

# PhelloCure

Skin protection and recovery  
from Exposome

the garden of  
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[www.naturalsolution.co.kr](http://www.naturalsolution.co.kr)

12-24, Gajangsaneopseo-ro, Osan-si, Gyeonggi-do, 18103, Republic of Korea

TEL: +82-31-374-5240 FAX: +82-31-374-5246



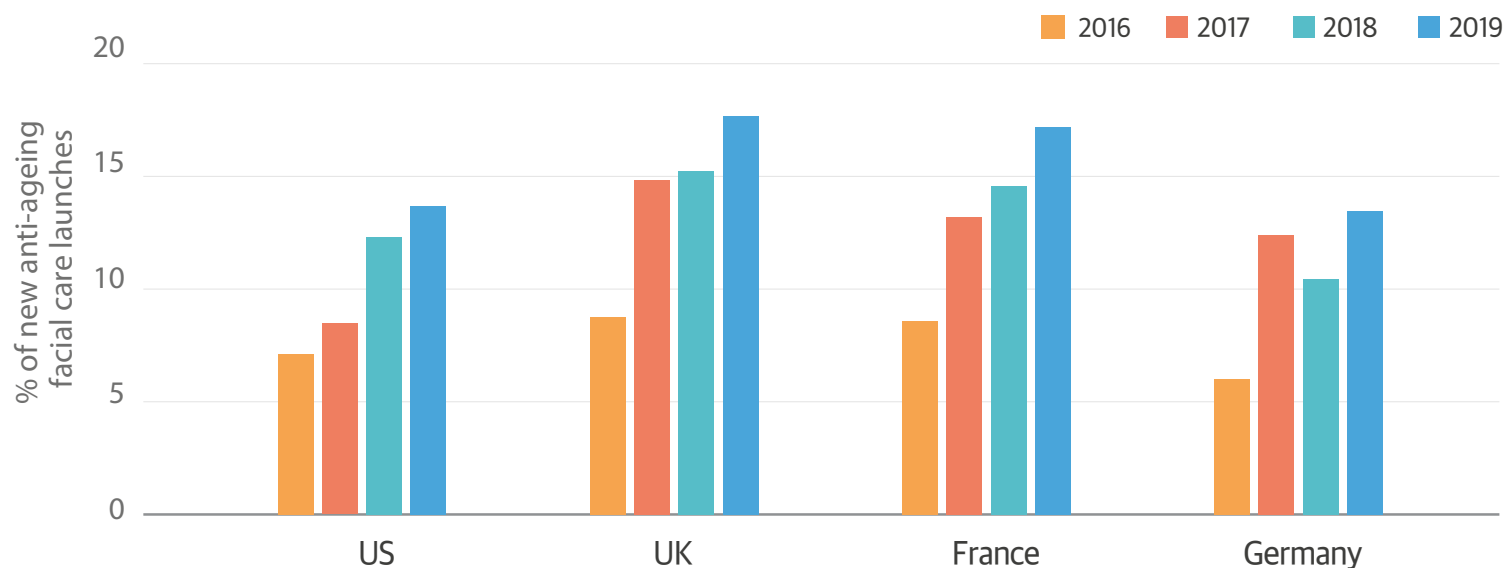


# PhelloCure

Skin recovery and protection product against Exposome  
using *Phellodendron amurense* bark.

# Trend Change: Combining pollution and anti-aging

% of new anti-ageing facial care launches with pollution in product description\*, by market, 2016-19 in Europe and US

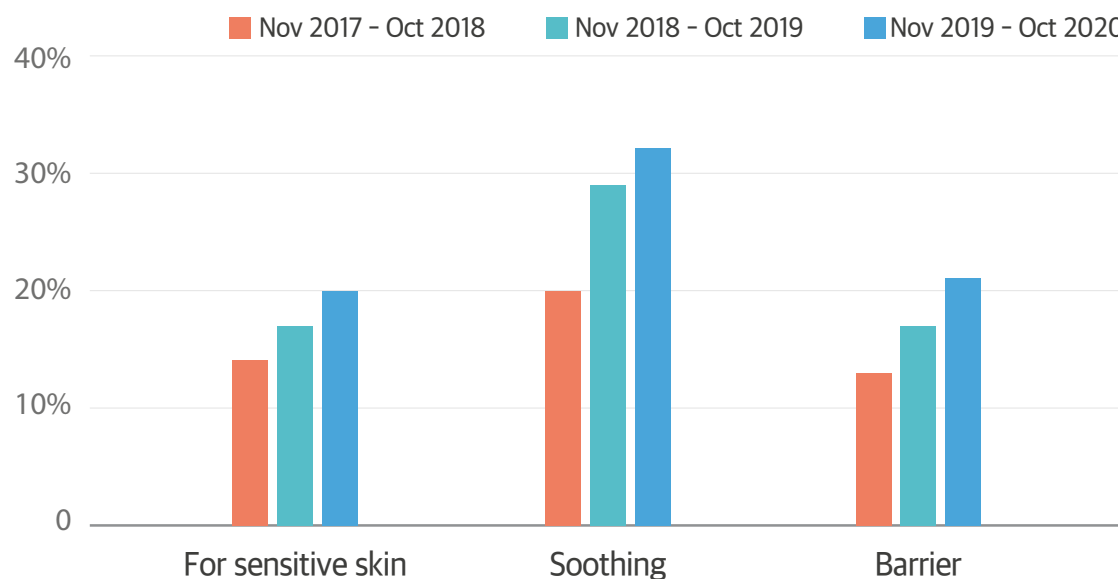


The anti-aging and anti-pollution combination claim is increasing in the US and Europe every year.

Source: Mintel GNPD

# Trend Change: Rising sensitive, soothing, and skin barrier claims

Sensitive skin, soothing and skin barrier claims in total facial skincare, Nov, 2017-Oct, 2020 in China



The environmental factors and the lifestyle are affected to our skin a lot these days. Due to this kind of external stress factors, skin sensitivity is common problem to us. **Skin barrier repair, and skin soothing effects are the key benefit treating skin sensitivity.** Actually, the claims targeting these fact are increased quite a bit in new facial skincare launches since 2017 in China.

