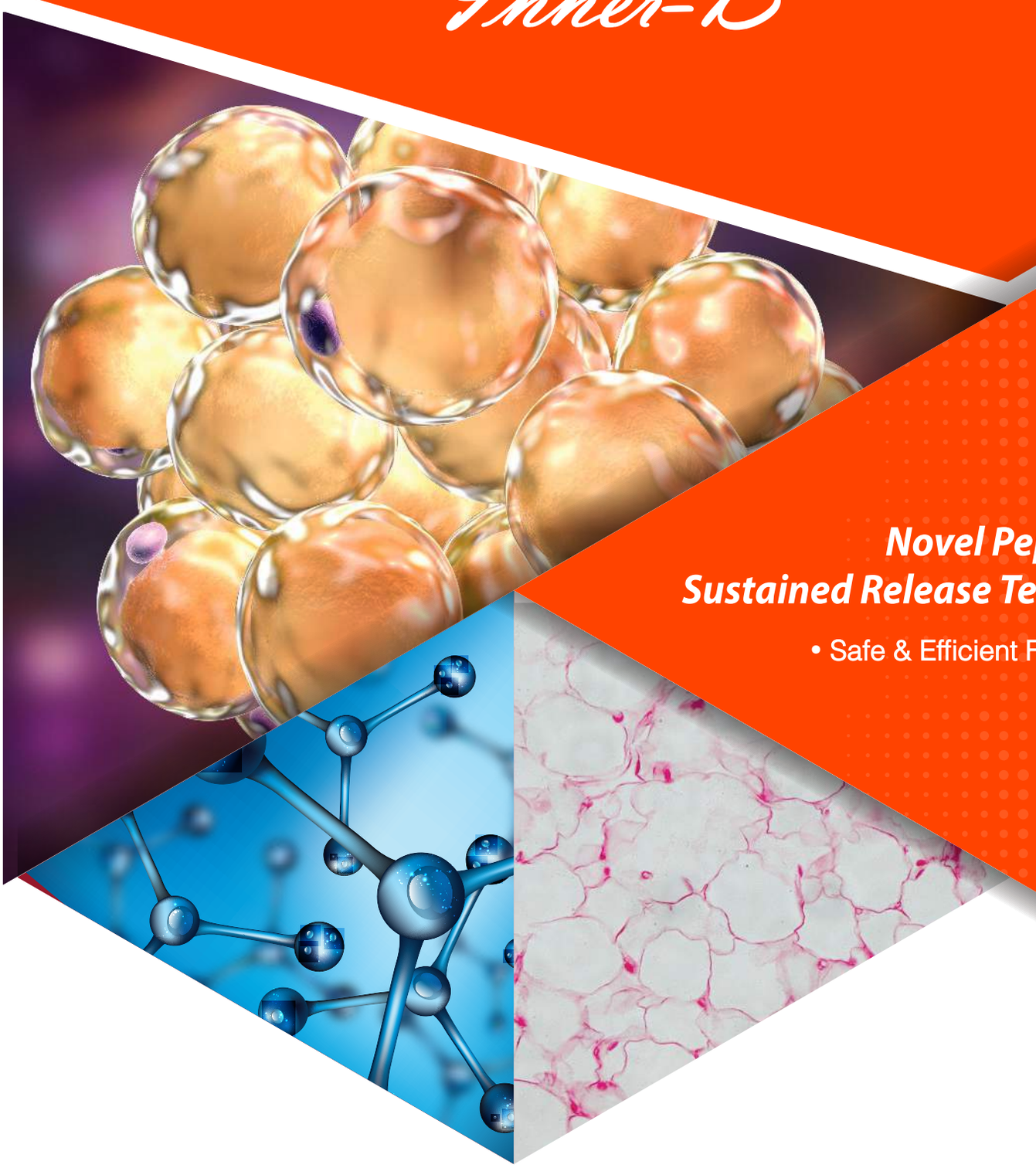
PROSTROLANE
Inner-B



Novel Peptide and Sustained Release Technology

- Safe & Efficient Fat Reduction

CAREGEN CO., LTD.

Innovative Features

- Peptide Sustained Release Technology
- Safe and Efficient Localized Fat Reudction
  (No Tissue Necrosis –〉 Control size of adipocyte)
- Super Painless
- No injection site reaction after procedure
  (No Edema, No Bruise, No Numbness, No erythema... etc)

PROSTROLANE
Inner-B

Prostrolane Inner B: 2 ml gel in prefilled syringe
Home Care: Inner-B RF Body Contouring Cream 100 ml

PART 1 GENERAL PRINCIPLES

PART 2 EFFICACY

PART 3 SAFETY

Part 1

GENERAL PRINCIPLES

PROSTROLANE *Inner-B*

GENERAL PRINCIPLES

Obesity

1

Introduction

Obesity is a medical condition in which excess body fat has accumulated to the extent that it may have a negative effect on health. Obesity increases the likelihood of various diseases and conditions, particularly cardiovascular diseases, type 2 diabetes, obstructive sleep apnea, certain types of cancer, osteoarthritis and depression. As a result, obesity has been found to reduce life expectancy. Obesity is most commonly caused by a combination of excessive food intake, lack of physical activity and genetic susceptibility. The view that obese people eat little yet gain weight due to a slow metabolism is not generally supported. Obesity is a leading preventable cause of death worldwide, with increasing rates in adults and children.

Localized fat accumulation

Localized fat accumulation means abnormal, excessive accumulation of fat on various parts of body, is generally related to disorders of fat metabolism and may be associated with exogenous obesity, in which case fatty deposition is widespread. Their condition often fails to respond to conservative measures such as dieting and exercises, and even in cases of marked weight loss the areas of bulging persist, giving the patient an ungraceful appearance.

Localized fat accumulation causes understandable psychological distress and despite the patient's self-control and careful choice of clothing, their body contour often fails to improve. In patients who acknowledge their existing deformity a considerable psychological and physical improvement can be obtained by the use of appropriate surgical procedures. It is therefore important to realize that patients suffering from localized fat deposition are quite of then disillusioned and disheartened.

Lipolysis

Lipolysis is the breakdown of Lipids and involves hydrolysis of triglycerides into glycerol and free fatty acids. Predominantly occurring in adipose tissue, lipolysis is used to mobilize stored energy during fasting or exercise. Lipolysis is directly induced in adipocytes by glucagon, growth hormone, atrial natriuretic peptide and cortisol and so on. In adipose tissue, intracellular triglycerides are stored in cytoplasmic lipid droplets. When lipases are phosphorylated, they access lipid droplets and through multiple steps of hydrolysis, breakdown triglycerides into fatty acids and glycerol. Each step of hydrolysis leads to the removal of one fatty acid. The first step and the rate-limiting step of lipolysis is carried out by adipose triglyceride lipase (ATGL). This enzyme catalyzes the hydrolysis of triacylglycerol to diacylglycerol. Subsequently, hormone-sensitive lipase(HSL) catalyzes the hydrolysis of diacylglycerol to monoacylglycerol and monoacylglycerol lipase (MGL) catalyzes the hydrolysis of monoacylglycerol to glycerol. Perilipin 1A is key protein regulator of lipolysis in adipose tissue. This lipid droplet-associated protein, when deactivated, will prevent the interaction of lipases with triglycerides in the lipid droplet and grasp the ATGL co-activator, comparative gene identification 58(CGI-58). When perilipin 1A is phosphorylated by PKA, it releases CGI-58 and it expedites the docking of phosphorylated lipases to the lipid droplet.

GENERAL PRINCIPLES

Global Market

2

Facial Injectables Market

The anti-aging market is booming due to changes in the medical paradigm of global aging, low birth rate, health care and quality of life. The anti-aging industry can be defined as' a high-tech industry that includes all of medicines, food, cosmetics, medical devices, and health programs that live a healthy life through prevention, treatment and improvement of aging and geriatric diseases. According to BCC research, the global anti-aging industry is expected to grow from $ 274.5 billion in 2013 to $ 420 billion in 2030.

Among the anti-aging related industries, the beauty cosmetics market has been growing steeply caused by the development of various simple and non-invasive treatment products, the decrease of treatment price. According to the American Society for Aesthetic Plastic Surgeons (ASAPS) data, minimally invasive procedures are expected to reach 13.9 million in 2014, a 4% increase from the previous year and 14.2 million in 2015, incased 2% YoY. Since 2000, surgical procedures have decreased by 10% from 1.9 million to 1.71 million, but minimally invasive procedures have increased by 158% from 5.5 million to 14.2 million. Especially, overall injectables saw a 10% increase in 2016. According to IMCAS 2014, market size of injectables will reach € 220 million in 2018, from € 150 million in 2012.

The development of various injections such as toxins and fillers brought these trends as the number of competitors in the toxin and filler industry has incased, led lowering of treatment price and expanding of treatment application with convenience of non-surgical procedures

Body slimming (localized fat reduction) Market

The global body slimming market size was valued at USD 214.7 billion in 2016 and is expected to grow at a CAGR of 8.3% over the forecast period. According to the Institute of Health Metrics and Evaluation, 30.0% of the world's population is either obese or overweight. The overweight and obese population reports a high prevalence of chronic diseases including hypertension, diabetes, and orthopedic diseases. Thus, growing number of obese and overweight population is driving the growth. An increasing preference toward junk food, physical inactivity, and the growing fast food industry is leading to an unhealthy & sedentary lifestyle, which results in weight gain. In addition, increasingly hectic routine and the growing stress are causing people to consume fast food, which is leading to untoward health effects. Thus, all these factors together are fueling the growth.

The body contouring medical device market is expected to achieve a compound annual growth rate of 7.9% between 2015 and 2022, according to a report from research and consulting firm GlobalData. This represents an annual increase from $671.8 million to over $1.1 billion.

The regional covered by the report across the 15 major markets (15MM: US, France, Germany, Italy, Spain, UK, Japan, China, India, Brazil, Australia, Canada, Mexico, Russia, and South Korea). By the end of the forecast period in 2022, the total market value will have grown to over $1.1bn, at a Compound Annual Growth Rate (CAGR) of 7.9%.

The report, which was generated by Brigitte Babin, a medical device analyst specializing in general surgery at GlobalData, notes that the body contouring market encompasses both noninvasive and minimally invasive fat reduction procedures like lipolysis and cryolipolysis.

