



# HINOLINE®

Natural anti-ageing composition with antimicrobial properties



PRODUCT CHARACTERISTICS

**ANTI-AGEING PROPERTIES**

**ANTI-MICROBIAL PROPERTIES**

**Does not affect human cutaneous microbiota**



**ORIGIN OF THE PRODUCT**

Natural Hinokitiol is extracted from sawdust of Aomori Hiba. (*Thujopsis dolobrata* (Thunb. ex L. f.) Siebold & Zucc.).

The Asunaro (or *Thujopsis dolobrata*) is a ornamental tree from Japan. It is used to a small extent in forestry in Japan, grown for the valuable wood, which is durable and scented.

Natural Levulinic acid is obtained by fermentation of sugar cane.

**THE ANTIMICROBIAL COMPOSITION HINOLINE HAS BEEN PATENTED BY GREENPHARMA.**

# Anti-ageing Properties

**HINOKITIOL** ACTS AS A CHELATORS OF IONS.  
IT HAS ANTI-AGING AT THREE LEVELS :

- by acting on the extracellular matrix by inhibiting MMPs
- by stimulating SOD and Catalase
- by inhibiting a series of pro-inflammatory cytokines.

**LEVULINIC ACID** HAS BEEN USED TO ENHANCE  
PERMEATION OF SEVERAL DRUGS.

It is known to influence stratum corneum lipid structures and cell permeability.

**HINOKITIOL is a promising and potent agent to inhibit UVB-induced MMP-1 and MMP-3 gene expression in skin fibroblasts.**

Preventive effects of  $\beta$ -thujaplicin against UVB-induced MMP-1 and MMP-3 mRNA expressions in skin fibroblasts.  
*Cheng JY et al., Am J Chin Med. 2012;40(2):387-98.*

**HINOKITIOL is an effective anti-inflammatory reagent that acts by inhibiting the Wnt/ $\beta$ -catenin signaling pathway and could be a promising therapeutic agent for the prevention and treatment of osteoarthritis.**

Hinokitiol reduces matrix metalloproteinase expression by inhibiting Wnt/ $\beta$ -Catenin signaling *in vitro* and *in vivo*.  
*Li J et al., Int Immunopharmacol. 2014 Nov;23(1):85-91. doi: 10.1016/j.intimp.2014.08.012. Epub 2014 Sep 6.*

**HINOKITIOL may be a potent anticancer candidate through down regulation of MMPs 9/2, reduction of OH $\cdot$  production and enhancement of antioxidant enzymes SOD and CAT.**

Hinokitiol Exerts Anticancer Activity through Downregulation of MMPs 9/2 and Enhancement of Catalase and SOD Enzymes: In Vivo Augmentation of Lung Histoarchitecture.  
*Huang CH et al., Molecules. 2015 Sep 25;20(10):17720-34. doi: 10.3390/molecules201017720.*

**HINOKITIOL inhibits ultraviolet B-induced apoptosis in keratinocytes and strongly suggest that the inhibitory mechanism is due to the antioxidant activity of metallothionein induced by the agent.**

Inhibitory effect of beta-thujaplicin on ultraviolet B-induced apoptosis in mouse keratinocytes.  
*Baba T et al., J Invest Dermatol. 1998 Jan;110(1):24-8.*

**HINOKITIOL may cure hair loss by suppressing factors that promote follicular apoptosis, such as TNF-alpha, in addition to stimulating new hair growth.**

Hinokitiol, a natural tropolone derivative, inhibits TNF-alpha production in LPS-activated macrophages via suppression of NF-kappaB.  
*Byeon SE et al., Planta Med. 2008 Jun;74(8):828-33. doi: 10.1055/s-2008-1074548. Epub 2008 Jun 6.*

**LEVULINIC ACID was already described to disturb lipid structure of cell membranes. In this publication, it is shown that the best chemical skin penetration enhancer for buprenorphine patch was LEVULINIC ACID.**

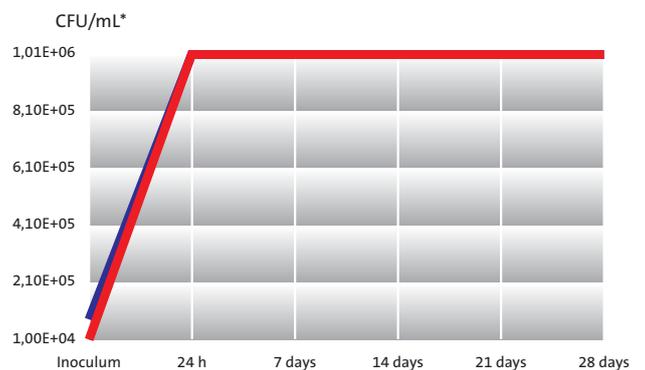
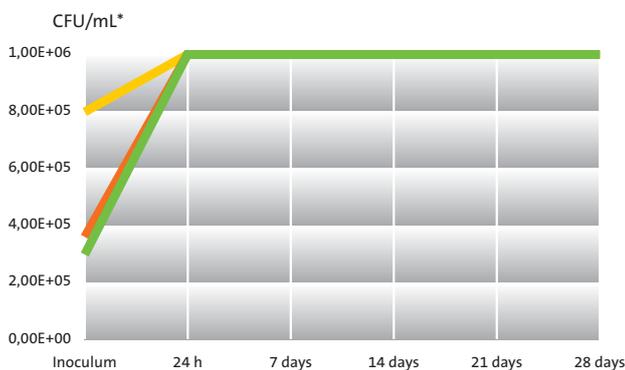
A statistical experimental design approach to evaluate the influence of various penetration enhancers on transdermal drug delivery of buprenorphine.  
*Mojtaba S. et al., Journal of Advanced Research (2015) 6, 155–162.*

