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### Asthashinesilver capsules: an excellent choice as kidney protector & as anti-diabetic in diabetes

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#### ABSTRACT

Globally, Diabetes Mellitus and its complications is the third largest killer. At the current rate, the diabetic population of 171 million will increase to 366 million by 2030. One of the most common complications associated with DM is nephropathy or kidney damage. Diabetes is strongly linked to oxidative stress as either a consequence of increased ROS production, reduced antioxidant status, or both. Oxidative stress in diabetes is brought on by consistent hyperglycemia (high blood sugar levels) from a very high carbohydrate diet, reduced cell carbohydrate uptake, and/or low insulin output from the pancreas. Astaxanthin could lessen oxidative stress in pancreatic beta cells (the cells in body that produce insulin) caused by chronic high blood sugar levels. In turn, this improves the body's ability to manage blood glucose levels by allowing the pancreatic cells to make the right amount of insulin when needed. Astaxanthin was found to improve pancreatic beta cell function and protect these cells from glucose toxicity, cell breakdown and death. L-Carnitine is a fatty acid oxidation facilitator which acts by interorganelle translocation of fatty acids. L-carnitine is a powerful aid due to its role in the conversion of fat into energy. L-carnitine is essential for beta-oxidation by transferring long-chain fatty acids from the cytosol to mitochondria. This article reviews the current available scientific literature regarding the effect of Astashine silver capsules as Antidiabetic in diabetes and as kidney protector.

**Keywords:** Astashine silver capsules, Antidiabetic, diabetes, kidney protector.

#### INTRODUCTION

The study shows that the antioxidant power of astaxanthin, which reportedly is 500 times stronger than that of vitamin E, can protect cells against the oxidative damage caused by high glucose (sugar) levels. High blood sugar levels and oxidative stress are associated with complications common among diabetics, including kidney disease, neuropathy (nerve damage), and diabetic retinopathy (vision problems).

In a Clinical study cells treated with high levels of glucose, and then exposed to astaxanthin. It is found that astaxanthin suppressed activities that damage cells and lead to complications associated with diabetes. Astaxanthin was also able to hinder lipid peroxidation (damage to fats in cell membranes by free radicals) and levels of total reactive species, superoxide, and nitric oxide (molecules that cause extensive cell damage).

Thus it conclude that the strong antioxidant properties of astaxanthin that allow it to reduce oxidative stress, inflammation, and cell death are the reasons why it could be an effective supplement to help prevent complications associated with elevated glucose levels in diabetics.

L-Carnitine, is a quaternary amine ( $\beta$ -hydroxy- $\gamma$ -N-trimethylammonium butyric acid-M.W. 161.2), and is known as a vitamin like and amino acid like substance. Synthetic carnitine occurs as both D & L isomers; however, only Lcarnitine is physiologically active. The main function of carnitine in the body is facilitation lipid oxidation by transporting long-chain fatty acids into the inner mitochondria region where they undergo  $\beta$ -oxidation. In order for fattyacids (from food intake or adipose tissue) to produce energy they must be changed into acylCoAs prior to  $\beta$ -oxidation; however, since acylCoAs cannot cross cell walls, carnitine comes into place to help with the transportation through the mitochondrial wall. Therefore, without carnitine, most of the dietary lipids cannot be used as an energy source and our body would accumulate fatty-acids resulting in obesity. In humans, L-carnitine is absorbed in the small intestinal mucosa by sodium-dependent active transport and by passive transport. In blood, carnitine does not need protein for a carrier, and is present in the free or acylcarnitine form. Clinical studies have shown the effects of L-carnitine on obesity & blood glucose control.

### Composition of Astashine silver casules

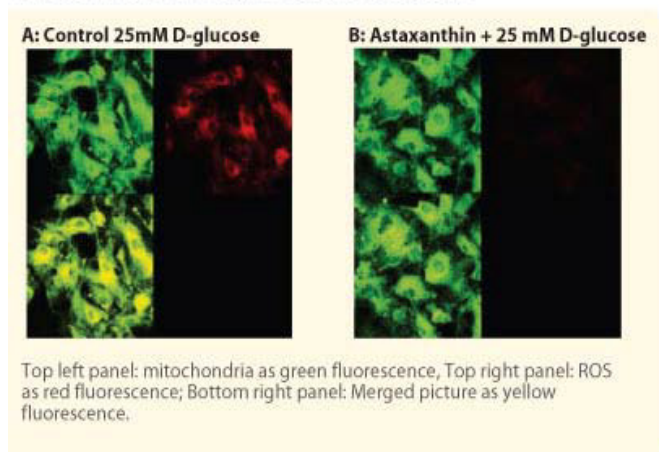
Astaxanthin - 2mg (Naturally derived from Haematococcus pulvialis algae extract, which is microencapsulated) & L-Carnitine L-Tartrate 368 mg.

