


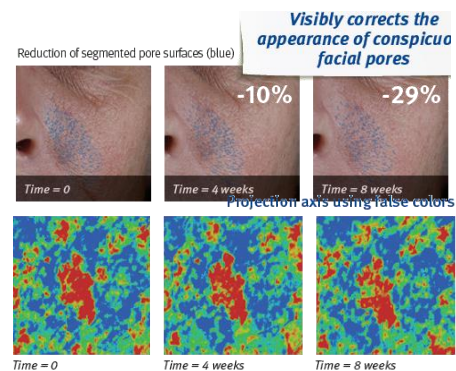
DSM사의 Skin Bioactives 국내 독점 대리점 ㈜인터케어 입니다.

BEAUACTIVE®

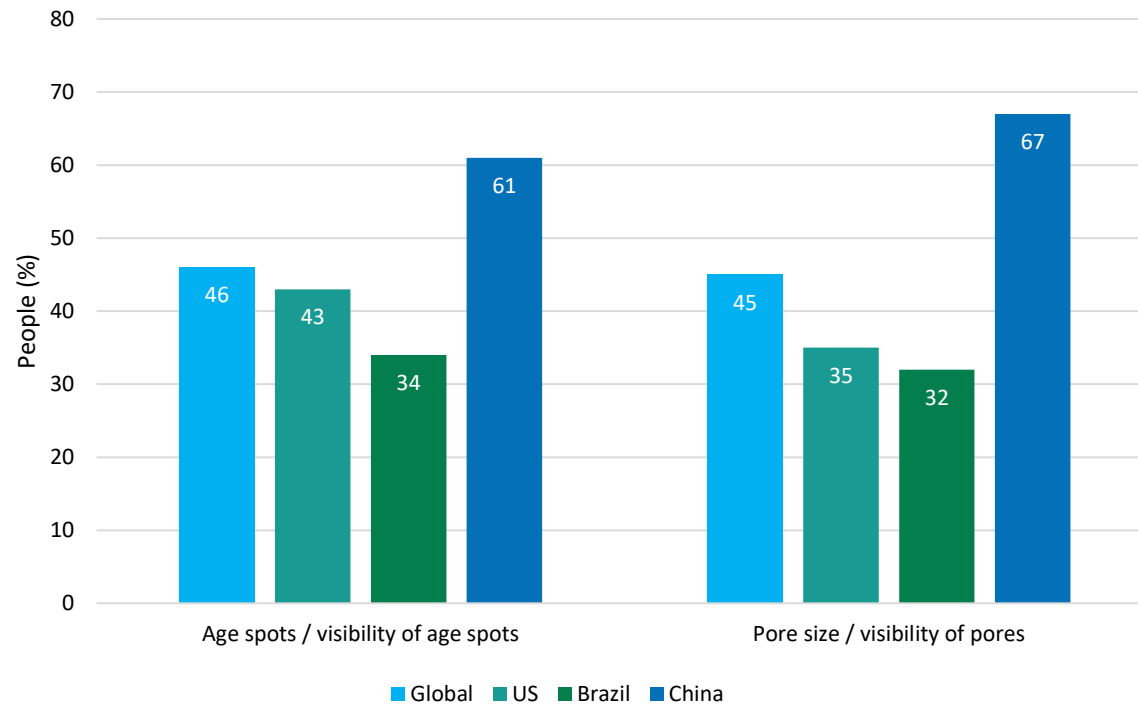
*corrects both conspicuous facial
pores and age spots*

Personal Care & Aroma | Bioactives | Technical & Performance Ingredients | UV Filters | Aroma Ingredients



원료명	BEAUACTIVE	제조원	DSM	공급원	(주)인터케어
INCI name	Hydroxystearic Acid				
한글 전성분	하이드록시스테아릭애씨드				
사용농도	0.2 ~ 1%	패킹 사이즈	1 KG		
원료특성 (story)	<div></div> <ul style="list-style-type: none">▪ DSM사의 생물 전환 기술로 개발한 모공과 기미를 해결하는 고순도 효능 액티브(세포보호, 기미 억제, 노화로 인한 모공감소 세가지 피부고민 해결)▪ 천연 유래 고순도(순도 99% 이상) 유용성 액티브 성분인 10-hydroxystearic acid는 발효 인삼에도 들어있는 성분으로 PPARα를 활성화해 UV로 인한 자극을 억제하고 UV 스트레스 마커인 p53을 억제해 멜라닌 형성이 감소. 진피층의 주요 콜라겐인 콜라겐 I과 III 합성을 촉진한다▪ 세포를 조절하는 마스터 셀 조절자인 PPARα를 여는 열쇠 역할을 하는 성분(in-silico model)▪ 친환경 기술(Green technology)로 원료 제조 : DSM사의 테크놀로지 센터에서 해바라기 유래의 올레익 산으로부터 생물전환기술(Bio-conversion)을 통해 개발한 고순도 액티브▪ 탄력 / 세로모공 케어 / 피부톤, 기미 개선 / 광노화 케어				
효능/효과 (메커니즘)	<ul style="list-style-type: none">▪ 콜라겐 I, 콜라겐 III 합성 촉진▪ UV로 인한 MMP-1 억제, 화상세포 감소(49%↓), 세포 손상의 마커인 p53 발현 억제(46%↓)		<ul style="list-style-type: none">▪ 1% Beauactive 함유 제품을 하루 2회 사용한 실험군 (38-65세)에서 기미와 모공 사이즈가 확연히 감소 <div><p>Visibly corrects the appearance of conspicuous facial pores</p><p>Reduction of segmented pore surfaces (blue)</p><p>-10%</p><p>-29%</p><p>Time = 0</p><p>Time = 4 weeks</p><p>Time = 8 weeks</p><p>Projection axis using false colors</p></div>		
기타	중국 수출 가능, EWG 1등급, 특허 등록, DSM사 SCIE 논문 보유, 80℃에서 유상 용해				

