



Capsaicin patch (Topical)

- Neuropathic pain management

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Capsaicin patch

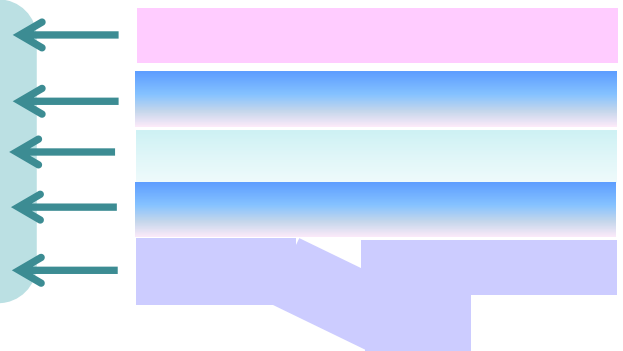
1. Composition

- Active Ingredient: capsaicin
- Type : highly affinity to the vanilloid receptor subtype 1 (VR1)
- Appearance : PET film laminate

2. System Design

- triple layered high penetration system

- PET backing layer
- Adhesive
- API
- Adhesive
- Release liner



3. Indication

- Management of neuropathic pain

4. Usage and dose

- One patch/ 3days and one day break

Business Model

- Product: capsaicin patch (neuropathic pain treatment)
- Strategy: administration method improvement
※ Capsaicin ointment (3 ~ 4 applications /day) → patch (1 / 3 days)

• Development status:

| | |
|-------------------------|------------|
| • Formulation, Scale-up | Done |
| • Phase I/II (Kor) | Done |
| • Phase III (Kor) | 1Q '13 ~ |
| • Process validation | '13 ~ |
| • Approval | 4Q '15 (E) |

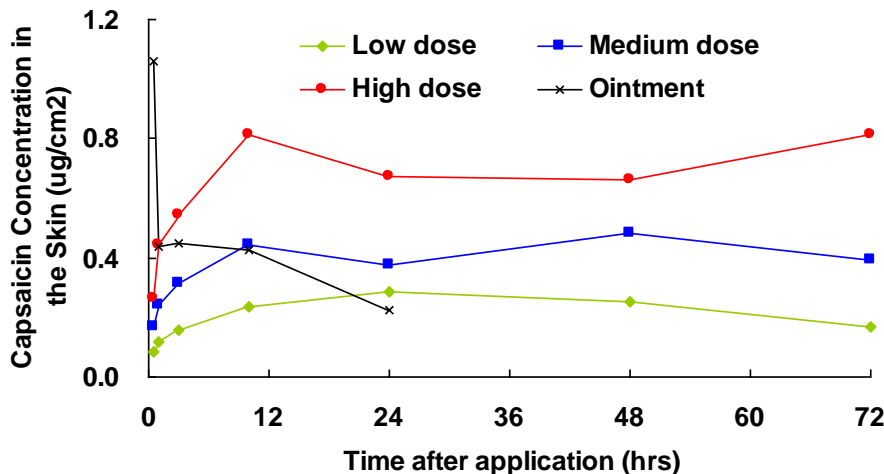
• Possible biz. model: (for Korean partner)

| | |
|----------------------|--|
| • Formulation | Samyang |
| • Scale-up | |
| • Phase I/II (Korea) | |
| • Phase III & PV | Co-dev. (cost sharing) |
| • After launch | <ul style="list-style-type: none"> • Manufacturing (Samyang) • MKT & Sales (Partner) |

