

FO<sup>TM</sup>

**FERMENTED OYSTER EXTRACT  
ESSENCE OF NATURAL GABA**

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**II** Highly Specialized Production Flow

**III** Proven Scientific Background

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# I. INTRODUCTION OF FO

## 1-1. RAW MATERIAL INFORMATION

### OYSTER IS A SUPER FOOD CONTAINING VARIOUS NUTRIENTS



- SCIENTIFIC NAME : *Crassostrea gigas*
- CHARACTERISTICS
  - Contain high levels of taurine and glutamic acid, a precursor of gamma amino butyric acid(GABA)
  - Super food containing 5 nutrients such as protein, carbohydrate, fat, minerals, and vitamins
  - Rich in calcium, potassium, phosphorus, zinc and iron including selenium and other vitamins
  - High levels of glycogen, taurine and lysine, etc.
- VARIOUS EFFICACIES
  - Zinc: necessary component for immunity and cell division
  - Taurine, nucleic acid, and iron : reducing cholesterol, anti-aging, and stamina enhancement
  - Vitamins : various vitamins such as A1, B2, B12, E, etc. Aid in metabolism of folic acid, and generation of energy

Reference : Korean Food Composition Table(9th revision) 2016

## 1-2. FO(FERMENTED OYSTER) EXTRACT

**BY OUR INNOVATING PATENTED, PROPRIETARY MANUFACTURING METHOD, FO CONTAINS HIGH-LEVELS OF GABA AND LACTATE, BIO-CONVERTED DURING FERMENTATION**

### ○ KEY FEATURES

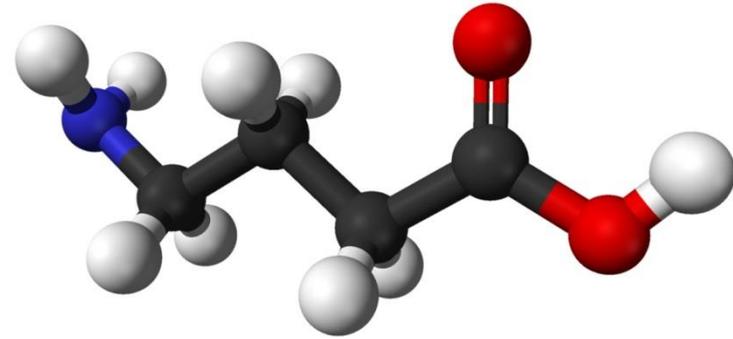
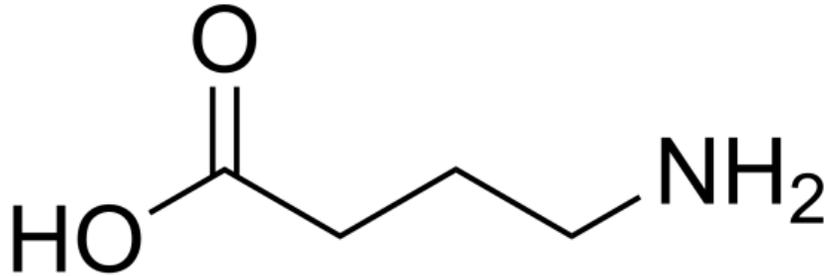
- Contains more than 10% of natural GABA and 4% Lactate ; Standard markers and active components
- Appearance : light yellow powder
- 100% water soluble ingredient easily applicable to various types of health food
- Achieved through safe and hygienic process (including autoclaving after fermentation)
- Special method to reduce typically, naturally occurring marine organism odor
- Improved flavor and texture to be easily adapted as a general food ingredient
- Rich in protein, essential amino acids, essential fatty acids, and vitamins
- Improved bioavailability through patented fermentation process with *L. brevis*BJ 20.

## 1-3. NUTRITIONAL CONTENTS and SAFETY of FO

Nutrients		Result
Calories (kcal/100g)		353.4
Carbohydrate (g/100g)		56.1
Crude Protein (g/100g)		31.8
Crude lipid (g/100g)		0.2
Saturated Fat (g/100g)		0.1
Trans Fat (g/100g)		0.0
GABA (g/100g)		13.0
Cholesterol (mg/100g)		0.0
Heavy metals	Plumbum (mg/kg)	0.0
	Arsenic (mg/kg)	0.7
	Cadmium (mg/kg)	0.0
	Total mercury (mg/kg)	0.0
	Coliform group (mg/g)	negative

Reference : COA of Korea AFRI of Busan Branch, 2020.

## 1-3. WHAT IS GABA

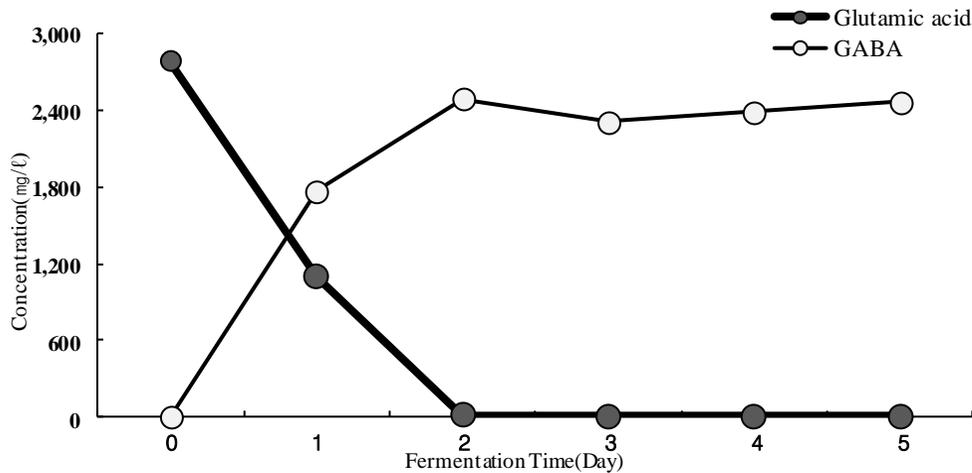


- GABA( $\gamma$ -aminobutyric acid) is a non-protein amino acid that is widely distributed in nature and functions as a major inhibitory neurotransmitter in the central nervous system(brain and spinal cord).
- GABA is well known for its physiological functions, such as the induction of hypotension, and diuretic and tranquilizer effects and has been used as a health food material since the mid-1980's. The market for GABA has been begun flourishing since 2001.
- GABA is made up of four carbons and is synthesized from glutamate via glutamate decarboxylase (GAD) by decarboxylation from the L-glutamate with pyridoxal phosphate as a cofactor.
- Multi-effects of GABA include brain enhancement, mental stability, decrease blood pressure, sleep induction, enhanced concentration, memory enhancement, promoting expression of growth hormone, hangover recovery, improved liver function, etc.

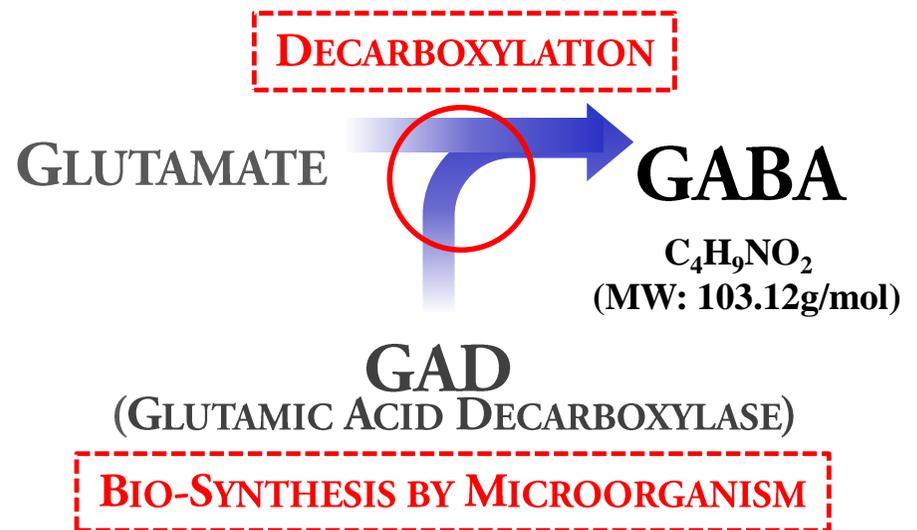
# 1-4. BIO-CONVERTED GABA: ACTIVE COMPOUND OF FO

## MECHANISM OF GABA SYNTHESIS:

GLUTAMIC ACID IN OYSTER IS CONVERTED TO GABA BY DECARBOXYLATION REACTION THROUGH FERMENTATION WITH *L. BREVIS* BJ20



Changes in Glutamic acid and GABA level during fermentation procedure of FO.



## 1-5. FREE AMINO ACID CONTENT : AFTER BIOCONVERSION

**GLUTAMATE CONTAINED IN OYSTER IS TRANSFORMED INTO GABA VIA GLUTAMATE DECARBOXYLASE DURING HIGHLY SPECIALIZED LACTIC ACID(L. BREVIS BJ20) FERMENTATION PROCESS**

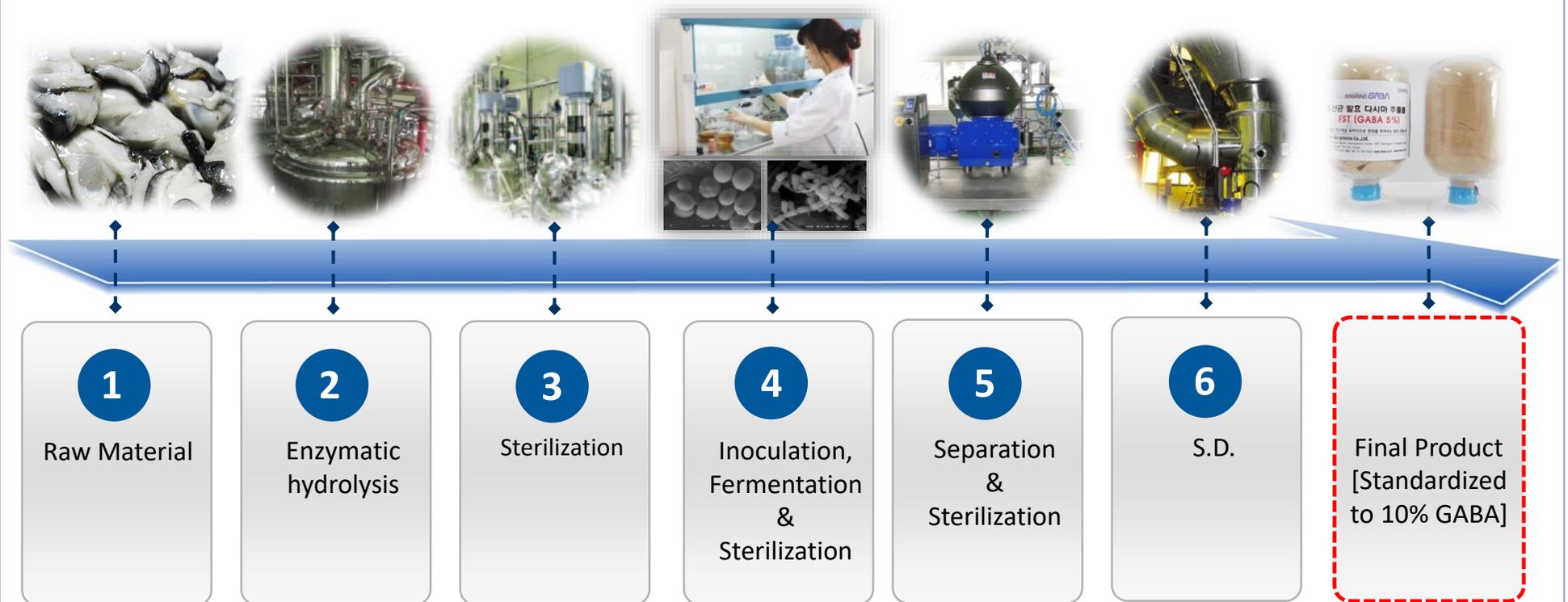
Free Amino Acid	Content (unit: mg/100g)
Phosphoserine	1569.5
Taurine	1131.0
Aspartic Acid	687.6
Glutamic Acid	277.6
Aspartic acid	687.6
Proline	785.1
Alanine	1322.5
GABA	14,784.9
threonine	604.9
Valine	907.3
lysine	772.2

Reference : COA of PKNU Food Analysis Center, 2019.