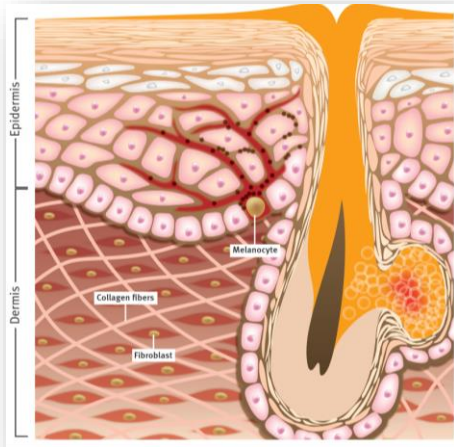
모공과 기미는 여성들이 흔히 느끼는 불만



**DSM survey 2014; Global Total- N= 468 US- N= 155 Brazil N= 156 China- N= 157*

중국 여성은 다른 나라 여성에 비해 모공과 기미에 큰 관심

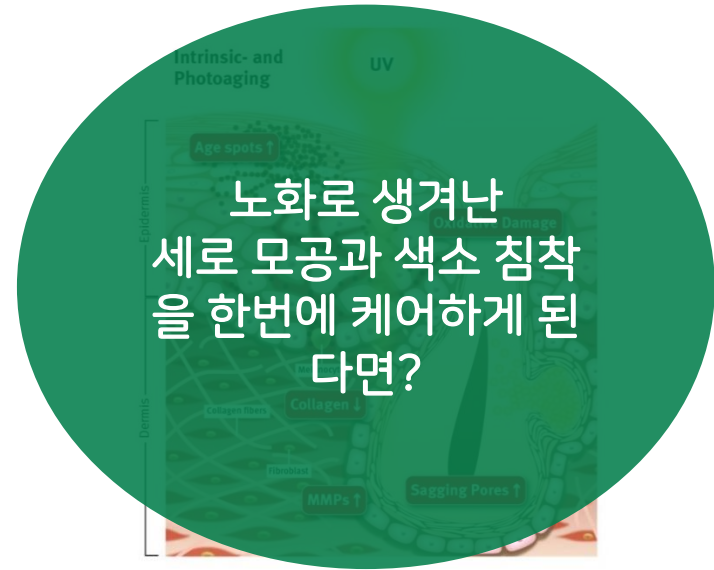
노화에 따른 모공과 기미의 변화



“10대”

모공이 커짐 / 기미 거의 없음

호르몬의 불균형 → 피지 분비량↑, 모공 사이즈 ↑
피지가 공기, 오염 물질과 엉켜 모공을 통과하는데
장애가 생기면 트러블을 유발



“30대 이후”

내인성 노화, 광노화 진행

산화 스트레스 → 세포 손상 ↑
MMP 증가로 콜라겐 ↓
→ 탄력 저하로 모공이 쳐지고 늘어남 (세로모공)
멜라노사이트 활동 증가 → 색소침착, 기미 발생

BEAUACTIVE



발효 인삼과 DSM의 BEAUACTIVE®의 공통점은?

건강 및 노화 방지 효과로 알려진 하이드록시스테아르산을 함유

Source: Journal of Medicinal Food (2016), 19(9), 817-822



BEAUACTIVE - Sustainable process

해바라기 유래의 올레익산 : 생물전환 기술(Bio-conversion)을 통해 개발된 고순도 액티브



Green Chemistry



Oleic acid

Oleate
hydratase
(bio-catalyst)



BEAUACTIVE®

Sustainable process



- 높은 수율로 고순도 제품 생산 > 99%
- 에너지 절약을 위한 공정

BEAUACTIVE

agonist는 세포내 수용체와 결합하여 수용체를 활성화시켜 생물학적인 반응을 유도하는 물질

PPARα의 작용제(agonist)의 역할에 대한 연구

- 표피 분화와 지질 대사를 조절*
- 표피 항상성과 장벽 기능에 영향*
- 노화 및 자외선으로 자극받은 피부를 개선
- 노화와 UV 스트레스에 따른 PPARα의 감소

- BEAUACTIVE는 핵내 수용체인 PPARα (peroxisome proliferator-activated receptor alpha)를 낮은 농도($EC_{50}=5.5 \mu M$)에서 활성화

BEAUACTIVE는 모공과 기미를 해결하는 성분임을 확인!!

PPARs는 세포를 여는 열쇠를 가지고 있어 세포가 환경에 의해 손상을 받으면 작용을 한다.

