formula to $C_{16}H_{22}O_8 + 2H_2O$ [19], and the reaction is described in **Reaction 1** using the current common notation.

In the next step, he oxidized coniferin with potassium dichromate in dilute sulfuric acid, triggering a vigorous reaction. After several weeks, colorless needles with an aromatic odor crystallized. He treated the crystals with a silver salt solution, resulting in the formation of elemental silver at the test tube [20]. Reacting it with sodium bisulfite yielded a solid substance [21]. Based on the results of these two reactions, he concluded that the resulting compound must be an aldehyde. The removal of the sugar with emulsin was simpler [22]. After just twelve hours, he obtained a white crystalline mass. He separated the sugar, and aromatic white crystals formed, which he named coniferogenin.

He could only determine the structure of the newly discovered compound through chemical reactions since the instrumental analytical techniques commonly used today were not known at that time. He melted the unknown substance with potassium hydroxide, neutralized it with hydrochloric acid, and obtained a compound with a faint clove-like odor, which, after purification, he identified as protocatechuic acid (3,4-dihydroxybenzoic acid), a molecule known at that time. It is formed from the molecule referred to by Haarmann as coniferogenin through demethylation of the potassium salt of vanillic acid according to the following **Reaction 2**:



Coniferogenin potassium salt of vanillic acid protocatechuic acid

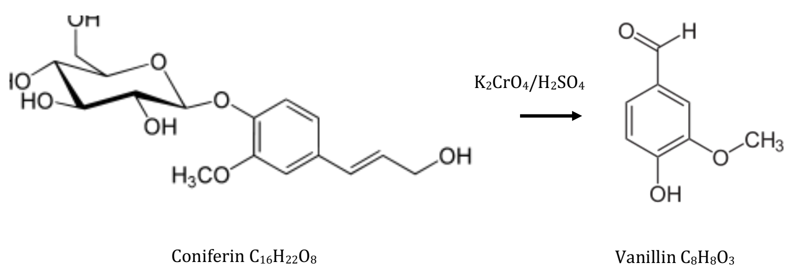
Reaction 2: Coniferogenin is converted to the potassium salt of vanillic acid using KOH/NaOH, which is subsequently transformed into protocatechuic acid through hydrochloric acid.

Haarmann had attended courses by Fittig and Hübner in Göttingen before going to Berlin. Hübner also evaluated his dissertation "On Some Derivatives of Glucosides Coniferin and Salicin" [23], which was completed with great diligence but unfortunately yielded little success. He was awarded a summa cum laude external doctoral degree in 1872 [24]. After his promotion, Haarmann, along with his brother Otto and Tiemann, went on a study trip to England, during which they visited factories in preparation for their future independence [25].

Vanillin, Company Foundation, Wedding

The small amount of coniferogenin obtained by Haarmann did not allow him to determine the structure of the newly discovered compound. Likewise, he did not know how to produce larger quantities of the aromatic substance. Haarmann and Tiemann joined forces. The results they had so far gave them hope that they could isolate the aromatic principle of vanilla and exploit it commercially. It took them another two years and countless experiments before they had a result to present.

First, they painstakingly collected cambial sap during the spring and summer of 1873 and were able to obtain approximately 2.5 kilograms of coniferin from it. With this, they could continue Haarmann's work. They repeated the experiment of oxidizing coniferin or its cleavage product, coniferyl alcohol, with a mixture of potassium dichromate and sulfuric acid. After 6 to 8 days, they obtained a white, fluffy crystalline mass. They identified Glucose and a compound whose composition, based on elemental analysis, could be described by the formula $C_8H_8O_3$ **(Reaction 3)**.



Reaction 3: Coniferin or coniferyl alcohol is oxidized with potassium dichromate to yield vanillin.

Tiemann reported the results of their investigations in the meeting of the German Chemical Society on March 23, 1874 [26]. They were convinced that the pleasant-smelling substance obtained from coniferin was a known compound, previously only produced by nature, which had been described by the French chemist Pierre-Paulin Carles (1845-1919) in 1872 and referred to as "vanilline" by him [27]. They believed that they had synthesized this crucial odor- and flavor-imparting component of vanilla pods and claimed that only this compound was responsible for the pleasant aroma of vanilla. Today, we know that vanillin is the dominant flavor component, but the complex aroma of vanilla is composed of several hundred components, of which approximately 35 contribute significantly to the typical aroma, even in small quantities [28]

Haarmann had no intention of pursuing an academic career. He wanted to commercially exploit the results of his dissertation and follow in his father's footsteps. It was a bold idea that Haarmann pursued, as who needed a synthetic replica of a luxury spice that only the wealthy used at the time.

His ancestors, whose lineage can be traced back to the 17th century, had always been involved in commercial activities, so it was not surprising when Wilhelm followed their example. Some investors, including his father, provided him with the necessary starting capital, and in 1874, he founded a start-up company in his hometown, a term that would be used today but the founding of start-ups was quite common in the German chemistry field in the 1860s.

The factory was intended for the production of vanillin from the wood of coniferous trees. Haarmann's Vanillin Factory in Holzminden was the first factory worldwide to produce a synthetic fragrance or flavor substance on an industrial scale [29].

During this period of Haarmann's life, he also got married to Luise Stieren (1855-1918) in 1876. In early 1877, their first son, Wilhelm (1877-1962), was born, named after his father. A year later, the twins Luise and Änne were born. The completion of their family planning came in 1890 with the birth of another son, Reinold.

In the summer of 1874, the newlywed 27-year-old factory owner went on his honeymoon to Gernsbach in the Black Forest and employed twenty to thirty women there, who worked on freshly felled trees and removed their bark, scraping and extracting the sap. The obtained liquid was concentrated to minimize the amount of water transported to the Weserbergland region.

Haarmann's business acumen was evident early on, as he applied for a patent for his invention, which he received on April 10, 1874, for a period of five years from the ducal Brunswick-Lüneburg district directorate. After the establishment of the German Empire in 1871, it took another six years for the Imperial Patent Office in Berlin to commence its operations on July 1, 1877. Haarmann obtained one of the first patents granted by the newly established office. The patent office awarded him a German Imperial Patent with the number 576 on July 12, 1877, valid for twelve years, for a method of artificially producing vanillin.

"I produce vanillin from coniferin or directly from the cambial sap of conifers containing coniferin, or finally from an extract of all parts of conifers in which coniferin is present. Coniferin is dissolved in water and treated with any oxidizing agent, such as potassium bichromate and sulfuric acid, potassium permanganate in aqueous solution, or nitric acid, and heated for an extended period. The solution is distilled with ether. The residue, consisting of vanillin and related compounds, is purified by repeated crystallization of the former, and the thus obtained vanillin is made available in the market." [30].

In theory, the process sounds very simple. However, in practice, it was very laborious to extract the cambial sap from the conifers. From a 20-meter-long trunk of a 70 to 100-year-old spruce tree, approximately one liter of cambial sap could be obtained, which in turn yielded 4 grams of coniferin. To obtain 1 kilogram of the desired sap, at least 250 trees had to be tapped, and a woman could extract about four to five liters per day. Trees have the highest sap content between May and July, a time when trees are only felled in parts of the country where it is not accessible during the winter. It was now the manufacturer's task to make agreements with the forest owners in these areas to access the raw material. With 20 women working on the 70 working days of the season, they could collect enough sap to convert into approximately twenty kilograms of coniferin, which was then painstakingly transformed into 7 kilograms of vanillin in the laboratory. This was the first year's production of his chemical factory. Haarmann sold vanillin for nine marks per gram. Assuming that he could sell all 7 kilograms, the first-year revenue was 63,000 Reichsmarks. The patents filed in the United States and the United Kingdom demonstrated the young entrepreneur's foresight [31].

In 1876, the first World's Fair outside of Europe took place in Philadelphia, featuring over 30,000 exhibitors from 35 countries. The Centennial International Exhibition was held in Philadelphia because it marked the 100th anniversary of the signing of the United States Declaration of Independence. Engineer Franz Reuleaux (1829–1905), who reported from the USA, did not have a favorable impression of German industry. He noted that they only wanted to produce cheaply. The patriotic motives behind the exhibited products created an unpleasant impression of nationalism and chauvinism, and there was a lack of innovation. Criticism of German industry had been expressed before, but the situation worsened due to the economic crisis after 1873. Under these circumstances, there were discussions in England about introducing a mandatory label "Made in Germany" to distinguish it from English quality goods. It is surprising that later "Made in Germany" became a seal of quality in light of these statements.

An exception was the presence of pharmaceutical, medical, and technical preparations. Opium and cinchona alkaloids, chloral hydrate, and salicylic acid produced according to Kolbe's patent could be found. Among all these glass cabinets from Schering and Kahlbaum, there was a narrow compartment with seven slender glass cylinders, which a reporter wrote about: *"They contain one of the most remarkable preparations in the German chemical section, namely the aromatic substance of the vanilla pod produced by Dr. Wilhelm Haarmann in Holzminden on the Weser River. [...] Vanillin, discovered in Hofmann's laboratory in Berlin two years ago, is already a significant commercial product that will eventually pose a formidable competition to the vanilla trade."* [33].

The vanilla plant belongs to the orchid family and is the only plant in this genus that produces edible fruits. Originally, it grew exclusively in the rainforests of Mexico. In the early 19th century, cuttings were brought to the botanical gardens of Paris and Amsterdam. European attempts to cultivate the plant in tropical regions outside of Europe failed due to the complicated pollination process of the orchid. It wasn't until 1837 that Belgian botanist Charles Morren (1807-1858) succeeded in unraveling the reproductive mechanism of vanilla and artificially pollinating its flowers in a greenhouse. In 1841, a twelve-year-old plantation slave named Edmond Albius (1829-1880) on Réunion Island discovered a manual pollination method. He simply opened the flower with a thin bamboo stick and transferred the pollen from the stamen to the stigma [34]. This method, which is still used today, involves labor-intensive artificial pollination using a wooden stick or straw. A skilled worker can pollinate about 1,000 to 1,500 flowers per day. The green fruits harvested after about eight months are initially tasteless and only develop their characteristic aroma through fermentation [35].

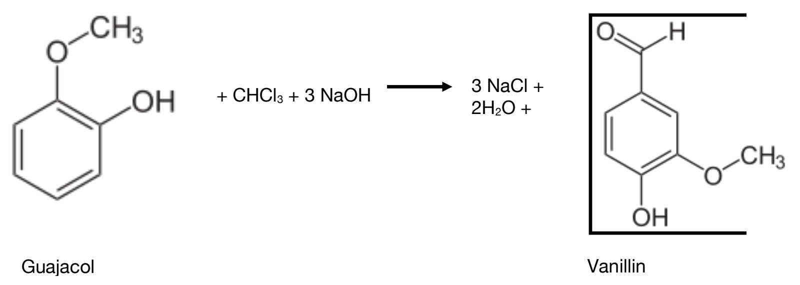
Haarmann's idea was to sell the product to large-scale entrepreneurs, such as the chocolate industry, as well as other sectors of the food industry, bakeries, ice cream manufacturers, and housewives. However, the acceptance of vanillin was low. In 1879, Haarmann complained and claimed that the French chemist Carles had already discovered vanillin as the only aromatic component of vanilla and that their vanillin was identical to the natural product [36].

