ACADEMIC MATERIALS

Academic materials



Oxidative Stress and Disease

ver 1.2

Institute for Advanced Study, Center for Basic Scientific Research, Gifu University, Tokai National University Institution Joint Research Lecture, Antioxidant Research Department, Antioxidant Research Institute

Gifu University Antioxidant Laboratory

Research objectives

Sunburns, hay fevers, acne, etc. that occur throughout the year, especially from early spring to summer, are all related to oxidative stress, which affects the quality of life and appearance, and causes a lot of mental stress. Besides, the old person smell and cognitive disorder that comes with aging are also related to oxidative stress, which unknowingly affects people around you.

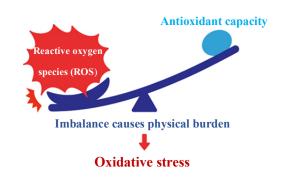
Oxidative stress is caused by a variety of factors and is related to many diseases. Therefore, routine inhibition of oxidative stress is good not only for yourself, but also for the people around you. As the saying goes, "almost all diseases are related to oxidative stress", in other words, "inhibition of oxidative stress every day can prevent and treat a variety of diseases."

Through various experiments, the lab aims to link the inhibition of oxidative stress with the prevention and treatment of diseases, and clarify its mechanism, with an ultimate goal to gain a lot of scientific evidence and contribute to a "healthy and longevity society".

What is oxidative stress?

The active energy needed to move the body is generated from daily food and oxygen absorbed through breathing by a small organ called mitochondrion inside cells.

However, it also synchronously produces a by-product called reactive oxygen species (ROS), which has higher reactivity. It is not only produced during energy generation, but also caused by various factors such as ultraviolet rays and radiation, infections caused by bacteria and viruses, air pollution and other external factors, as



well as lifestyle habits such as smoking and excessive drinking, diseases, and stress. This reactive oxygen species can destroy DNA, lipids, proteins and enzymes that are essential for health maintenance of the body. Therefore, to protect the body, it is necessary to remove this reactive oxygen species. This removing capacity called "antioxidant capacity" actually exists in our body. However, it's impossible to completely remove reactive oxygen species. What matters is the balance between the continuous production of reactive oxygen species, the ability to protect it and its antioxidant capacity. With the increase of active oxygen, once it's out of balance, the body will feel unwell. This status is called "oxidative stress".

I think everyone has seen rusty nails and discolored apples. These are all "oxidative phenomena" due to exposure to oxygen in the air. This is exactly what is happening in the body under oxidative stress.



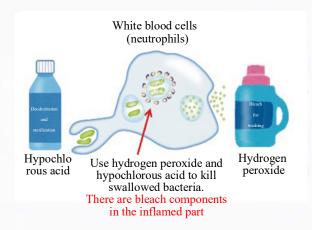
Discolored apple



Rusty nail

What is reactive oxygen species?

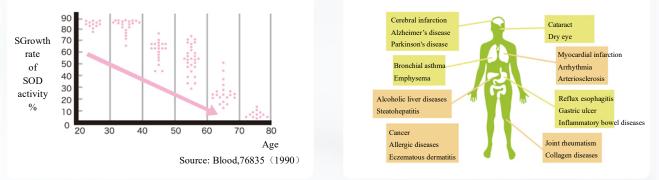
The reactive oxygen species producing oxidative stress refers to "oxygen that is more activated than oxygen in the air, that is, oxygen with higher reactivity". With high reactivity, it damages DNA and lipids, proteins, etc. in the body, and also causes inflammation. However, it not only has negative effect. This strong power can also be used to clear bacteria and viruses that invade the body, playing an important role in immunity. Let's describe it with familiar things around you.



There is a bleach that is commonly used in washing, whose raw material is hydrogen peroxide. There are also daily used deodorants and sterilizers, and its raw material is hypochlorous acid. Actually, both of them are reactive oxygen species, which are also produced in our body. Bleaches, deodorants, and sanitizers are all produced using this powerful bactericidal ability, and it is the white blood cells that work as the immune system that utilize this property in the body. Once invading bacteria are discovered, white blood cells engulf them and release hydrogen peroxide and hypochlorous acid to destroy the bacteria. Does the wound turn red, swell, or cause pain once it occurs? This is an inflammatory reaction caused by the accumulation of white blood cells for repair and release of a large amount of reactive oxygen species to the site. If it is believed that if a large amount of accumulated white blood cells releases both bleach and disinfectant into the blood, all parts of the body will start to "rust" as mentioned earlier. As a result, diseases will appear throughout the body, and the consequence would be unthinkable.

Relation with diseases

As mentioned earlier, our bodies have "antioxidant capacity" that fights oxidative stress. We are born with antioxidant capacity, which reaches its peak around the age of 20 and then gradually declines with age. As a result, once oxidative stress increases, the body rusts and causes inflammation and cell damage. The rusted status of the body, also known as the often said "aging" phenomenon, is even related to a variety of diseases. It is reported that there are more than 150 diseases related to oxidative stress.