Prof Wang Sun-Te,
Taiwan



BEAUACTIVE

In silico 모델 - BEAUACTIVE의 PPAR α 활성화 확인

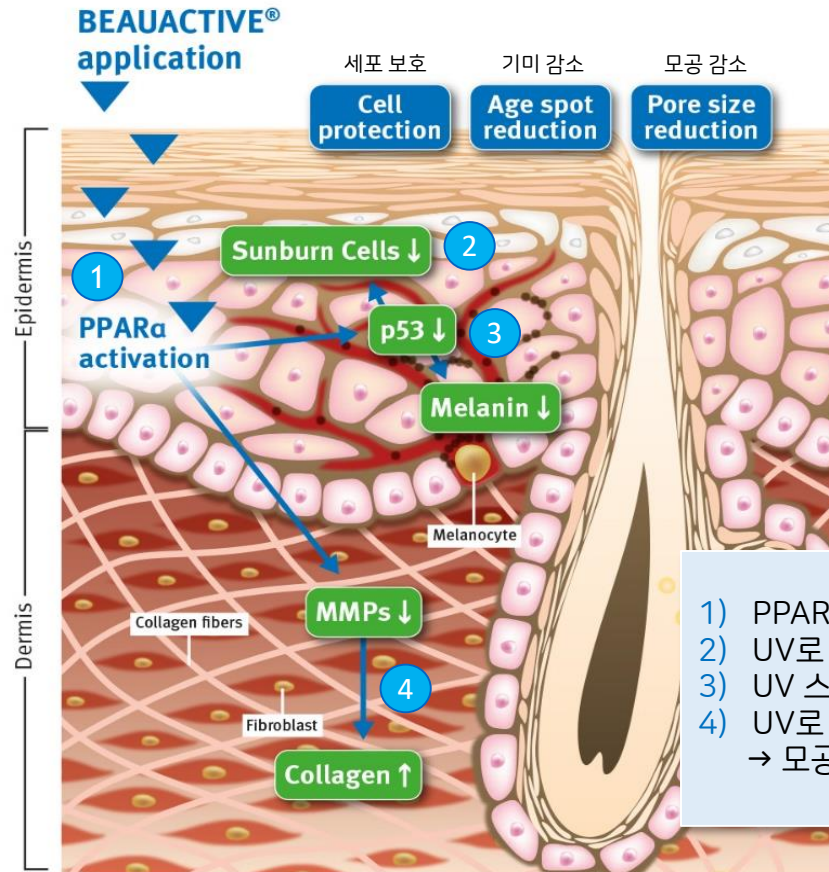


Tyr = 티로신; Ser = 세린; His = 히스티딘

BEAUACTIVE®의 PPAR α 에 결합

- 아미노산 His245, Tyr269, Tyr119, Ser85의 카복실산(-COOH)에 강하게 결합
- 아미노산 Ser85의 하이드록시기(-OH)에 강한 결합

BEAUACTIVE - 피부 메커니즘



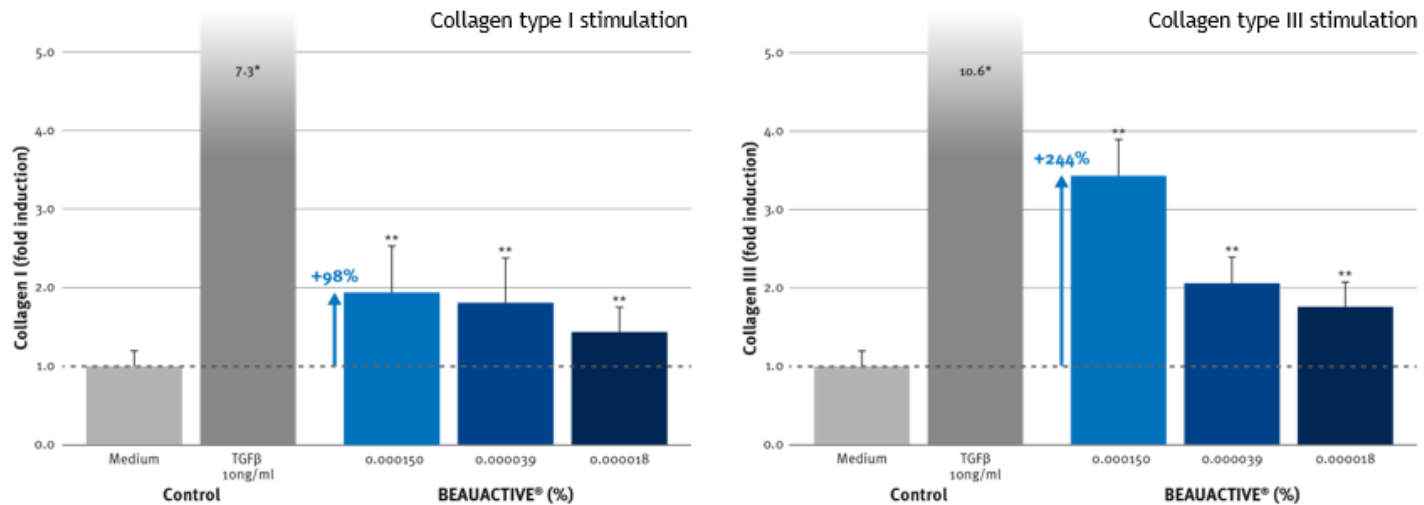
- 1) PPARα 활성화
- 2) UV로 인해 화상을 입은 세포 ↓ → 세포 보호 효과 ↑
- 3) UV 스트레스 마커인 p53 ↓, 멜라닌 형성 ↓ → 기미 ↓
- 4) UV로 인한 MMP 발현 ↓, 콜라겐 I, 콜라겐 III ↑ → 모공 사이즈 ↓

BEAUACTIVE

콜라겐 I, 콜라겐 III 합성 촉진 (세로모공 개선을 위한 주요 성분) - In-vitro



콜라겐 I과 III의 비율이 중요 : 노화가 될수록 피부의 콜라겐은 감소하며 특히 콜라겐 III의 비율이 급격하게 떨어지게 됨.



Collagen type I and type III stimulation in primary human dermal fibroblasts after 48 hours of incubation. Mean values \pm SD, n=3, ** p<0.01 relative to medium control

