



The Cataract Cure

and ground-breaking
therapies for other
eye conditions

By Marios Kyriazis, MD

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Dr. Kyriazis is one of Britain's top anti-aging physicians and is internationally recognised as a pioneer in the field. He is a bio-gerontologist with a medical degree and postgraduate degrees from King's College, London and the Royal College of Physicians. He has written many books for both the medical professional and the public alike and his articles have been widely published. In 1991 Dr. Kyriazis founded the British Longevity Society, one of the earliest societies in the field still operating today.

Prologue

Dr. Marios Kyriazis brings a wealth of medical expertise to one of the most important breakthroughs in recent times to help combat a disease called 'senile cataract,' a disease that affects one in five people over the age of 55.

In the past, the only treatment available for this chronic condition was surgery, which by its very nature can lead to serious complications. We must also consider that the replacement of a natural lens with a plastic one leads to a loss in accommodation; in brief a plastic lens is not as good as a natural one.

But now other non-surgical treatments are available, in particular the Russian development of N-acetyl-carnosine. In clinical trials this eye-drop treatment has shown dramatic and impressive results in treating age related cataracts.

Furthermore, The Cataract Cure also covers other associated eye disorders including;

- Glaucoma
- Macular degeneration
- Infection of the cornea
- Dry eye syndrome
- Computer vision syndrome
- Eyestrain
- vBlurred vision

The Cataract Cure is a resource for all persons interested in knowing about alternative approaches to eye care, approaches that are still proven, scientific and based in clinical experience.

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Foreword

As a researcher my work has taken me around the globe in search of new and exciting developments in the hunt for both preventative and curative therapies.

The world has many innovative products and technologies that are not well known and from time to time a particularly exciting development come to the fore; N-acetyl-carnosine eye-drops for cataract are just such an example.

In this publication Dr. Kyriazis highlights the background to its development and its studies and also looks at the clinical applications that make these eye-drops special. In addition, his patient examples and testimonials bring that intimate feeling that makes a discovery something personal and somehow even more important.

With an ever increasing 'older' population the incidences of age-related disorders such as senile cataract are ever more prevalent. As Dr. Kyriazis highlights in 'The Cataract Cure' this new research has proven that an eye-drop can slow, arrest and even reverse cataracts. Therefore, it not only represents an excellent example of 'antiaging medicine' at its best, it is also an important breakthrough for eye care.

Dr. Kyriazis book doesn't 'just' discuss the topic of cataracts, but includes additional information regarding other class leading therapies and nutrition; procedures that can ameliorate and improve many other troubling eye-sight problems including glaucoma and macular degeneration.

My recommendation is that anyone who is concerned about their failing eyesight and vision difficulties should digest and act upon the information presented here.

Phil Micans, MS, PharmB

Intro

Chapter 1: Introduction

History tells us that we now live longer than ever before. Scientific advances have ensured that many illnesses have been successfully eliminated and newer therapies are being discovered to deal with existing illnesses. Within the next 20 years we may experience an even more dramatic extension of the human life-span, made possible by discoveries in the field of genetics, stem cells, growth factors, calorie restriction mimetics and nanotechnology. Until that moment arrives, we need to deal with existing age-related disorders as best we can, and to be able to do this, we need to know exactly how aging works.

Most anti-aging researchers and physicians accept that a major factor involved in aging is damage caused by free radicals. These are a group of simple compounds with an electron missing from their chemical structure. The lack of electron makes free radicals very unstable. Due to reasons based on chemistry and chemical laws, free radicals need to obtain the missing electron from somewhere, and so they must seek out other molecules from which they can acquire an electron.

Examples of free radicals are:

- » Superoxide radicals

- » Hydrogen radicals
- » Hydroxyl and nitric oxide radicals

These reactive molecules destroy other molecules around them causing what we now call 'aging'. Free radicals affect every organ of your body, constantly. By the time you have finished reading this sentence, your DNA, proteins and cells have already been, minutely but irreversibly, damaged.

Therefore, it is important to keep free radicals under control, and Nature has made arrangements for this. We carry inside us a variety of antioxidants, natural chemicals which mop up free radicals and destroy them, keeping damage low. The problem is, with the passage of time, the effectiveness of these antioxidants worsens, and so we become unable to fight free radicals effectively. In this way, age-related damage accumulates until the time of death.

Apart from free radicals, another important cause of aging is glycation. During everyday metabolism, natural chemicals in your body such as glucose, fructose, aldehydes and ketones may attach themselves onto your proteins, during a process called glycation. This reaction is also sometimes called the Maillard reaction. It results

in a glycated protein, i.e. a protein carrying sugar (or similar) molecules on it. This glycated protein may then react with any other proteins resulting in irreversible bonding between the two. This bonding process is named 'cross-linking.'

Affected molecules can be anything from collagen and elastin (found in your skin, arteries or other internal tissues), to enzymes and proteins of the immune system. Facilitators during the cross-linking process are the carbonyl groups which act like glue, fixing the two proteins together. Carbonyls are fragments of chemicals which are formed as a result of a sugar (or an aldehyde or a ketone or a free radical) reacting with amino acids on a protein. Also, carbonyls can be formed in other situations involving fats or DNA. So, carbonyls may not only cause protein-to-protein cross-linking, but also protein-to-DNA, or protein-to-lipid cross-linking, which is equally damaging to your body.

Cross-linking results in formation of large insoluble amounts of damaged proteins in the tissues, including the eye. These damaged proteins are called AGEs (Advanced Glycation End products) and may then go on to combine with free radicals and cause yet more tissue injury (this is called 'chronic oxidation'). Although a steady rate of AGE formation happens as a result of normal aging (starting after the age of 20), formation of AGEs is accelerated during diabetes. AGEs then block activities within the cells, stimulate cells to produce more free radicals (such as superoxide and nitric oxide), and activate toxic chemical such as Tumour Necrosis Factor alpha (TNF- α) and interleukin 6. In this way, AGEs are contributing to age-related chronic diseases or even cancer.

Chronic diseases which can be caused by glycation and cross-linking are:

- » Diabetic complications
- » Poor immunity
- » Increased risk atherosclerosis and high blood pressure
- » Alzheimer's dementia
- » Kidney damage
- » Skin aging
- » Cataract (glycation, cross-linking and AGEs are particularly relevant to the eye where

they may cause significant harm as will be described below).

There are commercially available blockers of cross-linking (antiglycators). Examples of these include carnosine, aminoguanidine, metformin, acarbose, and pyridoxamine. Some of these (like acarbose and metformin) are already in use as drugs against diabetes, but new research coming to light is now emphasising their additional anti-cross-linking effects. However, only carnosine (under the form of N-acetylcarnosine) can be given in eye drops form for treatment of chronic eye conditions.

Three examples of effective anti-glycators are:

1. Carnosine

This combination of the amino acids beta alanine and L-histidine is a naturally-occurring agent found in muscle and nervous tissue. Carnosine has been hailed as one of the most promising cross-link inhibitors, and so it has been used against cataract as you will soon see. It has multiple actions and as such it has been called a pluripotent agent. One way carnosine works is by scavenging for free carbonyl groups. It is one of the few cross-link inhibitors that is not only active against protein-to-protein cross-linking but also against protein-to-DNA cross-linking.

Carnosine has a direct antioxidant action, and it also protects and activates many other antioxidants, such as glutathione. It is a strong chelator of heavy metals, mopping-up any toxic metal ions in your body which may result in accelerated free radical attack. Finally, it has a possible, yet unconfirmed, bond-breaking capability by dissolving certain bonds (S-S bonds) on cross-linked proteins. In measurements of arterial wall flexibility, carnosine seems to be able to relax the arterial wall and thus improve blood flow. This particular benefit of carnosine may be related to its ability to stimulate nitric oxide, a molecule that relaxes the muscles within the arteries.

Several experiments have highlighted carnosine's ability to reduce free radical

and glycation metabolism, both in humans and in animals. One of the most important developments regarding carnosine is its ability to prevent and cure age-related cataract, and possibly glaucoma and other chronic eye conditions. In this respect the form of carnosine used is N-acetylcarnosine. This curative action of carnosine is perhaps related to its ability to stimulate elimination of damaged proteins from the eye.

The dose of oral carnosine is anything from 50 mg to 300 mg a day, up to 500 mg to 1500 mg a day. With higher doses, there have been occasional reports of allergic reactions. Carnosine can also be obtained from a meat rich diet, particularly from chicken breast, rabbit, pheasant and other game (especially sprinting animals).

The interest in the use of carnosine and its derivatives for the treatment of cataract has been increasing over the past 3 years. Writing for a major peer-review journal, scientists from the Department of Ophthalmology, Christchurch Hospital, Christchurch New Zealand, have commented: "Since the last major review of medical treatment of cataract the search for an anti-cataract agent has advanced on many fronts. Some anti-cataract drugs, such as carnosine, have now reached clinical trials and showed encouraging results that warrant further investigation. The discovery of an effective medical treatment for cataract is likely to make global impact on eye health."

Reference: Toh T, Morton J, Coxon J, Elder MJ. Medical treatment of cataract. Clin Experiment Ophthalmol. 2007;35(7):664-71.

2. Metformin

Metformin is a frequently used drug used against diabetes (both against the insulin-dependent and against the non-insulin-dependent varieties). It can also lower cholesterol, reduce body fat, beef-up antioxidant defences and inhibit glycation. It limits the formation of AGEs, particularly those affecting collagen.

