Amino Acids (2014) 46:73–80
DOI 10.1007/s00726-012-1432-6

REVIEW ARTICLE

# Taurine and atherosclerosis

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Received: 6 July 2012 / Accepted: 16 November 2012 / Published online: 8 December 2012


**Abstract** Taurine is abundantly present in most mammalian tissues and plays a role in many important physiological functions. Atherosclerosis is the underlying mechanism of cardiovascular disease including myocardial infarctions, strokes and peripheral artery disease and remains a major cause of morbidity and mortality worldwide. Studies conducted in laboratory animal models using both genetic and dietary models of hyperlipidemia have demonstrated that taurine supplementation retards the initiation and progression of atherosclerosis. Epidemiological studies have also suggested that taurine exerts preventive effects on cardiovascular diseases. The present review focuses on the effects of taurine on the pathogenesis of atherosclerosis. In addition, the potential mechanisms by which taurine suppress the development of atherosclerosis will be discussed.

**Keywords** Taurine · Atherosclerosis · Cardiovascular disease · Artery

**Abbreviations**

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| CYP | Cytochrome P450 |
| HDL | High density lipoprotein |
| HepG2 | Human hepatocellular liver carcinoma cell line |
| HMG-CoA | 3-Hydroxy-3-methylglutaryl coenzyme A |
| HUVEC | Human umbilical vein endothelial cells |
| ICAM-1 | Intercellular adhesion molecule-1 |
| I-kB | Inhibitor of nuclear factorκ-B |
| LDL | Low density lipoprotein |
| LOX-1 | Lectin-like oxidized low density lipoprotein receptor-1 |
| NF-κB | Nuclear factor-κB |
| NO | Nitric oxide |
| PDGF | Platelet-derived growth factor |
| ROS | Reactive oxygen species |
| SMC | Smooth muscle cell |
| Tau-Cl | Taurine chloramine |
| TNF-α | Tumor necrosis factor-α |
| VLDL | Very low density lipoprotein |

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## Introduction

Taurine is one of the most abundant amino acids in mammals. In humans the endogenous synthesis of taurine from methionine and cysteine is low and the main source is therefore through the diet. Fish and seafood are rich in taurine (Kibayashi et al. 2000; Wójcik et al. 2010), and urinary taurine excretion is used as a marker of dietary intake of fish (Yamori et al. 2001). Taurine is involved in several biological and physiological actions, including bile acid conjugation, osmoregulation, anti-oxidation, intracellular ion regulation and immunomodulation (Huxtable 1992). Epidemiological studies have suggested that a high regular intake of taurine is associated with a reduced risk of developing cardiovascular disease (Yamori et al. 2001, 2009). It has also been reported that taurine is the second most abundant amino acid in the aorta (Kempf et al. 1970). A comparison of the arterial content of each amino acid in young and old cattle revealed that in contrast to that of other amino acids, the level of taurine is markedly reduced with age, suggesting that taurine exhibits different behaviors and

roles in arterial walls, than other amino acids (Kempf et al. 1970). An immunohistochemical study showed that taurine is present in vascular endothelial and smooth muscle cells (Terauchi et al. 1998). In addition, inflammatory cells, including leukocytes, monocytes, and platelets, which interact with endothelial cells, contain millimolar concentrations of taurine (Learn et al. 1990). These facts suggest that taurine may play important roles in the regulation of vascular functions (Abebe and Mozaffari 2011; Zulli 2011; Ito et al. 2012).

Atherosclerosis is one of the leading causes of morbidity and mortality worldwide. Accumulating results suggest that endothelial dysfunction induced by oxidative stress, hypercholesterolemia, hyperglycemia or inflammatory cytokines, is a key early event in the initiation of atherosclerosis. Endothelial dysfunction is followed by other key events of atherosclerotic plaque formation, such as inflammatory responses, cell proliferation and vasculature remodeling, which ultimately lead to vascular lesion formation, plaque rupture, thrombosis and tissue infarction (Libby 2002). Hypercholesterolemia constitutes an important risk factor for the onset of atherosclerosis. A growing body of evidence implicates inflammatory reactions in the development of atherosclerosis (Hansson and Hermansson 2011).