To achieve success with his synthetic product, Haarmann had to demonstrate that his vanillin was identical to natural vanillin and, furthermore, cheaper. Therefore, they had to develop a method to determine the vanillin content in the vanilla pods, as it was assumed to vary greatly among different varieties. In 1875, they developed a procedure to determine the vanillin content [37] depending on the harvest year and quality, and obtained values ranging from 0.75% to 2.9% [38]. With the price of vanilla pods in 1875 ranging between 192 and 240 Reichsmark, it was now possible to calculate the price of natural vanillin. The resulting values ranged from 6.60 to 25.60 Reichsmark per gram [39]. Thus, the "outrageous" price of 7 to 9 Reichsmark per gram for vanillin was justified.

Haarmann & Reimer particularly targeted chocolate manufacturers. According to their calculations, in 1879, these manufacturers consumed approximately 3,000 to 4,000 kg of vanilla in Germany, which cost them between 180,000 and 240,000 Marks. In contrast, the substitute, synthetic vanillin, would only cost 84,000 to 112,000 Marks. This meant potential savings of 96,000 to 128,000 Marks in Germany alone. Globally, the entrepreneurs estimated a consumption of 50,000 kg of vanilla, equivalent to 1,000 kg of vanillin, and a savings of 1,400,000 Marks [40].

Among housewives, the product found little appeal. A synthetic flavoring was something entirely new and initially met with resistance. A marketing campaign was needed to change this situation. Haarmann commissioned the well-known women's rights activist and cookbook author Lina Morgenstern (1830-1909) to write recipes that featured Haarmann & Reimer's patented vanillin. The booklet was distributed at the end of the 19th century, and influencer Morgenstern represented trustworthiness in synthetic flavorings.

Karl Reimer (1845-1883) also studied in Hofmann's laboratory and obtained his doctorate in 1871 with the dissertation "On some derivatives of fermentation alcohol." He then worked at the Royal Forestry Academy in Eberswalde under Theodor Hartig before being introduced by Hofmann to the Berlin Chemical Factory of C.A.F. Kahlbaum. Around 1875, he discovered that when chloroform reacts with phenol in the presence of alkalis, salicylaldehyde is formed, a previously inaccessible substance [41]. Reimer had discovered a generally applicable process that later became known as the Reimer-Tiemann reaction, as he worked closely with Tiemann, and they published the results, which went down in the history of chemistry under that name [42].



Reaction 4: Synthesis of vanillin from guaiacol using the synthetic method developed by Reimer.

Reimer reported in 1876 that he and Tiemann had succeeded in producing vanillin from guaiacol using the reaction mentioned above **(Reaction 4)** [43]. Through Tiemann's mediation, Reimer became a partner in Haarmann's vanilla factory, which changed its name to Haarmann & Reimer in 1876.

Unfortunately, the production process based on this method proved to be uneconomical and was not implemented in production. However, Tiemann had succeeded in producing vanillin inexpensively from eugenol, which is present in clove oil at 70-80% [44]. As a result, the selling price of synthetic vanillin was reduced from the original 7,000 to 9,000 Marks per kilogram to 750 Marks in 1885. Tiemann found a better alternative when he succeeded in directly converting eugenol into vanillin. In this process, he had to protect its hydroxyl group through acylation and then remove it after the oxidation was complete. Further cost reduction to 30 Marks was achieved when he discovered in 1891 that eugenol could be smoothly converted into isoeugenol, and vanillin could be obtained in significantly higher yields using peroxides.(45) With the significantly reduced production costs of vanillin, the synthetic variant now became a financially appealing alternative to natural vanilla.

The collaboration of the three men was successful. Unfortunately, Reimer died in 1883 from lung tuberculosis, which he had contracted during his military service and which had never properly healed. Haarmann was the powerful and visionary entrepreneur in the remaining duo, while Tiemann was the imaginative scientist who continuously came up with creative ideas for new products.

Competition and Diversification

The discovery of the synthetic route to vanillin was already recognized scientifically in 1876 when Haarmann and Tiemann were awarded the Cothenius Medal by the Leopoldina. The medal, which is awarded for outstanding scientific achievements, is made of solid gold and bears the inscription "Praemium virtutis salutem mortalium provehentibus sancitum" (As recognition of the ability of those who promote the well-being of mortals). Christian Andreas von Cothenius (1708-1789) bequeathed "one thousand gold talers" to establish it, with the stipulation that the interest be used every two years to award a golden commemorative coin adorned with the image of the benefactor for the best solution to a prize question from the field of practical medicine. However, it is also awarded to eminent researchers. Gustav Robert Kirchhoff (1824-1887) also received the award in 1876.

Shortly after the Franco-Prussian War, Hofmann facilitated a contact with France. During his trip in 1875, Tiemann met Hofmann's student Georges de Laire (1836-1908). After studying at the École polytechnique and the Conservatoire national des arts et métiers, de Laire had worked with Charles Girard (1837-1918) in the laboratory of Théophile-Jules Pelouze (1807-1867), a student of Joseph Louis Gay-Lussac (1778-1850). They synthesized fuchsine from aniline but could not sell the dye in France due to patent reasons. Therefore, Pelouze had it produced in England, where de Laire took charge of production from 1850 on and came into contact with Hofmann. He worked with Girard for some time in his laboratory, mainly on phenylated rosanilines. Back in Paris, they developed fuchsine blue and fuchsine violet. The beauty of these dyes led the inventors to establish their own dye factory in Ris-Orangis near Paris in 1872. Since the financial success of the new company failed to materialize, they sold their company in 1876 to pursue new ventures. Tiemann was able to convince de Laire to focus on synthetic vanillin, and de Laire agreed. Tiemann became a silent partner in the company, and a lifelong friendship was formed, which was remarkable so soon after the war. The new company occupied premises in Rue St. Charles-Grenelle. The rather shy de Laire went to the spruce forests himself in the spring, where trees were felled, and supervised the work. The trees were carefully debarked, and the sap was scraped out of the exposed cambium with wooden spoons and then concentrated. The crude coniferin was brought to Paris and converted into vanillin [46]. Over the years, the company developed into the largest producer of synthetic raw materials for the perfume industry.

More and more companies saw an opportunity to make money by manufacturing vanillin. To maintain their leading market position, Haarmann & Reimer, together with C.F. Boehringer & Söhne, Schimmel & Co., and the Chemical Factory on Actien, formerly Schering, formed the Vanillin Cartel [47]. Additionally, Haarmann & Reimer and de Laire secured the rights to a process from the Society for Chemical Industry, Basel, in 1895, for which they had to pay a considerable amount of license fees [48]. Cartels were not uncommon towards the end of the 19th century. The contractually established agreements initially focused on a joint pricing policy but were often expanded to regulate production quantities and sales conditions. Cartels aimed to restrict competition in order to control the market. In 1897, the legality of cartels was confirmed by the Supreme Reich Court, in contrast to the United States [49].

Further methods for producing vanillin were developed, and by 1925, more than ten patents for the production of vanillin using various methods had been granted [50]. Haarmann & Reimer got a taste of how difficult it was to defend intellectual property rights when they took action against the company Fritzsche & Co. from Hamburg. They had filed a patent for the production of vanillin from eugenol, which H&R considered a violation of their patent DRP 57,800. Tiemann was deeply affected when H&R lost the case.

The battle for the vanillin market was fiercely contested, and the price of synthetic vanillin declined. This led companies to adulterate vanillin with cheaper substances such as boric acid, benzoic acid, acetanilide, sugar, isoeugenol, or coumarin [51].

Heliotropin | Coumarin

During the first four years, Haarmann & Reimer exclusively produced vanillin in Holzminden. They then expanded their product range. In 1878, based on the work of Rudolph Fittig (1835–1910) and Wilhelm Mielck (1840–1896), they introduced piperonal to the market under the name heliotropin [52]. The production process was complex and expensive as the alkaloid piperine, which is found in black pepper at a concentration of 5 to 9%, had to be isolated and converted into piperonal through hydrolysis and oxidation. Initially, it was possible to successfully sell heliotropin, but the profitable times for the product soon faded. In 1885, Johan Frederic Eijkmann (1851–1915) recognized the familiar smell of piperonal when he oxidized shikimol with permanganate [53]. Theodor Poleck (1821–1906) also identified piperonal when he reacted safrole with permanganate [54]. Shikimol, a byproduct of camphor production, and safrole, the main component of sassafras oil, were identical and readily available compared to piperine.

In 1879, the next product introduced by the company was coumarin. Coumarin had been previously extracted from the tonka bean and was added to snuff tobacco due to its pleasant scent. In 1820, August Vogel (1778–1867) isolated the colorless crystals and suspected that they were benzoic acid based on their chemical properties.(55) Independently, Nicolas Jan Gaston Guibourt (1790–1867) also discovered coumarin and recognized it as a distinct substance [56]. In an essay presented at a session of the Académie royale de médecine, he named the substance "coumarine," derived from "coumarou," the French word for the tonka bean. The first synthesis was achieved by William Henry Perkin (1838–1907) when he reacted salicylaldehyde with acetic anhydride and sodium acetate [57]. Tiemann and Hermann Herzfeld (1853–1911) attempted to elucidate the reaction mechanism. They boiled a mixture of 3 parts salicylaldehyde, 5 parts acetic anhydride, and 4 parts sodium acetate for several hours, resulting in a crystalline mass that solidified upon cooling. By adding water, they obtained an oil that smelled of coumarin and acetic acid. In their opinion, acetylcoumaric acid or its mixed acetic anhydride was initially formed, and coumarin developed in a second phase upon heating. This understanding helped them implement the process in practice [58]. In 1879, Haarmann & Reimer introduced coumarin to the market.

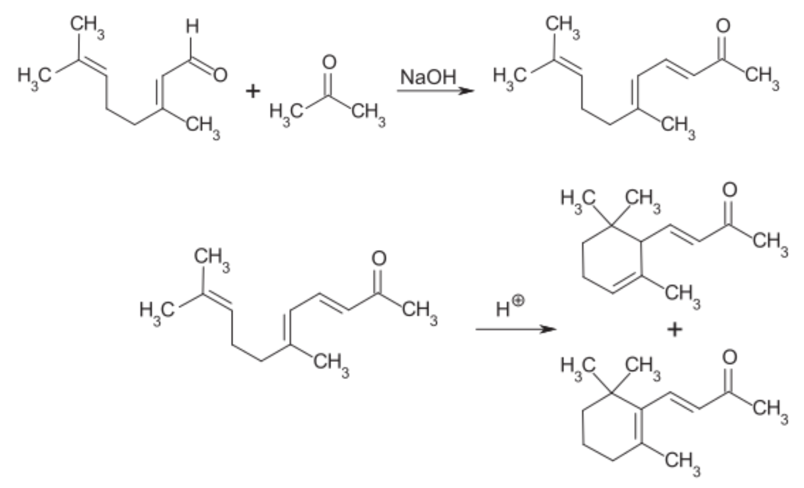
In 1883, Karl Köhler (1855–1890) joined the company and was responsible for expanding the production of heliotropin and coumarin. Otto Wallach (1847–1931), who later became a Nobel laureate, laid the foundation for the large-scale production of terpineol, and Paul Krüger (1859–1916), who joined the company in 1888, implemented the process in practice in 1889. Over time, the price of terpineol decreased from 100 Marks to 2 Marks, with an estimated annual demand of 100,000 kg.