Injectables for Body slimming (Localized fat reduction) Market

Cosmetic procedure which aims reduction of localized fat accumulations by intralesional injection of chemical substances that induce destruction of adipocyte most properly called injection lipolysis have been commonly associated with Mesothrapy.

The one common ingredient in all injection lipolysis formulations is phosphatidylcholine (PPC). In the United States, sodium deoxycholate (DC), a constituent of bile, is a second major ingredient used to keep the PPC soluble and in an injectable form without precipitating out of solution. Phosphatidylcholine (PPC) and sodium deoxycholate (DC) are both phospholipids, emulsifiers, and surfactants. PPC is the most abundant phospholipid component of cell membranes, a precursor to acetylcholine, and a constituent of lipoproteins. DC is a constituent of bile. Both substances are naturally present in the human body. In contrast to injections into the mesoderm, injection lipolysis treatments are delivered into the subcutaneous fat. In both cases, the depth of injection is critical to prevent damage to fascia. It has been hypothesized that treatment with PPC and DC reduces subcutaneous fat by adipocyte necrosis due to direct toxic or surfactant effects. Phosphatidylcholine (PPC) and sodium deoxycholate (DC) are both approved by the U.S. Food and Drug Administration (FDA) for use as surfactants and drug carriers, among other applications, but neither is approved for subcutaneous injection.

Subcutaneous injection of phosphatidylcholine formulations are associated with localized burning sensation, erythema & oedema, transient urticaria, ecchymoses & hematomas, infectious granulomatous reaction that spontaneously resolve within one month, skin ulceration that could be either due to injections placed too superficially or to compression of blood vessels in the area by severe edema. Common side effects of other injectables include injection site reactions (swelling, bruising, pain, numbness, redness, itching, warmth, hardness, tingling or burning sensation, skin tightness, nerve injury), headache, mouth or throat pain, high blood pressure (hypertension), nausea, or difficulty swallowing.

GENERAL PRINCIPLES

Development of Prostrolane Inner-B

3

Prostrolane Inner-B is a CE-approved injectable treatment that reduces lipid droplet(lipolysis) in fat cells of the treatment areas. Treatable areas are double chin, jowl, abdomen, upper arms, love handles, thighs and knees.

Caregen's past years were time for innovation and creation which Caregen has always gone through a difficult times with innovative products compared to competitors. Through endless lipolysis studies over the last 7 years, Caregen has been accomplished remarkable research achievements in targeted fat reduction and has developed Prostolane Inner-B.

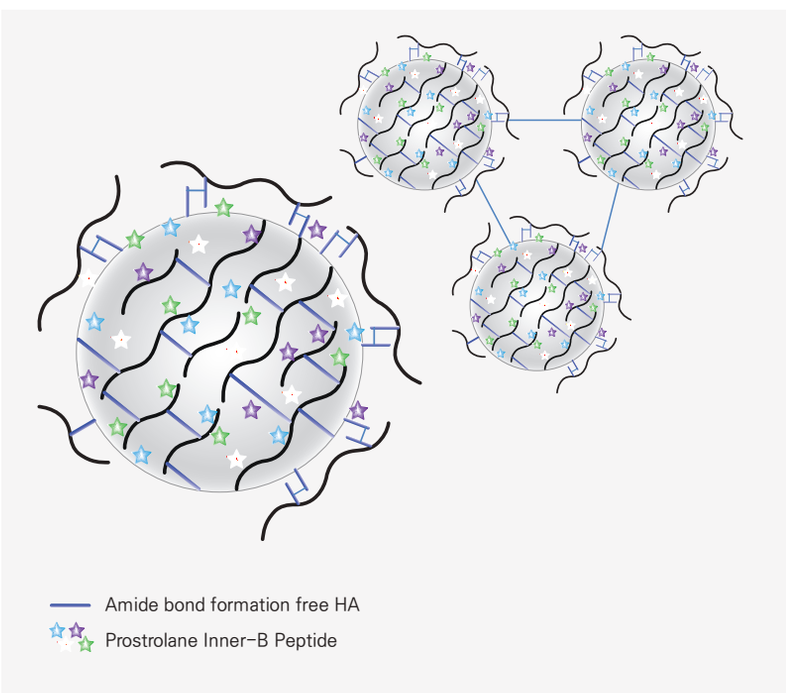
Many people around the world are suffering from obesity because of eating habits, lack of exercise and/or congenital problems. Lipolysis is one of the most difficult clinical parts to solve effectively in the medical esthetic field. Although many lipolytic products have been on the market for a long time, they were not meeting patients' needs due to their poor efficacy and side effects.

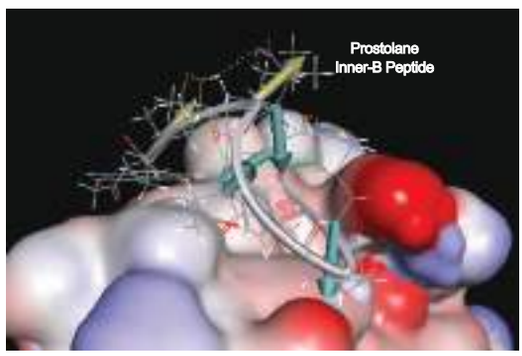
With noble lipolytic peptides and its sustained release technology, we developed very safe and effective product which can give the most satisfaction to patients and doctors.

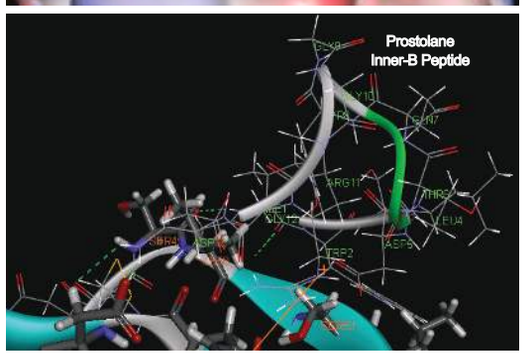
Looking at the benefits of Prostolane Inner-B

1) The size of adipose tissues are reduced without fat cells necrosis, so the side effect is dramatically reduced compared to other products.
2) The product can give continuous and most effective lipolytic effect for 2 weeks with one injection.
3) The formulation is very soft which gives minimized pain and super comfortability to patients and doctors.
4) Unique and exclusive patented technology makes it difficult for competitors to copy, so it can have a unique market position in the market.
5) The Product accelerating lipolysis, at the same time, and strongly down-regulating lipogenesis.

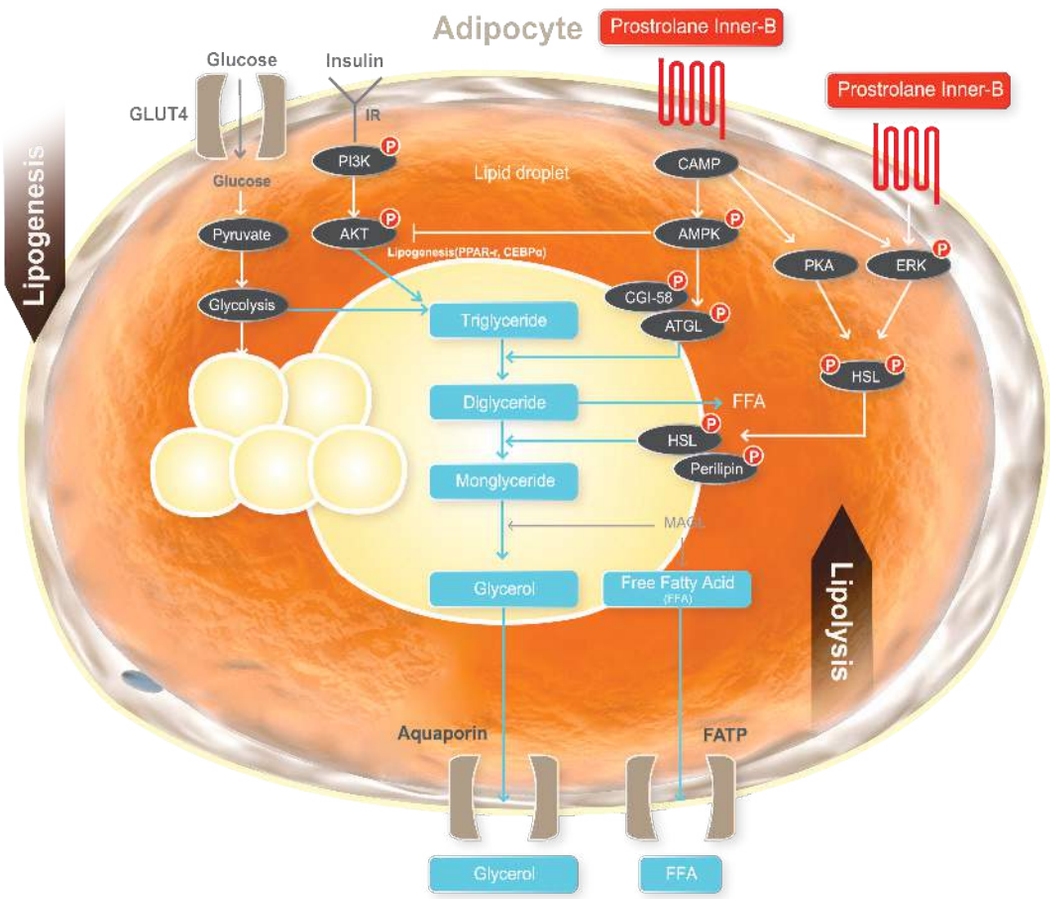
- Prostrolane Inner-B is a transparent gel supplied in a glass syringe. The product is for single use only. Prostrolane Inner-B is a sterile medical device, dermal resorbable implant that contains a Sodium hyaluronate and peptide complex (Nonapeptide-32, Pentapeptide-43, Tripeptide-41, Octapeptide-11).
- Site of application: Face (double chin, jowl), abdomen, upper arms, love handles, thighs and knees.







Mode of Action of Prostrolane Inner-B



Prostrolane Inner-B performs targeted fat reduction through activation of AMPK, PKA and ERK pathway which strongly increases lipolysis in accumulated lipid droplets by phosphorylation of ATGL and HSL.

In addition, Prostrolane Inner-B stimulates AMPK phosphorylation which leads inhibition of Lipogenesis by preventing PI3K-AK phosphorylation which is typical signaling pathway of triglyceride synthesis.

