

## **BioSpectrum Inc.**

### **Title (Name of Technology)**

Compositions for Improving Skin Conditions Comprising Alpha-Bisabolol  
as an Active Ingredient

## Executive Summary

BioSpectrum, Inc. is a leading developer and supplier of innovative specialty cosmetic ingredients. With profound knowledge and experience on PLANTS, formulation, and biological science, BioSpectrum is able to design and develop high-quality active ingredients for cosmetics. Our R&D team has put ceaseless efforts to search NATURE-derived candidates for skin care ingredients, which can be suggested as the alternatives for the currently using chemical cosmetic actives. BioSpectrum has optimized the concentration and formulation of each active ingredient based on professional knowledge and active research on skin disease, transdermal delivery system, skin cell-based screening system, and various liposome formulations.

Deok Hoon Park has developed skin-whitening agents (hereinafter referred to as 'α-bisabolol') which have efficacy (e.g., improvements of skin conditions, effect of anti-oxidant and anti-inflammation), safety and commercializing potential.

Skin color is determined by concentration and distribution of melanin in the skin. A multitude of approaches and researches have been made to improve skin conditions but have finally failed to effectively improve them.

② Industry Sector: 1. Academic/research (animal health), 2. Animal health (health & hygiene), 3. Biotechnology (assay system), 5. Drug delivery, 6. Drug discovery (combinatorial biology), 7. Medical service (wound closure) 8. Non-profit org./Government (organizations), 11. Service (clinical research)

③ Therapeutic Target: 2. Allergy (skin), 14. Metabolism (anti-oxidant)

④ Development phase: early stage

⑤ Type of business relationship sought (including licensing availability): development collaboration, or non-exclusive or exclusive licensing agreement

## Key Technology Highlights

### □ Notably multiple effects

The α-bisabolol of this invention had excellent effects on skin-whitening, anti-wrinkle, anti-obesity, inhibition of UV-irradiated hair loss and stimulation of hair growth.

### □ Significant reduction of melanin amounts

The α-bisabolol of this invention remarkably decreased melanin synthesis by inhibition of cellular tyrosinase activity compared with arbutin, which was verified in animal experiments using mice and human.

### □ Scavenging ROS (reactive oxygen species)

The α-bisabolol activated the activities of superoxide dismutase (SOD), increasing the clearance rate of superoxide anions ( $O_2^-$ ) in a concentration-dependent manner.

### □ Inhibition of COX (cyclooxygenase) activity

Anti-inflammatory activities of α-bisabolol were evaluated by determining the COX activities.

## Company Information Summary

### Company Description:

- CEO: Deok Hoon Park
- Established: April. 2000
- No. of Employees: 25
- Capital: US\$ 703,500

### Business Field:

- Biotechnology R & D
- Skin care ingredients
- Stem cell technology

### Company History

2000.04	Company established
2000.08.	Approved as a 'superior technology company' by Korea Technology Credit guarantee Fund (KTCGF)
2001.02.	Certificated as a model company with high technology by the Industrial Bank of Korea
2001.12.	Launching cosmetic ingredients to Korea market
2002.12	Strategic alliance with Green Cross Corp.(South Korea) - Dermaceuticals
2004.12.	Received R&D Fund from the Korea Ministry of Commerce, Industry, and Energy
2006.06.	The first exportation of MultiEx Naturotics in Germany
2006.11	Selection of promising small and medium enterprises
2007.09	Receive the commendation of Provincial Governor by Gyeonggi Venture Business Association

## Technology Overview

### ● Technology Platform

The core technology of BioSpectrum is to provide promising skin-whitening agents. The  $\alpha$ -bisabolol exhibits improvements of skin-whitening and anti-wrinkle, inhibition of UV-irradiated hair loss, stimulation of hair growth and anti-obesity.

**Background and unmet needs:** Skin color is determined by the accumulation and distribution of melanin which functions to block skin damages caused from the UV irradiation. The activities of tyrosinase is important to the synthesis of melanin. Therefore, the regulation of the activities of tyrosinase is a critical point for skin color.

A multitude of approaches and researches have been made to improve skin conditions but not effectively.

**Discovery and Achievements:** The  $\alpha$ -bisabolol of BioSpectrum has been developed on the basis of findings that camomile has multiple effects such as anti-inflammation, sedative activities and pain relief and  $\alpha$ -bisabolol is a main active component of camomile essence oil.

The  $\alpha$ -bisabolol derived from camomile is very effective in improving skin-whitening, anti-wrinkle and anti-obesity. In addition, the  $\alpha$ -bisabolol exhibits effects on inhibition of UV-irradiated hair loss and stimulation of hair growth.

