Natural Soothing Ingredient

BioSyn-Bisabolol

版本：2023.01

CONTENTS

Development Background

The market for sensitive skin care is growing steadily

Skin sensitivity and its symptoms, including redness, itching, and stinging and burning sensations, are now ***a top skincare concern*** among consumers globally. As between 2001 and 2017, incidences of sensitive skin among women increased by ***50%*** in the Western world and as much as ***56%*** in countries such as Japan.

Sensitive skin refer to a highly reactive state of the skin that occurs under physiological or pathological conditions. It is a complex process involving blood vessels, nerve conduction, and immune inflammation, characterized by symptoms such as itching, burning, and tingling, mainly occurring in the face.

About α-Bisabolol

α-Bisabolol is one of the many sesquiterpenoids found in nature, and has been used in traditional medicine for hundreds of years. It can protect the skin from daily stress and is particularly suitable for **sensitive skin, baby care, and after-sun applications**.

According to different sources, currently α-bisabolol can be divided into synthetic and natural sources. Synthetic α-bisabolol is generally extracted from farnesol as the initial material and purified by distillation to obtain racemic (±)-α-Bisabolol. Natural origin α-Bisabolol is generally extracted from the Brazilian shrub Candeia, but is limited to the scarcity of raw materials.

BioSyn-Bisabolol is a biologically active single form (-)-α- bisabolol. It is ***100%*** natural, which is in line with the development trend of **"Green and Natural"** high-end cosmetics raw materials at home and abroad.

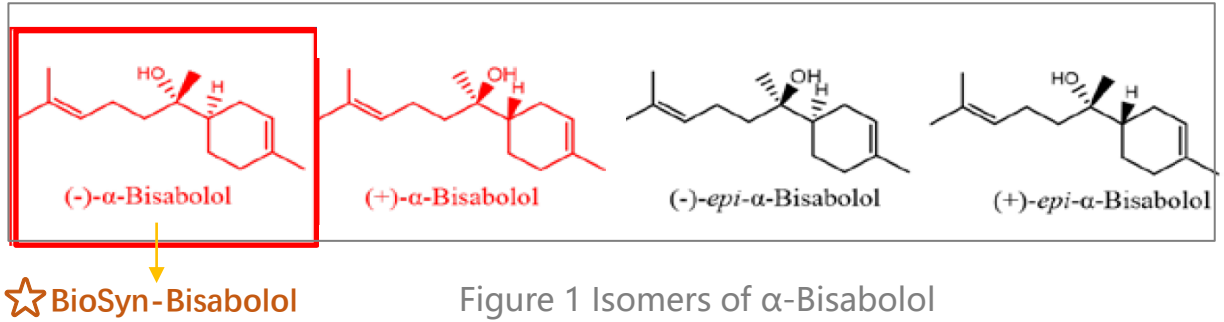


Figure 1 Isomers of α-Bisabolol

Comparison of α-Bisabolol on the market

- The purity of bisabolol supplied by ANECO is extremely high, and the assay of (-)-α-bisabolol is over ***95%***

Company Name	Product Name	INCI Name	CAS No.	Configuration, Assay	Origin
ANECO	BioSyn-Bisabolol	Bisabolol	23089-26-1	(-)-α-bisabolol, ≥95%	Fermentation
Givaudan Active Beauty	BisaboLife™	Bisabolol	23089-26-1	(-)-α-bisabolol, 90-100%	Fermentation
BASF	Bisabolol rac.	Bisabolol	515-69-5	(±) α-bisabolol, >85%	Synthesis
Symrise	Dragosantol® 100	Bisabolol	72691-24-8 515-69-5	(±) α-bisabolol, >95%	Synthesis
Citróleo	Citrue Bisabolol	Bisabolol	23089-26-1	(-)-α-bisabolol, 85%-95%-97%-99%	Plant
Vantage Personal Care™	Lipo™ Bisabolol	Bisabolol	23089-26-1	(-)-α-Bisabolol, ≥95%	Plant
Merck KGaA	RonaCare® Bisabolol Nat.	Bisabolol	23089-26-1	(-)-α-Bisabolol, ≥92%	Plant