GENERAL PRINCIPLES

Patent

4

No.	Nation	Code
1	United Arab Emirates	AE
2	ARPIO	AP
3	Australia	AU
4	Brazil	BR
5	Canada	CA
6	Chile	CL
7	Colombia	CO
8	EAPO	EA
9	Egypt	EG
10	EPO	EP
11	Hong Kong	HK
12	Indonesia	ID
13	Israel	IL
14	India	IN
15	Iran	IR
16	Japan	JP
17	Sri Lanka	LK
18	Mongolia	MN
19	Mexico	MX
20	Malaysia	MY
21	New Zealand	NZ
22	OAPI	OA
23	Philippines	PH
24	Saudi Arabia	SA
25	Singapore	SG
26	Thailand	TH
27	The United States of America	US
28	Viet Nam	VN
29	South Africa	ZA
30	China	CN

GENERAL PRINCIPLES

Reference

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1. World Health Organization: Fact sheet No. 311: obesity and overweight.
   http://www.who.int/mediacentre/factsheets/fs311/en/index.html. May 2012

2. Hasani-Ranjbar S, Nayebi N, Larijani B and Abdollahi M: A systematic review of the efficacy and safety of herbal medicines used in the treatment of obesity. World J Gastroenterol 15: 3073-3085, 2009.

3. Yin J, Zhang H and Ye J: Traditional Chinese medicine in treatment of metabolic syndrome.
   Endocr Metab Immune Disord Drug Targets 8: 99-111, 2008.

4. M. Ahmadian, Y.Wang, and H. S. Sul, "Lipolysis in adipocytes," International Journal of Biochemistry and Cell Biology, vol. 42, no. 5, pp. 555–559, 2010.

5. V. Large, O. Peroni, D. Letexier, H. Ray, and M. Beylot, "Metabolism of lipids in human white adipocyte," Diabetes and Metabolism, vol. 30, no. 4, pp. 294–309, 2004.

6. G.-Y. Carmen and S.-M. V´ıctor, "Signalling mechanisms regulating lipolysis,"
   Cellular Signalling, vol. 18, no. 4, pp. 401–408, 2006.

7. R. Li, H. Guan, and K. Yang, "Neuropeptide Y potentiates beta-adrenergic stimulation of lipolysis in 3T3-L1 adipocytes," Regulatory Peptides, vol. 178, pp. 16–20, 2012.

8. Fu Y, Zu Y, Chen L, Shi X, Wang Z, Sun S and Efferth T: Antimicrobial activity of clove and rosemary essential oils alone and in combination. Phytother Res 21:989-994, 2007.

9. L. Zhou, X. Wang, Y. Yang et al., "Berberine attenuates cAMPinduced lipolysis via reducing the inhibition of phosphodiesterase in 3T3-L1 adipocytes," Biochimica et Biophysica Acta, vol. 1812, no. 4, pp. 527–535, 2011.

10. X. Guo and K. Liao, "Analysis of gene expression profile during 3T3-L1 preadipocyte differentiation," Gene, vol. 251, no. 1, pp. 45–53, 2000.

11. S. P. Poulos,M. V. Dodson, andG. J.Hausman, "Cell linemodels for differentiation: preadipocytes and adipocytes," Experimental Biology and Medicine, vol. 235, no. 10, pp. 1185–1193, 2010.

12. M. Rodbell, "Metabolism of isolated fat cells: effects of hormones on glucose metabolism and lipolysis," The Journal of Biological Chemistry, vol. 239, pp. 375–380, 1964.

13. S. K. Fried and N.Moustaid-Moussa, "Culture of adipose tissue and isolated adipocytes,"Methods inMolecular Biology, vol. 155, pp. 197–212, 2001.

14. Weight Management Market Analysis By Diet (Meals, Beverages, Supplements), By Equipment (Fitness Equipment, Surgical Equipment), By Services (Fitness Centers, Slimming Centers, Online Weight loss Service), And Segment Forecasts, 2014 - 2025 Published Date: Feb, 2017.
   Report ID: GVR-1-68038-410-9.

Part 2

EFFICACY

PROSTROLANE *Inner-B*

EFFICACY

In vitro studies

1

01 Effect of Prostrolane Inner-B Peptide on lipogenesis

01 Principle

This study was conducted to evaluate the inhibitory effect of Prostrolane Inner-B Peptide on lipogenesis in pre-adipocytes.

This study has been done by determining expression levels of lipogenesis-related genes (PPARɣ, ACC, aP2) and lipid droplet production in 3T3-L1 cells treated with various concentrations of Prostrolane Inner-B Peptide in differentiation conditioned media.

This work has performed using RT-PCR and Oil Red O staining.

02 Materials and Methods

Cell	3T3-L1 (Mouse pre-adipocyte)
Culture condition	DMEM media, 37℃, 5% CO2 incubator
Differentiation conditioned media	DMEM containing 0.5mM IBMX, 0.25uM Dexamethasone and 1ug/ml Insulin
Treatment concentration	1uM Prostrolane Inner-B Peptide
Positive control	50nM human recombinant TNF-α
Treatment time	10 days
Method	RT-PCR / Oil Red O staining

03 Results

A.

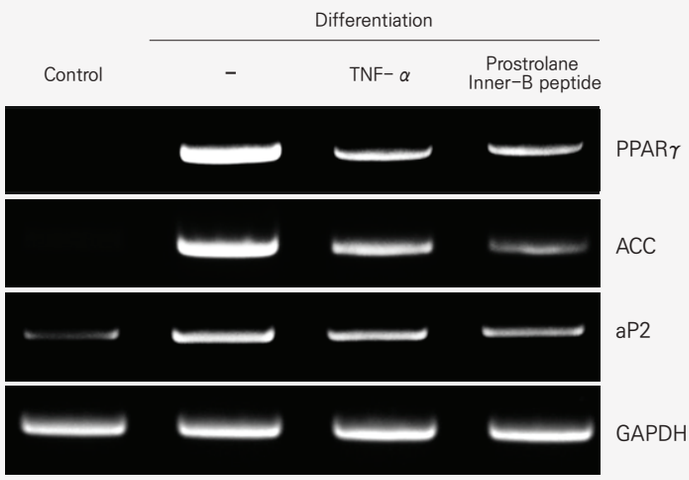


Figure 1. Increased Expression levels of lipogenesis-related genes (PPARɣ, ACC and aP2) were dramatically down regulated in Prostrolane Inner-B Peptide treated pre-adipocyte cells in differentiation conditioned media.
TNF-α : Positive Control

B.

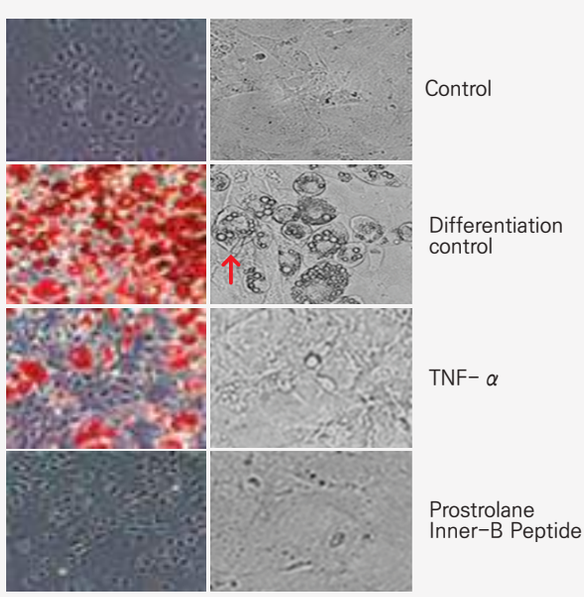


Figure 2. Differentiation conditioned Media induced lipid droplets were strongly decreased in Prostrolane Inner-B Peptide treated pre-adipocyte cells, which implied down regulation of lipogenesis by Prostrolane Inner-B Peptide.
TNF-α : Positive Control

EFFICACY

In vitro studies

1

02 Effect of Prostrolane Inner-B Peptide on lipolysis

01 Principle

This study was conducted to evaluate the stimulating effect of Prostrolane Inner-B Peptide on lipolysis in pre-adipocytes.

This study has been done by determining glycerol release level, triglyceride level, expression levels of lipolysis-related genes (CPT1a, Acox, HSL, ATGL, PLIN1, AMPKa), and lipolysis-related proteins (CPT1a, phospho-HSL, phospho-ATGL, phospho-AMPK1a) and lipid droplet accumulation in 3T3-L1 cells treated with various concentrations of Prostrolane Inner-B Peptide in differentiation conditioned Media.

This work was done using glycerol assay kit, triglyceride assay kit, RT-PCR, western blot and Oil Red O staining.

02 Materials and Methods

Cell	3T3-L1 (Mouse pre-adipocyte)
Culture condition	DMEM media, 37℃, 5% CO2 incubator
Differentiation conditioned media	DMEM containing 0.5mM IBMX, 0.25uM Dexamethasone and 1ug/ml Insulin
Treatment concentration	1uM Prostrolane Inner-B Peptide
Positive control	10, 50nM human recombinant TNF-α
Treatment time	Differentiation conditioned media treatment for 8 days followed by 1day sample treatment
Method	Glycerol release assay / Triglyceride assay / RT-PCR / Western blot / Oil Red O staining

03 Results

A.