At present, many diseases in the world are undergoing antioxidant therapy and research. However, despite detailed studies on its structure and preventive effect in test-tube and animal experiments, there are few drugs for prevention or treatment through antioxidant effects. Antioxidant substances that are versatile, have no side effects, and are effective in the prevention and treatment of many oxidative stress diseases, are highly anticipated. If the antioxidant capacity can be improved and the oxidative stress can be reduced, we can expect to prevent and improve aging and a variety of diseases.

Antioxidant compound developed

Scientific name: "Twendee X"



"Twendee X" is an anti-oxidant compound developed under the leadership of Haruhiko Inufusa, a specially-appointed professor of the lab, with 8 active ingredients including vitamin C and amino acids. It is an antioxidant formula product approved by radiation physicist Dr. Helmut (Germany) and ICDD (France) of oxidative stress measurement companies as *a substance with no side effects and the highest level of antioxidant capacity in the world*.

In 2019, it was recognized by the Medical Creation Committee of the Japan Society for the Prevention of Cognitive Disorder as Grade A in * % "Twendee X" is being sold with the name "Oxicut" by the manufacturer and dealer TIMA Tokyo Co., Ltd.

Active ingredients of "Twendee X" (raw materials)

All ingredients are natural inherent composition in our body.

Name of raw materials: Coenzyme Q10 (Made in USA) / Vitamin C (Sugar), L-Glutamine (Rice, Corn), L-Cystine (Chicken), Crystalline Cellulose, Stabilizer (Hydroxypropyl Cellulose), Magnesium Stearate, Fumaric Acid (Aromatic Hydrocarbon), Succinic Acid (Fumaric Acid), Microsilica, Calcium Carboxymethylcellulose, Vitamin B₂ (Glucose), Niacin (Amino Acid)

Scientific name: "Twendee Mtcontrol"



"Twendee Mtcontrol" is a product researched for further expanding the use of "Twendee X", whose initial form was completed in 2015. Infertility has become a social problem specially in recent years. Both men and women have factors causing infertility, but it's increasingly clear that most of them are caused by oxidative stress.

* "Twendee Mtcontrol" is being sold with the name "Mtcontrol" by the manufacturer and dealer TIMA Tokyo Co., Ltd.

Active ingredients (raw material) of "Twendee Mtcontrol"

Name of raw materials: Maltose (home made), Coenzyme Q10/Vitamin C (Sugar), L-Glutamine (Rice, Corn), L-Cystine (Chicken), Crystalline Cellulose, Stabilizer (Hydroxypropyl Cellulose), Fumaric Acid (Aromatic Hydrocarbons), Succinic Acid (Fumaric Acid), Magnesium Stearate, Microsilica, Lactoferrin (containing some milk components), Calcium Carboxymethylcellulose, Vitamin B₂ (Glucose), Niacinamide, Calcium Gluconate, Calcium Pantothenate, Vitamin B₁, Vitamin B₆, Folic Acid, Biotin, Vitamin B₁₂

Safety of Tw Safety of Twendee

INC Research Co., Ltd. (http://www.ina-research.co.jp/) was entrusted to carry out the safety testing in 2007.

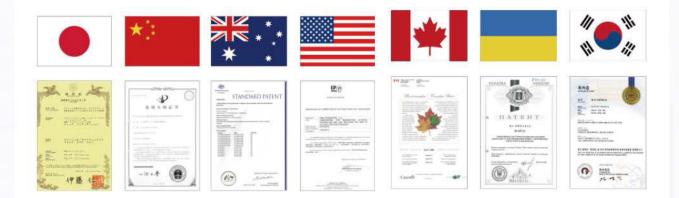
Carry out testing

Relevant effects of repeated administration in experimental mice in one week (INC Research test number: GL43080) Chromosomal abnormality test using mammalian cultured cells (INC Research test number: BV07158) Repeated oral administration toxicity test in experimental mice in 4 weeks (INC Research test number: BV07156) Back Mutation Experiment Using Bacteria (Except Cystine) (INC Research test number: BV07352) Side Effects Test in Human Clinical Studies (INC Research test number: NRP07-001)

All tests' safety has been confirmed. In addition, the report shows that the maximum safe intake per day is 2g or more per 1kg of body weight.

Patents obtained

Based on empirical data, patents are being filed in various countries around the world, led by the Japanese Patent Office Patent No. 5777821 "Composition for preventing cell damage effects", and various countries around the world (35 EU countries including Germany, the United States, Canada, China, Australia, Korea, and other European and Asian countries) have obtained formula patents.



※ Patent for Twendee Mtcontrol is being filed at present

In addition, several patents for the effects of the following items are also being filed.

- Whitening effect, sunscreen effect, reduction of snoring due to inflammation in the body (sleep apnea syndrome)
- Improve systemic capillary blood flow (improve muscle strength and endurance during exercise, inhibit gray hair, restore male function, etc.)
- Inflammatory bowel diseases (rheumatoid arthritis, etc.), metabolic diseases caused by oxidation (prevention of Alzheimer's disease, etc.)
- Degenerative diseases caused by oxidation (improve symptoms of Parkinson's disease), systemic diseases caused by oxidation (improve symptoms of chronic fatigue syndrome)
- · Dyscrasia caused by cancer (improve weight loss and fatigue at the end of cancer), improve diabetic peripheral nerve disorder
- Adjust biological clock (prevent jet lag syndrome), improve gestational hypertension syndrome, morning sickness (intensive morning sickness), gestational pruritus
- Fatigue recovery, etc.