Taurine has been demonstrated to prevent the development of atherosclerosis in both diet-induced hyperlipidemic animals (Murakami et al. 2010a) and genetic atherosclerosis-susceptible animals (Murakami et al. 2002a). The initiation and progression of atherosclerosis result from complex interactions in vessel walls between circulating factors and various cell types, including endothelial cells, smooth muscle cells, neutrophils, lymphocytes, monocytes and platelets (Ross 1999). Taurine has been shown to affect these cells and to prevent the development of atherosclerosis (Wójcik et al. 2010). Basic physiological actions, including osmoregulation, anti-oxidation and anti-inflammation, may be closely associated with the mechanisms responsible for the anti-atherosclerotic effects of taurine. The cholesterol-lowering effects achieved by taurine through the improvement of hepatic cholesterol metabolism are also related to the prevention of atherosclerosis. Therefore, both lipid and nonlipid mechanisms may contribute to the preventive effects that taurine exerts on the initiation and development of atherosclerosis.

## Anti-atherosclerotic effect of taurine

Taurine has been shown to prevent the development of atherosclerosis in various kinds of animal models, including mice (Murakami et al. 1999; Kondo et al. 2001; Matsushima et al. 2003), rabbits (Petty et al. 1990; Murakami et al. 2002a; Zulli et al. 2009) and quails (Murakami et al. 2010a). In one study, taurine supplementation prevented arterial lipid accumulation and decreased plasma levels of low density lipoprotein (LDL) and very low density lipoprotein (VLDL) cholesterol in mice fed with a high-fat/high-cholesterol diet (Murakami et al. 1999). In hyperlipidemia- and atherosclerosis-prone Japanese (LAP) quails, which develop severe atherosclerotic lesions in response to high-cholesterol diet, taurine supplementation markedly prevented the elevation of serum LDL and VLDL cholesterol levels and suppressed lesion formation (Murakami et al. 2010a). The data obtained from these diet-induced models of hyperlipidemia suggest that taurine prevents the elevation of non-high density lipoprotein (HDL) cholesterol and thereby retards the development of atherosclerosis.

It should be noted that anti-atherosclerotic effects exerted by taurine have also been observed in genetically hyperlipidemic animals, although taurine does not lower serum cholesterol levels. Taurine supplementation has been shown to reduce aortic lipid accumulation in apolipoprotein E (apoE)-deficient mice, a well-established animal model used for studying atherosclerosis (Kondo et al. 2001). Anti-atherosclerotic effects of taurine have also been demonstrated in Watanabe heritable hyperlipidemic (WHHL) rabbits, an animal model used for studying familial hypercholesterolemia (Murakami et al. 2002a). This rabbit is characterized by a deficiency of LDL receptors, increased plasma level of LDL cholesterol and early development of atherosclerosis. In addition, taurine has been shown to suppress the progression of atherosclerosis in spontaneously hyperlipidemic (SHL) mice, Japanese wild mice with apoE gene disruption (Matsushima et al. 2003). Therefore, in these genetically hyperlipidemic animals, taurine suppresses the development of atherosclerotic lesion formation without reducing serum cholesterol levels, suggesting the involvement of mechanisms other than cholesterol-lowering actions. Taurine supplementation has been shown to decrease serum and aorta levels of lipid peroxide in these animals (Kondo et al. 2001; Murakami et al. 2002a; Matsushima et al. 2003). Similar anti-oxidative effects of taurine have also been observed in rabbits fed with a high-cholesterol diet (Balkan et al. 2002). In addition, LDL from taurine-treated WHHL rabbits has been shown to be resistant to copper-induced oxidative modification (Murakami et al. 2002a). Therefore, anti-oxidative effect exerted by taurine, in addition to cholesterol-lowering effects, may be associated with the prevention of atherosclerosis.

