



NEW PRODUCT

ThorneVet Longevity Complex

A cutting-edge animal health supplement that combines a powerhouse of ingredients for beneficially influencing the body's longevity pathways and promoting healthy aging in companion animals. The ingredients synergistically balance the body's inflammatory processes, while reducing oxidative stress, in addition to providing key nutritional support for the veterinary cancer patient.

Key Calming Support Features

- | Contains nicotinamide riboside (NR), the most bioavailable and efficient precursor to NAD⁺, which is necessary to up-regulate the activity of the sirtuin proteins.
- | The formula's synergistic combination of polyphenol compounds – resveratrol, quercetin, curcumin, and green tea extract – beneficially influences the longevity pathways that promote healthy aging.
- | The carotenoid astaxanthin provides potent antioxidant support.
- | Includes the important amino acid taurine – which has been shown to enhance longevity in animals.

Introduction

There is substantial ongoing active research, as well as much considerable interest, in promoting longevity and understanding the biological and molecular targets that can influence the body's aging processes. Natural aging causes universal molecular, cellular, and physiological changes in the body – with most of these changes being negative. And although individual genetic makeup plays a significant role in the aging process, there are also non-genetic changes that can occur in the body as a result of the animal's daily environment – changes caused by lifestyle, nutrition, physical activity, obesity, exposure to pollutants and toxins, and illness. These non-genetic changes can contribute as much as 70 percent of the factors that cause the adverse expressions of aging. This non-genetic dynamic – referred to as **epigenetics** – allows for multiple avenues of positive interventions that can be designed and implemented to promote and enhance longevity and healthy aging.

Epigenetics is the term that describes changes in DNA expression that are not caused by the animal's underlying, inborn genetic makeup. In other words, **epigenetic changes** can alter the structure of the animal's DNA, and in doing so what would otherwise be the animal's natural patterns of gene expression are altered.¹

For example, there are several important points along the body's longevity pathways that can be beneficially influenced by either the up-regulation or the down-regulation of enzyme systems that control gene expression. Currently, there is considerable research looking at the **epigenetic influence** that nutritional supplements, pharmaceuticals, and lifestyle factors can have on enhancing anti-aging effects and promoting longevity. Each of these influences can have their own specific beneficial mechanism of action – for example, the up-regulation of the **sirtuin proteins**, or the down-regulation of mTOR to maintain optimal cellular metabolism, or the up-regulation of **AMPK1** to enhance cellular energy production. Although an in-depth discussion of these pathways is beyond the scope of this Product Information Sheet, some understanding of the body's longevity pathways is helpful to understand how supplementation with specific nutrients can beneficially impact longevity and healthy aging.

For example, the body's Krebs cycle produces cellular energy in the mitochondria of the body's cells. This energy production cycle is critical for every life process – in humans and animals alike. One important process of the Krebs cycle pathway is the production of **nicotinamide adenine dinucleotide** – or **NAD+**. The presence of newly produced **NAD+** in the mitochondria then becomes the fuel for oxidative phosphorylation and the electron transport chain, which in turn become the greatest producers of cellular energy within the mitochondria. It is for this supportive role in cellular metabolism, as well as for other notable reasons, that **NAD+** is now well-recognized as having numerous pro-longevity, healthy aging effects. In other words, the more **NAD+** the better! In addition, it should also be noted that physical activity and calorie restriction – both good things – can cause an increase in the level of **NAD+** within the cell.

As the level of **NAD+** within the cell increases, the increase is detected by the **sirtuin proteins** – a family of signaling proteins involved in the regulation of metabolism. In fact, the beneficial activity of the **sirtuin proteins** is dependent on **NAD+** being present because **NAD+** acts as a cofactor with these proteins. The **sirtuin proteins** undertake a host of important roles in controlling gene expression, in DNA repair, in oxidative stress response, in mitochondrial function, and in the synthesis of new cells. On the other hand, if there is down-regulation of **sirtuin protein** activity, that can lead to tissue-specific degenerative events that underlie multiple adverse health conditions, especially those related to aging.²

Up-regulation of the **sirtuin proteins** promotes the activation of the important enzyme – **AMP kinase (AMPK)**. **AMPK** is the primary regulator of cellular energy. The presence of **AMPK** has an inhibitory effect on another enzyme – the mammalian target of rapamycin (mTOR) enzyme – and when the mTOR enzyme is inhibited, then many beneficial cellular processes can commence and proceed within the cell, such as cellular repair processes. Thus, the net effects of **sirtuin protein** activation are both pro-longevity and anti-aging.³