Start of oxidative stress research

Dr. Helmut Durschlag of the Institute of Biophysics and Physical Biochemistry, University of Regensburg, was one of the survivors of the Chernobyl nuclear accident; due to his personal experience, he spent his life searching for substances that could reduce health hazards caused by radiation exposure through the lysozyme-irradiation experiment. In 2011, Dr. Helmut focused on the hypoglycemic effect of Twendee X and its formula. It is reported that from the lysozyme-irradiation experiment, the amount of Twendee X is about 1/7 of vitamin C, and has almost the same antioxidant effect as vitamin C. At this time, he asserts that Twendee X is the most powerful antioxidant in the world. To this end, in 2013, Inufusa opened the Antioxidant Research Department (now the Joint Research Lecture Antioxidant Research Department) at Gifu University, and began to research various pathologial and oxidative stress caused by Twendee X.

Helmut • Durschlag

Ph.D., Institute of Biophysics and Physical Biochemistry, University of Regensburg

I've been researching a variety of antioxidants.

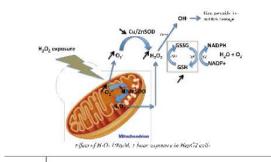
During the research, I became interested in the antioxidant activity of Twendee X and verified it in my own lab, and confirmed the beneficial data about Twendee, so I am now conducting a joint research with Dr. Inufusa's research team.

Antioxidant substances measurement through a third-party agency ICDD

While researching oxidative stress in 2014 to objectively evaluate the antioxidant effect of Twendee X, Inufusa entrusted ICDD, a French oxidative stress measurement company, to measure it.

The the measurement results of the antioxidant effect using a HHCC named HepG2 show that the oxidative stress of mitochondria is reduced by 63% at 60μ g/ml (equivalent to 20% of the daily amount of a human body weight of 60 kg), and the SOD of oxidative power is increased by 147%.

According to Dr. Natalie Compagnie, CEO of ICDD, there are no substances and formula products that have no side effects on the human body and have antioxidant power like Twendee X. That is to say, Twendee X is proven to be the most powerful antioxidant in the world.



Experimental condition	Dose	Effects on REDOX status in response to H_1O_2 exposure				
		mtROB	eROS	MESOD	6500	GSHtot
н,о,	10-ţeM	7" 80%	7*** 80%	≥ ² *** 32%	≥ *** 31%	71 8156
Twendee X	Opgial	N 83%	≥ 45%	7 147%	zi 60%	SI 40%
	1209 g/m1	77% צ	≥ 49%	71 104%	21 CO%	NG 🛛 15%
	244 jug/ml	N 65%	N 3746	NS 7138%	NS 7119%	N 20%

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Natalie Compagnie

ICDD (Innovative Concepts in Drug Development) CEO



ICDD has received entrustment for the measurement of oxidative stress from pharmaceutical, chemical, food, and cosmetic companies around the world. This company is better at researching antioxidants than any other companies in the world. In the experiments using our cells we have not found yet any substances that have no side effects in humans and have greater antioxidant effects than Twendee X.

Prevention of Cognitive Disorder

In recent years, the incidence rate of cognitive disorder has risen rapidly, and the number of affected people is expected to reach 7 million by 2025. The attack of cognitive disorder takes about 25 years, and prevention during this period is very important. Therefore, we invite the Nutritional Supplementary Food Class of the Medical Creation Committee of the Japan Society for the Prevention of Cognitive Disorder (Monitor: Professor Koji Abe, Department of Neurology, Okayama University) to carry out a clinical test of Twendee X's preventive effect on cognitive disorder.

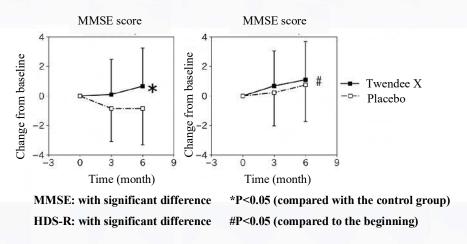
Test method: Positive, randomized double-blind test, control group, control standard group test carried on in 8 institutions across the country.

Administration period: 6 months, Twendee X and placebo.

Assessment method: Two assessments by MMSE and Hasegawa Dementia Modified Scale (HDS-R).

Results: Compared to decline in cognitive function from administration of placebo, that from administration of Twendee X is controlled. In addition, improvements are also seen in the MMSE assessment.

Comparison of Changes in the MMSE and Hasegawa-style (HDS-R) Dementia Scale with that at Beginning



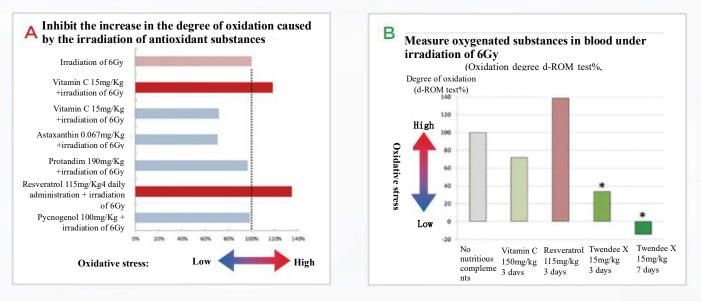
The research results were published in an American Medical Journal *Journal of Alzheimer's Disease* on August 24, 2019. In this regard, the Medical Creation Committee of the Japan Society for the Prevention of Cognitive Disorder rated it as Grade A "effectively preventing cognitive disorder ($\star \star \star$)" out of 6 grades of accreditation, and announced the accreditation on September 3, 2019.

