BoLCA+ BOTULIFE
Outperformer

WARMING UP

RELIEF

RECOVERY

RELAXING

The First Sports Cream with a **Botulinum Peptide** Component
that uses scientifically proven skin penetration technology.

JYPHARMTECH

The First Sports Cream with a Botulinum Peptide Component

Contents

JYPHARMTECH

Medicines, Medical Devices, Cosmeceuticals

IN & OUT product development and production

ABOUT US

Providing the best solution, grounded in various accumulated experiences of trial

JYPHARMTECH is a company supplying and exporting the medicines, medical appliances, and cosmetics for treatment procedures.

We have been participating in the research of the products related to the medical appliances and cosmetic surgeries, and supplying the PDO lifting threads and cosmetics for treatment procedures through OEM production. We have also been working as a Sourcing and Consulting Agent of domestic and international pharmaceutical firms.

- Distribution of prescription drugs including vaccines to domestic hospitals.
- Supply medicines and medical devices to Japanese cosmetic surgery.
- Supply medicines and medical devices to Russia, China, Southeast Asia, etc.
- Participation in product development and distribution of lifting thread and cosmeceuticals.

BPMed COSMETIC

ABOUT US

World Leader of the New Topycal Botulinum Toxin Era

Developing the product of true technology with excellent technical Cooperation partners

2014

2015

2016

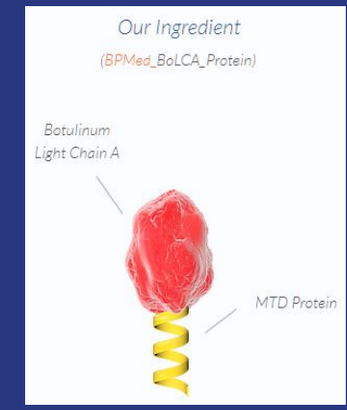
2017

2018

2019

Founded by members of the pharmaceutical industry, BPMED Cosmetics does not know how to advertise and sell cosmetics, but strives to create innovative cosmetics that pursue real effects.BPMED Cosmetic is the world's first to list ingredients derived from Botulinum in the international cosmetic ingredient collection.

The component derived from Botulinum's Botulinum uses MTD technology that penetrates the required protein to the dermis and actively penetrates the target cell, the neuron. Based on the ingredients that actually realize the effects of Botulinum in the dermis layer, BPME Cosmetic aims to develop into pharmaceutical ingredients in the future. We will continue to be the world leader in skin-penetrating botulinum toxin.



Product Introduction

BoLCA+ BOTULIFE
Outperformer
Dynamic Warming Up Gel

It is the first sports cream with a botulinum peptide component that uses scientifically proven skin penetration technology.
Preventing injury, improving muscle efficiency, and improving training ability by warming up before exercise.
It is absorbed quickly without stickiness and has no scent, so there is no repulsion even before and during exercise.

WARMING-UP | BOOSTER | INJURY PREVENTION

+ DEEP SOOTHING

The key ingredient of BoLCA+ BOTULIFE Outperformer is the ingredient of Botox, an anti-wrinkle injection. It is a substance derived from botulinum protein and is a recombinant protein made to allow skin penetration.

BENNEFITS

It is a world-recognized patented technology (MTD skin penetration technology) material that is quickly absorbed without stickiness.
Preventing injury, improving muscle efficiency.
Improving training ability by warming up before exercise.
Has no scent, so there is no repulsion even before and during exercise.
It helps warm up before exercise without artificial heat.
It helps calm skin and moisturizing.

MAIN INGREDIENTS

Methionyl r-Clostridium Botulinum Polypeptide-1 Hexapeptide-40
Arginine, Centella Asiatica Extract, Allantoin, Pinus Sylvestris Leaf Oil
Aloe Barbadensis Leaf Extract, Cucumber Fruit Extract

+

DEEP

SOOTHING

Product Introduction

BoLCA + BOTULIFE Outperformer

Relief and Recovery Lotion

It is the first sports cream with a botulinum peptide component that uses scientifically proven skin penetration technology.
It is quickly absorbed without stickiness to relieve muscle tension and pain.
Along with this, it contains natural plant extracts, which gives a feeling of refreshment to stressed skin and increases skin moisture and elasticity.

The key ingredient of BoLCA + BOTULIFE Outperformer is the ingredient of Botox, an anti-wrinkle injection. It is a substance derived from botulinum protein and is a recombinant protein made to allow skin penetration.

BENNEFITS

It is a world-recognized patented technology (MTD skin penetration technology) material that is absorbed into the muscles and fascia.
Giving tired body a refreshing feeling after exercise and helps recovery.
Relieving muscle tension and pain from exercise and stress.
Increases skin moisture and elasticity.

