SynergySWISSPHARMA

Tulobuterol Patch

www.synergypharma.ch

Tulobuterol patch

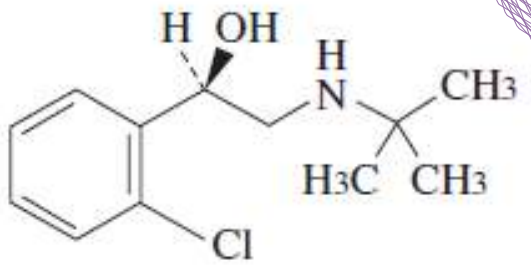
COMPOSITION	Tulobuterol 0.5mg/1.0mg/2.0mg
INDICATION	To control various symptoms such as dyspnea caused by the following obstructive airways diseases - Bronchial asthma - Acute bronchitis - Chronic bronchitis - Emphysema
USAGE	Once a day
APPEARANCE	Polyester film laminate Drug-in-adhesive multi-layered matrix
SIZE	2.5, 5, 10 cm^2
REMARKS	• Prolonged effects for 24 hours • Applied from 6 month infants to adults • Improvement of asthma symptom at night

Tulobuterol

- β_2-adrenocetor agonist

- **INDICATIONS**
  - Bronchial asthma
  - Acute bronchitis
  - Chronic bronchitis
  - Emphysema

- **PHYSICOCHEMICAL PROPERTIES**
  - Solubility : soluble in MeOH, EtOH, Acetic acid
    non-soluble in water
  - Chenical name :
    (RS)-2-*tert*-butylamino-1-(2-chlorophenyl) ethanol
  - Mw(g/mol): 227.73
  - Tm (°C): 92



Chemical structure of Tulobuterol
($C_{12}H_{18}ClNO$)

Bioequivalence test of Tulobuterol patch

STUDY DESIGN:

Open-label, single-dose, randomized,
two-period, crossover bioequivalence study

SUBJECTS:

Enrolled 34 healthy male subjects
(age 19-55 years)

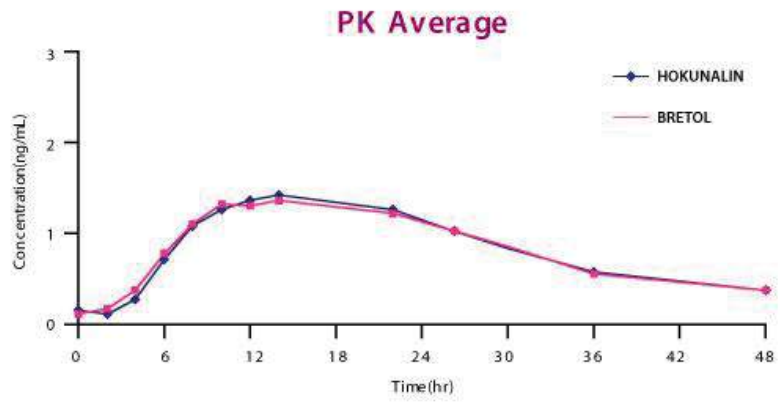
TEST AND REFERENCE PRODUCTS:

Test product – Tulobuterol (Tulobuterol 2.0mg)
Reference product - Hokunalin (Tulobuterol 2.0mg)

METHOD:

Tulobuterol patch was applied for 24 hours.
Venous blood was sampled in both periods over 48h.

BIOEQUIVALENCE TEST RESULT

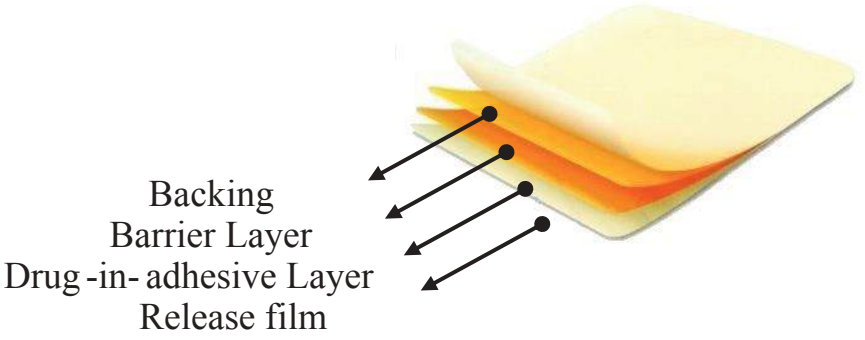


RESULTS:

Geometric Mean	Test-Tulobuterol*	Ref. – Exelon*	90% Confidence Interval
AUC_t (ng/ml)	34.91± 19.22	34.97± 19.22	$0.9095 \leq \delta \leq 1.0546$
C_{max} (ng/ml)	1.63 ± 0.58	1.63 ± 0.58	$0.8439 \leq \delta \leq 0.9942$

Tulobuterol patch design

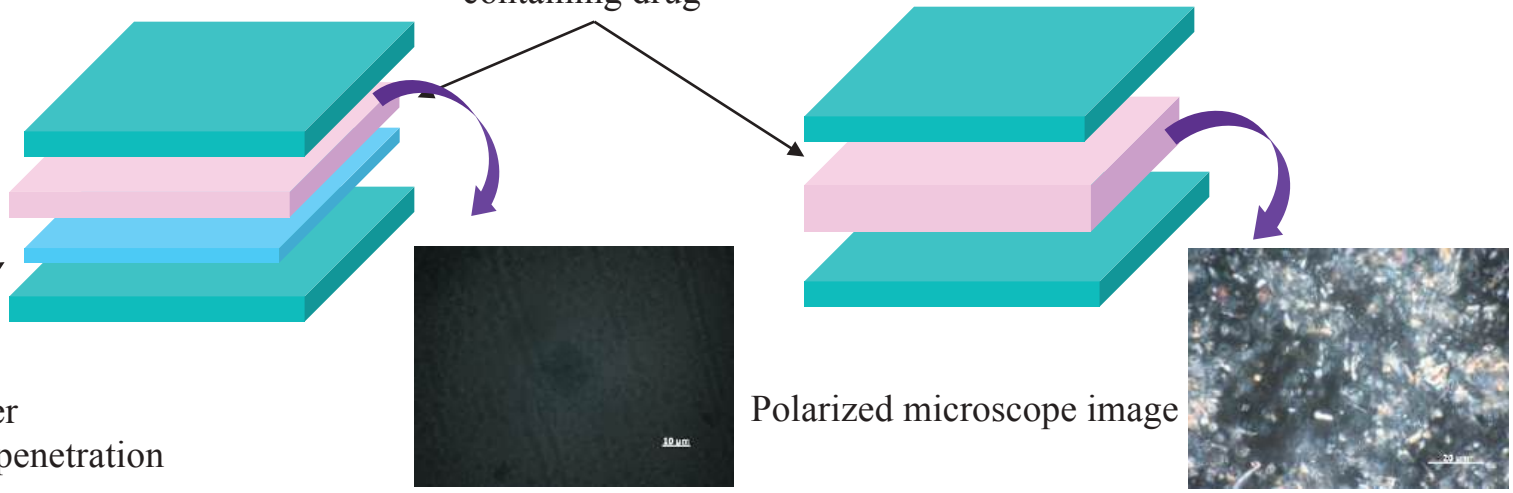
DRUG	Tulobuterol 0.5mg/1.0mg/2.0mg
BACKING	Polyester based film
DRUG LAYER	Rubber base adhesive single layer Thickness : 80 µm
LINER	Siliconized Polyester 100% film (75µm **film)**
MANUFACTURING PROCESS	Mixing, coating on liner, drying, laminating with backing, slitting, cutting & pouching process



Tulobuterol patch Vs. Hokunalin patch

Tulobuterol patch

HOKUNALIN (ABBOTT)



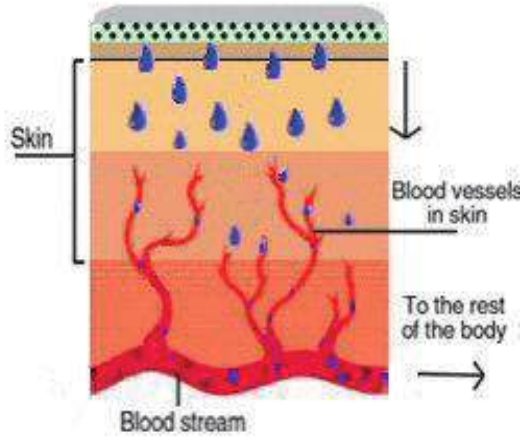
"DRUGS IS DISSOLVED COMPLETELY IN ADHESIVE"