Recent experiments show metformin to have widespread activities as a cross-link inhibitor. It reduces cross-linking of fibrin proteins which take part in the clotting of blood. Exaggerated cross-linking of fibrin results in abnormal blood clotting and therefore an increased risk of thrombosis with consequent heart disease or stroke.

There are no clinical studies evaluating metformin in cataract, but diabetic patients who are already on it are likely to be receiving its antioxidant, antiglycating benefits. Moreover, because it helps improve the circulation of the blood (by reducing the risk of thrombosis), it may be additionally useful in eye diseases such as macular degeneration, cataract and glaucoma.

Metformin is a calorie restriction mimetic which means it has many biological benefits associated with calorie restriction itself. Calorie restriction is the only proven method that can increase maximum lifespan, and reduces the likelihood of age-related conditions, including cataract.

3. Aminoguanidine

An agent structurally similar to metformin is aminoguanidine. As with the case of metformin, aminoguanidine also works by reducing the concentration of free carbonyl groups. In particular, it is active against certain aldehydes which contribute to cross-linking. It is effective mainly during the early stages of glycation.

Aminoguanidine is a potent inhibitor of any cross-linking which is initiated by glucose molecules but not as effective in situations involving ribose-related cross-linking. In any case, it prevents collagen cross-linking in tendons and skin, which shows its potential for prevention of muscle and joint age-related stiffness, and skin ageing (wrinkles). It limits the development of diabetic complications in animals (including eye complications), and it has shown promising effects in improving diabetic kidney disease. Also, it is a weak copper chelator. Copper chelation is important in AGE-induced damage, as high amounts of free copper are more likely to increase AGE-induced injury.

An additional action of aminoguanidine is that it prevents cross-linking between lipoproteins (proteins carrying fat molecules) and therefore reduces the risk of blockage of the arteries, particularly the small arteries that feed the small nerves of the eye. It should, therefore, be of use in eye conditions where blood supply is compromised. Experiments using aminoguanidine in eye drops form for prevention of cataract are currently under way.

Apart from anti-glycators, certain other agents have specific and promising benefits on eye disease. One such agent is melatonin.

Melatonin in some age-related eye conditions

In the eye, melatonin is produced in the retina, but production gradually declines with age. Adding extra oral melatonin supplements is believed to protect against many degenerative eye conditions. The presence of cell receptors for melatonin in the eye indicates that this substance has an important physiological role to play in several functions related to vision.

It has been shown that melatonin (N-acetyl-5-methoxytryptamine) prevents free radical damage to the tissues and also it scavenges and neutralises free radical in the eye.

Current evidence suggests that melatonin may protect against eye diseases such as cataract, keratitis, glaucoma, retinopathy and other injury to the eye. The cause of these conditions is thought to be, partly, due to oxidation damage which causes loss of cells (apoptosis), and degeneration of retinal neurons. Free radicals such as nitric oxide in the eye neurons and superoxide in the mitochondria of the axons produce dangerous toxins such as peroxynitrite. Among the substances that have actions against peroxynitrite is also melatonin.

Also see the paragraph below for further information of melatonin in the treatment of macular degeneration.

Cataract

In cancer patients undergoing radiotherapy, the

effect of irradiation on the eye can be significant, contributing to a worsening of cataract.

However, researchers from the Department of Radiation Oncology, Atatürk University, in Turkey have shown that melatonin supplements protect the lens of the eyes from radiation-induced cataract formation. The researchers suggest that supplementing cancer patients with melatonin may reduce the risk of radiotherapy-induced tissue injury.

Glaucoma

With regards to glaucoma, current research suggests that it could reduce intraocular pressure and so it can be of real help in this condition.

Reference: Mediero A, Alarma-Estrany P, Pintor J. New treatments for ocular hypertension. Auton Neurosci. 2009 11;147(1-2):14-9.

Note- this is believed to be due to melatonin's antioxidant effect, which is still being investigated.

Macular degeneration

Researchers from the Zhongshan Ophthalmic Center, Sun Yat-Sen University in China have reported that melatonin can help reduce the progression of macular degeneration. It is well known that melatonin controls eye pigmentation and so regulates the amount of light that reaches the visual receptors in the eye.

These researchers studied 100 patients suffering from either the wet or the dry form of macular degeneration. The patients were given 3 mg of melatonin every night, (the precise formula was designed by Dr. Walter Pierpaoli and also contained zinc and selenium in addition to the melatonin, it is called Melatonin Zn-Se or MZS™).

After a six month period, the scientists found that the patients' visual acuity was stable, i.e. there was a slowing down of the natural worsening of the condition. The scientists said: "We conclude that the daily use of 3 mg melatonin [with zinc and selenium] seems to protect the retina and to delay macular degeneration. No significant side effects were



These photographs (fundus pictures) attest to the slowing and reversal of both wet and dry forms of age related macular degeneration (ARMD). Patients took one MZS™ tablet (3mg melatonin, 50mg zinc and 50mcg selenium) nightly.

Top set: The left slide shows the eye of a 67 year old male before treatment, his vision had been deteriorating for 2-years. The right picture shows the same eye 2-months later after daily ingestion of one MZS™ tablet nightly. He now has stable visual acuity of 0.3 with remarkable improvements in sub-retinal macular hemorrhage.

Bottom set: The left slide shows the eye of a 71-year old female with ARMD before treatment. The right slide is her eye after 6-months of one MZS™ tablet nightly. Her vision improved from 0.2 to 0.4 (as indicated in the right slide).

Reference: Effects of melatonin in age related macular degeneration. Changxian Yi, Xiaoyan Pan, Hong Yan, Mengxiang Guo, Walter Pierpaoli. New York Academy of Science, volume 1057, 385-392, December 2005.

observed. “

A recent report by Austrian scientists confirms the antioxidant properties of melatonin with regards to the eye, commenting that patients with macular degeneration try to produce more melatonin as a defence mechanism against the condition.

Reference: Schmid-Kubista KE, Glittenberg CG,

et al. Daytime levels of melatonin in patients with age-related macular degeneration. Acta Ophthalmol. 2009;87(1):89-93.

So, to summarise, free radicals and glycation are two important causes of aging, and can cause a variety of chronic diseases, including cataract and other degenerative eye diseases. Certain nutrients and drugs are now commercially available, which may help protect against such

Chapter 2: Cataract

Age-related (senile) cataract is a chronic, progressive eye disease affecting the lens in the eye, resulting in reduced vision. The lens is a transparent, pale yellow structure made of special proteins (crystallins) and other clear material, allowing the light to pass through and focus onto the retina, so an image can be formed. It is found behind the pupil of the eye and it is surrounded by an elastic capsule. The lens is a relatively simple structure and it grows throughout life from the inside outwards.

When the lens is affected by age-related damage, it becomes opaque and cloudy, reducing the

amount of light reaching the inside of the eye and so vision is impaired.

Did you know?

Cataract is a Greek word, meaning ‘waterfall’. Indeed, the ancient Greeks compared the visual impairment of a patient with cataract to the difficulties in trying to see through a waterfall.

Cataract affects one in four people over the age of 65, and one in two people aged 80 and above.

About 28 000 new cases worldwide are reported every single day, and 17 million people across the world are blind due to cataract. Operations to treat cataract cost the US alone \$3.5 billion a year, and 43% of visits to eye specialists in the United States are associated with cataract. Therefore, there is considerable interest in finding ways to prevent the condition and reduce the burden upon health-providers.

The problem is that in developing countries cataract remains, on the whole, untreated due to lack of resources. In such countries it is a major cause of blindness. It is impossible to provide enough eye surgeons to manage all the cases of cataract in developing countries, not only due to the high cost involved but also due to lack of manpower.

Did you know?

Around 9 million people in developing countries (in Africa and Asia) are blind due to cataract. Put another way, one in every hundred residents of Africa is blind, and the frequency of the disease is increasing.

As we generally live longer than ever before, age-related diseases such as cataract are now becoming more frequent and affect people for longer. However, cataract does not only happen to older people. Younger groups are also affected. Apart from genetic causes of cataract, two well known causes are use of steroids and diabetes. Also, diet has been implicated as a cause. People who consume poor quality food are at a greater risk of cataract, and poverty is a risk factor making cataract more likely. This may be because a diet which is poor in high quality vegetables, protein and fruit does not provide enough nutrients to prevent the free radical damage to the eye.

You may remember from the discussion in Chapter 1 that free radicals and glycation cause proteins inside the lens to attach to each other, a process called cross-linking. This mass of abnormal proteins scatters the light and does not allow it to pass through. The crystallins in the lens become abnormally distorted and can

settle in different parts of the lens, for example the top, the middle, the outside, or the entire lens, causing different types of cataract. What is important here is that an opaque lens is not a useful lens, as the light must pass through it uninterrupted. Therefore, any treatment which reduces damage to crystallins is bound to result in effective clinical improvement of cataract.

From the nutritional point of view, lack of antioxidants in the diet has been shown to worsen the risk of cataract and other eye diseases such as glaucoma. Patients with cataract are frequently found to be deficient in antioxidants such as vitamin A, glutathione, lutein and zeaxanthin. Riboflavin (a member of the vitamin B group) is essential in modulating the activities of certain antioxidants in the eye.

Nutrients such as the following are all useful in providing protection against free radical in the tissues of the eye. Many experts recommend supplementing the diet with these nutrients as an extra insurance against eye disease.

