WHITE PAPER

KARNOZIN EXTRA

Abstract

Karnozin Extra is a high-quality food supplement with wide range of physiological activities in many different diseases and conditions. Karnozin Extra is formulation is based on the principles of mitochondrial medicine. Karnozin Extra improves mitochondrial function of every single cell in the body, allowing them to produce enough energy necessary for the body to function properly.

OUR AIM IS:
NATURAL, EFFECTIVE, SCIENTIFICALLY-PROVEN THERAPY, WITHOUT ANY SIDE EFFECTS.

Our R&D department is continuously working on designing and conducting many different studies that involve our main product Karnozin Extra.

So far, we have investigated its antioxidative potential, its effect on the nerve tissue using neuroblast cell line, *in vivo* model of multiple sclerosis, patients with multiple sclerosis, its effect on running wheel activity in rats and how it affects mitochondrial respiration in the human breast cancer cell line. The summary and results are presented in the following text.

Despite the very large number of known antioxidants, choosing one for effective use in a specific clinical situation is quite difficult.

Numerous references, as well as our own work experience, indicate that the antioxidant L-carnosine, meets almost all requirements for an ideal antioxidant. It is synthesized and contained in human muscle and nervous tissues, it is easily absorbed in the digestive tract, it penetrates through blood-brain barrier, and it has membrane-stabilizing properties. In addition, carnosine is not addictive, there is no danger of overdose, and it does not accumulate in the organism during long-term administration.

1 capsule of Karnozin Extra is composed of 6 ingredients:

L-Carnosine	125 mg
Coenzyme Q10	20 mg
L-carnitine	20 mg
Vitamin E	20 mg
Bilberry extract	20 mg
Grape seed extract	20 mg

L-carnosine is synthesized and contained in the human body, with the highest concentrations found in the skeletal muscles, heart and brain. The primary source of L-carnosine has traditionally been via dietary intake of meat and fish. However, due to the increased production and consumption of processed meat, the amount of L-carnosine derived from the modern diet is quite limited. Therefore, Karnozin Extra serves as a more ideal source of L-carnosine. It has a unique formulation on the market, complemented by bioflavonoids from two plant extracts, Bilberry extract and Grape seed extract, which are known for their rich content of beneficial flavonoids and polyphenols. It is far superior when compared to other L-carnosine products available worldwide. It has higher bioavailability, better absorption and stronger antioxidative properties.

In recent years, there has been an increased interest and great attention directed to the properties of carnosine, which is considered the substance of the 21st century. L-carnosine is being recognized as the basic medical preparation for people of all ages, especially those of 40 years or more. Studies on Carnosine are carried out in the USA, Australia, UK, Japan, Scandinavia, Russia, China and in many other countries worldwide. It is recommended by specialists as an important nutritional supplement in delaying the aging process. Since the level of L-carnosine reduces naturally with age, it is ideal that elderly people take L-carnosine supplements.

The deficiency of L-carnosine will for surely affect people's brain, muscles, heart and immune system. The activity of carnosine is based on its antioxidative, anti-glycation and anti-carbonyl-ation properties, in addition to the heavy metals chelation and the pH-buffering ability.

Basic biological functions of L-carnosine are:

- buffering of lactic acid – maintaining the pH value of muscles
- chelating heavy metals (detoxification of heavy metals);
- scavenging free radicals with its antioxidant effect;
- inhibition of protein glycation (binding sugars to proteins)
- inhibition of protein carbonylation (binding aldehydes to proteins)
- the role of neurotransmitter;
- reduction of the anti-inflammatory effect of cytokine IL-8.

Dietary supplementation with Karnozin Extra shows positive effects in many diseases and disorders such as autism, multiple sclerosis, all neurodegenerative and neuromuscular disorders, diabetes, heart diseases, psychiatric disorders and many others.

KARNOZIN EXTRA AND MITOCHONDRIA FUNCTIONING

Decreased mitochondrial ATP-production is a common finding during critical illness. It is associated with decreased activity of mitochondrial complexes in the electron transfer system. Adequate nutrient levels are essential for mitochondrial functioning. In addition to Q10, carnosine is one of these critical micronutrients since it has the ability to significantly increase the activity of complexes I-III of the electron transport chain. This results in an increase in ATP production and consequently leads to cytoprotection.

KARNOZIN EXTRA AND AUTISM

Autism is a severe developmental disorder with a poorly understood etiology. However, some facts are well researched so far. Lipid peroxidation markers are elevated in autism, indicating that oxidative stress is increased in this disease. Levels of major antioxidant serum proteins, namely transferrin (iron-binding protein) and ceruloplasmin (copper-binding protein), are decreased in children with autism. The alterations in ceruloplasmin and transferrin levels may lead to abnormal iron and copper metabolism in autism. Several studies have suggested alterations in the activities of antioxidant enzymes such as superoxide dismutase, glutathione peroxidase, and catalase in autism. Also, there is evidence that 20-50% of autistic patients have some kind of mitochondria defect. By reducing oxidative stress, improving mitochondrial function and removing toxic copper and iron ions from the brain of autistic patients, Karnozin Extra may help autistic children in various ways, mainly affecting the child's behavior and language skills, and it may enhance the functioning of the nervous system.

KARNOZIN EXTRA AND HEART MUSCLE

Healthy myocardium naturally contains a certain concentration of L-carnosine. However, L-carnosine supplementation significantly improves the strength and endurance of the heart muscle (by up to 30%). Studies have shown that carnosine can improve heart contractility, possibly by regulating cellular calcium levels. Also, carnosine can inhibit sympathetic nervous system activity that promotes hypertension, thus decreasing blood pressure.

Free radicals play a significant role in atherosclerosis. Oxidized LDL cholesterol is atherogenic and is thought to be important in the formation of atherosclerosis plaques. Furthermore, oxidized LDL is cytotoxic and can directly damage endothelial cells. Carnosine with its anti-glycation, anti-carbonylating, and anti-oxidative properties can help prevent harmful modifications of LDL cholesterol molecules that contribute to early stages of arterial plaque formation and thus prevent atherosclerosis as a whole.