Source: Mintel GNPD

# Exposome



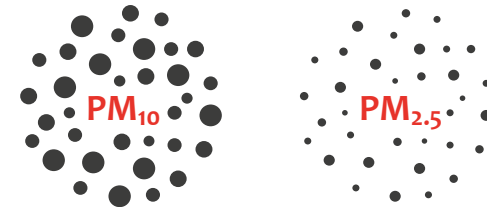
## EXPOSOME?

Exposome is referring to total exposure of human health. It could be UV, smoke, temperature, fine dust and so on.

# Exposome\_Air Pollution

Generally speaking, **air pollution was shown to be a major exposure to have a large impact on human skin aging.** (The Chemical Exposome of Human Aging, Misra et al., 2020, Front genet, 11, 574936)

- Dust, PM (Particulate Matter), floats or scatters in the air
- Classified as fine dust (PM<sub>10</sub>) or ultrafine dust (PM<sub>2.5</sub>) according to particle size
- PM<sub>10</sub> : Fine dust smaller than 10 µm in particle diameter such as dust, pollen, and mold
- PM<sub>2.5</sub> : Fine dust smaller than 2.5 µm in particle diameter, such as combustion particles, organic compounds, and metals

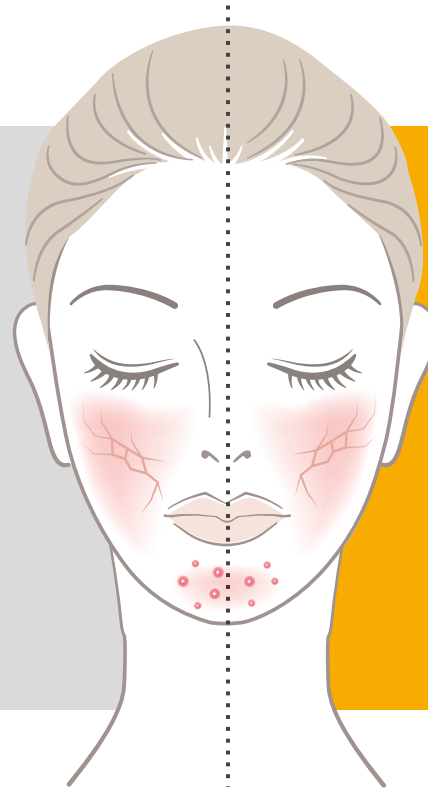


# Sensitized Skin by Exposome

## Same symptoms & different factors

### Sensitive Skin

- Congenital characteristic
- Allergy, asthma, rubeosis
- Thin skin (red skin that reflects blood vessel)
- Skin barrier easily gets weak by the thin skin and vulnerable to bacteria and allergic contactants



### Sensitized Skin

- Lifestyle, hormone, diet, smoking, drinking, UV, pollution
- Symptoms: dry skin, red spot, pimple, acne, rash, broken capillary vessel, uneasiness of skin after cleansing



# Ingredient of PhelloCure

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- The bark of the Hwangbaek tree (*Phellodendron amurense*) has yellow inner skin. It is collected by peeling the bark using more than 10 years old tree and has been used as a traditional medicinal plant.
- The main effects of *P. amurense* are to reduce the heat in the body, detoxification, and relief. It is prescribed to treat skin or scabies or ringworm, which are skin lesions in Donguibogam, which is a traditional medicinal book in Korea.
- Many scientific articles are available for *P. amurense* about anti-microbial, anti-inflammatory, and skin brightening effects.





# History of Medicinal Use

The bark of *P. amurense* used as a cure in a traditional medicinal book called Gwangjebigeup(廣濟秘笈) in Joseon dynasty (Korea)



○小兒膿瘡, 遍身不乾, 用黃柏末, 入枯礬少許摻之, 即愈. 《簡便》

*P. amurense* powder was used externally to treat pus on child's body.

○凍瘡裂痛, 乳汁, 調黃柏末, 塗之. 《專親》

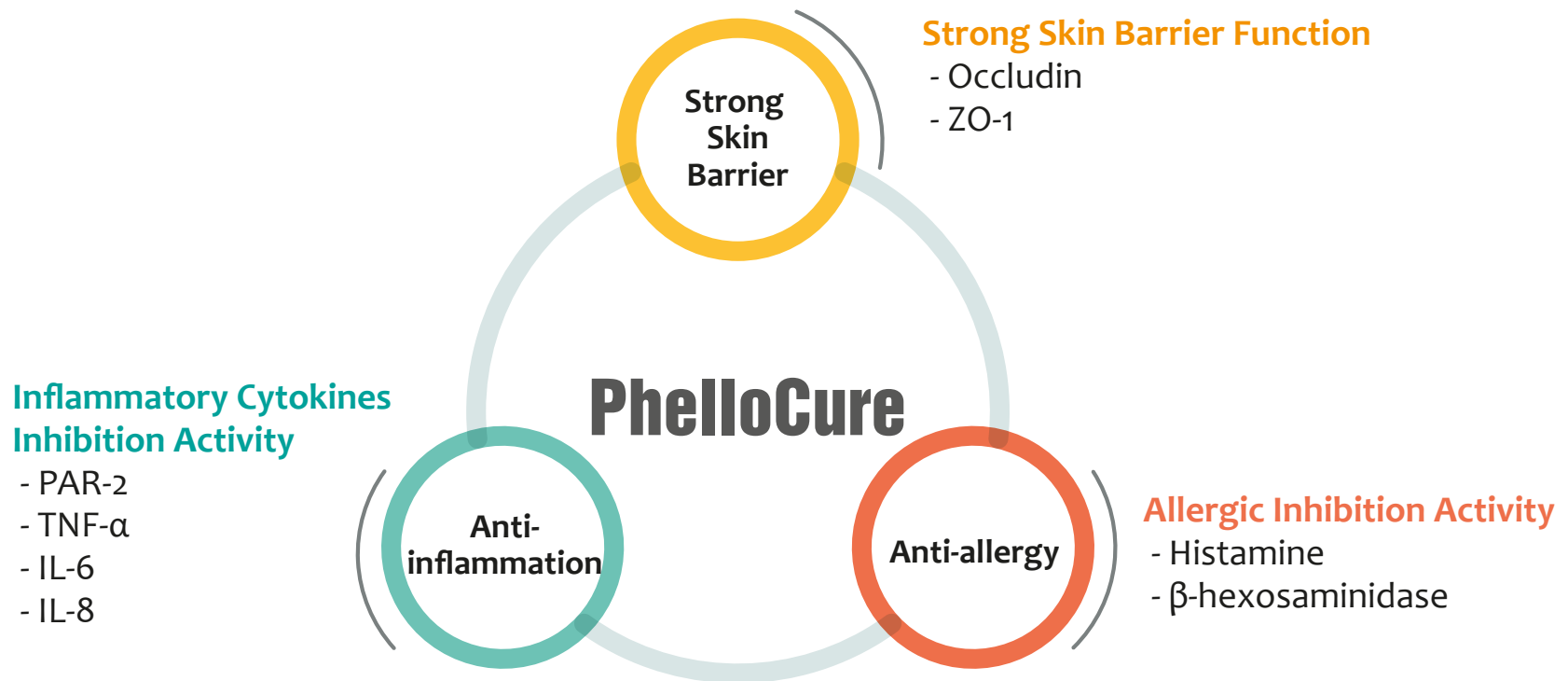
If you have a pain due to pernio, put *P. amurense* powder on your breast and apply it.