- » Pantethine
- » Folic acid
- » Bilberry

In diabetic patients, the risk of cataract is increased. This is believed to be due to an accelerated rate of destruction of the lens by glycation, in the presence of too much glucose in the blood. An enzyme which takes part in facilitating the reaction between sugars and proteins is called aldose reductase. Nutrients such as quercetin (from fresh fruit and dark vegetables) were found to specifically block the actions of aldose reductase, and so reduce the rate of protein destruction within the lens.

The point here is that cataract is due to an excessive rate of crystallin destruction within the lens, and that this rate can be accelerated by bad nutrition or diabetes:

- » Retinal detachment (0.8%)
- » Corneal swelling, needing a corneal transplant (1%)
- » Loss of accommodation (the inability to re-adjust the pupil of the eye according to the amount of light in the environment).

Another problem is that between 30% and 50% of patients who have had cataract operation may not be cured completely, their symptoms may re-occur and they may need an additional operation with laser.

Did you know?

In the USA, approximately 26,000 patients a year develop complications following cataract operation. Of these, approximately 7000 become irreversibly blind due to complications of the surgery.

In addition to the complications mentioned above, there is also a generally increased risk of dying following surgical treatments to the eye. Even the presence of cataract itself is associated with an increase risk of dying. When groups of people with cataract were compared to similar groups, and the statistics were adjusted to account for age, sex, and other illnesses, it was

found that those with cataract have a higher risk of dying. This does not mean that cataract itself causes death. It merely means that cataract is just an indication, a sign of accelerated aging which affects all parts of the body. This accelerated aging then increases the risk of death.

Writing for the Anti-Aging Bulletin™ in 2003, Dr. Robert Mason said: “It is difficult to support the argument that cataract research is unimportant with statistics as those cited above. The large and growing number of people with cataract and the significant complication rate should be sufficient reason to increase cataract research. A medical solution is required that will maintain the transparency of the lens. Even if the development of cataract can be delayed by 10 years, the overall benefits would be highly significant.”

So, any non-surgical treatment of cataract is particularly welcome, specifically in the case of eye drops which are considerably cheaper compared to the operation.

Chapter 3: N-acetylcarnosine eye-drops

Free radicals have been heavily implicated in causing cataract. These toxic by-products of your everyday metabolism combine with fat molecules on the cells and destroy them, during a process called lipid peroxidation. During the initial stages of cataract there is considerable build-up of chemicals which are a sign that lipid peroxidation has taken place. This means that the constituents of the lens have already been damaged. Once the lens is damaged, any further attacks by free radicals become even more harmful leading to a steadily progressing loss of vision.

The lens is protected by the aqueous humour, a fluid produced in the eye and containing fatty proteins. These fatty proteins can easily be harmed by free radicals worsening any initial damage to the inside of the lens and compounding the opacity of the lens.

Lipid peroxidation is a particularly vicious process in the eye (as well in other parts of the body). It is slow, progressive and devastating. Several experiments looking at how the lens is affected by free radicals have shown that the lipid content of the lens is vulnerable to the attack. The final result is a damaged lens with

cross-linked crystallin fibres, which reduce vision. Treatment with antioxidants such as glutathione was found to prevent cataract and slow down the progression of established cataract.

Did you know?

Even a small amount of free radicals in the lens, and consequently a small degree of lipid peroxidation, is enough to induce cataract.

In addition to free radicals created by your body, the lens can also be affected by ultraviolet (UV) light from the sun's radiation. This process is called 'direct photo-oxidation' which means that the light passing through your eye may interact with certain chemicals such as kynurerine. The resulting chemical reaction creates further free radicals and other toxic products (from lipid peroxidation) which combine with crystallins and cause more cross-linking. This process happens to all types of cataract, including to the type caused by aging, by diabetes and by drugs.

NAC activities and properties

N-alpha-acetyl-carnosine (NAC) is a naturally occurring compound, related to the nutrient carnosine (which is also called L-carnosine). Its molecular structure is similar to carnosine with the exception that it carries an additional acetyl group. What this means is that NAC is a more stable molecule which is not easily destroyed by any enzymes.

It is particularly active against lipid peroxidation in the different parts of the lens. Together with carnosine, NAC is an effective free radical scavenger, which circulates in your blood and tissues, identifies any free radicals and inactivates them. As mentioned above, NAC is not easily destroyed by the different chemical reactions that take place around the lens. This means that it can enter the lens and the tissues around it, where it then breaks down into the active form, L-carnosine. In turn, L-carnosine mops-up any free radicals and repairs the damage caused by any such free radicals which remain undetected. In this respect, NAC has

been described as a 'time release pro-drug' of carnosine, in the sense that it enters the tissues and then gradually breaks down to allow carnosine to work.

Some scientists believe that it would be difficult to administer pure carnosine directly into the eye, because the carnosine molecule would be inactivated by carnosinase (a natural enzyme which breaks carnosine down) and lose its effectiveness. But NAC is resistant to carnosinase in the eye and it is therefore ideal for administration as eye drops. Normally carnosine is present in the lens at an average concentration of about 25 microM. During the development of cataract this concentration drops to as little as 5 microM. However, administration of pure L-carnosine (1% solution) to the rabbit eye does not increase the concentration of carnosine in the lens. The use of NAC not only increases carnosine in the lens but also optimises the clinical effects of L-carnosine.

In addition, the exact way carnosine and NAC are manufactured is important. Carnosine extracted from meat substances has a low biological activity because it may be contaminated with impurities like hydrazine and heavy metal salts. It is quite difficult to purify carnosine using traditional ways such as chromatography. This is because as soon as carnosine is purified, it binds again to metal ions present in the mixture and so it becomes contaminated again. As you will see later in the book, the manufacturers of NAC devised a special method of purifying NAC which, in turn, releases carnosine in a controlled way.

The research

During early experiments performed at the Moscow Helmholtz Research Institute for Eye Diseases, scientists have used NAC eye drops (1% concentration) on rabbits in the laboratory. They compared this treatment with placebo (inactive eye drops). NAC was able to reach the inner parts of the eye (from the cornea to the aqueous humour) after about 15 to 30 minutes. During this process, NAC was broken down to form carnosine, which was then free to work against free radicals and glycation processes inside the eye. The advantage of using NAC

eye drops is that the active ingredient works both within the watery and within the fatty components of the cells, and so it reaches deep into the cell. During this experiment, no side effects were reported. The authors concluded that; "NAC is proposed as a treatment of eye disorders which are due to free radical damage, including cataract, glaucoma, retinal degeneration, corneal disorders, inflammation and complications of diabetes"

In a landmark study, a group of scientists who performed the earlier experiments on rabbits studied the effects of NAC eye drops on humans. The scientists selected 49 volunteers with an average age of 65 years, who had established age-related cataract. They then divided the patients into three groups:

- » Group one, was treated with 1% solution of NAC eye drops.
- » Group two was only treated with placebo eye drops.
- » Group three was left untreated.

The patients were examined at two and six month intervals. Several techniques were used to assess the patients' progress, for example, scanning of the lens, glare tests, slit-image and retro-illumination photography (a technique used by ophthalmologists to assess the state of the lens) and so on. The resulting photographs were then analysed by a computer. The results showed that, compared to the untreated patients:

- » After 6 months, approximately 41% of the eyes treated with NAC presented a significant reduction of the clouding of the lens.
- » 90% of the treated eyes showed a gradual improvement of vision.
- » 89% of the eyes showed an up to 100% improvement of sensitivity to glare.

The total period of this study was 24 months, and the results were sustained for the whole of this period. No significant side effects, allergies or eye irritation were reported. The authors of this study concluded that; "NAC appears to be suitable and acceptable for non-surgical treatment for senile cataract". Due to the

importance of this study, the entire abstract of the research is reproduced in Box 1 for those who are more technically-minded.

BOX 1: The abstract of the study as published in *Drugs R&D* 2002, 3(2):87-103

Title: Efficacy of N-Acetylcarnosine in the treatment of cataracts

Authors: Mark A. Babizhayev, Anatoly I. Deyev, Valentina N. Yermakova, Yuri A. Semiletov, Nina G. Davydova, Valerii S. Doroshenko, Alexander V. Zhukotskii and Ita M. Goldman

Purpose: To evaluate the effects of 1% N-acetylcarnosine (NAC) solution on lens clarity over 6 and 24 months in patients with cataracts

Trial design: Randomized, placebo-controlled study

Participants: 49 subjects (76 affected eyes) with an average age of 65.3±7.0 years, with a diagnosis of senile cataract with a minimum to advanced opacification in various lens layers.

Methods: 26 patients (41 eyes) were allocated to topical NAC 1% eye drops twice daily. The control group consisted of 13 patients (21 eyes) who received placebo eye drops, and 10 patients (14 eyes) who did not receive eye drops.

Main outcome measures: All patients were evaluated at entry and followed-up every 2 months for a 6 month period (trial 1), or at 6-month intervals for a 2-year period (trial 2), for best-corrected visual acuity and glare testing. In addition, cataract was measured using stereocinematographic slit-images and retro-illumination examination of the lens. Digital analysis of the lens images displayed light scattering and absorbing centers in two- and three-dimensional scales.

Results: The overall intra-reader reproducibility of cataract measurements (image analysis) was 0.830, and glare testing 0.998. After 6

months, 90% of NAC-treated eyes showed improvement in best corrected visual acuity (7-100%) and 88.9% showed a 27 to 100% improvement in glare sensitivity. Topographic studies indicated fewer areas of posterior sub-capsular lens opacity, and 41.5% of treated eyes had improvement in image analysis characteristics. The overall ratios of image analysis characteristics at 6 months compared with baseline measures were 1.04 and 0.86 for the control and NAC-treated group respectively ($p < 0.001$). The apparent benefits of treatment were sustained after 24 months' treatment. No treated eyes demonstrated worsening of vision. The overall visual outcome in the control group showed significant worsening after 24 months in comparison with both baseline and the 6-month follow-up examination. The overall clinical results observed in the NAC-treated group by the 24-month period of examination differed significantly ($p < 0.001$) from the control group in the eyes with cortical, posterior sub-capsular, nuclear or combined lens opacities. Tolerability of the eye drops was good in almost all patients, with no reports of ocular or systemic adverse effects.