**HINOLINE exerts a wide range of anti-aging effects thanks to its constituents.**

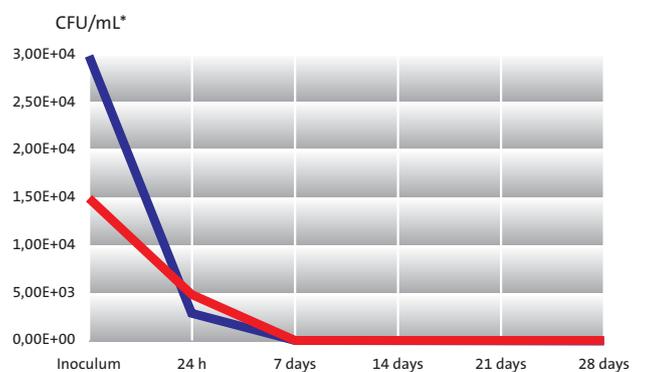
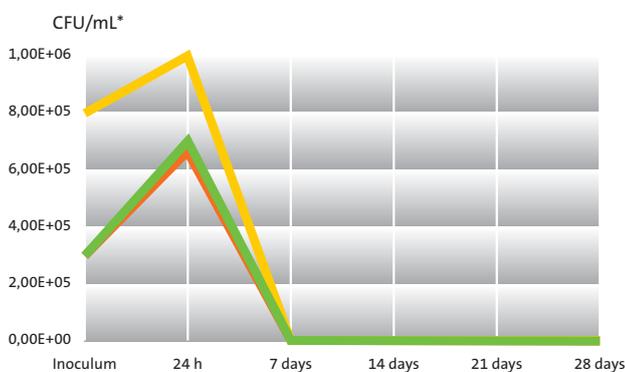
## Challenge-Test: Antimicrobial properties

We used a formulation highly sensitive to micro-organisms containing 70 % water.

### Formula without HINOLINE® 2 %



### Formula with HINOLINE® 2 %



■ *Escherichia coli* ATCC 8739  
■ *Staphylococcus aureus* ATCC 6538  
■ *Pseudomonas aeruginosa* ATCC 9027

■ *Candida albicans* ATCC 10231  
■ *Aspergillus brasiliensis* ATCC 16404  
 \* determined with Log of reciprocal dilution

**These results demonstrated a significant anti-microbial effect of HINOLINE. HINOLINE alone is able to reach the A criteria of the cosmetic ISO11930 standards.**

#### Recommandations of uses

- HINOLINE is a water soluble product
- Incorporation in formulations at 2-3 %
- Operating at a pH of 5.5 ± 0.5

#### Regulation :

China approved  
100% natural origin

## ANTIMICROBIAL SYNERGISTIC EFFECT

(MIC = Minimal Inhibitory Concentration)

Microbial Strains	MIC Control : Phenonip 5%	MIC PRODUCT ALONE		Mic Composition (%)	MIC HINOLINE		SI
		MIC Hinokitiol (%)	MIC Levulinic Acid (%)		MIC Hinokitiol (%)	MIC Levulinic Acid (%)	
<i>Escherichia coli</i>	0,31	0,0050	0,31	0,25	0,0038	0,038	0,87
<i>Staphylococcus aureus</i>	0,31	0,0050	0,63	0,25	0,0038	0,038	0,81
<i>Pseudomonas aeruginosa</i>	0,31	0,0500	0,5	1,00	0,0150	0,150	0,60
<i>Candida albicans</i>	0,31	0,0010	1,25	0,03	0,0005	0,005	0,47
<i>Aspergillus brasiliensis</i>	0,16	0,0030	1,25	0,13	0,0019	0,019	0,64

**The synergistic effect (SI) is calculated according to the Kull equation. The SI lower than 1 proves the synergistic effect.**

(« Kull FC et Al., Mixture of quaternary ammonium compounds and long-chain fatty acids as antifungal agents. *App Microbio* 1961, 9, 538-541).

**These results indicated a significant synergistic effect of the association Hinokitiol/Levulinic acid.**

## ANTIMICROBIAL PROPERTIES

**HINOKITIOL has significant antimicrobial and cytotoxic activities against oral pathogens and oral squamous cell carcinoma cell lines, respectively, and lower cytotoxic effects for normal human oral keratinocytes.**

*In vitro* antimicrobial and anticancer potential of hinokitiol against oral pathogens and oral cancer cell lines.

Yin-Hua Shih et al., *Microbiological Research*, Volume 168, Issue 5, 12 June 2013, Pages 254-262.

**HINOKITIOL has not only antifungal activity, but also insecticidal activity.**

Antifungal Activity of Hinokitiol-Related Compounds on Wood-Rotting Fungi and Their Insecticidal Activities.

Yoshihiko INAMORI et al., *Biological and Pharmaceutical Bulletin* Vol. 23 (2000) No. 8 P 995-997.

**The use of LEVULINIC ACID plus SDS as a wash solution may have practical application for killing foodborne enteric pathogens on fresh produce and uncooked poultry.**

Inactivation of Salmonella and Escherichia coli O157:H7 on Lettuce and Poultry Skin by Combinations of Levulinic Acid and Sodium Dodecyl Sulfate.

TONG ZHAO et al., *Journal of Food Protection*: May 2009, Vol. 72, No. 5, pp. 928-936.