## **II. HIGHLY SPECIALIZED PRODUCTION FLOW**

## 2-1. OUR PROPRIETARY PRODUCTION FLOW CHART

**OUR UNIQUE AND INNOVATIVE PRODUCTION TECHNOLOGY ENSURES HIGH QUALITY GABA PRODUCT (STANDARDIZED UP TO MIN. 10%)**



## 2-2. LACTIC ACID BACTERIA USED FOR FERMENTATION

### SCREENING

- Kimchi Group: 10 Cases
- Jeot-gal Group: 15 Cases

Ref1) Kimchi: Korean Traditional Fermented Cabbage

Ref2) Jeot-gal: Korean Traditional Salt-Fermented Seafood(Cod-Gut)

### ISOLATION

- *Lactobacillus* for GABA Formation

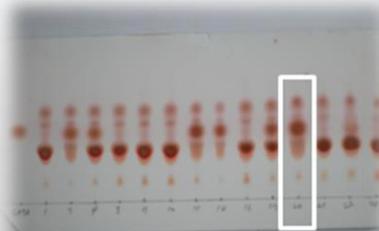


Fig. Result of TLC for GABA

### IDENTIFICATION

- 16s rRNA gene
- Characteristic of Biochemical and morphological

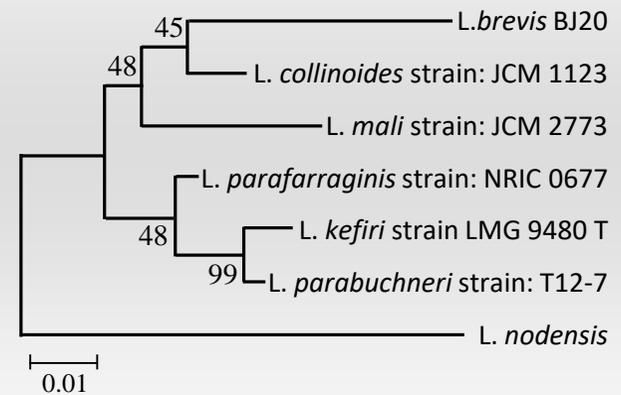


Fig. Result of 16s rRNA gene sequencing

## 2-3. SPECIFICATION OF LACTOBACILLUS STRAIN

### Name of Strain

• *Lactobacillus brevis* BJ20

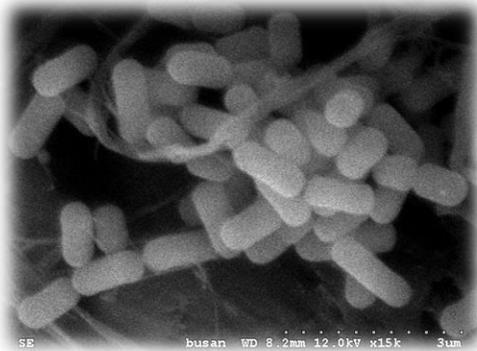


Fig. Scanning electron microphotograph of *L. brevis* BJ20

### Donation No.

• KCTC 1377BP

PROSPECT TREATY ON THE INTERNATIONAL REGISTRATION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSE OF PATENT PROCEDURE

**INTERNATIONAL FORM**  
**RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT**  
(second part) - to Rule 7.1

TO : Maru Bioprocess Co., Ltd.  
215, Marine Bio-Industry Development Center  
27 Hwangje-dong, Hwangje-myeon, Gyeonggi-do, Daejeon 305-912  
Republic of Korea

<b>I. IDENTIFICATION OF THE MICROORGANISM</b>	
<small>Identification reference given by the DEPOSITOR:</small> <i>Lactobacillus brevis</i> BJ20	<small>Accession number given by the INTERNATIONAL DEPOSITORY AUTHORITY:</small> KCTC 1377BP
<b>II. SCIENTIFIC DESCRIPTION AND/OR PROPOSED TAXINOMIC DESIGNATION</b>	
<small>The microorganism identified under I above was accompanied by: (*) a scientific description (*) a proposed taxonomic designation (*) other with a cross where applicable?</small>	
<b>III. RECEIPT AND ACCEPTANCE</b>	
<small>This International Depository Authority accepts the microorganism identified under I above, which was received by it on <b>August 19, 2008</b>.</small>	
<b>IV. RECEIPT OF REQUEST FOR CONVERSION</b>	
<small>The microorganism identified under I above was received by this International Depository Authority on _____ and a request to convert the original deposit to a deposit under the Budapest Treaty was received by it on _____.</small>	
<b>V. INTERNATIONAL DEPOSITORY AUTHORITY</b>	
<small>Name: Korean Collection for Type Cultures</small>	<small>Signature(s) of person(s) having the power to represent the International Depository Authority of authorized official(s):</small>
<small>Address: Korea Research Institute of Bioscience and Biotechnology (KIBS) 111 Gwahang-ro, Yuseong-gu, Daejeon 305-380 Republic of Korea</small>	 <small>Oki-Han-Mock, Director Date: <b>August 29, 2008</b></small>

Form 1014 (KCTC) - Page 1/2

### Characteristic

- Gram+ derived from Jeot-gal(Korean Traditional Salt-Fermented Seafood-Cod Gut)
- Rod Shape
- Lactobacillus strain suitable for GABA production
- Optimum Temperature for Growth and Development: 37°C
- Optimum pH : pH7
- Optimal NaCl concentration : 1%

## 2-4. ADVANTAGES OF FERMENTATION PROCESS

### ADVANTAGES AND MERITS OF FERMENTATION BY MICROORGANISMS

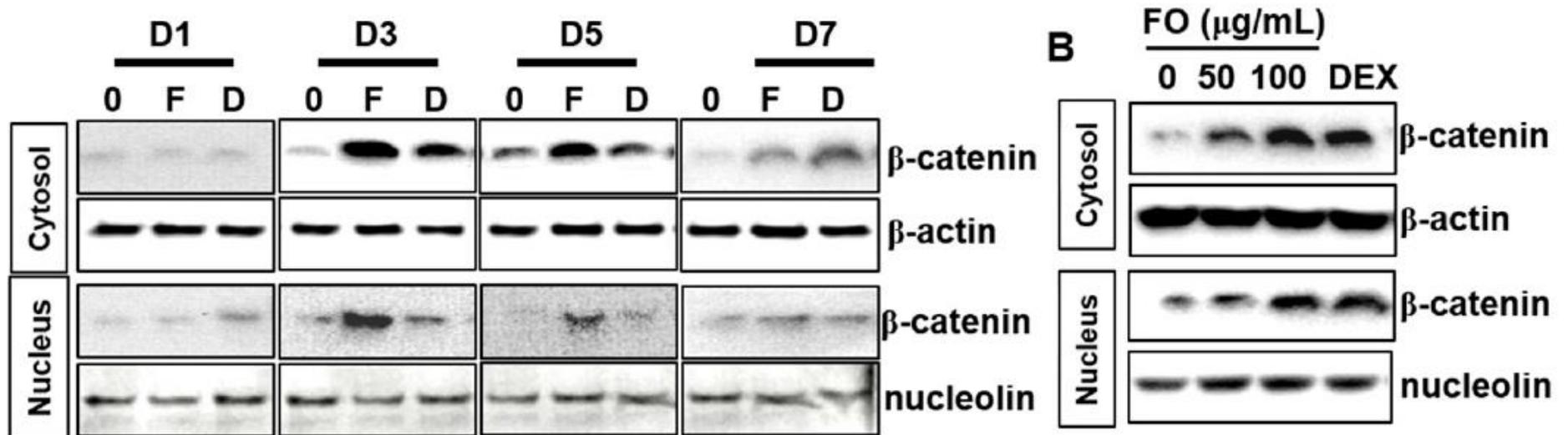


- FO IS PRODUCED UNDER STRICT QUALITY CONTROLLED AND SAFE, HYGIENIC PROCESS (AUTOCLAVING AFTER FERMENTATION)
- REDUCE ITS OWN NATURAL SEA ODOR BY OUR PATENTED FERMENTATION PROCESS
- IMPROVE FLAVOR AND TEXTURE APPLICABLE IN VARIOUS PROCESSED FOOD PRODUCTS
- ENHANCE BIOLOGICALLY ACTIVE COMPOUNDS AND INCREASED BIOAVAILABILITY RESULTING FROM IMPROVED EFFICACY

### **III. PROVEN SCIENTIFIC BACKGROUND**

## 3-1. Promotion of Bone Formation : IN-VITRO

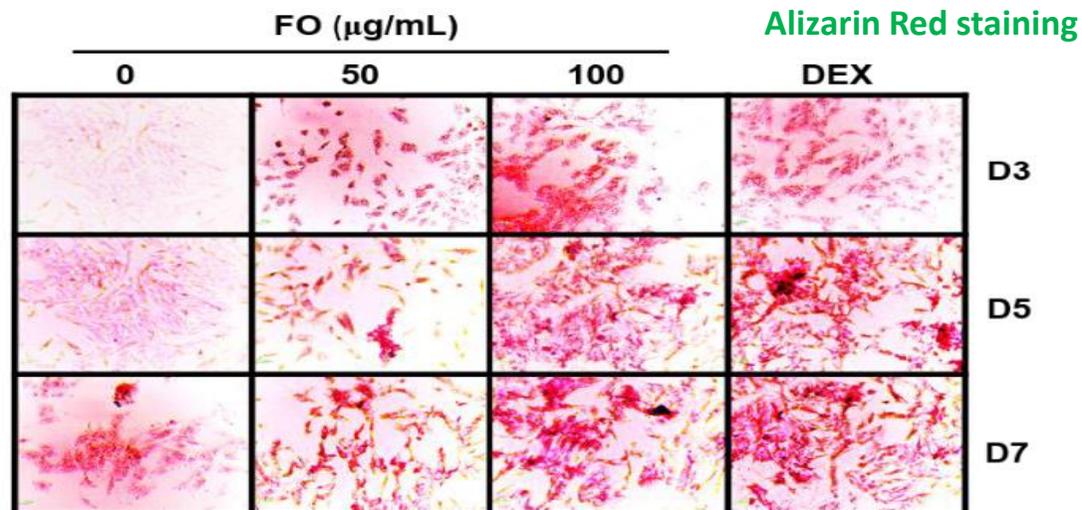
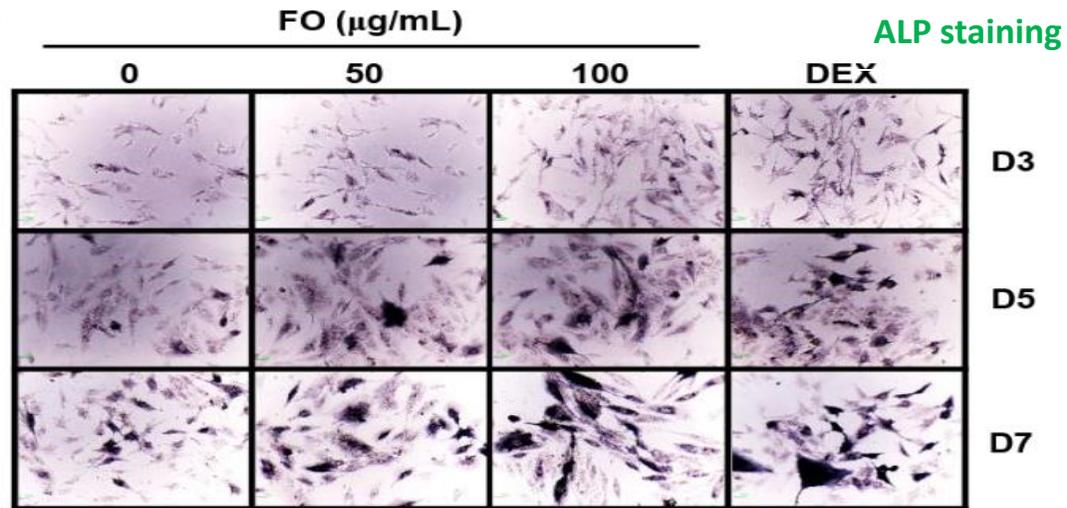
FO-mediated vertebrae formation is regulated via the  $\beta$ -catenin pathway



dexamethasone (DEX)

## 3-1. Promotion of Bone Formation : IN-VITRO

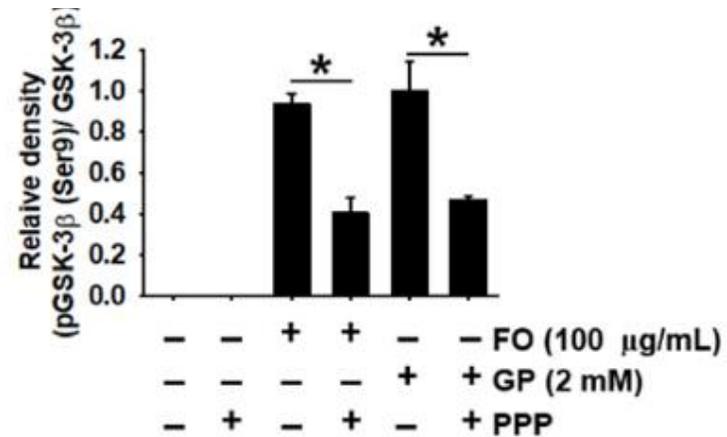
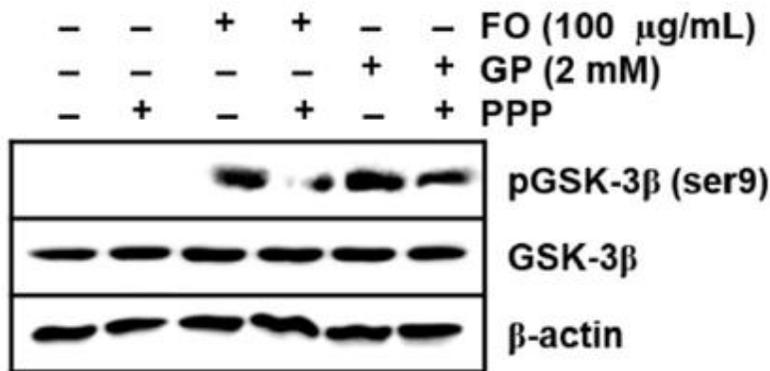
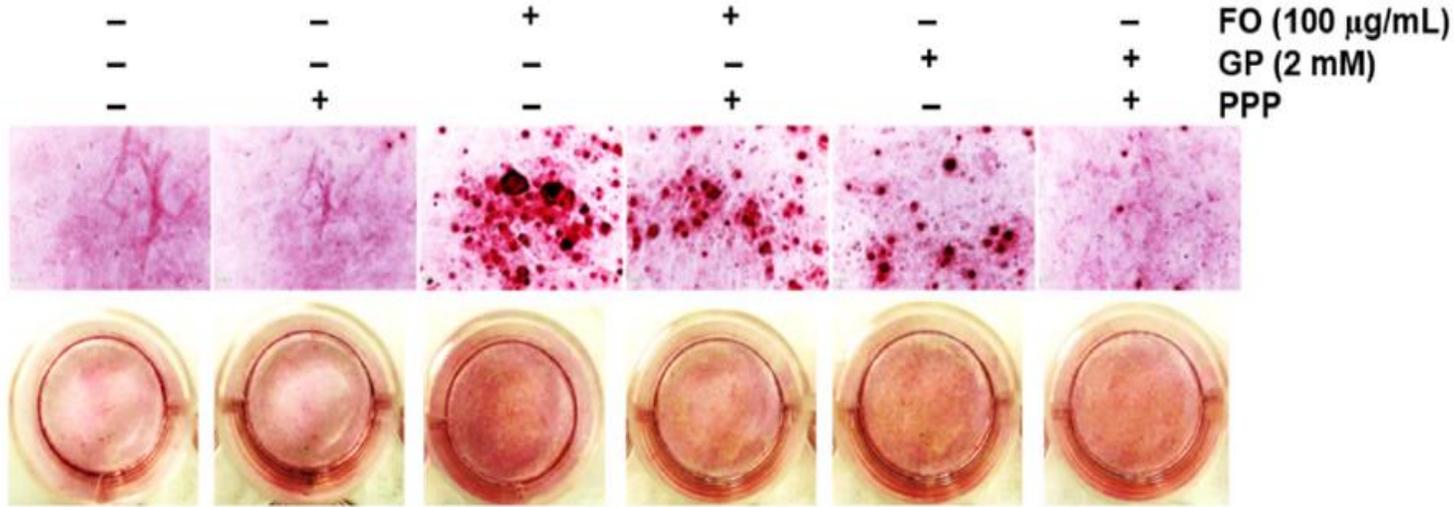
**FO elevates osteoblast differentiation along with mineralization and calcification**



Reference : Biomolecules 2019, 9, 711.