The most important of the various **sirtuin proteins** is **Sirt1**. **Sirt1** exerts beneficial effects on metabolic pathways, cell survival, cellular senescence (the destruction of worn-out cells), and the body's inflammatory response. In addition, the presence of **Sirt1** is thought to inhibit the progression of chronic conditions like diabetes, as well as pulmonary, neurodegenerative, and cardiovascular disorders.⁴ In addition to helping to maintain essential metabolic pathways – suggesting its activation is beneficial against metabolic disorders – **Sirt1** is also believed to play a beneficial role in the body's natural anti-cancer processes.⁴

In recent years, it has been found that certain natural compounds can beneficially influence and up-regulate **Sirt1** expression. **Sirt1** expression can then have positive downstream effects, such as balancing the body's inflammatory response, or perhaps even resisting the initiation or progression of cancer, while simultaneously promoting beneficial metabolic conditions; for example, increasing insulin sensitivity – all of which benefit longevity pathways and healthy aging. Interestingly, although these natural compounds can influence the longevity pathways by different mechanisms of action, they all mimic the known benefits that can result from calorie restriction. In any case, as a result, these compounds work to increase lifespan by improving metabolic function throughout the body.

ThorneVet's Longevity Complex includes the most bioavailable precursor to NAD⁺ production – Nicotinamide Riboside (NR) – along with potent polyphenolic compounds – Resveratrol, Quercetin, Curcumin – and potent green tea catechins – including EGCG, as well as the antioxidant Astaxanthin and a supplemental amino acid – Taurine. These ingredients work synergistically to up-regulate the activity of the sirtuin protein family, with the accompanying beneficial balancing of the body's inflammatory processes, along with promoting healthy aging and longevity, and, in the situation of the veterinary cancer patient, to provide substantial support for healing and recovery.