Jonone | Tiemann's Death

At the beginning of the 19th century, Marie Louise of Austria (1791–1847), Napoleon's wife and Duchess of Parma, promoted the cultivation of violets in Parma. She even convinced the Carthusian monks of the Annunziata Monastery to create the perfume "Violetta di Parma" (Violet from Parma) exclusively for her. Thanks to Marie Louise, the scent of violets became a hit in France.

The flower oil of the Parma violet and Victoria violet was one of the most precious ingredients in fine perfumery in the 19th century. The production cost for 1 kg of the oil amounted to 80,000 Marks. As an affordable alternative, the essential oil of iris root, which has a pleasant violet-like smell, presented itself. Tiemann therefore investigated the "violet root" [59] together with de Laire, Paul Krüger, and Richard Schmidt. They worked on the iris root project for seven years until they identified the iris aroma as a ketone present at 0.015% in the root. They named it "iron" and determined its formula as $C_{13}H_{20}O$ [60].

Finally, in 1893, they believed they had found a synthesis pathway. They condensed citral, an unsaturated aldehyde present in Indian lemongrass oil, with acetone in a basic environment using the Claisen reaction. They obtained a methyl ketone with an open chain, which they named "pseudojonone" and was nearly odorless. By heating it with dilute acid, they were able to close the ring and, luckily, obtained a fragrant substance that researchers named "jonone" and had the smell of violets **(Reaction 5)** [61].



Reaction 5: Synthesis of α- and β-Jonone from Citral.

Josef von Mering (1849-1908), to whom Tiemann gave the product, conducted a toxicological assessment of iron and jonone to evaluate their physiological effects. He reported the following:
"*Large rabbits received 1g of jonone multiple times in the form of an emulsion through a stomach tube without showing any disturbances. A dog weighing 8 kg received 1g of jonone suspended in 250 cc of water in its stomach for six consecutive days. The dog did not exhibit any abnormalities. It was lively, had a good appetite, and normal bowel movements. [...] After the above-mentioned animal experiments confirmed the non-toxicity of jonone at the administered doses, I myself took jonone several times - three times in one week and then for eight days, five drops each time - without experiencing any alteration in my general well-being. [...] I also conducted some experiments with iron, of which I had 5g available.*
A dog received 1 g twice without any adverse effects, and I myself took three drops several times in diluted brandy without experiencing any disturbances."[62].

The elucidation of the structure and synthesis of Iron was undertaken by Leopold Ruzicka (1887-1976), a future Nobel laureate, in 1919 after nearly two decades. It took until 1947 for him to discover the correct structure and publish a synthesis pathway [63].

Let's return to the synthesis of Jonone. The starting material was an acyclic monoterpene mixture consisting of the isomers geranial and neral. These isomers were discovered by chemists from the company Schimmel & Co. in the essential oil of Backhausia leaves in 1888. They had an intense lemon-like smell and were aptly named citral. It was later found that citral is also present in lemon oil and can be found in up to 80% in lemongrass oil. Years later, Semmler realized that citral structurally matched the terpene geranial, which he had first synthesized from geraniol in 1890 [64].

The company Franz Fritzsche & Co. also introduced a product under the name 'Veilchenöl künstlich' (artificial violet oil) to the market. According to Haarmann & Reimer, this product violated their patent. It should be noted that a chemical compound, even if previously unknown, is not patentable; only the process for its production is patentable. Haarmann & Reimer pursued a lawsuit at the Hamburg Regional Court. On January 28, 1897, the court issued a preliminary injunction, prohibiting Fritzsche & Co. from selling "Veilchen-Öl künstlich" under a penalty of 500 marks for each violation. However, the case was not yet concluded. There was an appeal and a request to overturn the judgment. Haarmann & Reimer also pursued legal action against the product introduced by Fritzsche & Co. in England and France. The dispute in Germany, France, and England, which required Tiemann's personal appearance, took a toll on him. After returning from a trip to London, he suffered a heart attack from which he would not recover, and he passed away shortly thereafter. Haarmann & Reimer won the legal battles in England and Germany.

A new industry emerges | Simple aroma compounds

With the work of Haarmann and the establishment of his company, an industry emerged that systematically searched for aroma compounds that could be produced through chemical means. Initially, the aromatic principle of the corresponding plant had to be identified in order to synthetically reproduce it. The interesting and profitable product group attracted the interest of other chemical companies, enticing them to claim a share of the market. Particularly, the chemical companies founded in the 1860s recognized the lucrative potential of aroma compounds. The Aktiengesellschaft für Anilinfabrikation, for example, realized that synthetic aroma compounds would complement their existing product portfolio. Significant quantities of nitrobenzene and benzaldehyde were produced during the production of aniline dyes, and these could be offered as aroma compounds in a particularly pure form as a substitute for bitter almond oil. They also acquired patents for the production of anthranilic acid methyl ester, which had an aroma reminiscent of orange blossoms [65]. This product was sold under the name "Irolène extra" and marketed as a synthetic replica of natural neroli oil, "faithfully reproduced, 1½ to 2 times stronger than real orange oil." [66]. Narcéol was a replica of natural jasmine oil, and the violet ketone "Agfa," which likely corresponded to Haarmann & Reimer's Jonone, was also offered by AGFA [67].

The industry of simple aroma compounds experienced a significant boom in Germany at the beginning of the 20th century. There were more than sixteen producers manufacturing over 150 different aroma chemicals [68]. The scope of this industry can be estimated from the statistics of the German Empire regarding the import and export of aroma compounds. Under the category of vanillin, coumarin, heliotropin, and similar synthetic aroma compounds, the exports exceeded imports by more than tenfold [69]. From 1907 to 1913, exports increased from 2,822,000 marks to 4,905,000 marks, representing a nearly 75% growth. To put it in perspective, the export of aniline and other coal tar dyes in 1907 amounted to 112,447,000 marks. The exports of synthetic aroma compounds accounted for approximately 2.5% of the export value of aniline and coal tar dyes.

The intense competition resulted in a significant drop in prices for many synthetic aroma compounds. The prices of vanillin decreased from 7,000 to 30 marks, coumarin from 500 to 25 marks, and heliotropin from 3,000 to 10 marks per kilogram. The profit margins in the early stages, while enjoying a monopoly, can be inferred from the fact that the price of nitromusk dropped to 5% of its previous value after the expiration of the patent. With the drastically reduced production costs of aroma compounds, perfumed products could be sold at much lower prices, attracting new segments of the population as customers by the end of the century [70].

The Period between 1880 and 1931

Privately, the year 1884 was particularly challenging for Haarmann. All three of his children fell seriously ill. His son Wilhelm hovered between life and death for weeks, and one of his daughters passed away. In the autumn, his 82-year-old father also passed away and had to be buried. There was some joy in 1890 when his second son Reinhold was born, and Haarmann began the Liebigstraße project. Like many entrepreneurs of his time, he supported his employees. In Liebigstraße, single-story half-timbered houses covered with Solling plates were built. The company assisted employees who wanted to purchase or build a house.

Over the next years, the company grew steadily. Since 1883, Haarmann had been hiring chemists for research, many of whom had previously worked with Tiemann at the University of Berlin and obtained their doctorates under him. In 1893, the staff consisted of director Wilhelm Haarmann, scientific advisor Ferdinand Tiemann, four chemists (Krüger, Ferdinand Sembritzki, Richard Schmidt, Georg Lemme, the latter joining in 1893), three administrative officers, and 39 workers. In the production department, there were two steam boilers with 234 square meters of heating surface, four steam engines with 29 horsepower and a waterwheel. In the same year, the company showcased Vanillin, p-oxybenzaldehyde, coumarin, heliotropin, terpineol, benzophenone, acetophenone, eugenol, isoeugenol, linalool, acetic acid linalool ester, as well as other compounds related to these substances at the World Exhibition. Haarmann continued to hire additional chemists who carried on Tiemann's legacy after his death. Max Kerschbaum joined in 1897, followed by Hermann Tigges and Johann Eduard Marwedel.

The newly introduced products were based on scientific research, and Otto Witt (1853-1915) wrote in his report on the 1893 World Exhibition to the Prussian Minister of Culture, Julius Robert Bosse (1832-1901):
"*One of the factories where the collaboration of science and technology in Germany is most evident is Haarmann & Reimer in Holzminden. This factory was established for the commercial exploitation of the synthesis of vanillin first accomplished by Tiemann and Haarmann. Gradually, the field of activity has expanded significantly, and the production of various aroma compounds through synthetic means has been undertaken, with almost every new technical achievement of the factory being a direct result of rigorous scientific research. The extensive range of exquisite products exhibited at the fair demonstrated the significant scale of the current operations of the company.*"[71].

Haarmann & Reimer also succeeded in replicating essential oils and introduced the first synthetic lily-of-the-valley oil to the market in 1909.

The relationship between the entrepreneur Haarmann and the social-democratic-influenced district became strained, leading Haarmann to move his residence to Höxter, located on the opposite side of the Weser River. In 1896, he had an exclusive villa constructed in Moroccan style with a view of the Weser, designed by the renowned architect Constantin Uhde (1836-1905) from Braunschweig **(Figure 2)** [72].

Since residing in Höxter, Haarmann had to endure a one-hour carriage ride across the Weser Bridge, completed in 1885, to reach Holzminden, where progress had slowly taken hold. A hospital was established in 1878, and in 1904, the sewer system was completed. In 1900, there were 46 telephone subscribers in Holzminden, and Haarmann & Reimer held the number 19. In 1901, the company transformed from a partnership into a GmbH (limited liability company).

Despite his many business trips, Haarmann found time for a usually four-week vacation on the North Sea island of Norderney with his family. His two sons also pursued chemistry studies, following in their father's footsteps. The elder son began in Freiburg in 1896, then transferred to Göttingen before completing his doctorate in Berlin in 1901. The younger son started his studies in Dresden and later moved to Kiel via Freiburg, where he earned his doctorate in 1915. Haarmann's wife passed away shortly before the end of World War I due to cancer. In 1917, he was appointed an honorary citizen of the city of Höxter for his numerous contributions, including the funding of a much-needed gymnasium.