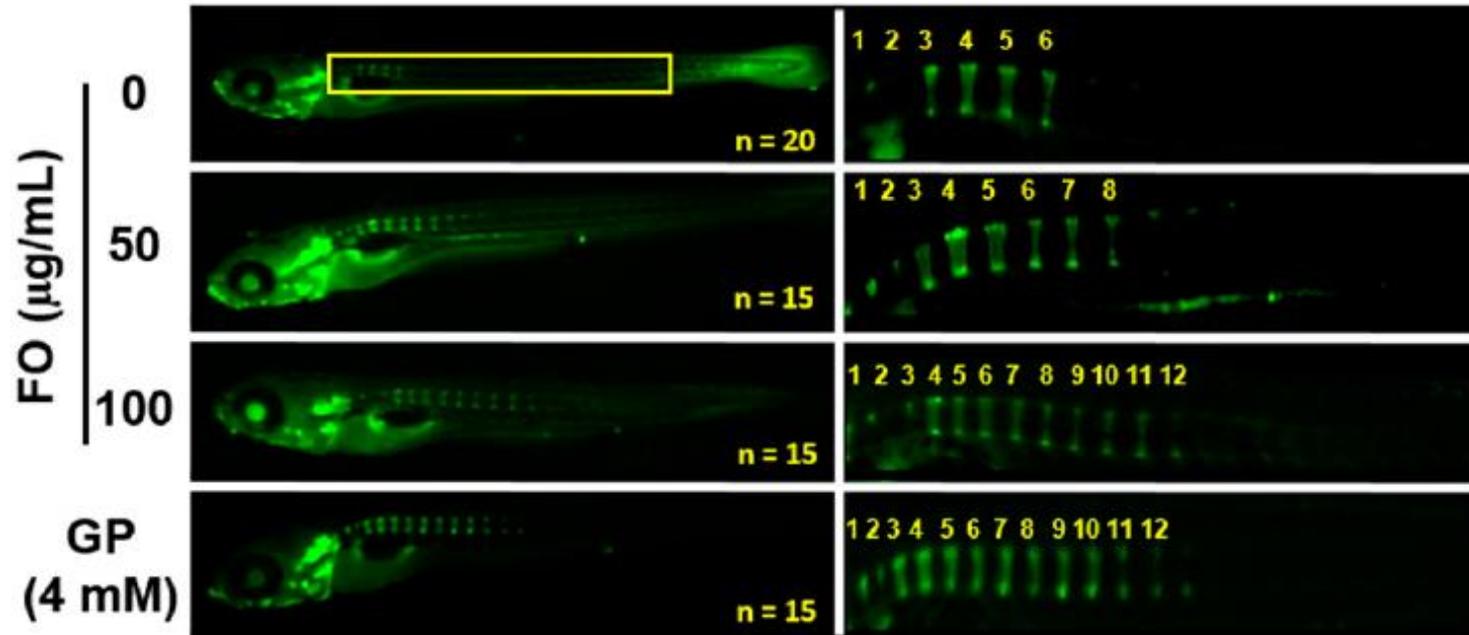
# 3-1. Promotion of Bone Formation : IN-VITRO

## FO inactivates GSK-3 $\beta$ through the IGF-1R signaling pathway



## 3-2. Promotion of Bone Formation : IN VIVO

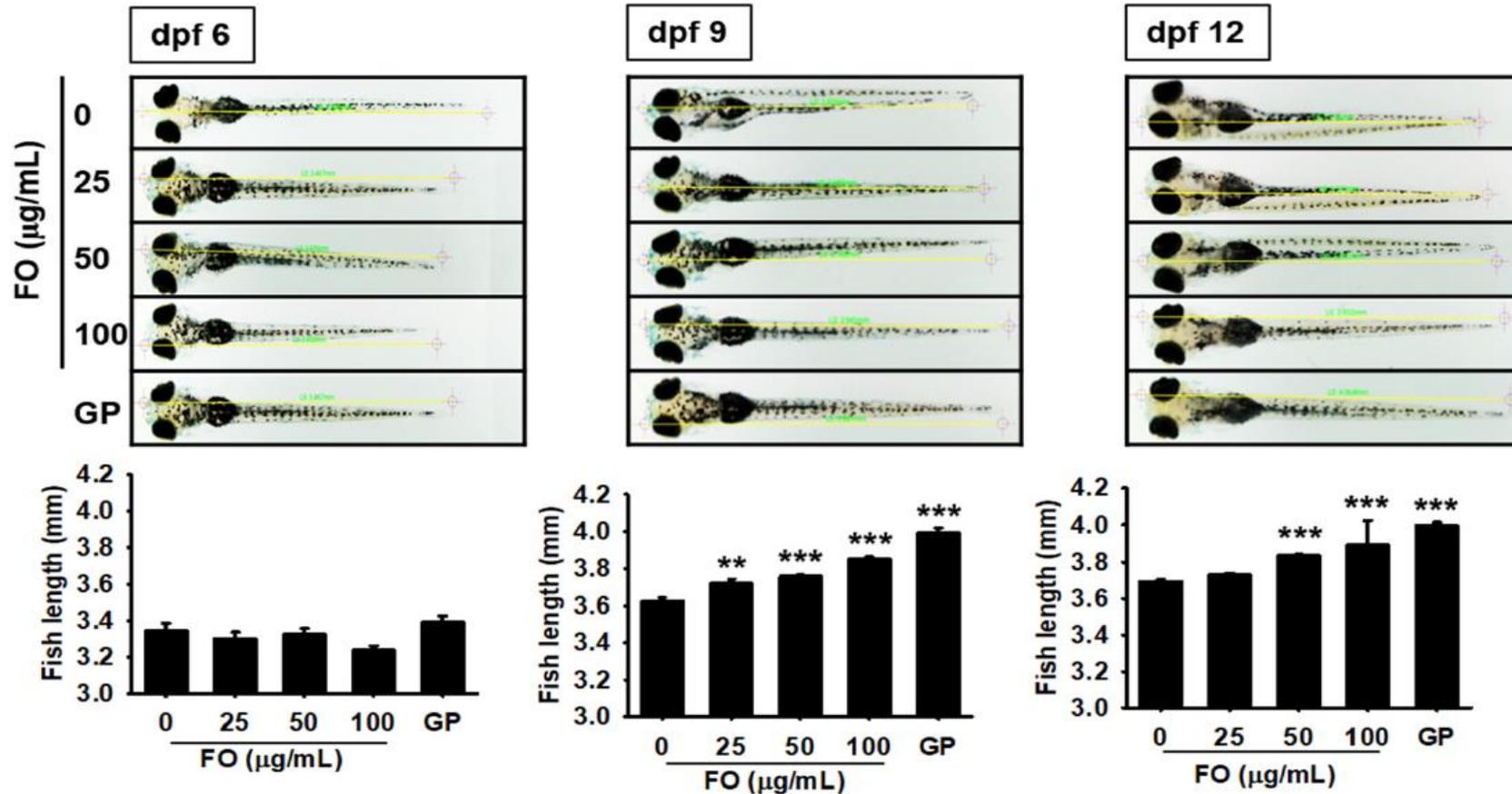
FO enhances bone formation by activating bone formation-promoting genes



β-glycerophosphate(GP)

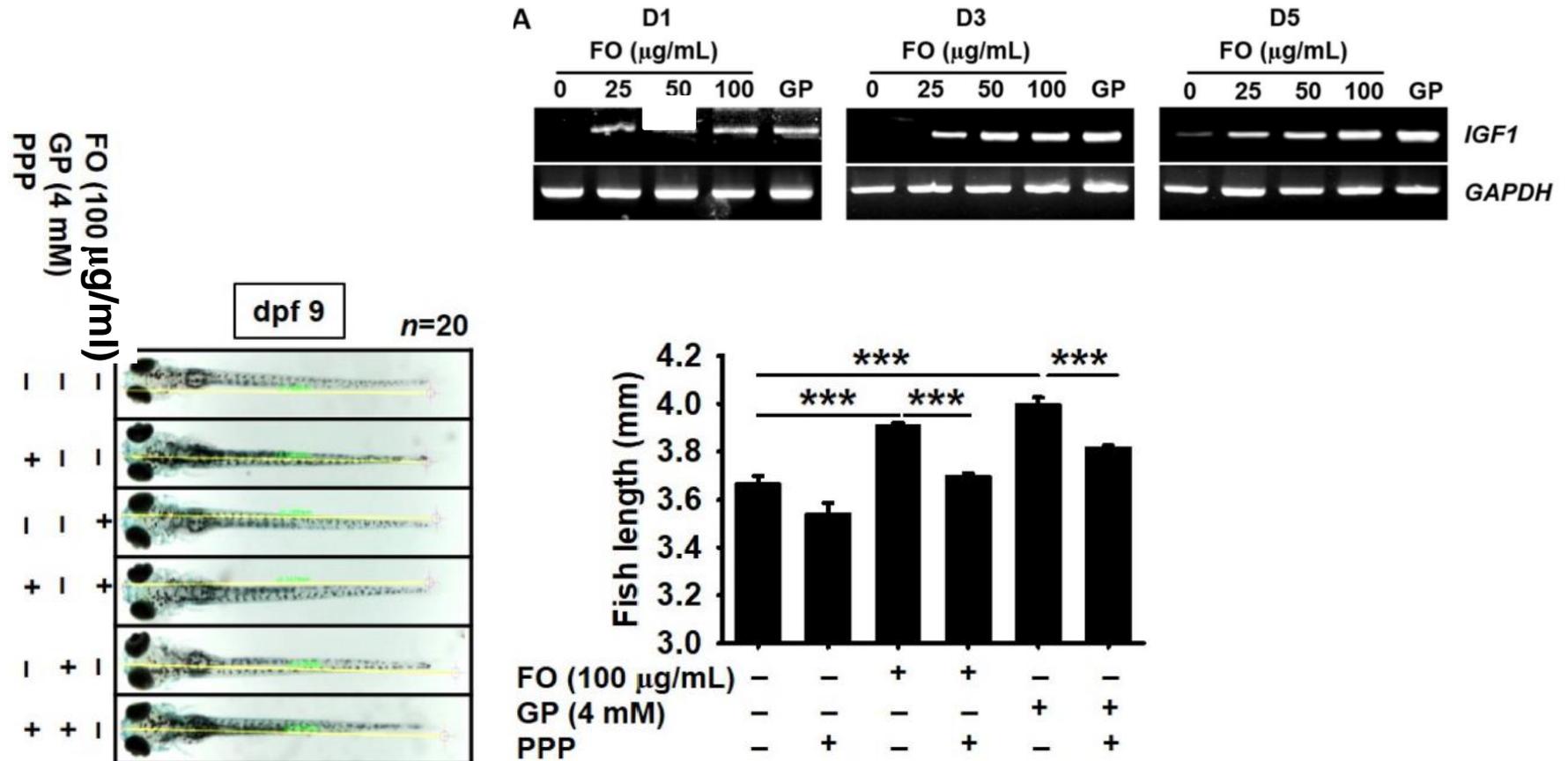
## 3-2. Promotion of Growth rate : IN VIVO

### FO promotes total growth rate in zebrafish larvae



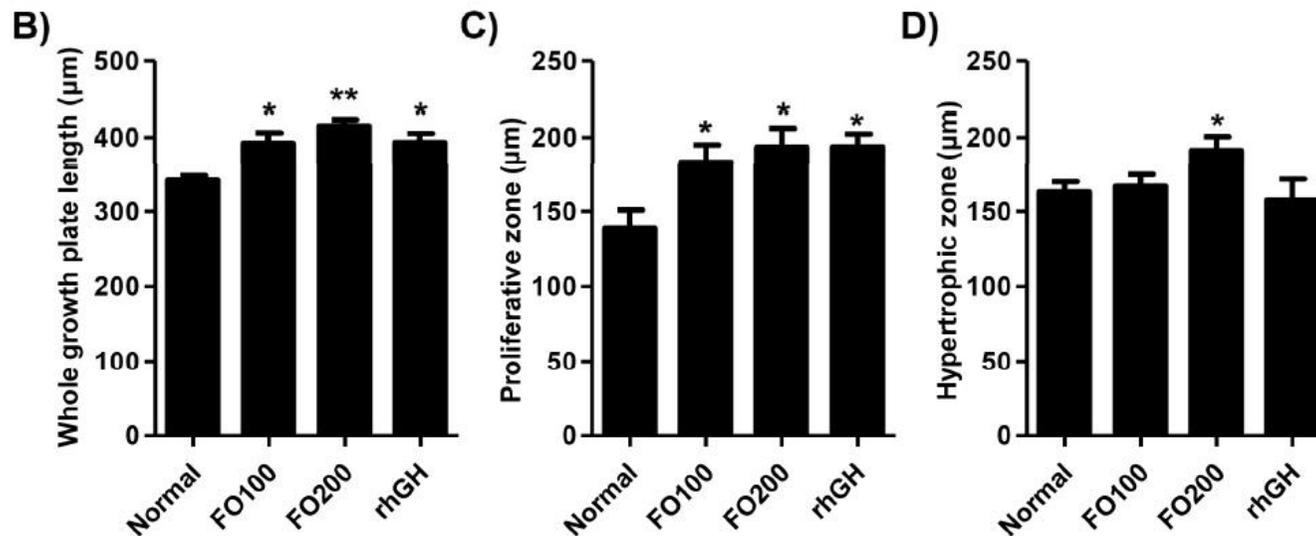
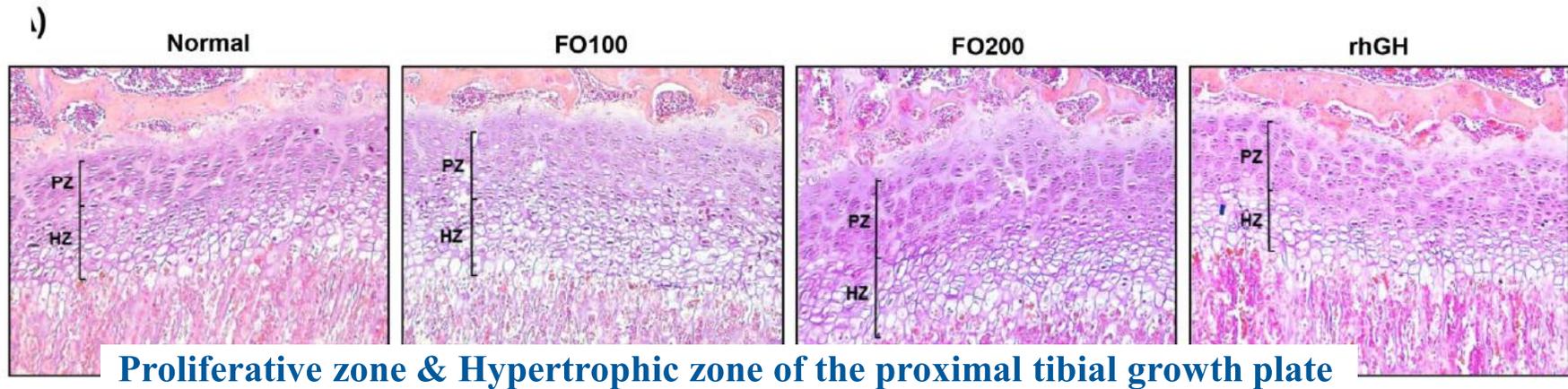
## 3-2. Promotion of Growth rate : IN VIVO

