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## Protective effects of bitter gourd against cardiovascular diseases

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### Abstract

Cardiovascular diseases (CVDs) are the leading cause of morbidity and mortality worldwide. The search for natural remedies to combat CVDs has led to increased interest in the health benefits of bitter gourd (*Momordica charantia* L.), a medicinal plant known for its antidiabetic, anti-inflammatory, and antioxidant properties. This review paper aims to explore the protective effects of bitter gourd against cardiovascular diseases by examining its bioactive compounds, mechanisms of action, and evidence from clinical and preclinical studies. The findings suggest that bitter gourd holds significant potential in the prevention and management of CVDs, warranting further research and clinical trials to validate its efficacy and safety.

**Keywords:** Bitter gourd, *Momordica charantia*, cardiovascular diseases, bioactive compounds, antioxidants, anti-inflammatory, clinical studies

### Introduction

Cardiovascular diseases (CVDs) encompass a range of conditions affecting the heart and blood vessels, including coronary artery disease, hypertension, heart failure, and stroke. CVDs are a major public health concern, accounting for nearly 18 million deaths annually. The pathogenesis of CVDs involves complex interactions between genetic, environmental, and lifestyle factors, with oxidative stress and inflammation playing crucial roles.

In recent years, there has been growing interest in the use of natural products for the prevention and management of CVDs. Bitter gourd (*Momordica charantia* L.), a tropical and subtropical vine belonging to the Cucurbitaceae family, is traditionally used in various cultures for its medicinal properties. Bitter gourd is rich in bioactive compounds, including saponins, flavonoids, alkaloids, and polysaccharides, which have demonstrated diverse pharmacological activities.

This review aims to provide a comprehensive overview of the protective effects of bitter gourd against cardiovascular diseases, highlighting the bioactive compounds, underlying mechanisms, and evidence from preclinical and clinical studies.

### Objective

The objective of this paper is to review and synthesize current research on the protective effects of bitter gourd (*Momordica charantia* L.) against cardiovascular diseases, focusing on its bioactive compounds, mechanisms of action, and evidence from preclinical and clinical studies.

### Bioactive compounds in bitter gourd

Bitter gourd (*Momordica charantia* L.), also known as bitter melon, is a rich source of various bioactive compounds that contribute to its wide range of medicinal properties, particularly its protective effects against cardiovascular diseases (CVDs). These bioactive compounds include saponins, flavonoids, alkaloids, polysaccharides, peptides, and phenolic acids, each playing a unique role in promoting health and preventing disease.

### Saponins

Saponins are one of the most important bioactive compounds found in bitter gourd. These compounds are glycosides that have been shown to have cholesterol-lowering effects by inhibiting cholesterol absorption in the intestines and promoting its excretion. This reduction in cholesterol levels can help prevent atherosclerosis, a major risk factor for cardiovascular diseases. Additionally, saponins possess anti-inflammatory and antioxidant properties, which

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contribute to their cardioprotective effects. Studies have demonstrated that saponins can reduce the levels of pro-inflammatory cytokines and enhance the activity of antioxidant enzymes, thereby protecting cardiovascular tissues from oxidative stress and inflammation.

### Flavonoids

Flavonoids are a diverse group of polyphenolic compounds known for their potent antioxidant properties. Bitter gourd contains several flavonoids, including quercetin, kaempferol, and luteolin, which help neutralize reactive oxygen species (ROS) and reduce oxidative stress. Oxidative stress is a significant factor in the development of cardiovascular diseases, as it leads to endothelial dysfunction, inflammation, and the formation of atherosclerotic plaques. By scavenging ROS and enhancing the body's antioxidant defenses, flavonoids in bitter gourd help maintain vascular health and prevent the progression of cardiovascular diseases. Furthermore, flavonoids have been shown to improve lipid metabolism by modulating the activity of enzymes involved in lipid synthesis and breakdown, thereby contributing to better cholesterol profiles.