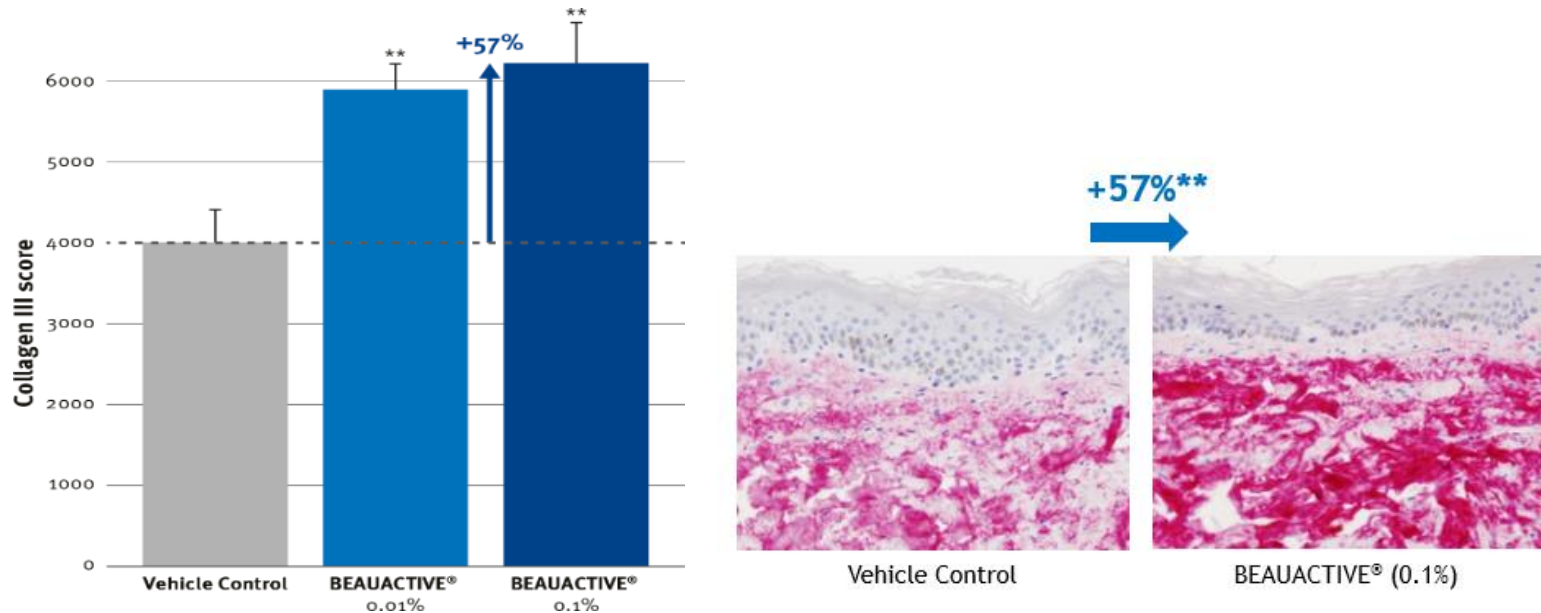
매우 낮은 농도에서 콜라겐 I (+98 %) 및 콜라겐 III(+244 %) 합성 촉진

BEAUACTIVE

콜라겐 III 합성 촉진 (세로 모공 개선을 위한 주요 성분) - Ex-vivo



콜라겐 I과 III의 비율이 중요 : 노화가 될수록 피부의 콜라겐은 감소하며 특히 콜라겐 III의 비율이 급격하게 떨어지게 됨.



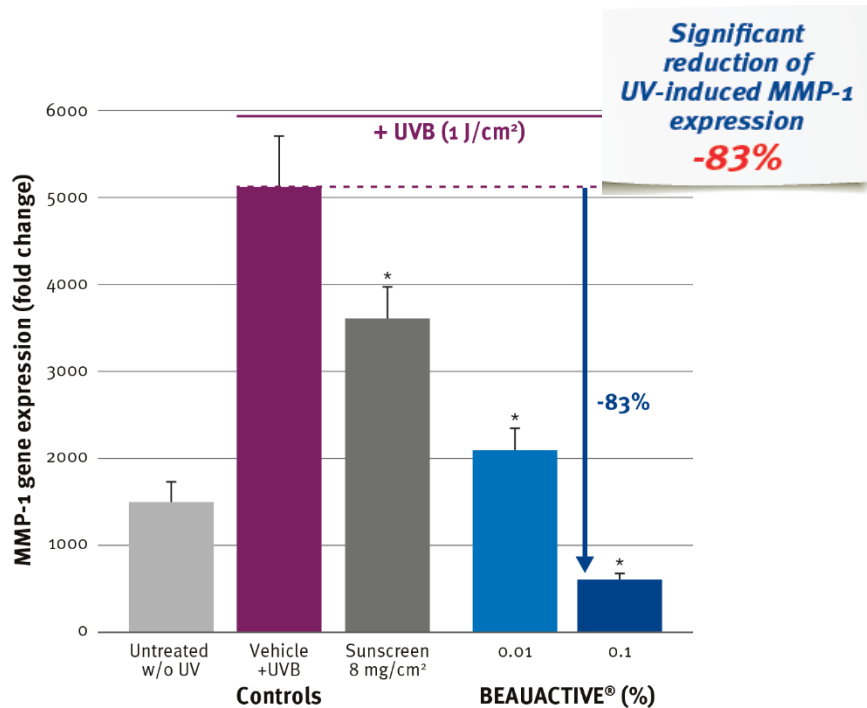
Quantification of collagen type III of IHC stained sections. Mean values \pm SEM, n=12. * $p < 0.05$, ** $p < 0.01$ significance relative to vehicle control.

IHC staining for collagen type III in human ex vivo skin. Comparison of vehicle (DMSO) vs. BEAUACTIVE® treatment (0.1%) at day 6.

