

Kittolife

HEALTH FROM NATURE LOVE OUR NEIGHBORS CONTINUAL FOCUSED RESEARCH

www.kittolife.co.kr





'Kitto Life' creates sound and healthy future with its customers respecting nature and life.

Kittolife Co., Ltd. is a bio venture company which develops diverse bio-technology products in order to manage healthy life by harmony with nature and human.

Since its establishment in 1992, it has focused on study for chitosan and chitooligosaccharide. It is studying and developing various value-added products such as cosmetics, household goods, health food, reagents, pharmaceutical intermediates, etc.

Kittolife Co., Ltd. is practicing will of globalization in Biotechnology area through future medical products, new materials, and new stuffs using Marine Biotechnology. It is making the best products only by raw materials of quality, updated facility system, etc. through continuous R&D.

Kittolife Co., Ltd. is going to be a global company responsible for health and welfare of human in 21st Century based on its philosophy of life respect.

CEO of Kittolife Co., Ltd.

Achievement

2010's

2016 2015 2014	Conducting test to apply to human body with supercritical pine nuts extract. (Kyunghee University Hospital) National certificate in Russia (two types including chitooligosaccharide par course prime) Obtained private certificate to reduce body fat from DFA in Korea (chitooligosaccharide). R&D and commercialization for A0 0814 coloring mass production technologies to improve dry eyes and visibility.	
2013	 (Agriculture and Life Industrial Technology Development Project and Agriculture, Forestry and Fisheries). Made R&D contract with Russian DIPLOMAT CLINIC. Clinical research on improving visceral fat of obese women. (Korea Food Research Institute) R&D and commercialization of functional materials controlling body fat using fine nuts extract (Agriculture, Forestry and Fisheries). 	heries)
2012	Obtained private approval license for obesity improvement from FDA (obtaining function of reducing body fact)	
	2000's	
	Recognized by Health and Welfare Minister Award Received Technology Manager Award from Industrial Technology Association Obtained clean workplace certificate	2010
	Contracted KITTOTAXOL-transfer technology contract Clinical test for obesity progenitor cell differentiation suppression A low molecular weight water-soluble chitosan nanoparticles for polrik acid gene-introduced carrier as a target ligand and applied for patent to manufacture it. (No 0882611)	2009
ļ	Applied for the patent of water-soluble low molecular weight chitosan nanoparticles encapsulated retinol and its manufacturing methods. [No. 821217] The sustained release of ciprofloxacin and biodegradable polylactide-glycolide copolymer and biodegradable nanoparticles and applied for patent for its manufacturing method [No. 0853309] Applied for US patent for Method for preparing water-soluble free amine chitosan [29 cases]	2008
Applied for	Applied for patent for N-acetylglucosamine production method by enzymatic degradation (No. 735826) Applied for patent for Transferrin receptor imaging agent and its manufacturing method (No. 735740) Applied for the patent for hydrophilic chitosan oligosaccharide nanoparticles with an anti-cancer agent and its manufacturing method (No.0762954) patent for high-purity water-soluble chitosan nano particles for transfer anti-cancer agents, components, and its manufacturing method. (No. 780014)	2007
Applied fo	or patent for water-soluble chitosan nanoparticles for transfer anti-cancer agent and its manufacturing method (No.578382) Certified K mark for water soluble free amine FACOS manufacturing tech. (No. 1658) Applied for patent in England for water soluble free amine (s-FACOS) producing method (Patent No. GB2397304) Selected as INNOBIZ second time	2006 2005
Transfe	Applied for patent for water soluble free amine chitooligosaccharide producing tech.(No.0441270) er of Poorly water-soluble anticancer drug paclitaxel accommodate Tues-related technology transfer (domestic and foreign)	2004
Tunot	Developed FACOS Chito oligosaccharides Developed the world-first FACOS Selected as INNO-BIZ company	2003 2002
	Developed first free amine chitooligosaccharide (FACOS) in the world Certified ISO 9001	2001
	1000/2	