### Clinical study reports of astaxanthin in astashine silver capsules

Scientists from the Kyoto Prefectural University of Medicine, Japan confirmed that astaxanthin significantly suppressed ROS production, biomarkers of oxidative damage and proinflammatory responses in mitochondria of Normal Human Mesangial Cells (NHMC) exposed to high-levels of glucose.

Manabe *et al.*, (2007) exposed NHMC to 25 mM D-glucose (equivalent to 400 mg/dl in humans) to investigate the oxidative damage reported in diabetic nephropathy or kidney damage (Figure 1). Chronic high-blood-glucose levels increase Reactive Oxygen Stress (ROS) production in mitochondria. ROS affects not only on the development of diabetes but also on its complications such as mesangial cell damage which leads to loss of kidney function. Since the progress of kidney damage is mostly irreversible and has an extremely poor prognosis, it is important to prevent the onset and progression of the nephropathy in the early stage of Diabetes Mellitus (DM) Type 2. [1]

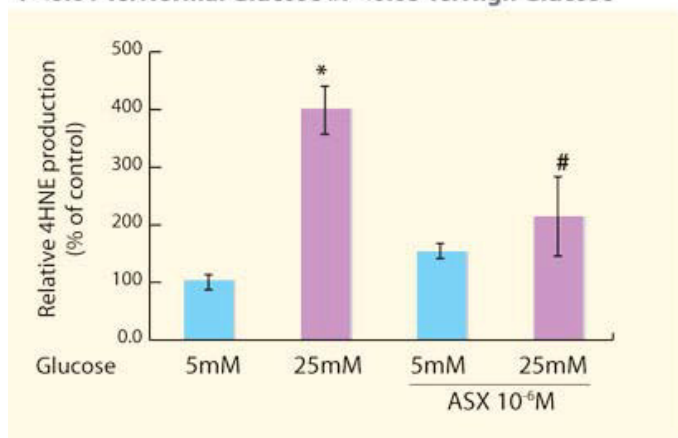
**Figure 1. Astaxanthin ( $10^{-6}$  M) reduced high-glucose-induced mitochondria-dependant ROS production in NHMCs. Detection by fluorescence technique. Astaxanthin reduced ROS production (indicated by no red fluorescence and no yellow fluorescence).**



The scientists from Kyoto Prefectural University of Medicine, Japan suggested using astaxanthin, a powerful antioxidant, to scavenge ROS in the prevention of diabetic nephropathy. Furthermore, an oxidative lipid peroxidation

marker, 4-hydroxy-2,3-nonenal (4HNE), was significantly reduced ( $P < 0.05$ ) by 50% with astaxanthin (Figure 2). Astaxanthin was also confirmed to localize in the cell mitochondrial membrane of NHMC by quantitative analysis.[2].

**Figure 2. Astaxanthin inhibited high-glucose induced production of 4-HNE oxidative stress-modified proteins in the mitochondria of NHMCs.**  
\*P<0.01 vs. Normal Glucose #P<0.05 vs. High Glucose