KARNOZIN EXTRA AND DIABETES

Together with excess formation of free radicals and decreased energy production, glycation process is also crucial in forming of almost all diseases. This chemical reaction can be described as the binding of protein molecules to molecules of sugar (glucose) and is followed by the creation of damaged, non- functional protein structures. It's a major factor in the aging process - and it's particularly devastating for diabetics. In diabetes, we have excess sugar molecules, so diabetic patients have up to triple more glycation damage compared to people who do not have diabetes. And that's the reason why people get cataract, atherosclerosis, other vascular issues and kidney problems. Glycation is responsible for all complications caused by diabetes. Karnozin Extra is effective against all forms of protein modification caused by glycation. L-carnosine has a chemical structure that allows it to bind with the aldehydes or sugar groups. Otherwise, if left alone - they would attack and bind with proteins. Also, L-carnosine is able to remove already formed glycated proteins, actually to remove sugar from proteins, and to make that protein fully functional again.

KARNOZIN EXTRA AND NEUROLOGICAL DISORDERS

Carnosine is a universal neuro-protectant. Evolution made sure that healthy and young nerve cells of the brain contain a sufficient amount of L-carnosine to protect these very important cells from damage and degenerative changes. The protective qualities are mainly related to the antioxidant effect of carnosine and prevention of glycation and carbonylation. Carnosine also acts as a neurotransmitter; anticonvulsant agent and chelating substance (bind heavy metals) and it has the ability to easily penetrate blood-brain barrier. Because of all these capabilities, it is a universal substance that protects the brain against a variety of neurological and mental disorders and diseases.

KARNOZIN EXTRA
CARNOMED RESEARCH PROGRAM

Carnomed is a company that produces and distributes all natural, high-quality food supplements. Our mission is to educate first ourselves, then patients, medical doctors and other professionals from different disciplines about the importance of L-carnosine, its role in the organism and its benefits in different medical conditions and problems.

The focus of the Carnomed research program is the idea that by improving the cellular respiration in the mitochondria we can affect human health and prevent the development of disease. Our supplement Karnozin Extra beneficially affects several target functions in the body, reducing the risk of disease and improving overall well-being.

In order to expand our knowledge and to make our company more competitive in the market, we decided to conduct a few very important scientific experiments in cooperation with the Government of the Republic of Serbia, and with our partners from different Universities in Serbia.

PRELIMINARY *IN VITRO* STUDY OF KARNOZIN EXTRA STABILITY

It is well-known that pure L-carnosine is quickly

degraded in the blood by the enzymes called carnosinases, which are splitting L-carnosine into 2 constituent amino acids beta-alanine and L-histidine, and therefore its bioavailability inside the cells is lower. During years of our work experience, we have been witnessing differences in patient's outcomes when using pure L-carnosine supplements and Karnozin Extra formulation. These observations suggested that L-carnosine in Karnozin Extra formulation is somehow protected from the carnosinase activity and in this *in vitro* study we wanted to prove that point.

First, we have determined UV/VIS spectra for pure L-histidine (Figure 1.) and pure L-Carnosine. (Figure 2.). The spectral analysis shows obviously different spectra. Then we incubated pure L-carnosine and Karnozin Extra in the same concentration with carnosinase enzyme for 10 minutes. After that, we analyzed spectra.

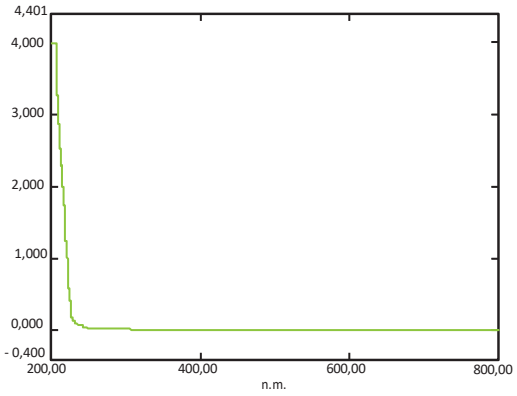


Figure 1. L-histidine

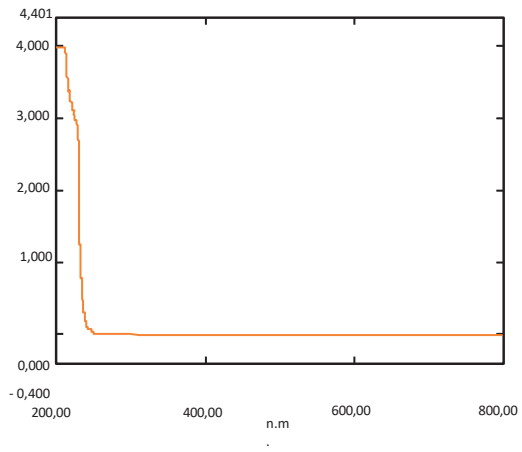


Figure 2. pure L-carnosine

L-carnosine incubated with carnosinase enzyme showed different spectra comparing to only L-carnosine (Figure 3.) (almost similar to the histidine spectra Figure 1.). These findings suggested that the carnosinase enzyme split L-carnosine into beta-alanine and L-histidine.

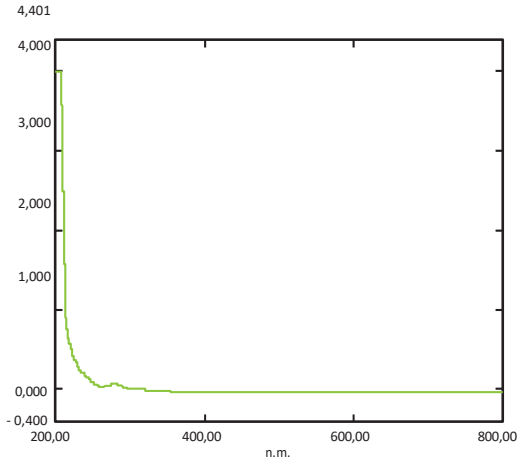


Figure 3. L-carnosine+ carnosinase

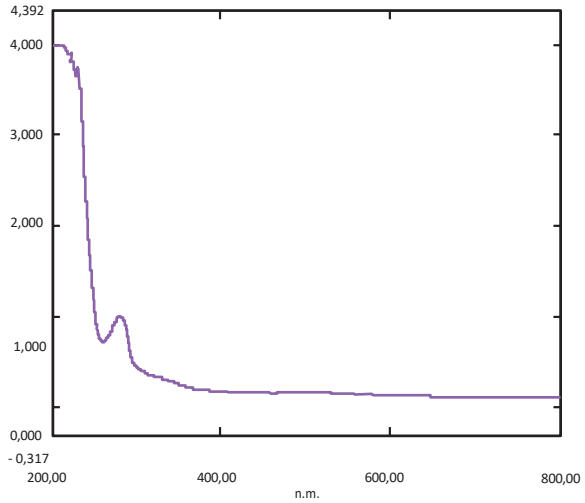


Figure 5. Karnozin Extra + carnosinase

However, when Karnozin Extra in the presence of carnosinase enzyme was analyzed, results showed that there was no difference between spectra of Karnozin Extra with and without enzyme (Figures 4 and 5).

