AOR™
Advanced Orthomolecular Research

THE TRUTH ABOUT RED YEAST RICE

THE GOOD, THE BAD, THE UGLY

AOR'S ANKASCIN 568-R: A POWERHOUSE FOR METABOLIC SYNDROME

THE TRUTH SERIES

THE TRUTH SERIES

As a discerning user of natural health products, you want what is best for your health. However, misinformation and deceptive marketing often makes it challenging to identify fact from fiction. The Truth Series was created by Advanced Orthomolecular Research (AOR) to share the evidence-based truth about the most controversial and confusing topics within the natural health industry. At AOR, we believe that truth and transparency are the most important values for any organization to uphold. As visionaries, we are committed to continuous innovation so that we can advance the world of natural health. As such, the Truth Series aligns with our vision of providing optimal products without compromise.

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WHAT IS RED YEAST RICE?

The Good, The Bad, The Ugly

Red yeast rice is a brick-red power food with medicinal properties and a long history. It is made by fermenting cooked white rice with a species of mold from the *Monascus* family, then drying the product and grinding it into a fine powder.

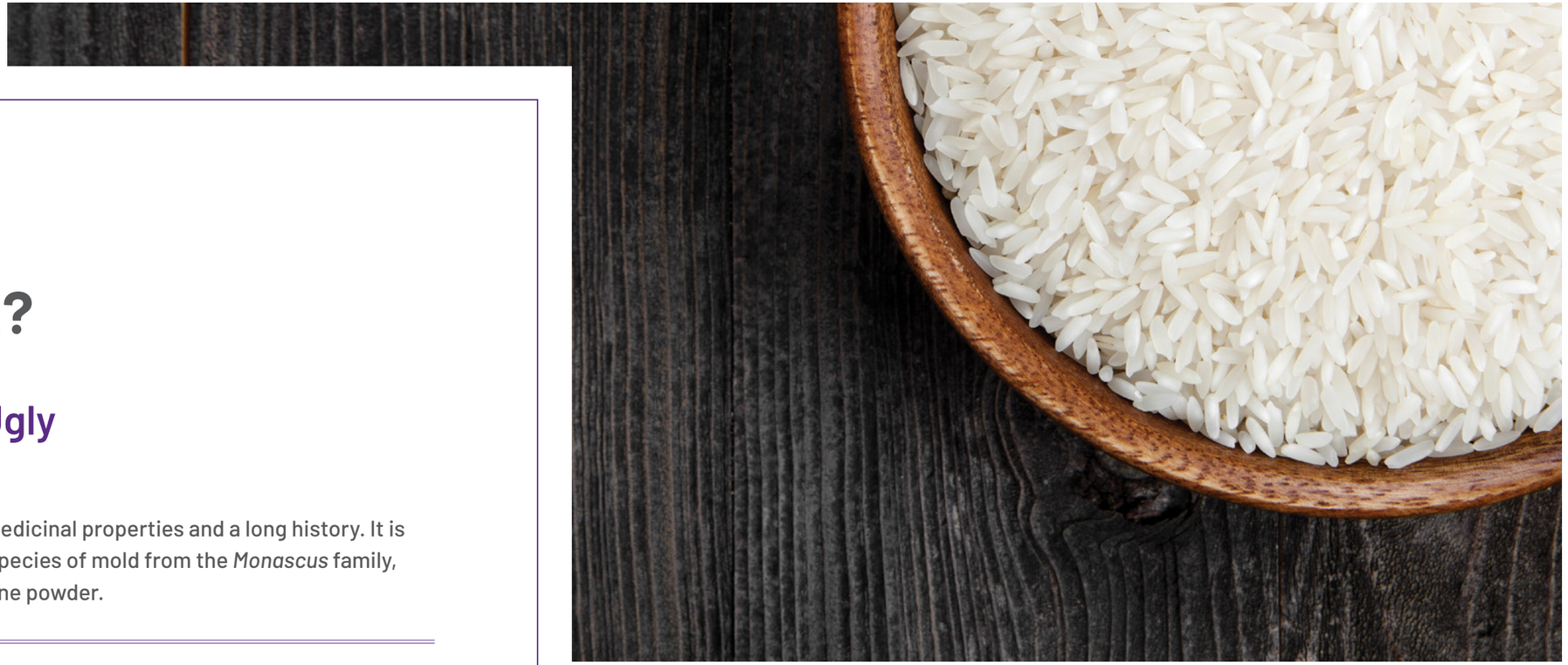
Red yeast rice has been a staple of Traditional Chinese Medicine and a food source for over a thousand years.

In addition to the vibrant color and rich flavour, *Monascus* adds many beneficial molecules to the rice. One of the most important additions is monacolin K, and it became the first drug ever prescribed to lower blood cholesterol levels. Discovered in 1979, the drug is still sold today under the brand names **Mevacor®** and **Altocor™**.

Monacolin K was the first member of what became a family of drugs called statins. While statins are effective at lowering blood cholesterol, they also come with serious side effects. These include: liver and kidney damage, muscle injury, digestive problems, and a higher risk of developing diabetes. These conditions can all be life-threatening if not caught and dealt with in a timely manner, and patients with these side effects must stop taking statins immediately.

Many red yeast rice supplements were effective at reducing blood cholesterol due to their high levels of monacolin K, but concerns about safety and side effects led to the banning of these supplements from the market in the USA and Canada.

Meanwhile, scientists noticed that some strains of *Monascus* that did not produce monacolin K, were still able to reduce blood cholesterol. Thus, a search for the active ingredients in *Monascus* led to the discovery and development of a new type of red yeast rice, called Ankascin 568-R. This form is safe, completely free of monacolin K, and is just as effective at managing blood cholesterol as the old supplements. The sale of Ankascin is approved by both Health Canada and the United States Food and Drug Administration (FDA), and its efficacy is supported by several clinical trials and dozens of research studies.



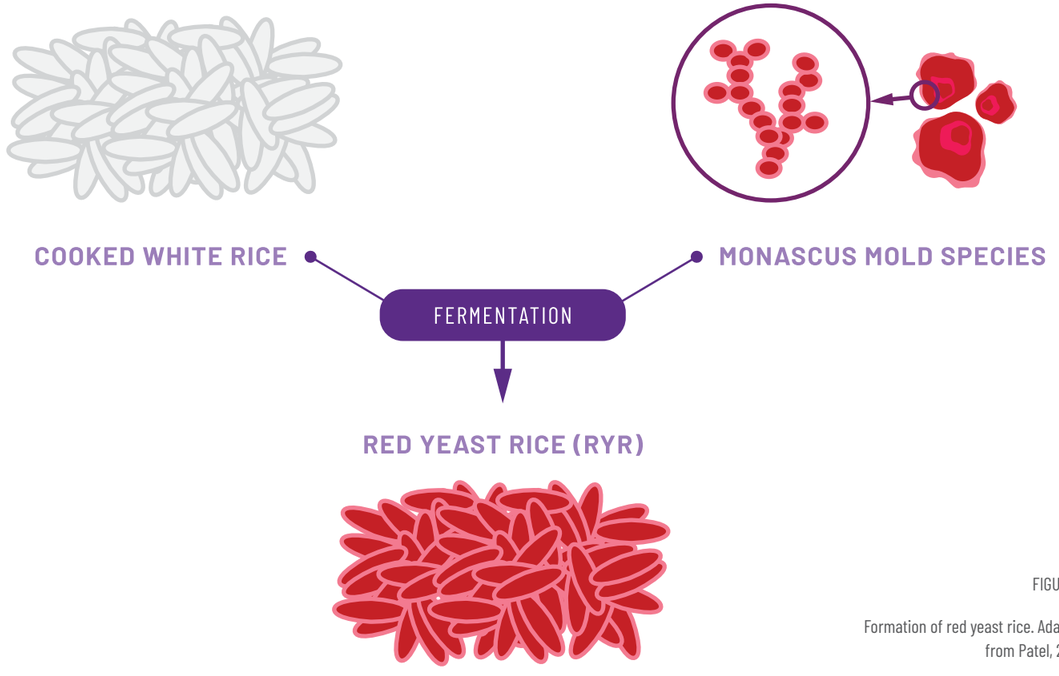


FIGURE 1.

Formation of red yeast rice. Adapted from Patel, 2016[6]

CARDIOVASCULAR DISEASE

Cardiovascular diseases are serious, life-threatening disorders that affect the heart and blood vessels.

THE MOST COMMON ONES INCLUDE THE FOLLOWING:

- Coronary heart disease, which affects the blood vessels serving the heart itself. This leads to heart attacks.
- Cerebrovascular disease, which affects the blood vessels that supply the brain. This leads to strokes.
- Hypertension, or high blood pressure, which worsens other forms of cardiovascular disease.
- Congestive heart failure, which happens when the heart becomes damaged or weakened.