MAIN INGREDIENTS

Methionyl r-Clostridium Botulinum Polypeptide-1 Hexapeptide-40, Menthol, Peppermint Leaf Extract, Pinus Sylvestris Leaf Oil, Shea Butter, Rosemary Extract ,Aloe Barbadensis Leaf Extract, Cucumber Fruit Extract

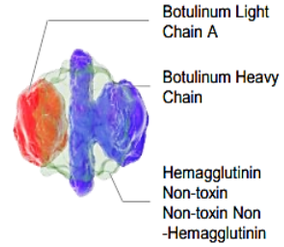
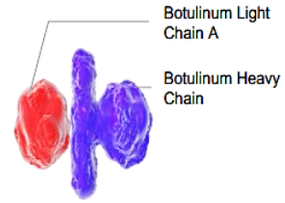
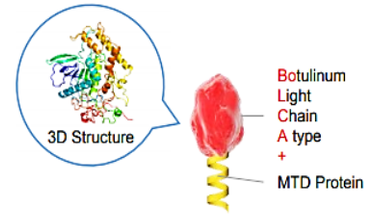
RELIEF | **RECOVERY** | **RELAXING**

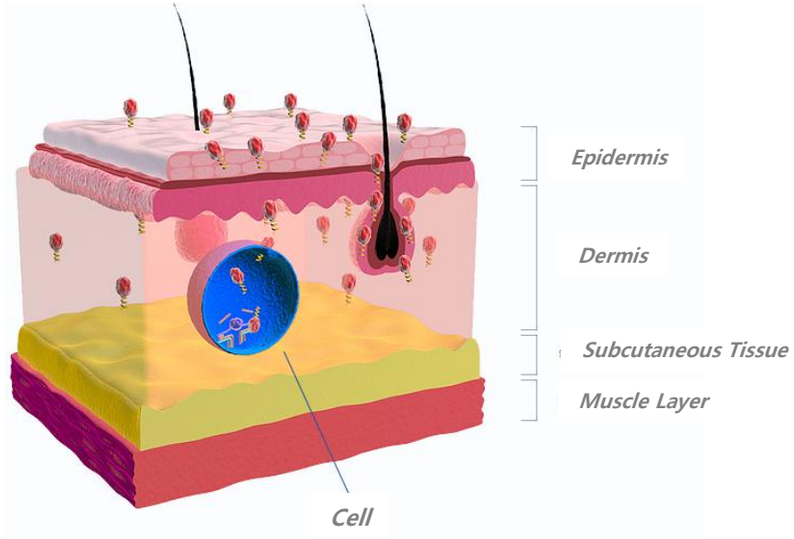
Key Ingredient Information

Methionyl r-Clostridium

Botulinum Polypeptide-1 Hexapeptide-40'

The key ingredient of BoLCA + BOTULIFE Outperformer is the ingredient of Botox, an anti-wrinkle injection. It is a substance derived from botulinum protein and is a recombinant protein made to allow skin penetration. Botulinum-Derivative Ingredient contains more than 95% of amino acids with type A of botulinum light chain and the remaining 5% of the core technology penetrates into the skin and acts on muscles and nerve cells.

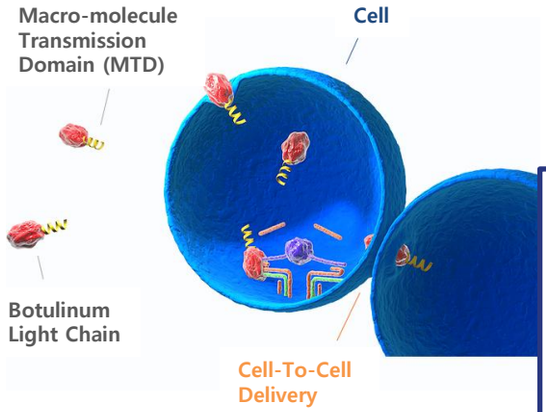
	Toxin Complex (Medical Injection)	Pure Toxin (Medical Injection)	BPMed-BoLCA (Skin Permeable)
Composition			
	Heavy chain : Nerve cell penetration **Light chain** : Botulinum Efficacy Part **Hemagglutinin** **Non-toxin Non-Hemagglutinin**	**Heavy chain** : Nerve cell penetration **Light chain** : Botulinum Efficacy Part	**Light Chain** : Botulinum Efficacy Part **MTD** : Macromolecular Transduction Domain (Skin & Nerve cell penetration) **Recombinant Protein**
Commercialization	1980	1995	2014
Example	BOTOX (Allergan, US) MEDITOXIN (Medytox, Korea)	XEOMIN (Merz, Germany)	BoLCA
	Not permitted to use in Cosmetic Product	Not permitted to use in Cosmetic Product	**The First** Botulinum Ingredient **on ICID** **BPMed Cosmetic has Exclusivity**
Molecular weight	900KDa	150KDa	53.6KDa



Platform technology to improve transdermal delivery of Methionyl r-Clostridium Botulinum Polypeptide-1 Hexapeptide-40'

1st Action
Improved penetration of functional materials into stratum corneum and other skin layers by MTD.