PRESS RELEASE	JSDP
(1) 利用 (1) 日 (1) (1) (1) (1) (1) (1) (1) (1) (1) (1)	
世界辺の部長度予防支援制 ~「認知症は酸化ストレス券」を意味は酸マ要加~	認定証書
●発展のボイント ・ 証明症の原因として離化ストレスが平等なファクターであることを、臨床対応により目界であ	
めて実証しました。 - 教授生社会員 Processex (Text) が、運生時年勤務事があると目界で読めて公開時会から歴史を	阿部 康二 殿
今にました。 ・ Tox に変更に募集されるそ年付加速からっているリブリスントであり、副か同たく活動中の 器構築からの後方が構築です。 ・ 考えの他にな想想を発展して成熟につながくことが条件されます。	犬房 春彦 瞬
岡山人孝人孝保臣皇紫武帝御京村御神道へ同学の尚藩原二帝法のグループは、米年人学育党	サブリメント「TwendeeX」は審議の結果、
低重・社会連携提供料でも完善まセンター会な状交換点、広路な状交換目の大原を影響に広報とし との共同研究により、認知点の素面として能なストレスが主要なファクターであることや、認知	当学会のエビデンス創出委員会にてグレード A
(MER-2)であっく名かで発展したした。 目前部分・したことれる見かいための記録であるためとのapation tenantian (ARE) で取らる。 分類点、シングへに、目前者、ジケロボーマントワールな人気強く強化、それ最近化容量ムケー ムであるAnstern (ボーン)を知道の認知は、スマルの3階級にとなった、人間的4時間から知知に一 長々では他们など時間 おかれ 4年前後回きたして、1000 日本目的100 日本目、した、本	(★★★)として認定します。
副会議書はようされば、米国の同学物語「Associed ModelsAnd Based」開始活動されました。 また、これにおいては、原知体予約等率にビデンの活動意味合いて読みる原始でしたで されば、「短期を予約する活動がある(ままた)」を受けました(特殊意志はなりまうには10回)。	2019年9月3日
■ 教夫方容 〈素長〉	
本料において設備性能器に増加しており、構造者の集まレンジプランによると 2025 年には有 会合教は 746 方人になると記念されています。 しかし 231 年 7 月の後、アルジンパマー連載問題	一般社团法人日本認知症于防学会
1 有知な真論は登場しておらず、今年経営運の防腐発売を全部が決通の開始のは働きす。 今回、数々の研究チームは、経営運動に開催として優化ストレスが豊富なシアクターであることと、	理事長 浦上 克赦。
K部に配合用でなくにより2000年が7時できることを世界であめて実施しました。 現在の問題では「今後期50年になる可能性の高い現実になり情報(ALC) たある」ことが判断し	エビデンス創出委員会 委員長 阿部 康二
ても実際を指导することはできません。月日の綺麗により利行して読み広とな話されてはじめてき 気が可能となるのです。しかし「空気発展」は安く発展ではありません。なぜなる読字の読み広報	SCITIS PHOP ARTICLES

Press Release by Okayama University

Grading certificate

Antioxidant effect



The oxidative stress in the body increases significantly after 3 days of exposure to radiation (6Gy). 3 days later, taking advantage of this feature, the mice were administered various nutritional supplements for 3 days, and were irradiated (6Gy) on the 4th day. 3 days later, the experimenters measured the oxidative stress in the blood and verified whether the rise in oxidative stress could be inhibited.

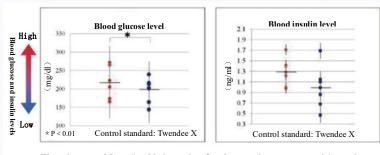
A The inhibitory effect on oxidative stress of representative antioxidant substances on the market.

In the usual dose (daily dose for a 60 kg human being converted into the body weight of a mouse), since the oxidative stress could not be reduced, astaxanthin and Protandim were administered at 100 times the usual dose for humans, and resveratrol and pycnogenol were administered at 4 to 5 times the usual dose for humans. 9 grams of Vitamin C (150 mg/kg) and high doses of astaxanthin and Protandim were taken, and the oxidative stress was reduced compared to the untreated group, but no significant difference was found.

B Inhibitory effect of Twendee X on oxidative stress.

Twendee X was administered 3 days before irradiation, for a total of 7 days before and after irradiation, and its inhibitory effect was compared with other antioxidants. It is clearly understood that the amount of Twendee X is 1/10 of Vitamin C, and the degree of oxidative stress is greatly reduced to 1/3 (green: p<0.05, t-test). The level of oxidative stress was reduced to -15% in the 7 days before and after administration to the mice. (Approval numbers: 25-64, 26-39, 27-94, 28-71, 29-97, 2019-041)

Changes in blood glucose and insulin levels after glycemic load



The mice were 27 weeks old, 5 months after the experiment starts, and 1 month after the administration of Twendee X. Continue a high-fat diet and feed cube sugar a week before the measurement.