1990's

2000	Constructed Chilgoe factory.
1999	Registered as a venture.
	Awarded from the Ministry of Maritime Affairs and Fisheries Sea on the fourth Marine Day.
1998	Obtained KT mark for domestic new technology from Korea Institute of Science and Technology.
	(Medical biotechnology sectors: No.0571))
	The third Gyeonggi Small & Medium Business Award: No.2538
	Performed certain projects from Maritime Affairs and Fisheries (industry-university cooperation).
1997	Constructed Songtan factory of Kittolife Co., Ltd. and opened R&D center.
	Obtained approval of heath Improvement and Supplements production (No. 21 from Incheon Department of Health and Human Services Agency.
	Started COS-KL225 (Powder), COS-KL235 (concentrate) production and sales.
	Presenting study on calcium absorption promotion action, anti-cancer, and anti-germ of Korean Chitin-Chitosan oligosaccharide (COS-KL 225) research meeting
	2nd chitin, chitosan Korea Research Symposium
1996	Successful in chitosan oligosaccharide commercialization of 100% enzymatic degradation
	- Launched chitin-chitosan research in Korea, appointed founding director.
1993	Successful in the first domestic chitin-chitosan food commercialization.
1992	Established in Kittolife Co., Ltd.



licence / Certification / Crape

of Grant of Patent



USA Patent

R (1

ne-

Q1111

No. 736740

(Transferrin Receptor)

21523.221







-	
- 944	

HE 221

Q 1.1.1 1

No. 780014

(High-Purity Water-Soluble hitooligosaccharide)

1 O





G

1. Aram



G	Ę
	- 55.77
* * 5	9
No. 0441270	N

(Free Amine Chitosan)

派对外行

Japanese Patent

No. 578382 (For Carrier of Anticancer Drugs)

-

E	5
	1
-	-
G	1.4.4.4

- Kittolife Co., Ltd.

We cherish and save nature and endeavor for customers' health continuously.



What is Chitooligosaccharide?

Chitooligosaccharide refers to low molecular weight sugar which 2-10 units of 6-carbon sugars (monosaccharides) are combined by treating the polymer chitosan with enzymes. Chitooligosaccharide is water-soluble. It is useful for our body like cholesterol improvement, etc.



Features of Chitooligosaccharide(FACOS)

It is a product commercialized and developed by collaborate research project of certain R&D project with Kittolife Co., Ltd. with Ministry of Maritime Affairs and Fisheries. Chitooligosaccharide (PACOS) from Kittolife Co., Ltd. disassembled 100% chitosan extracted from domestic crabs with zymolysis. It is a high-purity and high-guality functional materials separated and refined by using UMB. PACOS is water-soluble free-amine chitooligosaccharide which can be absorbed in our body. It applied for patent for its manufacturing technologies and certified from Ministry of Science and Technology.

Kittolife Co., Ltd. is a company specialized in chitosan and chitooligosaccharide. It holds domestic and overseas patent for chitosan and chitooligosaccharide. Also, it has submitted 60 different domestic and overseas research papers about its physiological functionality. In addition, it produces chitooligosaccharide in each Molecular Weight through UMB Automation System Engineering. From raw material supply to delivery of complete products, it produces chitooligosaccharide excellent in absorption rate through thorough quality control.



* The above data is a photograph showing the degree of absorption in the animal body organs according to molecular weight using chitooligosaccharide produced by using chitooligosaccharide (PACOS) produced by Kittolife Co., Ltd.

Source Journal of Controlled Release, v. 102, 2005, pp.383-394, Su Yong Chae, Mi-Kyeong Jang, Jae-Woon Nah

Chitooligosaccharides

What is cholesterol?

Chitooligosaccharide is a kind of fat with the animals. It is main component that makes up the cell membrane. It is used as a material of gall which is helpful for digestion of fat and controlling hormone. In particular, it is distributed to brain / overall body muscle / blood a lot. It is essential materials for our body.

Why is cholesterol harmful for our health?



Cholesterol in-taken by food or made inside our body moves around body through blood. Then, LDL carries cholesterol into cells and facilitates it to move around. However, LDL is easy to be oxidized to cause damages in the vascular tissue. As cholesterol gets accumulated in vascular tissue damaged, it tightens blood vessels and lowers function of vascular function. On the other hand, HDL scraps cholesterol attached on the walls of blood vessels and carries it to liver.