Regulatory Status

- **China — IECIC(2021 Edition)**

序号	中文名称	INCI名称/英文名称	淋洗类产品最高历史使用量（%）	驻留类产品最高历史使用量（%）	备注
02888	红没药醇	BISABOLOL			

- **Europe — CosIng**

#	INCI Name/Substance Name	CAS No.	EC No.	Restriction/ Annex/Ref #
1.	BISABOLOL	515-69-5 / 23089-26-1	208-205-9 / 245-423-3	

- **USA — PCPC**

MonoID	INCIName
304	Bisabolol

Test Data

Physical and Chemical Data

Specification

ITEMS	SPECIFICATION
Appearance	Colorless to pale yellow liquid
Odor	Characteristic odor
Assay	≥95%
Total plate count	≤100cfu/g
Yeast & Molds	≤100cfu/g
E. coli	Negative
Staphylococcus aureus	Negative
Pseudomonas aeruginosa	Negative
Candida albicans	Negative
Salmonella	Negative

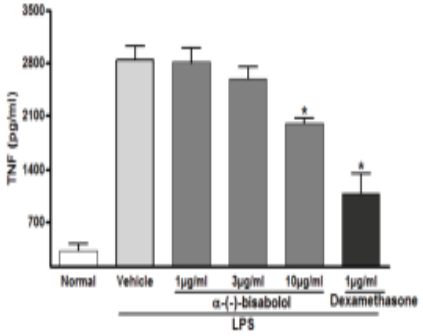
Efficacy Data

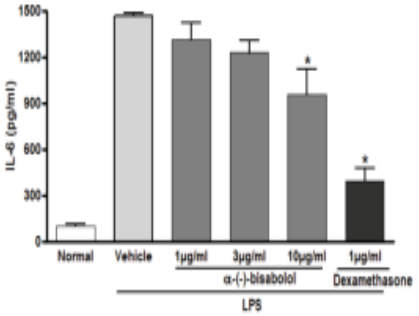
Anti-inflammatory and Soothing

- Inhibition of 5-lipoxygenase (5-LOX)

5-lipoxygenase (5-LOX) oxidizes arachidonic acid and produces proinflammatory leukotrienes through arachidonic acid metabolism

- Inhibition of proinflammatory factors IL-6 and TNF- α, PGE2, NO





- ***Figure d demonstrates that not cytotoxicity causes a decrease in inflammatory factors***

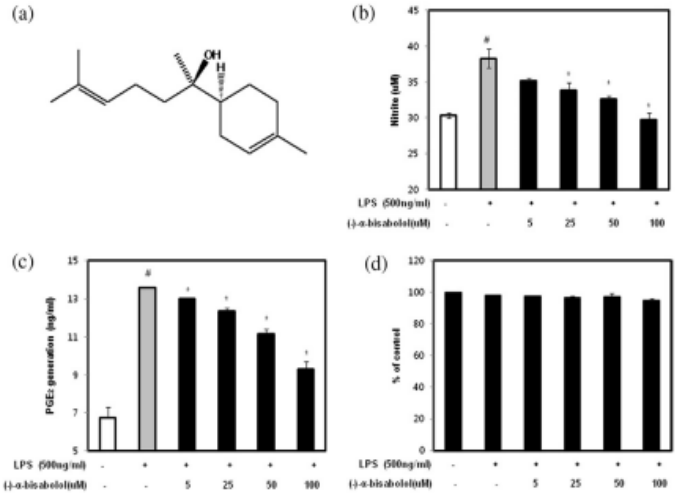


Fig. 1. (−)-α-Bisabolol inhibited NO and PGE_2 production in RAW264.7 cells. (a) Structure of (−)-α-bisabolol, (b) NO production, (c) PGE_2 production (d) Cell viability. Data are expressed as means ± S.D. *, $p < 0.05$ compared with LPS alone. #, $p < 0.05$ compared with vehicle control. Results were confirmed by three independent experiments.

Data Source: Baylac, Sabine, and Philippe Racine. "Inhibition of 5-lipoxygenase by essential oils and other natural fragrant extracts." International Journal of Aromatherapy 13.2-3 (2003): 138-142. K Maurya, Anil, et al. "α-(-)-bisabolol reduces pro-inflammatory cytokine production and ameliorates skin inflammation." Current pharmaceutical biotechnology 15.2 (2014): 173-181. Seungbeom, et al. "Inhibitory effects of (-)-α-bisabolol on LPS-induced inflammatory response in RAW264. 7 macrophages." Food and Chemical Toxicology 49.10 (2011): 2580-2585.