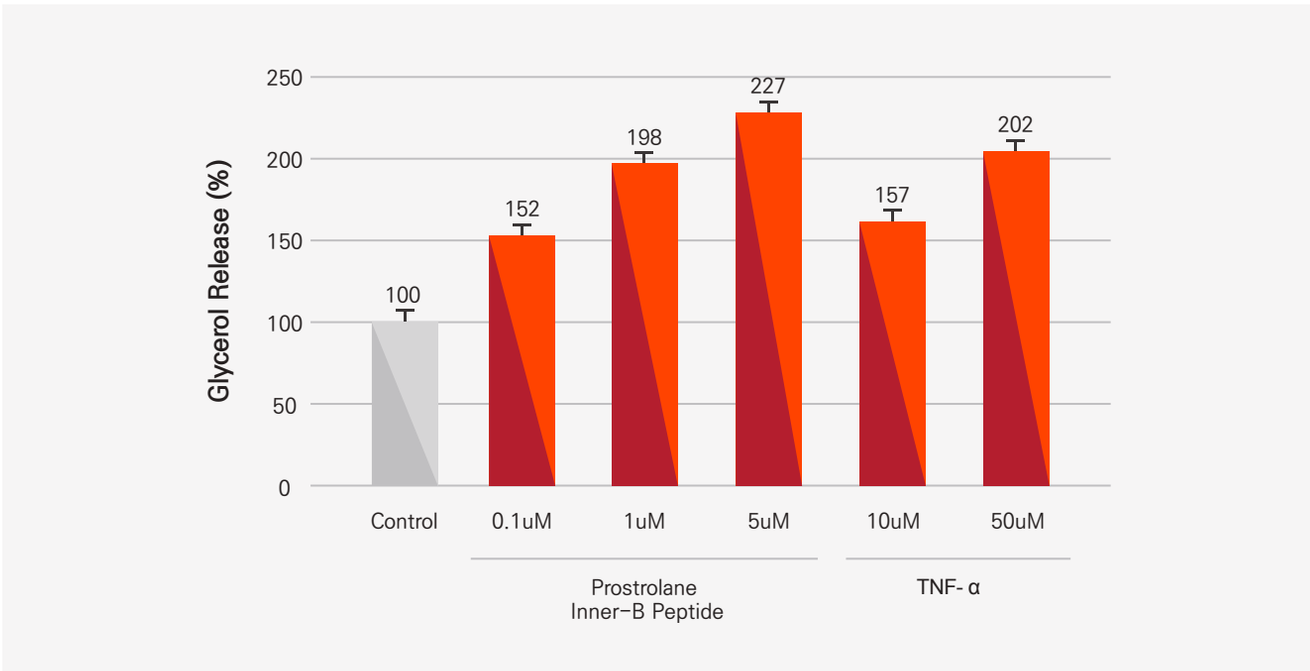


Figure 3. Glycerol release was accelerated with Prostrolane Inner-B Peptide treatment in a dose dependent manner in differentiated adipocytes.
TNF-α : Positive Control

B.

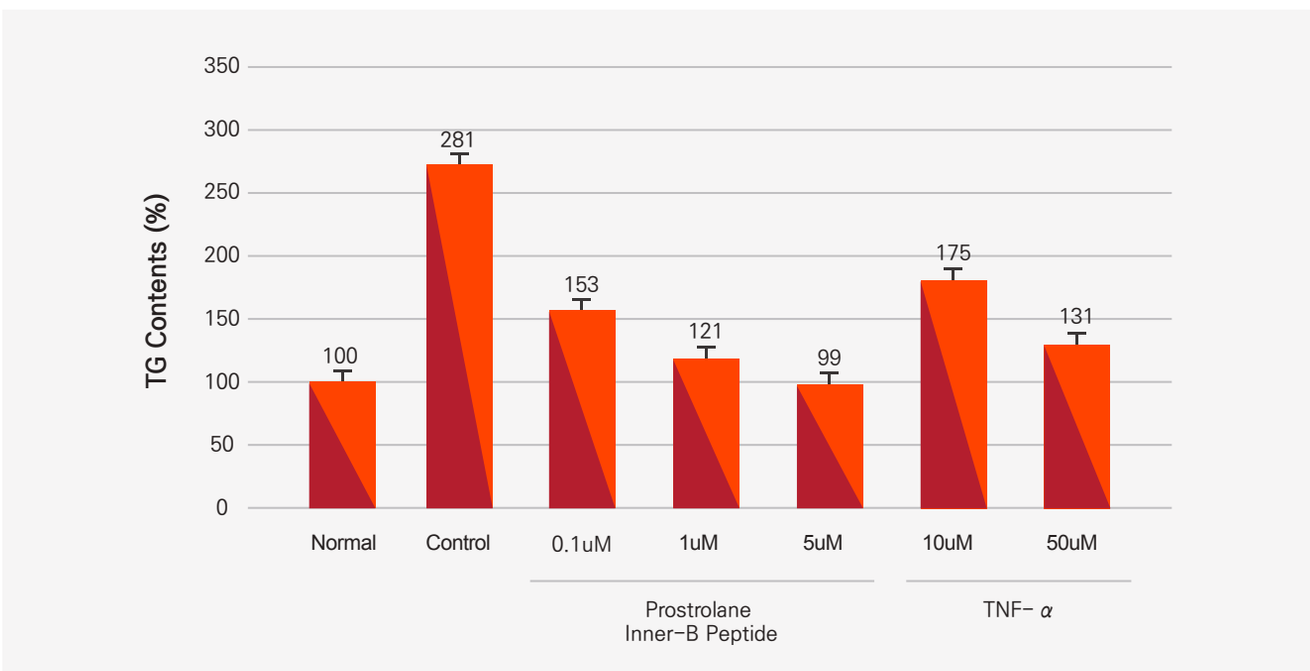


Figure 4. TG contents were dramatically decreased with Prostrolane Inner-B Peptide treatment which implied lipolytic effect of Prostrolane Inner-B Peptide.
TNF- α : Positive Control

C.

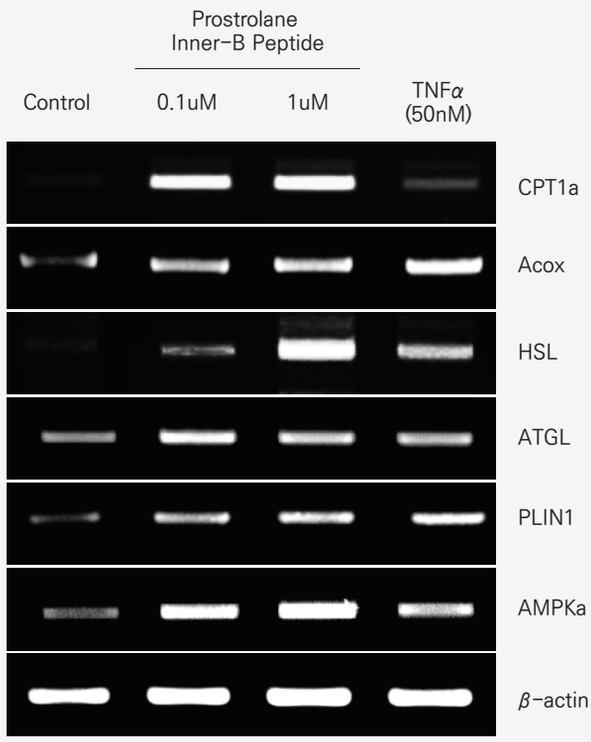


Figure 5. Expression levels of lipolysis-related genes were increased by Prostrolane Inner-B Peptide. TNF-α : Positive Control

D.

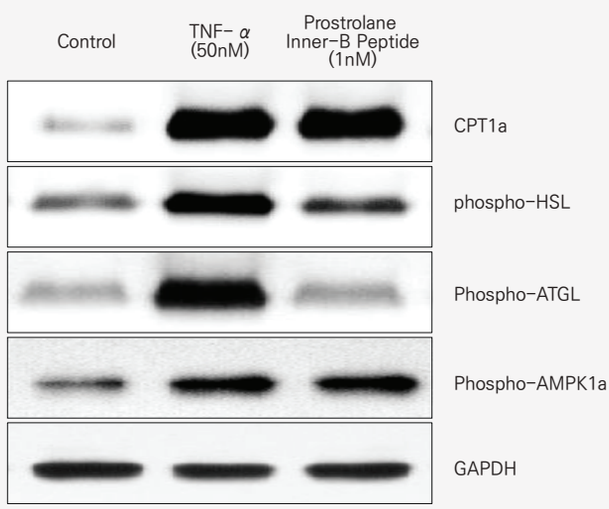


Figure 6. Expression level of lipolysis-related protein, CPT1a, and phosphorylation levels of lipolysis-related proteins, HSL, ATGL and AMPK1a were increased by Prostrolane Inner-B Peptide. TNF-α : Positive Control

E.

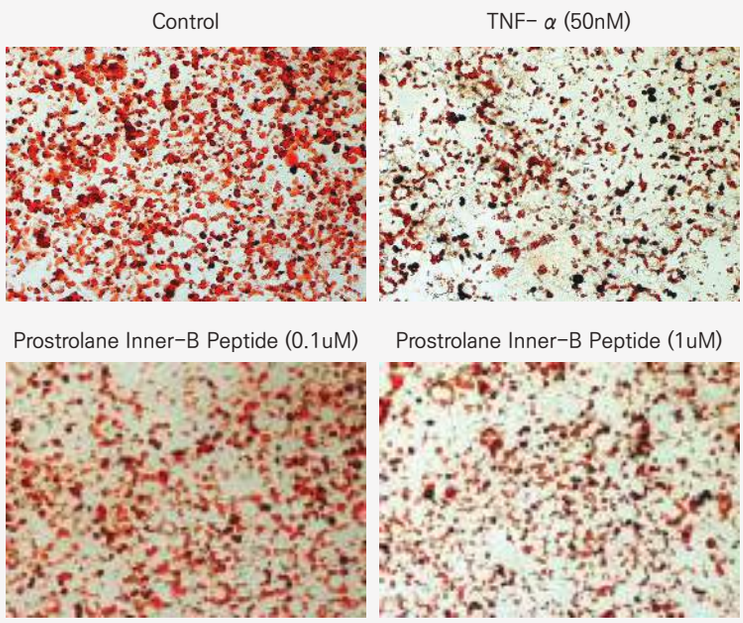


Figure 7. Lipid droplets in differentiated adipocytes were reduced by Prostrolane Inner-B Peptide.
TNF-α : Positive Control

EFFICACY

Ex vivo studies

❷

Effect of Prostrolane Inner-B Peptide on adipose tissue

01 Principle

This study was conducted to evaluate the stimulating effect of Prostrolane Inner-B Peptide on lipolysis in adipose tissue.

This was done by determining size of adipocytes, activity of lipolysis-related enzyme and expression levels of lipolysis-related genes (CPT1a, Acox, HSL, ATGL, PLIN1) and lipolysis-related proteins (phospho-HSL, phospho-ATGL) in 3T3-L1 cells treated with various concentrations of Prostrolane Inner-B Peptide in adipose tissue.

This work has performed using histology, RT-PCR and western blot.

02 Materials and Methods

Cell	Adipose tissue (isolated from mouse abdominal fat pad)
Culture condition	DMEM media, 37℃, 5% CO2 incubator
Treatment concentration	0.1~10uM Prostrolane Inner-B Peptide
Positive control	50nM human recombinant TNF-α
Treatment time	2days
Method	Histology (H&E staining and phospho-HSL immunostaining) / RT-PCR / Western blot

03 Results

A.