### FO induces bone formation and growth performance through the IGF-1R signaling pathway



## 3-2. Promotion of Growth rate : IN VIVO

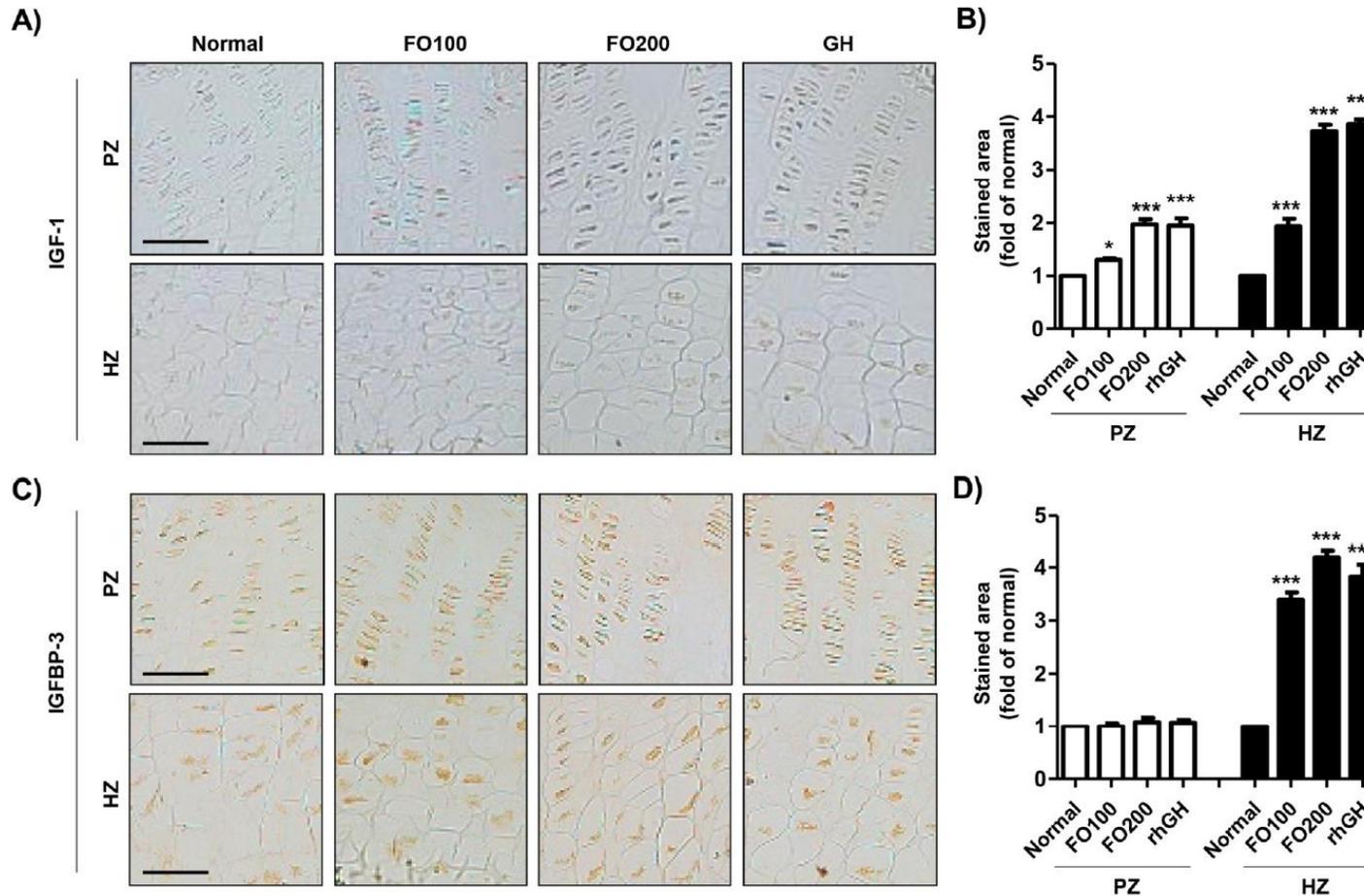
FO significantly increased the growth plate's total height compared to the normal group



## 3-2. Promotion of Growth rate : IN VIVO

**FO increased IGF-1 expression concentration dependently in both the proliferative and hypertrophic zones of the proximal tibial growth plate**

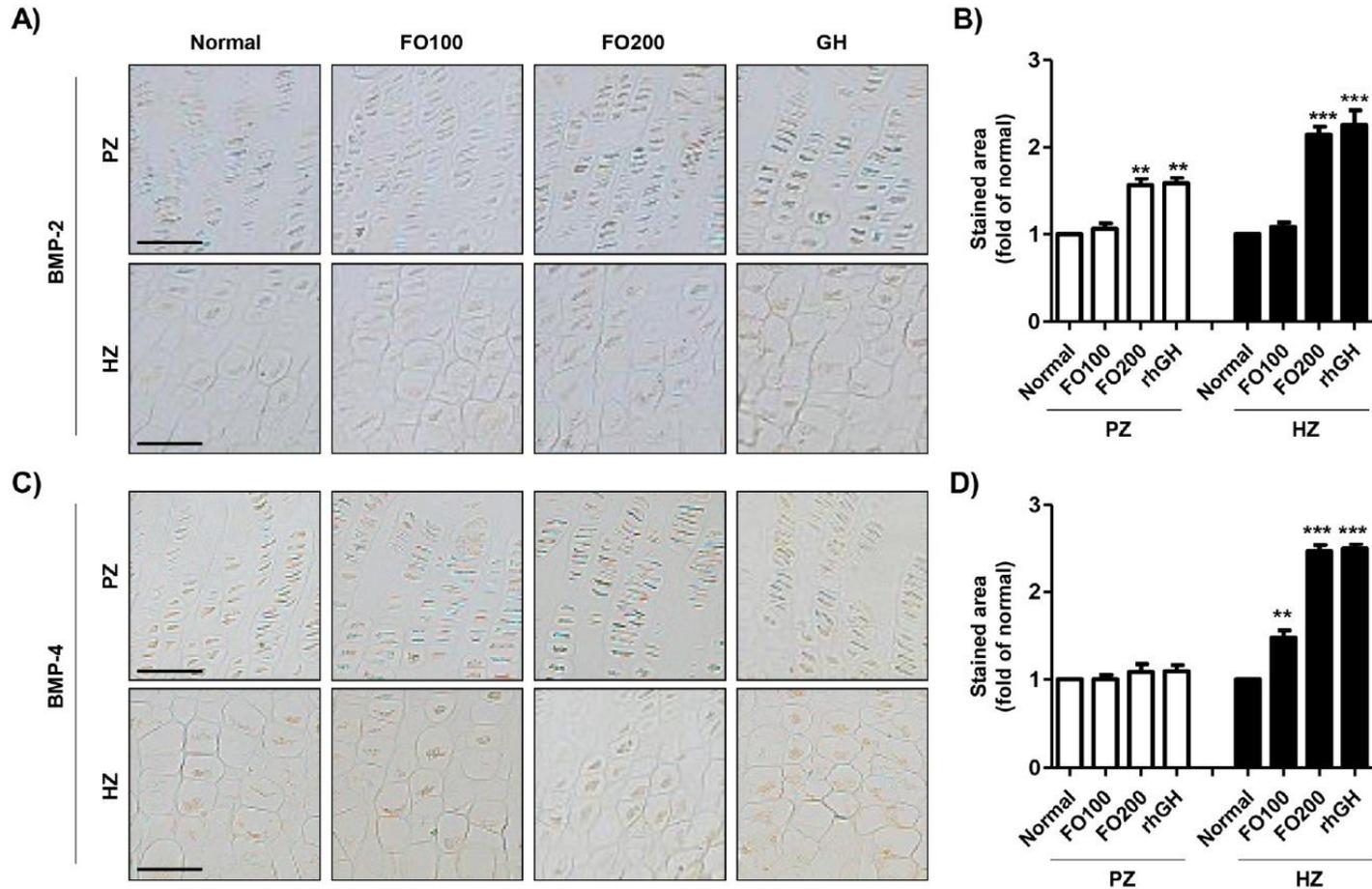
**The expression of IGFBP-3 in the hypertrophic zone was enhanced by FO administration**



## 3-2. Promotion of Growth rate : IN VIVO

The expression of BMP-2 was markedly increased by FO200 administration

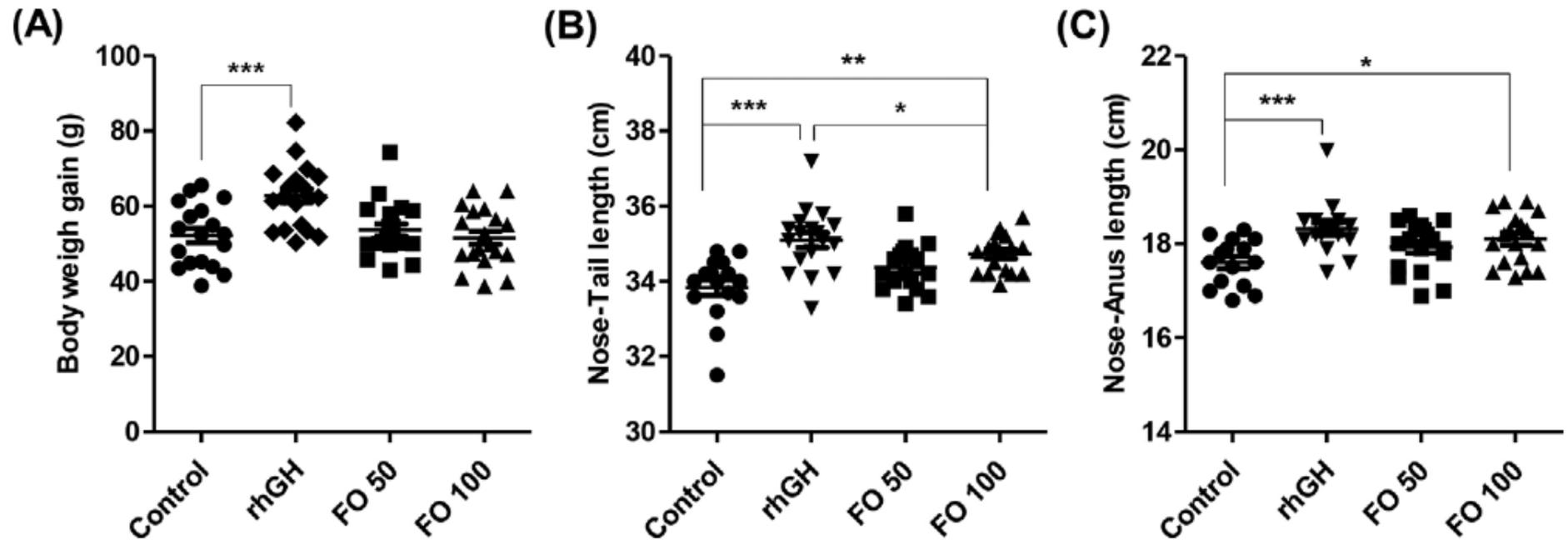
The expression of BMP-4 in the hypertrophic zone was enhanced by FO administration in a dose-dependent manner



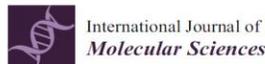
## 3-2. Promotion of Growth rate : IN VIVO

**FO promotes growth rate in SD rat**

**In the FO 100 group, the N-T length ( $p < 0.01$ ) and the N-A length ( $p < 0.05$ ) were significantly increased, respectively compared to the control group**



# PUBLISHED PAPERS



International Journal of  
*Molecular Sciences*



Article

## Protective Effects of Fermented Oyster Extract against RANKL-Induced Osteoclastogenesis through Scavenging ROS Generation in RAW 264.7 Cells

Jin-Woo Jeong <sup>1</sup>, Sung Hyun Choi <sup>2</sup>, Min Ho Han <sup>3</sup>, Gi-Young Kim <sup>4</sup>, Cheol Park <sup>5</sup>, Su Hyun Hong <sup>6,7</sup>, Bae-Jin Lee <sup>8</sup>, Eui Kyun Park <sup>9</sup>, Sung Ok Kim <sup>10</sup>, Sun-Hee Leem <sup>11</sup>, You-Jin Jeon <sup>4</sup> and Yung Hyun Choi <sup>6,7,\*</sup>



Article

## Fermented Oyster Extract Promotes Osteoblast Differentiation by Activating the Wnt/ $\beta$ -Catenin Signaling Pathway, Leading to Bone Formation

Ilandarage Menu Neelaka Molagoda <sup>1</sup>, Wisurumuni Arachchilage Hasitha Maduranga Karunaratne <sup>1</sup>, Yung Hyun Choi <sup>2</sup>, Eui Kyun Park <sup>3</sup>, You-Jin Jeon <sup>1</sup>, Bae-Jin Lee <sup>4</sup>, Chang-Hee Kang <sup>5</sup> and Gi-Young Kim <sup>1,\*</sup>



Article

## Fermented Oyster Extract Prevents Ovariectomy-Induced Bone Loss and Suppresses Osteoclastogenesis

Hye Jung Ihn <sup>1</sup>, Ju Ang Kim <sup>2</sup>, Soomin Lim <sup>2</sup>, Sang-Hyeon Nam <sup>2</sup>, So Hyeon Hwang <sup>2</sup>, Jiwon Lim <sup>2</sup>, Gi-Young Kim <sup>3</sup>, Yung Hyun Choi <sup>4</sup>, You-Jin Jeon <sup>3</sup>, Bae-Jin Lee <sup>5</sup>, Jong-Sup Bae <sup>6</sup>, Yeo Hyang Kim <sup>7</sup> and Eui Kyun Park <sup>2,\*</sup>