Conclusion: Topical NAC shows potential for the treatment and prevention of cataracts.

Looking at photographs of cataract below, it is possible to see a considerable improvement of the condition following use of NAC eye drops. This is obvious by comparing before and after pictures. Cataract usually shows as a whitish discoloration in the eye, which is reduced after a period of using NAC drops.

Did you know?

The reduction in the size of opacities has been named 'the snow melting effect'. As the snow melts and disappears, so the whitish discoloration of the lens 'melts away' and reduces in size after treatment with the drops.

In some cases involving experiments with dogs, this snow melting effect was found to take place within a month of starting the treatment.

Experiments with rabbits showed similar results, namely the reduction and improvement of lens opacities after using NAC eye drops from between one and three months.

Human experiments have broadly showed results similar to those found in animals (in addition to the experiment mentioned above). Transparency of the lens improved and the whitish colour of the eye reduced in size after using NAC eye drops at a concentration of 1% twice a day for four months. These results are not only relevant to mild cases of cataract but the improvements were also shown in cases of severe cataract (advanced mature cataract). The lens becomes more transparent and the overall quality of the lens improves, albeit the cataract does not completely disappear. Also, in cases of severe cataract the treatment needs to continue for long periods (at least five months) before an improvement can be identified.

In the latest reported experiment, scientists from the Moscow Helmholtz Research Institute of Eye Diseases, the Russian State Pirogov's Medical University and the Institute of Experimental Ophthalmology, University of Bonn, have studied N-acetylcarnosine as the commercially available preparation 'Can-C™' eye drops. The preparation was formed with:

- » 970 grams of de-ionized water
- » 13 grams Glycerine 1%
- » 10 grams N-acetylcarnosine 1%
- » 3 grams Carboxymethylcellulose 0.3%
- » 3 grams Benzyl alcohol 0.3%
- » 7.91 grams Potassium Borate, and
- » 3.47 grams Potassium Bicarbonate

All these ingredients help to stabilise and enhance the potency of N-acetylcarnosine, as well as acting as a lubricant to the eye. The scientists studied 30 dogs that had developed cataract (a total of 50 diseased eyes). These were treated with the above combination of ingredients (Can-C™ eye drops), twice a day for a six month period and the results were compared with two other groups of dogs, which were only treated with placebo or not treated at all.

In order to evaluate the progress of the treatment, these scientists used slit-images

and retro-illumination examination of the lens, the same two techniques used in the previous experiments described above. At the end of the experiment, 96% of the eyes treated with Can-C™ drops showed improvements of their condition, as demonstrated by the eye examination with the photographic techniques.

The improvement started from between four and six weeks of treatment and continued for the entire six month period. During that initial period, the effect of 'melting snow' was demonstrated, in other words, the cataract started to 'dissolve' within four weeks of the Can-C™ treatment. The improvements started from the edges of the lens and progressed towards the centre, to clear the entire lens from the cataract.

The scientists believe that this improvement is due to the transformation of N-acetyl-carnosine into carnosine inside the lens, and then due to carnosine reacting with toxic by-products of glycation, to reduce cross-linking. An additional possibility exists that carnosine may break existing bonds between the abnormally cross-linked crystallin proteins in the lens, by chemically reacting with certain parts of their structure and so release the proteins, allowing light to pass unhindered through the lens.

Specifically, carnosine, working together with glutathione can partially break the S-S bonds (bonds between sulphur-bearing groups on the protein molecule), so that the crystallin proteins become free to function again. In addition, carnosine accelerates the rate of elimination of abnormal proteins, in other words, even when the proteins are cross-linked, carnosine is able to dispose of them from the lens and leave the lens clear.

Latest research

A very recent clinical trial involving the use of NAC (under the commercial name Can-C™) comes to provide further evidence as to the usefulness of this compound. The Russian researchers who performed the original experiments with NAC, have studied a further 75 patients (age 53-83 years) suffering from age-related uncomplicated cataract. The treatment

was compared against a similar group of 72 healthy older patients (age from 54-78), who did not have cataract but who had problems with excessive sensitivity to glare. The study was double-blind placebo-controlled, meaning that neither the scientists nor the patients knew whether they were receiving the active treatment with NAC or just dummy treatment (placebo). The results were then evaluated independently

The treatment continued for nine months. The result showed a statistically significant improvement of patients who were taking the active treatment. There was improvement in visual acuity and in glare sensitivity, both of which can be a problem in cataract. Those patients who had the worst vision before the treatment were most likely to experience the most improvement. The treatment was very well tolerated, with no ocular or systemic adverse effects, and no signs of inflammation or allergy.

In addition to the above, these researchers have also analysed the sales results of Can-C™ and have reported that several thousand patients have used the product and approximately 500,000 vials have been used since it became available in 2001 (as of 2010)

In an experiment involving the use of N-acetyl-carnosine in dogs suffering from cataract, researchers found that its effects are more pronounced in the early form of the disease.

Scientists from the Department of Veterinary Medicine, University of Cambridge (UK), wanted to see if a topical antioxidant product containing N-acetyl-carnosine had any effect on dogs suffering from different stages of cataract. They examined 30 dogs of different breeds and used eye drops containing 2% N-acetyl-carnosine. The drops were used three times a day, and the dogs were examined at regular intervals, by using direct and indirect ophthalmoscopy and slit-lamp biomicroscopy (a method whereby the examiner looks directly and in detail into the eye). Specialist photographs were then taken. The results showed that improvement of cataract was found in all eyes examined, but this improvement was particularly relevant in cases where the cataract was in the early stages (immature cataract). The scientists concluded

(sic): “This study demonstrates some marginal reduction in lens opacification in a substantial number of cases of canine cataract with the use of a topical nutritional antioxidant formulation including N-acetyl carnosine. Lens opacification was improved with treatment in eyes with immature cataract or nuclear sclerosis while in eyes with mature cataract or cataract with associated intraocular inflammatory pathology less reduction.”

Reference: Williams DL, Munday P. *Vet Ophthalmol.* 2006;9(5):311-6. *The effect of a topical antioxidant formulation including N-acetyl carnosine on canine cataract: a preliminary study*.

Chinese scientists have confirmed that the antioxidant and antiglycating effects of the carnosine molecule can be the reason why it is effecting in delaying cataract development (Guo Y, Yan H. Yan Ke Xue Bao. 2006; 22(2):85-8. Preventive effect of carnosine on cataract development).

Another approach to improve the benefit of N acetyl carnosine is to combine it with the peptide carcinine. This is a molecule similar to carnosine and it is resistant to enzymatic hydrolysis, meaning that it is not easily broken down by enzymes. Remember that the carnosine molecule is sensitive to hydrolysis and can be broken down easily by the enzyme carnosinase. The combination of N-acetyl carnosine and carcinine may prove to be an ideal partnership, as neither of these molecules can easily be broken down and inactivated in the eye. Incidentally, this combination may be beneficial to skin health, because it protects its components against lipid peroxidation. Indeed, some manufacturers are now in the process of offering this combination as a product to be used by the general public.

Reference: Babizhayev MA. *Biological activities of the natural imidazole-containing peptidomimetics n-acetylcarnosine, carcinine and L-carnosine in ophthalmic and skin care products. Life Sci.* 2006;78(20):2343-57. *The combination of NAC and carcinine may be further enhanced by the addition of histidine which helps stabilize the action of carnosine.*

NOTE: Dr. Babizhayev and IVP have recently created an oral formula known as Can-C Plus™ containing these ingredients and which has been specially designed to work alongside the Can-C™ eye-drops.

A team of Russian scientists has recently reported that N-acetyl-carnosine together with the molecule pantethine work as chaperone molecules (for example, they help other molecules enter or exit the cell) and reduce the concentration of abnormal proteins in the lens, thus reducing the risk of cataract development. The same scientists have confirmed that UV radiation (from excessive exposure to sunlight for example) causes increased concentration of abnormal crystallins in the lens, thus contributing to cataract. However N-acetyl carnosine was able to slow down the formation of a particular form of abnormal crystalline, namely the beta I crystalline. They believe that this benefit is not due to antioxidant activities of N acetyl-carnosine, but due to other mechanisms. This shows that N-acetyl carnosine works in many different ways and attacks cataract in many fronts.

Reference: Avetisov SE, Polunin GS, et al. *Chaperon-like anticataract agents, the antiaggregants of lens crystallin. Communication 4: Study of the effect of a mixture of di- and tetrapeptides on a prolonged rat model of UV-induced cataract Vestn Oftalmol.* 2008;124(2):12-6.