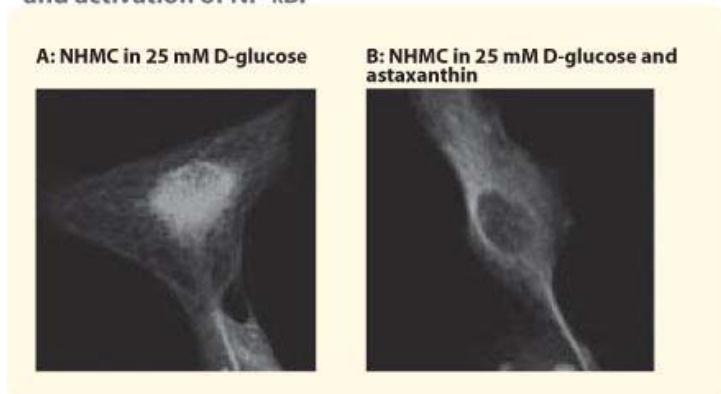


NHMCs pre-incubated with astaxanthin reduced the inflammatory response. For example, NF-κB activation and subsequent movement to the cell nucleus for Inflammatory gene activation was inhibited (Figure 3). Astaxanthin also reduced AP-1 activation and expression/production of COX-2, MCP-1, and TGFB1. If not suppressed, these factors will promote the pathogenesis and mesangial cell injury. Although the mechanism by which astaxanthin suppresses ROS is that astaxanthin may affect part of the electron transport chain and protect mitochondria from the detrimental effects of glucose toxicity. In summary, astaxanthin may scavenge excess ROS, reduce

ROS-protein damage, and inhibit inflammatory process. Therefore, the onset of nephropathy may expect to be prevented or delayed.[3]

In a separate study, randomized glycemic control reduced or normalized mitochondrial ROS production and delayed the onset and progression of early stage diabetic complications. Further, studies showed that astaxanthin reduced kidney damage in diabetic mouse models and many other biomarkers (reduced DNA damage, improved glucose-tolerance test, lowered NFκB). Studies demonstrated that astaxanthin could suppress ROS and reduce nephropathy.[4]

**Figure 3. Astaxanthin suppressed high-glucose induced nuclear translocation and activation of NF-κB.**



### Mechanism of Action of Astashine capsules in Type 2 Diabetes

In most cases, diabetes is treated with medication, although about 20% of diabetes may be managed by lifestyle changes. This means that even if we cannot change the genetic influences, fortunately, for most of us diabetes is preventable; for example, making dietary changes, taking

nutritional supplements and exercising. To highlight this, people in high risk groups who achieve a 5-7% cut in body weight will reduce risk of developing diabetes approximately 58% across all age and ethnic groups. research reveals a strong link between foods with high glycemic index and prevalence of type 2 diabetes. Excess blood glucose needs to be converted by insulin (produced by the

pancreas  $\beta$ -cells) into glycogen stores, however, when glycogen stores are full, glucose is converted into fat. Over time, the body's cells may eventually become desensitized to insulin. Astaxanthin displayed positive effects in a type 2 diabetes by reducing the disease progression by retarding glucose toxicity and kidney damage. This has profound implications for people who belong to high risk groups, display pre-diabetic conditions (impaired fasting glucose or impaired glucose tolerance) or want to manage advanced diabetic kidney problems (nephropathy).

Studies suggested that reactive oxygen species (ROS) induced by hyperglycemia contributes to the onset of Diabetes mellitus and its complications. Non-enzymatic glycosylation of proteins and mitochondria, prevalent in diabetic conditions, is a major source of ROS. For example, pancreatic  $\beta$ -cells kept in high glucose concentrations show presence of advanced glycosylation products, a source of ROS, which cause the following: i) reduction of insulin expression and ii) induction of cell death (apoptosis).  $\beta$ -cells are especially vulnerable to ROS because these cells are inherently low in antioxidant status and therefore, requires long term protection. A recent study demonstrated that antioxidant Astaxanthin exerted beneficial effects in diabetic conditions such as preservation of  $\beta$ -cell function.

Uchiyama *et al.*, 2002 demonstrated in obese diabetes type 2 mouse model that astaxanthin preserved pancreatic  $\beta$ -cell dysfunction against oxidative damage. Treated mice received 1 mg astaxanthin/day at 6 weeks of age and then tests performed at 6, 12 and 18 weeks. Observations of astaxanthin treated mice (N=8) included: i) significantly reduced fasting glucose sugar levels at 12 ( $P<0.01$ ) and 18 weeks ( $P<0.01$ ); and ii) decreased glucose ( $P<0.001$ ) and insulin ( $P<0.001$ ) levels in the blood serum. In additional, treated rats displayed better response profiles to the

intraperitoneal glucose tolerance test (IPGTT at 1g glucose/kg bodyweight). This showed that astaxanthin preserved pancreas function and insulin sensitivity.