According to the World Health Organization, more people die from cardiovascular disease every year than any other natural cause[1]. One in three American adults, and 1 in 12 Canadian adults has at least one form of cardiovascular disease[2,3]. Each year, it claims the lives of 63,000 Canadians, and 130,000 people receive a first diagnosis[4]. These sobering numbers highlight just how widespread the dangers of cardiovascular disease are in our daily lives.

A major problem with cardiovascular disease is that many people are unaware that they have it – a stroke or heart attack is the end result of many years of ongoing disease. The early stages have no warning signs or symptoms, and are not detectable even with modern testing methods. Most cases of cardiovascular disease result from lifestyle-related risk factors, and are thus preventable.

Given that 9 in 10 Canadians over 20 have at least one risk factor for cardiovascular disease[5], almost everyone can benefit from preventative lifestyle strategies to manage their heart health.

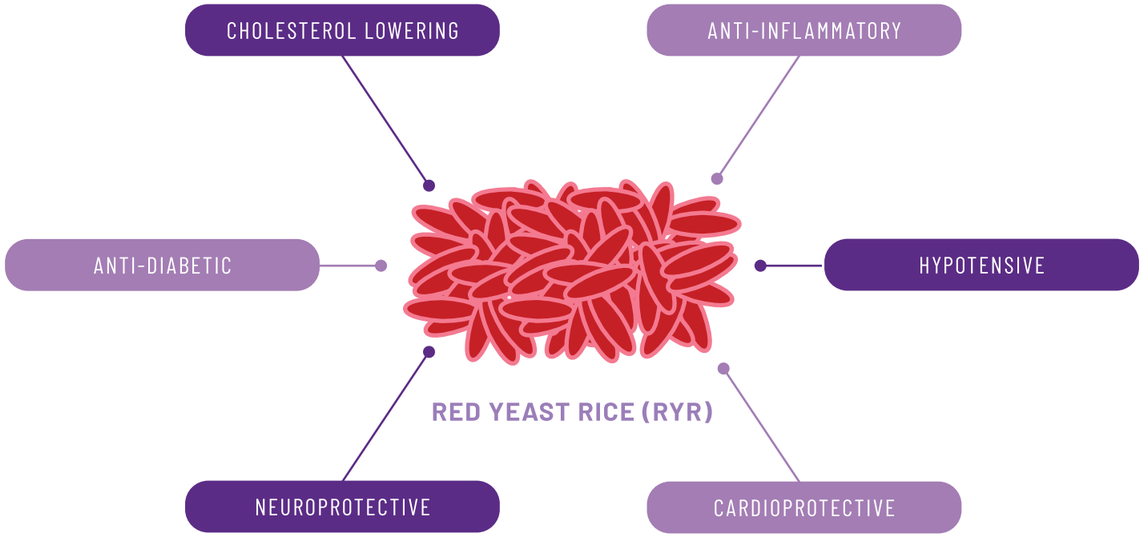


FIGURE 2.

Some therapeutic benefits of red yeast rice. Adapted from Patel, 2016[6].

RISK FACTORS FOR CARDIOVASCULAR DISEASE

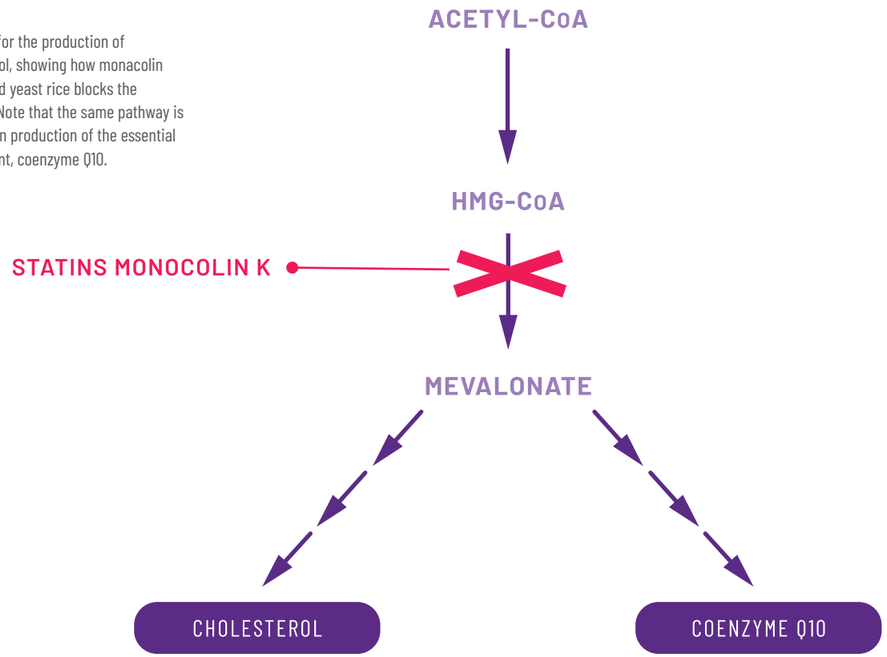
The major risk factors for cardiovascular disease include: smoking, stress, high blood pressure, and high blood cholesterol. In different ways, these factors increase the risk of developing congestive heart failure, heart attacks, and strokes.

Thousands of research studies over the last 60 years have shown that the risk of developing heart attacks and strokes is related to levels of low-density lipoprotein (LDL) cholesterol, or "bad cholesterol", in the blood[7]. LDL is a spherical protein package that transports most cholesterol around the body. In spite of its negative image, cholesterol is actually very important for normal health – we literally could not live without it. All cells make cholesterol to help maintain their shape and function, and to withstand stress. Cholesterol levels are at their highest in the brain, where brain cells use cholesterol to ensure that nerve signals travel quickly across the body. The liver produces most of our cholesterol from dietary fat, after which cholesterol is sent through the blood to the body's cells. These cells take as much cholesterol as they need from the blood, and produce the rest themselves.

LDL cholesterol turns "bad" when there is more of it available in the blood than the body needs. The excess cholesterol collects in the walls of major arteries, forming aggregates and clogs known as plaques. Over time, an artery clogged with cholesterol starts to look exactly like a pipe clogged with lime scale. Since this slows the flow of blood through blood vessels, the heart has to work harder to send blood around the body. This leads to high blood pressure, which puts extra stress on the heart and damages the blood vessels. Meanwhile, the cholesterol plaques are more likely to form blood clots that close off circulation altogether. The outcome of such clotting, depending on where it happens, is a life-threatening heart attack or a stroke. This potentially disastrous chain of events begins with elevated LDL cholesterol in the blood, making the management of cholesterol the focus of most treatment efforts.

FIGURE 3.

Pathway for the production of cholesterol, showing how monacolin K from red yeast rice blocks the process. Note that the same pathway is involved in production of the essential antioxidant, coenzyme Q10.



MANAGING CHOLESTEROL – STATINS AND RED YEAST RICE

From a medical standpoint, the most common way to reduce cholesterol in the blood is to force cells to use more of it. This is possible by keeping cells from making their own cholesterol. Doing this is a complex problem in chemistry; however, as is the case with many complex chemistry problems, nature provided a ready-made solution.

Red yeast rice has been used for over a thousand years in Traditional Chinese Medicine to treat circulatory disorders.The "yeast" used to ferment the rice is usually a mold from the Monascus family, with Monascus purpureus being among the most common of these. In 1979, a Japanese scientist named Akira Endo purified a molecule from Monascus that lowered blood cholesterol very effectively. This molecule, which he named monacolin K, became the first drug – generically known as lovastatin – used in humans for cholesterol management.

Lovastatin and other members of the "statin" class of drugs have the same mode of action, which is to block the function of a protein called 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) synthase (Figure 3).

Blocking this protein prevents most cells from making their own cholesterol. These cells in turn take up more cholesterol from the blood, leaving less circulating cholesterol available to be oxidized and to form artery-blocking plaques.