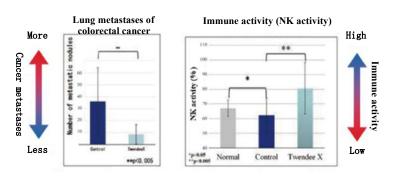
Measure body weight after a 16-hour fast, intravenously inject 0.3 g/kg glucose,

and measure its blood glucose and insulin levels after 15 minutes.

Diabetes is a representative disease related to oxidative stress. When the glucose concentration in the blood stays high for a long time, oxidative stress also increases, and insulin sensitivity deteriorates. Therefore, we created hyperglycemic mice by feeding them a high-fat diet for 5 months. We administered a normal dose of Twendee X continuously for one month, and compared with the mice (control standard) not administered Twendee X. After a 16-hour fast, we injected glucose intraperitoneally, and measured the blood glucose and insulin levels 15 minutes later. In this way, the effect of the diet of each mouse on the blood glucose could be eliminated.

Compared with the group of mice not administered Twendee X (control standard), Twendee X significantly reduced the differences in blood glucose and insulin levels. Insulin was supposed to lower blood glucose level, but Twendee X would also lower insulin level. It may be considered that by continuously taking Twendee X improved the metabolism, thereby lowering the blood glucose level. Since such metabolism did not use insulin, insulin level also dropped. Low insulin content indicates "mild and no stimulation to the pancreas". (Approval numbers: 25-63, 25-72, 26-40, 27-95, 28-70, 29-96, H30-154, 2019-043)

Cancer metastasis and immune activity



Mouse: BALB/cSlc nu/nu, 3, 6W, n=30 per group. Cell: RPMI4788(4×104 cells/0.2 ml) injected into the tail vein.

Control: Sterilized water for drink.

Twendee X: Twendee X (37mg/kg/day/mouse) dissolved in sterilized water for drink.

After 4 weeks of cell injection, NK activity was measured with LDH assay kit.

6 weeks after cell injection, some mouse was measured metastatic nodules on lung surface.

By injecting human colorectal cancer cells into the tail veins of nude mice, the cancer cells metastasize to the lungs. In addition, and oxidative stress also increases with the development of cancer, which makes it a kind of oxidative stress-related diseases. Therefore, mice injected with cancer cells were divided into two groups: one group was injected with Twendee X, while the other group was not injected with Twendee X (control standard 1); the groups of mice were raised for 6 weeks, and then the number of cancer cells metastasized to the lungs was measured. In the 4* week, the immune activity (the activity of natural killer (NK) cells that kill cancer cells) was measured in the same number of mice, and compared with normal mice of the same age (Normal). Twendee X was administered for 6 weeks after being injected with cancer cells. As a result, the number of cancer metastases to lungs in the Twendee X-administered group was reduced by 1/6 compared to the non-administration group. In terms of immune activity, it can be considered that although cancer metastasis causes lower activity, after taking Twendee X, the decreased NK activity nearly doubles, thereby improving immune function and reducing cancer metastases.

(Approval numbers: 25-63, 25-72, 26-40, 27-95, 28-70, 29-99 H30-154, 2019-043)

Questionnaire results

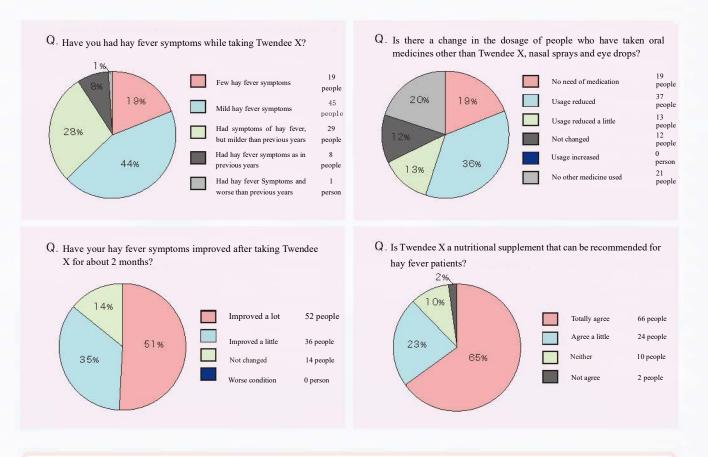
Implemented by: EYE'S Co., Ltd.

Hay fever monitoring

Implementation period: February 8 to May 7, 2017. Participants: 102 women over 20~50 (including 20~50).

Twendee X taking period: about 2 months, taken every day.

Results: actually 91% felt improvement in hay fever symptoms. After taking Twendee X, about 20% of people no longer needed the drug, and 90% of the people in the questionnaire wanted to use it if they have hay fever symptoms next year. Twendee X has no side effects against hay fever and is the best choice.