Furthermore, preliminary renal damage assessment measuring urinary albumin levels revealed significantly lower glomerular (kidney) damage. This was confirmed in another study by Naito *et al.*, 2004, who looked at diabetic nephropathy in the type 2 diabetic mouse model. astaxanthin can also circumvent high glucose toxicity which normally leads to increased oxidative stress and pathogenesis of kidney damage. Naito demonstrated that astaxanthin treated type 2 diabetic mice which normally shows renal insufficiency at 16 weeks of age in fact exhibited 67% less urinary albumin loss (N=5,  $P<0.05$ ) and figure 4 shows 50% less DNA damage (8-OHdG,  $P<0.05$ ). Furthermore, the increased protein loss was due to the vascular size ratio increase of 250% in the diabetic model. In astaxanthin treated mice, this area was significantly ( $P<0.05$ ) reduced by almost 54%.

Naito *et al.*, (2006) examined changes in the gene expression profile of glomerular cells in diabetic mouse model during the early phase of diabetic nephropathy. The mitochondrial oxidative phosphorylation pathway was most significantly affected by high-glucose concentration (mediated via reactive oxygen species). Long term treatment with astaxanthin significantly modulated genes associated with oxidative phosphorylation, oxidative stress and the TGF- $\alpha$ -collagen synthesis system.

### Astaxanthin and Type 2 Diabetes

Figure 4. Astaxanthin improved the glucose levels in the Intraperitoneally Glucose Tolerance Test (IPGT) in diabetic mouse model (Uchiyama *et al.*, 2002).

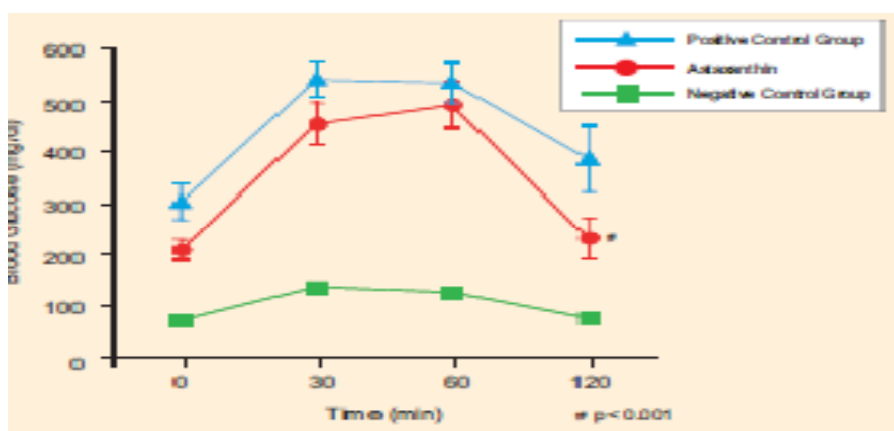


Figure 5. Astaxanthin preserved insulin sensitivity in the diabetic mouse model (Uchiyama *et al.*, 2002)

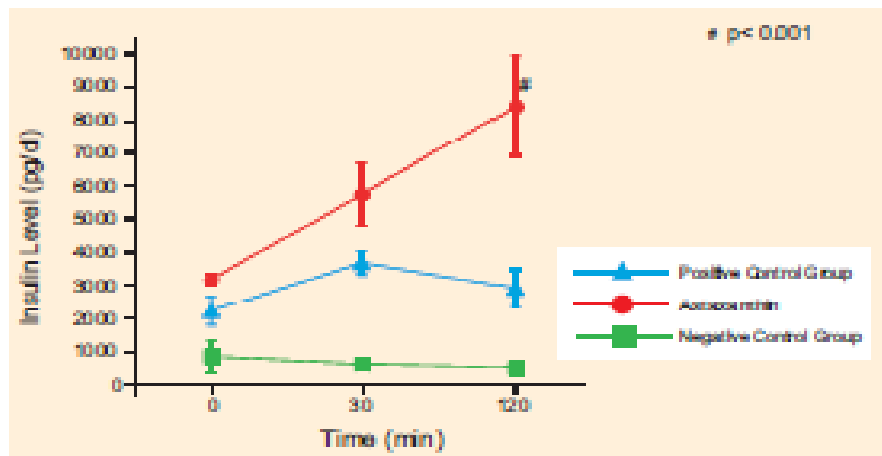


Figure 6. Astaxanthin protected kidney function measured by urinary albumin protein loss (Naito *et al.*, 2004)