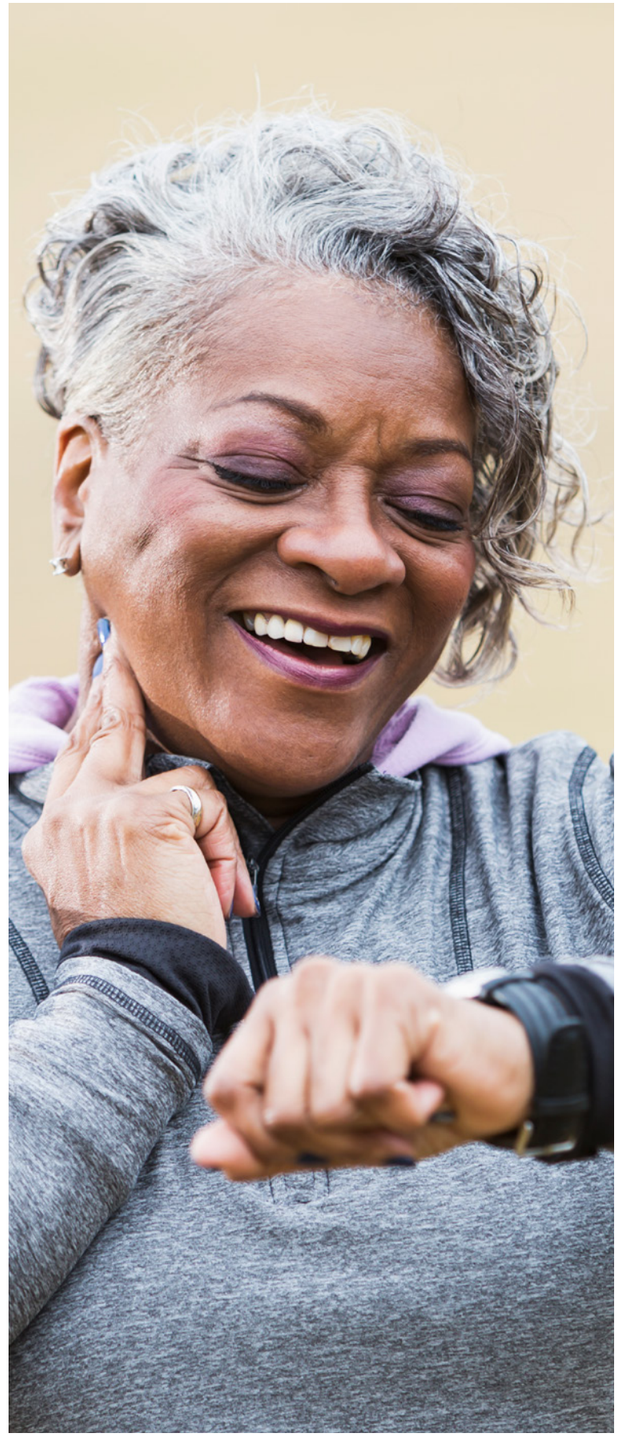
Statins effectively reduce the risk of death due to cardiovascular disease. Nevertheless, there are many cases in which the use of statins is either not enough or not suitable.

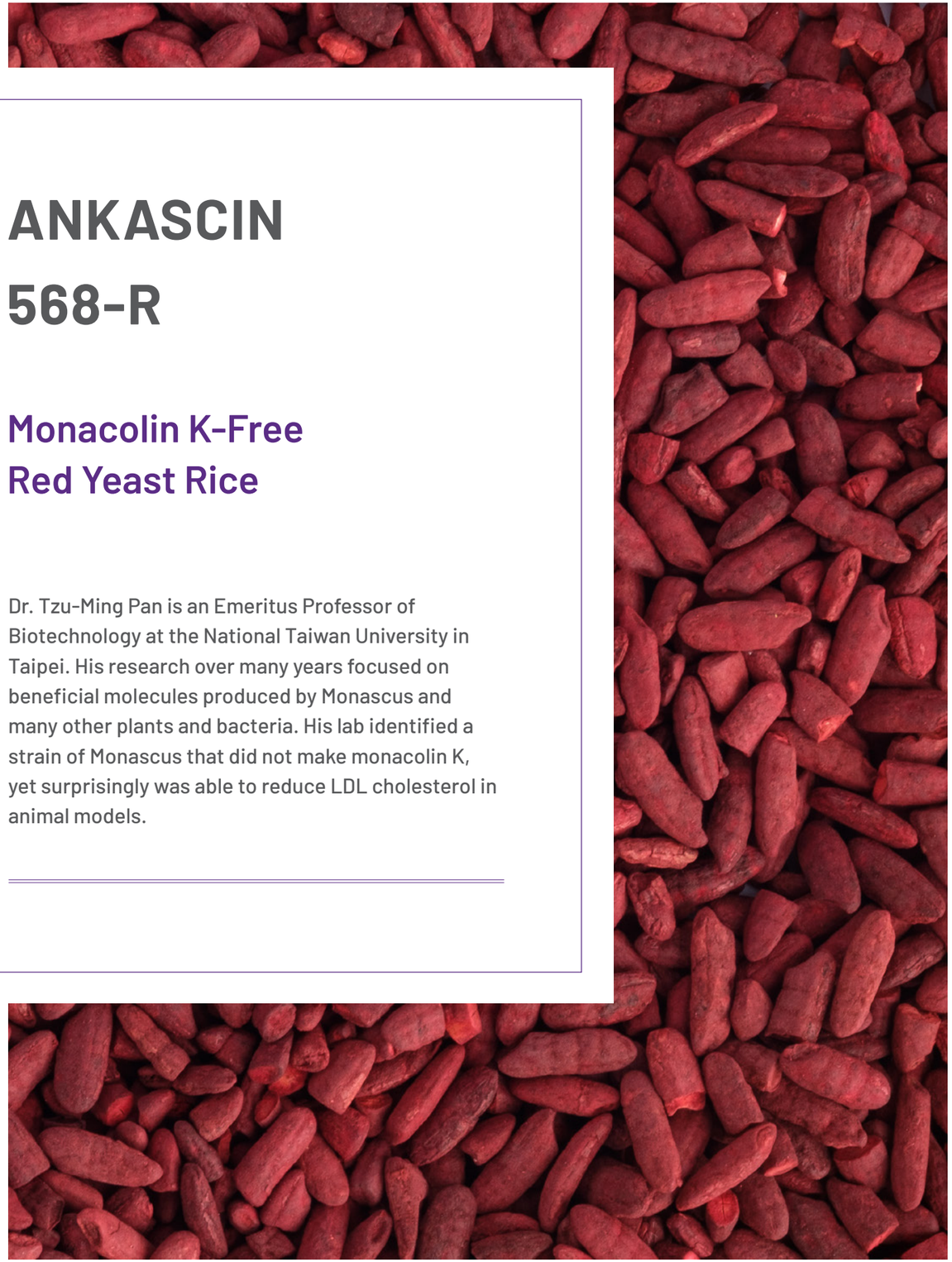
For instance, some patients cannot lower their cholesterol sufficiently with statins or similar treatments. Others have to stop using statins when they develop serious side effects such as liver and muscle damage[8]. Statins also cause heart and kidney failure by reducing levels of coenzyme Q10, an important antioxidant that is needed for proper heart and kidney functioning. Finally, people at high risk for cardiovascular disease due to family history or lifestyle may wish to reduce that risk by managing their cardiovascular health. Since statin use is not appropriate in such situations[9], there remains a need for safe, well-tolerated supplements to help people attain such health goals.

Red yeast rice supplements are not legal for sale in the USA and Canada if they contain more than trace amounts (one part per million of a 1.2 mg dose) of the natural statin, monacolin K. These supplements were banned by the FDA in the late 1990s because they contained variable and often dangerously high levels of monacolin K10. Some unscrupulous manufacturers even added the pharmaceutical form of monacolin K, lovastatin, directly to their supplements[11]. There is also the concern that such unregulated supplements may contain citrinin, a toxic by-product of the fermentation process. Importantly, all the disadvantages that apply to statins, including the possible serious side effects, applies to red yeast rice containing monacolin K, since the active agent is the same.

In spite of the prohibition against the sale of red yeast rice containing monacolin K, several supplements containing this statin are still on the market. A 2017 analysis of 28 red yeast rice supplements showed that almost all of them contained monacolin K, in highly variable quantities that were generally above the legal limit[12]. Such supplements are also frequently contaminated with high levels of the kidney toxin citrinin[13].

MONACOLIN K, BECAME THE FIRST DRUG – GENERICALLY KNOWN AS LOVASTATIN – USED IN HUMANS FOR CHOLESTEROL MANAGEMENT.





ANKASCIN 568-R

Monacolin K-Free Red Yeast Rice

Dr. Tzu-Ming Pan is an Emeritus Professor of Biotechnology at the National Taiwan University in Taipei. His research over many years focused on beneficial molecules produced by Monascus and many other plants and bacteria. His lab identified a strain of Monascus that did not make monacolin K, yet surprisingly was able to reduce LDL cholesterol in animal models.