Questionnaire results

- · Had no severe hay fever symptoms during spring.
- · Felt much better than last year, despite a lot of pollen this year. It would be better if it was cheaper.
- Very good physical condition. Make sure to indicate "improve hay fever" on the packaging. I am grateful for this wonderful product.
- · No problem with pollen in mild periods, but needed over-the-counter medications in peak periods.
- · Tried this product and took much fewer over-the-counter medicines than last year.
- The effective countermeasure against hay fever. The eye symptoms that bothered me every year were relieved, which is the most exciting thing.
- · Didn't have a cold in the past 2 months, and hardly had any symptoms such as sneezing, runny nose, itching around the nose, and itchy eyes.
- · In addition to hay fever, the symptoms of rough skin also eased, and I did not get tired easily.

Implemented by: EYE'S Co., Ltd.

Asthma monitoring

Implementation period: November 8, 2017 to March 18, 2018. Participants: 44 women over 20~50 (including 20~50).

<In the end>

Twendee X?

How many asthma attacks did you

have after 4 months of taking

1 ti

11%

Twendee X taking period: about 4 months, taken every day.

In the 4 months before taking the medicine, 60% had more than 5 attacks, but in the 2 months after taking the medicine, 90% had fewer than 4 attacks, which was a substantial improvement. In the last 4 months of taking, 65% had less than 4 attacks. In the second half of the 2-month period, which coincided with the period of hay fever, it was more likely to attack than usual, but it could be seen that there was still a great improvement compared with before taking it.

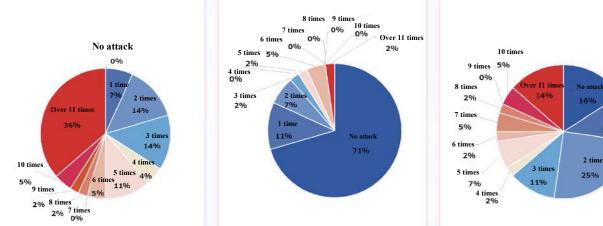
Questionnaire results about the number of asthma attacks (n=44/74 before, n=44 in middle, n=44 in the end)

<Before>

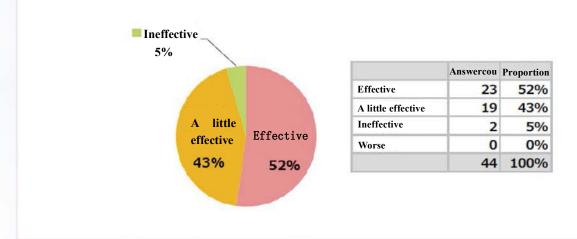
Please fill in the number of asthma attacks in the past 4 months (July to October).

<In the middle>

How many attacks did you have in the two months after you started taking Twendee X?



Q. Is Twendee X effective in inhibiting asthma attacks?



Implemented by: EYE'S Co., Ltd.

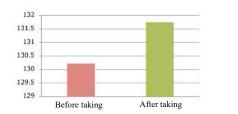
Intestinal bacteria monitoring

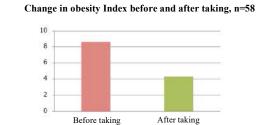
Implementation period: March 12 to May 29, 2018. Participants: 57 groups of healthy men and women

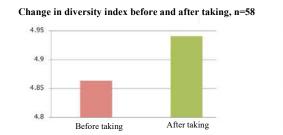
over 30.

Twendee X taking period:	1 month, taken every day.				
Analysis of intestinal	Takara Bio Co., Ltd.				
bacteria:	Analysis of intestinal bacteria: Takara Bio Co., Ltd.				
	ideal balance contains 20% g belonging to either. If such balan will be reduced, leading to a va improve the balance of intestina	a from the intestinal tract, where many intestinal bacteria live. The bod bacteria, 10% bad bacteria, and 70% ordinary bacteria no nee is disrupted by oxidative stress, the diversity of bacterial specie riety of diseases. Therefore, to stay healthy, it is very important to bacteria and the diversity of bacterial species.			
	bacteria and patency before and				
Changes in unbalanced bacteria	bacteria and patency before and	after taking Twendee X, and monitored the changes in intestina after. In the intestinal bacteria of healthy people, taking Twendee 2 ich greatly improved the patency.			
8	bacteria and patency before and also increased good bacteria, wh	after. In the intestinal bacteria of healthy people, taking Twendee 2			
unknown functions be	bacteria and patency before and also increased good bacteria, wh , regulator bacteria, and bacteria with efore and after taking, n=58 Bad bacteria	after. In the intestinal bacteria of healthy people, taking Twendee 2 ich greatly improved the patency.			
unknown functions b	bacteria and patency before and also increased good bacteria, wh , regulator bacteria, and bacteria with efore and after taking, n=58 Bad bacteria: increased Good bacteria: reduced	after. In the intestinal bacteria of healthy people, taking Twendee 2 ich greatly improved the patency. Change in number of strains before and after taking, n=58			
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changed Good bacteria: reduced or not changed Bad bacteria: reduced Good bacteria: Bad bacteria: red 3% Good bacteria: reduced or not changed reduced 12% 31%







Changes in defecation and defecate status



Monitoring of sleep apnea syndrome

Implemented by: Takashima ENT

In recent years, it has been reported that more than 70% (included) of patients with sleep apnea syndrome have elevated inflammatory markers, which indicates that there is inflammation somewhere in the airway, but ordinary anti-inflammatory agents cannot relieve symptoms. On the other hand, it's also reported that levels of reactive oxygen species are elevated in the blood of patients with sleep apnea syndrome, which means relation to oxidative stress.