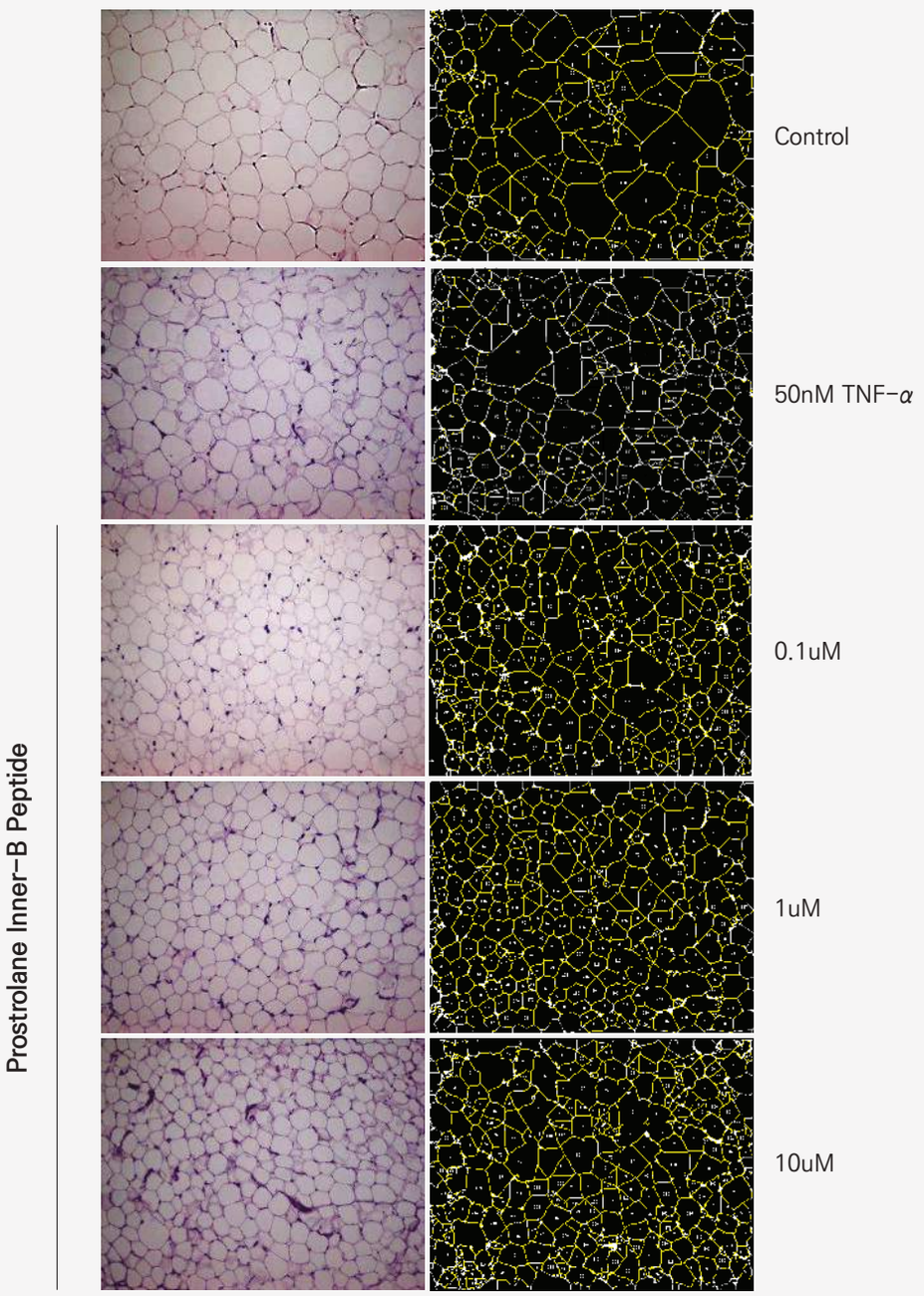


Figure 8. The size of adipocytes was dramatically reduced by Prostrolane Inner-B Peptide.
TNF-α : Positive Control

B.

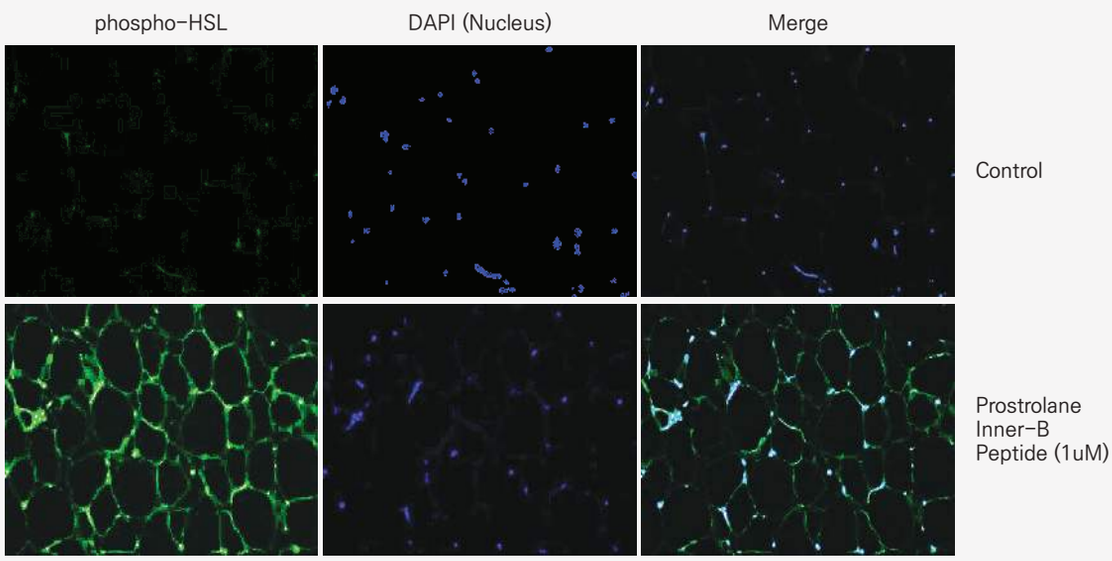


Figure 9. The phosphorylation level of lipolysis-related enzyme, HSL, was increased by Prostrolane Inner-B Peptide in adipose tissue.

C.

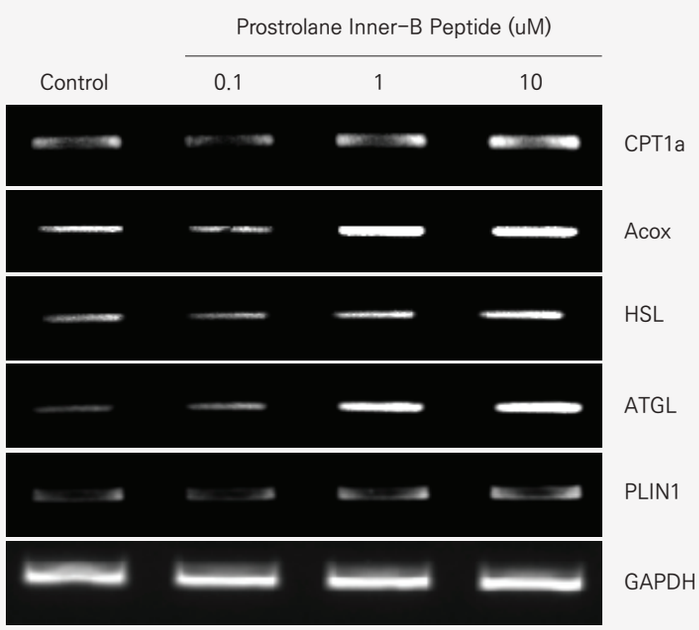


Figure 10. The expression levels of lipolysis-related genes were increased by Prostrolane Inner-B Peptide in adipose tissue.

D.

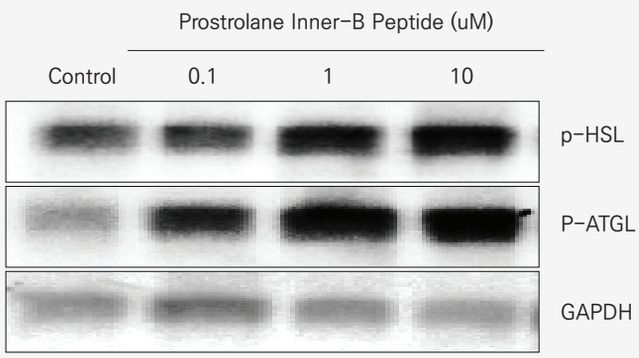


Figure 11. The phosphorylation levels of lipolysis-related proteins were increased by Prostrolane Inner-B Peptide in adipose tissue.

EFFICACY

In vivo studies

❸

Effect of Prostrolane Inner-B Peptide on weight loss of HFD-induced obese mouse model

01 Principle

This study was conducted to evaluate the weight-loss effect of Prostrolane Inner-B Peptide in HFD-induced obese mouse model.