Efficacy Data

Anti-inflammatory and Soothing

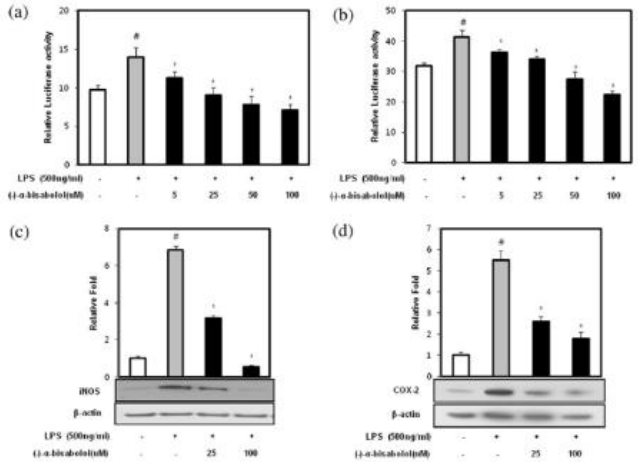


Fig. 2. (−)-α-Bisabolol inhibited LPS-induced expression of iNOS and COX-2 genes in RAW264.7 cells. To determine the effect of (−)-α-bisabolol on LPS-induced activation of (a) iNOS and (b) COX-2 promoters, RAW264.7 cells were transiently co-transfected with 2 μg of the firefly luciferase reporter gene under the control of iNOS or COX-2 responsible elements and 0.2 μg of Renilla luciferase expression vector driven by thymidine kinase promoter using the Superfect™ reagent (Qiagen), as described in Section 2. After 24 h, cells were stimulated with 500 ng/ml LPS in the presence or absence of (−)-α-bisabolol. Luciferase activity is expressed as a ratio of iNOS or COX-2-dependent firefly luciferase activity divided by control thymidine kinase *Renilla* luciferase activity (relative luciferase units). Data are expressed as means ± S.D. *, $p < 0.05$ compared with LPS alone. #, $p < 0.05$ compared with vehicle control. Results were confirmed by three independent experiments. Cells were treated for 2 h with different concentrations (25 and 100 μM) of (−)-α-bisabolol. LPS (500 ng/ml) was then added and cells were further incubated for 24 h. (c) iNOS and (d) COX-2 protein level were determined via Western blotting as described in Section 2. Data are expressed as means ± S.D. *, $p < 0.05$ compared with LPS alone. #, $p < 0.05$ compared with vehicle control. Results were confirmed by three independent experiments.

- iNOS is a mediator and regulator of inflammatory reactions; COX-2 is a key enzyme that regulates the production of prostaglandins, which are the main mediators of inflammation.
- ***α-bisabolol reduces the expression of iNOS and COX-2 genes by inhibiting NF-kβ And AP-1 (ERK and p38) signal channels, and plays a role in soothing inflammation.***

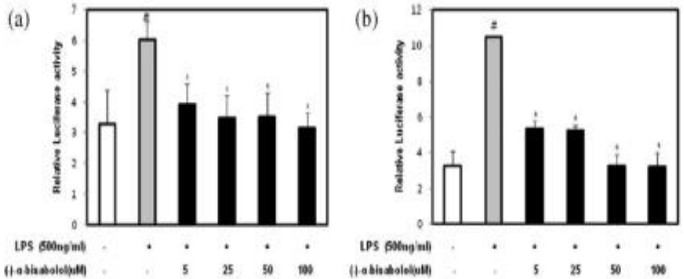


Fig. 3. (−)-α-Bisabolol inhibited LPS-induced activation of AP-1 and NF-κB promoters in transfected RAW264.7 cells. To determine the effect of (−)-α-bisabolol on LPS-induced activation of (a) AP-1 and (b) NF-κB promoters, RAW264.7 cells were transiently co-transfected with 2 μg of the firefly luciferase reporter gene under the control of AP-1 and NF-κB responsible elements and 0.2 μg of *Renilla* luciferase expression vector driven by thymidine kinase promoter by the Superfect™ reagent (Qiagen), as described in Section 2. After 24 h, cells were stimulated with 500 ng/ml LPS in the presence or absence of (−)-α-bisabolol. Luciferase activity is expressed as a ratio of AP-1 or NF-κB-dependent firefly luciferase activity divided by control thymidine kinase *Renilla* luciferase activity (relative luciferase units). Data are expressed as means ± S.D. *, $p < 0.05$ compared with LPS alone. #, $p < 0.05$ compared with vehicle control. Results were confirmed by three independent experiments.