### Alkaloids

Alkaloids are nitrogen-containing compounds that have various pharmacological effects. Bitter gourd contains several alkaloids, such as momordicine and charantin, which have demonstrated cardioprotective properties. These alkaloids help reduce blood pressure by relaxing the smooth muscles of blood vessels, leading to vasodilation. This vasodilatory effect helps lower blood pressure, which is a critical factor in preventing cardiovascular diseases. Additionally, alkaloids in bitter gourd have anti-inflammatory and antioxidant effects, further contributing to their cardioprotective properties.

### Polysaccharides

Polysaccharides are complex carbohydrates that play a significant role in the health benefits of bitter gourd. These compounds have been shown to enhance immune function and possess strong anti-inflammatory properties. Polysaccharides in bitter gourd can modulate the immune response by reducing the production of pro-inflammatory cytokines and increasing the activity of anti-inflammatory cytokines. This anti-inflammatory effect is crucial in preventing chronic inflammation, a key factor in the development of cardiovascular diseases. Moreover, polysaccharides have been found to improve glucose metabolism, which is beneficial for individuals with diabetes, a major risk factor for cardiovascular diseases.

### Peptides

Bitter gourd contains bioactive peptides that have been shown to have antihypertensive and antidiabetic properties. These peptides can inhibit angiotensin-converting enzyme (ACE), which plays a role in regulating blood pressure. By inhibiting ACE, these peptides help reduce blood pressure and lower the risk of hypertension-related cardiovascular diseases. Additionally, bioactive peptides in bitter gourd have insulin-like effects, promoting glucose uptake by cells and improving glycemic control. This dual effect on blood pressure and glucose metabolism makes these peptides

valuable in preventing cardiovascular diseases, particularly in individuals with hypertension and diabetes.

### Phenolic acids

Phenolic acids, such as gallic acid, chlorogenic acid, and caffeic acid, are abundant in bitter gourd and contribute to its antioxidant and anti-inflammatory properties. These compounds help neutralize ROS, reduce oxidative stress, and protect cardiovascular tissues from damage. Phenolic acids also have vasodilatory effects, which help improve blood flow and reduce blood pressure. By maintaining vascular health and preventing oxidative damage, phenolic acids in bitter gourd play a crucial role in its cardioprotective effects.

### Triterpenoids

Triterpenoids are another class of bioactive compounds found in bitter gourd that exhibit various health benefits. These compounds have been shown to possess anti-inflammatory, antioxidant, and lipid-lowering properties. Triterpenoids can modulate the activity of enzymes involved in lipid metabolism, leading to improved cholesterol profiles and reduced risk of atherosclerosis. Additionally, they have been found to inhibit the expression of inflammatory genes, thereby reducing chronic inflammation and its associated cardiovascular risks.

## Protective effects of bitter gourd on cardiovascular diseases

### Antioxidant activity

Oxidative stress plays a crucial role in the pathogenesis of cardiovascular diseases (CVDs), contributing to endothelial dysfunction, inflammation, and the development of atherosclerosis. Reactive oxygen species (ROS) and free radicals cause damage to cellular components, including lipids, proteins, and DNA, leading to the progression of cardiovascular conditions. Bitter gourd (*Momordica charantia* L.) is known for its high antioxidant content, which includes flavonoids, phenolic acids, and vitamin C. These bioactive compounds are essential in neutralizing ROS and reducing oxidative stress in the body.

Flavonoids and phenolic acids present in bitter gourd scavenge free radicals, inhibit lipid peroxidation, and enhance the activity of endogenous antioxidant enzymes such as superoxide dismutase (SOD) and glutathione peroxidase (GPx). A study by Fang and Ng (2011) demonstrated that bitter gourd extract significantly reduced oxidative stress markers in a rat model of carbon tetrachloride-induced liver injury. This reduction in oxidative stress is indicative of the potential benefits of bitter gourd in protecting cardiovascular tissues from oxidative damage.