The combination of oral N-acetylcysteine (600 mg) together with D-pantethine (90 mg) and other agents such as vitamin E (150 iu), zinc (15 mg), L-methionine (75 mg), L-histidine (300 mg) and carnosine (210 mg), has been shown to have a beneficial effect upon the treatment of cataract. These molecules work together, enhancing each other's potency and are thought to enhance the antioxidant action. In this respect, scientists have studied the effects of N-acetyl carnosine in eye drops used together with the above oral combination on patients suffering from well-established cataract. The treatment was applied twice a day for five months. At the conclusion of the experiment, the authors commented: “Our results show that combining imidazole-containing compounds

(such as carnosine, histidine and pantethine) at near physiological concentrations results in synergistic antioxidant activity. The oral consumption of N-acetylcysteine ingredient boosts the reduced glutathione level in the human crystalline lens. Age-related cataract is significantly reversed within 5 months of combined treatment. The clinical and experimental data demonstrate the effectiveness and safety of a combined treatment modality”.

Reference: Babizhayev M. Current Ocular Drug Delivery Challenges for N-acetylcarnosine: Novel Patented Routes and Modes of Delivery, Design for Enhancement of Therapeutic Activity and Drug Delivery Relationships. Recent Patents on Drug Delivery & Formulation, 3, 2009

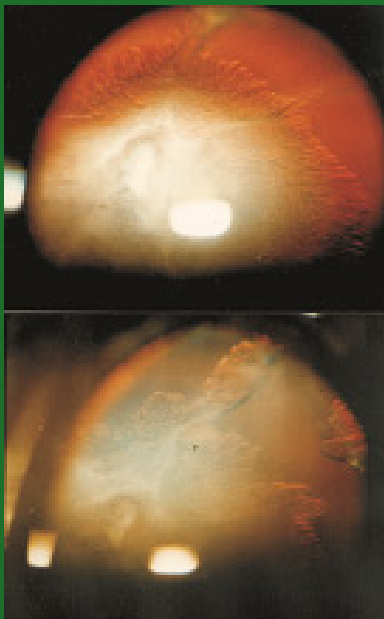
The oral combination is now available commercially under the name Can-C Plus™.

Photographs

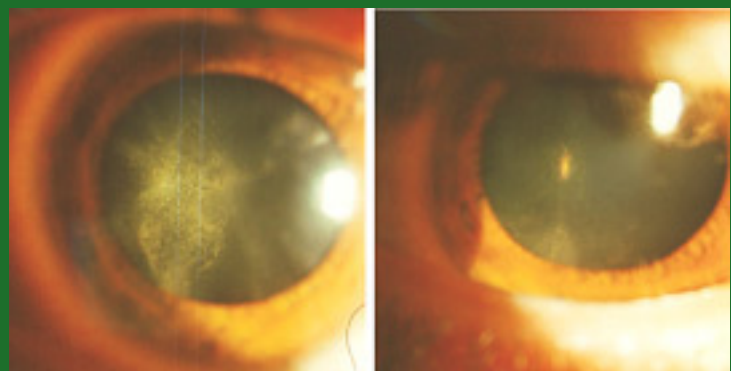
Here are some examples of animals and human eyes before, during and after treatment with Can-C™ eye-drops.



The photographs above show a large cataract in a rabbit's eye. The left eye is before treatment with Can-C™ eye-drops, the middle photo is during treatment, (4 drops daily) and shows a significant cataract reduction. The right hand photo is later still and highlights an even further reduction in the size of this cataract.



The top photograph shows the large milky cataract in a dog's eye before treatment. Just one month of treatment with Can-C™ eye-drops (4 drops daily) is shown in the lower photo. The cataract is seen to be 'breaking up,' an effect that for obvious reasons has been described as 'melting snow.' Can-C™ eye-drops work quite quickly in canines because they lack an enzyme (found in humans) called carnosinase that otherwise helps to break down/ destroy the active ingredient.



The photographs above are from a human (female) eye. The left hand one shows the size and shape of the cataract (resembling a bat in shape). The right hand photo is the same eye 5-months later after treatment with Can-C™ eye-drops 4-drops daily. The cataract has been removed and the opalescence and clarity is improved.

Other indications

NAC drops are not only useful in cataract. The drops can also benefit other eye conditions, most of which are due to, at least in part, free radical damage. Examples of these conditions include:

Glaucoma (in particular open-angle primary glaucoma)

Glaucoma is a disease causing loss of vision due to an increased pressure of fluid within the eye (the aqueous humour). The drops may help prevent free radical and glycation damage to the eye, while improving the flow of aqueous humour. The increased pressure can happen due to a variety of reasons but it is believed that free radicals have an important role to play in causing the basic biological problems in the production and elimination of this aqueous fluid. For example, the aqueous humour is produced by a net-like structure in the eye. Within this structure there are molecules called glycosaminoglycans which, by the way, are also found in other organs of your body such as the skin. A faulty production of these molecules may be caused by free radicals which are not kept under control by the natural antioxidants in the eye.

There is growing evidence that confirms the role of free radicals and oxidative damage in other parts of the eye in relation to glaucoma. The worse damage is found in retinal ganglion cells, (a special type of cells found in the eye). Free radicals can kill these cells directly but can also stimulate other toxins which then themselves kill the retinal ganglion cells. Free radicals also make other cells in the eye more sensitive to degeneration, through accumulation of AGEs (Advance Glycation End products). Finally free radicals, through oxidation, are involved in the activation of the immune response during glaucoma and change the way antigens are attached onto the cells. Thus, it is clear that free radicals play an important role during the formation of glaucoma.

In a study published in 2007 by researchers from the Department of Ophthalmology and Visual Sciences, University of Louisville School of Medicine, Kentucky, USA, it was confirmed

that AGEs play an important role in glaucoma, not only affecting retinal ganglion cells, but also other cells of the retina and the optic nerve, and extracellular tissues such as the laminar cribriform plates. Lamina cribrosa is a tissue that is generally affected during glaucoma, becoming rigid and causing several related events that contribute in clinical cataract. Therefore, the suggestion that, apart from antioxidants, we should also use AGE-preventors such as carnosine and carbinine, seem to be valid. Whilst in the subject of antioxidants, it is worth remembering that vitamin C, and glucosamine taken orally can protect and repair the glycosaminoglycan structure and thus improve production of the aqueous fluids. Other antioxidants used in glaucoma are:

- » Vitamin B12 and vitamin E
- » Magnesium and zinc
- » Lipoic acid
- » Melatonin
- » Ginkgo biloba
- » Forskolin

All of these, together with carnosine, have strong antioxidant actions and reduce the risk of damage to the eye tissues, thus reducing the risk of glaucoma. The use of NAC drops in glaucoma can be in association with existing traditional treatment with beta blockers. In addition, some sufferers use some or all of the above supplements.

Dry, tired and irritable eyes, (including problems related to computer screens such as Computer Vision Syndrome, contact lenses, air-conditioning etc).

Computer Vision Syndrome (CVS) has been defined by the American Optometric Association as “eye and vision problems related to the activities which stress the near vision and which are experienced in relation to the use of the computer”. Symptoms include sensitivity to light, double vision, watering of the eyes, eye fatigue, blurred vision, headaches, slow refocusing, burning feeling in the eyes, and dry or irritable eyes. A way to prevent CVS is to use suitable screens that reduce glare, have frequent breaks and use the correct angle of

vision in relation to the screen. Lubricant eye drops have been advised by researchers from the department of Ophthalmology, University of Texas in the USA. The proprietary preparation of N-acetyl carnosine (Can-C™) contains two lubricants, glycerin and carboxymethylcellulose, which have been proven to increase lubrication in the eye. These ingredients are also marketed separately in 'artificial tears' preparations. N-acetyl carnosine reduces inflammation in the eye, believed to be due to excessive blinking which causes micro-injury to the cornea. It also reduces sensitivity to glare.

Contact lenses

The lubricants contained in the Can-C™ drops improve the liquid film which protects the eye from outside irritants. In addition, NAC reduces lactic acid concentration in the eye, preventing irritation and redness. People who wear soft contact lenses may be able to wear them for longer and with more comfort when using Can-C™. When applied, contact lenses block the oxygen supply to the cornea and so they interfere with the normal metabolism of the outside layers of the eye. The different constituents of the cornea such as water content, minerals and glucose are under a finely-tuned balance mechanism and this balance may be interrupted by the contact lenses. An abnormal metabolism of the cornea causes production of chemicals such as lactic acid which causes the cornea to swell up, resulting in visual symptoms and pain. NAC and its derivative, carnosine, act as a buffer which means that the carnosine molecule identifies and inactivates any lactic acid molecules in the eye. This reduces the concentration of lactic acid and improves the overall metabolism of the cornea.

Dry eye syndrome

Two manifestations of the dry eye syndromes are called Lid Wiper Epitheliopathy and Lid Parallel Conjunctival Folds. These abnormalities affect contact lenses users and are believed to be related to mechanical forces during blinking. Normally, a mucus layer protects and shields the surface of the eye against the forces of blinking, but alterations in the composition of mucus reduce this protection. The lubricants

used in the commercial preparation of NAC (Can-C™) are useful in making the contact lenses feel more comfortable generally. The glycerin contained in the NAC lubricant preparation acts as a moisturizer of the ocular surface, reduces swelling and reduces the degree of haze by attracting water through the corneal epithelium. The dry eye syndrome can affect non-contact lenses users too, including people who live in dry, dusty environment, or certain patients with systemic disease (for example, Sjogrens syndrome or the menopause). The benefits of the drops are the same, irrespective of the cause of the syndrome.

BOX 2

With regards to dry or tired eyes, the Russian researchers who performed the original trials with NAC eye drops also performed research to evaluate the benefits of NAC on eyesight in general.

They studied patients aged between 48 and 60 years for a period to six months. These patients did not have cataract but were complaining of visual problems such as dry, tired eyes and poor vision.