○斂瘡生肌, 黃柏末, 麵糊調塗, 效. 《宣明》

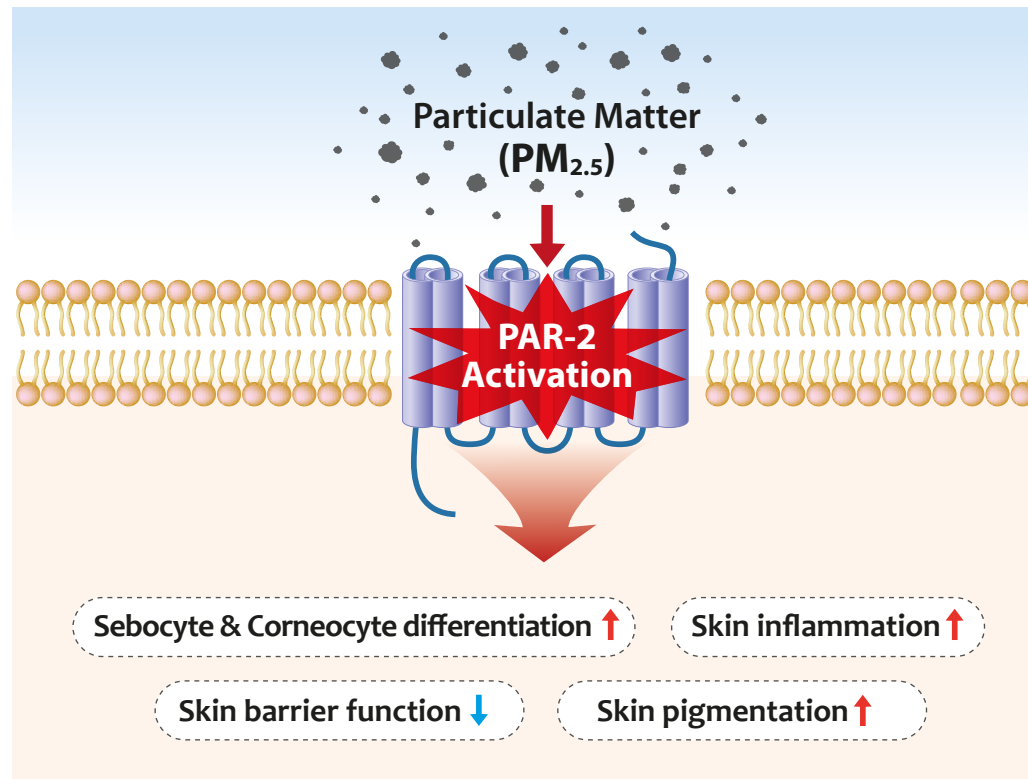
To heal furuncle and help new flesh grow, it is effective to apply *P. amurense* powder to flour paste.

Reference: Koran Traditional Medicine Knowledge Database

# PhelloCure and the Efficacies



# PAR-2 Mechanism by Exposome



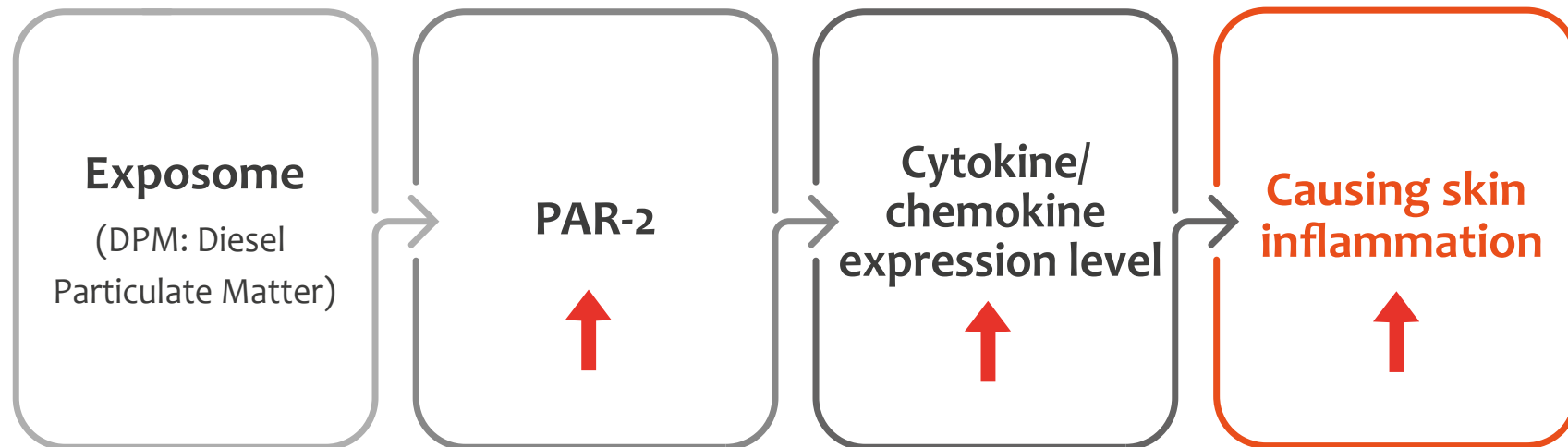
## Key Modulator **PAR-2**

**PAR-2** (Protease Activated Receptor-2) is present in keratinocyte, adipocyte, vascular endothelial cells, and produces various inflammatory reactions, pigments, and involved in skin barrier function.