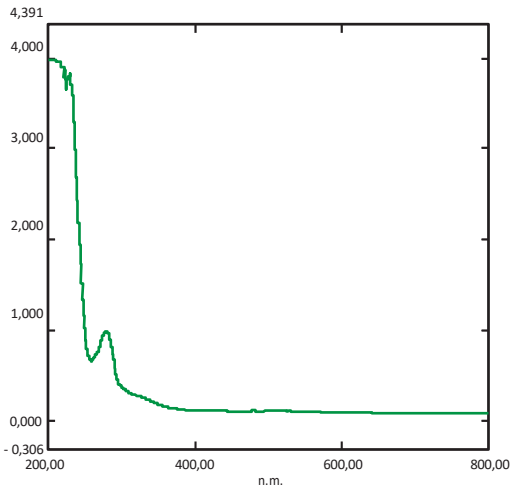


Figure 4. Karnozin Extra

According to those results, there is indicia that L-carnosine in Karnozin Extra is stabilized. Although the exact mechanism hasn't been found so far, by performing these analyses we can proudly say that the reason why Karnozin Extra is showing far superior effects in patients comparing to using the supplements that contain pure L-carnosine substance is its protection from the carnosinase enzyme degradation.

These analyses were performed at Institute for Biological Research 'Siniša Stanković' in Belgrade.

PhD, Dusko Blagojevic

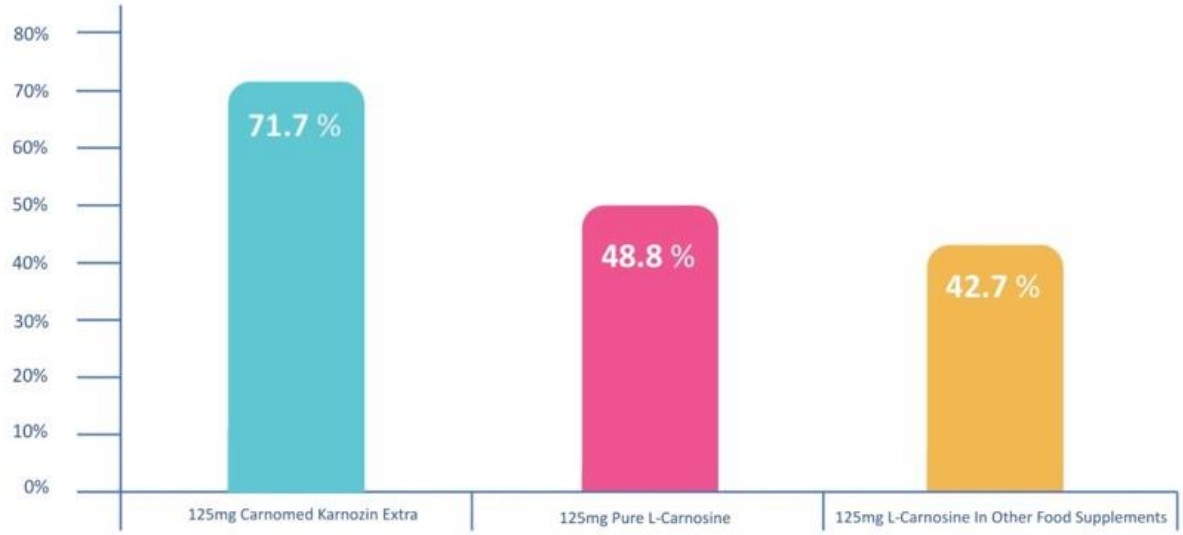
PhD, Aleksandra Nikolic Kokic

KARNOZIN EXTRA
ANTIOXIDATIVE CAPACITY

The first research Carnomed has performed is *in vitro* research of antioxidant capacity of our product Karnozin Extra. We quantitatively measured its ability to scavenge different type of free radicals. Also, we compared its antioxidant capacity with capacities of using the same amount of pure L-carnosine ingredient and L-carnosine from competitive food supplement producer.

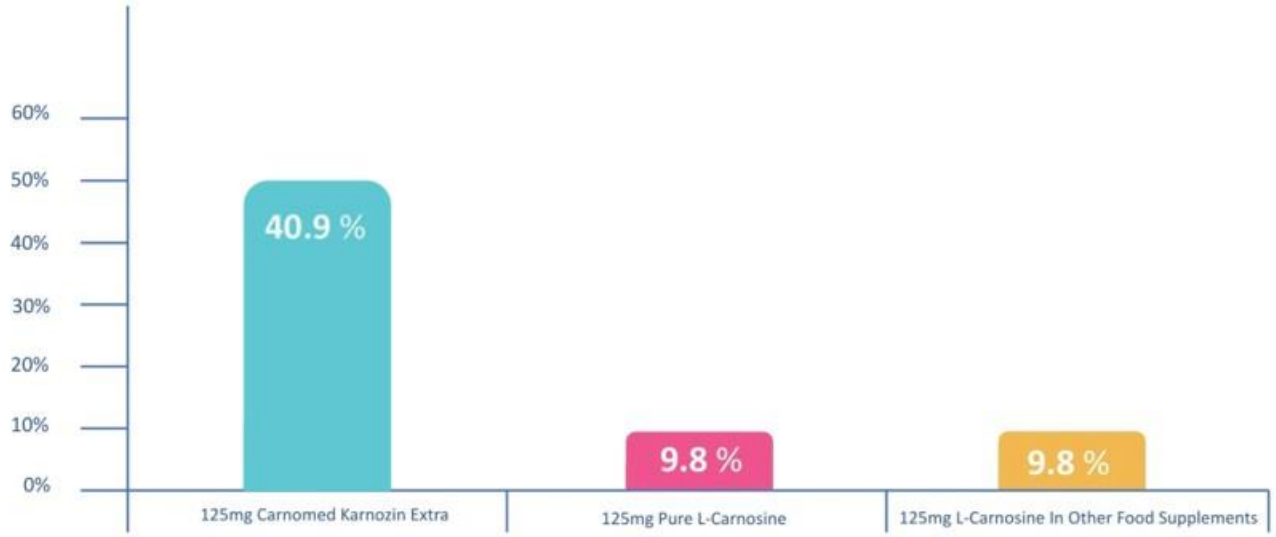
There is a variety of free radicals that are produced inside our cells. Some of them are useful in low concentrations, but others are extremely dangerous. There are some free radicals that are so harmful and reactive that they will steal an electron from anything, including DNA, proteins, lipids, and cell structures. **The hydroxyl radical** is highly unstable and it can damage virtually all types of macromolecules: carbohydrates, nucleic acids (mutations), lipids (lipid peroxidation), and amino acids. That is the most reactive radical known to chemistry.