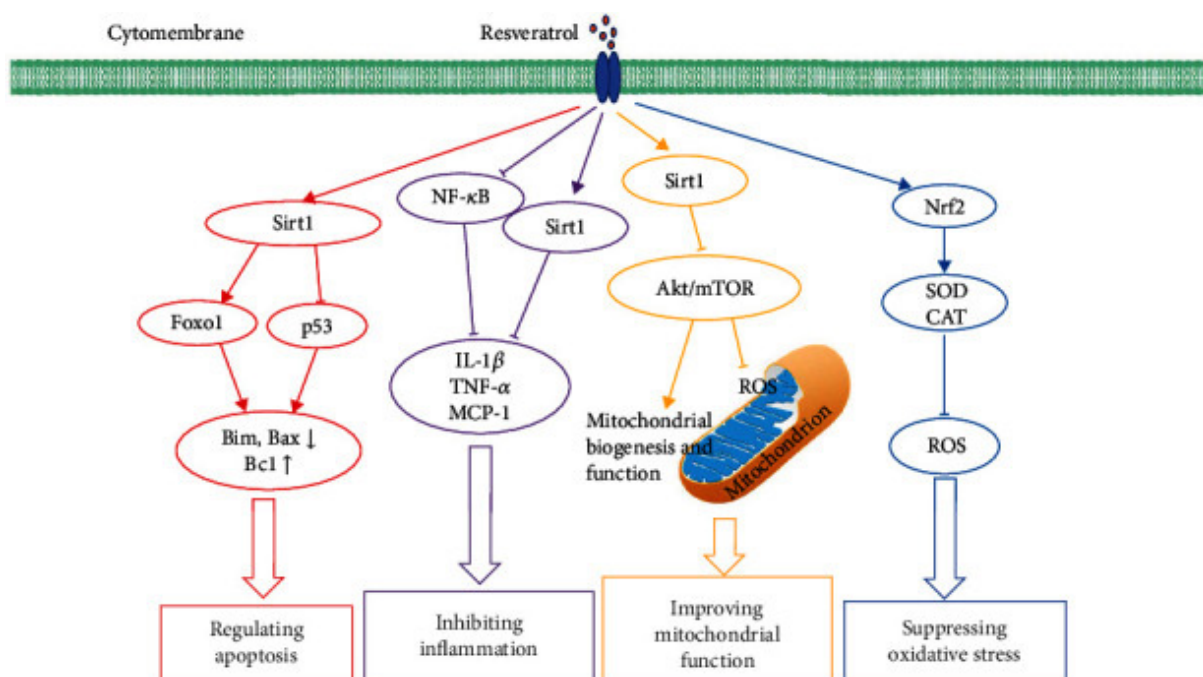
Polyphenol Compounds

Polyphenols are potent bioactive compounds – found extensively in plants – that have multiple health-promoting properties. The health-promoting properties of polyphenols include antioxidative and immuno-supportive benefits, as well as beneficial activity that moderates the body's inflammatory response and the gut's microbiota.⁵ **ThorneVet's Longevity Complex** incorporates a synergistic blend of multiple polyphenol compounds that help balance the body's inflammatory response, boost its antioxidant capacity, promote metabolic health, and, when adjunctive care is needed, provide substantial support to the veterinary cancer patient.

Trans-Resveratrol

Resveratrol is a polyphenol naturally found in grapes, blueberries, red wine, and peanuts. **Resveratrol** has been shown to have multiple beneficial bioactivities, including antioxidant, inflammatory response, and immune-supportive activity, as well as providing significant nutritional support in situations of cardiovascular disease, neurodegenerative disorders, obesity, and cancer.⁶ Numerous studies have shown **resveratrol's** importance in promoting healthy aging through suppressing oxidative stress, down-regulating imbalanced inflammatory responses, improving mitochondrial function, and up-regulating programmed cell death (apoptosis) as denoted in the diagram below.^{7,8} As can be seen in the diagram below, **resveratrol** upregulates **Sirt1**, which can then exert its many beneficial effects on multiple pathways as noted above, with the end result being enhanced longevity and healthy aging.

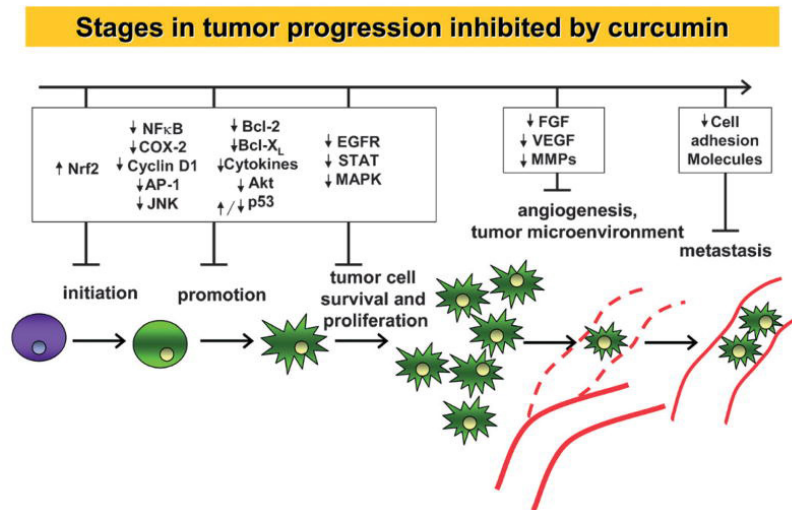
ThorneVet's Longevity Complex uses **Evolva's Veri-te Trans-resveratrol**, the most biologically active form of **resveratrol**, which is produced by fermentation processes, thus eliminating the use of solvents and increasing both the purity and the potency of the resulting end product.



Curcumin

Curcumin is a bioactive curcuminoid that comes from the rhizome of turmeric, a flowering plant in the ginger family. In addition to being used for thousands of years as a culinary spice, curcumin is also utilized for its many health-promoting benefits. Because curcumin by itself is poorly absorbed in the body, **Longevity Complex** contains **Indena S.p.A's Curcumin phytosome – CurcuVET®** – to ensure the highest bioavailability of this potent curcuminoid. **Indena S.p.A.**, headquartered in Milan, Italy, is the world's leading company dedicated to the identification, development, and production of high-quality, bioactive constituents derived from plants.