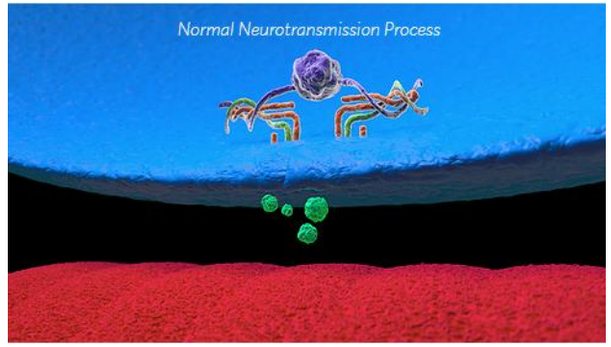
2nd Action
Maximized efficacy through the delivery of 'Methionyl r-Clostridium Botulinum Polypeptide-1 Hexapeptide-40' into specific targets.



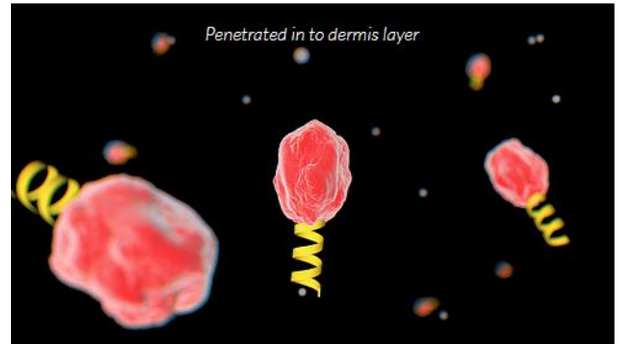
Modality of Intracellular delivery of MTD in 'Methionyl r-Clostridium Botulinum Polypeptide-1 Hexapeptide-40'

Intracellular penetration by MTD technology shows very high permeability and markedly less cellular damage than nano liposomes or general peptide component delivery technology (PTD)

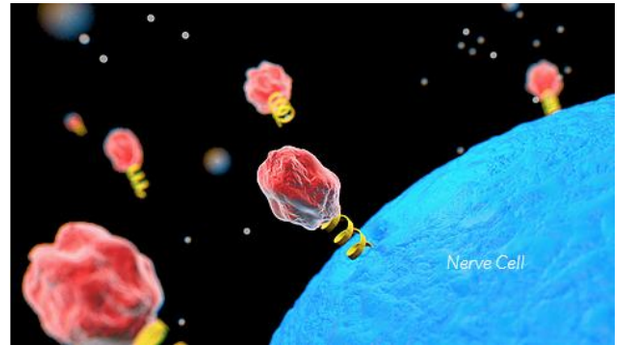
MECHANISM ON NERVE CELL



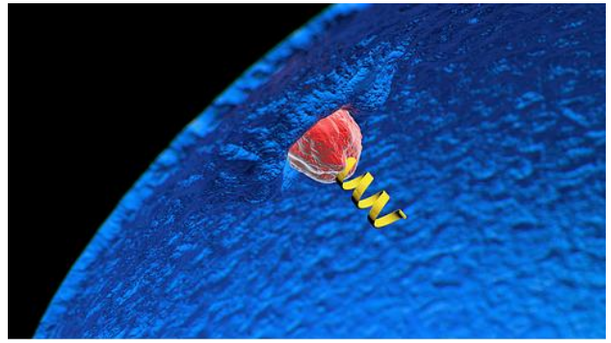
SNARE Complex Exocitosis Acetylcholine Diffusion
Binds to the Receptors on the Muscle



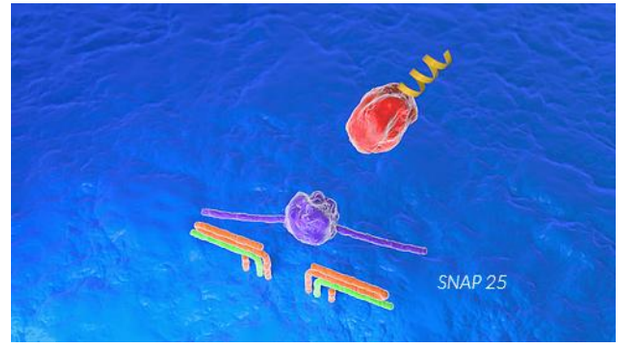
Methionyl r-Clostridium Botulinum
Polypeptide-1 Hexapeptide-40