The B16 murine melanoma (B-16 F10) was seeded into 6-well plate ( $1 \times 10^5$  per well) on DMEM and cultured at 37°C in 5% CO<sub>2</sub> until above 80%. The  $\alpha$ -bisabolol was treated to the samples at a concentration of 1 ppm, 5 ppm and 10 ppm and the samples were observed after 3 days of incubation. The amount of melanin per cells was measured at 490 nm using a microplate reader. The arbutin was served as a comparative agent.

**TABLE 1.  $\alpha$ -bisabolol reduces the production of melanin by inhibiting the activities of cellular tyrosinase.**

samples	Concentration (ppm)	Reduction rate on the production of melanin (%)	Inhibition rate on the activities of cellular tyrosinase (%)
arbutin	5	22	45
$\alpha$ -bisabolol	1	24	13
$\alpha$ -bisabolol	5	36	38
$\alpha$ -bisabolol	10	49	58

The  $\alpha$ -bisabolol exhibited the reduction of melanin amounts and inhibition of cellular tyrosinase activities in a concentration-dependent manner.

**TABLE 2. Skin external applications containing  $\alpha$ -bisabolol are safe.**

Test substances	Number of responsive subjects									Mean of Response Rate
	One week			Two weeks			Three weeks			
	1	2	3	4	5	6	7	8	9	
	± ± ± ±	± ± ± ±	± ± ± ±	± ± ± ±	± ± ± ±	± ± ± ±	± ± ± ±	± ± ± ±	± ± ± ±	
Control	2 - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	0.18
Test 1	3 - -	1 - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	0.37
Test 2	3 - -	1 - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	0.37
Total number of subjects	30	30	30	30	30	30	30	30	30	

To determine whether  $\alpha$ -bisabolol stimulate skin accumulation, various skin external application was tested. Mean of response rate was calculated as the following formula 1:

#### Formula 1

Mean of response rate =  $\frac{\{(\text{response index} \times \text{response rate}) / (\text{total subjects} \times \text{maximal point (4)})\} \times 100}{\text{trial number (9)}}$

In formula 1, high point means high response rate and the point of each  $\pm$ , + and ++ is 1, 2, 4. The test substances with mean of the response rate of not more than 3 are considered as a safe material applied on the skin. Therefore, skin external applications including  $\alpha$ -bisabolol are useful in the skin.

**TABLE 3.  $\alpha$ -bisabolol increases the clearance rate of superoxide anions ( $O_2^-$ ).**

samples	Concentration (ppm)	clearance rate of superoxide anions ( $O_2^-$ )
$\alpha$ -bisabolol	1	8
$\alpha$ -bisabolol	5	18
$\alpha$ -bisabolol	10	34

The  $\alpha$ -bisabolol had a significant effect on anti-oxidation in a concentration-dependent manner.

**TABLE 4.  $\alpha$ -bisabolol inhibits the activities of COX.**

samples	COX activity (%)
LPS (1 $\mu$ g/ml)	100
LPS (1 $\mu$ g/ml) + $\alpha$ -bisabolol (1 ppm)	95
LPS (1 $\mu$ g/ml) + $\alpha$ -bisabolol (5 ppm)	75
LPS (1 $\mu$ g/ml) + $\alpha$ -bisabolol (10 ppm)	67

In table 4, the  $\alpha$ -bisabolol effectively inhibited the COX activities in THP-1 cells, suggesting that the  $\alpha$ -bisabolol has an effect on anti-inflammation.

## Patents and Publications

BioSpectrum have patents issued or filed for application in PCT and Korea with regard to skin-whitening agent,  $\alpha$ -bisabolol.

**TABLE 5. List of Patents for Skin-Whitening Agent,  $\alpha$ -bisabolol**

Nation	Appln. No	Status	Description
PCT	PCT/KR08/01141	Published	COMPOSITIONS FOR IMPROVING SKIN CONDITIONS COMPRISING ALPHA-BISABOLOL AS AN ACTIVE INGREDIENT
KOREA	2007-0019899	Granted	COMPOSITIONS FOR IMPROVING SKIN CONDITIONS COMPRISING ALPHA-BISABOLOL AS AN ACTIVE INGREDIENT
JAPAN	2009-501364	Pending	COMPOSITIONS FOR IMPROVING SKIN CONDITIONS COMPRISING ALPHA-BISABOLOL AS AN ACTIVE INGREDIENT

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