Curcumin exerts many beneficial effects across various organ systems in the body. In addition to being a potent antioxidant, **Curcumin** enhances bile flow, thus promoting a normal cholesterol level, and it also exerts significant benefit in maintaining a balanced inflammatory response in the body.⁹ Like its co-ingredient **nicotinamide riboside malate**, **Curcumin phytosome** is included in **Longevity Complex** because of its ability to up-regulate the expression of **Sirt1**, thus promoting the body's programmed natural death of worn out cells, as well as improving mitochondrial function in the cells, increasing **AMPK** (thus enhancing cellular energy production), and reducing oxidative damage through increasing the expression of **Nrf2** – a transcription factor that promotes antioxidant effects.¹⁰ **Curcumin** has also been found to inhibit the development and progression of cancer from multiple pathways as denoted in the diagram below¹¹:



Quercetin

Quercetin (*saphora japonica*) is a **polyphenol flavonoid antioxidant** – more specifically it's a **flavonol** – which is found in many fruits and vegetables, including onions, grapes, berries, cherries, broccoli, seeds, nuts, and citrus fruits. Approximately 6,000 flavonoids have been identified in the plant world – with quercetin being the most abundant one. Like **curcumin**, **quercetin** by itself is not very bioavailable. For this reason, **ThorneVet's Longevity Complex** also utilizes **Indena's phytosome technology** to enhance **quercetin's** absorption and bioavailability – **quercetin** is complexed with **lecithin**, a readily absorbed **phospholipid** derived from sunflower. **Indena's** proprietary **phytosome** delivery system results in the enhanced absorption of **quercetin** because when the body readily absorbs the naturally absorbable **lecithin**, it also readily absorbs the **quercetin** that is complexed with the **lecithin**. In a human study with 12 participants, **Indena's Quercetin phytosome** demonstrated 20-times better absorption than unbound quercetin.

The beneficial effects of **quercetin** are well documented, and include its direct antioxidant effects, as well as its beneficial influence on enhancing signal transduction pathways – the cellular process in which signals are conveyed to change the activity of cells. In this context, **quercetin** displays inflammatory response benefits, immuno-protective benefits, neuro-protective benefits, and anti-aging benefits.¹²

Regarding its health aging benefit, **quercetin** is a **senolytic**. As cells age, a process called **senescence** takes place. Normally, cells continue to divide until they get old and die, when they are then removed from the body and replaced by new cells – like the billions of cells that die and are replaced in the body each day. However, during aging, some cells, although they stop dividing, they don't die. Even though they are useless, these cells, called **senescent cells** – or "**zombie cells**" – are not removed from the body. Some of the same factors that cause free radicals also cause **senescent cells**. **Senescent cells** can build up in the body and contribute to chronic health conditions because they secrete inflammatory chemicals that can damage healthy cells. Enter **quercetin**. Although the science of **senescence** is still in its infancy, it turns out that **quercetin** helps remove **senescent cells** from the body – making it a **senolytic**. And cellular senescence is up-regulated in the presence of **SIRT1**, which **quercetin** helps activate.

Nutritional flavonoids like **quercetin** are more potent antioxidants than vitamin C and vitamin E.¹³ By scavenging free radicals, by boosting the activity of the body's natural antioxidants, and by maintaining healthy inflammatory responses, **quercetin** encourages healthy aging and promotes longevity. **Quercetin** is also receiving attention for its apparent ability to slow the growth of cancer cells – research on **quercetin** is finding it does this by beneficially influencing the DNA processes that interrupt the growth of cancer cells, resulting in their subsequent naturally programmed death (apoptosis).¹⁴

Green Tea Extract

Green tea has been consumed in Asian cultures for its health-promoting properties for thousands of years. Several compounds found in **green tea** are responsible for these beneficial properties. The flavonoid polyphenols in **green tea** – called catechins – have been the most extensively studied. The group of catechins belonging to the various flavonoids in **green tea** include **epigallocatechin-3-gallate (EGCG)**, **epicatechin-3-gallate (ECG)**, **epigallocatechin (EGC)**, and **epicatechin (EC)**.¹⁵ Clinical studies confirm the positive inflammatory response and antioxidant effects of **green tea** polyphenols, benefits that are now considered to be the cornerstone of **green tea's** health-promoting properties. Numerous studies also show the polyphenols in **green tea** have therapeutic efficacy in benefitting the situation of cancer patients. Notably, polyphenols, including catechins, appear to hasten the death of cancer cells, while not adversely affecting surrounding healthy cells.¹⁶

There is much variability in the quantity and type of polyphenols present in **green tea extract**. This variability is influenced by growing conditions, time of harvest, and other variables involved in the processing and handling of the extracted material. To ensure the highest concentration of standardized catechins, including **EGCG**, **ThorneVet's Longevity Complex** uses **Indena S.p.A's Green Tea Phytosome (GreenSelect®)**, thus increasing the bioavailability of **green tea's** potent bioactive and therapeutic constituents.