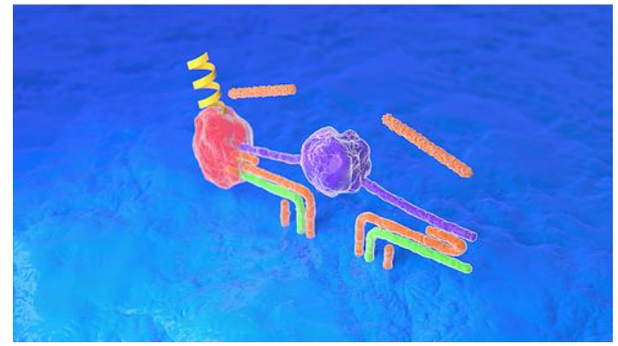
Approaching to the Cell



Direct Cell Membrane Translocation



Moves to the SNAP25



Cleaves SNAP25 by Light Chain Part

Test Results

SNAP25 Cleavage Diagra

Recombinant 'GST-SNAP25-EGFP' was purified to examine the clevis activity of the 'Methionyl r-Clostridium Botulinum Polypeptide-1 Hexapeptide-40' protein. The 'botulinum toxin light chain type A' that exists in the natural world is because it cleaves the C-terminal part of SNAP25.GST and EGFP are recombined to the size of 25 kDa at each N-terminal and C-terminal and purified again to confirm the clevis form. 75kDa 'GST-SNAP25-EGFP' is a 50kDA and 25kDa protein by 'Methionyl r-Clostridium Botulinum Polypeptide-1 Hexapeptide-40'It becomes Clevis.

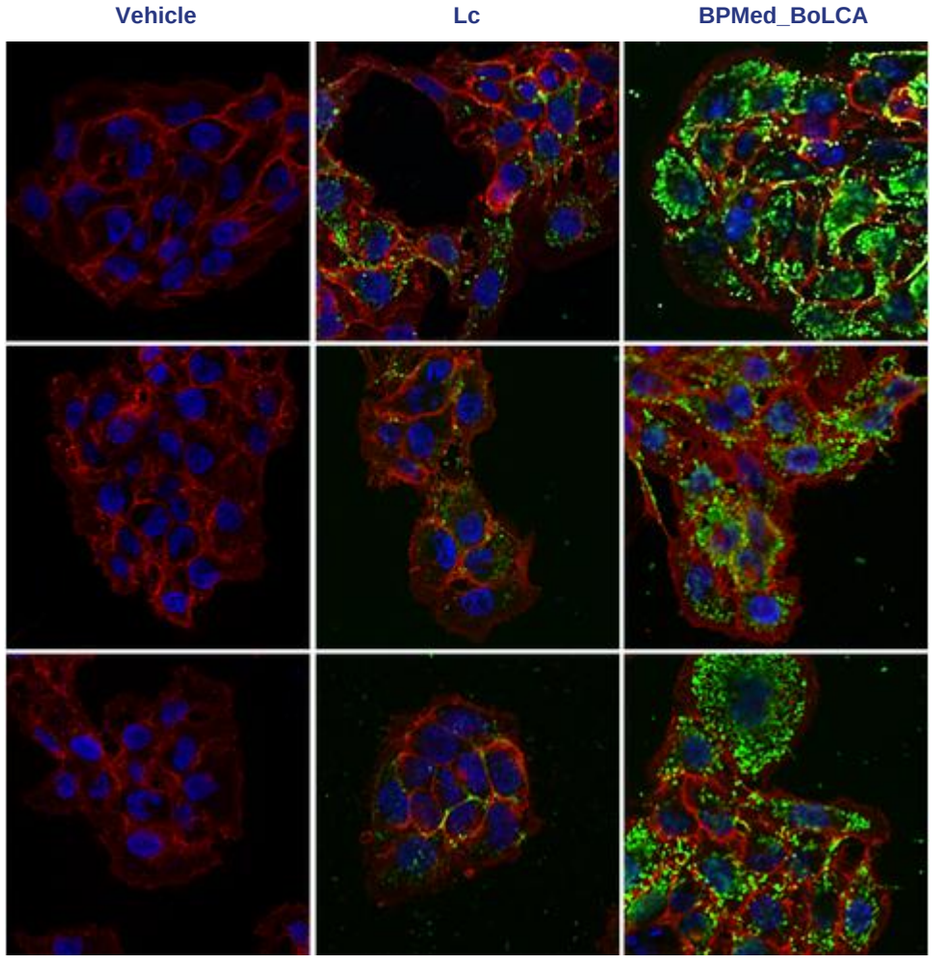
SNAP25 Cleavage

Size alteration after GST-SNAP25-EGFP cleavage

in vitro SNAP25 Cleavage Assay

Confirming that the GST-SNAP25-EGFFP protein is cleaved by 'Methionyl r-Clostridium Botulinum Polypeptide-1 Hexapeptide-40'For GST-SNAP25-EGFR protein in-vitroReact with Methionyl r-Clostridium Botulinum Polypeptide-1 Hexapeptide-40 '.As a result, the GST-SNAP25-EGFP protein is cleaved with GST-SNAP25 (50kDa) and EGFP (25kDa), and is proportional to the dose of ‘Methionyl r-Clostridium Botulinum Polypeptide-1 Hexapeptide-40’.