Efficacy of drug, Tack & other physical properties are stable

"DRUGS IN CRYSTAL FORM"

- Drug crystal on surface make the tack of adhesive worse
- Crystal size is depend on temperature & humidity -> Efficacy of drug is varied

In - vitro skin permeation of Tulobuterol patch

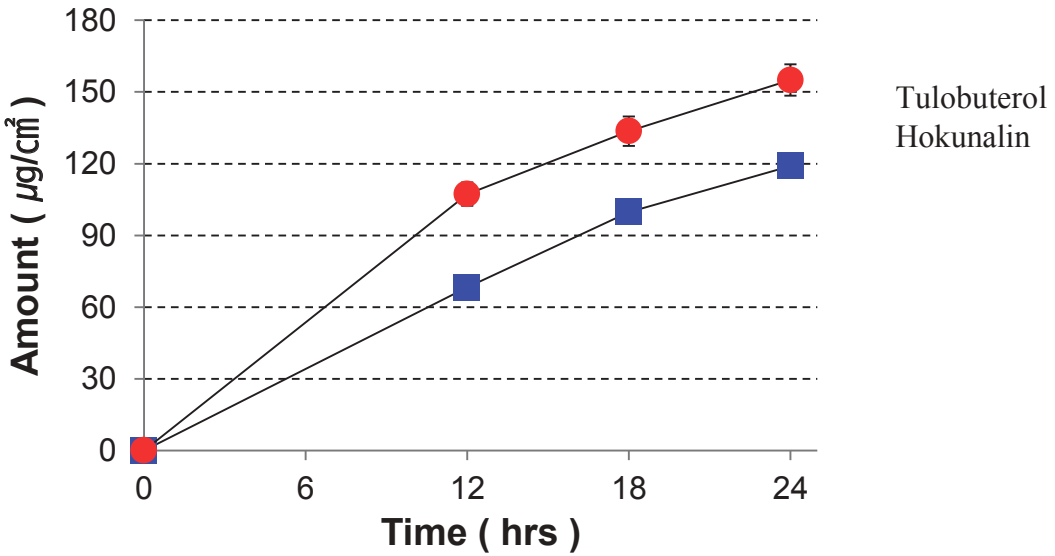


TEST METHOD

According to OECD guideline for skin absorption: *in vitro* method
Using Franz diffusion cell

MATERIALS

Skin : Human cadaver skin (stratum cornium, 80mm thickness)
Sample area : 0.636 cm^2
Receptor : PBS buffer solution, pH 7.4



Tulobuterol patch 2mg, 1mg, 0,5mg

LONG-ACTING TRANSDERMAL BRONCHODILATOR

- Prolonged effect for 24 hours applying one patch daily.
- Improvement of asthma symptom at night


2mg


1mg


0.5mg

Long-acting transdermal bronchodilator

- Prolonged effect for 24 hours applying one patch daily.
- Improvement of asthma symptom at night

1. Easy and simple application.

As a patch type, Tulobuterol patch has a great compliance. Panicularly, Tulobuterol patch is more convenient to use for children and the aging people who have difficulty to take oral preparations such as tablets, capsules etc. as well as inhalation, and for asthma patients who have GI troubles or disorders.

2. Long-acting effects

Tulobuterol patch is applied to the skin surface one patch daily as it is a long acting β_2--agonist preparation and the effects last for 24 hours. Tulobuterol patch can effectively prevent asthma attack at night and early in the morning when respiratory function usually declines.

3. Low adverse reactions

Tulobuterol patch has less frequent adverse reactions than oral prepartions which drug concentration in blood is rapidly increased right after administration. So, Tulobuterol patch can be used for children aged over 6 months.

4. Recommended management of COPD

Tulobuterol patch is indicated for treatment of dyspnea caused by airways obstration due to bronchial asthma, acute and chronic bronchitis, emphysema.