In vitro & Pre-Clinical Study

1. Dermatopharmacokinetics Study

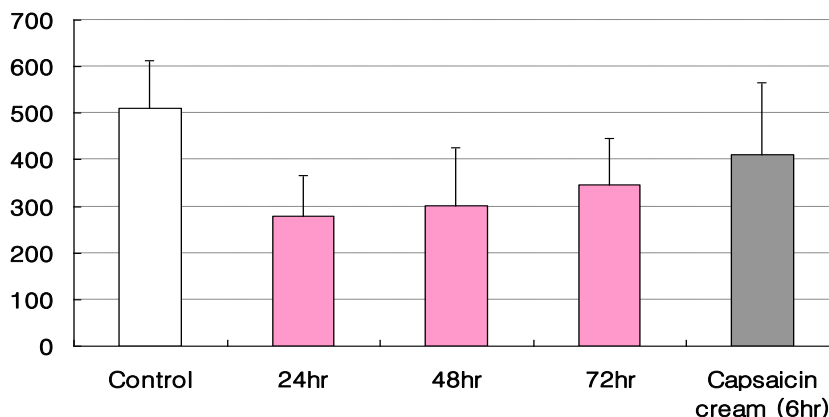
- Animal : male SD rat (4 groups, n=5 per group)
- Test drugs: capsaicin patch (25, 50, 100 $\mu\text{g}/\text{cm}^2$) & capsaicin ointment (0.075%)



► Capsaicin was delivered and maintained in the skin for 72 hours with single application of Samyang capsaicin patch

2. Efficacy

- Model: formalin induced licking paw test - *Bellasio et al. 2003*
- Animal: male SD rat (5 groups, n=20 per group)
- Test drugs: capsaicin patch (100 $\mu\text{g}/\text{cm}^2$) & capsaicin ointment (0.075%)



► Capsaicin patch groups showed higher efficacy than ointment group (i.e., the number of licking counts of patch was reduced by ~ 25% compared to ointment)

3. Toxicity: Skin irritation test

- Test facility : GLP facility (*Biotoxtech Co., Ltd, Korea*)
- Animal : male New Zealand White Rabbit (n=6)
- Test drugs : placebo patch & capsaicin patch (25, 50, 100 $\mu\text{g}/\text{cm}^2$)
- Evaluation: Draize's Primary Irritation Index at 24, 48, and 72 hours after application

| Sample | P.I.I. * | Results |
|--|----------|---------------|
| Capsaicin patch (25 $\mu\text{g}/\text{cm}^2$) | 0.0 | No irritation |
| Capsaicin patch (50 $\mu\text{g}/\text{cm}^2$)** | 0.0 | |
| Capsaicin patch (100 $\mu\text{g}/\text{cm}^2$)** | 0.0 | |
| Capsaicin ointment (0.075%, 15 ug/cm²) | 0.46 | |

* P.I.I: Primary Irritation Index

** No skin irritation for 7 times of repeated application for 28 days

Phase I/II Clinical Study

1. Synopsis of the Study

- **Objective: Evaluation of Efficacy and Safety**
- **Test Sample & Subject**
: Capsaicin patch 50, 100 ug/cm², Placebo patch, Capsaicin cream 0.075%
- **Regimen: 6 weeks/subject**
- **Evaluation Criteria**
 - ✓ **Efficacy: Daily Pain Rating Scale, Daily Sleep Interference Scale**
Quality of Life Assessment (EQ-5D)
 - ✓ **Safety : Adverse Event, the Concentration of Capsaicin in Blood**

2. Result of the Study

- **Efficacy**
 - ✓ **Daily Pain Rating Scale: Significant pain decrease**
(Capsaicin patch 50ug/cm² & Capsaicin cream)
- | | SY Patch 50μg/cm² | Placebo | Cream 0.075% |
|---|--|----------------|---------------------|
| Pain reduction evaluated by patients | 91.67% | 58.33% | 61.54% |
- ✓ **Daily Sleep Interference Scale**
: All groups showed reduced sleep interference except placebo patch
 - **Safety**
 - ✓ **Adverse Event (AE)**
: 2 case of "severe" AE for capsaicin cream, none for SY patch
- Paraesthesia, Constipation
 - ✓ **Analysis of Capsaicin concentration in blood**
: showed that capsaicin patch is locally acting but not systemically

3. Conclusion

- Capsaicin patch has the similar efficacy compared to capsaicin cream
- Capsaicin patch is acting locally but not systemically
- No serious adverse event rather than 2 severe case for capsaicin cream
- Finally, Capsaicin patch is safe with improved convenience of administration