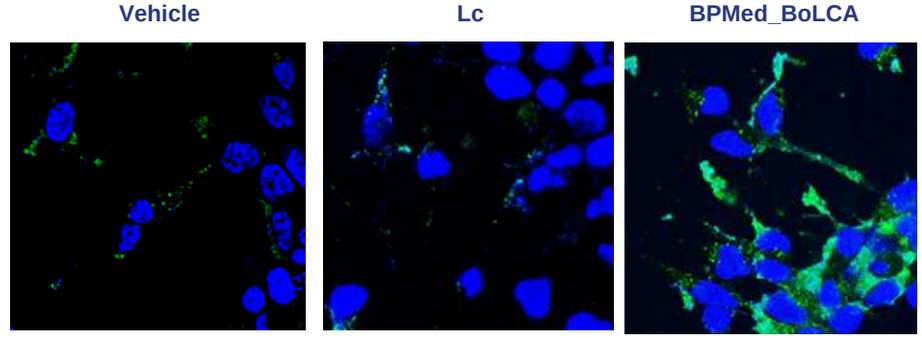
Buffer condition: 1mM DTT, 1mM HEPES,1mM NaCl, 2uM $ZnCl_2$
Reaction : 37℃ 3hrs. SDS-PAGE loading condition - 12% SDS-PAGE - volt : 120V



*** Treatment condition**
- HaCaT cell
- Peptide : 5μm

Permeation of keratinocytes

FITC-bound 'Methionyl r-Clostridium Botulinum Polypeptide-1 Hexapeptide-40' protein was applied to keratinocyte skin cells, and it was confirmed that the protein was observed within 1 to 6 hours. This result shows that 'Methionyl r-Clostridium Botulinum Polypeptide-1 Hexapeptide-40' can penetrate the skin.

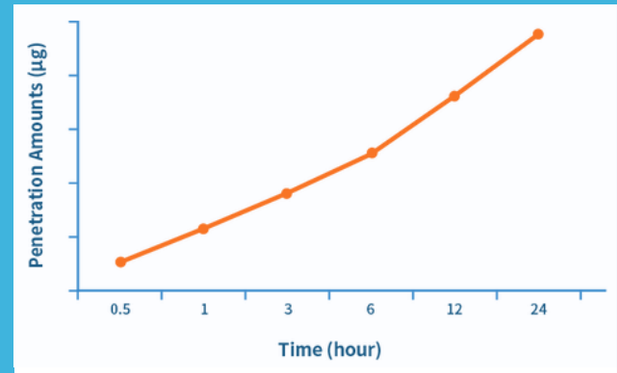


*** Treatment condition**
- FITC conjugated : 5μg
- Time : 3hrs
- Method : confocal

'Methionyl r-Clostridium Botulinum Polypeptide-1 Hexapeptide-40' cell penetrate test

Potential in human neuronal cell

Transfer ability in human nerve cellsFITC-coupled 'Methionyl r-Clostridium Botulinum Polypeptide-1 Hexapeptide-40' protein was applied to differentiated SiMa cells (human neuroblastoma). After 3 hours, you can see that the protein is observed within the cells. These results show that 'Methionyl r-Clostridium Botulinum Polypeptide-1 Hexapeptide-40' is delivered to human nerve cells, the most important destination of botulinum protein.



'Methionyl r-Clostridium Botulinum Polypeptide-1 Hexapeptide-40' transdermal diffusion test

Transdermal Diffusion

Dermal spread‘ Performs a percutaneous diffusion test using Millipore's Strat-M membrane products. The amount of 'Methionyl r-Clostridium Botulinum Polypeptide-1 Hexapeptide-40' penetrating from 30 minutes to 24 hours is converted to a cumulative frequency using ELISA. You can see that it continues to infiltrate after 24 hours.

Reference

Botulinum toxin has been used for the treatment of many clinical disorders by producing temporary skeletal muscle relaxation. In pain management, botulinum toxin has demonstrated an analgesic effect by reducing muscular hyperactivity, but recent studies suggest this neurotoxin could have direct analgesic mechanisms different from its neuromuscular actions. At the moment, botulinum toxin is widely investigated and used in many painful diseases such as myofascial syndrome, headaches, arthritis, and neuropathic pain. Further studies are needed to understand the exact analgesic mechanisms, efficacy and complications of botulinum toxin in chronic pain disorders.

Application of Botulinum Toxin in Pain Management

Woo Seog Sim Department of Anesthesiology and Pain Medicine,
Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea.

Botulinum toxin (BTX) is a pre-synaptic neuromuscular blocking agent that triggers chemical denervation by temporarily suppressing secretion of acetylcholine at motor nerve endings; therefore, **BTX injections are useful for diseases with increased involuntary muscle activity or tension**

New therapeutic indications for botulinum toxins.

Cordivari C. Misra VP. Catania S. Lees AJ. Mov Disord. 2004 Mar;19 Suppl 8:S157-61.

Trials of BTX in painful conditions are ongoing mainly on refractory tension headache, migraine, and backache as well as dystonia-complex regional pain syndrome and myofascial pain with promising results.