Between 1897 and 1918, Haarmann established more than 15 foundations, such as the Haarmann Foundation and the Foundation for the Hospital and Marienstift in Höxter, as well as the Foundation for Cancer Research in Münster. After his sons joined the company, Haarmann enjoyed a somewhat quieter life. He had a fondness for technological innovations and equipped his laundry room with electrical appliances as soon as possible. He also enjoyed crafting toys for his grandchildren and, as his leisure time expanded, developed an interest in history and cherished his extensive library. His love for travel cost him his life when he suffered rib fractures and a chest contusion during a stormy sea voyage, from which he never recovered. He passed away on March 6, 1931.

How Background Shapes the Professional Profile

The majority of entrepreneurs during the Industrial Revolution in Germany came from artisanal and commercial professions. Haarmann was an exception as he opened his own business immediately after completing his studies. However, among the group from which entrepreneurs mainly emerged were the sons of factory owners. Haarmann came from a family of entrepreneurs, with his father managing the Sollinger quarries and his uncle overseeing the ceramics factory founded by his grandfather. He grew up surrounded by entrepreneurs. What qualities must entrepreneurs possess, and under what conditions must they operate?

Entrepreneurs often work under conditions of uncertainty, risk, urgency, complexity, and resource scarcity. Entrepreneurship is defined by activities that involve identifying, evaluating, and exploiting new business opportunities. The aim of entrepreneurship is to introduce new products or services, new forms of organization, new markets, new processes, or new materials. This is accomplished through the establishment of organizations.(73)

After successfully synthesizing vanillin in 1874, Haarmann founded Haarmann's Vanillin Factory in Holzminden. It is considered the first factory to technically produce a fragrance or aroma substance. In collaboration with Ferdinand Tiemann and Karl Reimer, both of whom, like Haarmann, had learned

Fig. 2 Villa Haarmann. *Source: Psychogerd Wikimedia Commons*

in the laboratory of August Wilhelm Hofmann, the company, renamed Haarmann & Reimer, became one of the largest and leading manufacturers of flavors and fragrances. Haarmann demonstrated a willingness to take risks, as he expanded his activities to France early on, a country that he and his colleagues had been fighting against until recently. The company constantly sought new substances and successfully brought them to the market. Haarmann proved to be a powerful and visionary entrepreneur who had to compete against strong competitors. He was highly successful and achieved significant wealth.

References *(German language)*:

[1] *Albert Ellmer*, „Dr. Wilhelm Haarmann †", in: Riechstoff Industrie 6 (1931). S. 102-105

[2] *Georg Schwedt*, Betörende Düfte, sinnliche Aromen, Weinheim 2008.

[3] *Margot Vogelmann*, „Dr. Wilhelm Haarmann und seine Zeit" in: Jahrbuch Landkreis Holzminden 4 (1986). S. 58-99.

[4] *Björn Bernhard Kuhse*, Vanillin – Historie und Schulrelevanz: Die Geschichte einer regionalen Riechstoffindustrie und deren Verwendung in einem praxisorientierten Chemieunterricht, Göttingen 2010.

[5] *Björn Bernhard Kuhse*, Wilhelm Haarmann auf den Spuren der Vanille: Forscher, Unternehmer und Pionier der Riechstoffe, Holzminden 2012.

[6] *Björn Bernhard Kuhse*, Der Herr der Düfte: Mit der Vanille zum Multimillionär, Ein Wissenschaftsroman, Holzminden 2014.

[7] *Björn Bernhard Kuhse*, Hofmann: Ein Chemiker begeistert Queen Victoria, Göttingen 2018.

[8] *Georg Schwedt*, Am Anfang war das Vanillin. Die Väter der Aromen-Industrie in Holzminden, Norderstedt 2017. Ders., Am Anfang war das Vanillin. Die Väter der Aromen-Industrie in Holzminden. iBooks.trie/id1275508050?mt=11. Heruntergeladen: 29. September 2017.

[9] *Klaus, Stanzl*, Die Entstehung der Riechstoffindustrie im 19. Jahrhundert: Die synthetischen Riechstoffe. Stuttgart 2019.
Klaus Stanzl, „Die Industrie der Riechstoffe im 19. Jahrhundert", in: Mitteilungen der Fachgruppe Chemie der Geschichte 26 (2020), S. 142-167.

[10] *Werner Jahns*, „Die Privatisierung des staatseigenen Betriebes "Administration der Sollinger Steinbrüche" und die Familie Haarmann", in: Jahrbuch Landkreis Holzminden 17 (1999), S. 31-50

[11] „Konstituierende Versammlung", in: Berichte der deutschen chemischen Gesellschaft 1 (1) (1868)

[12] „Statuten der deutschen chemischen Gesellschaft zu Berlin", in: Berichte der deutschen chemischen Gesellschaft, 1(1), (1868). S. 5–8.

[13] *zitiert aus: Margot Vogelmann*, „Dr. Wilhelm Haarmann und seine Zeit", in: Jahrbuch Landkreis Holzminden 4 (1986). S. 74.

[14] *zitiert aus: Margot Vogelmann*, „Dr. Wilhelm Haarmann und seine Zeit", in: Jahrbuch Landkreis Holzminden 4 (1986). S. 77

[15] *Wilhelm Haarmann*, „Über einige Derivate des Salicylaldehyds", in: Berichte der deutschen chemischen Gesellschaft 6 (1873). S. 338-341

[16] *Wilhelm Kubel*, „Coniferin, ein Glucosid aus dem Cambialsaft der Nadelhölzer", in: Journal für praktische Chemie 97 (1866). S. 243

[17] *Wilhelm Kubel*, „Coniferin, ein Glucosid aus dem Cambialsaft der Nadelhölzer", in: Journal für praktische Chemie 97 (1866). S. 243 – 246

[18] *Wilhelm Haarmann*, Über einige Derivate der Glucoside Coniferin und Salicin, Dissertation Berlin 1872. S.

[19] *Ferdinand Tiemann und Wilhelm Haarmann*, „Über das Coniferin und seine Umwandlung in das aromatische Princip der Vanille", in: Berichte der deutschen chemischen Gesellschaft 7 (1874). S. 608-623

[20] Die Reaktion wird 1882 von Bernhard Tollens auf Nachweis für reduzierende funktionelle Gruppen beschrieben und wird Tollensprobe genannt werden. B. Tollens," Ueber ammon-alkalische Silberlösung als Reagens auf Aldehyd", in: Chem. Ber. 15 (1882). S. 1635–1639

[21] Die Bisulfit-Reaktion ist eine nukleophile Addition von Natriumhydrogensulfit an Carbonylverbindungen, wobei ein Feststoff entsteht.

[22] Emulsin ist eine β-Glucosidase, die Moleküle mit Glucose hydrolisiert.

[23] *Wilhelm Haarmann*, Über einige Derivate der Glucoside Coniferin und Salicin, Inaugural-Dissertation, Berlin 1872.

[24] Universitätsarchiv Göttingen. Signatur: Phil. Fak. 157, S. 432-439

[25] *Margot Vogelmann*, „Dr. Wilhelm Haarmann und seine Zeit", in: Jahrbuch Landkreis Holzminden 4 (1986). S. 58-99

[26] *Ferdinand Tiemann und Wilhelm Haarmann*, „Über das Coniferin und seine Umwandlung in das aromatische Princip der Vanille", in: Berichte der deutschen chemischen Gesellschaft 7 (1874). S. 614

[27] *Pierre-Paulin Carles*, „Étude chimique du givre de vanille", Bulletin de la Societé Chimique de France 17 (1872). S. 12-16.

[28] *Elisabeth Vaupel*, „Betört von Vanille. Seit 500 Jahren begehrt - und immer noch Forschungsthema", in: Kultur & Technik, 26/1 (2002). S. 47–51

[29] *Otto N. Witt*, „Ferdinand Tiemann. Ein Lebensbild", in: Berichte der deutschen chemischen Gesellschaft 34/3 (1901), S. 4402–4455

[30] Deutsches Reichspatent 579

[31] US Patent No.: 151,119 (May 19, 1874); Wilhelm Haarmann, "Patent No.: 709", in: Chemical News and Journal of Physical Science 30 (1874). S. 230

[32] *Franz Reuleaux*, „Briefe aus Philadelphia". Braunschweig 1877. S. 3-5

[33] *zitiert aus: Margot Vogelmann*, „Dr. Wilhelm Haarmann und seine Zeit", in: Jahrbuch Landkreis Holzminden 4 (1986). S. 61-62

[34] *Signe Mikulane*, „Vanille: Geschichte, Zucht / Veredlung und wirtschaftliche Bedeutung", in: Île de la Réunion. Abschlussbericht zur großen Exkursion. Geographisches Institut der Universität Heidelberg 2006. S. 103-110

[35] *Elisabeth Vaupel*, „Betört von Vanille. Seit 500 Jahren begehrt - und immer noch Forschungsthema", in: Kultur & Technik 26 (2002). S. 47–51

[36] Haarmann und Reimer, „Über das Vanillin", in: Chemiker Zeitung 3 (1879). S. 635

[37] *Ferdinand Tiemann und Wilhelm Haarmann*, „Über eine Methode zur quantitativen Bestimmung des Vanillins in der Vanille", in: Berichte der deutschen chemischen Gesellschaft 8 (1875), S.1115–1122

[38] *Ferdinand Tiemann und Wilhelm Haarmann*, „Über die Bestandteile der natürlichen Vanille", in: Berichte der deutschen chemischen Gesellschaft 9 (1876), S. 1287–1292

[39] *Margot Vogelmann*, „Aus der Geschichte der Riechstoffindustrie", in: Chemiker Zeitung 99 (1975) S. 49–53

[40] *Haarmann und Reimer*, „Über das Vanillin", in: Chemiker Zeitung 3 (1879). S. 781

[41] *Karl Reimer*, „Über eine neue Bildungsweise aromatischer Aldehyde", in: Berichte der deutschen chemischen Gesellschaft, 9 (1876), S. 423–424.