Integrative Medicine Research 9 (2020) 100412

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Integrative Medicine Research

journal homepage: [www.imr-journal.com](http://www.imr-journal.com)



Original Article

## Effect of fermented oyster extract on growth promotion in Sprague–Dawley rats



Hyesook Lee <sup>a</sup>, Hyun Hwang-Bo <sup>a</sup>, Seon Yeong Ji <sup>a</sup>, Min Yeong Kim <sup>a</sup>, So Young Kim <sup>a</sup>, Minji Woo <sup>b</sup>, Young-Sam Keum <sup>c</sup>, Jeong Sook Noh <sup>d</sup>, Joung-Hyun Park <sup>e</sup>, Bae-Jin Lee <sup>e</sup>, Gi-Young Kim <sup>f</sup>, Eui Kyun Park <sup>g</sup>, Young-Chae Chang <sup>h</sup>, You-Jin Jeon <sup>f</sup>, Yung Hyun Choi <sup>a,\*</sup>



Article

## Fermented Oyster Extract Promotes Insulin-Like Growth Factor-1-Mediated Osteogenesis and Growth Rate

Ilandarage Menu Neelaka Molagoda <sup>1</sup>, Jayasingha Arachchige Chathuranga Chanaka Jayasingha <sup>1</sup>, Yung Hyun Choi <sup>2</sup>, Eui Kyun Park <sup>3</sup>, You-Jin Jeon <sup>1</sup>, Bae-Jin Lee <sup>4</sup> and Gi-Young Kim <sup>1,\*</sup>



Article

## Gamma Aminobutyric Acid-Enriched Fermented Oyster (*Crassostrea gigas*) Increases the Length of the Growth Plate on the Proximal Tibia Bone in Sprague-Dawley Rats

Hyesook Lee <sup>1,2</sup>, Hyun Hwangbo <sup>1,3</sup>, Seon Yeong Ji <sup>1,2</sup>, Min Yeong Kim <sup>1,2</sup>, So Young Kim <sup>1,3</sup>, Da Hye Kim <sup>1,4</sup>, Su Hyun Hong <sup>1,2</sup>, Su Jeong Lee <sup>5</sup>, Freshet Assefa <sup>5</sup>, Gi-Young Kim <sup>6</sup>, Eui Kyun Park <sup>5</sup>, Joung-Hyun Park <sup>7</sup>, Bae-Jin Lee <sup>7</sup>, You-Jin Jeon <sup>6</sup> and Yung Hyun Choi <sup>1,2,\*</sup>

### 3-3. CHILD HEIGHT GROWTH EFFECT : CLINICAL TRIAL

- **DESIGN** : A randomized, placebo-controlled trial approved by the IRB of the Pusan National University Korean Medicine Hospital(PNUKHIRB-2019002)
- **TARGET** : Children with stature in the 25<sup>th</sup> percentile by age(age of 6-11 years)

- **CHARACTERISTICS OF PARTICIPANTS** :

	Control (n=50)	FO Group (n=50)
Age (years)	8.30±1.64	8.58±1.79
Height (cm)	124.14±9.26	126.17±10.61
Weight (kg)	25.12±5.31	27.28±6.50

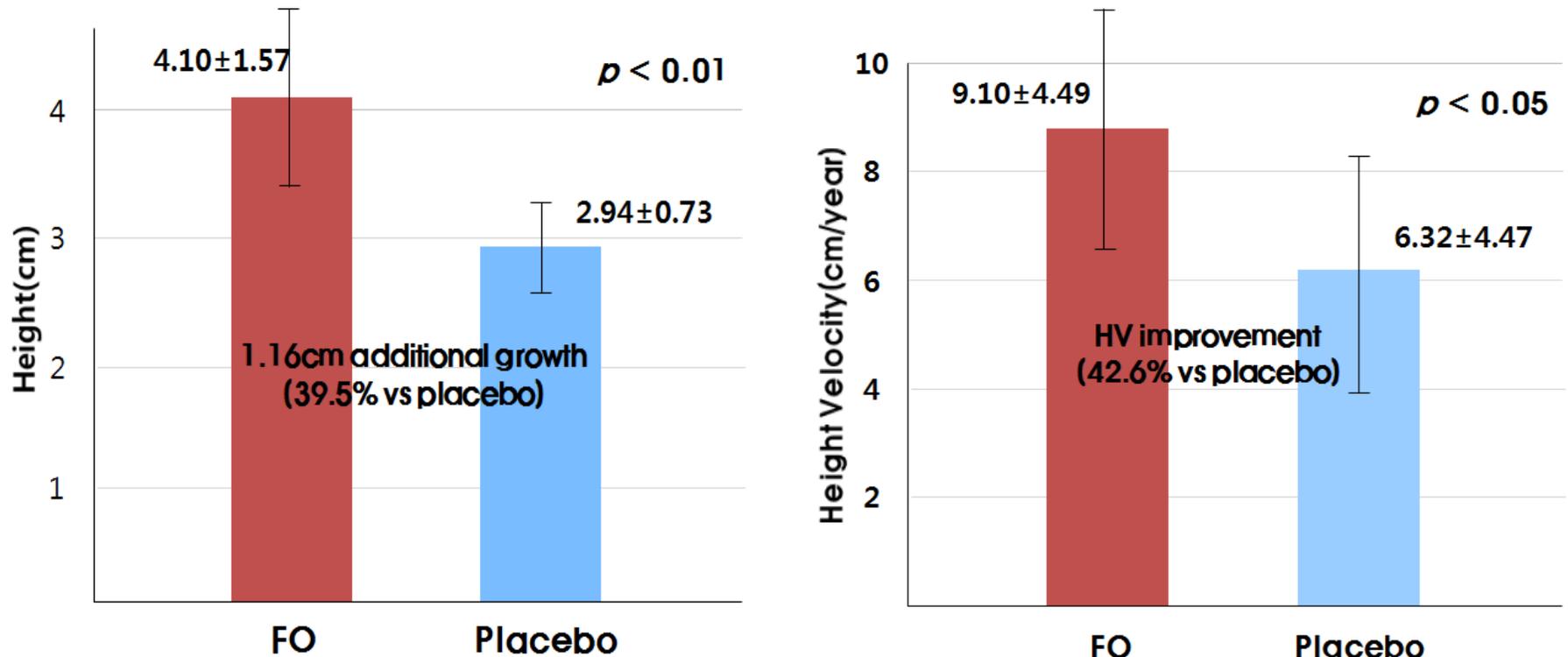
Most of the demographic data, except gender didn't significantly differ at the baseline between the two groups. Values are means ± SD.

- **ADMINISTRATION** : FO(n=50) or Control(n=50) groups were administered one time per day for 24weeks
- **DOSAGE** : 500 mg FO per day (1 stick orally once daily before bedtime)

### 3-3. CHILD HEIGHT GROWTH EFFECT : CLINICAL TRIAL

FO showed a significant increase in height gain compared with the placebo ( $p = 0.004$ ).

The mean difference in the pre and post-change of HV in the FO was significantly increased compared with the placebo at the 24th week from the baseline.

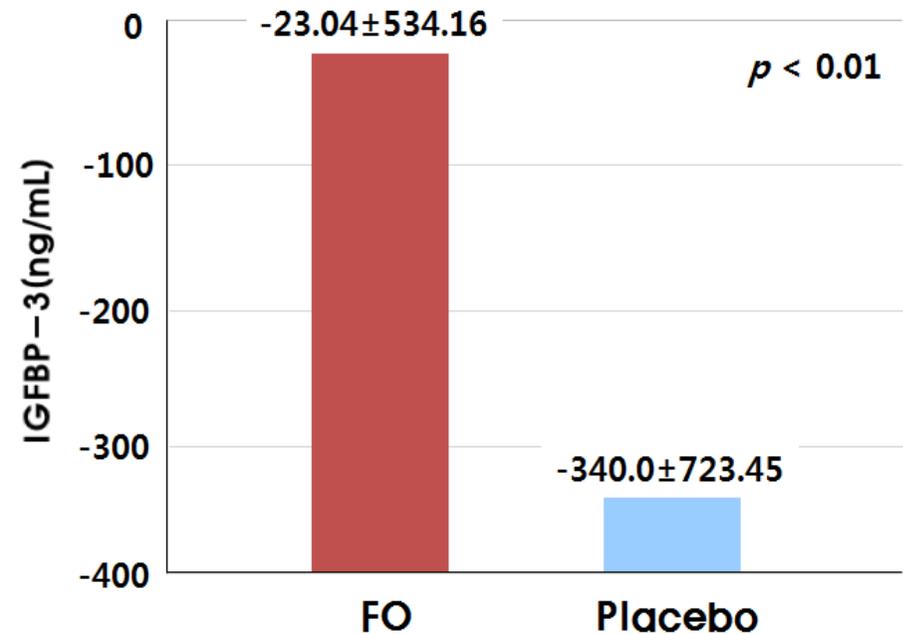
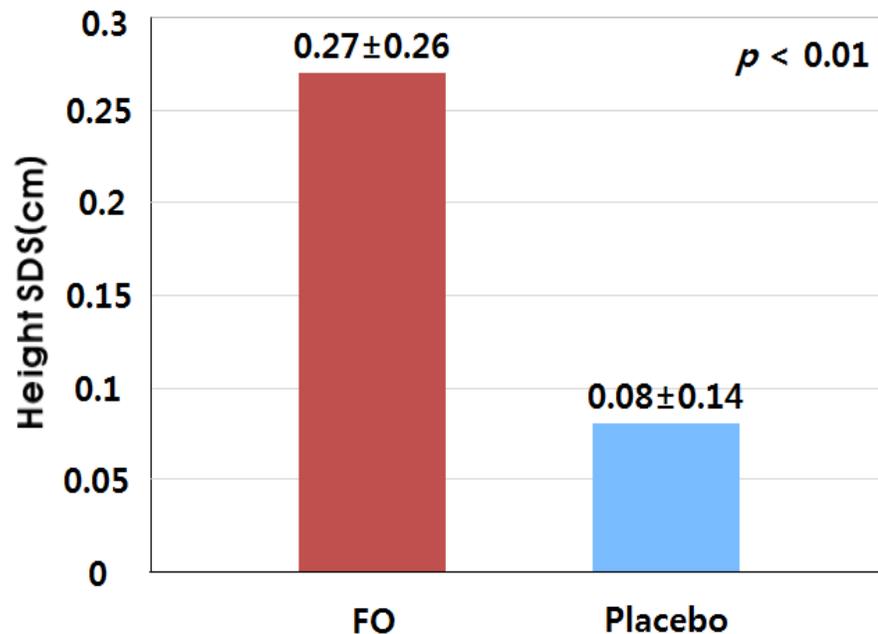


○ Reference : A randomized, placebo-controlled trial Report of Pusan National University Korean Medicine Hospital (PNUKHIRB-017, 2020.06.09); Integrative Medicine Research, 2020, 100691.

### 3-3. CHILD HEIGHT GROWTH EFFECT : CLINICAL TRIAL

The height SDS was significantly increased in the FO compared with the placebo ( $p < 0.01$ ).

The serum IGFBP-3 level showed a significant difference between the two groups. The decrease in the IGFBP-3 level in the FO was less than that in the placebo.



○ Reference : A randomized, placebo-controlled trial Report of Pusan National University Korean Medicine Hospital (PNUKHIRB-017, 2020.06.09); Integrative Medicine Research, 2020, 100691.



Original Article

## Efficacy and safety of fermented oyster extract for height of children with short stature: a randomized placebo-controlled trial

Aram Jeong <sup>a</sup>, Beom-Chan Park <sup>b</sup>, Hee-Yeon Kim <sup>c</sup>, Jun-Yong Choi <sup>d</sup>,  
Jinhong Cheon <sup>b,c</sup>, Joung-Hyun Park <sup>e</sup>, Bae-jin Lee <sup>e</sup>, Kibong Kim <sup>b,c,\*</sup>

<sup>a</sup> Department of Korean Pediatrics, School of Korean Medicine, Gachon University, Seongnam 3, Republic of Korea  
<sup>b</sup> Department of Korean Pediatrics, School of Korean Medicine, Pusan National University, Yangsan, Republic of Korea  
<sup>c</sup> Department of Korean Pediatrics, Korean Medicine Hospital, Pusan National University, Yangsan, Republic of Korea  
<sup>d</sup> Department of Internal Medicine, School of Korean Medicine, and Korean Medicine Hospital of Pusan National University, Yangsan, Republic of Korea  
<sup>e</sup> Marine Bioprocess Co. Ltd., Busan, Republic of Korea

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RCT  
Height  
Short stature

ABSTRACT

**Background:** Some experimental studies have established the effect of oysters on the promotion of body growth. Yet, there is a lack of human clinical studies. The objective of this study was to evaluate the effect of a fermented oyster (FO) extract on the increase in the height of children with stature in the 25th percentile by age.  
**Methods:** In total, 100 children (6–11 years old) were randomly divided into two (FO or control) groups. For 24 weeks, the subjects in the FO group took the FO extract once daily before sleeping, whereas the control group took placebo extracts, simultaneously. We evaluated the height gain, height velocity (HV), height standard deviation score (SDS), urine deoxyypyridinoline (DPD), growth hormone (GH), insulin-like growth factor (IGF-1), and IGF binding protein 3 (IGFBP-3).  
**Results:** The height gain and height SDS were significantly higher in the FO group than in the placebo group after 24 weeks (height gain:  $p < 0.001$ , height SDS:  $p < 0.005$ ). The HV was also significantly higher in the FO group than in the placebo group after the 6th and 24th week ( $p = 0.001$ ,  $p = 0.004$ ). After 24 weeks, we observed a decrease in GH, IGF, and IGFBP-3 in both groups. However, serum IGFBP-3 level in the FO group reduced less than placebo group.  
**Conclusion:** FO supplementation may help to increase the height of children, and the effect might be mediated via effects on the IGFBP-3 levels.  
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1. Introduction

Complex environmental factors, including heredity and nutrition, affect the increase in height in children.<sup>1</sup> Short stature is defined as a height that is more than two standard deviations (SD) below the mean, which is near the third percentile.<sup>2</sup> However, children in a range that does not correspond to short stature receive growth hormone (GH) treatment because of the increasing interest in height in pediatrics and socio-economic development.<sup>3</sup>

For more than fifty years, GH treatment has been prescribed to

been reports of several adverse effects such as rash and pain at the injection site, pre-pubertal gynecomastia, arthralgia.<sup>5</sup> Additionally, GH treatment during the pre-pubertal period does not affect the final adult height compared to that of untreated children.<sup>6</sup>