Recently, the fastest growing use for BTX toxin has been in the cosmetic applications.

Botulinum Toxin for the Treatment of Myofascial Pain Syndromes Involving the Neck and Back: A Review from a Clinical Perspective

José M. Climent,[1] Ta-Shen Kuan,[2] Pedro Fenollosa,[3] and Francisco Martin-del-Rosario[4]

There is evidence that botulinum toxin could be useful in specific myofascial regions such as piriformis syndrome. It could also be useful in patients with refractory MPS that has not responded to other myofascial injection therapies.

Botulinum toxin for myofascial pain syndromes in adults

Adriana Soares, Régis B Andriolo, Álvaro N Atallah, Edina MK da Silva

Botulinum toxin is a protein produced by the bacterium Clostridium botulinum and is a potent neurotoxin that eventually inhibits muscle contractions. It is capable of selectively weakening painful muscles and interrupting the pain cycle.

A comparative trial of botulinum toxin type A and methylprednisolone for the treatment of myofascial pain syndrome and pain from chronic muscle spasm.

Porta M Pain. 2000 Mar;85(1-2):101-5.

These results **indicate the superior efficacy of BTX-A over conventional steroid treatment in patients suffering from MPS, when combined with appropriate physiotherapy.**

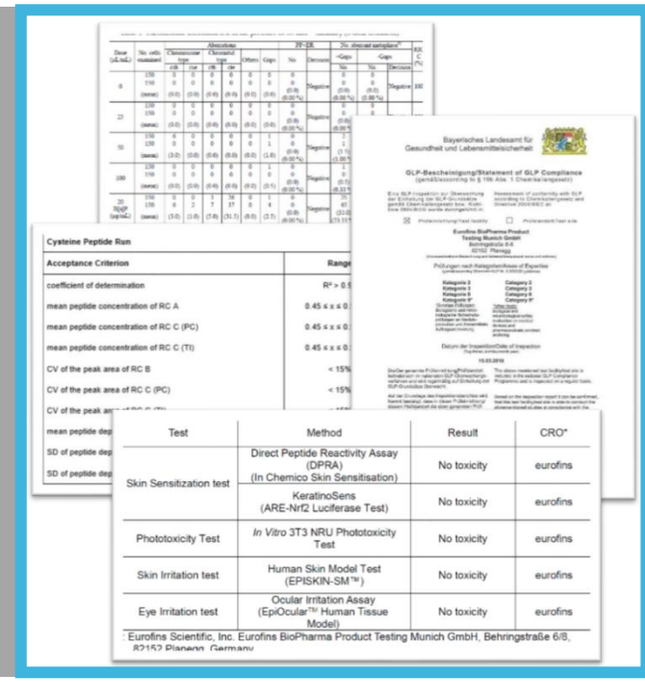
Safety Tests

The following safety tests were performed on the raw material " Methionyl r-Clostridium Botulinum Polypeptide-1 Hexapeptide-40 ".

- Cell toxicity (in-House Lab.)
- Bacterial Reverse Mutation Assay test (GLP Lab.)
- Chromosomal test (GLP Lab.)

The following additional tests are conducted on the safety of 'Methionyl r-Clostridium Botulinum Polypeptide-1 Hexapeptide-40' and animal testing of this ingredient is never carried out.

- Skin Irritation using EPISKIN
- Eye Irritation using EpiOcular test
- Skin Sensitization : Local Lymph node Assay : BrdU-ELISA)
- in vitro 3T3 NRU Photoxity Test

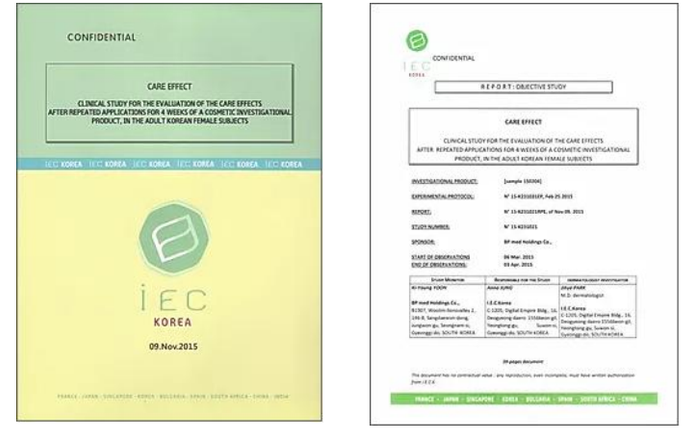


Test	Method	Result	CRO*
Skin Sensitization test	Direct Peptide Reactivity Assay (DPRA) (In Chemico Skin Sensitisation)	No toxicity	eurofins
	KeratinoSens (ARE-Nrf2 Luciferase Test)	No toxicity	eurofins
Phototoxicity Test	*In Vitro* 3T3 NRU Phototoxicity Test	No toxicity	eurofins
Skin Irritation test	Human Skin Model Test (EPISKIN-SM™)	No toxicity	eurofins
Eye Irritation test	Ocular Irritation Assay (EpiOcular™ Human Tissue Model)	No toxicity	eurofins