[42] *Karl Reimer und Ferdinand Tiemann*, „Über die Einwirkung von Chloroform auf alkalische Phenole", in: Berichte der deutschen chemischen Gesellschaft, 9 (1876) S. 824–828; Karl Reimer und Ferdinand Tiemann, „Über die Einwirkung von Chloroform auf Phenole und besonders aromatische Oxysäuren in alkalischer Lösung", in: Berichte der deutschen chemischen Gesellschaft, 9 (1876), S. 1268–1278

[43] *Karl Reimer*, „Bildungsweise aromatischer Aldehyde", in: Berichte der deutschen chemischen Gesellschaft 9 (1876), S. 423–424

[44] *Ferdinand Tiemann*, „Über eine Bildungsweise der Vanillinsäure und des Vanillins aus Eugenol und über die Synthese der Ferulasäure", in: Berichte der deutschen chemischen Gesellschaft, 9 (1876), S. 52–54

[45] Deutsches Reichspatent 93,938

[46] *Otto N. Witt*, „Georges de Laire" in: Berichte der deutschen chemischen Gesellschaft 34 (1909). S. 3-5

[47] *Elisabeth Vaupel*, „Betört von Vanille. Seit 500 Jahren begehrt - und immer noch Forschungsthema", in: Kultur & Technik 26 (2002). S. 47–51

[48] *Björn Bernhard Kuhse*: Wilhelm Haarmann auf den Spuren der Vanille. Holzminden 2012, S. 66

[49] *Jürgen Kocka*, Unternehmen in der deutschen Industrialisierung. Göttingen 1975

[50] Deutsches Reichspatent 63,007; Deutsches Reichspatent 80,195 / Deutsches Reichspatent 92,794 / Britisches Patent 27,236 / Britisches Patent 164,715

[51] "Semi-Annual Report of Schimmel & Co. (Fritzsche Brothers)", eds. by Schimmel and Company, Miltitz near Leipzig, London and New York. 1904, S. 131

[52] Rudolph Fittig und Wilhelm Mielck: „Untersuchungen über die Konstitution des Piperins und seiner Spaltprodukte Piperinsäure und Piperidin", in Liebigs Annalen der Chemie 152 (1869). S. 25-58

[53] Johan Frederic Eijkmann, „Sur les principes constituants de l'Illicium relegiosum. (Shikimi-no-ki en japanais)", in: Recueil des Travaux Chimiques des Pays-Bas 4 (1885). S.32-54

[54] Theodor Poleck, „Über die chemische Struktur des Safrols", in: Berichte der deutschen chemischen Gesellschaft 19 (1886). S. 1094-1098

[55] August Vogel, „Darstellung von Benzoesäure aus der Tonka-Bohne und aus den Melioliten oder Steinklee", in: Annalen der Physik 64 (1820). S. 161-166

[56] Nicolas Jan Gaston Guibourt, „De la semence Tonka", in: Histoire Abregée des Drogues Simple. Paris 1820. S. 160-161

[57] William H. Perkin, "On the Artificial Production of Coumarin and Formation of its Homologues", in: Journal of the Chemical Society, 22 (1868), S. 53–63

[58] Ferdinand Tiemann und Hermann Herzfeld, „Zur Synthese des Cumarins aus Salicylaldehyd", in: Berichte der deutschen chemischen Gesellschaft, 10 (1877), S. 283–288

[59] „Veilchenwurzel" ist eine ältere Bezeichnung für den Iris-Wurzelstock, und nicht mit der Wurzel des Wohlriechenden Veilchens (Violae odoratae radix) zu verwechseln

[60] Ferdinand Tiemann und Geroge de Laire, „Über Iridin, das Glucosid der Veilchenwurzel", in Berichte der deutschen chemischen Gesellschaft 26 (1893). S. 2010-2044

[61] Ferdinand Tiemann und Paul Krüger, „Über Veilchenaroma", in: Berichte der deutschen chemischen Gesellschaft 26 (1893). S. 2675-2708; Deutsches Reichspatent 73,089.

[62] Ferdinand Tiemann und Paul Krüger, „Über Veilchenaroma", in: Berichte der deutschen chemischen Gesellschaft 26 (1893). S. 2675-2708. S. 2708

[63] *Leopold Ruzicka*, „Über die Beziehungen zwischen den Jononen und Iron", in: Helvetica Chimica Acta 2 (1919). S. 352-362
Leopold Ruzicka, Casimir F. Seidel, Hans Schinz und Max Pfeiffer, „Veilchenriechstoffe. Die Konstitution des Irons", in: Helvetia Chimica Acta 30 (1947). S. 1807-1810
Hans Schinz, Leopold Ruzicka, Casimir F. Seidel, Ch. Tavel, „Produits à odeur de violette. Synthèse de la d,l-α-irone", Helvetia Chimica Acta 30 (1947). S. 1810-1814
Leopold Ruzicka, Casimir F. Seidel und Hans Schinz, „Veilchenriechstoffe III. Über die Bruttoformel und einige Umsetzungen des Irons", Helvetica Chimica Acta 16 (1933). S. 1143-1154

[64] *Friedrich Wilhelm Semmler,* „Über Citral (Geranial) und Lemongrasöl", Berichte der deutschen chemischen Gesellschaft 31 (1898). S. 3001-3003
Friedrich Wilhelm Semmler, „Über indisches Geraniumöl. II. Oxidation des Geraniols", in: Berichte der deutschen chemischen Gesellschaft 23 (1890). S. 2965-2968

[65] Erdmann: DRP 110 386

[66] *H. Mann*, Die moderne Parfümerie, Augsburg 1904. S. 542

[67] *Albert Ganswindt*, Die Riechstoffe. Ihre Geschichte, ihr Vorkommen, ihre Gewinnung, ihre Eigenschaften, ihre Prüfung und ihre Anwendung in der Parfümerie, Kosmetik, Pharmazie, Medizin, Technik und Likörfabrikation, 8. Aufl., Leipzig 1922.

[68] *Georg Cohn*, „Synthetische Riechstoffe", in: Handbuch der kosmetischen Chemie, hrsg. von Hans Truttwin, Leipzig 1920, S. 209–242.

[69] Statistisches Jahrbuch für das Deutsche Reich 1900 bis 1915

[70] *Albert Hesse*, „Bilder aus der Riechstoffindustrie", in: Zeitschrift für angewandte Chemie, 25 (1912), S. 337–365; Eugénie Briot, "From Industry to Luxury. French Perfume in the Nineteenth Century", in: Business History Review, 85 (2011), S. 273–294.

[71] *Otto N. Witt*, Die chemische Industrie auf der Weltausstellung zu Chicago und in den Vereinigten Staaten von Nordamerika im Jahre 1893, Berlin 1894, S. 136-137.

[72] Quelle/Informationen über Haarmann von Heinrich Steude, einem Ur-Enkel

[73] *Scott Shane*, A General Theory of Entrepreneurship. The Individual-opportunity Nexus (= New Horizons in Entrepreneurship). Cheltenham 22005.

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Think Globally, Buy Locally – New Approaches to Professional Cleaning and Care

T. Kimmel, T. Potstada, A. Leismüller, R. Kreische, L. Kalz

On May 22nd and 23rd, 2023, stakeholders from the cleaning and hygiene industries gathered in Constance for the annual conference of the SEPAWA Professional Cleaning & Care Specialist Group.

This conference is aimed at manufacturers and users of professional products and has been providing information on current developments in this field for over fifteen years. The conference was moderated by **Tobias Potstada** and covered three thematic areas.

Due to the disrupted supply chains caused by the COVID-19 pandemic, two presentations focused on supply security. One presentation highlighted the issue from the perspective of an association **(Mr. Entner, Presentation 1)**, and the other from the perspective of a distributor **(Mr. Heimbach, Presentation 2)**.

Environmental protection has a strong influence on formulations in the field of cleaning and care due to various existing or anticipated regulations. The topic of microplastic avoidance has been a concern in the industry for some time and will continue to be so, as the filtration of fibrous microplastics in washing machines will be mandatory in France from 2025. Three presentations showcased the range of challenges in this regard. These included an examination of legislative aspects within the framework of ECHA regulations **(Mr. Entner, Presentation 4)**, a presentation of findings on the formation and prevention of microplastics during washing **(Brandt, Presentation 3)**, and an exploration of the handling of microplastics in floor care by a polymer manufacturer **(Ms. Mannheim and Mr. Bach, Presentation 5)**. Thus, there is a need for biodegradable components in floor care products, such as polymers based on PU **(Mr. Bernhard Sölle – Presentation 6)**, wood-derived glycols **(Mr. John, Presentation 7)**, or natural waxes **(Dr. Krendlinger, Presentation 8)**.

A practical perspective rounded out the program. One presentation provided an update on the current state of solar cleaning from a manufacturer of solar cleaning systems **(Mr. Kneiber, Presentation 9)**, while another took a closer look at questionable cleaning methods from the perspective of a cleaning product manufacturer **(Ms. Nerowski, Presentation 10)**.

As usual, on the first day's evening, attendees had the opportunity to exchange information and industry news on the lakeside terrace. The next conference is expected to take place in May or June 2024 in Constance.

Presentation 01: Raw Material Supply in Uncertain Times (Marcello Entner, Austrian Federal Economic Chamber / Association of the Chemical Industry of Austria (FCIO))

In his presentation, Mr. Marcello Entner from the Association of the Chemical Industry of Austria (FCIO) described the economic situation of the European chemical industry. Based on current data, he referred to the positive development of sales in recent years, particularly since 2021. However, this trend in sales figures is primarily attributed to inflation, as the production volumes have not increased to the same extent.

One of the main drivers of price increases mentioned by Mr. Entner is the rising energy prices, which have currently stabilized at a high level after a significant increase. For example, this trend in energy costs led to a 17% increase in manufacturer prices for soaps and detergents in the EU compared to the previous year. Consequently, this will result in a competitive disadvantage for Europe.

The chemical industry is also concerned about the shortage of skilled workers. 72% of the surveyed companies stated that they are heavily affected by the shortage of skilled workers, which has a significant impact on business operations and expansion efforts. The prevailing inflation also drives up labor costs and exacerbates the situation further.

Despite the significant economic challenges, Mr. Entner concluded his presentation with a cautiously positive outlook, partly because the sentiment in the chemical sector is gradually improving.

Presentation 02: Supply Security and Supply Chain Issues from the Distributor's Perspective (Daniel Heimbach, Julius Hoesch GmbH & Co. KG)

The past few years have certainly not been easy for producers of cleaning and care products in terms of product availability, marked by volatility and fluctuations. However, this challenging time has brought about significant changes not only for customers but also for raw material distributors. Mr. Daniel Heimbach, Head of Sales & Procurement at Julius Hoesch, explained in his presentation how the supplier of industrial and specialty chemicals has dealt with these challenges. The three phases of the supply chain – procurement, production, and distribution – have faced unprecedented problems within a short period of time:

Due to the pandemic, demand plummeted within a few weeks, and even in recovering markets, supply chains remained disrupted. This was further compounded by long-standing trade disputes between the US and China, the Ukraine conflict, and individual events such as the Ever Given container ship incident. At the same time, new regulatory requirements such as the Supply Chain Due Diligence Act came into effect. These challenges were further compounded by a shortage of skilled workers in the logistics sector.

To better mitigate these events, which are beyond the distributor's control, and to prevent supply shortages in the future, various strategies have been defined. These include diversifying suppliers, strengthening the sourcing strategy in Europe, and establishing transparent supply chains. Additionally, inventory management is being optimized.

To reduce risks in the long run, a sustainable multi-supplier strategy is being pursued. Moreover, awareness of the relationship between price and performance must be established, allowing for a confident stance against the "cheap is good" logistics and procurement mentality.