NEUTRALIZATION OF HYDROXYL RADICAL

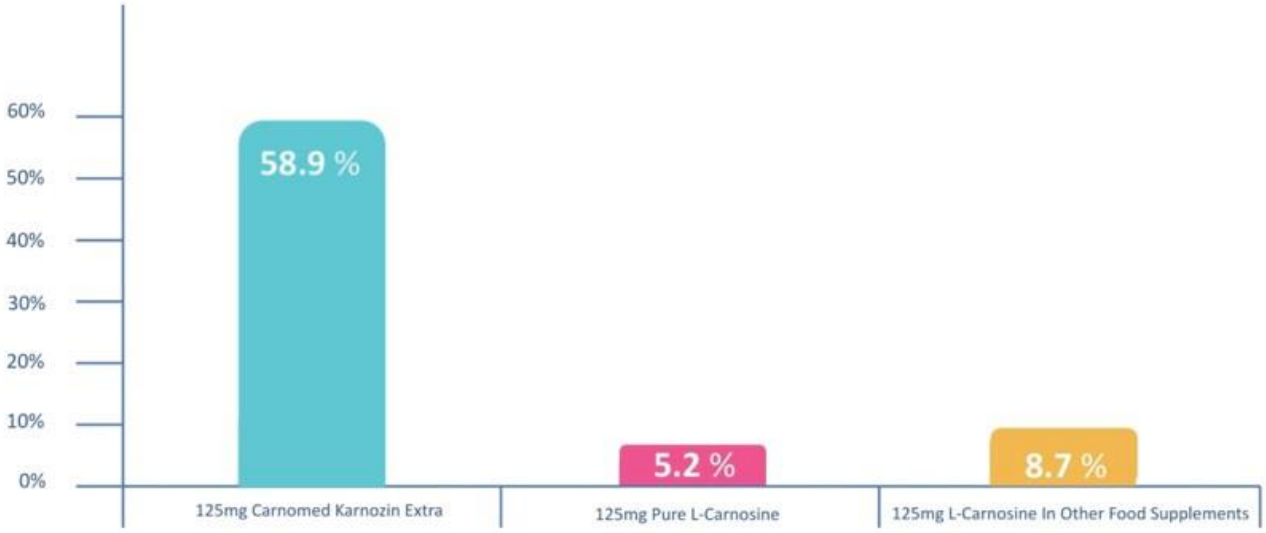


The small, free radical molecule nitric oxide has been identified as a major signal transduction molecule in humans and animals. Nitric oxide free radical is involved in the process of apoptosis. When produced excessively, it can disregulate this important way of cell defense system. Also, nitric oxide is involved in oncogene expression, meaning that his role in forming cancer is well described. Moreover, it can damage our DNA through DNA oxidation.

NEUTRALIZATION OF NITRIC OXIDE RADICAL



NEUTRALIZATION OF LIPID PEROXIDATION PROCESS



These findings suggest that Karnozin Extra possesses far superior antioxidative potential comparing to pure L-carnosine compound and may be translated to any disease and disorder where oxidative stress plays a large role.

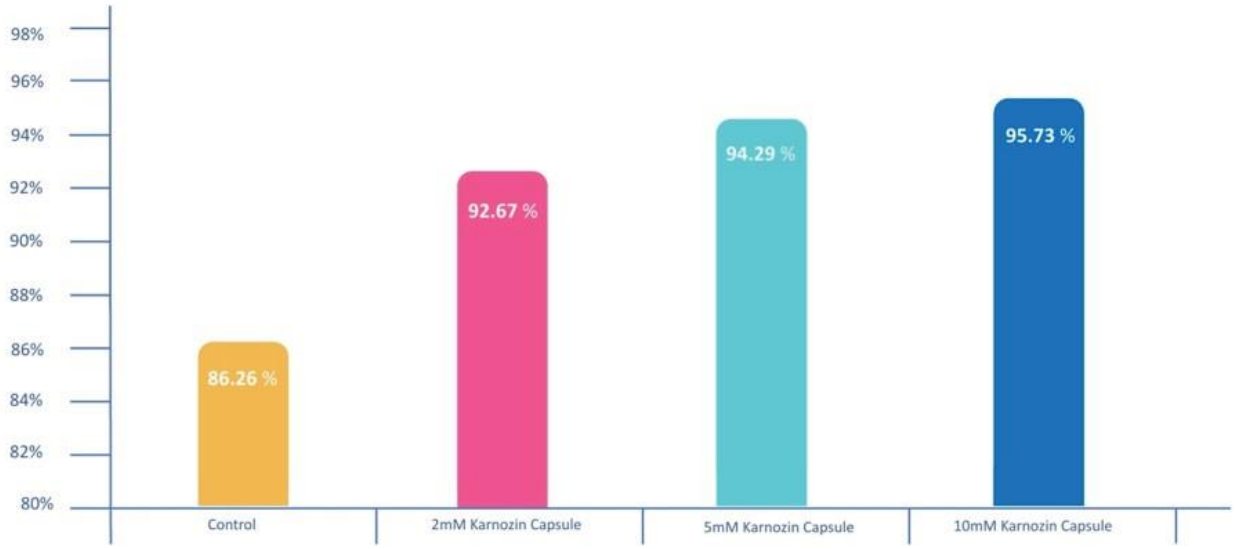
Above mentioned experiments were performed at Medical Faculty, University of Novi Sad.