Eurofins Scientific, Inc. Eurofins BioPharma Product Testing Munich GmbH, Behringstraße 6/8,

Clinical Tests

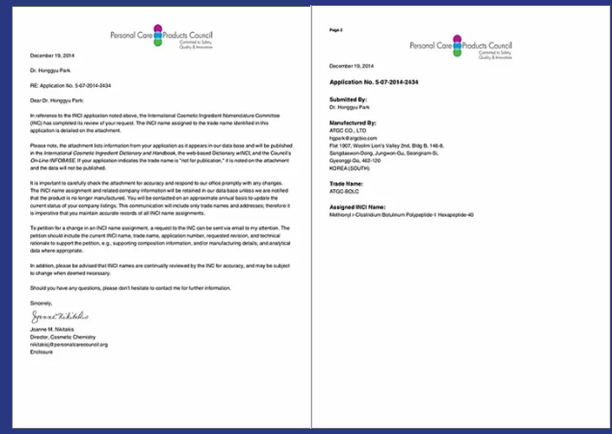
Single Human Patch Test
Bolca Anti-Wrinkle Facial Serum
(I.E.C. Korea @ Chonnam National Univ. Hospital)



Clinical Test (I.E.C. Korea)
Bolca Anti-Wrinkle Facial Serum
(I.E.C. Korea)

Registration Status

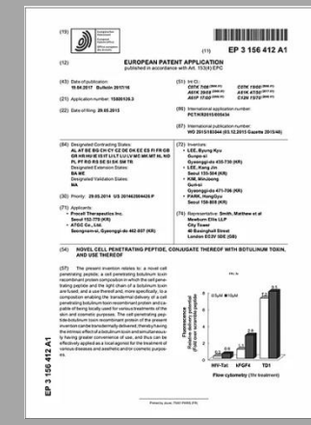
ICID



'Methionyl r-Clostridium Botulinum Polypeptide-1 Hexapeptide-40' was listed in the International Cosmetic Ingredients (ICID) in December 2014. This can be found on page 2096 of the International Cosmetic Ingredient Dictionary (ICID) 2016 Vol.2. The INCI name '' Methionyl r-Clostridium Botulinum Polypeptide-1 Hexapeptide-40 'is not determined by the applicant company. This is the name given for classification by PCPC in Washington, which is hosting the ICID, and global cosmetic companies. The 'Clostridium Botulinum', included in the INCI name, proves that this raw material is actually derived from 'botulinum toxin'.

However, the name 'Clostridium Botulinum' is not the only thing that matters. Even if it penetrates into the skin with '' Botulinum Toxin Light Chain ', it cannot exert its efficacy because it cannot penetrate into nerve cells. The MTD core technology that realizes the penetration into the skin and the penetration of nerve cells is applied to create the botulinum-derived raw material that we dreamed of. Although it is possible to develop a raw material containing the name 'Clostridium Botulinum', it cannot imitate its technology and efficacy.

PATENT



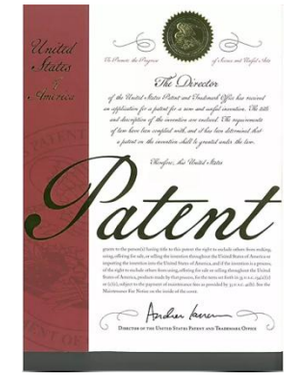
PCT / KR2015 / 005434

Novel cell permeable peptide and botulinum toxin conjugate and Their use "Methionyl r-Clostridium Botulinum Polypeptide-1 Hexapeptide-40" is currently in the process of filing for patents in eight major countries in the world. This technology patent was developed through joint research between ET Co., Ltd., which possesses 'botulinum toxin' technology, and Procell Terrafutics Co., Ltd., which possesses skin and target cell penetration technology and exclusive use of substances.

BPMed Cosmetic Co., Ltd. owns the exclusive right to use the patent and the exclusive right to use the material.

- *Completed patent registration in Korea (KR.10-1882461)*
- *Completed patent registration in Japan (JP.6243577)*
- *Completed patent registration in Russia (RUS.2670135)*