Presentation 03: New Insights into Sources, Sinks, and Solutions for Fibrous Microplastics (Stefan Brandt, University of Applied Sciences Niederrhein, Krefeld)

At the beginning of the presentation, Mr. Brandt explained the definition and differences between specifically fibrous microplastics from textiles and microplastics in general. Microplastics are defined as particles with a diameter of less than 5 mm. In contrast, fibrous microplastics are usually only a few micrometers thick, which allows them to easily reach wastewater treatment plants. However, the microplastics retained there are not disposed of through incineration but are instead, to a significant extent, spread as fertilizer on fields through sewage sludge, thus remaining in the environment. In Germany, approximately 80 g of fiber abrasion from synthetic textile washing is released per person annually. According to an estimate from 2017, fibrous microplastics from synthetic textiles account for 35% of the microplastics in the world's oceans. This high contamination is caused by the large proportion of polyester fibers in textiles, accounting for about 50% **(Figure 1)**.

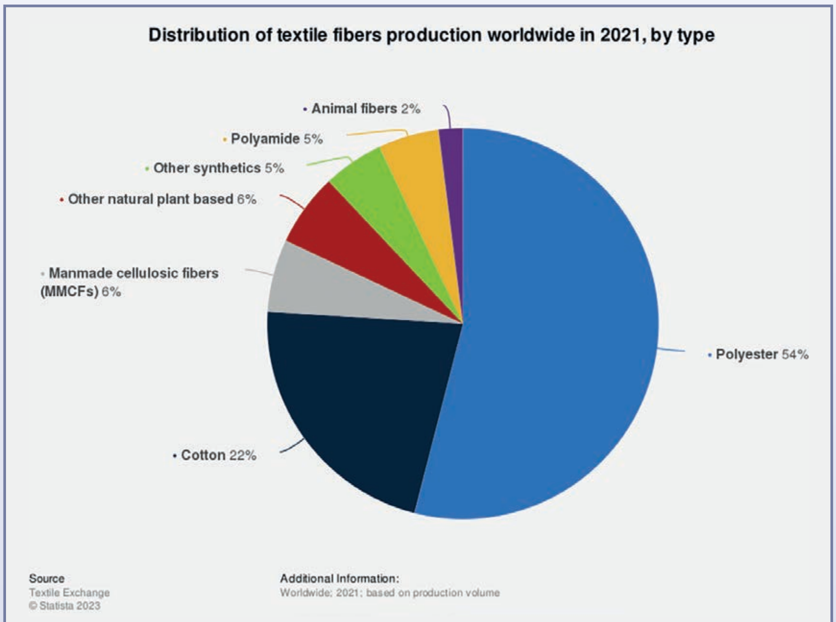

Fig. 1 The global distribution of fiber types in fiber production in 2021 shows that polyester dominates the world fiber market with 54%. *Source: Statista based on data from Textile Exchange.*

These fibers are mainly used in outdoor clothing, which has a high growth rate, as well as in bulky knits (fleece®).

The TextilMission project was launched in 2017, involving various partners (University of Applied Sciences Niederrhein, Technical University of Dresden, WWF, Henkel, Miele, BSI, adidas, VAUDE, and POLARTEC). Through interdisciplinary collaboration, analyses were conducted, and solutions for reducing fibrous microplastics were identified.

To determine the impact of domestic laundry on microplastics, washing tests were carried out under various conditions. Small washing loads of selected top-selling outdoor and sports apparel were washed with liquid detergent in a household front-loading washing machine using the Easy Care 40°C program. Subsequently, the wastewater from the washing machines was filtered sequentially through different steel filters (1.5 mm, 0.5 mm, 0.15 mm, 50 µm, and 5 µm). The amount of retained microplastics was determined gravimetrically. The quantification of the found polymers was performed in the laboratory using TED-GC/MS. At the filter sizes of 50 µm and 5 µm, 99% of the captured samples were quantified as PET originating from the textiles. The other polymers likely originated from contamination with other types of microplastics found in households and laboratories **(Figure 2)**.

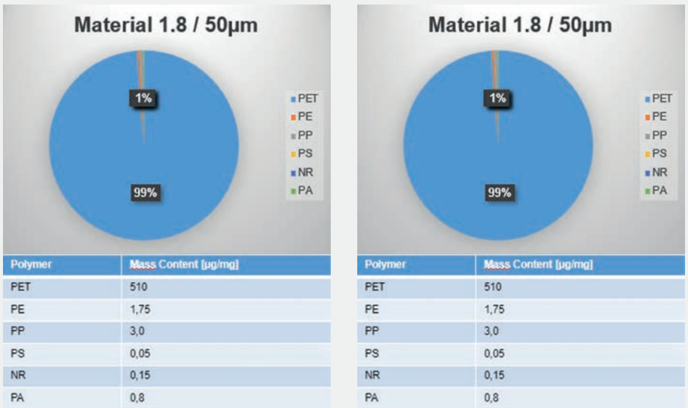

Fig. 2 Quantification of polymers retained by various filters with mesh sizes of 50 µm and 5 µm. The respective proportions were determined by the laboratory method TED-GC/MS by the Federal Institute for Materials Testing.

An important finding was that a significant amount of fibrous microplastics is released, particularly during the first and second washes. When the microplastic quantities from the first 10 washing cycles are added together, approximately 50% of the total amount is released during the first wash **(Figure 3)**.

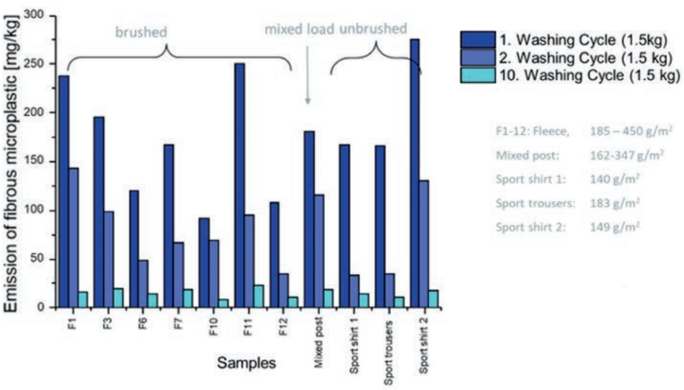

Fig. 3 The release of fibrous microplastics during the first wash accounts for 40-60% of the sum of the first ten washes.

Based on these results, Mr. Brandt, on behalf of the TextilMission project, recommended avoiding "fast fashion" and opting for high-quality fibers or clothing. The more frequently the fiber is washed, the lower the loss of fibrous microplastics. Additionally, the release can be reduced through higher load quantities and optimized utilization of washing machine capacity.

According to the EU Textile Strategy, various measures are aimed at avoiding or reducing microplastics throughout the product life cycle, including mandatory requirements for product design, controlled manufacturing processes, promotion of innovative materials, optimized washing machine filters and detergents, as well as setting microplastic limits. Mr. Brandt sees the enzymatic degradation of PET fragments in wastewater treatment plants and the development of new materials for innovative fiber types that possess better biodegradability as perspectives for addressing the issue.

Presentation 04: Microplastic Restriction Sales according to ECHA (Marcello Entner, Austrian Federal Economic Chamber / Association of the Chemical Industry Austria (FCIO))

Mr. Marcello Entner summarized the planned microplastic restrictions of the EU regulation, which will come into effect in the third quarter of this year, in another presentation. He first addressed the definition of microplastics or "Synthetic Polymer Microparticles" (SPM). SPM particles are defined as particles containing an encapsulation or solid polymer content of ≥ 1% (w/w). Such particles with a diameter of ≤ 5 mm or fibers with a length of ≤ 15 mm and a diameter of ≤ 3 mm fall under the restrictions of the forthcoming regulation.

Products that add SPM to achieve certain properties at more than 0.1 weight percent are affected by the restriction. However, if the release of SPM into the environment can be prevented by the chemical or physical properties of the product in its end use or if emissions are already avoided by other regulatory measures, there are exceptions to the prohibition of placing on the market (§ 4 and 5).

This point was highly debated among the participants during the event on both days. For example, is the application of floor care products and subsequent removal of the coating with cleaning agents considered an introduction into the environment or not? The fact is that floor polish products are explicitly listed in the regulation. Clarification on this point will likely have to await accompanying guidance documents. The exceptions for which the regulation does not apply include:

- Natural polymers
- Polymers that do not contain carbon
- Water-soluble polymers (solubility ≥ 2 g/L)
- (Biologically) degradable polymers

After the regulation comes into effect, authorities can request mandatory information on polymer identity. This request must be responded to within a feedback period of 7 days. The requested detailed information may include names (IUPAC), CAS, EC number, molecular weight (range), analytical data, associated methods, and information on the function of the polymer. If the information is not yet available, there is a

30-day feedback period for the supplier. Transition provisions apply to various product categories, with the following deadlines listed below:

- Rinse-off cosmetics (4 years)
- Detergents, waxes, polishes like floor polish (5 years)
- Encapsulated fragrances (6 years)
- Leave-on cosmetics (6 years)
- Makeup, lip, and nail products (12 years)

Furthermore, according to the regulation, there is an obligation to provide information on SPM/microplastics in the product on labels, packaging, package inserts, and safety data sheets starting from the second year after the regulation comes into effect. Digital tools such as QR codes are only permitted as complementary means.

In conclusion, Mr. Entner provided an outlook on forthcoming regulatory measures regarding SPM that will impact the industry in the future, such as regulations on dishwasher and laundry detergent capsules.

Presentation 05: Microplastic – A Challenge in Floor Care from a Polymer Manufacturer's Point of View (Christelle Mannheim & Armin Bach, Zschimmer & Schwarz Group)

After the legal classification, the challenges faced by floor care products with microplastic-containing formulations were presented. The entry of microplastics through cleaning and care products is very low, but there is a clear need for action. Every measure counts, and everyone must take responsibility. For example, it was pointed out that the use of cleaning agents in the North East Atlantic region leads to an annual entry of 100,000 kg of microplastics into the marine environment. The most radical step would be to completely eliminate the use of floor care products. However, it is also argued that the use of these products can help reduce environmental impact by increasing the lifespan of floor coverings and reducing cleaning efforts. In addition, the ingredients are only partially affected by microplastic restrictions since, for example, the micro-particles contained in floor coatings form a closed layer during film formation and are therefore no longer subject to the restrictions. However, it is expected that regulations will become stricter in the long term, so proactive planning should be considered. Another problem is that conventional ingredients of floor care products, such as polymers (acrylates) and waxes, often contain polyethylene (PE), both of which are poorly biodegradable.

The company calls for new global standards, increased investments in research for sustainable and biodegradable substitutes, and more green innovations. They aim to lead by example.

Presentation 06: Biodegradable Polymers for PU-based Floor Care Products (Bernhard Sölle, Polymer Competence Center Leoben GmbH (PCCL))

To address the challenges arising from the SPM restrictions in the field of floor care, Mr. Bernhard Sölle reported on initial research results from his dissertation on biodegradable PU-based polymers for floor care products, supported by the Austrian Research Promotion Agency. The project aimed to find substitution options for the predominantly used acrylates in the field of floor care, which are non-biodegradable or have low biodegradability.