The cause of this inflammation lies in reactive oxygen species, but it is unclear whether the increase in reactive oxygen species is caused by inflammation. However, among patients with sleep apnea syndrome who took Twendee X to eliminate fatigue, several patients' apnea symptoms disappeared. Therefore, we surveyed people whose family members reported sleep apnea symptoms, asked them to take Twendee X continuously for at least three weeks, and conducted a questionnaire about their symptoms before and after taking.

Questionnaire results

Questionnaire results	Yes	No	No	Improvem
Less snoring	30	5	0	85.7%
Less waking up at midnight due to breathing difficulties	28	5	2	84.8%
Become sound asleep	32	3	0	91.4%
Less sleepy during the day	27	5	3	84.3%
Less depressed mood	26	4	5	86.6%
Focused during the day	26	4	5	86.6%
No more apnoea in sleep according to family members.	30	5	0	85.7%
No more serious snoring according to family members.	30	5	0	85.7%
Go to the toilet less at midnight	18	7	10	72.0%
No headache after waking up in the morning	16	7	12	69.5%
Decreased symptoms of thirst after waking up in the morning	22	6	7	78.6%
No more serious snoring even after drinking alcohol	20	5	10	80.0%

Questionnaire respondents

35 men whose family members pointed out their sleep apnea syndrome an the symptoms persisted for more than one year (including one year).

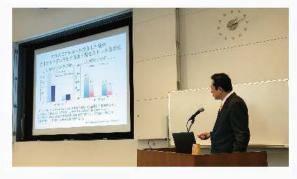
The average age was 57.2 years.

Complications: 21 people with diabetes, 7 people with hypertension, and 26 people with obesity. Take 1 piece of Twendee X (the active ingredient of Twendee X is converted to 13.3~17.6 mg/kg) every 15~20 kg of body weight when waking up, and take it for more than 3 consecutive weeks (including 3 weeks). Then a questionnaire survey was conducted (TIMA Japan Co., Ltd.).

Society publication

Foreign societies

 October 2020, The 22nd World Conference on Oxidative Stress Reduction, Redox Homeostasis & Antioxidants.
 "COVID-19 infection is oxidative stress disease. Twendee will be best solution to prevent and avoid severe symptoms."



- October 2020, The 22nd World Conference on Oxidative Stress Reduction, Redox Homeostasis & Antioxidants.
 - "Does continuous OS reduction prevent and ameliorate through species diversity of intestinal bacteria?"
- 3. October 2019, Sustainable Industrial Processing Summit & Exhibition. "Brain Disease and OxidativeStress: Ischemia and Dementia".
- 4. October 2019, Sustainable Industrial Processing Summit & Exhibition. "Cancer and Oxidative Stress".
- 5. October 2019, Sustainable Industrial Processing Summit & Exhibition. **"Does continuous oxidative stress reduction** prevent and ameliorate diseases through species diversity of intestinal bacteria?"
- 6. October 2019, Sustainable Industrial Processing Summit & Exhibition. "Role of Anti-oxidant Twendee X for Maintenance of Voice and Swallow".
- 7. October 2019, Sustainable Industrial Processing Summit & Exhibition. "Exposome-induced Oxidative Stress and Protective Effects of Antioxidants in Rats".
- 8. November 2018, Sustainable Industrial Processing Summit and Exhibition. "Oxidative stress: Can We Reduce Oxidative Stress in Various Diseases?"

Domestic Societies

- 1. October 2019, the 9th Academic Meeting of the Japan Society for the Prevention of Cognitive Disorder, "The role of Twendee X in cranial nerves"
- 2. October 2019, The 61st Japan Brain Nutritional Supplements Society, "Clinical Effect of Antioxidant Nutritional Supplement Twendee X"
- 3. October 2019, The 1st Japan Brain Nutritional Supplements Society, "Can the antioxidant nutritional supplement Tewndee X function as a body regulator?"
- 4. September 2020, The 61st Academic Conference of the Japanese Neurological Society, "Antioxidative Treatment of Neurological Diseases Infinite Potentials of Twendee X-"
- 5. June 2019, The 72nd Academic Meeting of the Japanese Society for Oxidative Stress, "Antioxidant compound Twendee X's effect of reducing oxidative stress"
- 6. In December 2018, the 16th Japan Functional Food Medical Association General Conference "Discussion on the administration of antioxidant compound Twendee X for allergic diseases"
- September 2018, The 8th Academic Meeting of the Japan Society for the Prevention of Cognitive Disorder, "Progress in the Proof for Cognitive Disorder Prevention of Antioxidant Nutritional Supplement - Twendee X"
- 8. In September 2018, the 8th Academic Meeting of the Japan Society for the Prevention of Cognitive Disorder, "What will happen once oxidative stress declines? Basic and clinical data for cognitive disorder, cerebral infarction, hay fever, asthma, chronic sinusitis, fatigue and other diseases."
- 9. May 2018, The 18th General Assembly of Japan Anti-Aging Medical Society, "What happens once oxidative stress is reduced?"