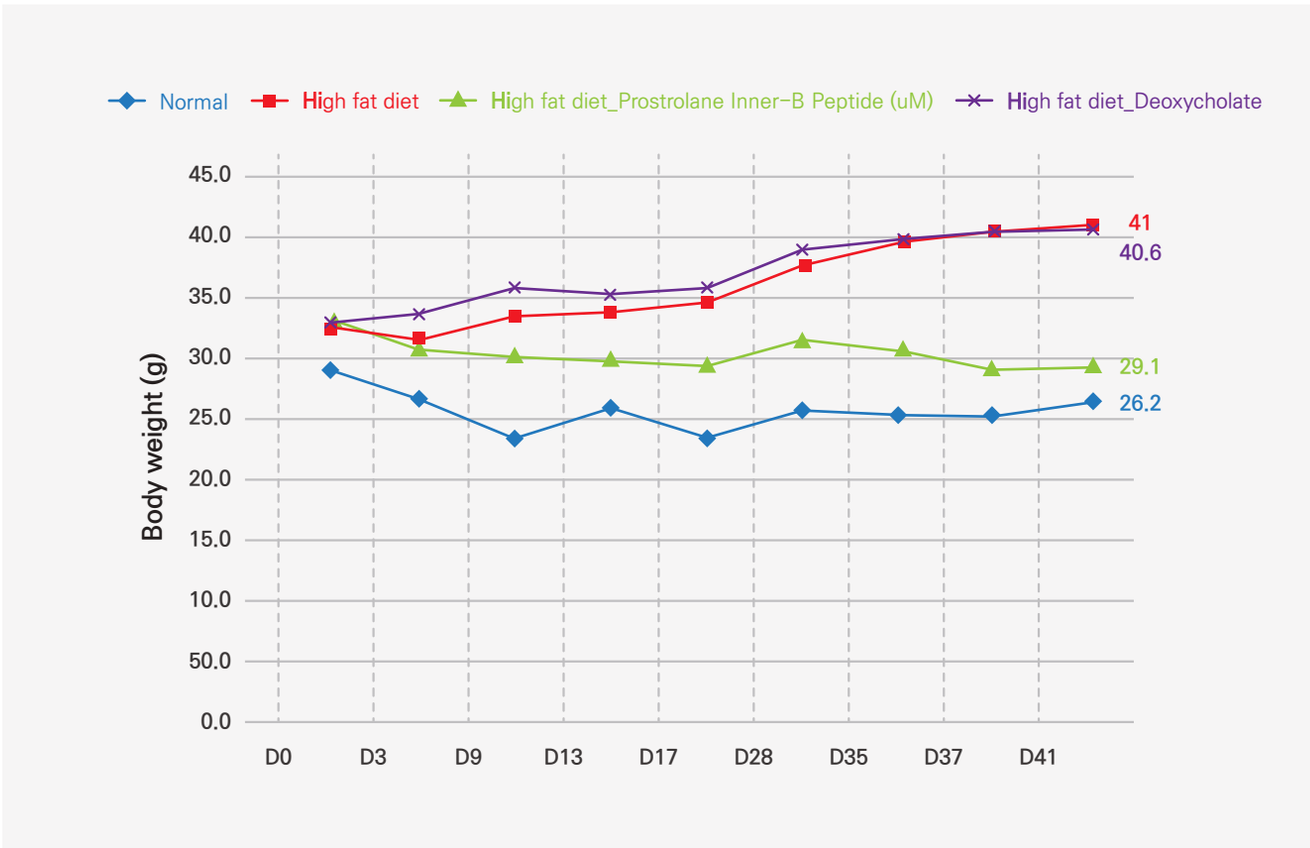
This work has been done by measurement of body weight in HFD-induced obese mouse model.

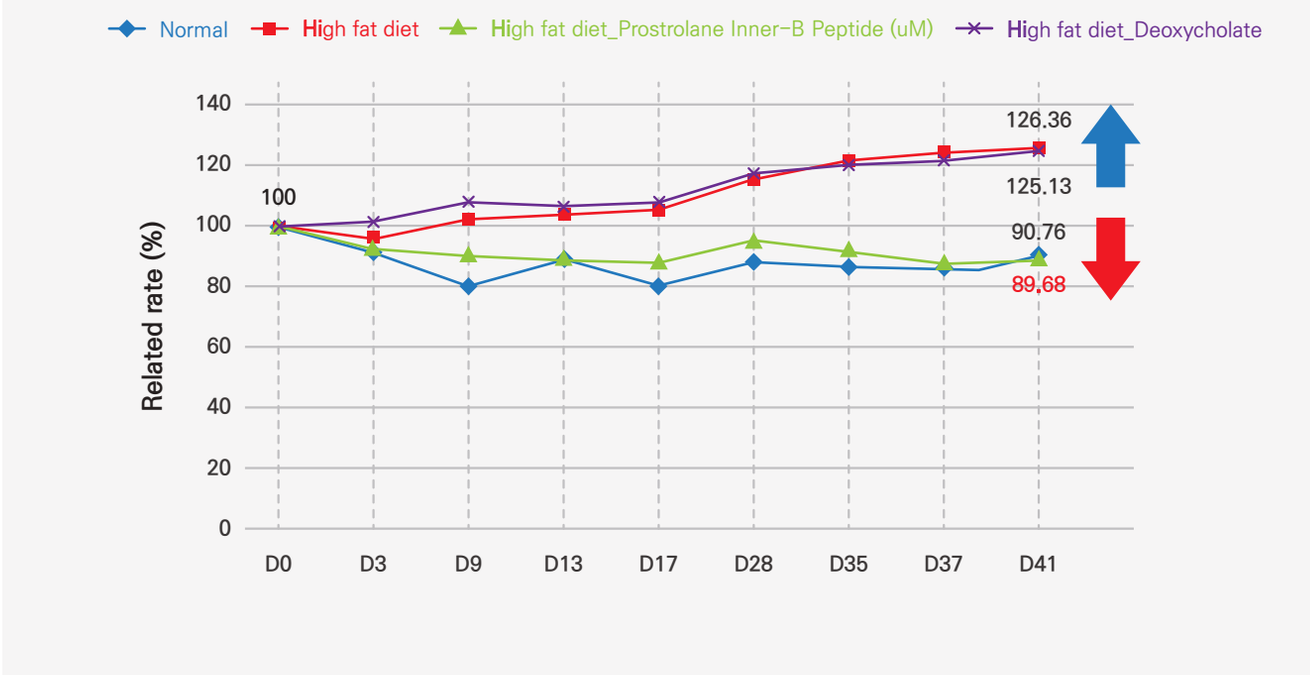
02 Materials and Methods

Animal	HFD-induced obese mouse: 15 weeks, Male, C57/BL6 mouse treated with high fat diet for 9 weeks. (5 heads/group) Normal mouse: 15 weeks, Male, C57/BL6 mouse treated with normal diet (5 heads/group)
Treatment	Dose: 2mg/head Prostrolane Inner-B Peptide or 2mg/head Deoxycholate (Positive control) Injection point: abdominal fat pad Frequency: twice a week Duration: 6 weeks
Measurement	Body weight

03 Results

A.


Normal
High fat diet
High fat diet_Prostrolane Inner-B Peptide (uM)
High fat diet_Deoxycholate
Body weight (g)
45.0
40.0
35.0
30.0
25.0
20.0
15.0
10.0
50.0
0.0
D0
D3
D9
D13
D17
D28
D35
D37
D41
41
40.6
29.1
26.2


Normal
High fat diet
High fat diet_Prostrolane Inner-B Peptide (uM)
High fat diet_Deoxycholate
Related rate (%)
140
120
100
80
60
40
20
0
D0
D3
D9
D13
D17
D28
D35
D37
D41
100
126.36
125.13
90.76
89.68

	Body weight (g)				Related rate (%)			
	Normal ←	High fat diet model (HFD) →			Normal ←	High fat diet model (HFD) →		
		Control	Prostrolane Inner-B Peptide	Deoxycholate		Control	Prostrolane Inner-B Peptide	Deoxycholate
D0	**28.9**	**32.4**	**32.8**	**33.0**	**100**	**100**	**100**	**100**
D3	26.5	31.4	30.6	33.5	91.63	96.63	93.19	101.64
D9	23.2	33.3	30.0	35.7	80.52	102.77	91.30	108.21
D13	25.7	33.7	29.6	35.2	89.03	103.86	90.21	106.66
D17	23.2	34.5	29.2	35.7	80.48	106.39	88.97	108.23
D28	25.5	37.6	31.4	38.9	88.33	115.88	95.70	117.87
D35	25.1	39.6	30.1	39.8	86.95	122.04	92.65	120.60
D37	25	40.4	28.9	40.4	86.60	124.51	88.08	122.41
D41	**26.2**	**41.0**	**29.1**	**40.6**	**90.76**	**126.36**	**89.68**	**125.13**

Figure 12. The Average body weight of HFD control group had 35% higher than that of normal diet mouse group after forty one days feeding.
Prostrolane Inner-B Peptide treatment group showed similar body weight of normal group which has clearly implied that Prostrolane Inner-B Peptide has controlled weight-loss in treatment group.

A.

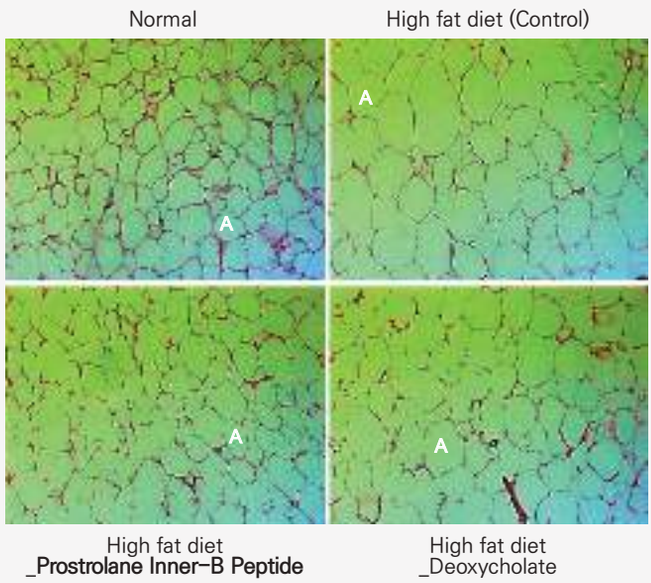


Figure 13. The size of Abdominal white adipose tissues of normal and HFD mice were analyzed. Adipocytes of Prostrolane Inner-B Peptide treated mouse was much smaller than that of High fat diet control and Deoxycholate treated mouse.
A: Adipocyte

B.

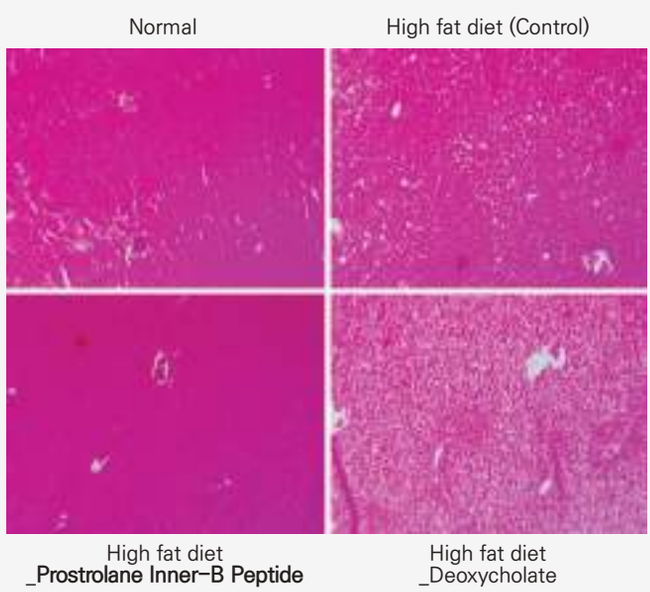


Figure 14. Hepatic tissues of normal and obese HFD mice analyzed. Hepatic steatosis (Fatty liver) was shown in high fat diet control and Deoxycholate treated mice. But Prostrolane Inner-B Peptide treated mouse showed much decreased lipid droplets in hepatocytes.