Therefore, Mr. Sölle primarily synthesized polymers with "labile" groups, such as ester groups, to enhance biodegradability. However, pure polyesters proved to be too "soft" or not sufficiently resistant for use in heavily stressed floor care coatings. Consequently, he focused on the synthesis of polyurethanes in the further course of the research project. By using different polyester diols in the synthesis, it is possible to adjust various polymer properties, such as biodegradability and hardness/resistance.

After a brief overview of step-growth reactions such as polycondensation and polyaddition, Mr. Sölle detailed the polymer syntheses conducted in his work and the possibilities to influence the desired properties accordingly.

Initial formulations of floor care coatings showed promising results but exhibited lower resistance and poorer soil repellency compared to standard coatings upon closer examination. However, external tests of biodegradability according to OECD 302B already showed biodegradabilities of up to 30% for the polymer prototypes.

As another highlight of the project, Mr. Sölle introduced covalently bound fluorescent markers (naphthalimide derivatives) into the polymer structure during the synthesis to enable the detection of SPM (microplastic particles) in wastewater, sludge, etc., for better tracking of the fate of SPM in the environment.

Presentation 07: Circular Economy: Bioglycols from Wood (Holger John, UPM Biochemicals, Helsinki)

In his presentation, Mr. Holger John from UPM Biochemicals in Helsinki reported on the development and production of glycols from renewable raw materials. Ethyleneglycol and propyleneglycol can be produced from wood as the base material. Initial samples have already been made available and tested. The CO_2 footprint has been determined and certified by DEKRA. FSC-certified beech wood is used for production, which is harvested within a radius of 150-600 km around the Leuna production site.

The share of beech trees in German forests is 16% (2021), and it is projected to increase to 21% by 2050 through the cultivation of mixed wood. Wood is a renewable and climate-neutral resource. Sustainable forest management and forestry practices are essential to achieve global CO_2 sequestration goals. This involves controlled harvesting and replanting, as young trees can absorb more CO_2, creating a renewable cycle.

The hardwood from the tree trunk is used in the furniture industry, but a large proportion of the remaining tree components are currently only used for energy generation. The plan is to produce bioglycols from this combustion wood and the ongoing thinning wood.

Mr. John highlighted the following advantages: Bioglycols are 100% bio-based and can have a better carbon footprint and CO_2 impact compared to fossil fuels. The beech wood is sourced and distributed regionally and is vegan. Bioglycols can also replace conventional glycols as a raw material for PET production, enabling a bio-based content of up to 30%.

Presentation 08: Natural and Biodegradable Waxes for Use in Microplastic-Free Floor Care Products (Dr. Ernst Krendlinger, EPW GmbH)

Dr. Krendlinger, former Head of Development at Clariant, Lubrizol, and Deurex, as well as a recipient of the European Inventor Award, illustrated the possibilities of using natural waxes in polymer coatings, both theoretically and with practical examples.

Due to the upcoming restrictions on the intentional use of microplastics, traditional fossil-based PE and PP waxes in floor care products are facing limitations. One solution is to look to nature, as natural waxes are not covered by the planned ECHA regulation. In addition to the well-known but too soft for floor coatings beeswax, the properties of the much harder and already industrially used Brazilian carnauba wax were discussed. The lesser-known but still relevant candelilla and sunflower waxes, with a melting point of around 70°C, were also examined practically with provided samples.

A waste product of sugar production is sugarcane wax, which is present in the sugarcane itself at only 0.1%, but can be found in the bagasse (filter cake) at 8-10%. This bagasse, which has been deposited in landfills in the main cultivation areas for decades, can now be exploited through landfill mining. With a high melting point and low acid value, the properties relevant to floor care products align with the new rising star: rice (bran) wax. This wax exhibits properties that can compete with the synthetic hydrocarbon waxes used so far.

Even more exotic waxes were mentioned to illustrate that waxes can be found in unusual places, such as the wax properties of earwax and the particularly hard wax from scale insects used in shellac production.

Presentation 09: Practical Insights from PV Cleaning (Josha Kneiber, TG hyLIFT GmbH)

Germany's ambitions regarding the expansion of photovoltaic (PV) systems are evident with the Renewable Energy Sources Act, which came into effect in 2023. According to this act, the currently installed PV capacity is set to increase by over 330% by 2030. The necessity and benefits of sustainable energy should be generally known. In his presentation, Josha Keiber, Managing Director of TG hyLIFT GmbH, discussed the importance of PV system cleaning and the associated challenges.

The type and intensity of dirt accumulation vary depending on the region, type of installation, location, season, and weather conditions. However, it is clear that higher dirt accumulation leads to greater loss of energy yield. In Germany, not cleaning the PV panels can result in a loss of around 10%, while in "dusty weather conditions without rain," this figure can quickly exceed 20%. Therefore, cleaning is necessary. The use of unsuitable techniques and methods, such as using a freely moving robot on a steep surface and/or using the wrong cleaning chemicals, can lead to the robot sliding off the roof, making the investment in cleaning far from profitable. Similarly, treating a concrete plant's PV system with water to remove cement dust would be counterproductive. Too abrasive bristles could damage anti-reflective coatings, reducing the system's energy yield despite cleaning. The use of certain chemicals requires the capture of wash water, making the cleaning of large systems economically unfeasible.
In summary, it is important to differentiate that not every cleaning method is suitable for every PV system. While simple handheld brushes may be suitable for smaller, easily accessible systems, it is recommended to invest in expensive specialized equipment or hire specialized service providers for other systems.

Presentation 10: Critical Examination of Questionable Cleaning Methods (Bianca Nerowski, TANA Chemie GmbH)

In the last presentation, Bianca Nerowski discussed the issues with various cleaning methods. She started with a brief summary of the definition of dirt (misplaced matter) and cleaning (removal of dirt). Then, Ms. Nerowski presented three cleaning methods that are often marketed as supposed solutions for private and building cleaners: UV-C light, ozone, and dry steam.

The DNA-damaging effect of UV-C light (wavelength of 200 to 280 nm) has been known for decades and is used, for example, for surface disinfection in hospitals. However, criticisms of this method include non-compliance with disinfection times, inadequate safety labeling that prohibits entering the treated areas, and the lack of effectiveness on shaded surfaces.

Dry steam refers to water vapor heated to 150 °C, where, unlike conventional (wet) steam, there is no liquid phase present. This medium can be used in appropriate cleaning devices to cause adhering dirt on surfaces to simply peel off through rapid heating. It is often claimed that 99.9% of germs on the surface are killed. However, this advertising claim is criticized because a germ reduction of a factor of 10^5 ("99.999%") is usually required to speak of disinfection. Nevertheless, slogans such as "No more health-endangering chemical disinfectants: Steam works faster than disinfectants!" are used in advertising. Ms. Nerowski emphasized that contrary to these claims, this method is also ineffective against house dust mites and therefore does not provide relief for allergy sufferers.

Finally, ozone (O3) is discussed as a problem-solving method. Due to its strong oxidative properties, ozone decomposes odor molecules and kills microorganisms, making it suitable for disinfection and odor elimination. However, the use of ozonated water in washing machines and dishwashers is criticized because the ozone molecule is unstable. It decomposes in distilled water after about 30 minutes and in the presence of dirt, it only takes a few seconds. Thus, there is not enough time for a disinfecting effect. Ozone spray bottles are often marketed as cleaning agents for quick and comprehensive "hygienization," although the precise meaning of this term remains open to interpretation for the recipient.

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CosmeticBusiness
International Trade Show of the Cosmetics Supplying Industry

LEIPZIG, 26 JUNE 2023

CosmeticBusiness 2023 closed on 15 June with very satisfied exhibitors and visitors. At the international trade show of the cosmetics supplying industry, 414 exhibitors and represented companies from 27 countries presented innovations and trends for the creation of future cosmetics products in three fully-booked exhibition halls at MOC Munich. A major focus of the event was sustainable product solutions. Trade visitors travelled to this top industry event from 43 countries and were impressed by its scope which included the Spotlight novelty show, several themed routes and a broad conference programme offering inspiration for product development.


Picture Credits: Leipziger Messe GmbH / Tom Schulze

CosmeticBusiness 2023: Leading Event Provides Powerful Inspiration for the International Cosmetics Industry

"*Three fully-booked exhibition halls, more than 70 new exhibitors, numerous start-ups and very satisfied exhibitors: CosmeticBusiness is continuing its success story*", reports a satisfied **Markus Geisenberger**, Managing Director of Leipziger Messe. "Exhibitors and visitors alike have made this international industry get-together a place for exchanging expertise, developing new business contacts and coordinating project details", he adds. "CosmeticBusiness is the cosmetics industry's main event and a fixed item in the trade show calendar."

Expanded Exhibition Area for Ingredients and Increased International Participation

From ingredients and manufacturing to packaging, CosmeticBusiness combines every aspect of cosmetics manufacturing and packaging at one central venue, thereby reflecting the industry's entire value chain. At this year's edition of the international trade show, 414 exhibitors and represented companies from 27 countries presented their range of products and services across 11,000 m^2 of exhibition space. This represents an increase of 25 per cent compared to the last edition of CosmeticBusiness. The proportion of exhibitors from abroad rose from 32 per cent in 2022 to 37 per cent this year.

Another noteworthy development was the larger exhibition area for ingredients. With a total of 148 exhibitors and represented companies, this was a third larger than at last year's event, offering industry visitors even more inspiration.

Dr Oliver Reimelt, Country Sales Manager at Croda GmbH, says: "*At CosmeticBusiness, we were able to meet our regular customers and acquire new ones. The mix at CosmeticBusiness is ideal because it includes everything from procurement and research to logistics and packaging. We can meet customers we otherwise wouldn't have the opportunity to speak with.*"

Positive Mood Among Exhibitors

The vast majority of exhibitors say they are very satisfied with their participation at CosmeticBusiness. A survey conducted by the independent marketing research company Gelszus Messe-Marktforschung found that 9 of 10 exhibitors regarded their presence at the trade show as a success and were optimistic about good post-trade-show business. 94 per cent of respondents praised the visitors' expert qualifications and 91 per cent were pleased with the quality of their contacts.

Johannes Schick, CEO of the Linhardt Group, also confirms this: "*CosmeticBusiness is the most important trade show for us. It's much better this year than last year which still had a pandemic aftertaste. This year, everyone's enthusiasm for the trade show is back. All the products and services are concentrated in three halls, and everyone who really has something to exhibit is here. With regard to participation and visitor fre-*

quency, it was a very successful trade show. I am very satisfied with it."

Klaus Grabowsky is the CEO of Cosmetic Service GmbH and was pleased to make numerous new business contacts: "*We are exhibiting at CosmeticBusiness for the first time and have made a huge number of contacts here so far. We certainly achieved our quantitive goals – we couldn't possibly have had more conversations. It's also important for us to meet customers we have previously only seen digitally or were finding it difficult to arrange meetings with.*"

Positive Visitor Reviews

The visitor survey conducted during the event showed that 97 per cent of respondents would recommend CosmeticBusiness to others. Nearly as many visitors (92 per cent) hope to attend the trade show again next year, and 90 per cent say their attendance at this year's event was worth it.