콜라겐 III (+57%) 합성 촉진 효과

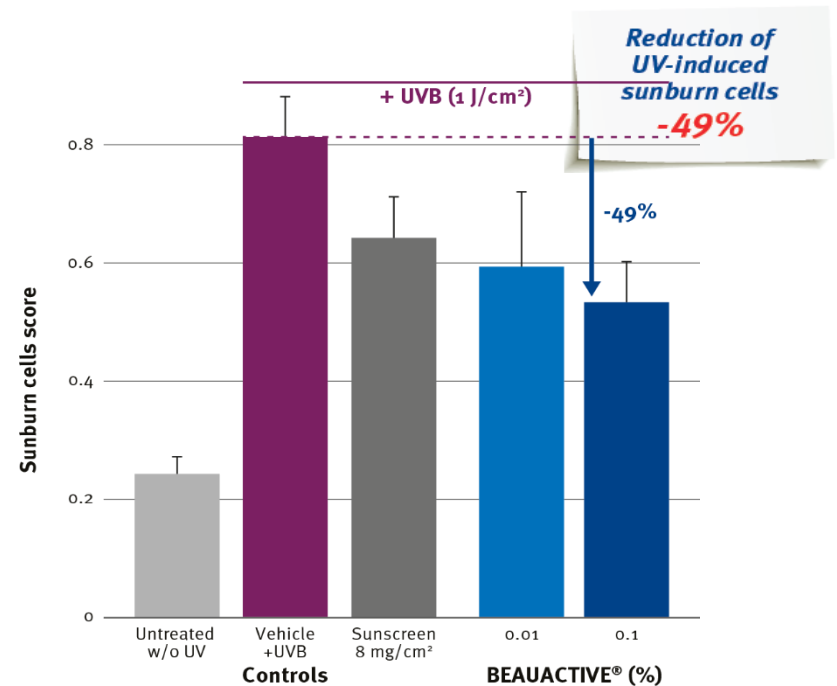
BEAUACTIVE

세로 모공의 주요 원인인 MMP-1 억제 - Ex-vivo



UVB-induced MMP-1 (1J/cm²) gene expression from skin sections by RT-qPCR after one day.
Mean values \pm S.E.M, n = 12; * p<0.05 vs. vehicle control (DMSO) + UVB

UV에 의해 야기되는 화상 세포 형성 억제 - Ex-vivo

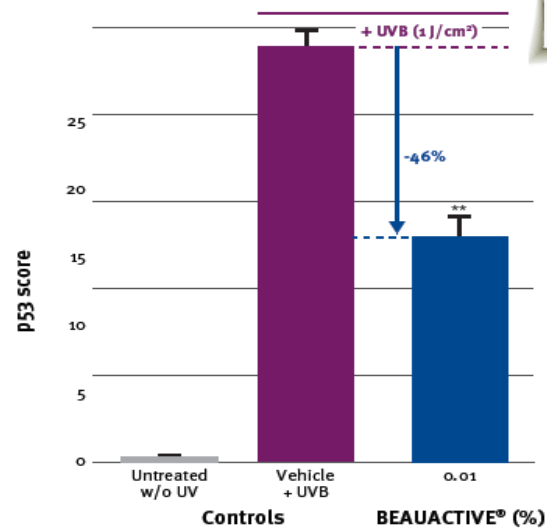


Comparison of ex vivo treatments vs. vehicle (DMSO) 24 h after UVB irradiation. Sunburn cells quantification on H&E-stained skin sections. Mean values \pm S.E.M, n = 12; * p<0.05 vs. vehicle control (DMSO) + UVB.

BEAUACTIVE

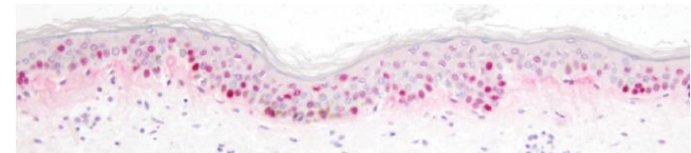
UV 스트레스 마커인 p53 억제 (세포손상과 색소침착 유발) - Ex-vivo

Tests performed on p53 IHC stained skin sections by image a

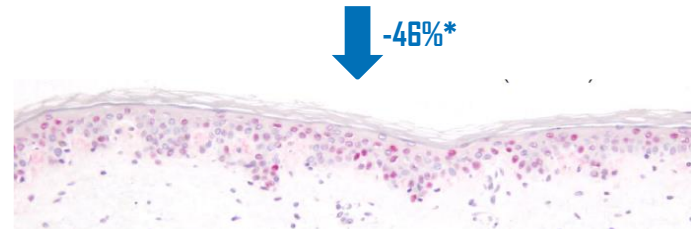


IHC stained skin section for p53 analysis Image analysis of p53-stained skin sections.

Mean values \pm SEM, n = 12, ** p<0.01 significance vs. vehicle (DMSO) control.



Vehicle Control/UVB



BEAUACTIVE® (0.01%)/UVB

BEAUACTIVE

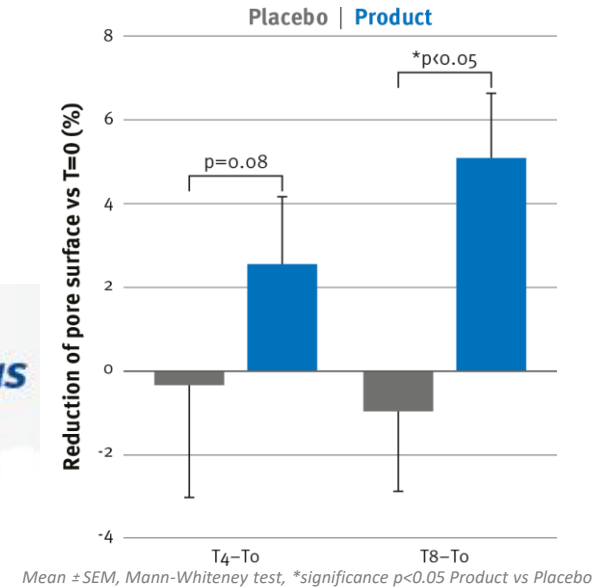
8주 후, 모공 감소 효과

IN VIVO TEST 백인 여성 37명(38-65세), 1% BEAUACTIVE 사용 8주 간 하루 2회 사용
고해상도 사진 (VISIA CR), 이미지 분석 (모공 및 기미)

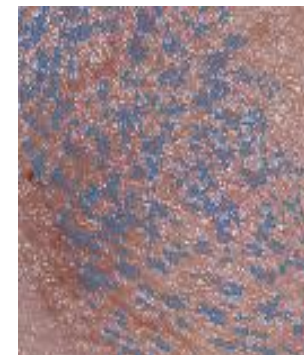
Reduction of segmented pore surfaces (blue)



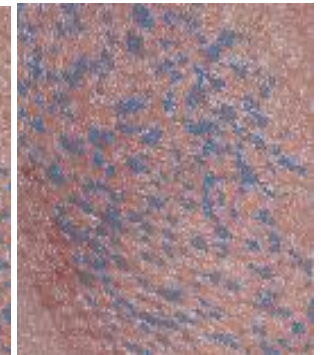
*Visibly corrects the
appearance of conspicuous
facial pores*