Reference: Update on protease-activated receptor 2 in cutaneous barrier, differentiation, tumorigenesis and pigmentation, and its role in related dermatologic diseases, Mason Henehan, Anna De Benedetto, 2019, Experimental Dermatology, 28, p.877-8

1. Anti-inflammation
2. Skin Barrier Function
3. Anti-allergy

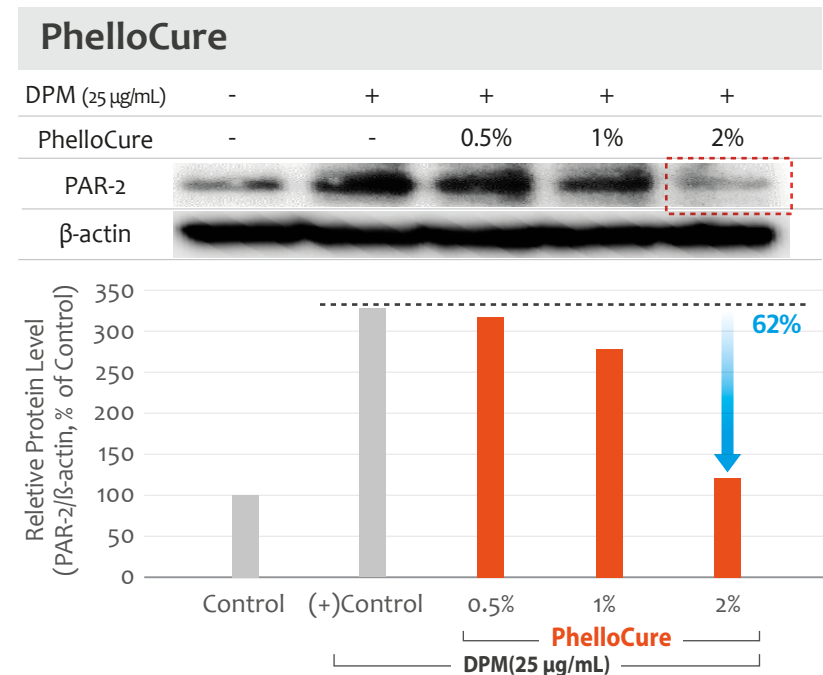
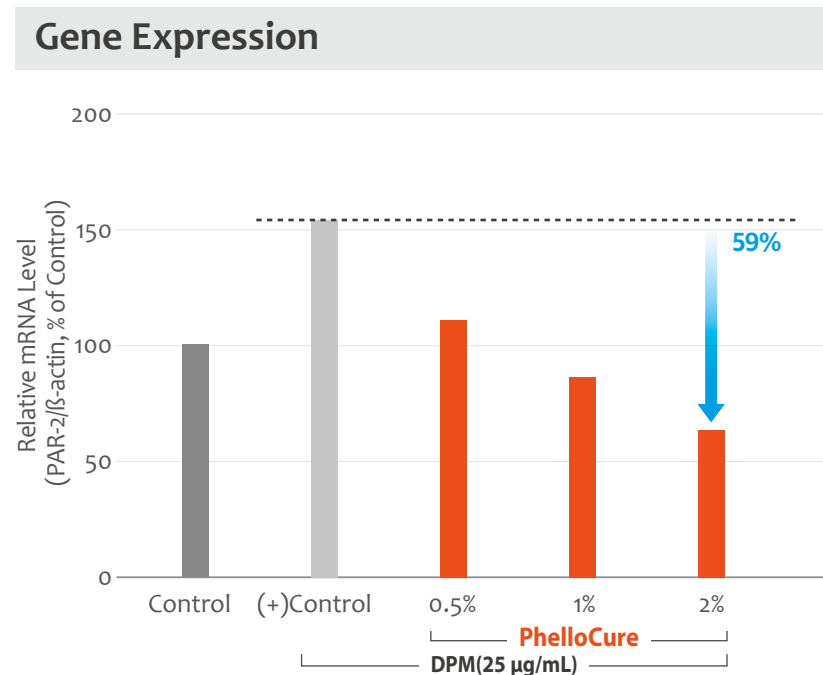
# Skin Inflammation Mechanism by Exposome



1. Anti-inflammation
2. Skin Barrier Function
3. Anti-allergy

# In vitro Evaluation: Anti-inflammatory Effect

## DPM-induced PAR-2 Expression in Human Keratinocyte (HaCaT)



When treated PhelloCure 2% in DPM-induced cell, PAR-2, the key modulator for inflammatory response, was inhibited over 50% in both gene and protein expression level.

