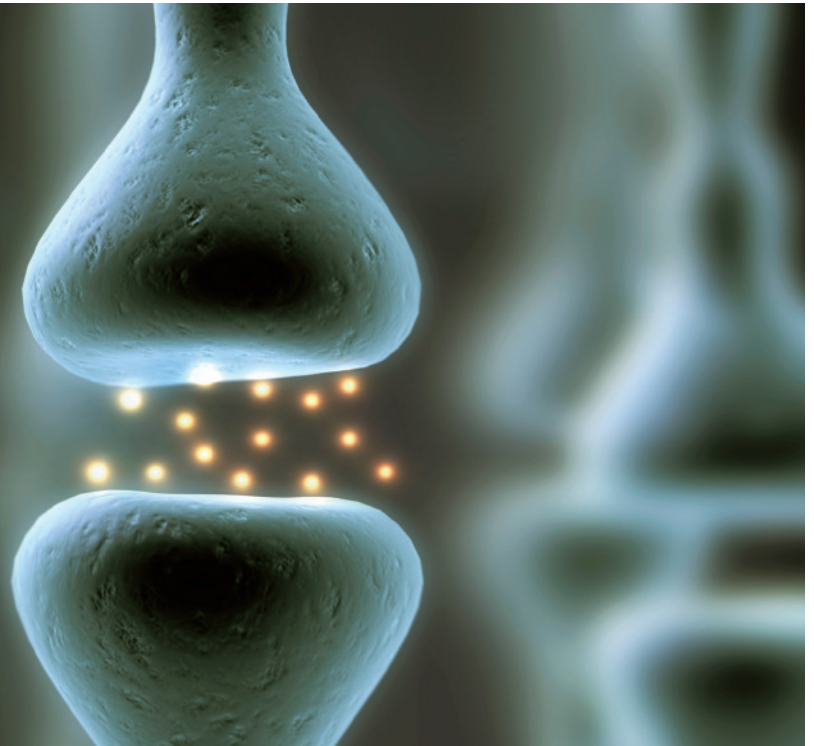


# HotFlux®

Long-Lasting,  
Low-Irritation

## Impart Exotic and Delicate Warming Sensation



## HotFlux®

### INCI Declaration

Vanillyl Butyl Ether

### Benefits

- Impart exotic warming sensation
- Enhance microcirculation
- Help stimulate hair growth

### Applications

- Massage
- Slimming
- Spa
- Pain relief
- Intimacy
- Hair & scalp care

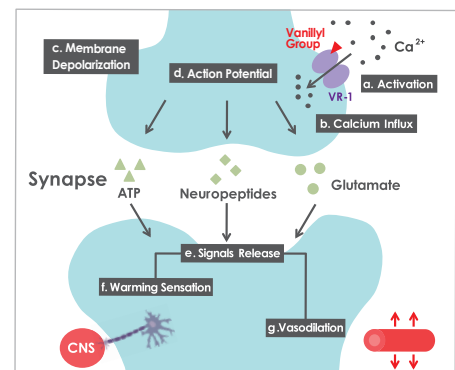
Sometimes, a small amount of additive can light up the sensory experience of a formulation. Substances known to impart a sensation of warmth upon application are called warming agents. HotFlux®, vanillyl butyl ether, is a mild warming agent that imparts an exotic, gentle and long lasting warming effect. It has a low irritation profile when compared to similar acting materials. HotFlux® can also induce natural hair growth cascade through enhanced microcirculation and stimulation of key neurotransmitters. It can be introduced into many types of applications to provide psychophysical relaxation, pain relief, as well as increased blood flow and delivery of nutrients to the hair shaft.

### The Mechanism of Warming Sensation

The vanillyl group of HotFlux® is the functional group that plays the key role in inducing the warming sensation via nervous system. The sensory neurons are activated through the binding of the vanillyl group to its receptor, named vanilloid receptor-1 (VR-1). It is a non-selective cation channel that naturally responds to noxious stimuli, such as high temperatures or acidic pH. Upon ligand/receptor binding, the channel opens and leads to an influx of predominant calcium ions through the channel pore. In turn, this action causes membrane depolarization that generates an action potential once it reaches a threshold. That action potential then propagated along the axon to the synapse.