5. Combination therapy

Tulobuterol patch is more beneficial as add-on controller for patients receiving inhaled corticosteroid, first-line controller as interactions with inhaled corticosteroids play a role in improving bronchial responsiveness.

LABA (Long acting beta2 agonist)

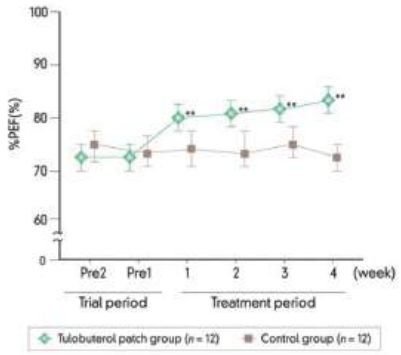
Selectively activating to adrenergic β2 recector agonise, Tulobuterol patch relieves dyspnea and cough of asthma patients as it expands the airways by relaxing bronchial smooth muscle and decreases stretch secretory gland.

INDICATIONS

To control various symptoms such as dyspnea caused by the following obstructive airways disease:

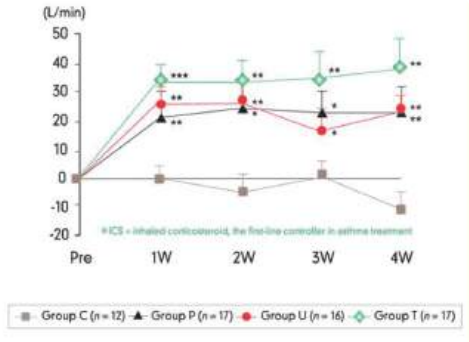
- Bronchial asthma
- Acute bronchitis
- Chronic bronchitis
- Emphysema

Tulobuterol Patch alone increases predicted value of %PEF (Peak Expiratory Flow)



Changes in % predicted value of morning peak expiratory flow (PEF) before to during rhe four-week trearmenc period in the Tulobuterol parch and control groups. Values are presented as means and standard errors of the mean (SEM). **p < 0.0l vs (Pre 2 and Pre l)/2.

Combination therapy with ICS significantly improves morning PEF value than with other drugs



Effects of addition of pranlukast, slow-release theophylline and Tulobucerol parch to a regimen of inhaled corticosteroid on difference in morning PEF before to after trearment(PEF). Abbreviations:Group C, control group; Group P,pranlukast group; Group U, slow-release theophylline group; Group T, Tulobuterol patch group. *p < 0.05, **p < 0.01, ***p < 0.001 vs Group C

Reference) Allergology International 2009;58:509-518

Tulobuterol patch 2mg, 1mg, 0,5mg

COMPOSITIONS

Each parch contains:
Tulobuterol.....0.5mg (2.5cm')
Tulobuterol.....1.0mg (5cm')
Tulobuterol ..... 2.0mg (l0cm')

DESCRIPTION

Rectangular, rounded corners and translucent sustained release transdermal patch

INDICATIONASN DU SAGE

To control various symptoms such as dyspnea caused by the following obstructive airways disease

- Bronchial asthma
- Acute bronchitis
- Chronic bronchitis
- Emphysema

DOSAGE AND ADMINISTRATION

Tulobuterol Patch should be applied the following dosage once daily.
The site of application is clean, dry, hairless, intact healthy skin of chest, back or upper arm.

- 6 months to 3 years of age : 0.5mg
- 3 to 9 years of age : 1.0mg
- 9 years of age and older : 2.0mg

CONTRAINDICATIONS

1) Patients who is receiving catecholamine preparation (epinephrine, isoproterenol etc.)
2) Patients with hypersensitivity to this medicine or ingredients contained.

PRECAUTIONS

1) Hyperthyroidism patients (Symptoms may be worse)
2) Hypertension patients (Blood pressure may be increased)
3) Heart disease patients (Palpitation and arrhythmia may occur.)
4) Diabetes mellitus patients (Glucose metabolism may occur and blood glucose level may be increased)
5) Atopic dermatitis patients (Itching around applied skin, skin rash may occur)
6) The aging people

STORAGE

Store at a hermetic container at room temperature (1 ~30°C)

SHELF-LIFE

24 months from the manufacturing date.