\*DPM: Diesel Particulate Matter

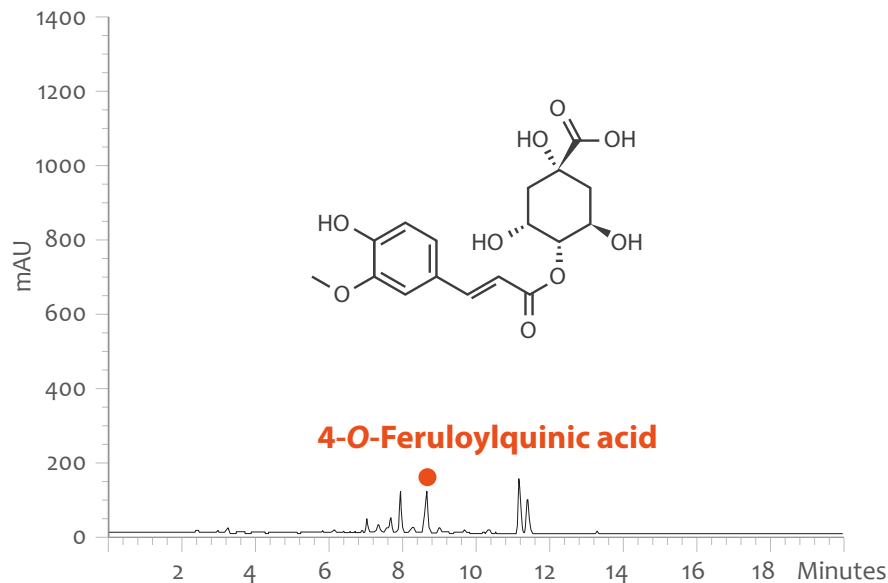


1. Anti-inflammation
2. Skin Barrier Function
3. Anti-allergy

# In vitro Evaluation: Anti-inflammatory Effect

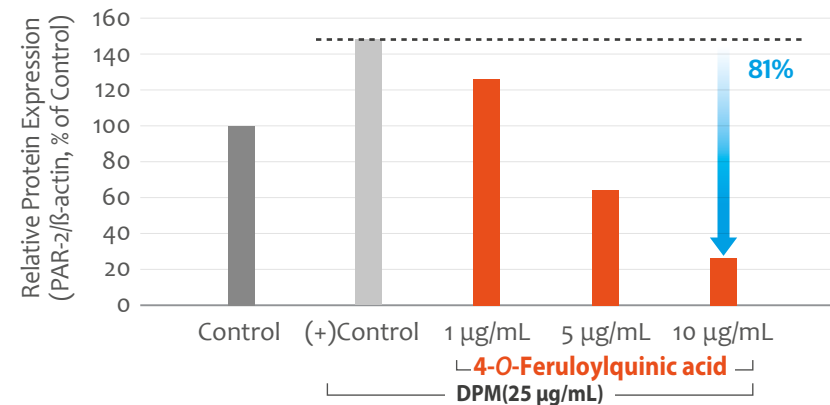
## DPM-induced PAR-2 Expression by 4-O-Feruloylquinic acid in Human Keratinocyte (HaCaT)

HPLC Profile of PhelloCure



Protein Expression

DPM (25 µg/mL)	-	+	+	+	+
4-O-Feruloylquinic acid	-	-	1 µg/mL	5 µg/mL	10µg/mL
PAR-2					
β-actin					

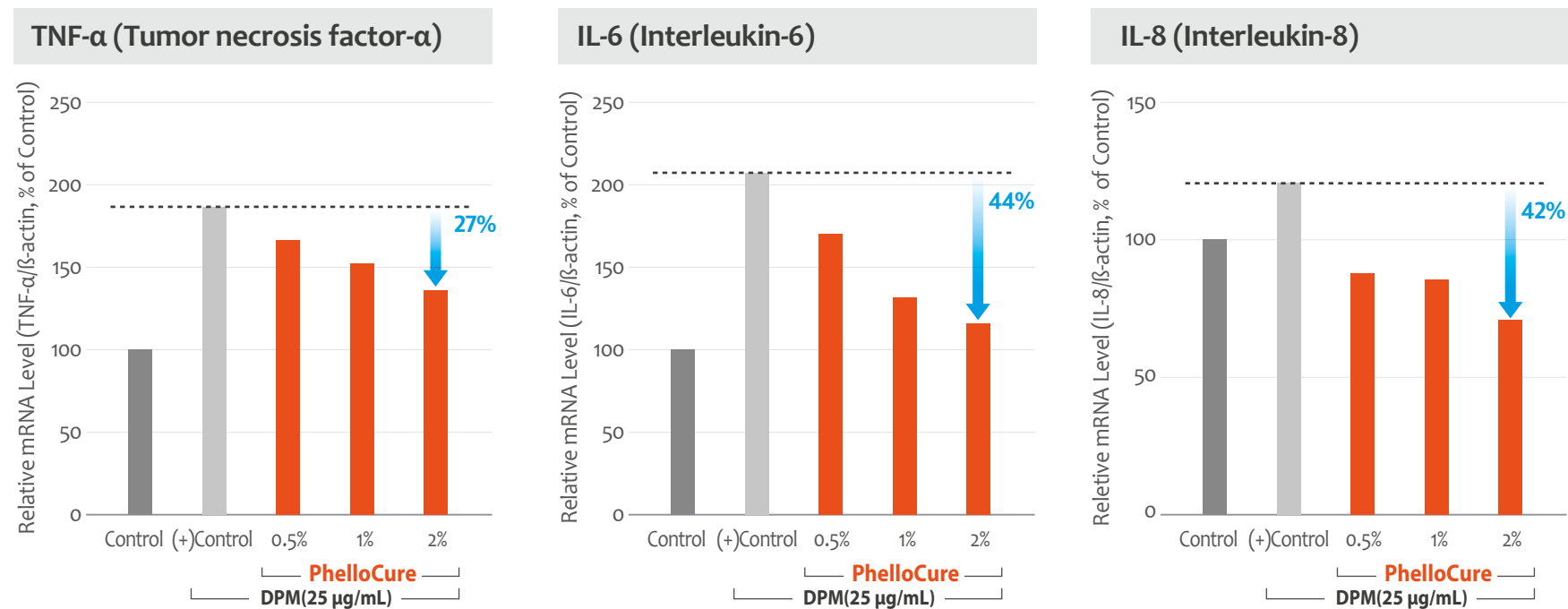


4-O-Feruloylquinic acid, an active compound isolated from *P. amurense* bark showed anti-inflammatory efficacy by inhibiting over Expressed PAR-2 protein level that causes skin inflammation.

1. Anti-inflammation
2. Skin Barrier Function
3. Anti-allergy

# In vitro Evaluation: Anti-inflammatory Effect

## DPM-induced Cytokines Gene Expression in Human Keratinocyte (HaCaT)



PhelloCure inhibited the gene expression of inflammatory cytokines, TNF-a, IL-6 and IL-8 strongly in Human Keratinocyte.