Activated sensory neurons will release glutamate, ATP and a variety of neuropeptides as neurotransmitters from the synapse. These neurotransmitters eventually reach the central nervous system and launch a cascade of warm-

ing sensation, which can also be similarly triggered by temperature of  $\geq 43^{\circ}\text{C}$ . Among the neurotransmitters, calcitonin gene-related peptide (CGRP) is one of the known neuropeptides released upon activation, which acts on vascular endothelial cells to trigger vasodilation, therefore increases the blood circulation.



# HotFlux®

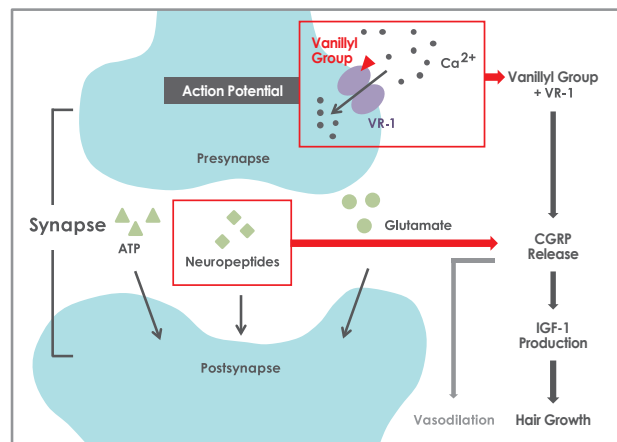
## Efficacy Study

2.1

### Rejuvenate Hair Growth:

#### The Role of Vanillyl Group in Hair Growth

Hair loss is the most distressing problem of the scalp that approximately 1.8% of the world population is experiencing. HotFlux®, as a potential ingredient that enhances microcirculation, could serve as an anti-hair loss treatment by activating its functional vanillyl group. HotFlux® facilitates the delivery of nutrients to hair follicles; it also helps to increase insulin-like growth factor (IGF-1), which is important for the proliferation of hair stem cells, by stimulating the release of CGRP.

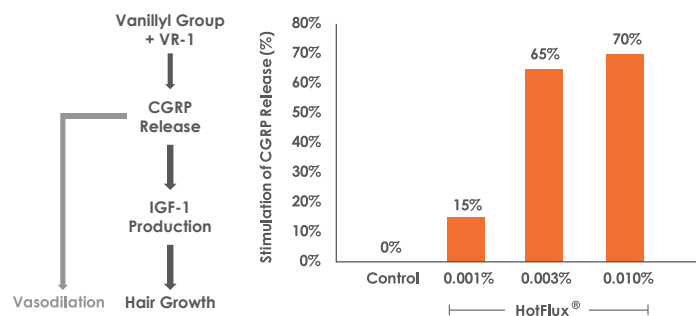


2.2

### Rejuvenate Hair Growth:

#### Stimulation of CGRP

CGRP is a neuropeptide which not only induces the synthesis of IGF-1 but also serves as a vasodilator. It is reported that oral administration of capsaicin can improve hair growth in patients of alopecia. HotFlux®, on the other hand, contains the same vanillyl group as capsaicin and was assessed to investigate if similar effect exists. Data shows that a concentration-dependent release of CGRP by sensory neurons without any cytotoxic effect, when different concentrations of HotFlux® were applied.