## Epidemiological study

Although there is no direct evidence for anti-atherosclerotic effects of taurine in humans, worldwide

epidemiological studies have indicated the beneficial effects of taurine intake on cardiovascular disease prevention. Yamori et al. (2001, 2009) reported in a multicenter cross-sectional study that the mortality rates of stroke and coronary heart disease are inversely related to urinary taurine levels, a marker of dietary taurine intake. Moreover, subjects with higher levels of urinary taurine excretion have lower body mass indices, systolic and diastolic blood pressures, plasma total cholesterol levels and atherogenic indices (total cholesterol/HDL cholesterol) than those with lower levels of urinary taurine excretion (Yamori et al. 2010). These observations support the notion that dietary taurine intake is beneficial to prevent hypertension, hypercholesterolemia and obesity and reducing the risk of cardiovascular disease.

## Mechanisms responsible for the anti-atherosclerotic effects of taurine

Atherosclerosis is a complex multifactorial disease that develops in arterial walls (Libby 2002). Hypercholesterolemia is one of the most well-established risk factors for developing atherosclerosis. In addition, inflammation and oxidative stress are closely associated with the initiation and progression of atherosclerosis. Endothelial dysfunction is a common feature of all phases of atherosclerosis, and supports lesion formation by promoting both early and late mechanisms of atherosclerosis, including up-regulation of adhesion molecules, chemokine secretion, leukocyte adherence, cell permeability, LDL oxidation, platelet activation, cytokine elaboration and vascular smooth muscle cell (SMC) proliferation and migration. Many studies show that the cholesterol-lowering, anti-inflammatory and antioxidative actions of taurine are closely associated with the suppression of atherosclerosis.

### Effects of taurine on serum cholesterol levels

Hypercholesterolemia and elevated levels of LDL cholesterol in particular, have been shown to be strongly related to the initiation and development of atherosclerosis. Intervention trials have demonstrated that lowering LDL cholesterol levels reduces the clinical manifestations of atherosclerosis (Vaughan et al. 2000). Hypercholesterolemia decreases the bioavailability of nitric oxide (NO) and causes endothelial dysfunction.

The cholesterol-lowering effects of taurine has been studied extensively in rats (Murakami et al. 1996; Yokogoshi et al. 1999), mice (Murakami et al. 1999), hamsters (Murakami et al. 2002b) and quails (Murakami et al. 2010a). Taurine prevents the elevation of LDL and VLDL cholesterol levels induced by a high-fat/high-cholesterol diet. In contrast, the effects of taurine on HDL cholesterol levels seem to vary according to experimental conditions.

Several studies have shown that taurine supplementation stimulates bile acid production by increasing the expression of cholesterol 7α-hydroxylase (CYP7A1), a rate-limiting enzyme of bile acid synthesis (Murakami et al. 1996; Yokogoshi et al. 1999). Since taurine is involved in the conjugation of bile acids, enhancement of bile acid production is thought to be a major mechanism responsible for the cholesterol-lowering actions of taurine (Chen et al. 2012). Taurine supplementation up-regulates the mRNA expression and enzymatic activity of CYP7A1, leading to increase in bile acid production and its fecal excretion. A reduction of bile acids in the enterohepatic circulation results in derepression of CYP7A1 activity and a further increase in bile acid synthesis. The liver compensates for a loss of cholesterol by increasing cholesterol synthesis and up-regulating hepatic LDL receptor activity. In hamsters, the cholesterol-lowering effects of taurine have been shown to be associated with the up-regulation of hepatic CYP7A1 activity and 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase activity and the stimulation of hepatic LDL clearance (Murakami et al. 2002b). A liver perfusion study conducted in rats indicates that taurine reduces the hepatic accumulation and secretion of cholesterol ester (Yamamoto et al. 2000). In addition, taurine enhances ketone body production and fatty acid oxidation (Fukuda et al. 2011). Taurine inhibits the secretion of apolipoprotein B and cholesterol ester in human hepatoblastoma HepG2 cells (Yanagita et al. 2008). These events may be related to stimulation of bile acid production from cholesterol and reduced hepatic cholesterol pool by taurine.