Patent Registration Competion Korea



Patent Registration Competion USA

Patent Registration Competion Japan

Patent Registration Competion Russia

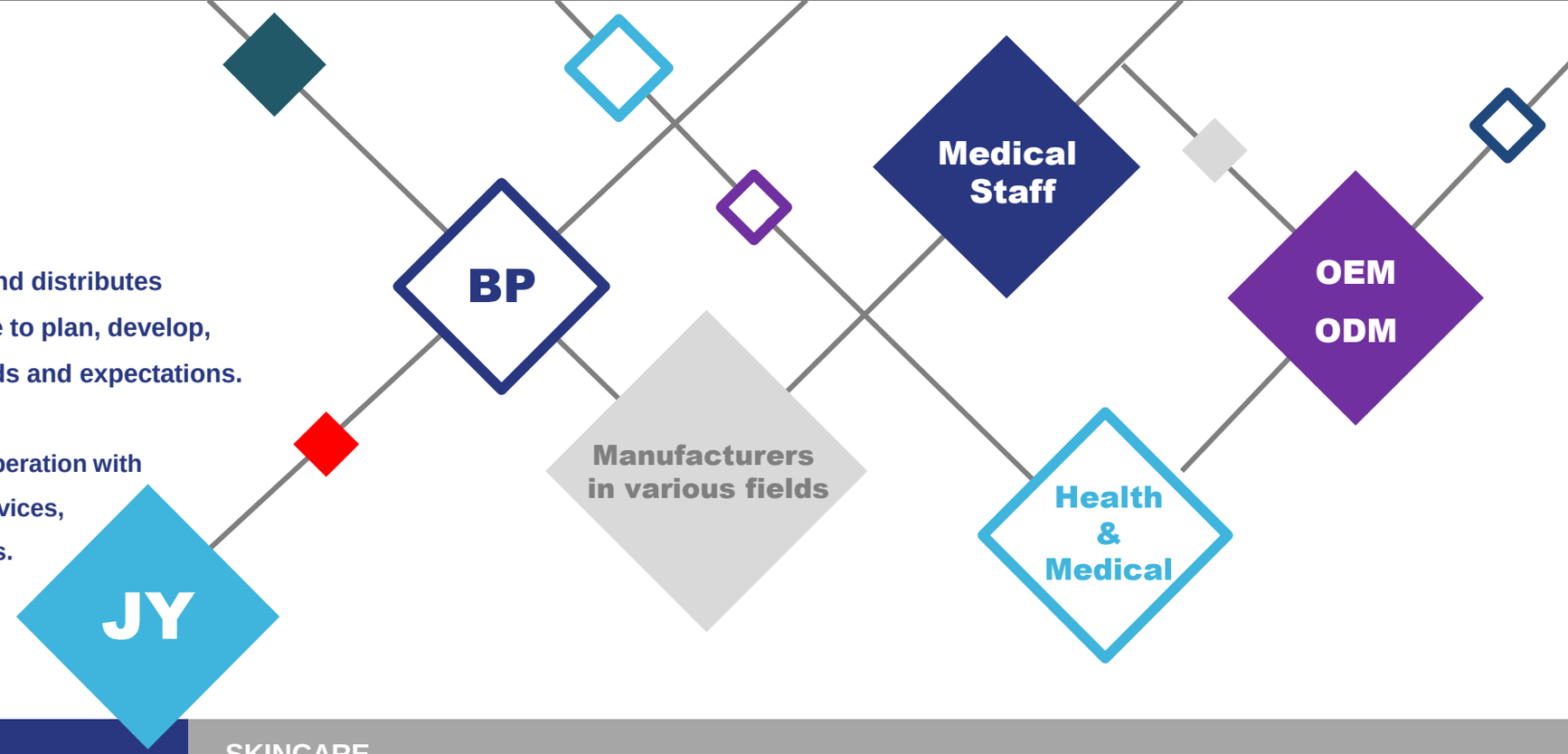
Patent Registration Competion China

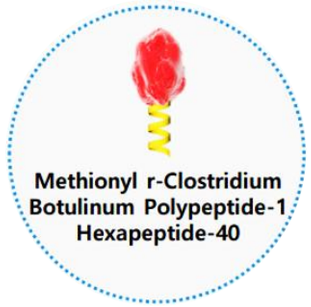
Patent Registration Competion Canada

OUR ABILITY

JYPHARMTECH is a company that participates in and distributes product development in various fields. It is possible to plan, develop, and manufacture products that meet customer needs and expectations.

JYPHARMTECH can develop various products in cooperation with BP MED as well as manufacturers such as medical devices, beauty devices, health functional foods and cosmetics.





“Methionyl r-Clostridium Botulinum Polypeptide-1 Hexapeptide-40”

We can develop various products in cooperation with BP MED

SKINCARE

Botulinum Toxin A cosmetic procedure product that can expect the same effect as a dermal layer injection procedure and a highly functional home care product. Expected effects: Improve fine lines, improve elasticity, control sebum, improve acne.

SPORTS CREAM

Botulinum Toxin is the first sports cream to be used as a peptide component. It has no fear of muscle weakness and muscle loss, unlike the Botulinum Toxin topical procedure.

HAIR LOSS

Expected the same effect as injecting Botulinum Toxin into the scalp and proceeded a case study. As a result, prevention of hair loss and improvement

DEVELOP A NEW MEDICINE

Development of migraine treatment and hair loss treatment. Clinical trials conducted at medical institutions (Severance Hospital). The results of the case study proved the effectiveness and confirmed the possibility of development.