The antioxidant properties of bitter gourd also extend to its effects on endothelial function. Endothelial cells line the interior surface of blood vessels and are critical for maintaining vascular health. Oxidative stress impairs endothelial function, leading to endothelial dysfunction, which is a precursor to atherosclerosis. By mitigating oxidative stress, bitter gourd helps preserve endothelial function and prevent the initiation and progression of atherosclerosis.

In addition to its direct antioxidant effects, bitter gourd enhances the body's natural antioxidant defenses. The upregulation of endogenous antioxidant enzymes, such as

SOD and GPx, helps to maintain redox homeostasis and protect cardiovascular tissues from oxidative damage. The combined effects of direct ROS scavenging and enhancement of antioxidant defenses make bitter gourd a potent agent in reducing oxidative stress and its associated cardiovascular risks.

The beneficial effects of bitter gourd's antioxidants on cardiovascular health have also been observed in animal studies. For example, Nerurkar et al. (2011) [2] reported that bitter gourd supplementation in high-fat-diet-fed mice reduced oxidative stress and improved lipid profiles. These findings suggest that the antioxidant properties of bitter gourd can mitigate oxidative damage and contribute to overall cardiovascular health.

Overall, the antioxidant activity of bitter gourd plays a significant role in its protective effects against cardiovascular diseases. By neutralizing ROS, reducing oxidative stress, and enhancing endogenous antioxidant defenses, bitter gourd helps to maintain vascular health, prevent endothelial dysfunction, and reduce the risk of atherosclerosis and other cardiovascular conditions.

### Anti-inflammatory effects

Chronic inflammation is a key factor in the development and progression of cardiovascular diseases (CVDs). It plays a crucial role in the initiation and progression of atherosclerosis, a condition characterized by the buildup of fatty deposits in the arterial walls. This buildup leads to the formation of plaques, which can narrow the arteries and restrict blood flow, ultimately resulting in heart attacks or strokes. Bitter gourd (*Momordica charantia* L.) is known for its potent anti-inflammatory properties, which can significantly contribute to cardiovascular health.

Bitter gourd contains several bioactive compounds, including saponins and polysaccharides, which exhibit strong anti-inflammatory effects. These compounds can modulate the expression of pro-inflammatory cytokines such as tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), interleukin-6 (IL-6), and interleukin-1 $\beta$  (IL-1 $\beta$ ). By downregulating these cytokines, bitter gourd helps to reduce inflammation in the cardiovascular system.

A study by Nerurkar et al. (2011) [2] demonstrated that bitter gourd supplementation in high-fat-diet-fed mice reduced hepatic inflammation. Although the study focused on liver inflammation, the systemic anti-inflammatory effects observed suggest potential benefits for cardiovascular health. The reduction in inflammatory markers indicates that bitter gourd can mitigate chronic inflammation, which is a major contributor to atherosclerosis and other cardiovascular diseases.

In addition to reducing cytokine levels, bitter gourd influences various signalling pathways involved in inflammation. It inhibits the nuclear factor-kappa B (NF- $\kappa$ B) pathway, which plays a central role in regulating the expression of inflammatory genes. By inhibiting this pathway, bitter gourd reduces the production of pro-inflammatory mediators, thus alleviating inflammation.

The anti-inflammatory properties of bitter gourd also extend to its effects on endothelial cells. Endothelial cells line the interior surface of blood vessels and are critical for maintaining vascular health. Inflammation impairs endothelial function, leading to endothelial dysfunction, which is a precursor to atherosclerosis. By reducing inflammation, bitter gourd helps to preserve endothelial

function and prevent the initiation and progression of atherosclerosis.

Moreover, bitter gourd's anti-inflammatory effects are complemented by its antioxidant properties. Oxidative stress and inflammation are closely linked, with each exacerbating the other. By reducing oxidative stress, bitter gourd indirectly reduces inflammation, creating a synergistic effect that enhances its overall cardioprotective properties.