The overwhelming majority (85 per cent) say they achieved their goals for the trade show. The most important goals for visitors included making business contacts, finding out about new products and industry trends as well as gaining a general overview of the market. Inspiration was provided by the well-established Spotlight novelty show with product presentations from 32 companies, themed routes for sustainable solutions as well as innovations and a comprehensive conference programme.

Visitors came to CosmeticBusiness this year from a total of 43 countries. Most of them travelled from Austria, Switzerland, Italy, the Netherlands, Poland, the Czech Republic, Spain, France and Belgium.

Trade visitor Sebastian Wölke, Managing Director of no planet b, reports: "*Once again, it was truly an industry get-together and I met many former colleagues from the FMCG sector. When it comes to product-related suppliers (packaging, formulating, filling), CosmeticBusiness is by far the most significant event in German-speaking Europe. In my experience, other industry players feel the same way*."

Launching Pad for Industry Newcomers

For the second time, CosmeticBusiness fulfilled its role as a hub of innovation for the cosmetics industry by offering start-ups a platform in the Innovation Corner for exchange with the international trade audience. Newcomers to the industry presented their innovations in detailed lectures, inspiring visitors with fresh new ideas. Julie Cortal, Head of Business Development at NoPalm Ingredients, says: "*We are a young start-up and are still in the early stages of our journey to bring innovative ingredients to the cosmetics industry. For us, CosmeticBusiness offers the opportunity to meet potential new industry and market partners who could work together with us and demonstrate the potential of our ingredients to them. We haven't yet broken into the German market. Here, we can find the industry experts and partners to help us do so.*"

Optimistic Industry Outlook for the Future

The cosmetics industry rates the current business climate considerably more positively than last year. 70 per cent of respondents regard the current situation as positive which is six per cent higher than in 2022. The view of the coming months is also optimistic. More than half of the respondents expect their business to improve this year, a third expect no change, and only six per cent expect conditions to worsen.

Date for CosmeticBusiness 2024

The next CosmeticBusiness will take place from **5 to 6 June 2024** at MOC Munich.

About CosmeticBusiness

CosmeticBusiness is the only international trade show in Europe where the cosmetics industry meets exclusively with its suppliers and finds solutions for the development of all cosmetic products, from active ingredients to manufacturing and packaging. As the only industry meeting place in Germany, the largest cosmetics market in Europe, the B2B trade show exhibition is a trend barometer for decision-makers from management, product management and development, marketing, as well as purchasing and production. The next edition of CosmeticBusiness will take place from 5 to 6 June 2024 at MOC Munich.

About Leipziger Messe

The Leipziger Messe is one of the ten leading German trade fair companies and one of the top 50 worldwide. It organises events in Leipzig and at various locations all over Germany and abroad. With its five subsidiaries and the Congress Center Leipzig (CCL), Leipziger Messe is a comprehensive service provider covering the entire chain of the events business. It is due to this level of professionalism, that customers and visitors in 2022 voted the Leipziger Messe the service champion of the trade fair industry in Germany's largest service ranking for the ninth time in a row. The Leipzig fairgrounds comprise an exhibition area of 111,900 m^2 and an open-air exhibition area of 70,000 m^2. Every year, over 270 events take place – from trade fairs, exhibitions and congresses to events. Leipzig was the first German trade fair company to be certified according to the Green Globe standards. Sustainability is a recurring theme in the Leipziger Messe's corporate activities.

www.cosmetic-business.com

Cosmetic Business

Naturally Boosted – Smoothing Eye Cream

CH0119

Part	Ingredient/INCI Name	Functionality	% w/w
A	**Water** (Aqua)	–	71.50
	ChromaPur CV2 (Cellulose)[1]	Skin blurring agent	5.00
	Sodium Benzoate[4]	Preservative	0.30
	Potassium Sorbate[4]	Preservative	0.20
B	**Crodafos CES** (Cetearyl Alcohol (and) Dicetyl Phosphate (and) Ceteth-10 Phosphate)[1]	Emulsifier	5.00
	Crodamol™ ISIS (Isostearyl Isostearate)[1]	Emollient	5.00
	Crodamol™ MM (Myristyl Myristate)[1]	Emollient	3.00
	Crodamol™ SSA (Decyl Isostearate (and) Isostearyl Isostearate)[1]	Emollient	3.00
	Syncrowax™ HRC (Tribehenin)[1]	Structure	2.00
C	**Fruitliquid Kumquat** (Glycerin (and) Water (and) Citrus Japonica Fruit Extract)[3]	Botanical extract	3.00
	Synchrolife (Glycerin (and) Pentylene Glycol (and) Rosmarinus Officinalis (Rosemary) Leaf Extract (and) Palmitoyl Tetrapeptide-7 (and) Chrysin)[2]	Anti-pollution active	2.00

Suppliers: **1: Croda 2: Sederma 3: Crodarom** 4: VWR Chemicals

This formulation was developed in the United Kingdom. Contact your local sales representative with enquiries as ingredient availability can vary by region.

PROCEDURE:

Combine **Part A** and **Part B** separately and heat to 75-80°C. Add **Part B** to **Part A** with fast stirring. Mix with an Ultra-Turrax homogeniser for 1 minute per 100g at 10,000rpm. Stir slowly to cool. Add **Part C** below 40°C and continue stirring to cool. Adjust to pH 5-6 with TEA.

CHEMICAL PSYCHICAL PARAMETERS:

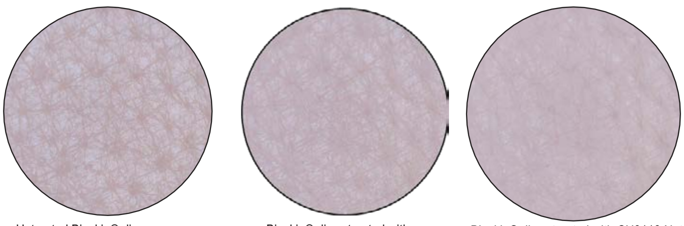
Appearance: White cream;
pH: 5.46 ± 0.5;
Viscosity: 36,160 cP ± 10% DV2T 5rpm, spindle 5, ambient temperature
Stability: 3 months at 4, 25, 40, 45, 50, 7x -10/+40 24hr freeze/thaw cycles

DESCRIPTION:

Brighten up your eyes with a natural boost. This rich eye cream, more than 90% derived natural according to ISO 16128, will help every skin type and skin age to look their best. **ChromaPur™ CV2** instantly blurs skin's imperfections, including fine lines and wrinkles, whilst **Synchrolife™** tackles signs of fatigue and helps resynchronise the skin against digital pollution damage. **Fruitliquid™ Kumquat**, a superfruit extract, adds a touch of vitality and reenergises the skin, whilst the addition of **Crodafos™ CES** helps to achieve this soft and velvety sensory that makes the application a pleasant moment.

SUPPORTING DATA:

To demonstrate the soft-focus effect provided by **ChromaPur CV2**, image of the CH0119 Naturally Boosted Smoothing Eye Cream on Bioskin® discs representing skin age 50 were compared to a control formulation and an untreated Bioskin® discs.



Untreated Bioskin® discs — Bioskin® discs treated with control formulation — Bioskin® discs treated with CH0119 Naturally Boosted Smoothing Eye Cream containing ChromaPur CV2 at 5% inclusion level

As can be seen, CH0119 Naturally Boosted Smoothing Eye Cream show a soft-focus effect compared both to the untreated Bioskin® discs and the control..

www.crodapersonalcare.com.

sederma

Genderless essential care mascara

with SILVERFREE™ (*) and WIDELASH™ (**) (SE0231E)

Part	Ingredient/INCI Name	Functionality	% w/w
A	Water Deionised (Aqua)	–	To 100
	Potassium Sorbate	Preservative	0.10
B	Glycerin	Humectant	14.00
	Dimethyl Isosorbide	Humectant	2.50
	Microcare® Emollient DCP (Pentylene Glycol (and) Caprylyl Glycol (and) Decylene Glycol)[3]	Antimicrobial	1.50
	Xanthan Gum FNCS-PC (Xanthan Gum)[4]	Rheology modifier	0.80
	Genuvisco® Carrageenan CG-131 (Carrageenan)[5]	Rheology modifier	0.50
C	Alcohol	Solvent	5.00
	Lait d'amande[2]	Fragrance	0.10
D	**Silverfree™** (Glycerin (and) Aqua (and) Palmitoyl-Dipeptide-52)[1]	Hair repigmenting active ingredient	1.50
E	**Widelash™** (Glycerin (and) Aqua (and) Panthenol (and) Biotinoyl Tripeptide-1)[1]	Lash enhancer active ingredient	2.00

Suppliers: **1: Sederma 2: Parf'ex** 3: Thor 4: Jungbunzlaeur 5: CP Kelco

(*) Patent N° FR3 115 209; WO2022/084255; WO2014/080376; EP2 922 864; US,9,534,0155
(**) Patent N°FR 2 974 297; WO 2012/143845; EP 2 699 223

Microcare® is a registered trademark of Thor; Genuvisco® is a registered trademark of CP Kelco

This formulation was developed in France. Contact your local sales representative with enquiries as ingredient availability can vary by region.

PROCEDURE:

Weigh and mix **Part A** with normal helix stirring. Weigh and mix **Part B**. Combine **Part B** to **Part A** with helix stirring. Allow swelling for 60 minutes. Weigh and mix **Part C**. Add **Part C** to **Part A+B**. Weigh and add **Part D** to the previous part. Weigh and add **Part E** to the previous part. Mix well.

CHEMICAL PSYCHICAL PARAMETERS:

Appearance: Off-white opaque gel;
pH: 6.30 ± 0.5;
Viscosity: 30.000 cps ± 10% Sp.93, 2.5rpm, 1 min, 25°C, Brookfield DV-I Prime
Stability: 3 months at 4°C, 25°C, 45°C and 1 month at 50°C
Centrifuge 10min @ 3000rpm and 1 x -80°C/+25°C 24 hours freeze-thaw cycle and autoclave 20min @120°C

DESCRIPTION:

This 'less is more' residue free mascara has a light and non-greasy texture for maximum tolerance. It is designed to allow thicker and fuller lashes upon application. Thanks to **Silverfree™** the hair's natural colour is protected, and greying is counteracted in the long run while **Widelash™** promotes hair growth and thickness. With this hair care mascara your authentic beauty is highlighted. To be ACTIVEly committed, the formulation is cold processed and has a natural origin content >95%* according to the ISO 16128-1 and ISO 16128-2 standards.

Since the publication of the two parts of the ISO 16128-1 & ISO 16128-2 standards, we are aware of the ins and outs thanks to our involvement in different internal and external task forces at the international level. So, the following values are provided* ***according to our interpretation of the standard ISO 16128. They are likely to evolve along the way of discussions with professional federations of cosmetic industry.*

FORMULATIONS

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