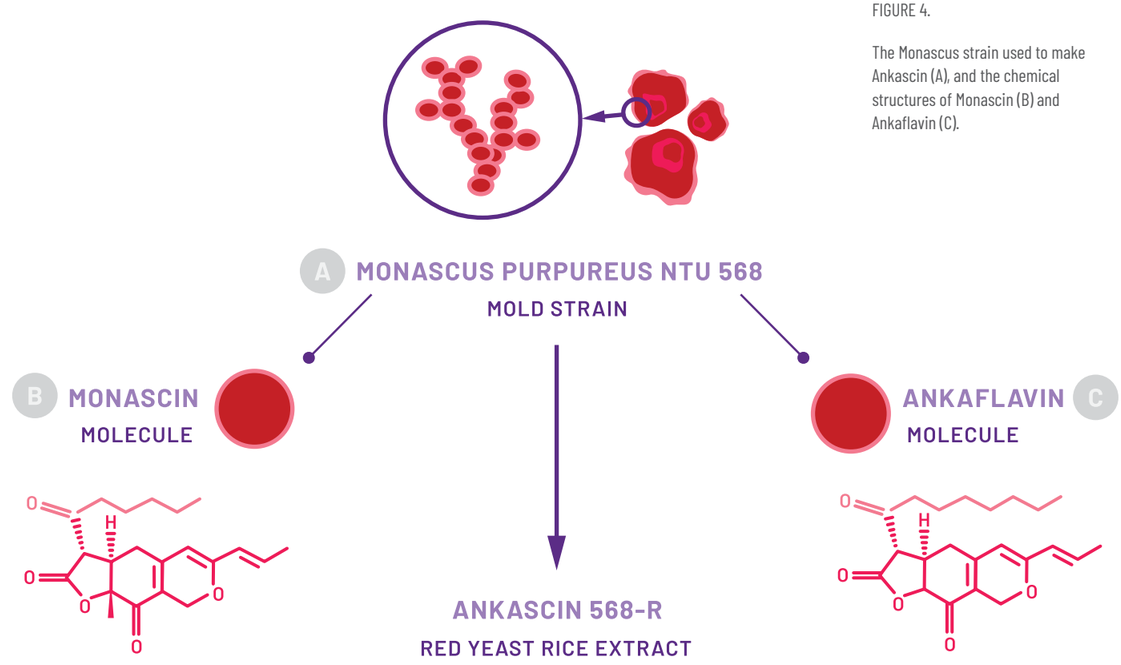


FIGURE 4.

The Monascus strain used to make Ankascin (A), and the chemical structures of Monascin (B) and Ankaflavin (C).

After several years of work, Dr. Pan and his group isolated two molecules from red yeast rice that were responsible for this cholesterol lowering effect. These molecules, named monascin and ankaflavin, are chemically very similar (see Figure 4), suggesting that they function in similar or complementary cellular pathways. In fact, they turned out to have other remarkable properties: not only could monascin and ankaflavin lower LDL cholesterol levels in the blood, they also helped in the management of blood pressure, blood sugar, and Alzheimer's disease. Dr. Pan's group and others have published almost 100 research papers in the last 10 years that reported these findings. The red yeast rice extract they produced was called Ankascin 568-R. It is enriched with monascin and ankaflavin, and its safety and efficacy have been demonstrated in several clinical trials for different treatment conditions.

This data led to the inclusion of Ankascin in the FDA's list of New Dietary Ingredients that are reasonably expected to be safe[14]. It also received approval for sale by Health Canada's Natural and Non-Prescription Health Products Directorate. As a supplement that is free of both monacolin K and citrinin, it is safe and effective for both short and long term use.

NOT ONLY COULD MONASCIN AND ANKAFLAVIN LOWER LDL CHOLESTEROL LEVELS IN THE BLOOD, THEY ALSO HELPED IN THE MANAGEMENT OF BLOOD PRESSURE, BLOOD SUGAR, AND ALZHEIMER'S DISEASE.

MANAGEMENT OF CARDIOVASCULAR DISEASE

with Ankascin – Clinical Research

The key findings relevant to the use of Ankascin red yeast rice to manage blood cholesterol came from an experimental study in hamsters.

Unlike other animals commonly used in research, hamsters develop many of the key characteristics of human cardiovascular disease when fed a diet that is high in fats and sugar[15].

The positive effects of monascin and ankaflavin in animal models led to human clinical trials to evaluate the ability of these molecules to manage blood cholesterol, blood pressure, and blood sugar.

STUDY:

MONASCIN AND ANKAFLAVIN ACT AS NOVEL HYPOLIPIDEMIC AND HIGH-DENSITY LIPOPROTEIN CHOLESTEROL-RAISING AGENTS IN RED MOLD DIOSCOREA

AUTHORS: Tzu-Ming Pan, Chun-Lin Lee, & colleagues

JOURNAL: Journal of Agricultural and Food Chemistry

PUBLICATION YEAR: 2010

DESIGN: Experimental

POPULATION: Hamster model of cardiovascular disease

PROCEDURES: Cardiovascular disease was induced in hamsters by feeding them a high-fat diet. They were then given a diet containing purified monacolin K, monascin or ankaflavin for 8 weeks.

RESULTS: Monascin and ankaflavin reduced LDL cholesterol levels by 34 and 42%, respectively, a reduction comparable to that seen with monacolin K treatment. Blood levels of fat (triglycerides) decreased by 63% (with monascin) and 58% (with ankaflavin), and by 42% with monacolin K. These effects were associated with reduced plaque buildup in the aorta, which is the major artery delivering blood from the heart.

KEY CONCLUSIONS: Monascin and ankaflavin were comparable to monacolin K at reducing blood cholesterol and cardiovascular disease.

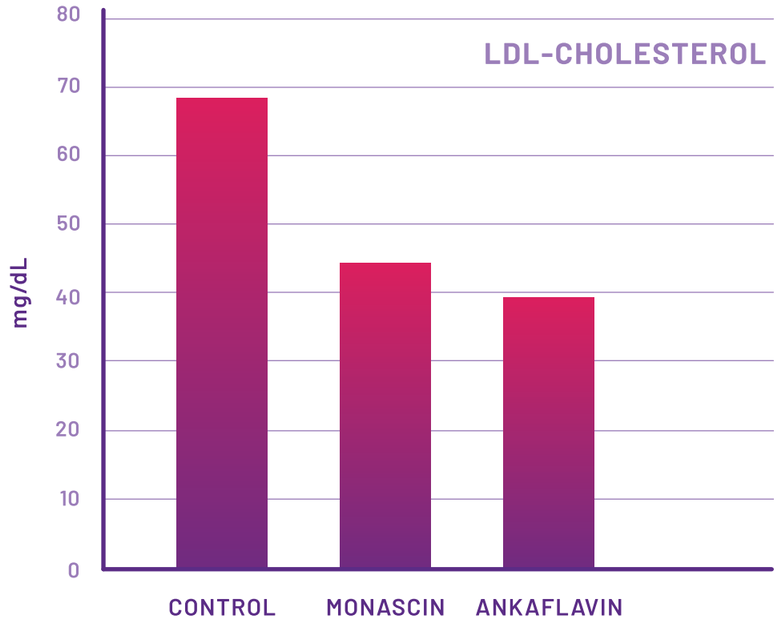


FIGURE 5.

Effects of Monascin and Ankaflavin on LDL cholesterol in hamsters.

AUTHORS: Tzu-Ming Pan, Sheng-Fu Liu and colleagues

JOURNAL: Journal of Food and Drug Analysis

PUBLICATION YEAR: 2017

DESIGN: Randomized, double-blind, placebo-controlled clinical trial

POPULATION: 40 participants with borderline high blood cholesterol

DOSE: 110 mg of Ankascin per day

DURATION: 8 weeks, followed by a 4-week washout

EVALUATION: Weeks 0 (baseline), 4, 8 and 12 (follow-up)

RESULTS: There was a 19% reduction in LDL cholesterol in participants receiving Ankascin for 4 weeks, and a 20% reduction after 8 weeks. This reduction disappeared when participants stopped taking Ankascin after 8 weeks. LDL cholesterol in the control group did not change over the study period. There were no reports of liver, kidney or muscle toxicity.

KEY CONCLUSIONS: Ankascin safely and effectively reduces LDL cholesterol within 4 weeks of treatment.

STUDY:

A RANDOMIZED, DOUBLE-BLIND CLINICAL STUDY OF THE EFFECTS OF ANKASCIN 568 PLUS ON BLOOD LIPID REGULATION

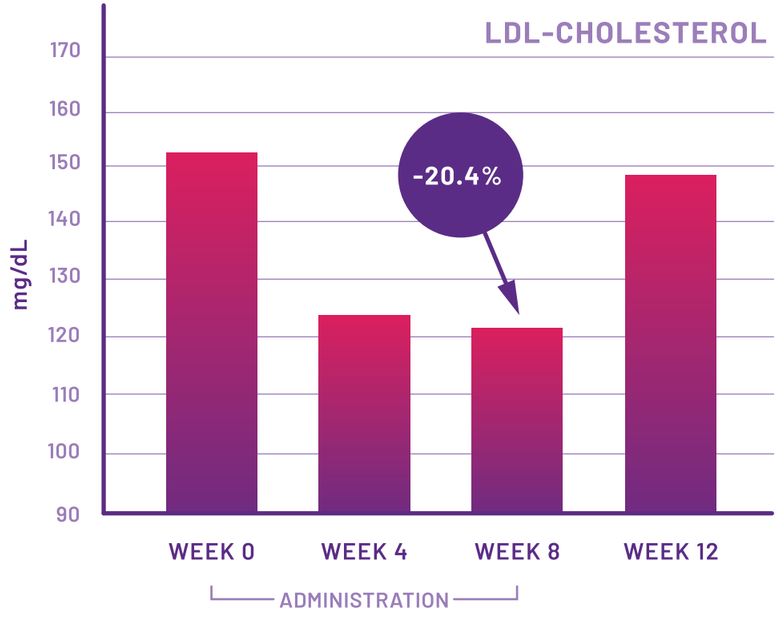


FIGURE 6.