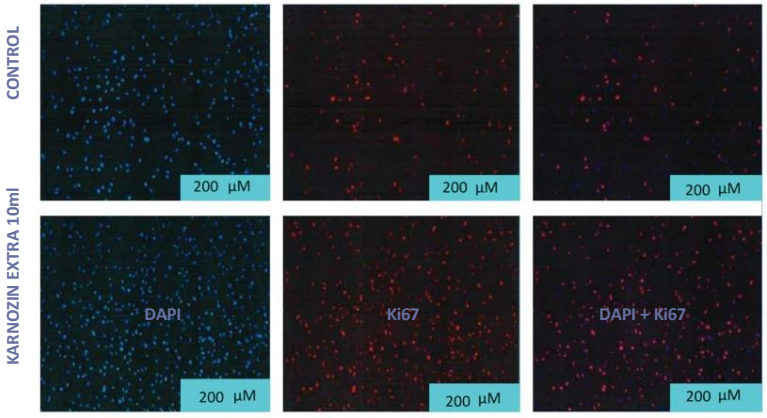
PhD, Biljana Bozin

PhD, Nebojsa Kladar

KARNOZIN EXTRA
AND NEUROBLAST CELL LINE

The second research Carnomed performed was the *in vitro* determination of the neuromodulatory potential of Karnozin Extra on neuroblasts cell culture. Neuroblasts are precursors of neurons and can divide to form new type of neuronal cells. We used neuroblast cell culture in our research to explore what effect our product has on the nerve tissue. When Karnozin Extra was administered into the culture in increasing concentrations (2mM, 5mM, 10mM), increased proliferative power of neuroblast was observed. This finding points to the positive trophic potential of Karnozin EXTRA preparation onto neuroblast cells in *in vitro* conditions, suggesting that Karnozin Extra functions something like a growth factor in the nerve tissue. And this might be a reason why Karnozin Extra is showing outstanding results in conditions where we observe the loss of neurons or diminished synaptic activity. Those disorders include autism, epilepsy, ischemic strokes, Alzheimer's and Parkinson's disease.





The research was conducted at Medical Faculty, University Of Novi Sad, under supervision of:

MD, PhD, Ivan Capo

MD, Dejan Miljkovic

KARNOZIN EXTRA AND *IN VIVO* MODEL OF MULTIPLE SCLEROSIS

The third research is an animal model of autoimmune encephalomyelitis, which is the model that in experimental conditions represents multiple sclerosis.

Multiple sclerosis (MS) is a condition of the central nervous system, interfering with nerve impulses within the brain, spinal cord and optic nerves. It is characterized by multiple lesions or scars. These scars occur within the central nervous system and depending on where they develop, manifest into various symptoms. MS affects more than two million diagnosed worldwide. Most people are diagnosed between the ages of 20-40, but it can affect younger and older people too. There is currently no known cure for MS and MS represents a significant clinical issue nowadays.

The study design was as following: There were 3 groups of mice, one control group, one that received the dose of 140mg/kg that corresponds to 2 capsules of Karnozin Extra in humans, and the third group received the dose of 420mg/kg that corresponds to 6 capsules of Karnozin Extra per day. We fed all 3 groups for 25 days, which corresponds to 2-2, 5 years in human lifespan.

BRIEF CONCLUSIONS:

- Administering the aqueous suspension of Karnozin Extra (Carnomed) in a daily dose of 140 mg/kg and 420 mg/kg for 25 days did not lead to statistically significant changes in body weight of mice.
- Administering the aqueous suspension of Karnozin Extra (Carnomed) in a daily dose of 140 mg/kg for 25 days (equivalent to a daily human dose of 2 capsules) **did not cause histologically visible changes and damages** to the kidney, liver, spleen, heart, pancreas, testis, digestive tubes and brain.
- Administering the aqueous suspension of Karnozin Extra Carnomed in a daily dose of 420 mg/kg for a 25 day period (equivalent to a daily human dose of 6 capsules) **did not cause histologically visible changes and damage** to the kidney, liver, spleen, heart , pancreas, testis, digestive tubes and brain.
- Administering the aqueous suspension of Karnozin EXTRA (Carnomed) in a daily dose of 140mg/kg for 20 days (equivalent to a daily human dose of 2 capsules), to animals with previously induced autoimmune encephalitis, **did not make the significant neuronal and glial-protective potential** relative to the control group of individuals without treatment.
- Administering the aqueous suspension of Karnozin EXTRA (Carnomed) at a daily dose of 420 mg/kg for 20 days to animals with previously induced autoimmune encephalitis **produced a potentially significant neuronal and glial-protective potential** relative to the control group of the animals without treatment.

Qualitative analysis of the tissue characteristics among the investigated groups with AIE showed that there were no significant differences between the control group AIE (group 1) and the experimental group with the use of Karnozin EXTRA in a dose of 140 mg/kg (group 2) with respect to the intensity of brain damage. However, in the group of mice with 6 capsules per day, it is observed less demyelinating areas and less inflammation. Those mice were in better shape and condition.

There were no observed morphological, histological and functional changes in lung, liver, kidney, heart, pancreas, brain, and spleen and testis tissues, even in high doses (6 capsules per day). That qualifies our product Karnozin Extra as highly safe for usage.

Research has been conducted at Medical faculty, University of Novi Sad, under supervision of:

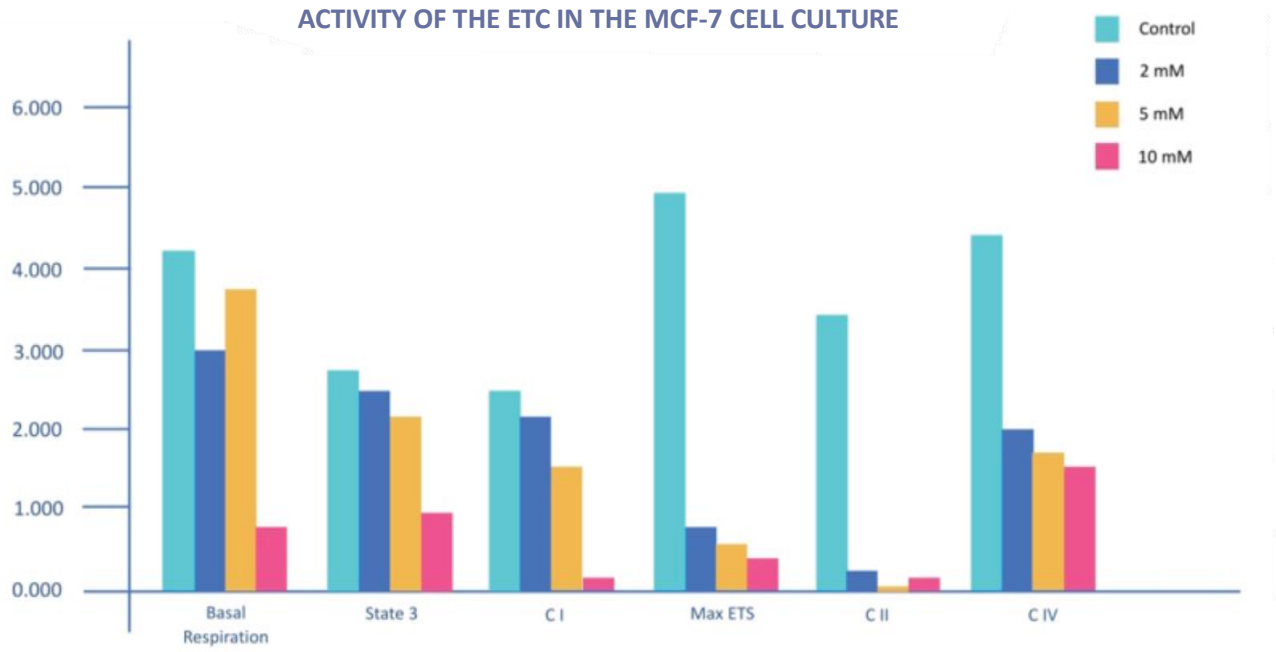
MD, PhD, Ivan Capo

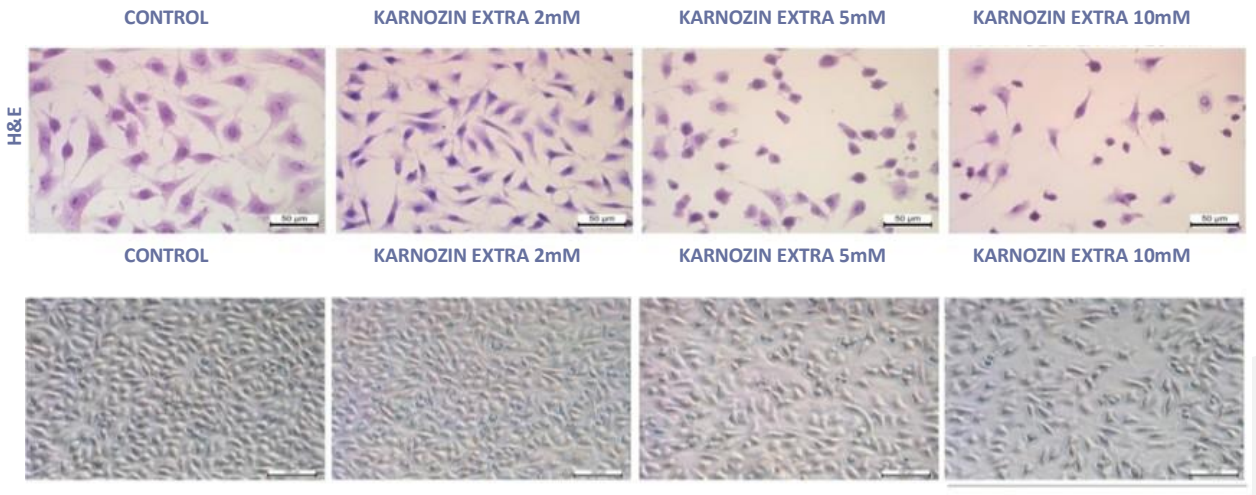
MD, Dejan Miljkovic

KARNOZIN EXTRA
AND MITOCHONDRIAL FUNCTION OF THE CANCER CELLS

We decided to investigate the effects of Karnozin Extra on oxidative phosphorylation, electron transport chain and production of ATP in the cancer cells. We have measured oxygen consumption in examined cell lines. The research has been completed at The Medical Faculty, University of Novi Sad.

We took human breast cancer cell line (MCF-7). And we made 4 groups out of this culture. The first was control group. In the second we added 2mM of Karnozin Extra, in the third we added 5 mM of Karnozin Extra, and forth one was with 10mM of Karnozin Extra.





WE HAVE LEFT THE CANCER CELLS TO GROW, AND HERE'S WHAT WE HAVE OBSERVED AFTER SOME TIME:

1. We have measured the basal respiration of the cancer cells. In other words, we measured how the cells breathe as a whole. We can see at this graph how 10mM of Karnozin Extra has significantly decreased the basal respiration of these cancer cells.

2. Furthermore, in the second measurement we added ADP to the cells in order to speed up the electron flow along the ETC. Basically, we measured the mitochondrial breathing or cellular respiration in this case. Again, the cellular respiration has significantly decreased after administration of 2, 5 and especially 10mM of Karnozin Extra

3. In the third measurement, we investigated how Karnozin Extra influences the activity of the first protein complex (NADH dehydrogenase) in the ETC. Again, significant reduction of the first complex activity has been observed after administration of Karnozin Extra, especially in higher concentration.

4. In the next measurement, we added the substrate to the cancer cells to speed up respiration to the maximum capacity. 2,5 and 10 mM of Karnozin Extra succeeded to decrease cellular respiration in this case.

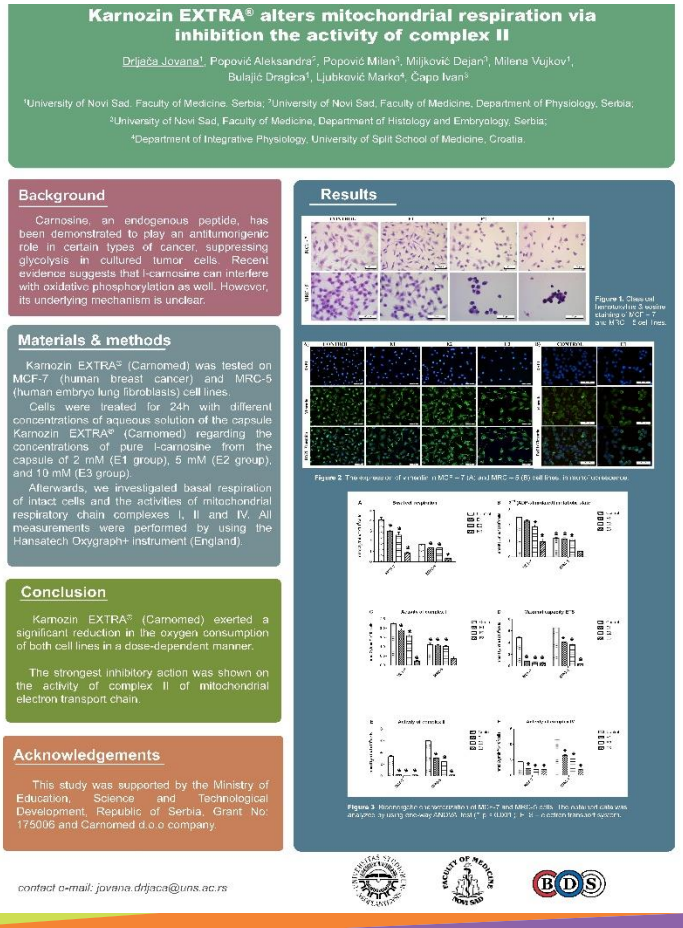
5. In the 5th measurement, we have observed decreased activity of the second protein complex in the ETC after administration Karnozin of Extra. Actually, Karnozin Extra showed its greatest inhibitory effect on the complex II, succinate dehydrogenase.