Therefore, LDL accumulated on blood vessel is bad cholesterol. HDL lowering cholesterol in the blood is known as good cholesterol.

Total cholesterol (mg/dl)	Classification Responding	
Less than 200	Normal	Regular check
200-239	Border level	Diet and exercise needs
Over 240	High risk group	Diet and exercise needs

Levels of Maintaining Cholesterol in Blood

The role of chitooligosaccharide

To interfere with the re-absorption of bile acid can assist in lowering cholesterol levels.

It can be helpful to improve cholesterol levels among bloods by controlling HDL and LDL.

Chitooligosaccharide absorbs the harmful cholesterol (LDL) and discharge out of body. It also increases level of HDL to improve and control cholesterol.

Relevant Documents

Korean Chitin, Chitosan Journal, 2001, v. 6 (3), pp. 107–110, Yun-Hee Son, Kyung-Su Nam J, Agric. Food Chem, 2003, v. 51, pp. 4624–4627, Pyo-Jam Park, Jae-Young Je, Se-Kwon Kim Journal of agricultural and food chemistry, 2003, v. 51, pp. 4930–4934, Pyo-Jam Park, Jae-Young Je, Se-Kwon Kim Carbohydrate Polymers, 2004, v. 55, pp. 17–22, Pyo-Jam Park, Jae-Young Je, Se-Kwon Kim Bioorganic & Medical Chemistry, 2005, v. 13, pp. 3449–3455, Ronghua Huang, Eresha Mendis, Se-Kwon Kim Korea Food and Nutrition Journal, 2005, v. 34 (1), pp. 35–41, Gil-Nam Kim, Eun-Suk Joo, Gyu-Il Kim, Se-Gwon Kim, Hyun-Pil Yang, Yu-Jin Jeon Carbohydrate Polymers, 2006, v. 63, pp. 122–129, Ronghua Huang, Niranjan Rajapakse, Se-Kwon Kim



Chitooligosaccharide(FACOS)

Chitooligosaccharide of Kittolife Co., Ltd. (FACOS) is chitooligosaccharide (PACOS) from Kittolife Co., Ltd.disassembled 100% chitosan extracted from domestic crabs with zymolysis. It is a high-purity and high-quality functional materials separated and refined by using UMB. PACOS is water-soluble free-amine chitooligosaccharide which can be absorbed in our body. It obtained certificate of domestic manufacturing mark (KT mark), being applied for its two technologies such as (chitooligosaccharide manufacturing technology with high bio-activation: No.0571) (water-soluble free-amine chitooligosaccharide which can be absorbed in body: No.1658).

Types of raw materials

- For food use : Chitooligosaccharide PACOS, zero zone PACOS, chitooligosaccharide powder (H), polymer chitosan (KL-245)
- Reagents for research : Chitooligosaccharide in each molecular weight
- Medical use : s-FACOS
- Functional raw materials : Collagen peptides from fish scale

Chitooligosaccharide for food use - Patent registration No. 0291308

Experiment items	riment items Chitooligosaccharide PACOS Chitooligosacchari		
	Powder without flavor	Powder without flavor	
Appearance	and odor with unique colors	and odor with unique colors	
	and flavors	and flavors	
Moisture	Under 10% Under 10%		
Chitooligosaccharide content	ooligosaccharide content Over indicated value (800mg) Over indicated value		
Cadmium (Cd) Under 1mg/kg Under 1mg/k		Under 1mg/kg	
Hydrargyrum (Ag) Under 1mg/kg Under 1mg		Under 1mg/kg	
Lead (Pb)	Lead (Pb) Under 3mg/kg Under 3mg/kg		
Captain aureus	Negative	Negative	



Chitooligosaccharide for research reagents

Chitooligosaccharide has different bio-activations in each molecular weight. diverse experiments are available using it. Kittolife Co., Ltd. purifies and separates by using precise and multi-stage membrane system. Chitooligosaccharide for research reagents of different molecular weights is produced. Through recognition by the biggest global reagent company, Sigma-Aldrich, COS-KL225 / chitosan oligosaccharide lactate is listed in Aldrich index as a global standard.