Effect of Ankascin treatment on blood cholesterol levels.

AUTHORS: Tzu-Ming Pan, Yin-Ruei Wang and colleagues

JOURNAL: Journal of Food and Drug Analysis

PUBLICATION YEAR: 2016

DESIGN: Randomized, double-blind, placebo-controlled clinical trial

POPULATION: 39 diabetic patients

DOSE: 110 mg of Ankascin per day

DURATION: 12 weeks, followed by a 4-week washout

EVALUATION: Weeks 0 (baseline), 6, 12 and 16 (washout)

RESULTS: In patients receiving Ankascin, fasting blood glucose dropped by 8.5% within 6 weeks of treatment. This reduction increased to 9.3% by the end of the treatment period (12 weeks), but had largely disappeared within 4 weeks of the end of treatment. There were no changes in fasting blood glucose in the control group.

KEY CONCLUSIONS: Six weeks of Ankascin treatment was enough to reduce blood glucose levels in diabetic patients.

STUDY:

A RANDOMIZED, DOUBLE-BLIND CLINICAL STUDY TO DETERMINE THE EFFECT OF ANKASCIN 568 PLUS ON BLOOD GLUCOSE REGULATION

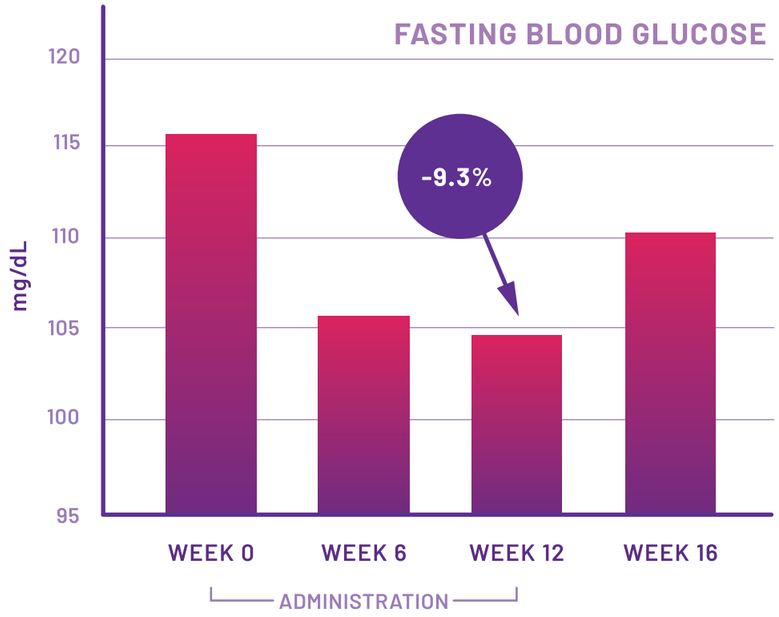


FIGURE 7.

Effect of Ankascin treatment on blood glucose levels.

STUDY:

A RANDOMIZED, DOUBLE-BLIND CLINICAL STUDY ON BLOOD PRESSURE REDUCTION AND IMPROVEMENT OF BLOOD LIPID PROFILE WITH TREATMENT OF ANKASCIN 568

AUTHORS: Tzu-Ming Pan, Chien-Li Chen and colleagues

JOURNAL: Chinese Journal of Physiology

PUBLICATION YEAR: 2017

DESIGN: Randomized, double-blind, placebo-controlled clinical trial

POPULATION: 21 patients with hypertension

DOSE: 220 mg of Ankascin per day

DURATION: 8 weeks, followed by a 2-week washout

EVALUATION: Weeks 0 (baseline), 2, 4, 6, 8 and 10 (washout)

RESULTS: Systolic and diastolic blood pressure in the treatment group had dropped by an average of 7.7% after 4 weeks of treatment, and returned to baseline levels within 2 weeks of the end of treatment.

KEY CONCLUSIONS: Ankascin may be effective in managing blood pressure in hypertensive patients.

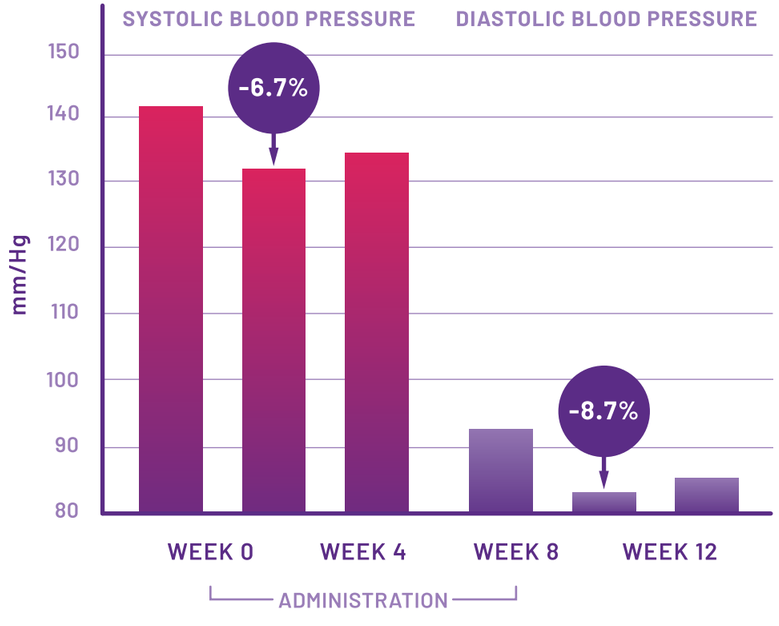
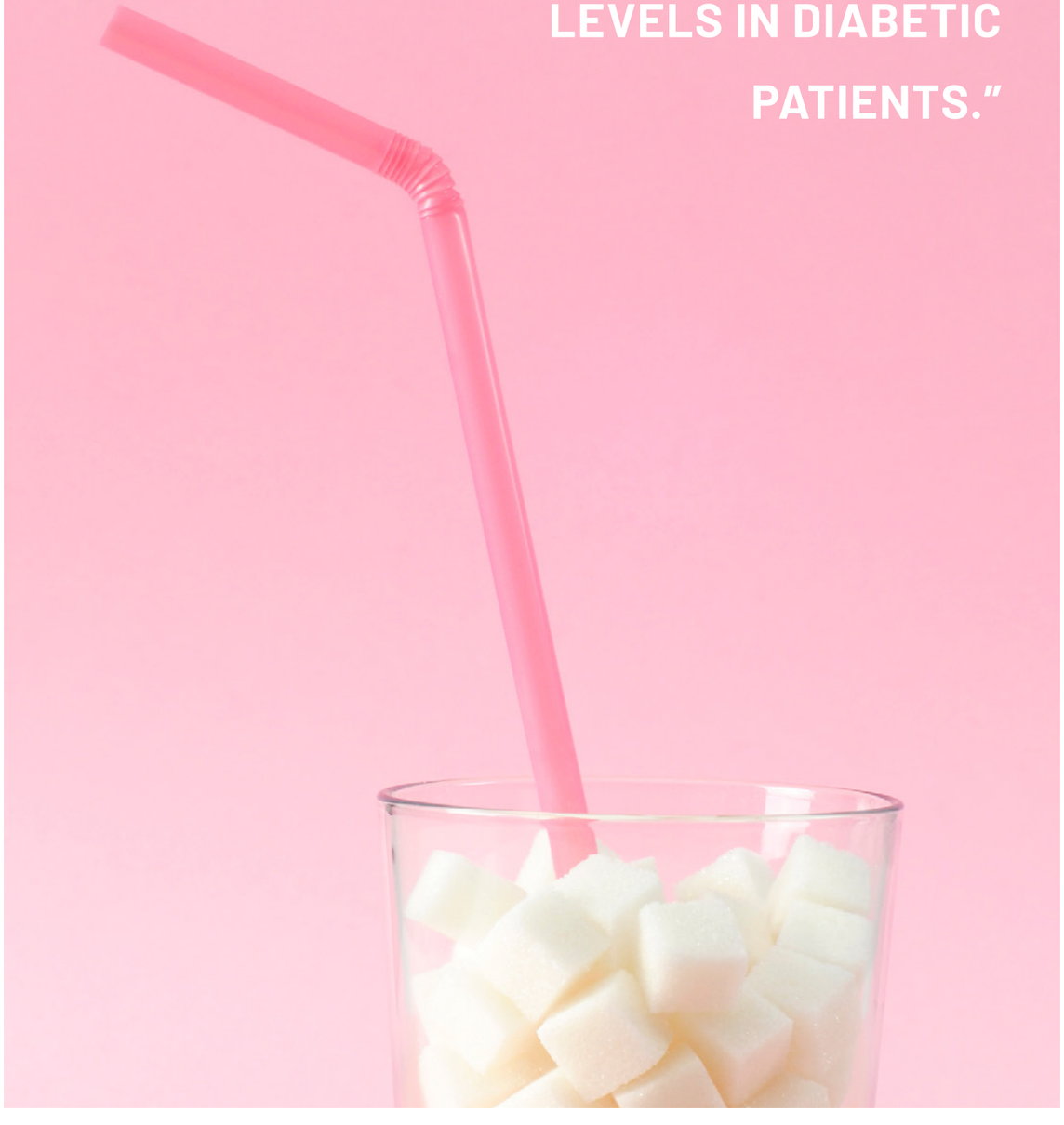


FIGURE 8.