T=0
모공 표면 (파랑)



T=8w
모공 표면 (파랑)



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4주 후, 기미 개선 효과

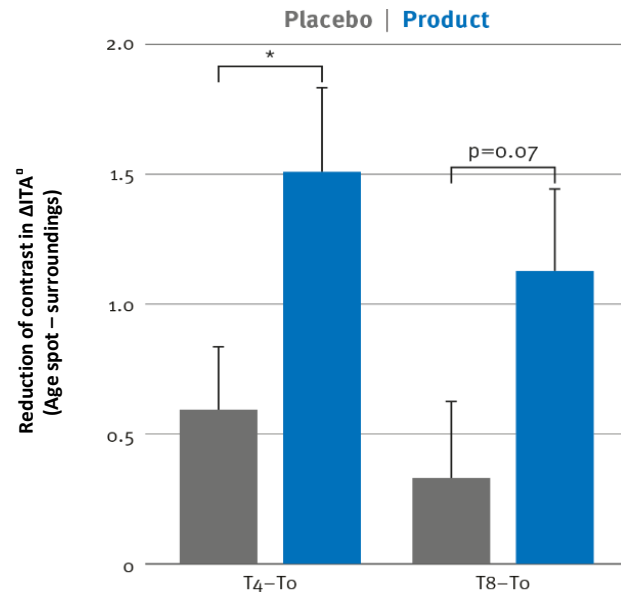
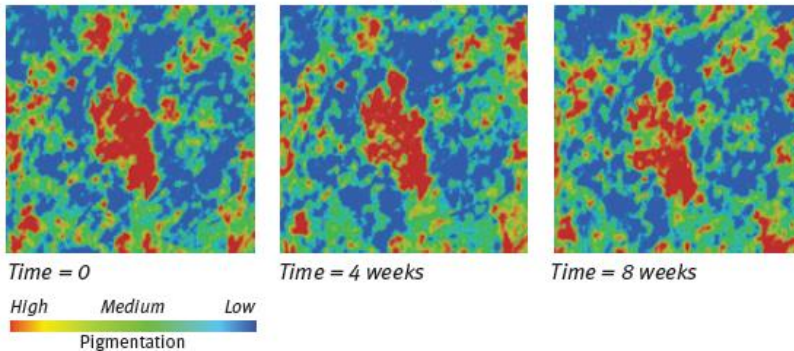
IN VIVO TEST 백인 여성 37명(38-65세), 1% BEAUACTIVE 사용 8주 간 하루 2회 사용
고해상도 사진 (VISIA CR), 이미지 분석 (모공 및 기미)

Selected age spot of Subject #20
treated with 1% BEAUACTIVE®

Cross-polarized images



Projection axis using false colors



-ITA° (개별 유형학적 각도)는 밝기(L *)와 노란색 매개 변수 (b *)를 포함하여 피부 색소 침착 정도 확인
-대비 = 주변 피부 값과 기미 사이의 ΔITA° 차이
- ΔITA° 값의 대비 감소는 연령대에 유리한 색소 침착 감소를 반영

BEAUCTIVE

트렌스포밍 샤벳 제형 구현

1% BEAUCTIVE로 고체 타입의 샤벳 제형 구현이 가능 (0.5%까지는 일반적인 에멀전 제형)

피부에 발랐을 때 가벼운 수분감을 주면서 녹아내리는 트렌스포밍 멜팅 제형 구현



Phase	Ingredients	INCI Name	% w / w	Supplier
A	WATER DEM.	AQUA	Ad 100	
	Euxyl PE 9010	PHENOXYETHANOL, ETHYLHEXYLGLYCERIN	1.00	100444
	Dekaben CP	CHLORPHENESIN	0.20	100665
A1	CremerGlyc Refined Glycerine	GLYCERIN	4.00	101003
A1	Organic Keltrol CG-T	XANTHAN GUM	0.20	100400
B	Tego Care CG 90	CETEARYL GLUCOSIDE	1.50	100415
	Lanette O	CETEARYL ALCOHOL	1.00	100037
	Myritol 318	CAPRYLIC/CAPRIC TRIGLYCERIDE	5.00	100037
	Massocare HD	ISOHEXADECANE	5.00	101025
	BEAUCTIVE®	HYDROXYSTEARIC ACID	1.00	100288
	Sepinov EMT 10	HYDROXYETHYL ACRYLATE/SODIUM	0.50	100313
		ACRYLOYLDIMETHYL TAURATE COPOLYMER		
C	Frag 49454695 Sail Away	PARFUM	0.20	101007

SK-E-101017-472

Patent application filed

특허

등록 특허 : 유럽/만료일 EP3206659B1/2035-10-15

(19)



Europäisches Patentamt

European Patent Office

Office européen des brevets



(11) EP 3 206 659 B1

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(51) Int Cl.:
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A61Q 17/04 (2006.01) A61Q 19/00 (2006.01)
A61Q 19/08 (2006.01)

(21) Application number: 15780898.1

(22) Date of filing: 15.10.2015

(86) International application number:
PCT/EP2015/073912

(87) International publication number:
WO 2016/059169 (21.04.2016 Gazette 2016/16)

(54) USE OF A COSMETIC COMPOSITION COMPRISING 10-HYDROXYSTEARIC ACID

KOSMETISCHE VERWENDUNG EINER ZUBEREITUNG ENTHALTEND
10-HYDROXYSTEARINSÄURE
UTILISATION COSMÉTIQUE D'UNE COMPOSITION CONTENANT DE L'ACIDE
10-HYDROXYSTÉARIQUE

- (84) Designated Contracting States:
AL AT BE BG CH CY CZ DE DK EE ES FI FR GB
GR HR HU IE IS IT LI LT LU LV MC MK MT NL NO
PL PT RO RS SE SI SK SM TR