Data Source: Seungbeom, et al. "Inhibitory effects of (-)-α-bisabolol on LPS-induced inflammatory response in RAW264. 7 macrophages." Food and Chemical Toxicology 49.10 (2011): 2580-2585.

Efficacy Data

Antioxidant (scavenging free radicals)

A large number of exogenous or endogenous stimuli can produce a local protective tissue response, commonly referred to as "inflammation.". Inflammatory processes recruit different types of cells (especially polymorphonuclear neutrophils, PMNs) and simultaneously produce inflammatory mediators that activate the "stress signaling pathway". PMN recruitment is initially a protective mechanism, but their activation can lead to a "respiratory burst" and subsequent release of reactive oxygen species (ROS), which can damage target cells and surrounding cells (lipid peroxidation, amino acid oxidation, protein fragmentation, and DNA damage), leading to a self-sustaining inflammatory cycle and oxidative stress.

The purpose of the Luminol Amplified Chemiluminescence (LACL) study was to examine whether bisabolol interferes with ROS production during PMN respiratory bursts and determine the minimum concentration at which it still exerts antioxidant activity. LACL has been widely used to detect ROS generated by PMN under various conditions.

Table 1. Effects of various concentrations of bisabolol on LACL of PMN respiratory burst induced by *C. albicans*

	Control		Control + ethanol 0.5%		Bisabolol									
					31 µg/ml		15.5 µg/ml		7.7 µg/ml		3.8 µg/ml		1.9 µg/ml	
	peak	T_{peak}	peak	T_{peak}	peak	T_{peak}	peak	T_{peak}	peak	T_{peak}	peak	T_{peak}	peak	T_{peak}
	66.3	17; 10	78.0	21; 40	38.5	18; 00	56.0	17; 50	59.3	17; 00	75.6	18; 25	81.9	20; 21
	42.3	19; 20	32.6	20; 20	22.4	13; 40	23.5	18; 10	24.0	18; 40	29.0	20; 35	30.9	18; 50
	31.5	17; 30	31.6	20; 40	7.1	11; 50	16.3	16; 30	24.2	18; 00	29.4	19; 30	34.2	18; 00
	75.3	14; 30	84.6	15; 30	29.6	17; 40	50.7	16; 40	56.2	15; 10	71.0	16; 10	83.7	15; 00
Mean ± SEM	53.90 ± 10.18	17; 07 ± 1; 00	56.57 ± 14.16	19; 32 ± 1; 23	24.44 ± 14.25*	15; 17 ± 1; 31	36.68 ± 9.84*	17; 17 ± 0; 25	41.18 ± 9.90*	17; 12 ± 0; 46	51.29 ± 12.78	18; 40 ± 0; 57	57.71 ± 14.62	18; 03 ± 1; 07

Peak in millivolts, T_{peak} in minutes and seconds. * $p \leq 0.05$ versus control + ethanol 0.5%.

Table 2. Effects of various concentrations of bisabolol on LACL of PMN respiratory burst induced by fMLP