Effect of Ankascin treatment on blood pressure.

“SIX WEEKS OF ANKASCIN TREATMENT WAS ENOUGH TO REDUCE BLOOD GLUCOSE LEVELS IN DIABETIC PATIENTS.”



MECHANISMS OF ACTION

Ankascin works by normalizing cellular mechanisms that are disrupted in the previous clinical studies.

High cholesterol, high blood pressure and high blood sugar are part of a group of related conditions called metabolic syndrome. This develops when the body loses the ability to properly manage its sources of energy, which are mostly fats and carbohydrates. Patients with this syndrome are at much higher risk for developing diabetes and cardiovascular disease. Many of the effects of metabolic syndrome are due to long-term inflammation and oxidative stress.

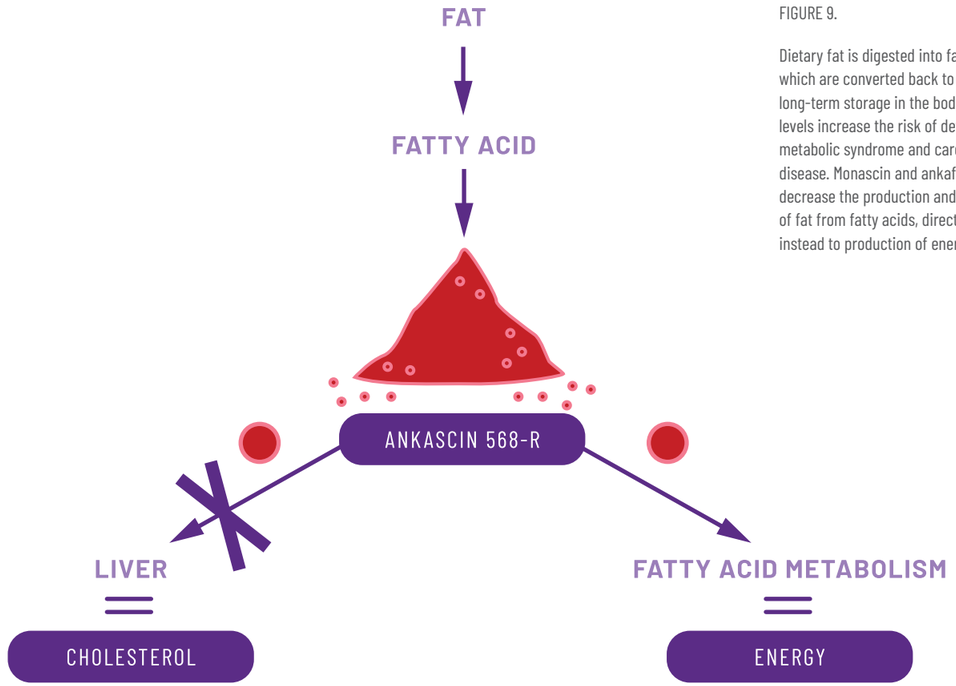


FIGURE 9.

Dietary fat is digested into fatty acids, which are converted back to fat for long-term storage in the body. High fat levels increase the risk of developing metabolic syndrome and cardiovascular disease. Monascin and ankaflavin decrease the production and storage of fat from fatty acids, directing them instead to production of energy.

However, both of which are reduced by monascin and ankaflavin. For instance, monascin reduces the production of inflammatory cytokines such as interleukin-6, interleukin-1β, and tumor necrosis factor a16. Monascin and ankaflavin also activate a cellular sensor of oxidative stress known as Nrf2; once activated, this sensor drives the production of many antioxidants to protect the body against damage[16,17]. Oxidation of cholesterol is an important first step in the production of plaques. By preventing this, monascin and ankaflavin reduce both inflammation and the increased blood pressure that normally develops with cardiovascular disease.

Ankascin has many ways of reducing LDL cholesterol, but among the most important of these is its ability to control how fat is made and used by the body. Dietary fat is digested into fatty acids, which the liver turns into cholesterol. It is for this reason that a high-fat diet, even if it is low in cholesterol, can increase your risk of cardiovascular disease. Ankascin reduces the conversion of fatty acids to cholesterol, by increasing their use in the production of energy. A diagram summarizing these effects is shown in Figure 9.

Monascin and ankaflavin prevent the development of metabolic syndrome by controlling blood sugar and the response of cells to insulin. Type 2 diabetes is common among patients with metabolic syndrome, and occurs when cells no longer respond to insulin by increasing their uptake of glucose[23].

This results in dangerously high levels of blood glucose, which is responsible for the serious health problems associated with this disease. Insulin resistance is due, at least in part, to constant, high levels of inflammation, which directly blocks the cellular pathway necessary for cells to respond to insulin[24].

Monascin acts to restore normal functioning of this pathway by reducing inflammation and its associated negative effects. Ankaflavin increases glucose uptake in the liver, increases insulin production by the pancreas, and decreases production of metabolites that increase the risk of diabetes[25,26].

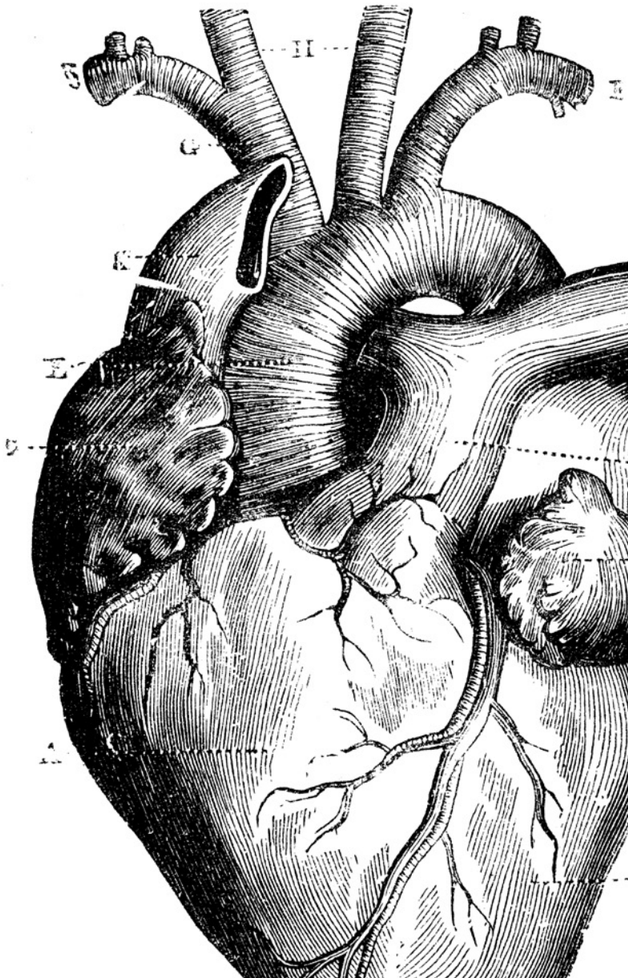
Monascin and ankaflavin also act to reduce the elevated blood pressure that occurs in hypertension. Chronic high blood pressure is associated with damaging changes in the structure of blood vessels, leading to a loss of elasticity and flexibility. Both *Monascus* metabolites use different mechanisms to prevent these alterations. Furthermore, treatment with monascin and ankaflavin lead to increased production of nitric oxide, which dilates the blood vessels and reduces blood pressure[27]. Notably, nitroglycerin, which is one of the most important pharmaceuticals for the treatment of hypertension and heart attacks, functions through the same mechanism[28]. Monascin and ankaflavin also prevent the production of proteins that stiffen and inflame the blood vessels. Since inflamed blood vessels are also more likely to develop plaques, there is a two-fold effect of Ankascin here in reducing the risk of cardiovascular disease.

Moreover, unpublished data from Dr. Pan's lab provides extra insight into the mechanism of action of ankaflavin in reducing blood pressure. The renin-angiotensin system is a signaling pathway used by the body to regulate blood volume[29]. Activation of this pathway increases salt and water retention, but also increases blood pressure. Consequently, the pathway is a major target of pharmaceuticals designed to treat hypertension. Ankaflavin counteracts this pathway and normalizes blood pressure, through several different mechanisms. First, it increases production of a hormone which directly opposes the activity of the renin-angiotensin system. Second, it blocks production of the hormone directly responsible for water and sodium retention by the kidneys. Finally, ankaflavin increases the activity of another pathway, the effect of which is to increase the production of nitric oxide, reduce inflammation and reactive oxygen species, reduce formation of blood clots, and to dilate blood vessels[30].