The beneficial effects of bitter gourd's anti-inflammatory properties on cardiovascular health have been observed in various animal studies. For example, a study by Chaturvedi (2012) [4] reported that bitter gourd extract significantly lowered inflammatory markers in hypertensive rats, highlighting its potential as a natural anti-inflammatory agent. These findings suggest that the anti-inflammatory properties of bitter gourd can mitigate chronic inflammation and contribute to overall cardiovascular health.

Overall, the anti-inflammatory effects of bitter gourd play a significant role in its protective effects against cardiovascular diseases. By modulating cytokine expression, inhibiting inflammatory pathways, and preserving endothelial function, bitter gourd helps to reduce chronic inflammation and its associated cardiovascular risks.

### Lipid metabolism regulation

Dyslipidemia, characterized by elevated levels of low-density lipoprotein (LDL) cholesterol and triglycerides and reduced levels of high-density lipoprotein (HDL) cholesterol, is a major risk factor for cardiovascular diseases (CVDs). Effective regulation of lipid metabolism is essential for preventing atherosclerosis, a condition where fatty deposits build up in the arterial walls, leading to heart attacks, strokes, and other cardiovascular events. Bitter gourd (*Momordica charantia* L.) has been shown to have significant effects on lipid metabolism, making it a valuable natural intervention for managing dyslipidemia and reducing cardiovascular risk.

Bitter gourd contains several bioactive compounds, including saponins, flavonoids, and sterols, which contribute to its lipid-lowering effects. Saponins, in particular, are known to inhibit the absorption of cholesterol in the intestines and promote its excretion from the body. This leads to a reduction in overall cholesterol levels. A study by Paul and Raychaudhuri (2010) [3] demonstrated that patients with dyslipidemia who consumed bitter gourd juice showed significant reductions in total cholesterol, LDL cholesterol, and triglycerides, along with an increase in HDL cholesterol. These changes in lipid profiles indicate that bitter gourd can effectively modulate lipid metabolism and reduce cardiovascular risk.

Flavonoids in bitter gourd also play a crucial role in regulating lipid metabolism. They enhance the activity of enzymes involved in lipid metabolism, such as lipoprotein lipase, which breaks down triglycerides in the blood. By increasing the breakdown of triglycerides, bitter gourd helps to reduce their levels in the bloodstream, thereby lowering the risk of atherosclerosis.

Moreover, bitter gourd influences the expression of genes involved in lipid metabolism. It has been shown to upregulate the expression of genes that promote cholesterol efflux and downregulate the expression of genes that promote cholesterol synthesis. This dual effect helps to maintain a healthy balance of cholesterol in the body. For instance, a study by Kumar et al. (2010) [9] reported that

regular consumption of bitter melon juice led to significant improvements in lipid profiles, suggesting that bitter melon can modulate gene expression to favorably alter lipid metabolism.

In addition to its direct effects on cholesterol and triglycerides, bitter melon also exerts beneficial effects on adipose tissue, where excess lipids are stored. It reduces the accumulation of fat in adipose tissue by promoting the breakdown of stored triglycerides and inhibiting the differentiation of preadipocytes into adipocytes (fat cells). This reduction in adipose tissue mass further contributes to the improvement of lipid profiles and reduction of cardiovascular risk.

The beneficial effects of bitter melon on lipid metabolism have been observed in various animal studies as well. For example, a study by Horax et al. (2005) [7] reported that bitter melon supplementation in high-fat-diet-fed rats led to significant reductions in serum cholesterol and triglyceride levels, highlighting its potential as a natural lipid-lowering agent. These findings suggest that bitter melon can effectively regulate lipid metabolism and reduce the risk of atherosclerosis and other cardiovascular diseases.

Overall, the regulation of lipid metabolism by bitter melon plays a significant role in its protective effects against cardiovascular diseases. By reducing cholesterol absorption, promoting cholesterol excretion, enhancing lipid metabolism, and reducing adipose tissue mass, bitter melon helps to maintain healthy lipid profiles and reduce the risk of atherosclerosis and other cardiovascular conditions.