Society publication

Education/Seminar, etc

August 2019, The 2nd Antioxidant Summit - Cognitive Disorder and Health & Longevity - Open Seminar, Osaka August 2019, The 2nd Antioxidant Summit - Cognitive Disorder and Health & Longevity - Open Seminar, Tokyo September 2019, Oxidative Stress and Disease, Special Lecture

January 2019, Lifespan and Oxidative Stress. Open Seminar on Antioxidant Research ~Health & Longevity and Allergic Diseases~

November 2018, Lifespan and Oxidative Stress. The 1st Health & Longevity and Antioxidant Summit

September 2018, Nagoya Small and Medium Business Promotion Association, Managers Forum "Proposal for a truly diet and lifestyle for longevity ~ Prevent body rust, cancer, diabetes, hypertension, cognitive disorder ~"

August 2018, ITbM Seminar, "Lifespan and Oxidative Stress"

- January 2018, The 36th Health Fair Seminar, "Body rust can cause cognitive disorder, and adult diseases such as cognitive disorder, cancer, diabetes, hypertension, hay fever, acne are also caused by oxidative stress!"
- January ~ March 2018, "Allergic diseases are caused by rust!?" 1st on hay fever, 2nd on dermatitis, 3rd on ulcerative colitis (Aichi, Gifu, Mie)

Papers published

- Yang Fuhua, Tanaka Sho, Marcus, Mathusika, Gleifencrow, Yoshikawa Toshiichi, Okada Naomi, Haruhiko Inufusa. Twendee X, the world's first anti-oxidant tablet to prevent cognitive disorder, challenges the super-aged society. BIO Clinica Vol.35 No.10 Sep. 2020.
- Koh Tadokoro, YasuyukiOhta, Haruhiko Inufusa, Alan Foo Nyuk Loon, Koji Abe. Prevention of Cognitive Declinein Alzheimer's Disease by Novel Antioxidative Supplements. Int J Mol Sci. 2020 Mar; 21(6)
- Yang Fuhua, Tanaka Sho, Marcus, Mathusika, Gleifencrow, Yoshikawa Toshiichi, Okada Naomi, Haruhiko Inufusa. The world's first
 prevention of cognitive disorder was achieved (process of preventing cognitive disorder through the anti-oxidant research department's
 compound Twendee X). Medical Science Digest, Vol45(13), 2019.11.
- Yang Fuhua, Tanaka Sho, Marcus, Mathusika, Gleifencrow, Yoshikawa Toshiichi, Okada Naomi, Haruhiko Inufusa. The world's first prevention of cognitive disorder was achieved- the relations with oxidative stress, inflammation and immunity. BIO Clinica Vol.35 No.4 Apr. 2020.
- Koh Tadokoro, Ryuta Morihara, Yasuyuki Ohta, Nozomi Hishikawa, Satoko Kawano, Ryo Sasaki, NamikoMatsumoto, Emi Nomura, Yumiko Nakano, Yoshiaki Takahashi, Mami Takemoto, Toru Yamashita, SetsukoUeno, Yosuke Wakutani, Yoshiki Takao, Nobutoshi Morimoto, Yumiko Kutoku, Yoshihide Sunada, KatsushiTaomoto, Yasuhiro Manabe, Kentaro Deguchi, Yasuto Higashi, Haruhiko Inufusa, Fukka You, Toshikazu Yoshikawa,Markus Matuschka von Greiffenclau, Koji Abe. Clinical Benefits of Antioxidative SupplementTwendee X for Mild Cognitive Impairment: A Multicenter, Randomized, Double-Blind, and Place-bo-Controlled Prospective Interventional Study. J Alzheimers Dis. 2019; 71(3): 1063-1069
- Shizuo Hirano, Haruhiko Inufusa, Sugiyama Yuichiro, Kaneko Mami, Yoshikawa Toshiichi. Voice and Anti-aging, Journal of the Japanese Anti-aging Medical Association, Vol. 15, No. 2, 214-219. 2019.4.

About the lab

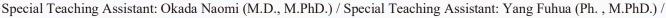
Lab member

Chief Researcher: Haruhiko Inufusa (M.D., M.PhD.)

Born in Okayama Prefecture in 1957. Majored in and graduated from the Department of Surgery, Institute of Medical Sciences, Kinki University after graduating from the Faculty of Medicine, Kinki University (Kinki University Ph.D. (Medicine))

After that, he successively served as a professor in the Department of Clinical Medicine, Faculty of Medicine, Kinki University, a visiting professor at the European Institute of Telesurgery, University of Strasbourg, and a visiting professor at the Surgical Classroom of the University of Barcelona, Spain. He has been in his current position since 2013.

Chief Researcher at the Antiacidification Lab of the Louis Pasteur Medical Research Center / Executive Member of the Certification Creation Committee of the Japan Society for the Prevention of Cognitive Disorder/ Council Member of the Japanese Society for Gastroenterology (Tokai Region) / Council Member of the Japan Society for Endoscopic Surgery Member / Director of Japan Brain Nutritional Supplements Society



Academic Research Assistant: Harakawa Yoshitsune

Contact Information of Co-researchers

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Contact Information

For joint research and interviews with our lab, please contact us by email. Meanwhile, we also accept questions from the public about antioxidant research.

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Videos posted on YouTube's "Antioxidant Channel"





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