6. And finally, complex IV, cytochrome C oxidase. Similarly to other complexes, Karnozin Extra was able to reduce its activity in the dose dependent manner.

To summarize, Karnozin Extra blocks and inhibits the cellular respiration in the breast cancer cell line, acting on different components of the ETC in the mitochondria. The strongest inhibition is clearly seen on the complex II (succinate dehydrogenase). Moreover, Karnozin Extra shows its anticancer potential in the dose dependent manner. When higher concentrations of Karnozin Extra (10mM) were added to the culture, cancer cells have used less oxygen, and their respiration was compromised. Although this was *in vitro* examination on the cell cultures and not in the living organism, these findings suggest that it makes sense to further investigate Karnozin Extra anticancer potential in the animals and eventually show that Karnozin Extra can do the same in the human organism affected by cancer.

Project leader:
MD, PhD, Ivan Capo

Poster presented at Serbian Biochemical Society Conference



KARNOZIN EXTRA AND MOLECULAR BIOLOGY

Faculty of Natural Science in Novi Sad, Department for Molecular Biology has completed the research on rats using our supplements. We have fed middle aged rats with Karnozin Extra for 2 months (equivalent 6 years in human lifespan). The dosage we used in this experiment was only 2 capsules per day. **In this experiment we looked for their ability and will to run more than the control group.** We recorded their physical activity every 6 minutes, every day and night during 60 days, by using highly sophisticated software.

After statistical evaluation of data, it has been shown that group of rats that received Karnozin Extra run 40% more comparing to the control group.

The gathered data suggest that Karnozin Extra provided more energy to the rats, they were capable to run more and they had more will and initiative to move.

PhD, Silvana Andric

PhD, Tatjana Kostic

PRECLINICAL AND CLINICAL STUDY ON METABOLIC SYNDROME

Since it has been already proven in scientific literature that pure L-carnosine inhibits glycation, oxidation of LDL cholesterol and protects from atherosclerosis, we thought it would be a good idea to perform similar experiments with our product - Karnozin Extra. We obtained Regulatory and Ethics Committee approvals and the research is currently ongoing at Department of Pharmacology at Medical Faculty, University of Novi Sad. It includes *in vivo* model, more than 100 mice and rats are included and 50 patients with diabetes type 2. We are measuring their glucose, insulin and cholesterol levels, their antioxidant capacity and inflammatory markers, before and 3 months after taking our supplement. Also, biological activity of Karnozin Extra will be quantitatively compared with the commonly used drugs, metformin and simvastatin. Actually, this will be the PhD thesis of one of the students from Medical Faculty, University of Novi Sad, Serbia.

Preliminary results suggest very strong hepatoprotective properties of Karnozin Extra. Paracetamol-induced hepatotoxicity was developed in the control group of animals after administrating high doses of paracetamol. However, group of animals pretreated with Karnozin Extra had normal levels of liver enzymes.

MD, PhD, Aleksandar Raskovic

KARNOZIN EXTRA AND MULTIPLE SCLEROSIS - PATIENT-REPORTED OUTCOMES

We have been invited to present our scientific abstract at World Congress of Neurology which was held in Dubai on October 27-October 31. The abstract is related to 51 MS patients and their outcomes while taking Karnozin Extra supplement. They have reported reduced fatigue and increased quality of life after just 4 months of supplementation. The abstract is available online. The poster on the right side presents the study which was presented at the World Congress of Neurology in Dubai.

Medium-Term Carnosine Supplementation Positively Affects Patient-Reported Outcomes in Multiple Sclerosis

Jasna SIMICIC, Sergej M. OSTOJIC
Applied Bioenergetics Lab, University of Novi Sad, Serbia

WCN 2019 XXIV WORLD CONGRESS OF NEUROLOGY DUBAI, UNITED ARAB EMIRATES, OCTOBER 27-31 2019

ABSTRACT

Multiple sclerosis (MS) is a potentially disabling autoimmune disease of the central nervous system, with a rather uncertain prognosis and no cure. Supplemental carnosine seems to be beneficial for balancing contractile function and reducing fatigue while these functions are altered in MS; however, the effects of carnosine as an element of management of MS remain unclear. **PURPOSE:** In this preliminary study, we evaluated the effects of medium-term carnosine administration on Multidimensional Fatigue Inventory (MFIS) and Short Form Survey Instrument (SF-36) in adult patients with MS. **METHODS**: During 2018 (from March to November) 51 patients with MS (age 44.9 ± 8.4 years; 15 men and 36 women) were recruited and examined by a certified health care professional. All patients were allocated to an open-label treatment trial with supplemental carnosine (500mg/day) administered during the four months, with patients evaluated at baseline and at post-intervention follow-up. **RESULTS:** A total MFI score dropped after carnosine intervention (64.1 ± 19.1 at baseline vs. 52.5 ± 19.1 at follow-up; $P < 0.05$), indicating reduced self-reported fatigue for 18.1% in patients suffering from MS. This was accompanied by improved SF-36 scores for 14.5% at 4-month follow up. **CONCLUSION:** Supplemental carnosine is effective in reducing fatigue in mid-age patients with MS.