1. Anti-inflammation
2. **Skin Barrier Function**
3. Anti-allergy

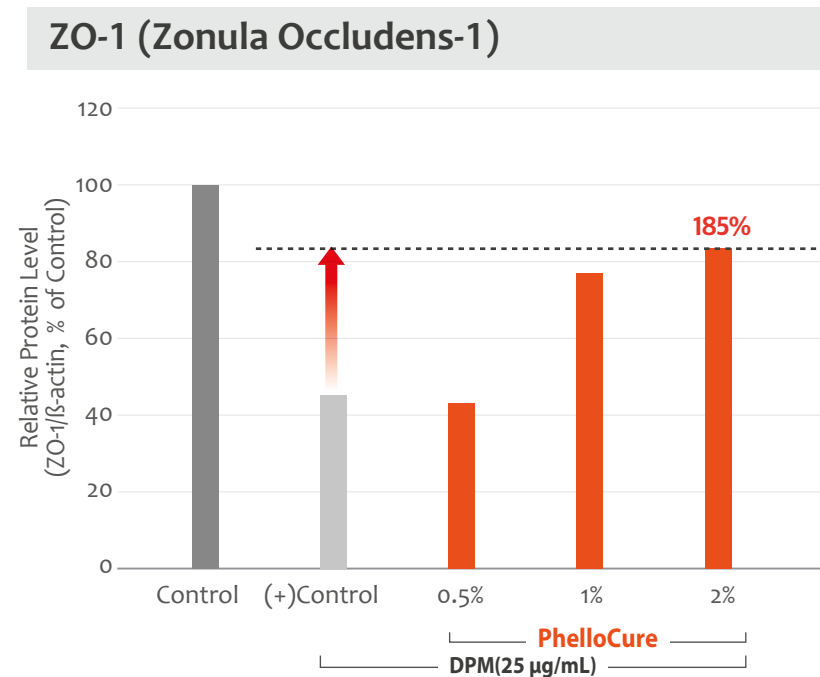
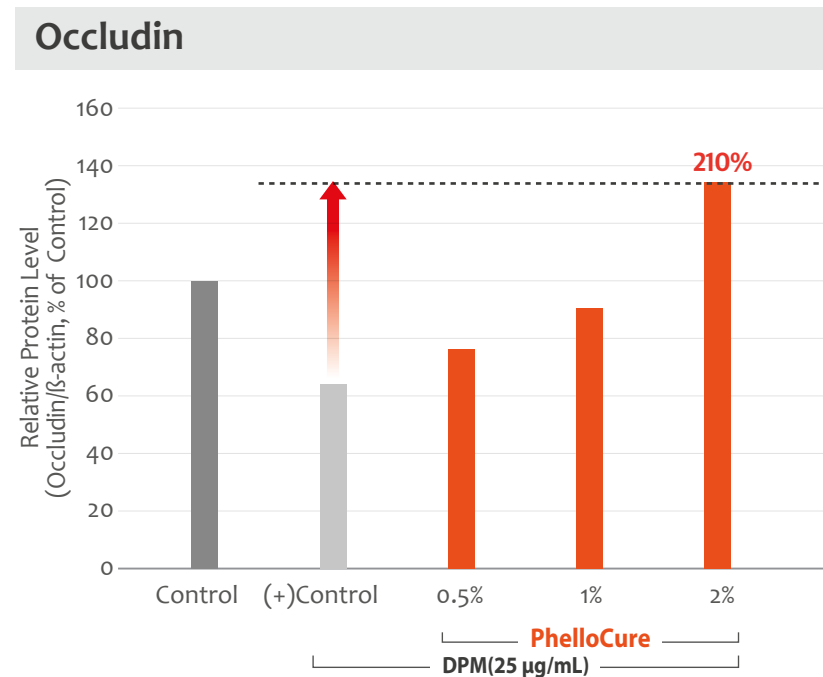
# Skin Barrier Mechanism by Exposome



1. Anti-inflammation
2. Skin Barrier Function
3. Anti-allergy

# In vitro Evaluation: Skin Barrier Function

## DPM-induced Occludin and ZO-1 Protein Expression in Human Keratinocyte (HaCaT)

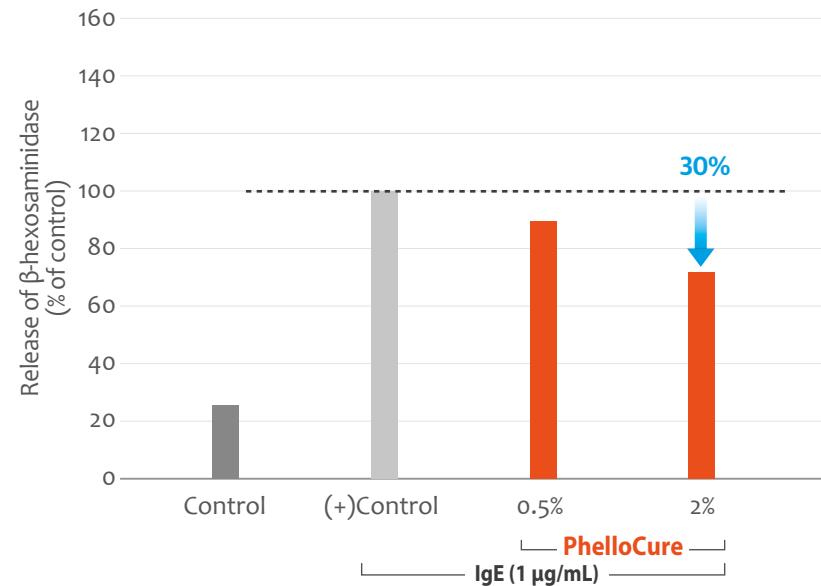


Phellocure stimulates skin barrier function by increasing tight junction proteins such as Occludin and ZO-1.