According to Bonchogangmok (a Chinese book published in 1596), oysters are reported to be effective in removing dampness and phlegm in body, so they have been widely used for the treatment of furuncle, hyperhidrosis and stress.<sup>7</sup> Oysters have been known to promote bone generation because of their high calcium content.<sup>8</sup> Several studies have indicated the effects of oys-

## 발효굴추출물의 경구 섭취가 소아 신장 성장에 미치는 효과 및 안전성 평가를 위한 무작위배정, 이중눈가림, 위약 대조 인체적용시험: 인체적용시험 프로토콜

김희연<sup>1,5</sup> · 박범찬<sup>1,5</sup> · 천진홍<sup>1,5</sup> · 최준용<sup>2,5</sup> · 안병민<sup>3</sup> · 박정현<sup>4</sup> · 이배진<sup>4</sup> · 김기봉<sup>1,5,\*</sup>

<sup>1</sup>부산대학교한방병원 한방소아과, <sup>2</sup>부산대학교한방병원 한방내과, <sup>3</sup>제너러론바이오텍,  
<sup>4</sup>제이랩바이오프로세스, <sup>5</sup>부산대학교 한의학전문대학원

Abstract

### Randomized, Double-blind, and Placebo-controlled a Human Study for Growing of Stature via the Analysis of Effect of Ferment Oyster Extract: Study Protocol

Kim Hee-Yeon<sup>1,5</sup> · Park Beom-Chan<sup>1,5</sup> · Cheon Jin-Hong<sup>1,5</sup> · Choi Jun-Yong<sup>2,5</sup> ·  
An Byeong-Min<sup>3</sup> · Park Joung-Hyun<sup>4</sup> · Lee Bae-Jin<sup>4</sup> · Kim Kibong<sup>1,5,\*</sup>

<sup>1</sup>Department of Korean Pediatrics, Pusan National University Korean Medicine Hospital  
<sup>2</sup>Department of Korean Internal Medicine, Pusan National University Korean Medicine Hospital  
<sup>3</sup>General Biotech, <sup>4</sup>Marine Bioprocess Co. Ltd.  
<sup>5</sup>School of Korean Medicine, Pusan National University

Objectives

The purpose of this study is to confirm the efficacy and safety of the treatment of with fermented oyster extract on height growth in children with short stature.

Methods

A total of 100 people, between 6 and 11 years old, will be participated in a randomized, double-blind, and placebo-controlled human study. The fermented oyster group will take 500 mg of fermented oyster extract once a day for 24 weeks. The placebo group will take 3400 mg of fructooligosaccharide as placebo once a day for 24 weeks. The outcomes of the intervention will be measured at the baseline, 6 week, 12 week, 18 week, and 24 week. The primary outcome is the changes in height from the baseline. The secondary outcomes are growth rate, height SDS, bone age, GH, IGF-1, IGFBP-3, osteocalcin, BALP, DPD, and LH.

Results

This trial was approved by the institutional review board of Pusan National University Korean Medicine Hospital (registry number: PNUKH-HRB-2019002). Recruitment of the research participants will be opened from May 2019 till December 2019.

Conclusions

This study will provide clinical information to determine the efficacy and safety of the treatment with fermented oyster extract on height growth in children with short stature

## **IV. APPENDIX**

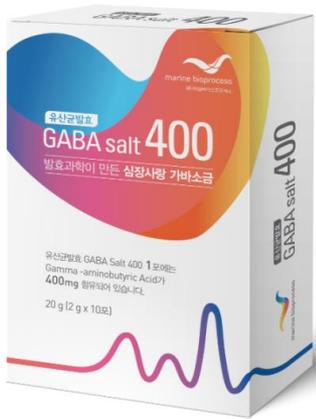
## 4-1. PATENTS

Status		Title	REG No
IPs	Application	<b>Composition for height growth comprising fermented oyster extract</b>	10-2020-0149129
	Registration	<b>COMPOSITION FOR IMPROVING BONE HEALTH, INCLUDING FUNCTIONAL FERMENTED MATERIAL USING OYSTERS</b>	10-2132862
	Registration	Composition for prevention and treatment of muscular disorders or improvement of muscular functions comprising functional fermented material using oyster	10-2136886
	Registration	<b>COMPOSITION FOR IMPROVING BONE HEALTH, INCLUDING FUNCTIONAL FERMENTED MATERIAL USING OYSTERS</b>	EP.19180523.A
	Application	<b>COMPOSITION FOR IMPROVING BONE HEALTH, INCLUDING FUNCTIONAL FERMENTED MATERIAL USING OYSTERS</b>	JP.2019111568.A
	Application	<b>COMPOSITION FOR IMPROVING BONE HEALTH, INCLUDING FUNCTIONAL FERMENTED MATERIAL USING OYSTERS</b>	US.201916441131.A

## 4-2. PUBLISHED PAPER LIST

No.	TITLE	JORNAL	Year	SCI(E)
1	Fermented Oyster Extract Promotes Osteoblast Differentiation by Activating the Wnt/ $\beta$ -Catenin Signaling Pathway, Leading to Bone Formation	Biomolecules	2019	SCIE
2	Fermented Oyster Extract Promotes Insulin-Like Growth Factor-1-Mediated Osteogenesis and Growth Rate	Marine Drugs	2020	SCIE
3	Gamma Aminobutyric Acid-Enriched Fermented Oyster ( <i>Crassostrea gigas</i> ) Increases the Length of the Growth Plate on the Proximal Tibia Bone in Sprague-Dawley Rats	Molecules	2020	SCIE
4	Effect of fermented oyster extract on growth promotion in Sprague–Dawley rats	Integrative Medicine Research	2020	SCIE
5	Efficacy and safety of fermented oyster extract for height of children with short stature: a randomized placebo-controlled trial	Integrative Medicine Research	2020	SCIE
6	Protective Effects of Fermented Oyster Extract against RANKL-Induced Osteoclastogenesis through Scavenging ROS Generation in RAW 264.7 Cells	International Journal of Molecular Science	2019	SCIE
7	Randomized, Double-blind, and Placebo-controlled a Human Study for Growing of Stature via the Analysis of Effect of Ferment Oyster Extract: Study Protocol	J Pediatr Korean Med	2019	KCI

# Lactic acid bacteria fermentation Lacto **GABA(10%)** Salt (Probiotics Alive & Not ) Proposal



# Fermentation(Lacto)GABA Salt, WHY ?

IT/의학

## [토요이슈]"천일염, 정제염, 재제염... 그 소금이 그 소금"

Microplastic detection in all commercial salts

시판 모든 소금에서 미세플라스틱 검출 '충격'

목포대 연구팀 6종 분석결과 국내외제품 모두 검출  
갯벌 심층에서도 나와, 인도 소금에서도 대부분 검출

Unconditional low-salt diet? A little salty in summer, less than 5g in other seasons

## 무조건 저염식? 여름엔 조금 짜게, 다른 계절엔 하루 5g 이내로

입력 : 2019-06-16 17:38 | 수정 : 2019-06-17 01:37

'양날의 검' 소금, 건강한 섭취법

The secret of excessive salt intake "Serotonin"

## 과도한 소금 섭취의 비밀 '세로토닌'

2020.02.11. 10:24



**편당성공**  
111 %달성  
5,554,700 원 판매  
74 명의 시포터

나트륨을 낮춰주는 천연 만능 72발효소금  
서울산업진흥원 펙티브와 함께합니다.

목표 금액 5,000,000원 | 판매기간 2017.10.17-2017.11.10  
100% 이상 오려면 판매에 성공하는 프로젝트  
이 프로젝트는 판매 마감일까지 목표 금액에 100% 오르지 않으면 판매가 진행되지 않습니다.

프로젝트 스토리

나트륨을 낮춰주는 천연 만능 72발효소금을 소개합니다.



## REAL Fermentation ? Safe?

## Let's relieve stress with cooking 요리로 스트레스를 해소하자



스타 셰프들이 스트레스 해소를 위해 '집에서 만들어 먹는 음식 9'

건강한 식단 | 건강한 요리법 | 쉬운 요리법 | 다이어트 요리법 | 음식 요리법 | 건강한 야



# Salt: It is essential to sustain life, **warning WHY?**

세계의 소금 특별전  
Special Exhibition 'Salt of the World'

소금 없이 살 수 없는 인간  
Humans who cannot live without salt

**호모 소금 사피엔스**  
Homo Salinus Sapiens  
Salt, the Source of Human Wisdom

소금을 가진 지혜의 인간

하루에 필요한 소금의 양, **3g이면 충분!**  
3 grams of salt needed per day is enough



Message du Chef

Salt flavors and pepper influences mood  
**소금은 맛을 내고 후추는 기분을 좌우한다.**

가장 큰 비밀은 가장 작은 소금이었고  
가장 큰 영향을 주는 것은 몇 알의 후추였다.

백년 면역력을 기우는

**짠맛의 힘**

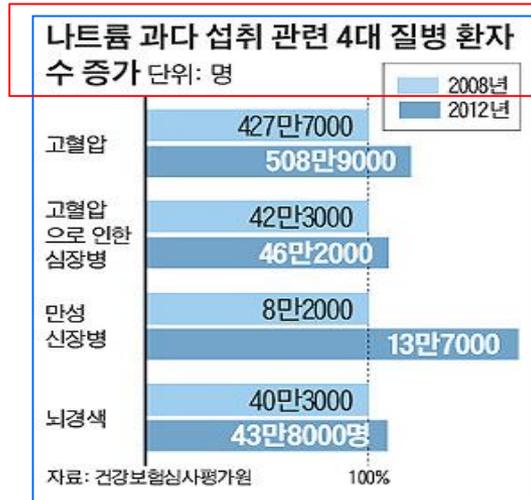
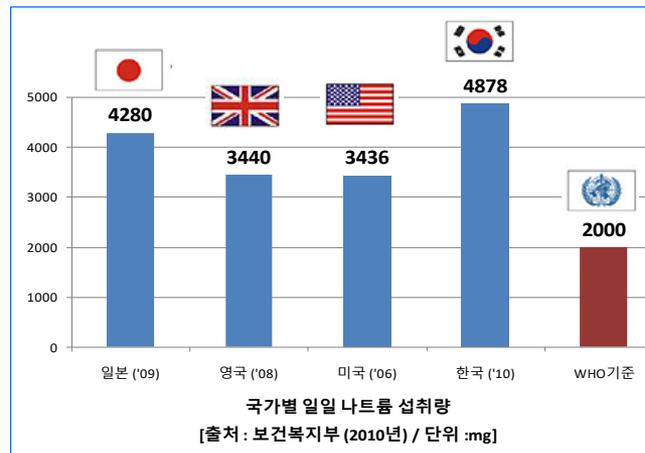
원인 모를 염증과 만성질환에서 탈출하는 최상의 소금 사용설명서

Increasing number of patients with four diseases associated with excessive sodium intake

소금 적게 먹으면 심혈관질환 발생  
적당한 소금을 섭취하는 것이 중요  
Eating less salt causes cardiovascular disease

인체 내 나트륨의 역할

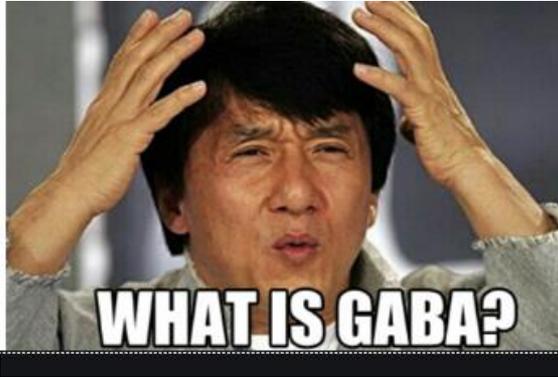
- 신진대사 촉진
- 신경통의 전달
- 지방과 당분기스의 흡착과 배설
- 소화 작용
- 근육의 수축
- 산소와 영양물질을 세포 내로 이동





# What is GABA?

## GABA (Gamma-Amino Butyric Acid ): 비단백질성 아미노산



Approved by the Korean Food and Drug Administration  
Individual recognition approval (Lotte Shopping)  
Helps improve blood pressure

**GABA-containing powder derived from L-glutamic acid (GABA 20mg/day)**



Prevent hypertension diabetes



무농약 가바쌀 효녀밥상  
www.hyonyeo.com

갈색 쌀로 당뇨를 이겨냈다?

**'천기누설' GABA 편**

Brown rice helps lower blood pressure

가바 성분은 기억력 증진 혈당치 상승 억제  
혈압 저하에 도움을 준다는 갈색 쌀

본방송 천기누설 목요일 밤 11시

# GABA's International Journal Publications Other Efficacy Materials



**GABA**

Gamma-AminoButyric Acid

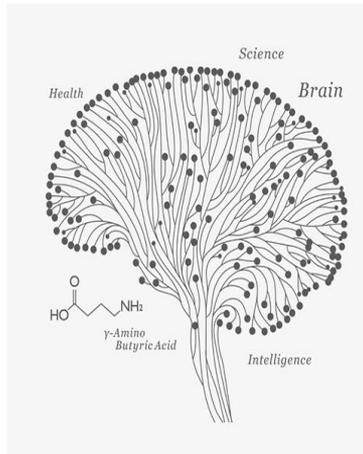
## '가바' 처음 들어 보셨다구요?

뇌 대사 향상, 의욕 저하 등의 치료에 사용되어 브레인푸드 Brain-food라고도 불리는 '가바GABA'는 뇌와 중추신경계의 중요한 억제성 신경전달물질로, 뇌의 대사와 순환 촉진작용을 한다고 알려져 있어요.

### 출처

임상동, 김기성, 한국식품연구원, GABA의 효능과 이용, 한국유기농기술과학회지, Vol. 27 No.1, pp. 45-51, 2009

임상약이연구회(민순, 이현수, 윤형운, 정은서 감수), 의학·간호 약어해설사전, 대광의학, 2016



미국, 유럽 등 선진국의 신경의학, 약리학 분야에서는 가바에 대한 임상연구가 활발하게 이루어지고 있어요. 최근 논문 몇가지만 소개해 드릴게요.

Let me introduce you to some recent papers.