The scientists found that, after treatment, the patients claimed that their vision was clearer, their eyes felt generally better, relaxed and less tired. No signs of allergy were found, and no side effects were reported.

Macular degeneration

This is a chronic degenerative disorder of the eye resulting in distorted and diminished vision. Free radicals and UV radiation have been named as causative factors, in addition to genetic and other unknown causes. NAC eye drops have been proven effective in reducing glare and improving colour vision. The mechanism of action is similar to other chronic eye conditions namely protection against free radical damage and improvement of blood circulation to the eye. However, there have been concerns that using the eye drop form may not be as useful as using the tablet form in this particular condition.

One reported adverse reaction was in relation to a patient who had both cataract and a degree of macular degeneration. The use of NAC eye drops worsened the macular degeneration, albeit temporarily. Until further research clarifies this point, it is best to only use carnosine in oral form.

Infection and inflammation of the cornea

Published research shows that carnosine has anti-inflammatory benefits, not only in the case of eye conditions but also within other organs of your body. Chinese scientists have discovered that when carnosine is given by mouth, it may help reduce inflammation and promotes wound healing. Other researchers have also found that NAC eye drops are helpful in reducing the risk of certain eye infections such as keratitis or iritis.

This is not to say that the drops should be used instead of antibiotics, but that those who already use the drops as a security against cataract may be also be getting an additional anti-infective benefit.

A Russian study published in 2006 found that carnosine eye drops at a 5% concentration could reduce the concentration of noxious enzymes in the eye following injury. The treatment also increased the effectiveness of other treatments used in conjunction with the carnosine eye drops.

Ref. Volkov OA, Neshkova GA, Moshetova LK, Iarovaia GA. The effect of carnosine on inflammatory processes during contusion of the eyeball. Biomed Khim. 2006;52(2):188-91.

Chapter 4: Composition and purity

Commercially available eye drops used against cataract (such as Can-C™, for example) contain special formulations of N-acetyl-carnosine and also other ingredients. The combination of these ingredients ensures that the NAC molecule remains stable and its concentration is finely balanced.

The inventors of Can-C™ eye-drops are a company called Innovative Vision Products (IVP), with branches in Moscow (Russia), and Delaware (USA). They are the holders of worldwide patents for the use of NAC eye drops, manufactured to match the exact combination of ingredients as that used in the clinical research experiments.

IVP has filed a European patent for these drops in 1993, and other patents in the USA and across the globe. The company emphasizes that it is very important to use the exact combination of eye drops ingredients for maximum efficiency. They say:

“There is a very fragile and highly specific balance of purity for this formulation that must be maintained to ensure the safe and effective use of N-acetyl-carnosine eye drops. Therefore, it must be clearly understood that only formulas made to this specific purity and methodology, the patented formulas, that have been proven in animal and human clinical trials to be efficacious and, most importantly, safe in the long-term”.

In an announcement made in February 2004, Dr. Mark Babizhayev, who holds the rights to the patents declared:

“Unfortunately there are a few amoral companies, attempting to capitalize on this discovery, which are illicitly fabricating and touting inferior N-acetyl-carnosine for senile cataracts without the benefit of the specific purity level required to ensure efficacy and safety for eye use. A number of these deceptive companies are actually referencing my research, to promote their sub-standard product, thereby damaging my reputation. In addition, some are attempting to make their products more attractive with the addition of vitamins such as vitamin A and E. These vitamins while, by themselves, may be beneficial to the eye, have branched hydrocarbon skeletons that inhibit the activity of N-acetyl-carnosine, particularly in the cornea and conjunctiva of the eye. More importantly, combinations of vitamins and N-acetyl-carnosine have not got any published clinical trials for either efficacy or safety. This could lead to damage of the eye surface with long-term use, as was shown with L-carnosine (eye drops) in our trials. Therefore, as the publisher of much research on this subject I feel a responsibility to inform consumers of the fraudulent and dangerous products being promoted to the public”.

These are important statements which highlight the need to use only products that have been proven as effective and safe following research. Dr. Babizhayev believes that the addition of extra vitamins to the eye drop preparation may be damaging to the eye, so it is important to only use N-acetyl-carnosine patented by Innovative Vision Products (IVP), which does not contain any vitamins.

The IVP formulation has been developed using certain specific technical ways which purify NAC. The eye drops also contain a balanced amount of trace metal ions (minute amounts of minerals) which stabilize the NAC molecule. IVP says that it is the exact combination of these ions that give NAC its full potential. Too many or too few metal ions were found to significantly affect the performance of the eye drops.

With the correct combination of ingredients, the carnosine molecule which is released after N-acetyl-carnosine reaches the eye is much more effective against lipid peroxidation. On the other hand, if a different combination of ingredients is added into the NAC components (as it is the case with some other commercial preparations) the end result may be that N-acetyl-carnosine may not be able to transform to its active variant L-carnosine, rendering the whole process useless. More worryingly, the manufacturers of Can-C™ believe that this addition of extra vitamins or other compounds may cause the NAC to transform into histamine which may then cause allergic reactions and inflammation of the eye.

Although media and internet reports say that the discovery of the benefits of NAC eye drops on cataract is credited to other scientists, only Dr Mark Babizhayev and his team have published research listed on Medline (the gold standard indexing service, which lists all legitimate research publications). Other names of scientists or professors who are advertised as having done research on NAC eye drops do not appear on Medline. Therefore, in the absence of other research, it seems prudent to follow the advice given by scientists who have studied NAC on humans, until further research with NAC plus vitamins becomes available.

Testimonial

“I just wanted you to know that the improvement in my vision is amazing. I had got to the point where I could no longer drive due to haziness from my cataract. Now I feel very secure and am able to see almost as well as before my cataract was diagnosed. Also I have not noticed any kind of side effects. I just wanted to tell you how happy I am and that I am definitely recommending Can-C eye drops to all my friends with similar problems. If you need me for any referrals or statistics I would be happy to help. Please keep on with the great work.”

- Andrea Bea, Michigan

The use of vitamins in improving cataract has been supported by several research studies. However, all of these studies were performed

using oral vitamins (taken by mouth) and not in eye drop form. Also, none of these studies evaluated the effectiveness of combining vitamins with NAC. On the contrary, at least one research report has highlighted the problems with using vitamins in eye drop form. Researchers from the Department of Ophthalmology, Kuala Lumpur Hospital, in Malaysia, have reported a case of a patient using vitamin C eye drops for some months. This patient went on to develop corneal deposits (crystal material on the outside of the eye) which made vision worse.

In another study, two Bulgarian researchers examined the effects of substances used against vitamin C-induced modifications of the lens. They started from the known fact that vitamin C given by eye drops can induce changes in the lens. These changes include an increase in carbonyl groups, the chemical agents which facilitate glycation. The scientists then studied several agents, including carnosine, for their effects against these carbonyls. They concluded that carnosine, as well as aminoguanidine (which has actions similar to carnosine) are effective at reducing carbonyls in the lens, thus protecting against glycation. Remember, that on this occasion, carbonyls were created by vitamin C. The point of this is to remind you that although certain vitamins may be beneficial against cataract if given by mouth, the same vitamins may be damaging if given by eye drops.

Looking at the benefits of oral vitamins, scientists from the Biometry and Nutrition Group, Agharkar Research Institute, in India found that certain vitamins and nutrients may be effective in preventing cataract. They assessed the diet content of a group of 143 patients with cataract (aged between 50 and 70 years), compared to the diet of 100 people of similar characteristics who did not have cataract. They then studied the levels of nutrients such as vitamin A, C, minerals and selenium (a known antioxidant). All patients with cataract were found to have subnormal levels of vitamins in their blood, together with high levels of free radicals and cross linked material. A higher concentration of vitamins and antioxidants was associated with a lower risk of cataract.

Because NAC is an acetylated form of carnosine, this acetyl group may interact and neutralize other molecules such as vitamin E. There are published experiments which show that using vitamins such as vitamin E, together with acetyl chemicals makes the concoction ineffective, with regards to the vitamin. Therefore the use of vitamins together with NAC in one liquid mixture appears not to be a good idea, as it makes the mixture useless.

So, in summary, although antioxidant vitamins (like vitamins A, C and E) taken by mouth may have a positive impact on cataract, the use of these vitamins in eye drop forms and/or in association with NAC, has not been proven to work and may even be associated with eye damage.

Chapter 5: Further information

The RCO is a respected body of eye specialists who base their clinical practice on published scientific research. They have issued the following public statement about N-acetyl carnosine:

Statement by the Royal College of Ophthalmologists: N-acetyl carnosine for cataracts:

“The evidence for the effectiveness of N-acetyl carnosine eye-drops is based on experience on a small number of cases carried out by a Russian research team. To date, the research has not been corroborated and the results replicated by others. The long-term effect is unknown. Unfortunately, the evidence to date does not support the ‘promising potential’ of this drug in cataract reversal. More robust data from well conducted clinical trials on adequate sample sizes will be required to support these claims of efficacy. Furthermore, we do not feel the evidence base for the safety is in any way sufficient to recommend its use in the short term. More research is needed.”

- Mr Winfried Amoaku FRCS FRCOPHTH PHD.
Vice President Chairman, Scientific Committee
August 2008

Since the publication of this statement, the results of new scientific trials have been made available to the Scientific Committee of the RCO. These peer-reviewed papers included newly published research elaborating on how the drops work at the molecular level and how a further sample of patients has been studied with positive results. This corroborates the earlier findings of the Russian researchers. In addition, evidence was made available to show that, over the past seven years, approximately 500,000 vials of Can-C™ (N-acetyl carnosine) have been sold world-wide, and that the rate of re-purchasing was high. This shows that the patients themselves felt that the drops were working. No negative experiments were published, and there is no evidence to show that the drops are unsafe in the long-term. In fact,

there is positive evidence showing that the drops **are** safe.