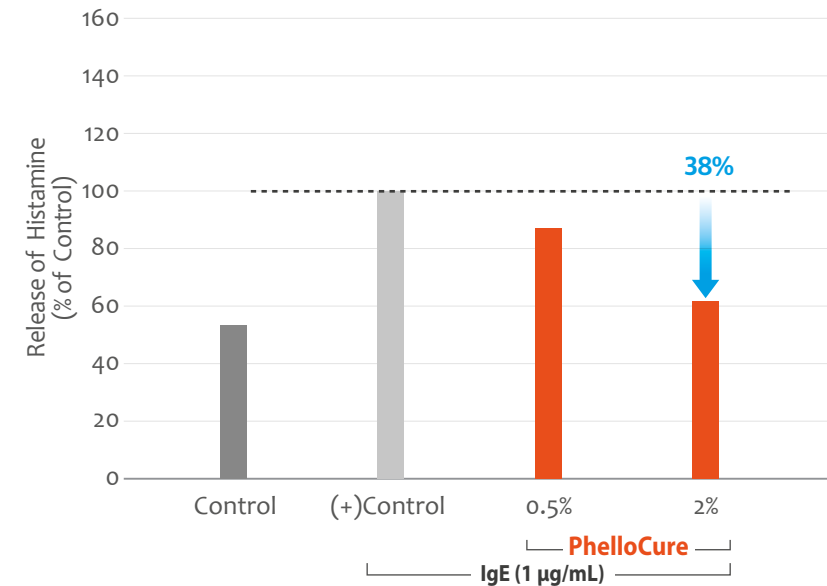
1. Anti-inflammation
2. Skin Barrier Function
3. **Anti-allergy**

# In vitro Evaluation: Anti-allergic Effect

## Inhibition of $\beta$ -hexosaminidase Release in Mast cells



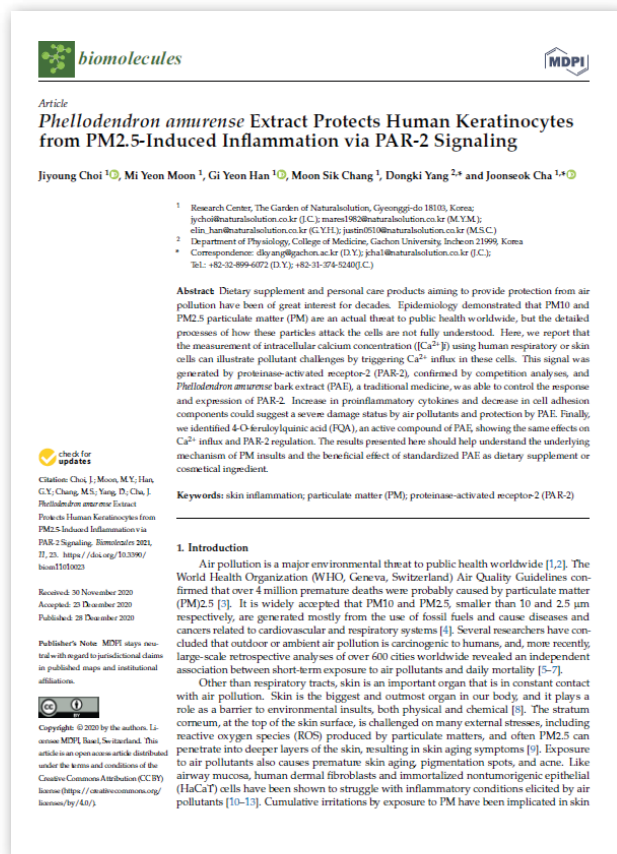
## Inhibition of Histamine Release in Mast cells



Phellocure can reduce allergic reaction by inhibiting  $\beta$ -hexosaminidase and histamine by 30% and 38% respectively.



# Published Article and Patent about PhelloCure



**biomolecules** MDPI

Article  
**Phellodendron amurense Extract Protects Human Keratinocytes from PM2.5-Induced Inflammation via PAR-2 Signaling**

Jiyoung Choi <sup>1</sup>✉, Mi Yeon Moon <sup>1</sup>, Gi Yeon Han <sup>1</sup>✉, Moon Sik Chang <sup>1</sup>, Dongki Yang <sup>2,\*</sup> and Joonseok Cha <sup>1,\*</sup>✉

<sup>1</sup> Research Center, The Garden of Natural Solution, Gyeonggi-do 18103, Korea; jychoi@naturalsolution.co.kr (J.C.); mnam1983@naturalsolution.co.kr (M.Y.M.); elin\_han@naturalsolution.co.kr (G.Y.H.); jstain0510@naturalsolution.co.kr (M.S.C.)  
<sup>2</sup> Department of Physiology, College of Medicine, Gachon University, Incheon 21999, Korea  
 \* Correspondence: dkyang@gachon.ac.kr (D.Y.); jcha1@naturalsolution.co.kr (J.C.); Tel.: +82-32-999-6072 (D.Y.); +82-31-974-6240 (J.C.)

**Abstract** Dietary supplement and personal care products aiming to provide protection from air pollution have been of great interest for decades. Epidemiology demonstrated that PM10 and PM2.5 particulate matter (PM) are an actual threat to public health worldwide, but the detailed processes of how these particles attack the cells are not fully understood. Here, we report that the measurement of intracellular calcium concentration ( $Ca^{2+}$ ) using human respiratory or skin cells can illustrate pollutant challenges by triggering  $Ca^{2+}$  influx in these cells. This signal was generated by proteinase-activated receptor-2 (PAR-2), confirmed by competition analyses, and *Phellodendron amurense* bark extract (PAE), a traditional medicine, was able to control the response and expression of PAR-2. Increase in proinflammatory cytokines and decrease in cell adhesion components could suggest a severe damage status by air pollutants and protection by PAE. Finally, we identified 4-O-teruloylquinic acid (TQA), an active compound of PAE, showing the same effects on  $Ca^{2+}$  influx and PAR-2 regulation. The results presented here should help understand the underlying mechanism of PM insults and the beneficial effect of standardized PAE as dietary supplement or cosmetic ingredient.