C.

	Normal	High fat diet model		
		Control	Prostrolane Inner-B Peptide	Deoxycholate
Glucose	203	263	179	260
Triglyceride	79	94	66	131
Total Cholesterol	66	135	102	118
Lipase	17	47	22	37
LDL	8	13	12	12
HDL	58	122	90	106
APO-A1	1	0.8	1.1	1
APO-B	0.6	1	0.6	0.5
APO-B/A1	0.6	1.3	0.5	0.5

Figure 15. Serum glucose, lipid profile and lipid metabolism-related factors were analyzed. Glucose and lipid levels in Prostrolane Inner-B Peptide treated mouse were lower than that in high fat diet control mouse. Apolipoprotein A-I (APO-A1) is the major protein in high-density lipoprotein (HDL) and Apolipoprotein B (APO-B) is the major protein in low-density lipoprotein (LDL). The ratio, APO-B/APO-A1, was lower in Prostrolane Inner-B Peptide treated mouse than in High fat control mouse. This results shown improvement of serum lipid metabolism by Prostrolane Inner-B Peptide.

D.

	Normal	High fat diet model		
		Control	Prostrolane Inner-B Peptide	Deoxycholate
AST (< 40)	105	**426**	66	271
ALT (< 45)	27	**83**	21	43
ALP (30-120)	123	93	84	88

Figure 16. Hepatotoxicity-related factors were analyzed in mouse serum. AST (Aspartate transaminase) and ALT (Alanin transaminase) levels increased in High fat diet mouse serum and those were lower in Prostrolane Inner-B Peptide treated mouse serum.
This results shown that Prostrolane Inner-B Peptide Protected hepatocytes from hepatic steatosis-induced inflammation.

EFFICACY

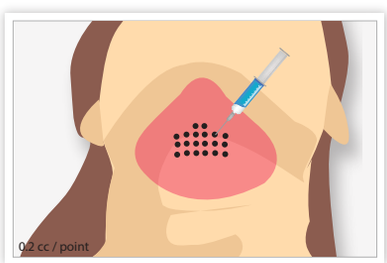
Human clinical tests

4

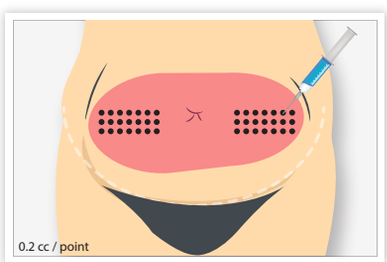
Study Title : The clinical study to evaluate the safety and efficacy of Prostrolane Inner-B

Test Product: Prostrolane Inner-B

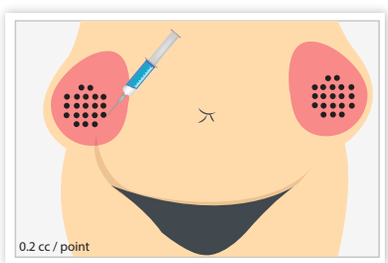
Protocol



Double chin

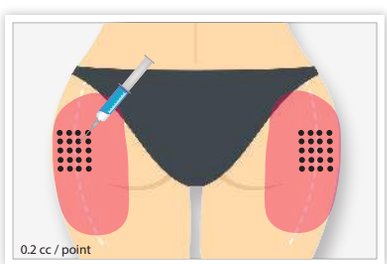


Abdomen

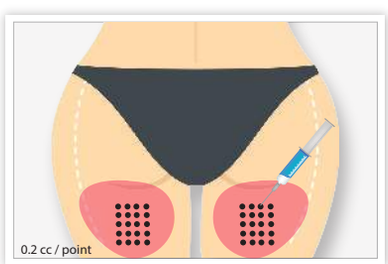


Love Handles

Upper arms



Outer thighs



Inner thighs

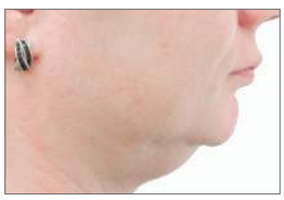
No.	Injection Site	Interval between sessions	Number of Total sessions
1	Double Chin	2 weeks	3 sessions
2	Abdomen	2 weeks	4 sessions
3	Love Handles	2 weeks	4 sessions
4	Upper arms	2 weeks	3 sessions
5	Thighs	2 weeks	4 sessions
6	Jowl	2 weeks	3-4 sessions
7	Knees	2 weeks	4 sessions

01 Double chin

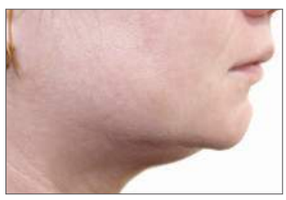
2 syringes per session (3 sessions)

Case. 1

Before



After



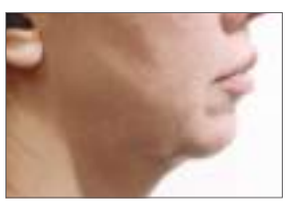
Before

After

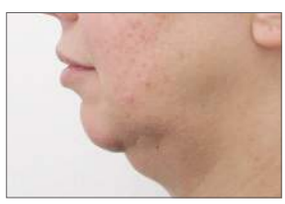
Case. 2

Before

After



Before



After

Case. 3

Before

After

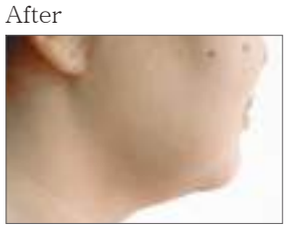
Before

After

Case. 4

Before

After



Before

After

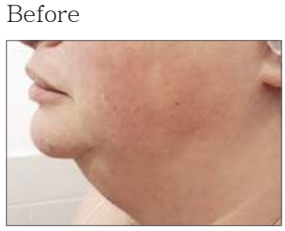
Case. 5

Before

After

Case. 6

Before



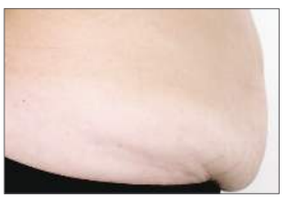
After

02 Abdomen

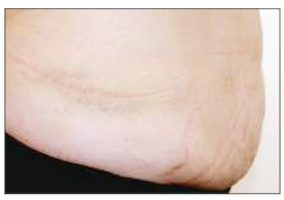
4 syringes per session (4 sessions)

Case. 1

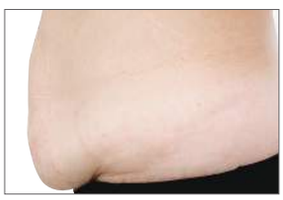
Before



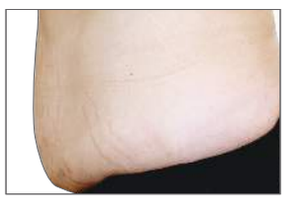
After



Before

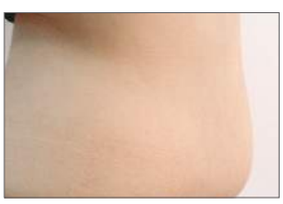


After



Case. 2

Before



After

Before

After

Case. 3

Before

After

Before

After

Case. 4

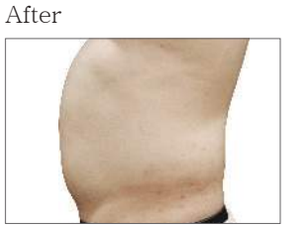
Before

After

Case. 5

Before

After



Case. 6

Before

After

Case. 7

Before

After

Case. 8

Before After

Case. 9

Before After

Case. 10

Before After

Case. 11

Before After

Case. 12

Before After

Case. 13

Before After

03 Love Handles

2 syringes per session (4 sessions)

Case. 1

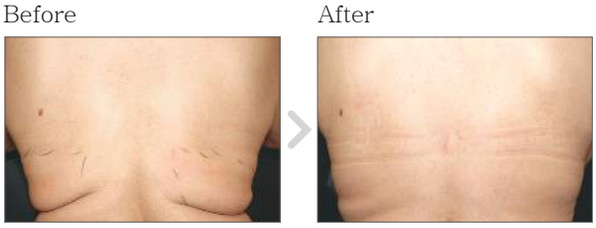
Before After

Case. 2

Before After

Case. 3

Before After



Case. 4

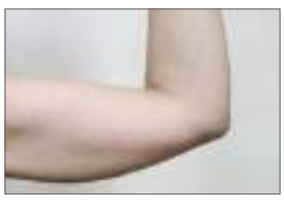
Before After

04 Upper Arms

2 syringes per session (3 sessions)

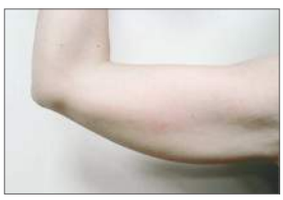
Case. 1

Before



After

Before



After

Before

After

05 Thighs

4 syringes per session (4 sessions)

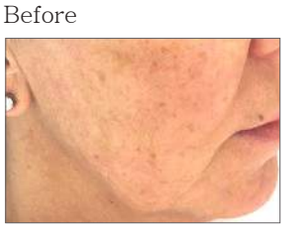
Before

After

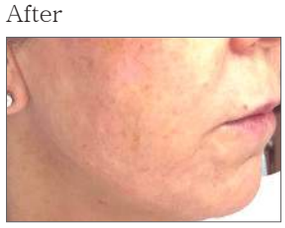
06 Jowl

1 syringes per session (3 sessions)

Before



After

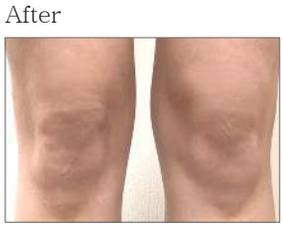


07 Knees

2 syringes per session (4 sessions)

Before

After



Part 3

SAFETY

PROSTROLANE *Inner-B*

SAFETY

Statistical Summary

1

Study Title: The Biocompatibility study to evaluate the safety of Prostrolane Inner-B

Test Product: Prostrolane Inner-B
Test Site: KTC (Korea Testing Certification)