	Control		Control + ethanol 0.5%		Bisabolol									
					31 µg/ml		15.5 µg/ml		7.7 µg/ml		3.8 µg/ml		1.9 µg/ml	
	peak	T_{peak}	peak	T_{peak}	peak	T_{peak}	peak	T_{peak}	peak	T_{peak}	peak	T_{peak}	peak	T_{peak}
	179.0	2; 40	171.3	2; 00	51.9	1; 20	109.4	1; 00	141.2	2; 40	161.4	2; 10	175.2	1; 05
	129.4	1; 30	118.0	2; 00	30.1	1; 40	74.0	1; 40	94.1	1; 40	105.2	2; 00	116.2	1; 50
	152.1	1; 50	148.8	2; 20	54.1	1; 00	111.2	2; 00	120.5	2; 30	129.1	1; 50	153.7	2; 00
	123.9	2; 10	124.6	2; 10	17.0	1; 00	63.0	2; 50	94.3	2; 10	108.9	2; 20	118.1	1; 40
Mean ± SEM	146.10 ± 12.55	2; 02 ± 0; 15	140.67 ± 12.17	2; 07 ± 0; 16	38.05 ± 8.81**	1; 30 ± 0; 13	89.40 ± 12.28**	1; 52 ± 0; 23	112.52 ± 11.39**	2; 15 ± 0; 13	126.15 ± 12.87*	2; 05 ± 0; 06	140.80 ± 14.35	1; 24 ± 0; 27

Peak in millivolts, T_{peak} in minutes and seconds. * $p \leq 0.05$ and ** $p \leq 0.01$ versus control + ethanol 0.5%.

Dtat Source: Braga, Pier Carlo, et al. "Antioxidant activity of bisabolol: inhibitory effects on chemiluminescence of human neutrophil bursts and cell-free systems." Pharmacology 83.2 (2009): 110-115

Efficacy Data

Antioxidant

Table 3. Effects of the different concentrations of bisabolol on chemiluminescence SIN-1 cell-free test

	Control		Control + ethanol 0.5%		Bisabolol									
					31 µg/ml		15.5 µg/ml		7.7 µg/ml		3.8 µg/ml		1.9 µg/ml	
	peak	T_{peak}	peak	T_{peak}	peak	T_{peak}	peak	T_{peak}	peak	T_{peak}	peak	T_{peak}	peak	T_{peak}
	37.6	8; 50	44.4	9; 10	21.7	10; 00	34.5	8; 05	37.5	7; 50	37.8	7; 40	42.3	8; 30
	24.8	10; 30	27.7	10; 45	15.2	9; 10	15.0	8; 20	20.9	9; 23	24.2	8; 21	29.0	9; 25
	69.3	7; 22	69.2	8; 10	33.8	8; 40	45.5	6; 40	50.5	6; 10	60.5	6; 30	66.9	7; 45
	25.5	7; 55	25.8	7; 05	8.9	7; 35	12.3	7; 50	18.6	7; 49	21.9	8; 10	23.6	8; 05
Mean ±	39.30 ±	8; 39 ±	41.77 ±	8; 47 ±	19.90 ±	8; 51 ±	26.82 ±	6; 44 ±	31.87 ±	7; 50 ±	36.10 ±	7; 40 ±	40.45 ±	8; 26 ±
SEM	10.42	0; 41	10.05	0; 47	5.32*	0; 30	7.95*	0; 57	7.50*	0; 39	8.86	0; 25	9.65	0; 22

Values are in millivolts at peak, T_{peak} in minutes and seconds. * $p \leq 0.05$ versus control + ethanol 0.5%.

Table 4. Effects of various concentrations of bisabolol on chemiluminescence in the $H_2O_2/HOCl^-$ test

	Control		Control + ethanol 0.5%		Bisabolol									
					31 µg/ml		15.5 µg/ml		7.7 µg/ml		3.8 µg/ml		1.9 µg/ml	
	peak	T_{peak}	peak	T_{peak}	peak	T_{peak}	peak	T_{peak}	peak	T_{peak}	peak	T_{peak}	peak	T_{peak}
	536.1	0; 05	531.0	0; 06	155.5	0; 07	277.6	0; 06	345.4	0; 06	386.3	0; 06	483.7	0; 05
	527.8	0; 08	538.8	0; 07	184.0	0; 07	235.3	0; 06	311.2	0; 08	372.1	0; 08	484.3	0; 06
	652.2	0; 10	669.7	0; 08	305.7	0; 09	416.0	0; 09	518.1	0; 07	549.7	0; 06	663.2	0; 08
	534.3	0; 06	545.1	0; 07	263.3	0; 07	320.1	0; 07	383.6	0; 09	485.8	0; 06	548.3	0; 09
Mean ±	562.60 ±	0; 07 ±	571.15 ±	0; 07 ±	227.12 ±	0; 07 ±	312.25 ±	0; 07 ±	389.57 ±	0; 07 ±	448.47 ±	0; 06 ±	544.87 ±	0; 07 ±
SEM	29.92	0; 01	32.98	0; 00	34.73**	0; 00	38.67**	0; 01	45.32*	0; 01	42.17*	0; 00	42.25	0; 01

Values are in millivolts at peak, T_{peak} in minutes and seconds. * $p \leq 0.05$ and ** $p \leq 0.01$ versus control + ethanol 0.5%.