**Keywords:** skin inflammation; particulate matter (PM); proteinase-activated receptor-2 (PAR-2)

**1. Introduction**  
 Air pollution is a major environmental threat to public health worldwide [1,2]. The World Health Organization (WHO, Geneva, Switzerland) Air Quality Guidelines confirmed that over 4 million premature deaths were probably caused by particulate matter (PM)2.5 [3]. It is widely accepted that PM10 and PM2.5, smaller than 10 and 2.5  $\mu$ m respectively, are generated mostly from the use of fossil fuels and cause diseases and cancers related to cardiovascular and respiratory systems [4]. Several researchers have concluded that outdoor or ambient air pollution is carcinogenic to humans, and, more recently, large-scale retrospective analyses of over 600 cities worldwide revealed an independent association between short-term exposure to air pollutants and daily mortality [5–7].  
 Other than respiratory tracts, skin is an important organ that is in constant contact with air pollution. Skin is the biggest and outermost organ in our body, and it plays a role as a barrier to environmental insults, both physical and chemical [8]. The stratum corneum, at the top of the skin surface, is challenged on many external stresses, including reactive oxygen species (ROS) produced by particulate matters, and often PM2.5 can penetrate into deeper layers of the skin, resulting in skin aging symptoms [9]. Exposure to air pollutants also causes premature skin aging, pigmentation spots, and acne. Like airway mucosa, human dermal fibroblasts and immortalized nontumorigenic epithelial (HaCaT) cells have been shown to struggle with inflammatory conditions elicited by air pollutants [10–13]. Cumulative irritations by exposure to PM have been implicated in skin

check for updates  
 Citation: Choi, J.; Moon, M.Y.; Han, G.Y.; Chang, M.S.; Yang, D.; Cha, J. Phellodendron amurense Extract Protects Human Keratinocytes from PM2.5-Induced Inflammation via PAR-2 Signaling. *Biomolecules* 2021, 11, 23. <https://doi.org/10.3390/biom1101023>  
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## 출원 번호 통지서

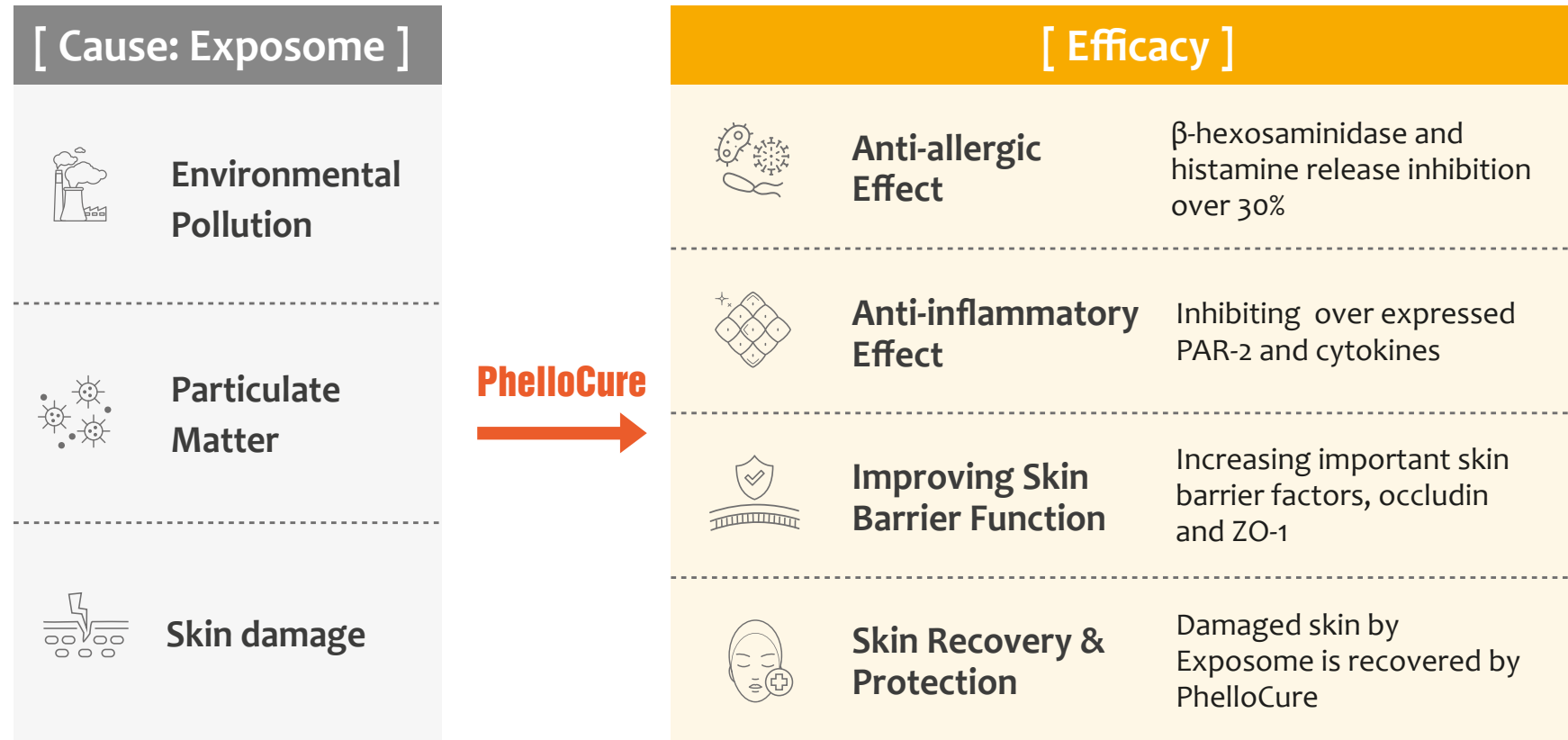
출원 일자	2020.12.11
특기 사항	심사청구(유) 공개신청(무)
출원 번호	10-2020-0173272 (접수번호 1-1-2020-1347123-18) (DAS접근코드 C978)
출원인 명칭	주식회사 더가든오브내추럴솔루션(1-2011-046155-1)
대리인 성명	이재영(9-2005-000390-1)
발명자 성명	한기연 최지영 차준석 장문식
발명의 명칭	환벽나무 추출물을 유효성분으로 포함하는 기능성 화장품 조성물 및 그의 제조방법

특 허 청 장

▲ Patent application in Korea

◀ We have published a scientific article about *P. amurense* in *Biomolecules* on 2021.

# Summary



**PhelloCure**  
→

# Product Information

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- **Product Name:** PhelloCure(GPD)-RSPO
- **INCI Name:** Phellodendron Amurense Bark Extract
- **Dosage:** 1 – 3%
- **Formulation:** Add to the formulation when the temperature is lower than 55°C.  
Recommended to add after the cooling process.
- **Storage:** Avoid direct light or UV.  
Keep it in a dry area at room temperature.



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*" We are always upgrading to serve you better"*