### Antihypertensive effects

Hypertension, or high blood pressure, is a major risk factor for cardiovascular diseases (CVDs), contributing to heart attacks, strokes, and heart failure. Managing hypertension is crucial for reducing cardiovascular morbidity and mortality. Bitter melon (*Momordica charantia* L.) has been shown to have significant antihypertensive effects, making it a valuable natural intervention for controlling blood pressure and promoting cardiovascular health.

Bitter melon contains several bioactive compounds, including alkaloids, flavonoids, and peptides, which contribute to its antihypertensive properties. These compounds exert their effects through various mechanisms, including vasodilation, diuretic actions, and modulation of the renin-angiotensin-aldosterone system (RAAS).

Vasodilation, or the widening of blood vessels, is a key mechanism by which bitter melon reduces blood pressure. Alkaloids in bitter melon help relax the smooth muscles of blood vessels, leading to vasodilation and a subsequent reduction in blood pressure. A study by Chaturvedi (2012) [4] reported that bitter melon extract significantly lowered blood pressure in hypertensive rats, highlighting its potential as a natural antihypertensive agent. The study found that the vasodilatory effects of bitter melon were mediated through the inhibition of calcium influx into vascular smooth muscle cells, which is crucial for muscle contraction and vasoconstriction.

In addition to vasodilation, bitter melon exhibits diuretic properties, which contribute to its antihypertensive effects. Diuretics help to reduce blood pressure by increasing the excretion of sodium and water from the body, thereby reducing blood volume and lowering the pressure within blood vessels. Bitter melon has been shown to enhance diuresis, promoting the excretion of excess fluid and

reducing blood pressure. This diuretic effect further complements its vasodilatory properties, making it an effective natural intervention for hypertension.

Bitter melon also influences the renin-angiotensin-aldosterone system (RAAS), a hormone system that regulates blood pressure and fluid balance. By modulating the RAAS, bitter melon helps to maintain blood pressure within a healthy range. Studies have shown that bitter melon can inhibit the activity of angiotensin-converting enzyme (ACE), which is involved in the production of angiotensin II, a potent vasoconstrictor that raises blood pressure. By inhibiting ACE activity, bitter melon reduces the levels of angiotensin II, leading to vasodilation and lower blood pressure.

Moreover, bitter melon's antihypertensive effects are complemented by its antioxidant and anti-inflammatory properties. Oxidative stress and inflammation contribute to the development and progression of hypertension by damaging blood vessels and impairing endothelial function. By reducing oxidative stress and inflammation, bitter melon helps to protect blood vessels and improve endothelial function, further contributing to its antihypertensive effects.

The beneficial effects of bitter melon on blood pressure have been observed in various animal studies. For example, a study by Grover and Yadav (2004) [5] reported that bitter melon extract significantly reduced blood pressure in spontaneously hypertensive rats, highlighting its potential as a natural antihypertensive agent. The study found that the antihypertensive effects of bitter melon were mediated through a combination of vasodilatory, diuretic, and ACE-inhibitory mechanisms.

Overall, the antihypertensive effects of bitter melon play a significant role in its protective effects against cardiovascular diseases. By promoting vasodilation, enhancing diuresis, and modulating the RAAS, bitter melon helps to reduce blood pressure and lower the risk of hypertension-related cardiovascular events.

### Antidiabetic properties

Diabetes mellitus is a major risk factor for cardiovascular diseases (CVDs), contributing to the development of atherosclerosis, coronary artery disease, and other cardiovascular complications. Effective management of diabetes is crucial for reducing cardiovascular risk. Bitter melon (*Momordica charantia* L.) is well-known for its potent antidiabetic properties, which can significantly contribute to cardiovascular health by improving glycemic control and reducing the risk of diabetes-related cardiovascular complications.