(30) Priority: 17.10.2014 US 201462065102 P

(43) Date of publication of application:
23.08.2017 Bulletin 2017/34

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(74) Representative: Berg, Katja
DSM Nutritional Products Ltd
Patent Department
Wurmisweg 576
4303 Kaiseraugst (CH)

(56) References cited:
EP-A2- 0 744 175 WO-A1-2007/039057
WO-A1-2014/016517 WO-A1-2014/084676
KR-B1- 100 693 292 US-A- 4 424 234
US-A- 5 747 051 US-A1- 2010 286 102

공개 특허 : 한국 10-2017-0066419



(19) 대한민국특허청(KR)

(12) 공개특허공보(A)

(11) 공개번호 10-2017-0066419

(43) 공개일자 2017년06월14일

(51) 국제특허분류(Int. Cl.)
A61K 8/365 (2006.01) A61K 8/67 (2006.01)
A61Q 17/04 (2006.01) A61Q 19/00 (2006.01)
A61Q 19/08 (2006.01)

(52) CPC특허분류
A61K 8/365 (2013.01)
A61K 8/671 (2013.01)

(21) 출원번호 10-2017-7009641

(22) 출원일자(국제) 2015년10월15일
심사청구일자 없음

(85) 번역문제출일자 2017년04월10일

(86) 국제출원번호 PCT/EP2015/073912

(87) 국제공개번호 WO 2016/059169
국제공개일자 2016년04월21일

(30) 우선권주장 62/065,102 2014년10월17일 미국(US)

(71) 출원인
디에스엠 아이피 어셋츠 비.보이.
네덜란드 엔엘-6411 타이 헤르렌 헤트 오버문 1

(72) 발명자
임펠트 도미니크
스위스 체하-4303 카이제라우그스트 부르미스베르
576 디에스엠 누트리셔널 프로덕츠 리미티드 파텐
트 데카르트먼트
라드스펠러 알렉산더
스위스 체하-4303 카이제라우그스트 부르미스베르
576 디에스엠 누트리셔널 프로덕츠 리미티드 파텐
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루트 볼프
스위스 체하-4303 카이제라우그스트 부르미스베르
576 디에스엠 누트리셔널 프로덕츠 리미티드 파텐
트 데카르트먼트


(74) 대리인
제일특허법인

전체 청구항 수 : 총 15 항

(54) 발명의 명칭 10-하이드록시스테아르산을 포함하는 화장품 조성물의 용도

(57) 요약

본 발명은 피부의 상태 및 외관의 개선을 위해, 보다 특히 주름 방지제로서, 균일한 피부톤의 촉진을 위해, 모공 크기의 감소를 위해, 광 보호제로서 및/또는 피부 장벽 기능의 개선을 위해 인간 피부에 도포하기 위한 10-하이드록시스테아르산, 또는 이의 염 또는 에스테르를 포함하는 국소용 조성물의 화장품 용도에 관한 것이다.

 INTERCARE

Fermented Ginseng Contains an Agonist of Peroxisome Proliferator Activated Receptors α and γ

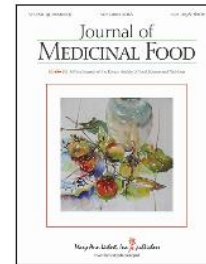
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ABSTRACT Peroxisome proliferator activated receptor (PPAR) is a nuclear receptor that is one of the transcription factors regulating lipid and glucose metabolism. Fermented ginseng (FG) is a ginseng fermented by *Lactobacillus paracasei* A221 containing minor ginsenosides and metabolites of fermentation. DNA microarray analysis of rat liver treated with FG indicated that FG affects on lipid metabolism are mediated by PPAR- α . To identify a PPAR- α agonist in FG, PPAR- α transcription reporter assay-guided fractionation was performed. The fraction obtained from the MeOH extract of FG, which showed potent transcription activity of PPAR- α , was fractionated by silica gel column chromatography into 16 subfractions, and further separation and crystallization gave compound **1** together with four known constituents of ginseng, including 20(R)- and 20(S)-protopanaxadiol, and 20(R)- and 20(S)-ginsenoside Rh1. The structure of compound **1** was identified as 10-hydroxy-octadecanoic acid by ¹H- and ¹³C-NMR spectra and by EI-MS analysis of the methyl ester of **1**. Compound **1** demonstrated much higher transcription activity of PPAR- α than the other isolated compounds. In addition, compound **1** also showed 5.5-fold higher transcription activity of PPAR- γ than vehicle at the dose of 20 μ g/mL. In the present study, we identified 10-hydroxy-octadecanoic acid as a dual PPAR- α/γ agonist in FG. Our study suggested that metabolites of fermentation, in addition to ginsenosides, contribute to the health benefits of FG.

KEYWORDS: • DNA microarray • fermented ginseng • PPAR alpha • PPAR gamma • 10-hydroxy-octadecanoic acid



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약용 식품 저널

Fermented Ginseng Contains an Agonist of Peroxisome Proliferator Activated Receptors α and γ

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techniques, was shown to have a wide variety of pharmacological activities. FG extracts were shown to exert an antihyperglycemic effect in T2DM mice.¹⁷ However, the active constituents of FG for metabolic disorders have not yet been clarified. We previously reported the protective effect of FG against acetaminophen-induced rat liver injury,¹² in which the transcription activity of PPAR- α indicated a tendency to be increased by FG treatment in rats. This observation suggested the presence of a PPAR- α agonist in FG, which prompted us to perform this investigation. As part of our study on the beneficial health effects of FG, we performed a search for a PPAR- α agonist in FG using bioassay-guided fractionation, which resulted in the isolation of its active constituent. We describe herein the isolation and characterization of this compound.

발효 인삼이 함유하는 PPAR α Agonist를 확인, 다양한 의약품 효능!!