Nicotinamide Riboside Malate (NRM)

As described in the **Introduction**, **nicotinamide adenine dinucleotide (NAD⁺)** is a critical coenzyme that is necessary for the generation of cellular energy inside the mitochondria of the cell, as well as being an essential cofactor in the metabolic reactions involving the **sirtuin proteins**. **NAD⁺** both directly and indirectly influences multiple key cellular functions, including metabolic pathways, DNA repair, chromatin remodeling (to maintain normal gene expression), cellular senescence, and immune cell function. These cellular processes and functions are necessary for maintaining metabolic balance (**homeostasis**) as a component of healthy aging.¹⁷

Just as in humans, an animal's **NAD⁺** level declines with aging, and this change is associated with many age-related adverse health conditions, including cognitive decline, metabolic disorders, sarcopenia (muscle wasting), frailty, and, as is becoming more apparent, possibly even cancer. It is now thought that many aging-associated conditions can be slowed down, and possibly even reversed, by maintaining or restoring **NAD⁺** to an optimal level.¹⁷ **NAD⁺** can be formed in the body naturally from precursors or from intermediates that are consumed in the diet, such as meat, dairy, eggs, and certain types of wheat.

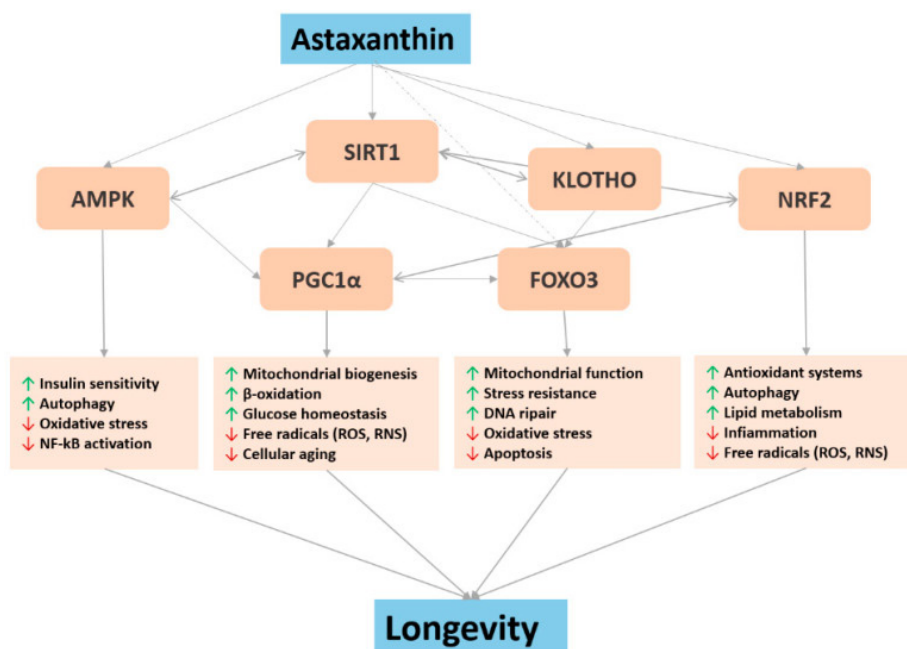
In 2004, it was discovered that **nicotinamide riboside** is a highly efficient precursor of **NAD⁺** because it requires the least amount of bodily energy to produce **NAD⁺** when **nicotinamide riboside** is present. Accumulating evidence on **nicotinamide riboside's** health benefits has validated its efficacy across numerous animal and human studies for the treatment of a number of cardiovascular, neurodegenerative, and metabolic conditions.¹⁸ Supplementation with **nicotinamide riboside** has been shown to increase the level of **NAD⁺** in multiple tissues, concurrent with increased activity of the **sirtuin proteins**, improved mitochondrial function, and regenerative stem cell potential.¹⁸

The **nicotinamide riboside** ingredient in **ThorneVet's Longevity Complex** is **nicotinamide riboside hydrogen malate**. This is an ingredient that is exclusive to **ThorneVet** and is a unique form of **nicotinamide riboside**. **ThorneVet** sources its **nicotinamide riboside malate** from a European supplier, and **ThorneVet** is the only animal health product company in the United States using this unique form of **nicotinamide riboside** in a companion animal health supplement. **Nicotinamide riboside malate** is **nicotinamide riboside** bound to **hydrogen malate salt**, which is another Krebs's cycle organic acid, thus further supporting **nicotinamide riboside's** cellular energy production capability.