Typesof products

- Chitooligosaccharide under 1,000 of molecular weight (under MW 1,000)
- Chitooligosaccharide over 1,000 under 3,000 of molecular weight (MW 1,000~3,000)
- Chitooligosaccharide over 3,000 under 5,000 of molecular weight (MW 3,000~5,000)
- Over 5,000 molecular weight (Over MW 5,000)

Chitooligosaccharide for medical use(s-FACOS®) - Patent registration No.0441270

's-FACOS' applied by chitooligosaccharide for medical use is next-generation chitooligosaccharide which has been developed for three years as collaborate study with professor Na Jae Wun's research team from polymer engineering at Suncheon University and Pyeongtaek Technology Research Center. It is water-soluble free-amine chitosan of chitooligosaccharide state. It attracted high attention by representing its manufacturing method, basic features, contents for use as DNA carrier on domestic and overseas journals. It has been recognized as an innovative gene-carrier to different research groups and companies which tried to develop previous non-virus gene medicine. It is expected to facilitate product development along with relevant researches. It applied for domestic and overseas patents (PCT). In addition, chitooligosaccharide has features of conveying medicines from cells and mucoadhessive, and so on. Therefore, it is expected to be used and applied in diverse forms for the relevant researches.

Types of products

– s-FACOS(low molecular water soluble chitosan) : Used to DDS and GDS

• Reference to study materials in clause 6

Bio-NAG(Zymolysis NAG : Alternative Raw Materials for Glucosamine)

NAG is new material which is reported for its excellent ingredient to improve wrinkles as a cosmetics and Arthritis treatment material, promoting the generation of cartilage in medical world in the form of Chitin monomer unit. Production methods can be classified synthesis NAG and enzyme decomposition NAG. A lot of products using most NAG synthetic have been released than the natural NAG because of manufacturing difficulties and high manufacturing cost. However, our company produces only 100% enzyme decomposition NAG with our state-of-art technology.

Features – Patent Registration No.735826

• High-purity enzyme-decomposition products

- Enzyme-decomposing NAG product which is produced by decomposing Chitin with chitinase.
- Produced by applying world best enzyme-decomposing chitoolgosaccharide producing technologies.
- High-purity product over 95% purity
- Excellent sitological characteristics
- Color (white), flavor (about one-half of the sugar for sweetness), low hygroscopicity, high solubility, high-temperature stability
- No browning reaction at high temperature and in room temperature No minerals like CL- ion, etc. are included.
- High stability is kept under diverse food processes.

Excellent safety

Synthesis NAG produced by the acetylation of glucosamine may not occur any troubles in contact with the skin as a cosmetics or by in-take of a small amount of drugs. However, ingesting it in a large amount can cause safety trouble. Only NAG (Bio-NAG) close to natural type in the course of production can ensure its safety.



Other raw materials

Collagen peptides from fish scale : Patent Registration No. 1020312

- Raw materials
- Tilapia fish scale
- Usage
 - Health functional food, food, beverage, cosmetics
- Features
- White powder
- No flavor, no odor
- Excellent Solubility
- Low molecular weight (average molecular weight 1,500)



Collagen peptides from fish scale

Anthocyanin derivatives

- Raw materials
- Grape skin extract, fermentation culture
- Usage
- Health food, food, beveragescosmetics
- Features
- Produce an anthocyanin contained in the grape skins in the body derived anthocyanins 2-6 molecules using enzymes
- Solubility in water, oil, excellent
- Having an effective bioactivity



Anthocyanin derivatives

Kittolife | Marine Biotechnology Venture Company www.kittolife.co.kr

Experiment of Immunostimulatory Effect

Experiment raw materials(Wonkwang University Hospital)

• FACOS produced in Kittolife

• Average molecular weight: 3.5kDa

Experiment method

• Subjects of experiment: Healthy adult without immune abnormalities from 74 to 86 years.