The British distributors of the drops have offered a free supply of Can-C™ eye drops and have invited the RCO to set up an independent, ‘no-strings-attached’ clinical trial in order to provide further evidence on the effectiveness of NAC in cataract.

All of the above are currently being considered by the Scientific Committee of the RCO and any new developments will be announced soon.

Frequently Asked Questions

How long do I need to use the drops for prevention of cataract?

The current recommendation is to use one to two drops for at least five or six months. The free radical assault on the lens is continuous throughout life, and so it is necessary to protect the lens for as long as possible. After this period one can use a lower dose, long-term. Cataract does not improve with age and therefore it is recommended to use the drops indefinitely. It is likely that when you stop the treatment, the condition may worsen with time, but it is not very clear whether this progression will be the same rate as one who has not used the drops in the past.

Testimonial

“I wanted to tell you about my experiences with the special Russian eye drops. At first I didn’t think there were any real differences, but I persisted in using the drops twice a day in the affected eye. Now, after about three months, I believe that there are significant changes to my vision. It has been a fairly gradual thing which may explain why I didn’t appreciate any changes early on, but now it is obvious to me that my eyesight has improved. The changes are slower than I anticipated but, I for one am sold on the drops.”

- Charles Lee, Hong Kong

Why can't I use carnosine eye-drops directly?

Pure L-carnosine, although works wonders as a capsule, it does not concentrate sufficiently in the eye tissues if given as eye drops. The aqueous humour of the eye contains high concentrations of carnosinase which destroys carnosine. NAC is able to pass through the aqueous humour unaffected by carnosinase, reach the lens and then release carnosine which, in the lens, is protected against carnosinase. The carnosine then goes on to work as discussed in this book

Why do you think that positive experiments on animals necessarily show that humans will also benefit?

Because the animals lenses studied so far (from rabbits and dogs) are more or less similar in composition to ours. All benefits seen with NAC eye drops in animals were also replicated and found true in humans. Although animal research is cheaper and easier to conduct than human research, the results are comparable.

What other supplements or nutrients can I use to complement NAC drops?

To help prevent cataract, glaucoma and age-related macular degeneration, some nutritionists recommend lutein, zeaxanthin, melatonin, aminoguanidine, oral vitamins, glutathione, ginkgo biloba and selenium. A diet rich in berries, dark colored fruit and vegetables is also recommended. However, it has also been suggested that excessive use of lutein causes accumulation of lutein in the lens, and this depresses the action of other natural antioxidants in the eye. This can exacerbate cataract progression, because the lens antioxidant enzymatic activity (SOD, glutathione reductase, glutathione peroxidase) is reduced in the presence of lutein. On the other hand, N-acetyl-carnosine and carnosine can protect the natural enzymatic activity in the lens, even when are applied topically. There is mounting evidence however that lutein supplements may impede the action of the NAC eye-drops, therefore it may be prudent to avoid lutein containing supplements whilst using the NAC eye-drops in order to maintain their maximum efficacy.

Any other advice for prevention of cataract?

Cataract and some other chronic degenerative eye diseases (such as macular degeneration) may be worsened by UV light, as well as by external free radicals. So, avoid smoking and pollution, and always wear sunglasses when out in the strong sunlight. Use glasses which filter UV light completely and, if you are particularly vulnerable to chronic eye disease, choose wrap-around glasses which protect the eye from the sides also.

Why are NAC eye-drops not marketed for the 'cure' of cataract?

Experiments show that these drops may actually dissolve cataract and therefore cure existing cataract. However, due to licensing regulations, only registered physicians can prescribe and dispense treatments that cure any given condition. In order to be able to offer this treatment to as many members of the public as possible, the manufacturers of these drops marked them only as a lubricant, which does not require a physician's prescription. However, it is advised that you only use the drops under medical supervision.

I saw anti-cataract drops featured in popular chat shows on television. Does this mean that the drops are officially approved?

Only the official authorities can approve a drug or a treatment directed at a specific disease. In the US it is the FDA, while in the UK it is the MHRA (Medical and Healthcare Regulatory Agency). You need to understand that any product may be featured on television or in a newspaper, without actually any research to back the claims up. The makers of Can-C™ affirm that their drops are scientifically researched and that the research is published in peer-review scientific journals.

You said that NAC is protected by a patent. What are the technical details?

The patent is in the names of Babizhayev MA, Bozzo Costa E. Pharmaceutical composition containing N-acetyl-carnosine for the treatment of cataracts. Patent PCT/EP 94/03340 SCB

PCT, 10.10.1994, together with a similar Italian patent registered a year earlier (15.10.1993)

What makes ‘Can-C’ N-acetyl-carnosine so different from other brand names of N-acetyl-carnosine?

There are different ways of manufacturing N-acetyl-carnosine (NAC). Some varieties contain the contaminant hydrazine which may cause toxicity. Can-C’s NAC is manufactured using a specific cGMP process in Japan by following certain guidelines which are a trade secret of the company. This process ensures that only NAC of an exact level of purity is used to make the Can-C drops.

How can I make sure that the drops I use are made using this specific process?

Look on the label. It should say that the drops were formulated by Innovative Vision Products (IVP). The manufacturers say that if this is not indicated on the label, then the product will either be ineffective or possibly dangerous to the eye.

I live in a very hot climate. How do I store the drops?

Whilst the drops in unopened bottles are stable at room temperature for long periods, it is probably advisable that they are best kept in the refrigerator at a temperature between 2 and 8 C. However they should not be allowed to be frozen. A vial, once opened it usually remains active for three-four weeks. Use the eye drops as directed by your physician or eye specialist. The general dose is one or two drops in the effected eye twice a day.

If the experiments are so promising, why isn’t the treatment used by all eye specialists?

Most conventional eye specialists wait for a substantial amount of research to be made available before they start using a product. This may take decades. In the meantime the disease can progress beyond repair. NAC has been used since 2001, and according to the manufactures tens of thousands of patients have been treated.

No significant side effects have been reported

Can I use it to treat cataract affecting my dog?

Yes, N-acetyl-carnosine drops have been used to treat cataract-related loss of vision in dogs, cats, horses, and even pet rabbits. It works along the same principles as in the human eye, however due to the lack of carnosinase in dogs eyes (the enzyme that breaks down carnosine) beneficial results may be seen more quickly than in humans.

BOX 3: Case study

Background: Pam S. is a 64 year old woman living in the South of England. She worked as a secretary for several years, and now she is working part-time as a clerical assistant in a firm of solicitors. Pam enjoys driving to see friends all over the country.

Problems: She is relatively healthy, exercises regularly and smokes 5-10 cigarettes a day. Apart from a slightly raised blood pressure, she rarely had any reason to visit her doctor. During the past two or three years however, she noticed that driving at night started to become difficult. Cars coming from the opposite direction had too strong headlights, or so she thought. She was momentarily blinded by these headlights, and found that she became slightly confused and disoriented by them.

Cataract: Her doctor told her that this is increased sensitivity to glare, a common problem in older drivers, but also a sign that visual problems may be present. With time, the problem worsened and she also noticed that her vision started to become blurred. After a visit to the optician, she was told that she had the beginnings of cataract, mainly in the left eye but also in the right. Understandably, she was upset to hear this, particularly as her doctor told her that the only solution was to wait until the problems got worse and then have an operation to remove the diseased cataract.

Treatment: She started asking other people and she also checked the internet for any other

possible treatments. Eventually she came across N-acetyl-carnosine eye drops and decided to try these. However, she found several suppliers offering different brand names and making too-good-to-be-true claims about more or less instant or complete cure. Her confusion worsened when she read reports about the dangers of using certain brands of the eye drops. A friend of hers recommended a knowledgeable physician who had an interest in eye diseases, so she went to see him.

Can-C™: The physician explained that, according to published research, the best brand to use at present is Can-C™, as it is the only one patented and shown not to have any adverse effects during research. So, Pam tried Can-C™ twice a day in each eye for several weeks. After about six weeks of treatment, she noticed that her vision was becoming clearer and she was not so much disturbed by other cars' lights at night. During a check up with her doctor, she was told that the cataract has not progressed, in fact if anything it was more limited. She now continues the use of Can-C™ and is under regular evaluation.

Other users of NAC eye drops have said:

- » My mother's eyesight has been improved, it is amazing.
- » My ophthalmic physician has not seen anything like it in the 20 years of assisting people with cataract.
- » I took some other drops for four months, and these did nothing. I've been only taking Can-C™ eye drops for 4 weeks and can already notice the difference.
- » I feel that having to avoid surgery; these eye drops have given me great hope for the future.

These case studies and testimonials show that the public at large is beginning to benefit from the positive actions of NAC eye drops. But it is not just the general public who has discovered the treatment. Medical professionals are also becoming increasingly aware of the potential of these eye drops.

A physician from California writes: "As a medical doctor, at first I was quite dubious of

such a breakthrough. I believed that, if the drops were as effective as claimed, the medical establishment would have known about it. Reluctantly, I have decided to try the drops on my mother who had moderate cataract and was so keen to try a medical treatment rather than have an operation. Over time, she has noticed considerable improvement in her eyesight. The results have been very impressive. I then looked into the science behind the eye drops and it all made sense. I am now researching the matter further and I want to pass the good news to as many of my colleagues as I can".