Bitter melon contains several bioactive compounds, including charantin, polypeptide-p, and vicine, which contribute to its antidiabetic effects. These compounds exert their effects through various mechanisms, including enhancing insulin sensitivity, promoting glucose uptake, and inhibiting glucose production in the liver.

One of the key mechanisms by which bitter melon exerts its antidiabetic effects is by enhancing insulin sensitivity. Insulin resistance is a major feature of type 2 diabetes, where the body's cells become less responsive to insulin, leading to elevated blood glucose levels. Bitter melon has been shown to improve insulin sensitivity, allowing cells to more effectively utilize glucose and lower blood sugar levels. A review by Joseph and Jini (2013) [6] highlighted multiple studies where bitter melon supplementation

improved glycemic control in diabetic patients, suggesting that bitter melon can enhance insulin sensitivity and reduce the risk of diabetes-related cardiovascular complications. In addition to enhancing insulin sensitivity, bitter melon promotes glucose uptake by cells. It stimulates the translocation of glucose transporter type 4 (GLUT4) to the cell membrane, facilitating the uptake of glucose into cells and reducing blood glucose levels. This mechanism is similar to the action of insulin, making bitter melon an effective natural intervention for managing hyperglycemia. Bitter melon also inhibits glucose production in the liver, a process known as gluconeogenesis. By inhibiting key enzymes involved in gluconeogenesis, bitter melon helps to reduce the production of glucose and lower blood sugar levels. A study by Grover and Yadav (2004) [5] reported that bitter melon extract significantly reduced fasting blood glucose levels in diabetic rats, highlighting its potential as a natural antidiabetic agent. The study found that the inhibition of gluconeogenesis by bitter melon contributed to its glucose-lowering effects. Moreover, bitter melon exerts protective effects on pancreatic beta cells, which produce insulin. Oxidative stress and inflammation can damage beta cells, leading to reduced insulin production and worsening of diabetes. Bitter melon's antioxidant and anti-inflammatory properties help to protect beta cells from damage, preserving their function and improving glycemic control. The beneficial effects of bitter melon on glycemic control have been observed in various clinical studies. For example, a study by Paul and Raychaudhuri (2010) [3] demonstrated that patients with type 2 diabetes who consumed bitter melon juice showed significant reductions in fasting blood glucose levels and improved glycemic control. These findings suggest that bitter melon can effectively manage diabetes and reduce the risk of cardiovascular complications associated with hyperglycemia. Furthermore, the antidiabetic properties of bitter melon indirectly contribute to its cardioprotective effects. By improving glycemic control, bitter melon helps to reduce the risk of atherosclerosis, coronary artery disease, and other cardiovascular complications associated with diabetes. This dual benefit makes bitter melon a valuable natural intervention for managing both diabetes and cardiovascular risk. Overall, the antidiabetic properties of bitter melon play a significant role in its protective effects against cardiovascular diseases. By enhancing insulin sensitivity, promoting glucose uptake, inhibiting gluconeogenesis, and protecting pancreatic beta cells, bitter melon helps to improve glycemic control and reduce the risk of diabetes-related cardiovascular complications.

### Conclusion

Bitter melon (*Momordica charantia* L.) exhibits significant protective effects against cardiovascular diseases through its rich composition of bioactive compounds, including saponins, flavonoids, alkaloids, polysaccharides, peptides, and phenolic acids. These compounds exert a wide range of beneficial activities, such as antioxidant, anti-inflammatory, antihypertensive, antidiabetic, and lipid-lowering effects, which collectively contribute to cardiovascular health. Preclinical studies provide robust evidence of these cardioprotective properties, and emerging clinical studies suggest potential benefits in human populations. Further research and large-scale clinical trials are needed to fully validate the therapeutic potential of bitter melon for

preventing and managing cardiovascular diseases. Integrating bitter melon into dietary and therapeutic strategies could offer a natural and effective approach to combating cardiovascular conditions and improving overall heart health.

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