Bio-derived hydroxystearic acid ameliorates skin age spots and conspicuous pores

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Keywords: age spots, chemical synthesis, computer modelling, hydroxystearic acid, pores, skin physiology/structure

Abstract

INTRODUCTION: We report on the preparation and efficacy of 10-hydroxystearic acid (HSA) that improves facial age spots and conspicuous pores.

METHODS: The hydration of oleic acid into HSA was catalysed by the oleate hydratase from *Escherichia coli*. Following treatment with HSA, collagen type I and type III was assessed in primary human dermal fibroblasts together with collagen type III, p53 protein levels and sunburn cells (SBC) after UVB irradiation (1 J cm⁻²) by immunohistochemistry on human *ex vivo* skin. UVB-induced expression of matrix metalloproteinase-1 (MMP-1) was determined from full thickness skin by RT-qPCR. Modification of the fibroblast secretome by HSA was studied by mass-spectrometry-based proteomics. In a full-face, double blind, vehicle-controlled trial HSA was assessed for its effects on conspicuous facial pore size and degree of pigmentation of age spots in Caucasian women over an 8-week period.

RESULTS: HSA was obtained in enantiomeric pure, high yield (≥80%). Collagen type I and type III levels were dose-dependently increased (96% and 244%; $P < 0.01$) *in vitro* and collagen type III in *ex vivo* skin by +57% ($P < 0.01$) by HSA. HSA also inhibited UVB-induced MMP-1 gene expression (83%; $P < 0.01$) and mitigated SBC induction (−34% vs. vehicle control) and reduced significantly UV-induced p53 up-regulation (−46% vs. vehicle control; $P < 0.01$) in irradiated skin. HSA modified the fibroblast secretome with significant increases in proteins associated with the WNT pathway that could reduce melanogenesis and proteins that could modify dermal fibroblast activity and keratinocyte differentiation to account for the alleviation of conspicuous pores. Docking studies *in silico* and EC50 determination in reporter gene assays (EC50 5.5×10^{-6} M) identified HSA as a peroxisomal proliferator activated receptor- α (PPAR α) agonist. Clinically, HSA showed a statistically significant decrease of surface and volume of skin pores ($P < 0.05$) after 8 weeks of application and age spots became significantly less pigmented than the surrounding skin (contrast, $\Delta \geq 0.05$) after 4 weeks.

CONCLUSION: HSA acts as a PPAR α agonist to reduce the signs of age spots and conspicuous pores by significantly modulating the expression of p53, SBC, MMP-1 and collagen together with major changes in secreted proteins that modify keratinocyte, melanocyte and fibroblast cell behavior.

Résumé

INTRODUCTION: voici notre rapport sur la préparation et l'efficacité de l'acide 10-hydroxystéarique (AHS) qui atténue les taches de vieillesse faciale et améliore l'apparence des pores.

MÉTHODES: L'hydratation de l'acide oléique en AHS a été catalysée par l'hydratase d'oléate à partir de *Escherichia coli*. Après un traitement par AHS, les collagènes de type I et de type III ont été analysés dans des fibroblastes dermiques humains primaires, ainsi que le taux de collagène de type III et de protéine p53, et les cellules provenant de coups de soleil (sunburn cells, SBC) après irradiation par UVB (1 J cm⁻²) par immunohistochimie sur de la peau humaine *ex vivo*. L'expression de la matrice métalloprotéase-1 (MMP-1) induite par les UVB a été déterminée à partir d'un échantillon de pleine épaisseur de peau par RT-qPCR. La modification du sécrétome des fibroblastes par l'AHS a été étudiée par analyse protéomique basée sur une spectrométrie de masse. Dans une étude du visage entier, en double aveugle, contrôlée par excipient, l'AHS a été évaluée pour ses effets sur la taille des pores apparents du visage et sur le degré de pigmentation de taches de vieillesse chez des femmes de race blanche sur une période de 8 semaines.

RÉSULTATS: L'AHS a été obtenu à un haut rendement, énantiomérique pur (≥80 %). Les taux de collagènes de type I et de type III ont augmenté *in vitro* en fonction de la dose (96 % et 244 %; $P < 0.01$) et le collagène de type III dans de la peau *ex vivo* de +57 % ($P < 0.01$) lors d'un traitement par AHS. L'AHS a également inhibé l'expression génique MMP-1 induite par les UVB (83%; $P < 0.01$) et a atténué l'induction des SBC (−34 % par rapport à l'excipient), et a réduit significativement la régulation à la hausse du p53 induite par les UV (−46 % par rapport à l'excipient; $P < 0.01$) sur de la peau irradiée. L'AHS a modifié le sécrétome des fibroblastes avec des augmentations significatives des protéines associées à la voie WNT qui pouvaient réduire la mélanogenèse et des protéines qui pouvaient modifier l'activité des fibroblastes dermiques et la différenciation des kératinocytes pour une atténuation des pores apparents. Des études de docking *in silico* et la détermination de l'EC50 dans les dosages des gènes rapporteurs (EC50 5.5×10^{-6} M) ont identifié l'AHS comme un agoniste du récepteur- α activé par les proliférateurs de peroxysomes (peroxisomal proliferator activated receptor- α , PPAR α). Cliniquement, l'AHS a permis une diminution statistiquement significative de la surface et du volume des pores de la peau ($P < 0.05$) après 8 semaines d'application, et les taches de vieillesse sont devenues significativement moins pigmentées par rapport à la peau environnante (contraste, $P < 0.05$) après 4 semaines.



Figure 7 Reduction of conspicuous facial pores on subject #20 after treatment with product formulation (1% hydroxystearic acid). VISIA-AR images taken at T = 0, 4, and 8 weeks: Parallel-polarized photos and pore surface topography near the nose (as shown as in blue).

PPAR alpha agonist(작용제) 10-Hydroxystearic acid(HSA)는 p53, SBC(화상 세포), MMP-1과 콜라겐을 조절해 노화의 징후인 기미와 모공을 줄여준다!!

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