History of NAC development, based on comments made by Dr. Mark Babizhayev

The work on NAC and its use in eye diseases started back in 1991, in association with Italian researchers. After the initial period of research, it was realized that NAC can be broken down and transformed into carnosine which is active within the eye. The first research on NAC and cataract was published in *Clinical and Chim Acta* in 1996.

This initial research was performed on laboratory animals such as rabbits and, later, dogs. It was shown that NAC eye drops can have the 'melting snow' effect which means that the cataract was slowly dissolved from the outside inwards until it improved completely. This effect was shown to happen as early as within one month of the treatment. Following the encouraging animal results, it was the turn of human trials. Before this however, it was necessary to develop efficient and accurate ways of measuring the results. So, Dr Babizhayev and his team developed techniques of glare tests which are very sensitive to very tiny changes of the lens opacities. The actual techniques used were stereocinematographic image and retro-illumination photography with digital analysis and 3D computer graphics. These helped monitor the light scattering and the light absorption from the lens.

They found that NAC drops would improve the visual symptoms and the visual parameters of patients with cataract, and also that as long

as the treatment continued; there was no recurrence of cataract. Patients using NAC eye drops continually have been evaluated for a maximum of 24 month period. Since the original

experiments, patients have used the eye drops for an additional year at least, with no signs of side effects, and with the benefits remaining.

Testimonials

"I have been using the Can-C™ eye drops since last September. I had my vision checked on January 2 (2004). My vision has improved four times and my lens is clearing. I will get my vision checked again and let you know of my progress. Can-C™ drops have been a godsend to me."
- Bill Kline, Illinois

"I used the Can-C™ drops for three or four months. I certainly noticed cleared vision (I have cataract). I stopped using the drops and vision became fuzzy again, so I restarted the drops about two weeks ago. I definitely will continue to use them. The results were good, but I now know that I need to use them on an ongoing basis. Thank you." - Edith Koln, Utah

"I'd like to thank you for researching and developing Can-C. During an eye exam, they informed me I had the start of cataracts and would likely need surgery in about 5 yrs. I was 56 and horrified, especially as I am the designated driver for my social unit: me, mom and our diabetic friend who's legally blind from retinopathy. I searched the net and learned about Can-C. Calling around to double-check their safety, I was shocked to learn that there was no NIH (National Institute of Health) or other government studies. One researcher I talked to said that as long as there was an effective treatment- meaning surgery, there would be little chance of any studies being done, at least he was honest about the entrenched nature/power of the cataract surgery crowd. Anyway, I started the drops 2-drops each eye twice a day, within 3 weeks; there was a significant and dramatic improvement which continued for awhile longer. Now I use 1-drop in each eye daily; 2-drops if I indulge in lots of carbohydrates. Plus the drops are especially soothing when my eyes are tired and gritty feeling." - Linda Palmer, California

"I used Can-C for 4-months with amazing results. My vision in my left eye improved from 20/40 to 20/25 and upon renewal of my driving license, the eye glass restriction was eliminated! With less glare and near perfect vision I now drive in the evenings and early morning without glasses, much as I did in my youth 30-years ago! Since birth, my right eye could only identify the big "E" on the eye chart. After 4-months of Can-C treatment, I can now read the 3rd line on the eye chart. It's truly amazing to be nearly blind in my right eye for 60-years and now regain some sight!" - Dr. Richard Lippman, Hawaii.

"I just wanted you to know that the improvement in my vision is amazing. I had gotten to the point where I could no longer drive due to haziness from my cataracts, and now I feel very secure and am able to see almost as well as before my cataract was diagnosed. Also, I have not noticed any kind of side effects. I just wanted to tell you how happy I am." - Anthony Boulton, Kansas

As mentioned above, the drops can also be used in pets because the same pathology is involved. Indeed, some of the experiments on NAC have been performed on dogs or rabbits. A relevant comment in this respect is the following:

"I would like to relay to you my great satisfaction with the Can-C™ cataract drops! I have been administrating the product for approximately 2 ½ months to my 5-year-old Yorkshire terrier who has diabetic induced cataracts. The cataracts were completely opaque and she had no sight in either eye. The left eye is already partially clear of cataract and the right shows signs of clearing. Partial vision has returned. I was considering eye surgery when she was first diagnosed, but with the results I have seen so far I feel it's not warranted. I would highly recommend this product to anyone! Again, thank you for this life saver!" - Lynne Carver, New Jersey

BOX 4: Reported side effects

Very few problems associated with the use of these eye drops have been reported. Some people (one in every thousand users) have reported stinging after using the drops. The level of stinging varies from person to person depending on the pH of the eye.

People who have something in their eye (contact lens, a piece of grit etc) may also notice stinging. It is best to remove your contact lenses, wash your eye and then use the drops. Then, wait for 15 minutes before reinserting the contacts to allow for the complete passage of the product into the aqueous humour.

Sometimes the vision becomes cloudy after using the drops. This happens in very rare cases (one in ten thousand) and improves after a few hours. The cause of this is believed to be due to the interaction of benzyl alcohol in the drops and yeasts in the eye (usually during an undiagnosed yeast infection such as candida/thrush). In order to overcome this problem you need to cure the yeast infection first.

Summary and Conclusion

Cataract is an important and growing cause of visual loss throughout the world. It is caused by changes in the eye resulting in a clouded lens which does not allow the light and visual images to reach the retina. The majority of these changes are caused by free radicals and glycation, both of which are connected with aging, diabetes and other chronic diseases. N-acetyl-carnosine eye drops were found to easily penetrate the eye, reach the lens and chemically change into carnosine which then attacks free radicals, prevents glycation, eliminates damaged material from the lens and dissolves some cross-linked proteins.

As a result, the lens becomes clearer and the vision improves. Experiments have only studied the efficacy and safety of Can-C™, a commercial brand of N-acetyl-carnosine which contains certain specific ingredients (as well as specially prepared N-acetyl-carnosine). The efficacy and safety of other brands, some of which may contain vitamins has not been studied sufficiently, and there are fears that such brands may actually be damaging to the eye in the long term.

Chapter 6: Resource Guide

Glossary

Antioxidants = chemical substances which reduce or inactivate free radicals

Calorie restriction mimetics = drugs or nutrients that mimic the benefits of calorie restriction

Carnosinase = an enzyme found naturally in the body, which has only one aim: to break carnosine down to its ingredients (which are the amino acids alanine and histidine)

Cross-linking = the binding of one molecule to another, rendering both molecules ineffective

Crystallins = special type of proteins inside the lens of the eye

Glycation = the attachment of sugar molecules on proteins or DNA

Molecule = a structure with individual chemical properties. Examples of molecules are DNA, proteins, amino acids, vitamins, enzymes etc.

Ophthalmoscopy = looking in the inside of the eye using special instruments

Placebo = Dummy or sham treatment. Used in research to compare it with the active treatment

Suppliers of Can-C™

International Antiaging Systems is the exclusive worldwide supplier, by permission from the original patent holders of N-acetylcarnosine.

Contact at: www.antiaging-systems.com

A specific site for Can-C™ and Can-C™ Plus purchase is www.can-c.net

Selected References

Further reading about Carnosine:
Anti-Ageing Medicines
By Marios Kyriazis, MD
Watkins Publishing, London 2005, ISBN 1842931474

These are provided for information. A full list of references is available from the suppliers of the eye drops.

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Websites

1. www.antiaging-systems.com the official supplier of the Can-C™ eye drops. This site also contains extensive information on age-related diseases, antiaging products, books and conferences.
2. www.nacetylcarnosine.com with full and regularly updated information on NAC, testimonials, questions and answers etc.
3. www.thebls.org the website of the British Longevity Society, with information and articles about developments in living longer.
4. www.melatoninznse.com the suppliers of Dr. Pierpaoli's specially formulated melatonin + zinc + selenium compound (MZS™); the same as used in the Chinese study showing efficacy with age related macular degeneration.

Biography

Marios Kyriazis, MD, is one of Britain's top anti-aging physicians and is internationally recognized as a pioneer in the field. He is a Biogerontologist with a medical degree as well as post-graduate degrees from the University

of London and the Royal College of Physicians. He has a portfolio of over 700 articles, lectures and interviews on aging. He has presented his research at international conferences and has worked with academic researchers from across the world on variety of age-related projects. He has also featured in almost all daily and weekly national newspapers, radio and television in the UK, and internationally.

Professional Review

“The Cataract Cure describes clearly and succinctly, in a step-by-step way the innovative treatment now available for reversing senile cataract. With its practical approach, it demystifies the subject and is an invaluable reference guide to all eyecare practitioners requiring an introduction to surgical treatment alternatives.”

- Dr. Robert Montague Ophthalmologist, (Dr. Montague has been a practicing ophthalmologist since 1976).

Customer Reviews

“After reading this book and speaking to my eye-care specialist I embarked on a program of n-acetyl-carnosine eye-drops. Six weeks on, I have already noticed a significant difference in my overall eye sight. My vision is much clearer, the glare I used to suffer at night whilst driving has almost disappeared. I would recommend ANYONE who is suffering with senile cataracts to read this book and investigate these eye-drops; it could stop your need for surgery!”

- David Lehavre, Illinois

“There is much to be learnt in this book, I for one am very pleased that there is now an option such as eye-drops for cataract. Dr. Kyriazis does explain all the ins-and-outs of quality assurance etc. and there is lots of good information contained within.”

- Michael York, Monaco

CAN-C

For further information or to speak to our business development managers about your requirements please contact us in the following ways:

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