Background

Multiple sclerosis (MS) is a prevalent inflammatory-demyelinating disease, with fatigue and impaired quality of life often reported among key MS pathognomonics. Supplemental *L*-carnosine (dipeptide composed of beta-alanine and *L*-histidine) could be effective in reducing fatigue and improving quality of life in MS patients due to its antioxidative, anti-carbonylating, anti-glycation, neuroprotective and chelating properties yet no human trial evaluated this hypothesis.

Methods

In this open-label interventional preliminary study, 51 MS patients aged 20 to 65 years received oral *L*-carnosine formulation (500 mg per day b.i.d.) during 4 months; most of the patients (83.0%) had relapsing-remitting MS. At baseline and at each month follow-up visits, patients completed two questionnaires: (1) Multidimensional Fatigue Inventory (MFI), a 20-item self-report instrument designed to measure fatigue; and (2) Short Form Survey Instrument (SF-36), patient-reported survey of patient health.

Results

Compliance with the intervention (determined by capsule counts at final visit) was high (88.0 ± 11.4%). Total MFI score improved from 52.5 ± 19.1 at baseline to 64.1 ± 19.1 at 4-month follow-up ($P < 0.05$) (Figure 1). MFI subscales analysis revealed a significant change for cognitive and physical domain after an intervention ($P < 0.05$). This was accompanied by improved SF-36 scores for 14.5% at 4-month follow up (Figure 2).

Conclusion

Medium-term supplementation with *L*-carnosine resulted in a significant fatigue reduction and improved health-related quality of life in men and women suffering from MS, while a treatment protocol was well tolerated. Therefore, oral *L*-carnosine may become an important adjuvant to the pharmacological therapeutics available for the management of MS-related fatigue and quality of life. Long-term well-sampled studies are highly warranted to confirm these preliminary results.

Figure 1. Changes in total MFI score and MFI subscales during the study. Values are mean ± SD. Asterisk denotes significant difference ($P < 0.05$) baseline vs. 4-month follow-up.

Figure 2. Total SF-36 score at baseline and at each follow-up visit. Values are mean ± SD. Asterisk denotes significant difference ($P < 0.05$) baseline vs. 4-month follow-up

Poster presented at World Congress of Neurology held in Dubai, October 2019

KARNOZIN EXTRA AND MULTIPLE SCLEROSIS-PILOT CLINICAL STUDY

Multiple sclerosis (MS) is a complex autoimmune disorder that affects millions of people around the world, negatively interfering with different aspects of health and everyday life. Being the most frequently seen demyelinating disease, MS prevalence varies considerably, from high levels in North America and Europe to low rates in Eastern Asia and sub-Saharan Africa. Due to its rather high prevalence in developed countries, the development of effective and applicable strategies to prevent or manage.
MS becomes a must for the medical community.

Among other factors, it appears that low levels of tissue carnosine and mitochondrial dysfunction accompany MS (Keytsman et al, 2018), with oral carnosine might be applicable to tackle impaired bioenergetics and oxidative stress in MS, and perhaps win back neuromuscular function (Eijnde. Carnosine loading in MS. clinicaltrials.gov ID: NCT03418376). However, several formulations of carnosine have shown limited applicability due to restraints in brain delivery or tissue performance (Sariev et al, 2015) thus pushing both industry and researchers to find bioavailable and effective formulation of carnosine. No human studies so far evaluated the impact of inn ovative L-carnosine formulation (Karnozin Extra) in MS. Here, we will evaluate the impact of supplemental carnosine on neuromuscular performance, brain biomarkers of carnosine metabolism, and health-related quality of life in a case series of patients with MS.

We are the first in the world who are investigating the association between L-carnosine and multiple sclerosis.

The first clinical pilot study related to Karnozin Extra and Multiple Sclerosis (CARMUS) was initiated in June 2019 at Applied Bioenergetic Lab, University of Novi Sad. It included 3 MS patients, where we measured their work capacity, autonomic nervous system function, blood analysis and levels of L-carnosine and other metabolites in the brain using MR spectroscopy before and after 8 weeks of supplementation with Karnozin Extra.

The study was completed in December 2019 and we obtained promising results. All patients experienced reduced fatigue accompanied by improved walking capabilities. Brain levels of significant metabolites increased, specifically there was an average increase of 18.9% in choline-containing substances, 21.2% in creatine and 12.3% in myo-inositol. Additionally, lactate levels decreased by 23.5%. Analysis of cardiovascular reflexes indicated normalized parasympathetic and sympathetic function in all patients. Total antioxidant capacity increased up to 49% after 8 weeks of Karnozin Extra administration These findings suggest that Karnozin Extra presents an important adjuvant treatment in multiple sclerosis. The results are published in the peer-reviewed journal Nutrition Research. The abstract was accepted for presentation at Nutrition 2020 Congress, held in Seattle, WA, the US from May 30 - June 2.

The Principal Investigator:
MD, PhD, Sergej Ostojic

KARNOZIN EXTRA AND AUTISM

After Dr. Michael Chez had published study about autism and L-carnosine in Child Neurology in 2002, we haven't investigated enough the relation between L-carnosine and autism. Therefore, Carnomed decided to conduct clinical study where we will include 35 children with autistic spectrum disorders age 3-7. The study title: Efficacy and safety of a combined antioxidant supplement for children with autism: A prospective, follow-up study with Karnozin Extra®

We will evaluate their behavior and social skills using different standardized behavior scales before and after 12 weeks of using our Karnozin Extra.

Project leader and Principal Investigator:

MD, PhD, Dejan Stevanovic

We are also very proud and would like to point out that today we have more than 20 respected University Professors, from different disciplines (medicine, biology, chemistry, agriculture and technology) involved in Carnomed scientific work. They truly support us and all references about our collaborative work are available upon requests.

CONCLUSION

Karnozin Extra is perfectly safe supplement that can be used in a wide range of diseases and disorders. It is well tolerated and has no identified side effects or adverse drug interactions. The dosage should be from 1-2 capsules for infants, up to 10 capsules per day in neurodegenerative disorders that are present in elderly population. As a prevention of the aging process, 2-3 capsules per day are recommended. With its multitargeted physiological actions Karnozin Extra serves to prevent age-related diseases such as cognitive decline and dementia, to promote exercise comfort and performance, to slow progression of metabolic conditions such as diabetes, and to defend against atherosclerosis and heart disease.

Education is very important to us, and so is spreading our knowledge, research and findings. We really hope that all our committed work, supported with scientific background, clinical and other studies, all evidence-based, will help us to reach and to introduce to as many people as possible the product that might change their lives.

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