1) FACOS ingestion-free group(20 persons)

2) FACOS ingestion group(20 persons) : FACOS 5.1 g / day, intake for 8 weeks

Experiment Evaluation

- Serum separation from the vein of the subjects
- IL related to immune function (Interleukin)-1ß IL-2, IL-4, IL-10, IL-12 Measurement of IFN- γ and TNF- α

The effect of FACOS on the serum cytokine

- FACOS intake group
- IL-12 and IFN-y value is significantly increased compared to the control group

	Experimental group (n=20/group)			
Cytokine	Control group (pg/mL)	FACOS intake gro up (pg/mL)		
IL-1β	390.6 ± 216.4	369.6 ± 209.4		
IL-2	510.9 ± 125.5	586.8 ± 113.7		
IL-4	16.3 ± 8.2	27.9 ± 6.9		
IL-12	98.6 ± 68.0	358.9 ± 124.3 [°]		
TNF-α	79.7 ± 35.1	56.9 ± 40.7		
IFN-γ	834.2 ± 223.8	1,589.5 ± 343.4°		

* IL-12: Secretes B cell, mononuclear leukocytes and macrophages * IFN-γ: Induces differentiation of Th1 (delay-type immune response)

ightarrow Activation of macrophages and NK cell

The level of significance was $\mathsf{P} < .05$ for all statistical tes.

Improvement Effect in Abdominal Fat(Clinical Trials)

Catholic University, Seoul Sungmo Hospital (Professor of Family Medicine, Kim Kyung Su), Sookmyung Women's University (Professor of Food Science and Nutrition, Sung Mi Kyung)

*** Additional analysis(BMI, waist circumference, visceral fat / area ratio of subcutaneous fat) ***

1) Results of analysis based on MBI 30kg/m²

- There are differences in terms of body fat volume, visceral fat area, subcutaneous fat area, and total abdominal fat area for the groups over BMI 30kg/m².

2) Results of analysis based on waist circumference, abdominal obesity standard

- There are significant differences only in body fat for 90cm or less-waist male and 85cm or less-waist female.
- There are significant differences in body fat weight and total abdominal fat area for 90cm or more-waist male and 85cm or more-waist female.
- Results of analysis based on sub-cutaneous fat and visceral abdominal fat area ratio which classifies sub-cutaneous abdominal fat and visceral abdominal fat.
 - There are significant differences for 0.4 or less groups(sub-cutaneous fat) visceral fat and subcutaneous fat area ratio.
 - There are significant differences among 0.4 or more groups(visceral abdominal fat) in terms of body fat and visceral fat/ subcutaneous fat area ratio.



< Comparison of DEXA and CT change of group with BMI over 30 kg/m² (ITT set)>

* Conclusion: Check of the reduction effect of abdominal fat (visceral fat + subcutaneous fat) Significant fat reducing effect was realized compared to the control group in terms of abdominal obesity of visceral abdominal fat.

Clinical Trial - Body Fat Reduction Effect

- Clinical trial : Andong Seongso Hospital 90 Seodongmun-ro Andong-si Kyungbuk (Double-blind, Randomization, Placebo-contrast)
- Clinical target : Adult females over 20 years and under 50 years (over BMI 25kg/m²)

Comparison of body fat quantity changes through DEXA(PP set)





Comparison of weight and body mass index changes(ITT set)



Summary of Clinical Test Results

- 1) Results of analysis targeting ITT set about body fat volume, primary efficacy variable
 - After 12-week intake, body fat volume in chitooligosaccharide test group tends to decrease in comparison of that of placebo group. Significant changes were observed at correction by dietary caloric intake and energy consumption among two groups. (p=0.042)
- 2) The results of analysis targeting PP set about body fat volume, primary efficacy-evaluating variable -Body fat reduction in chitooligosaccharide statistical test group was

Weight reductions were 2.08 \pm 0.27kg for the chitooligosaccharide test group and 1.34 \pm 0.27kg for the placebo group. Chitooligosaccharide intake group tends to reduce more than the plabo group. Significant changes were observed at correction by dietary caloric intake and energy consumption among two groups. (p=0.041)

- 3) Weight reductions (ITT set) were 1.74 \pm 0.27kg for the chitooligosaccharide test group and 1.17 \pm 0.14kg/m² for the placebo group.
 - Body mass index reductions were 0.73 \pm 0.27kg for the chitooligosaccharide test group and 0.52 \pm 0.14 kg/m² for the placebo group. Significant changes were observed in body weight and body mass index corrected by dietary caloric intake and energy consumption during exercise (p=0.032, p=0.040).