Thus, by regulating the key cellular pathways involved in hypertension, ankaflavin successfully reverses the negative effects of lifestyle, genetics, and other factors that predispose individuals to cardiovascular disease.

It is clear that both monascin and ankaflavin have several beneficial activities in controlling cellular pathways that are affected in metabolic syndrome. Thus, dietary supplementation with Ankascin may support against symptoms of metabolic syndrome.

BY REGULATING THE KEY CELLULAR PATHWAYS INVOLVED IN HYPERTENSION, ANKAFLAVIN SUCCESSFULLY REVERSES THE NEGATIVE EFFECTS OF LIFESTYLE, GENETICS, AND OTHER FACTORS THAT PREDISPOSE INDIVIDUALS TO CARDIOVASCULAR DISEASE.



ANKASCIN FOR MENTAL HEALTH

Alzheimer's Disease

While most studies on red yeast rice supplements have focused on their use in managing cardiovascular health and diabetes, there is evidence to support beneficial effects of Ankascin on memory and overall brain function.

Alzheimer's disease is the most common cause of dementia, and affects about 300,000 Canadians over the age of 65[32]. The number of new cases in Canada has risen dramatically (over 20%) in the past 10 years. The main symptoms include memory loss, declining language skills, and loss of the ability to care for oneself.

Unfortunately, since there is no cure, most treatment efforts focus on managing symptoms and reducing the loss of capabilities that come with advanced disease.

A number of important features of Alzheimer's disease are visible when the brain is examined under the microscope. A loss of brain cells causes the brain to shrink dramatically. The area most affected by this loss is called the hippocampus, which is a major part of the brain involved in formation of new memories. Not surprisingly, memory loss, and a difficulty in forming new memories, are the earliest signs of Alzheimer's disease. The brain of an Alzheimer's patient also becomes filled with hard, dense material called amyloid plaques. Unlike the cholesterol plaques that form in blood vessels, these ones are made from aggregates of a protein called amyloid beta. Whereas amyloid beta is normally removed quickly from a healthy brain, in Alzheimer's disease the protein accumulates to form plaques that are highly toxic to brain cells. Scientists believe that it is this accumulation of amyloid beta into plaques that causes Alzheimer's disease. Consequently, research and treatment efforts have focused on ways to either prevent production of amyloid beta, or to remove it from the brain before it aggregates into amyloid plaques.

The important events in the development of Alzheimer's disease – specifically, amyloid beta aggregation, plaque formation, and brain shrinkage – begin approximately 30 years before any symptoms of Alzheimer's disease appear. Given that the resulting damage to the brain is irreversible, it becomes critically important to prevent the onset of disease through maintenance of good nutrition and mental health.

ALZHEIMER'S DISEASE AND CHOLESTEROL

Several years ago, it was observed that patients with advanced cardiovascular disease were far more likely to have amyloid plaques in their brains than individuals without cardiovascular disease[33]. High blood cholesterol was also linked to the development of Alzheimer's earlier in life[34]. Similarly, people who effectively managed their cholesterol with statin treatment were less likely to develop Alzheimer's and similar dementias than individuals with high and unmanaged cholesterol[35]. Taken together, the data suggests a strong connection between cholesterol and Alzheimer's disease.

There are several possible reasons for the connection. Cardiovascular disease due to high blood cholesterol also affects blood vessels in the brain.

Cholesterol plaques in blood vessels reduce the efficiency with which amyloid beta and similar toxins are removed from the brain; thus, increasing the likelihood that amyloid plaques will form. A key characteristic of cardiovascular disease is inflammation, which is also associated with Alzheimer's disease. People who use anti-inflammatory drugs over a long time period are less likely to develop Alzheimer's disease[36]. Inflammation increases both the formation of amyloid beta and its deposition into amyloid plaques; thus, promoting both the development and progression of Alzheimer's disease[37,38]. This means that natural health products which lower cholesterol and reduce inflammation may protect the brain from Alzheimer's disease.

ANKASCIN AND ALZHEIMER'S DISEASE

Dr. Pan made the surprising and welcome discovery that red yeast rice supplements containing monascin and ankaflavin effectively reduced the signs and symptoms of Alzheimer's disease.

Researchers in Dr. Pan's laboratory used several methods to verify this finding. It is possible to mimic the early stages of Alzheimer's disease in rats by injecting amyloid beta aggregates into their brains. The researchers used this approach with rats that were also fed high-fat diets, to simulate the high-cholesterol risk conditions associated with early onset Alzheimer's disease. They treated some of these rats daily with either monascin or ankaflavin for 4 weeks, and then tested their ability to learn and remember how to escape from a maze. The amyloid beta-injected rats had difficulties in both learning and remembering the escape task. In contrast, the performance of rats supplemented with monascin or ankaflavin performed just as well as normal, healthy rats[39]. This suggested that monascin and ankaflavin could reverse the cognitive decline seen in Alzheimer's disease.

Dr. Pan's group used another method to evaluate the use of Ankascin in this context. High levels of aluminum in the brain can induce Alzheimer's disease by making amyloid beta more likely to form plaques[40,41]. In this experiment, rats with aluminum-induced Alzheimer's disease were treated with Ankascin, or with donepezil (a drug used to treat Alzheimer's) for 1 month, after which their symptoms were evaluated. As expected, the aluminum caused several symptoms of Alzheimer's disease, including memory problems, higher amyloid beta production, and amyloid plaques. However, rats supplemented with Ankascin had none of these symptoms[42]. Remarkably, the only effect of donepezil was to improve short-term memory, and had no benefit against the plaques themselves.These exciting results showed that Ankascin was actually more effective at treating Alzheimer's disease than a prescription drug.

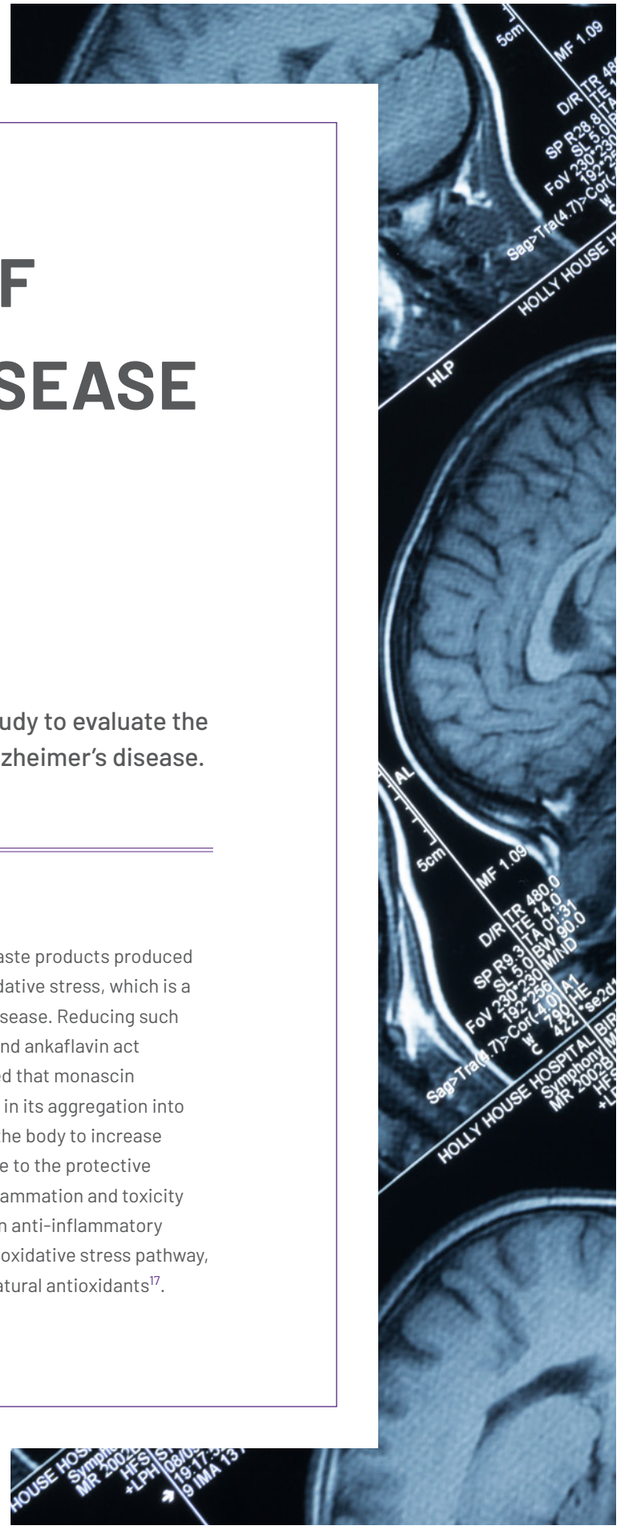
MANAGEMENT OF ALZHEIMER'S DISEASE

With Ankascin – Clinical Research

Dr. Pan's group recently completed a clinical study to evaluate the use of Ankascin to manage the symptoms of Alzheimer's disease.