After stimulation with Candida albicans, significant concentration-dependent inhibition of LACL was observed at concentrations ranging from 7.7 to 31 g/ml of erythritol; After stimulation with fMLP, significant inhibition of LACL was observed at concentrations ranging from 3.8 to 31 g/ml. Similar effects were observed in SIN-1 and H2O2/HOCl- systems.

Dtat Source: Braga, Pier Carlo, et al. "Antioxidant activity of bisabolol: inhibitory effects on chemiluminescence of human neutrophil bursts and cell-free systems." Pharmacology 83.2 (2009): 110-115

Efficacy Data

Antibacterial

- For Candida albicans (equivalent to 1%), Staphylococcus aureus (equivalent to 0.03%~0.3%), etc.

	Antimicrobial activity (mM)			
	S. aureus[1]	*B. cereus*[2]	*E. coli*[3]	*C. albicans*[4]
Alcohols				
(-)-α-bisabolol	143.9±0.0	>143.9±0.0	>143.9±0.0	36.0±0.0
geraniol	38.9±18.2	51.9±0.0	25.9±0.0	19.5±0.0
(±)-linalool	77.8±37.0	103.7±29.8	51.9±29.8	38.9±0.0
(E- & Z-)-(±)-nerolidol	>143.9±0.0	>143.9±24.7	>143.9±24.7	143.9±0.0

Data Source: Van Zyl, Robyn L., et al. "The biological activities of 20 nature identical essential oil constituents." Journal of Essential Oil Research 18.sup1 (2006): 129-133.

Efficacy Data

Increase bioavailability: increase permeability coefficient

- In a liquid carrier, α-bisabolol can significantly increase the permeability coefficient of dapiprazole base (DAP-B) (up to 73 times).

It may work by reversibly altering the barrier properties of the stratum corneum and by increasing drug distribution to the skin barrier.
Among them, the activity of optically active (-) terpenes as DAP-B penetration enhancers is twice that of (±) α-bisabolol.

(±) α-bisabolol enhances the penetration of two model drugs with different lipophilicity, 5-fluorouracil and triamcinolone acetonide, through human skin.

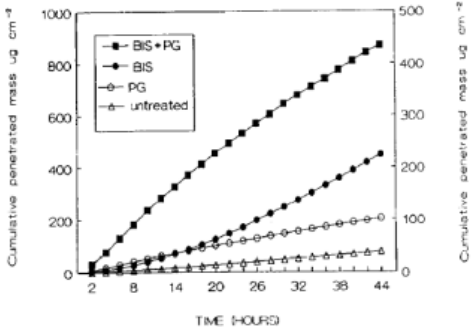


Fig. 2. Example cumulative penetration curves of 5-fluorouracil delivered from its saturated aqueous solution to untreated and enhancer treated human epidermis at 32°C. The left ordinate refers to the α-bisabolol/propylene glycol-treated skin and the right ordinate refers to all other curves.