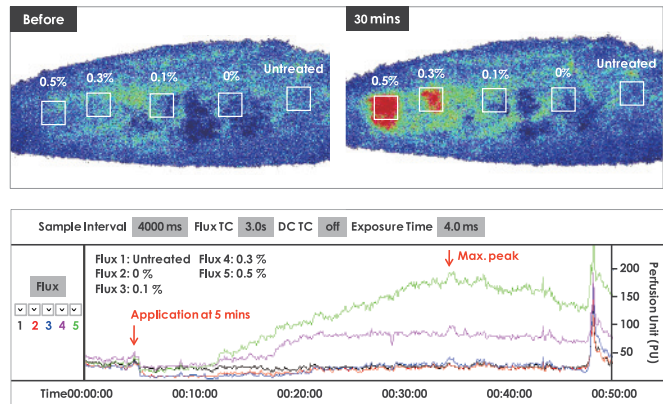


## Efficacy Study

1.1

### Microcirculation Enhancement: Increase of Blood Flow

21 volunteers, aged between 21 to 40 years old, participated in a microcirculatory study using Laser Doppler Flowmetry. The local blood cell flux (BCF) was evaluated when different concentrations of HotFlux® were applied to the subjects' forearm. Results show that HotFlux® at 0.3% and 0.5% can exhibit significant increase in BCF as shown from the laser images as well as changes in the blood flow (PU) curve. HotFlux® also provides prolonged microcirculation enhancement for over 30 minutes.



1.2

### Microcirculation Enhancement: Analysis of Blood Perfusion and Warming Sensation

A more in-depth analysis and other parameters were explored in the study. HotFlux® showed a great performance that 30.24% and 66.4% of blood perfusion was increased, respectively, when 0.3% and 0.5% of sample creams were applied. Over 90% of the subjects felt warming sensation after treatment. The onset and maximum peak of the warming effect occurred more rapidly when HotFlux® was treated at higher concentration. The average duration of the perfusion in all volunteers was more than 30 minutes with no reports on pain or discomfort on the treatment sites throughout the process.

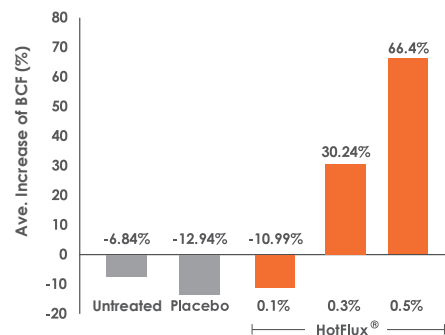


Table 1

| Conc. (%) | Measurable Response (n / total) | Warming Sensation (n / total) | Ave. Percentage Increase (%) | Initial Response Time (min) | Max. Peak Onset Time (min) | Ave. Duration Time (min) |
|-----------|---------------------------------|-------------------------------|------------------------------|-----------------------------|----------------------------|--------------------------|
| Untreated | 4/21                            | 0/21                          | -6.84                        | n.a.                        | n.a.                       | n.a.                     |
| 0         | 3/21                            | 0/21                          | -12.94                       | n.a.                        | n.a.                       | n.a.                     |
| 0.1       | 5/21 (23.81%)                   | 10/21                         | -10.99                       | 14.93                       | 28.6                       | >30.8                    |
| 0.3       | 17/21 (80.95%)                  | 19/21                         | 30.24                        | 10.47                       | 23.5                       | >30.8                    |
| 0.5       | 14/21 (76.19%)                  | 19/21                         | 66.40                        | 9.58                        | 22.1                       | >32.0                    |

# HotFlux®

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## Claim Ideas

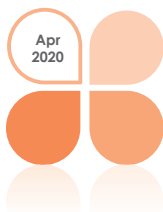
- Impart exotic warming sensation
- Enhance microcirculation
- Help stimulate hair growth

## Applications

- Warming cream/ lotion (head, hand, foot and body)
- Spa product (massage, scrub)
- Slimming product
- Hair & scalp product
- Personal lubricant
- Color cosmetics (lip gloss)
- Pain-relief product (ointment, patch)
- Anti-cellulite product

## Marketing Benefits

- Safer than other warming agents
- Non mutagenic and less irritating
- Longer lasting duration
- REACH compliant, China approved and Halal approved



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