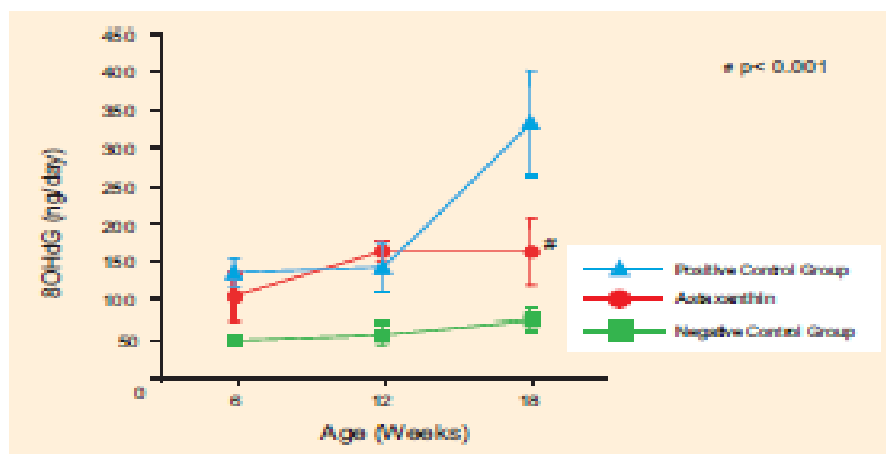
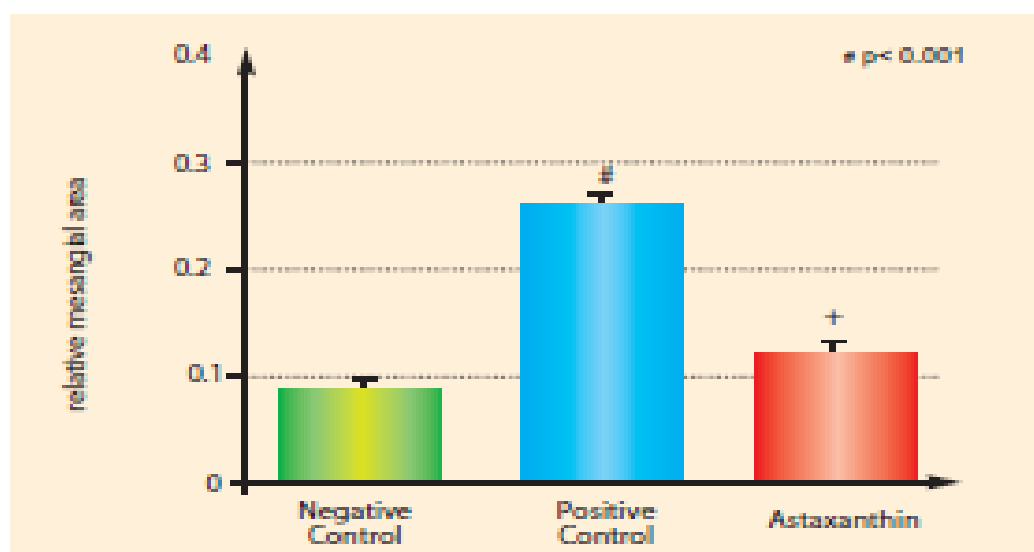


Figure 7. Astaxanthin preserved the relative mesangial area.  $+p < 0.05$  vs positive control (Naito *et al.*, 2004)



## Clinical study reports on l-carnitine in astashine silver capsules

### Diabetes/Insulin Resistance

A study that was published in the November 2010 issue of "Fundamental and Clinical Pharmacology" evaluated the benefits of using L-carnitine in combination with the conventional drug Orlistat to improve sugar and fat levels as well as for weight management. The researchers found that the subjects who took both Orlistat and L-carnitine had better improvement in body weight, inflammatory markers, glucose and lipid profiles compared to the subjects who took the conventional drug alone.

Another study published in the April 2010 issue of "Nutrition and Metabolism" assessed the benefits of L-carnitine for various health conditions. In relation to diabetes, researchers concluded that there is increased evidence that supplementing with L-carnitine helps improve cardiovascular conditions, may help reduce obesity and improves glucose intolerance.