Astaxanthin

Astaxanthin, a **ketocarotenoid**, is a potent antioxidant, well known for its vibrant red color, that can cross the blood-brain barrier. **Astaxanthin** has the greatest antioxidant capacity among the 730 known **carotenoids**, including **beta carotene**, **lycopene**, and **lutein**. **Astaxanthin** is initially produced by microalgae and phytoplankton which, after they are consumed, the carotenoid works its way up the food chain to eventually become the source of the deep pink color of ocean fish, like salmon. Due to its unique chemical structure, **astaxanthin** acts as a scavenger of free radicals in the internal membrane layer of the cell, while simultaneously controlling oxidation on the outside surface of the cell membrane – effectively protecting both the inside and outside of the cell membrane. These characteristics are the main reasons for the exceptional antioxidant capacity of **astaxanthin**, which is approximately 10 times more effective than **beta-carotene** or **lutein** and about 100 times greater than **alpha-tocopherol**.¹⁹ In addition to directly inhibiting free radicals, **astaxanthin** has been shown to further inhibit oxidative damage by activating several beneficial genes that are linked to longevity and healthy aging. Furthermore, recent research reveals that **astaxanthin** activates mitochondrial function and enhances the biogenesis of mitochondria; i.e., the production of new mitochondria.

The following diagram highlights the effects of **astaxanthin** on the body's longevity pathways. **Astaxanthin** directly and beneficially interacts with **AMPK**, **Sirt1**, **FOXO3**, and **Nrf2** gene expression, thus promoting longevity by moderating inflammatory responses, reducing oxidative stress, and promoting optimal mitochondrial function — all of which are beneficial anti-aging effects.¹⁹



ThorneVet's Longevity Complex uses a superior **astaxanthin** ingredient – from **AstaReal®**. **AstaReal's astaxanthin** is derived from the microalgae called **Haematococcus pluvalis**, a fresh-water unicellular microalgae (like Chlorella and Spirulina); therefore, it is plant-based and vegetarian friendly. **AstaReal's astaxanthin** has been studied in more than 70 published clinical trials. An excellent description of **AstaReal's astaxanthin** ingredient, and its many benefits for health and longevity can be found at astareal.com/en/astaxanthin.

Taurine

Taurine, an abundant amino acid in all living organisms, is involved in a wide variety of life processes. While early studies showed that an optimal **taurine** concentration is correlated with good health, it has been found more recently that the body's concentration of **taurine** naturally decline with aging. A 2023 study published in *Science* reveals that in both mice and monkeys, supplementation with **taurine** is able to improve both life span and health span. Investigations into the mechanisms of action through which **taurine** supplementation improves the health span and life span reveal that **taurine** positively affects several hallmarks of aging. For example, **taurine** reduces cellular senescence (the natural aging of cells), protects against telomerase deficiency, suppresses mitochondrial dysfunction, decreases DNA damage, and balances the body's inflammatory response.²⁰

There are multiple ways to incorporate Longevity Complex into your pet's health care. ThorneVet's Longevity Complex can be used in preventative fashion to maintain health, promote vitality, and ward off disease. Longevity Complex can also be used as part of a comprehensive protocol in treating metabolic disorders, as well as immune system disorders, including autoimmune diseases and cancer.



Longevity Complex

Synergistic ingredients that enhance the body's longevity pathways to promote healthy aging in companion animals



Cats: 1/2 soft chew 1-2 times daily



1 soft chew per 25 pounds body weight 1-2 times daily

V985-SC / 90 Soft Chews



PRODUCT FACTS

Active Ingredients per 3-gram Soft Chew:

Taurine	500 mg
Nicotinamide Riboside Hydrogen Malate	100 mg
Quercetin Phytosome (Saphora japonica extract (flower) / Phospholipid complex from Sunflower)	75 mg
Curcumin Phytosome (Curcuma longa extract (root) / Phospholipid complex from Sunflower) (CurcuVET®)	50 mg
Green Tea Phytosome (Camellia sinensis extract (leaf) decaffeinated / Phospholipid complex from Sunflower) (GreenSelect®)	50 mg
Trans-Resveratrol (Veri-Te®)	40 mg
Astaxanthin (from AstaReal®)	3 mg

Inactive Ingredients (soft chew matrix):

Arabic gum, bacon flavor (vegan), buffered white distilled vinegar, chick pea flour, citric acid, coconut glycerin, coconut oil, guar gum, rosemary extract, sunflower lecithin, sunflower oil, tapioca starch, water.

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