## γ-Aminobutyric acid (GABA) administration improves action selection processes: a randomised controlled trial

Steenbergen L. et al., *Scientific Reports*, 2015 July 31; 5:12770

가바의 투여가 갑작스럽거나 복잡한 요구에 대한 수행력, 즉 **사고력과 직무 수행능력을 향상시켰다**는 연구 결과



## Oral intake of γ-aminobutyric acid affects mood and activities of central nervous system during stressed condition induced by mental tasks

Yoto A. et al., *Amino Acids*, 2012 Sep; 43(3):1331-7

가바 섭취 30분 경과 후, 가바를 투여한 그룹이 위조약(Placebo) 그룹에 비해 **스트레스가 물리적으로 더 완화**되었다는 연구 결과



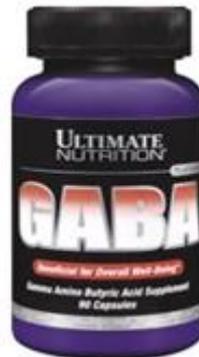
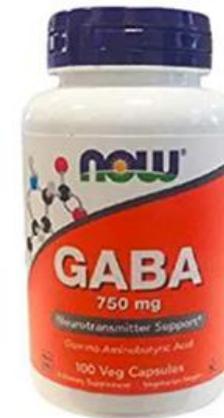
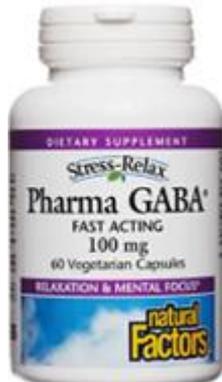
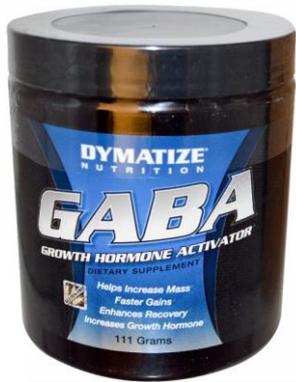
## GABA dramatically improves glucose tolerance in streptozotocin-induced diabetic rats fed with high-fat diet

Sohrabipour S. et al., *European Journal of Pharmacology*, 2018 May 5; 826:75-84

가바가 당뇨 쥐의 **혈당, 인슐린 레벨, IPGTT, ITT, 글루코겐 생성경로, 글루카곤 수용체, 체중 및 체지방을 개선**시켰다는 연구 결과

# Global market **GABA SUPPLEMENT** commercialization status

Efficacy in relieving stress, strengthening concentration, improving sleep, height and muscle growth

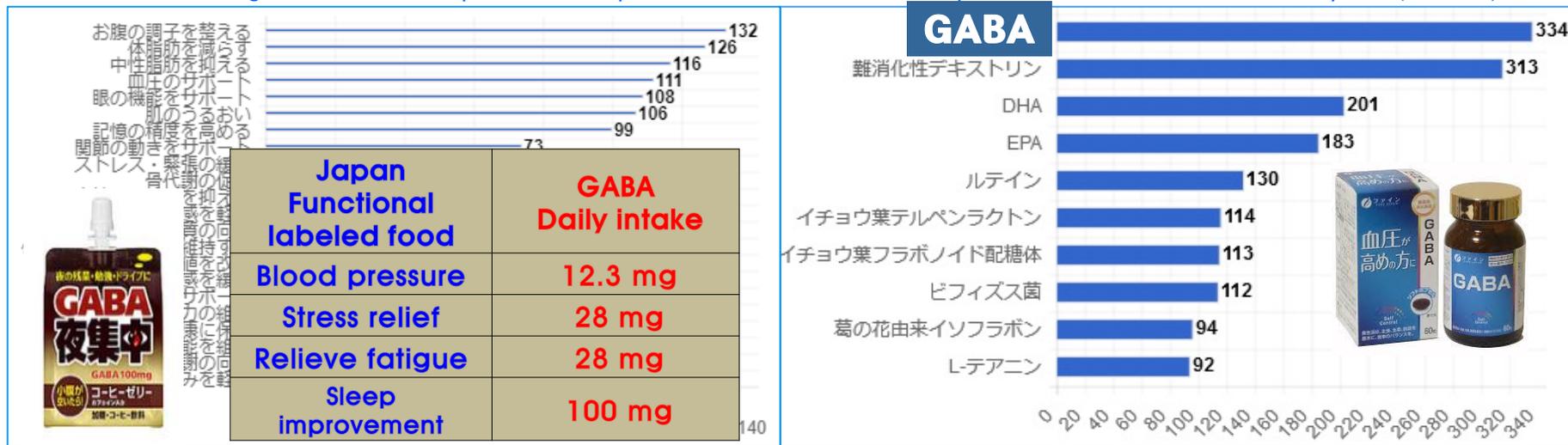


# Application of functional GABA materials in Korea / Japan

Korea Food and Drug Administration GABA material (individually recognized)  
functional ingredient approval status

Material name	Indicator material	Function	Intake (indicator substance/day)	Manufacturer (country)	right holder
Derived from L-glutamic acid GABA-containing powder	GABA	Blood pressure improvement	20mg	JAPAN	Lotte Shopping

Status of Involved Ingredients and acceptance of a report After Introduction of the Japanese Functional Labeled Food System (2020.04)



# Improved blood pressure containing GABA Current status of functional food labeling in Japan



전체보기 **시장동향** 수출입동향 무역장벽 안전성

08.02 2019 기능성 식품\_GABA가 들어간 야채들

현재 일본에서는 혈압을 낮추는 효과 등이 있는 「GABA」의 기능성 표시식품이 증가하고 있다. 여기에 비타민, 미네랄 등 영양소가 풍부하게 함유되어 있어 매일 식탁에 오르지만 판매 시에 그 효과를 전달하기는 어렵다. “GABA 함유”를 명확히 표시함으로써 야채의 소비확대를 꾀하고 있는 추세이다.

おむすびの GABA

지사 yes@at.or.kr

New リニューアル!

第1位

機能性表示食品

血圧が気になる方へ

食塩不使用 中華ドレッシング

化学調味料・保存料 無添加

日本初 ドレッシング

塩分削減 さらさら食味の GABAで 血圧を下げる

イチョウの健康効果 セサミンUP↑

黒酢の健康効果者 アミノ酸20種以上 体にうれしい必須アミノ酸が豊富に含まれる





# Current Status of Commercialized Foods Containing GABA in Korea



브레인 가바치 스테디메이트  
브레인 에너지 가바(GABA)로 만들어  
집중력 향상에 좋은 브레인 음료  
스튜디오 메이트



브레인 에너지 가바 충전으로  
집중력을 100% 끌어올리자

브레인 에너지  
가바 GABA

국내산  
100%

VST  
특허 추출방식



# manufacturing process and specifications

**Role of fermented lactic acid bacteria: high concentration GABA production + sodium reduction (10%) + probiotics**

Refined Sea Salt  
+  
Glucose  
Yeast Extract  
Glutamic Acid



*Lactobacillus 2 types*  
inoculation

Fermentation  
For 72Hrs

Sterilization  
Filtering

or

None  
Sterilization

Spray-drying  
Packing  
(powder)

or

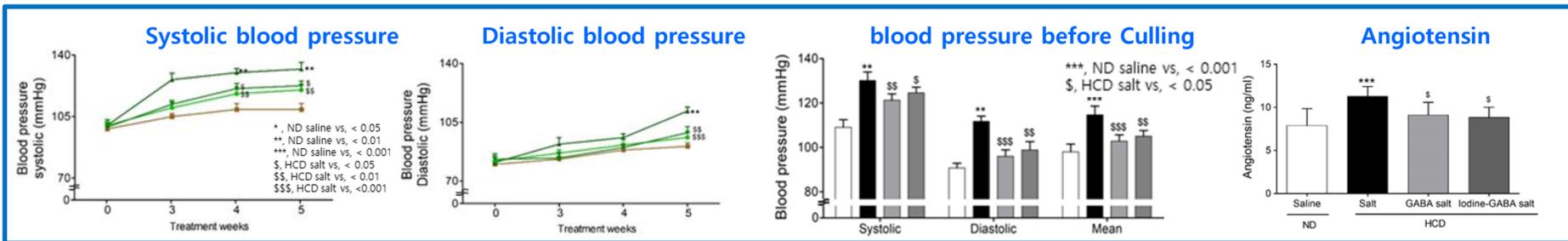
Concentration  
Packing  
(solution)

## Products OF Lacto GABA Salt

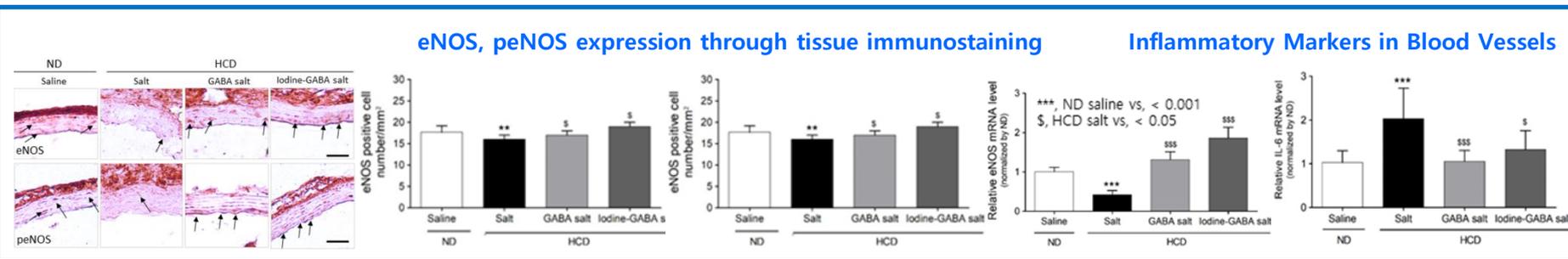
Name	Quality characteristics	Packaging (Formulation)	Remark
(生) Lacto GABA Salt FOB BUSAN \$40/kg	GABA>10%, Nacl>60%, Lactate>0.5% Probiotics Alive : log10 (CFU/g) over 4 Lactobacillus culture (dead cells): log10 (CFU/g) over 8	Powder Paper plastic bag (bulk) Bottle, PE, Stick Pouch	None MSG
Lacto GABA Salt FOB BUSAN \$35/kg	GABA>10%, Nacl>60%, Lactate>0.5% Lactobacillus culture (dead cells) : log10 (CFU/g) : over 9	Powder Paper plastic bag (bulk) Bottle, PE, Stick Pouch Solution(bulk) IBC Tank, Vinyl pack	None MSG
Low Na Lacto GABA Salt	GABA>10%, Nacl>60%, Lactate>0.5% Totally soluble in water	Powder Paper plastic bag (bulk) Bottle, PE, Stick Pouch Solution(bulk) IBC Tank, Vinyl pack	None MSG

## Blood Pressure Index Change

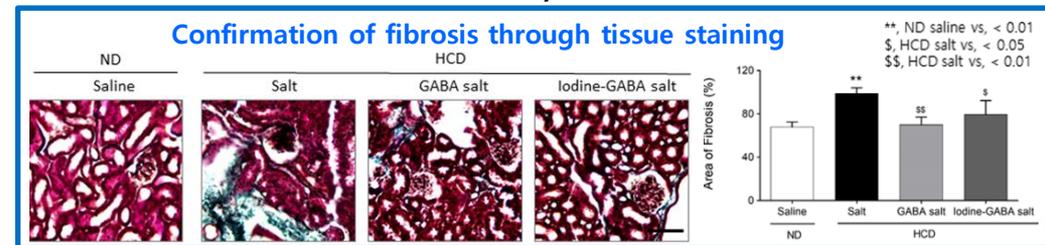
Gachon University team of Professor Byun