In a clinical study Healthy volunteers and type 2 diabetics received an infusion of L-carnitine or saline, after which plasma glucose and insulin levels were analyzed. Insulin-mediated glucose uptake was significantly higher in both groups receiving L-carnitine compared to the saline groups, indicating improved insulin sensitivity from carnitine.[5] A Clinical study found 500-mg intramuscular injections of L-carnitine twice daily for 15 days resulted in improvement in painful diabetic neuropathy.[6]

### Safety of astashine silver capsules

Astaxanthin has demonstrated safety in numerous human clinical trials. In one open-label clinical study on subjects with metabolic syndrome (n=17). Astaxanthin (16 mg/day, for three months) significantly raised blood bilirubin ( $p \leq 0.05$ ), potassium ( $p \leq 0.05$ ), and creatine kinase ( $p \leq 0.01$ ), although all three values remained within normal range. Also, astaxanthin significantly lowered the liver enzyme gamma-glutamyl transpeptidase (GGTP;  $p \leq 0.05$ ). Since the researchers noted this enzyme was abnormally elevated in 11 of the 17 subjects at baseline, this astaxanthin effect may have been beneficial. Animal experiments have investigated astaxanthin at levels well over 120 mg/day in human equivalents, without causing

apparent harm. Hoffman-La Roche confirmed its safety with extensive tests, including acute toxicity, mutagenicity, teratogenicity, embryotoxicity, and reproductive toxicity. L-carnitine is listed as pregnancy category B, indicating animal studies have revealed no harm to the fetus but that no adequate studies in pregnant women have been conducted. L-carnitine has been given to pregnant women late in pregnancy with resulting positive outcomes. The racemic mixture (D,L-carnitine) should be avoided. D-carnitine is not biologically active and might interfere with the proper utilization of the L isomer. In uremic patients, use of the racemic mixture has been correlated with myasthenia-like symptoms in some individuals.

### Supplement Facts

- **Presentation:** 60 capsules
- **Usage:** As a food supplement combination of antioxidants to improve health and vitality.
- **Contra-indications:** Product is contra-indicated in persons with Known hypersensitivity to any component of the product hypersensitivity to any component of the product.
- **Recommended usage :Adults:** two capsules per day along with food.
- "Do not exceed the recommended daily dose"
- **Administration:** Taken by oral route at anytime with food.
- **Precautions:** Food Supplements must not be used as a substitute for a varied and balanced diet and a healthy lifestyle. This Product is not intended to diagnose, treat, cure or prevent any diseases. Do not exceed the recommended daily dose.
- **Warnings:** If you are taking any prescribed medication or has any medical conditions or have any medical conditions (seizures) under age group 17 year always consults doctor or healthcare practitioner before taking supplements.
- **Side Effects:** Mild side effects like nausea, headache and vomiting in some individuals have been reported.
- **Storage:** Store in a cool, dry and dark place.
- Keep out of reach of children.

## SUMMARY & CONCLUSION

Clinical studies shows that the antioxidant power of astaxanthin, which reportedly is 500 times stronger than that of vitamin E, can protect cells

against the oxidative damage caused by high glucose (sugar) levels. High blood sugar levels and oxidative stress are associated with complications



common among diabetics, including kidney disease, neuropathy (nerve damage), and diabetic retinopathy (vision problems).

Astaxanthin suppresses activities that damage cells and lead to complications associated with diabetes. Astaxanthin was able to hinder lipid peroxidation (damage to fats in cell membranes by free radicals) and levels of total reactive species, superoxide, and nitric oxide (molecules that cause extensive cell damage).

The strong antioxidant properties of astaxanthin that allow it to reduce oxidative stress, inflammation, and cell death are the reasons why it could be an effective supplement to help prevent complications associated with elevated glucose

levels in diabetics and to further benefit people at risk of diabetic complications such as diabetic kidney disease. L-carnitine has a useful effect on several diabetic risk parameters, including plasma lipids and lipoprotein. L-Carnitine decreases triglycerides synthesis, and increases mitochondrial beta oxidation of fatty acids. Studies indicated that L-carnitine decreases serum cholesterol, triglycerides, and free fatty acids. L-carnitine supplementation causes a significant decrease in LDL-C, cholesterol and triglycerides in patients who received L-carnitine supplementation. Thus ASTASHINE SILVER CAPSULES offers an Excellent Choice as Antidiabetic in Diabetes & as Kidney protector.

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