Sponsor: CAREGEN

SECTION 1 : Chemical and Physical Tests

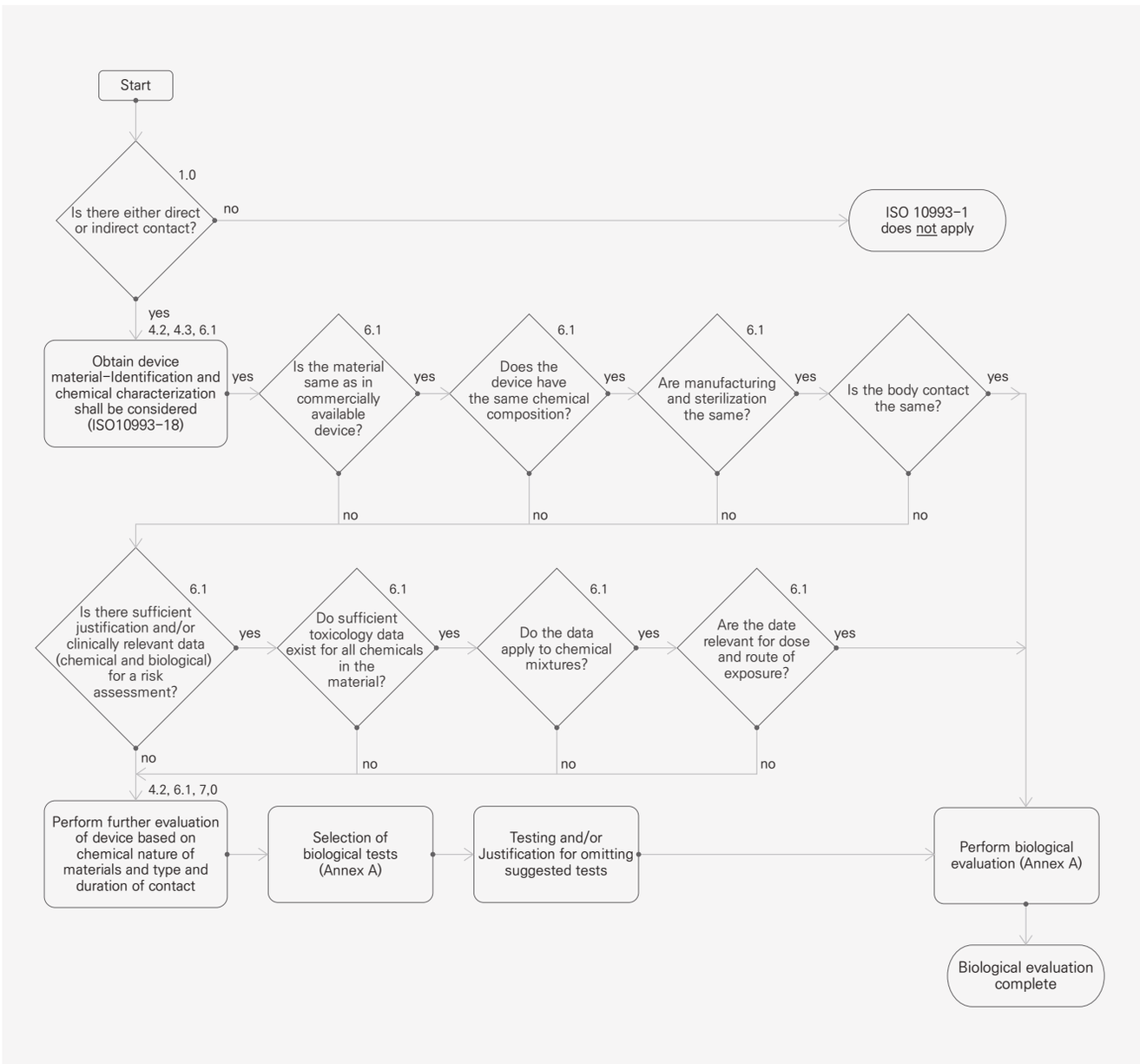
1. Chemical and Physical Test Items

1.1. Property
1.2. Determination of Volume of Injection in containers
1.3. pH
1.4. Heavy Metals
1.5. Sodium Hyaluronate Contents
1.6. Osmolarity
1.7. Complex viscosity
1.8. Sterility Test
1.9. Bacterial Endotoxin Test

SECTION 2 : Biological Tests

1. Biological Test Items

systematic approach to a biological evaluation of medical devices as part of risk management process (ISO 10993-1: 2009).



2. Categorization of Medical devices by ISO 10993-1:2009 Chapter 5

Chapter 5 ISO 10993-1	Device
5.2 Body contact	5.2.3 Implant devices a) Tissue / bone
5.3 Duration of contact	b) Prolonged contact (〉 24h to 30d)

3. Selection of Biological evaluation test

(According to ISO 10993-1:2009, Annex A / Table A.1-Evaluation tests for consideration)

Test Items	By ISO 10993-1	Evaluation test study
Cytotoxicity test	V	V
Sensitization test	V	V
Intracutaneous (intradermal) Reactivity test	V	V
Acute Systemic toxicity test	V	V
Subchronic toxicity (subacute toxicity)	V	V
Genotoxicity test	V	V
Implantation	V	V
Haemocompatibility	N/A	N/A

3.1 Cytotoxicity test

Reference: ISO 10993:2009, Biological evaluation of medical devices - Part 5: Tests for in vitro cytotoxicity (indirect contact - agar diffusion Test) / (Refer to Appendix 5, Test Report No. MD 2015-00259)

3.2 Sensitization test (guinea pig maximization test)

Reference: ISO 10993 : 2010, Biological evaluation of medical devices - Part 10: Tests for irritation and skin sensitization, 7.5 Guinea pig maximization test / (Refer to Appendix 6, Test Report No. MD 2015-00259)

3.3 Intracutaneous (Intradermal) Reactivity test

Reference: ISO 10993 : 2010, Biological evaluation of medical devices - Part 10: Tests for irritation and skin sensitization, 6.3 Animal intracutaneous (intradermal) reactivity test. / (Refer to Appendix 7, Test Report No. MD 2015-00259)

3.4 Acute Systemic toxicity test

Reference: ISO 10993:2006 Biological evaluation of medical devices - Part 11: Tests for systemic toxicity, 5. Acute Systemic toxicity / (Refer to Appendix 8, Test Report No. MD 2015-00259)

3.5 Genotoxicity test (Ames test: Bacterial Reverse Mutation Test)

Reference: ISO 10993:2014, Biological evaluation of medical devices - Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity, 4. Genotoxicity tests
- OECD : 1997, Guidelines for the Testing of Chemicals - 471 : Bacterial Reverse Mutation Test / (Refer to Appendix 10, Test Report No. MD 2015-00259)

3.6 Genotoxicity test: mammalian Erythrocyte Micronucleus Test

Reference: ISO 10993:2014, Biological evaluation of medical devices - Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity, 4. Genotoxicity tests
OECD : 1997, Guidelines for the Testing of Chemicals - 474 : Mammalian Erythrocyte Micronucleus Test / (Refer to Appendix 11, Test Report No. MD 2015-00259)

3.7 Implantation Test

Reference: ISO 10993:2007, Biological Evaluation of Medical devices – Part 6: Tests for local effects after implantation, Annex C. Test methods for implantation in muscle (Refer to Appendix 12, Test Report No. MD 2015-00259)

3.8 Subacute systemic toxicity Test

Reference: ISO 10993:2006, Biological evaluation of medical devices - Part 6 : Tests for Systemic Toxicity, Repeated exposure systemic toxicity (Subacute systemic toxicity) / (Refer to Appendix 1, Test Report No. T2016-10747)

SECTION 3 : Stability Tests

The purpose of stability test is to provide evidence on how the quality of Prostrolane Inner_B varies with time under the influence of a variety of environmental factors such as temperature, humidity and to establish a retest period for the substance or a shelf life for the product and recommended storage conditions.
(Accelerated Aging test Setting in accordance with ASTM F 1980: Standard guide for accelerated aging of sterile Barrier Systems for medical device)
We verified shelf-life of Product by Accelerated Aging test.

SAFETY

The summary of Test result

2

No.	STUDY LIST	Standard	Results
1	Property	When observing it with the naked eye, test solution should be clear and have no foreign particles	Pass
2	Determination of Volume of injection in Containers	When tested in accordance with the korean phamaceutical determination of volume of injection in containers, the volume should be more than the volume which is a given information by manufacturer	Pass
3	pH	When testing the test solution according to general test, process and apparatus of KP, the pH should be within 6.3~8.3	7.32
4	Heavy Metals	When testing the extracted solution in accordance with korean pharmacopoeia, atomic absorption method, the overall content of lead, tin, zine and iron should be 5mg/L and less, and cadmium should be 0.1mg/L and less	Not detected
5	Cytotoxicity Test	ISO 10993-5, Tests for in vitro cytotoxicity (indirect contact-agar diffusion test)	0 grade
6	Guinea Pig maximization test	ISO 10993-10, Guinea pig maximization test (GPMT)	Negative
7	Intra cutaneous (intradermal) Reactivity Test	ISO 10993-10, Intracutaneous (intradermal) reactivity test	0.0
8	Acute systemic toxicity test	ISO 10993-11, Acute systemic toxicity	Non-toxic
9	Bacterial Endotoxin test	USP〈85〉 Bacterial Endotoxin test	〈0.005
10	Genotoxicity test (Bacterial reverse mutation test	ISO 10993-3, Test for Genotoxicity test, Bacterial Reverse Mutation Test	Negative
11	Genotoxicity test (Mammalian Erythrocyte micronucleus test)	ISO 10993-3, Test for Genotoxicity test, Mammalian Erythrocyte Micronucleus test	Negative
12	Implantation test	ISO 10993-6, Tests for local effects after implantation	Non-irritant
13	Sterility test	The korean pharmacopoeia eleventh edition	None

PROSTROLANE *Inner-B*

CAREGEN CO., LTD.

Head Office. 46-38, LS-ro 91beon-gil, Dongan-gu, Anyang-si, Gyeonggi-do 14119 South Korea
Tel. +82-31-420-9200 **Fax.** +82-31-452-3869 **E-mail.** sales@caregen.com
Creative Village. 16-27, LS-ro 91beon-gil, Dongan-gu, Anyang-si, Gyeonggi-do, South Korea
1st Manufacturing. 272 Gongdan-ro, Gunpo-si, Gyeonggi-do, South Korea
2st Manufacturing. 270 Gongdan-ro, Gunpo-si, Gyeonggi-do, South Korea

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