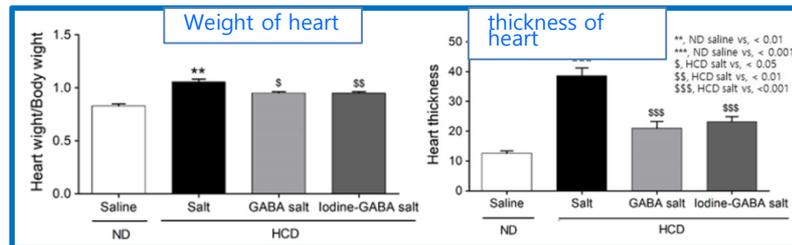
## Vascular and Inflammatory Markers



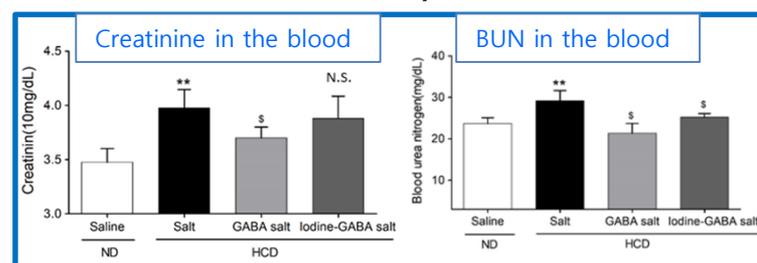
## Kidney structure



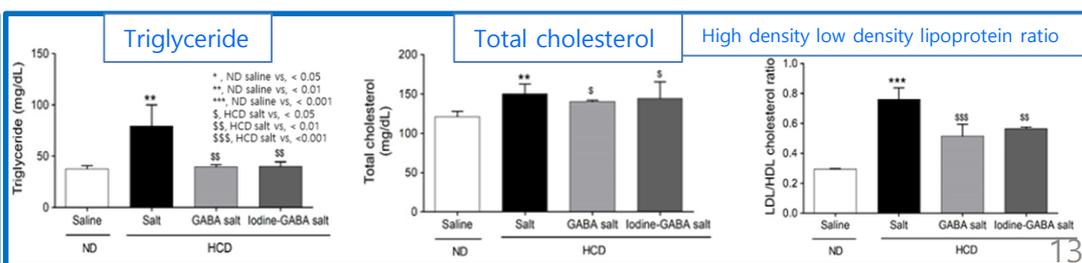
## Cardiac index



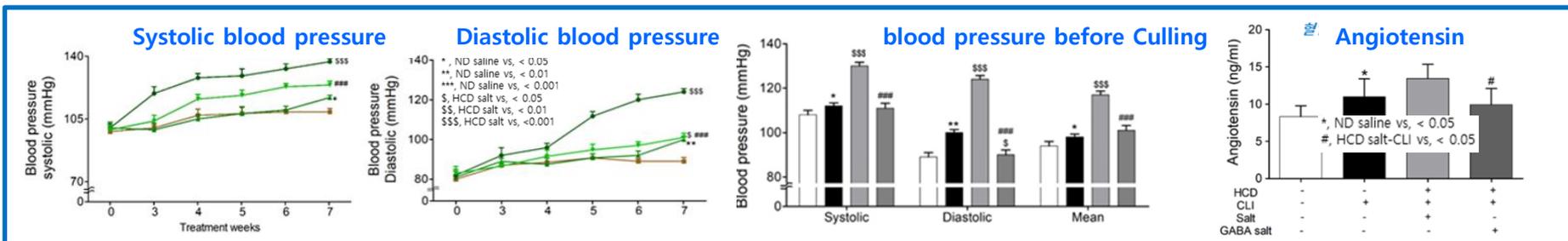
## Kidney Index



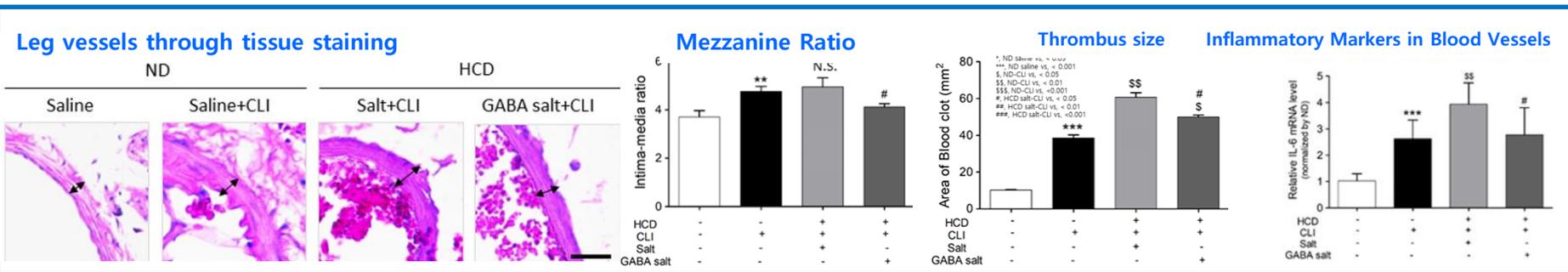
## Blood index



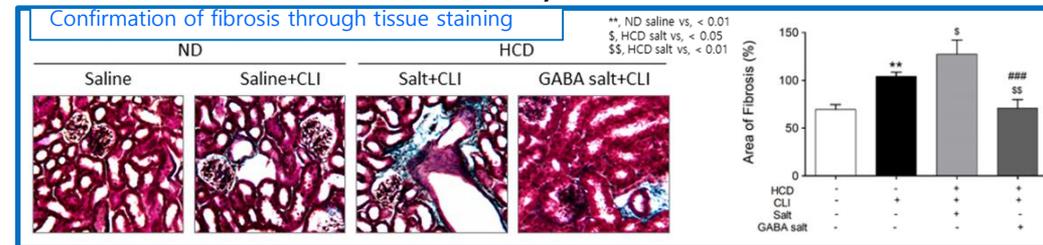
### Change of Blood Pressure Index



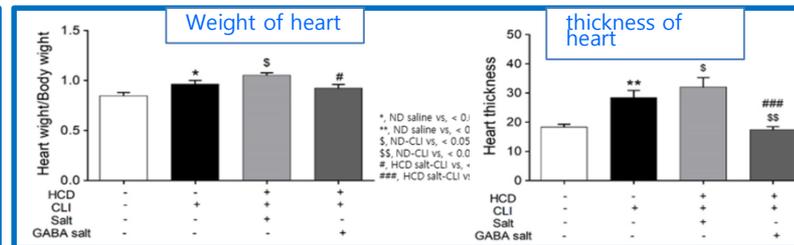
### Vascular and Inflammatory Markers



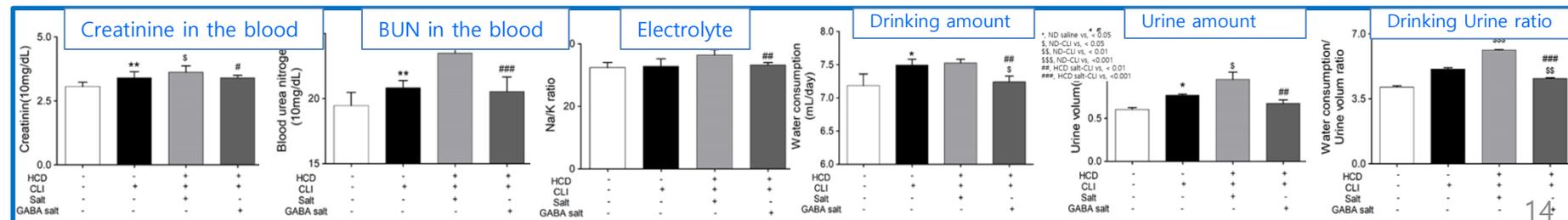
### Kidney structure



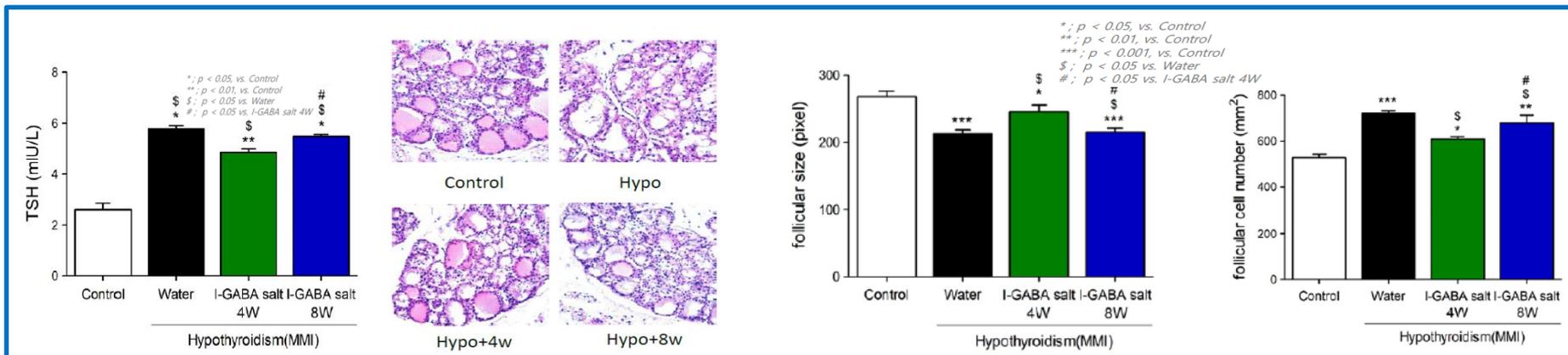
### Cardiac index



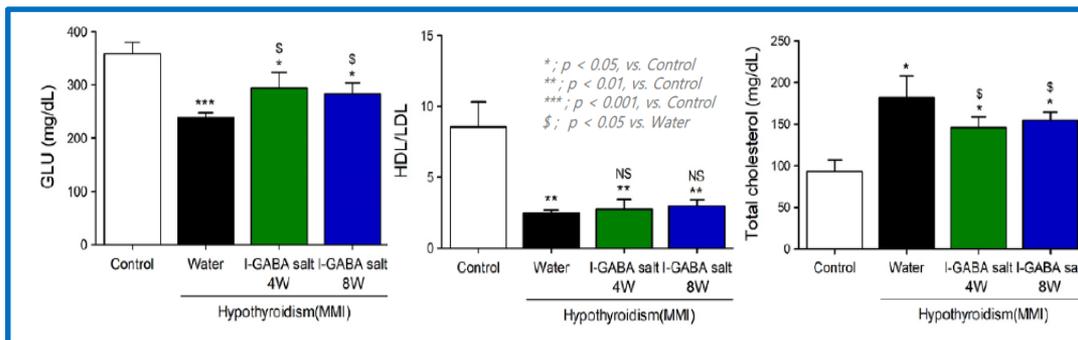
### Kidney indicators



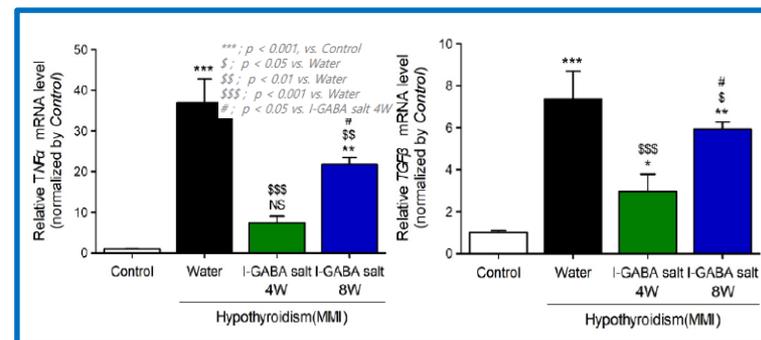
## Changes in thyroid indicators (hormones, cells, tissues)



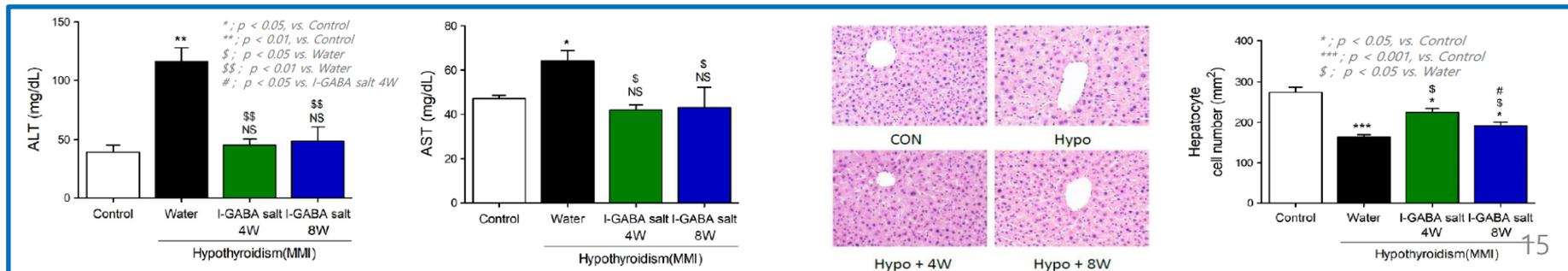
## Changes in blood indicators (blood sugar, cholesterol)



## Immunomarker (Cell) Change



## Changes in liver indicators (enzymes, tissues, cells)



# New concept for Healthy Cooking Lacto GABA Salt



**Low Sodium**  
**Lacto GABA Salt**

Fermentation: low Na(10%)  
(B2B, B2C)

**Infant-friendly,**  
**CARE FOOD**

Blood pressure improvement  
: Contains GABA 10%

( intake: GABA 13-20mg/day )

Ramen, porridge, salted food,  
fermented food



**Postbiotics (生菌)**  
**Lacto GABA Salt**

Contains probiotics  
(B2B, B2C)

**Non-heated food,**  
**for healthy cooking**  
( Cooking Over 60 ° )

Contains 10%  
of functional material  
GABA

Baby food, salad, grilled meat  
Kimchi, pickles, cod roe, salad



**Postbiotics (死菌)**  
**Lacto GABA Salt**

Contains  
lactic acid bacteria culture  
(B2B, B2C)

**Heated food, for**  
**healthy cooking**  
( Cooking Under 60 ° )

Contains 10%  
of functional material  
GABA

**HMR, CARE FOOD, MEAL KIT**  
**(ALL FOOD)**

# Iodine GABA Salt Global Market demand

## Fermentation of Seaweed & Sea Salt

THE LANCET  
Diabetes & Endocrinology



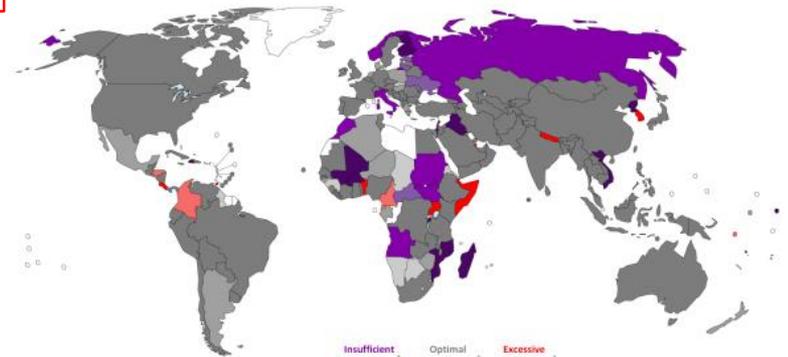
REVIEW | VOLUME 3, ISSUE 4, P286-295, APRIL 01, 2015

### Iodine deficiency and thyroid disorders

Prof Michael B Zimmermann, MD • Kristien Boelaert, MD

Published: January 12, 2015 • DOI: [https://doi.org/10.1016/S2213-8587\(14\)70225-6](https://doi.org/10.1016/S2213-8587(14)70225-6)

Global scorecard of iodine nutrition in 2019  
in the general population based on median urinary iodine concentration (mUIC) in school-age children (SAC)<sup>1</sup>



Insufficient iodine intake <sup>1</sup> mUIC <100 µg/L	Optimal iodine intake <sup>2</sup> mUIC 100-299 µg/L	Excessive iodine intake <sup>3</sup> mUIC >300 µg/L
--------------------------------------------------------------	------------------------------------------------------------	-----------------------------------------------------------

Nationally representative data, recent surveys (2004 – 2018)

14	105	9
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Sub-national data (any administrative level), recent surveys (2004 – 2018)

7	16	5
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National and sub-national data, surveys conducted before 2004

4	13	0
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요오드 함유 소금

**MORTON**

물든

요오드가 함유된 물든 소금을 아시나요 ??? 세계인이 찾는 요오드강화 ...

엄마들이 왜, 요오드 소금을 찾을까요?

- 성장기 어린이 및 청소년 발육과 두뇌발달에 꼭 필요한 요오드를 함유한 소금입니다. [출처 Wikipedia, '요오드 결핍' 정의 인용]
- 국, 무침, 찜개 등 어느 요리에도 잘 어울리는 감칠맛 나는 맛있는 소금입니다.
- 160년 역사의 물든사가 최초로 개발 현재 미국인 60% 이상이 먹고 있습니다.

요오드란?

예조류, 우유 등에 풍부한 요오드는 성장발육과 두뇌발달에 꼭 필요한 영양소로 적정량의 섭취가 중요합니다. 캐나다를 비롯한 산간지방에서는 요오드 부족을 극복하기 위해 소금에 요오드를 첨가하며 밀가루, 우유 등의 식품에도 요오드가 함유되어 있습니다. [출처 Wikipedia, '요오드 결핍' 정의 인용]

4 LB NET WT 1.8 kg