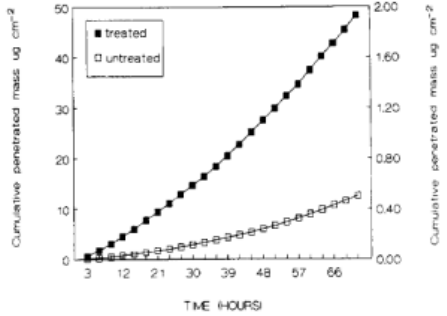


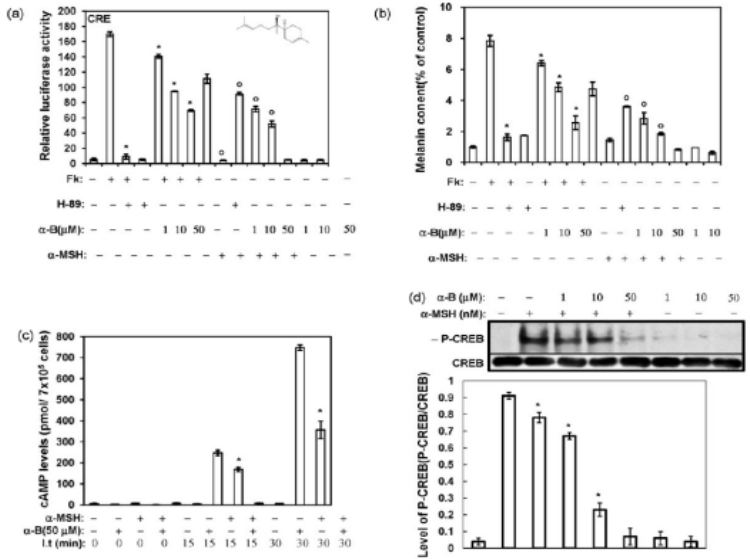
Fig. 4. Cumulative penetration curves of triamcinolone acetonide, delivered from its saturated 1:1 propylene glycol-water solution to untreated and enhancer treated (1:1 α-bisabolol/propylene glycol) human epidermis at 32°C (example plots). The left ordinate refers to the treated skin and the right ordinate refers to the untreated skin.

Data Source: Monti, D., et al. "Enhancement of transdermal penetration of dapiprazole through hairless mouse skin." Journal of controlled release 33.1 (1995): 71-77. Kadir, Ron, and Brian W. Barry. "α-Bisabolol, a possible safe penetration enhancer for dermal and transdermal therapeutics." International journal of pharmaceutics 70.1-2 (1991): 87-94

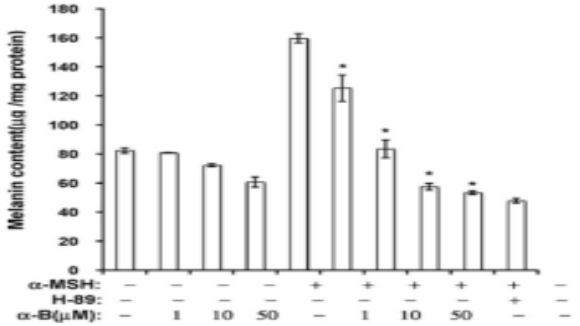
Efficacy Data

Whitening

Increased enzyme activity of melanocytes and increased melanocytes may cause excessive cytochrome deposition in the epidermis and dermis. The cyclic adenosine monophosphate (cAMP) response factor CRE is involved in α-Melanocyte stimulating hormone (α-MSH).



- As shown in Figure a, α-bisabolol inhibited α-MSH induced activation of the CRE luciferase reporter gene.
- As shown in Figure b, α-MSH induced melanin content is decreased by α-bisabolol.
- As shown in Figure c, α-bisabolol decreased α-MSH induced cAMP production.
- As shown in Figure d, CREB phosphorylation is also inhibited by α-bisabolol.
- ***The above indicates that α- bisabolol operates upstream of the cAMP production step.***



Data Source: Kim S, Lee J, Jung E, Huh S, Park JO, Lee JW, Byun SY, Park D. Mechanisms of depigmentation by alpha-bisabolol. J Dermatol Sci. 2008 Dec;52(3):219-22

Formulation Applications

Brand Applications

Essence

Primer

Cleansing milk

Night cream

Lotion

Cleansing Cream

Mask

Lipstick

Sunscreen

Shampoo

Product Advantages

Product Advantages

- Advanced sustainable biotechnology
- Biologically active single form
- Up to 99% or higher assay
- 100% natural

Classification	Name
Presentation	Presentation
Technical Documents	SPEC (Specification)
	TDS (Technical Data Sheet)
	MSDS (Material Safety Data Sheet)
	COA (Certificate of Analysis)
	Composition Breakdown
	Flow Chart
	Formulation Guideline
Declaration Document	Non-Animal Testing Statement
	Non Nanomaterials Statement
	SVHC Statement
	California Prop 65 Statement
	CMR Statement
	BSE/TSE Free Statement
	Halal Statement
	Kosher Statement
	Vegan Statement
	Regulation Compliance Statement
	Country of Origin Statement

Company Laboratory & Certification System

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