4) In the case of hip circumference

- In PP set, hip circumference reductions were 2.12 ±0.33cm for the chitooligosaccharide test group and 0.96 ± 0.43cm for the placebo-control group. A statistically significant difference was found between the two groups compared (P=0.036).

s-FACOS(LMWSC) Patent and Thesis

Technology name		Registration (Patent Application No.)	Remarks	
Patent	High-quality water-soluble chitosan oligosaccharide, composition comprising the same and method for the preparation thereof		PCT/KR2005/003598	PCT patent application
	Methode of producing water-soluble free amine chitosan		No. 0441270	Domestic patent
	Method for preparing water-soluble free amine chitosan		GB2397304	English patent
	Method for preparing water-soluble free amine chitosan		ZL02823379.4	Chinese patent
	Method for preparing water-soluble free amine chitosan		US 7,345,165 B2	U.S. patent
	Water soluble chitosan nanoparticle for delivering an anticancer agent and preparing method thereof		US 7,883,723	U.S. patent
	Water soluble chitosan nanoparticle for delivering an anticancer agent and preparing method thereof		No. 5116108	Japanese patent
	Method for enhancing the solubility of paclitaxel		GB2436745	English patent
	Applied chemistry, 5(2), 2001. 36-39	Biodegradability of microspheres prepared using low molecular water soluble chitosan.		
	Journal of polymer science:part A 40, 2002. 3796-3803	Spectroscopic characterization and preparation of low molecular, water-soluble chitosan with free-amine group by novel method		
Thesis	Applied chemistry, 6(2), 2002. 611-614	The synthesis of LMWSC for pharmaceutical application.		
	Journal of controlled release, 102, 2005. 383-394	Influence of molecular weight on oral absorption of water soluble chitosans.		
	Food science and biotechnology 15(6), 2006. 937-941	Absorption behavior in the body of chitosan oligosaccharide according to molecular weight; an in vitro and in vivo study		

s-FACOS(LMWSC) Chitosan for Medical Use



- Raw materials for DDS and GDS use
- Salts-removed soluble free amine chitosan
- High-purity chitooligosaccharides which is comparative with other products
- A variety of physiological activation

Body Absorption Rate



Low molecular-weight, water-soluble chitosan (MW 3,500)





s- FACOS Optimal Nanocapsule (finished technology development)

Cytotoxicity



Gene Carrier Patent and Thesis

Technology name		Registration (Patent Application No.)	Remarks	
Patent	Low-molecular weight, water-soluble chitosan nanoparticle for gene delivery with folic acid conjugated thereto as target ligand and preparation method thereof		PCT/KR2007/005711	PCT patent application
	Water soluble chitosan nanoparticle for delivering an anticancer agent and preparing method thereofering an		US 7,883,723	U.S. patent
	Water soluble chitosan nanoparticle for delivering an anticancer agent and preparing method thereof		No. 5116108	Japanese patent
	Method for enhancing the solubility of paclitaxel		GB2436745	English patent
	Journal of Controlled Release 109 (2005) 330- 344	Deoxycholic acid-conjugated chitosan oligosaccharide nanoparticles for efficient gene carrier		
	Journal of Controlled Release, 116(3), 2007	Chitosan-g-polyethyenimine as gene carrier		
Thesis	Polymer (Korea), published, 2007. 12.	Development of gene carrier fractioned low molecular-weight water soluble chitosan (LMWSC)		
	Polymer(Korea), 31(5), 454-459, 2007	Characterization and Preparation of low molecular weight water soluble chitosan nanoparticle modified with cell targeting ligand for efficient gene delivery		
	Journal of Applied Polymer Science 102 (2006), 3545-3551	DNA Delivery Using Low Molecular Water-Soluble Chitosan Nanocomplex as a Biomedical Device		

Gene carrier(Plattform technology)

Replaceable with previous virus vector by combining ions among genes and chitosan

- Developing next-generation gene therapy
- Selective treatment for genetic defect parts



Transfection of LMWSC-pEGFP



73, Sandan-ro 197beon-gil, Pyeongtaek-si, Gyeonggi-do, Korea Tel. 82-2-579-7003 Fax. 82+2-579-7572 Homepage www.kittolife.co.kr