HOW IT WORKS

Antioxidants protect the body against the harmful effects of waste products produced by our cells. These waste products create a state known as oxidative stress, which is a major aspect of both cardiovascular disease and Alzheimer's disease. Reducing such stress can slow the development of both disorders. Monascin and ankaflavin act as powerful antioxidants. Recent work from Dr. Pan's lab showed that monascin prevents oxidation of amyloid beta protein, which is a first step in its aggregation into amyloid plaques[43]. Furthermore, monascin assists the cells of the body to increase the production of various antioxidant genes that also contribute to the protective effect. The net effect of these actions is to reduce both the inflammation and toxicity associated with amyloid beta buildup. Ankaflavin also acts as an anti-inflammatory agent through different mechanisms[44]. It activates the cellular oxidative stress pathway, which leads cells to respond by producing large quantities of natural antioxidants[17].



STUDY:

CLINICAL STUDY FOR THE EFFECT OF ANKASCIN 568 IN ALZHEIMER'S PATIENTS

AUTHORS: Tzu-Ming Pan, Ya-Wen Hsu and colleagues

JOURNAL: Submitted for publication

PUBLICATION YEAR: 2018

DESIGN: Placebo-controlled clinical study

POPULATION: 10 patients with mild to moderate Alzheimer's disease

DOSE: 440 mg of Ankascin per day

DURATION: 10 months

EVALUATION: Monthly

RESULTS: After 9 months of treatment, patients receiving Ankascin showed fewer signs of dementia as compared to a decline in the control group. Ankascin patients also exhibited less distress and agitation, in addition to a reduction in blood LDL cholesterol and triglycerides.

KEY CONCLUSIONS: Ankascin may be effective in managing symptoms associated with Alzheimer's disease.

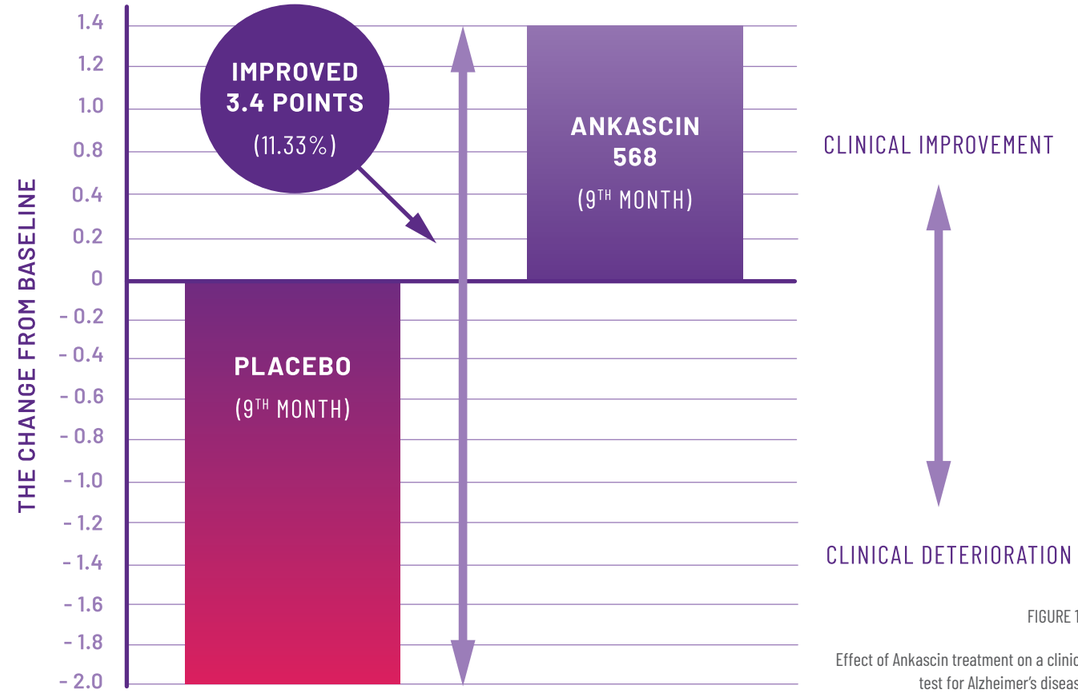


FIGURE 10.

Effect of Ankascin treatment on a clinical test for Alzheimer's disease.

SAFETY OF ANKASCIN

Red Yeast Rice

Long-term use of statins, or of red yeast rice containing monacolin K, produces toxic side effects on the liver, kidneys, and skeletal muscle.

These side effects are worsened by interactions with drugs that increase the biological activity of statins (see Table 1)[45]. Toxicity is a major reason why patients discontinue statin therapy, which in the absence of a suitable replacement leaves these patients at a high risk of heart attacks or strokes. Ankascin red yeast rice is statin-free, and has no reported side effects. Evidence for this safety comes from clinical trials, in which patients receiving Ankascin were monitored carefully for signs of toxicity.

Blood tests were conducted for aspartate aminotransferase and alanine aminotransferase. These are liver enzymes that are released into the blood when the liver is damaged. In all clinical studies, blood levels of these enzymes remained normal.The scientists involved in these clinical studies also tested for creatine phosphokinase, which is released from skeletal muscle upon damage, and for creatinine and various electrolytes that are elevated with kidney damage. Levels of all these metabolites remained normal, even with treatments lasting up to 10 months. These results show that, unlike statins and other red yeast rice supplements, use of Ankascin comes with no toxic side effects.

Ankascin red yeast rice is on the FDA's list of New Dietary Ingredients[14]. To be included on this list, a manufacturer must demonstrate that the product is reasonably expected to be safe.

SAFETY TESTS FOR ANKASCIN INCLUDED THE FOLLOWING:

- 90-day oral toxicity study in rats, at 230 times the usual dosage.
- In vitro chromosomal aberration assay, to determine if it is carcinogenic.
- Micronucleus assay, to determine if it is genotoxic.
- Ames test, to also determine genotoxicity.

All of these tests were negative for Ankascin, providing further evidence of its safety for sustained use.

INTERACTING DRUGS & SUBSTANCES
ITRACONAZOLE
CYCLOSPORINE
DILTIAZEM
KETOCONAZOLE
POSACONAZOLE
BOCEPREVIR
TELAPREVIR
ERYTHROMYCIN
NEFAZODONE
GRAPEFRUIT JUICE

TABLE 1.

Partial list of drugs and substances that interact with statins such as monacolin K. None of these interactions apply to Ankascin red yeast rice.

FREQUENTLY ASKED QUESTIONS

1. WHO CAN TAKE AOR'S RED YEAST RICE WITH ANKASCIN?

Ankascin is safe for most people; however, it should be taken with caution under certain conditions. Consult a healthcare practitioner if you are breastfeeding, taking other medications (including, but not limited to, cyclosporine, blood thinners, blood lipid-lowering medications, blood pressure medications or anti-diabetic drugs), if you suffer from liver or kidney disease, if you have received an organ transplant, or for use beyond 8 weeks. If you experience muscle pain, tenderness and/or weakness, discontinue use and consult a healthcare practitioner. Do not use if you are pregnant or plan to become pregnant.

2. WHICH AOR PRODUCTS SUPPORT CARDIOVASCULAR HEALTH IN SYNERGY WITH ANKASCIN?

Several AOR products act in different ways to help support cardiovascular health. The primary effect of Ankascin red yeast rice is to reduce blood levels of cholesterol and sugar. Oxidation of cholesterol can lead to the formation of plaques, even in individuals with healthy cholesterol levels. In this case, antioxidants will support healthy blood vessels by maintaining the cholesterol in its normal reduced state. Useful AOR antioxidants in this regard include Opti-Cholest, *Acta*-Resveratrol and Active Green Tea. Individuals who are also using statins to manage their cholesterol will have reduced levels of the essential antioxidant coenzyme Q10, leading to muscle pain[46]. This can be managed by use of AOR's Coenzyme Q10 supplement.

3. ARE THE BENEFITS OF RED YEAST RICE WITH ANKASCIN DUE ENTIRELY TO MONASCIN AND ANKAFLAVIN?

Many different molecules are produced by *Monascus* in the fermentation process that produces red yeast rice, and many of these may contribute to the beneficial effects of this supplement. These molecules include unsaturated fatty acids, pigments (monascin and ankaflavin are yellow pigments), and phytosterols. Many of these have positive biological activity. For instance, the red pigments monascorubrin and rubropunctatin are effective antibiotics[47], and may reduce blood cholesterol through separate mechanisms[48].

4. WHAT IS THE IDEAL DOSE?

The recommended dose of 1-2 capsules per day is based on evidence from clinical trials that 110-220 mg/day were sufficient to see beneficial effects. Consult a healthcare practitioner before exceeding this dose.

5. WHICH DRUGS ARE SAFE TO TAKE ALONG WITH ANKASCIN RED YEAST RICE?

There are no known drug interactions involving Ankascin. However, one should seek the advice of a healthcare practitioner to discuss their own individual situations.

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