### Effects of taurine on endothelial cells

Endothelial cells play a pivotal role in the maintenance of normal vascular functions, and disturbance of this balance is a key early event in the initiation and development of atherosclerotic vascular disease. Vascular endothelium actively regulates vascular tone, lipid breakdown, thrombogenesis, inflammation and vessel growth, all of which are important factors in the development of atherosclerosis.

Taurine has been shown to be present abundantly in endothelial cells and to contribute to the protection of these cells (Abebe and Mozaffari 2011). An immunohistochemical analysis revealed that vascular endothelial cells are stained intensely with taurine antibodies (Terauchi et al. 1998). The existence and regulation of taurine transporter have been demonstrated in endothelial cells (Qian et al. 2000). Taurine has an important role in the regulation of osmolarity in endothelial and other cells. Hypo-osmotic swelling activates the efflux of taurine from endothelial cells (Manolopoulos et al. 1997). Alfieri et al. (2002)

showed that taurine enables endothelial cells to adapt to hypertonic stress, protecting them from apoptosis.

It has been reported that taurine protects endothelial cells from LDL, oxidized LDL, or high glucose. Tan et al. (2007) showed that taurine protects against oxidized LDL-induced endothelial dysfunction related to nitric oxide production. Ulrich-Merzenich et al. (2007) showed that taurine protects human umbilical vein endothelial cells (HUVEC) from endothelial dysfunction induced by hyperglycemia and/or oxidized LDL through the down-regulation of apoptosis and adhesion molecules. Wu et al. (1999) demonstrated that taurine attenuates hyperglycemia-induced HUVEC apoptosis through the inhibition of reactive oxygen species (ROS) production and intracellular $Ca^{2+}$ modulation. Wang et al. (1996) noted that taurine reduced the necrosis and apoptosis of HUVECs induced by activated neutrophil or calcium ionophore A23187 and suggested that these effects are attributed to the anti-oxidant activity and modulation of intracellular $Ca^{2+}$ exerted by taurine. In streptozotocin-induced diabetic rats, blunted response of endothelium-dependent vasodilator to acetylcholine, increase in serum oxidized LDL and soluble intercellular adhesion molecule-1 (ICAM-1) levels as well as overexpression of lectin-like oxidized low density lipoprotein receptor-1 (LOX-1) and ICAM-1 were all significantly attenuated by taurine supplementation (Wang et al. 2008). Casey et al. (2007) also reported that taurine reduced diabetic microvascular inflammatory injury by preventing leukocyte adhesion and migration, endothelial cell apoptosis and ICAM-1 expression in diabetic rats. Taurine has also been shown to ameliorate rolling velocity and to reduce the number of adherent leukocytes, thereby inhibiting the transendothelial migration of leukocytes, in rats infused with lipopolysaccharide (Egan et al. 2001).

In a human trial of young smokers, treatment with taurine attenuated impaired endothelial-dependent vasodilatation (Fennessy et al. 2003). In addition, when HUVECs were cultured with monocyte-conditioned medium from smokers who had been treated with taurine, the levels of NO and endothelin-1 returned to control levels.

LOX-1, a lectin-like receptor for oxidized LDL, is present primarily on endothelial cells and is involved in endothelial dysfunction and the subsequent pathogenesis of atherosclerosis (Ogura et al. 2009). Up-regulation of LOX-1 has been identified in the atherosclerotic arteries of several animals and humans. Some experiments have revealed that taurine treatment reduces the expression of LOX-1. Taurine supplementation has been shown to inhibit the expression of endothelial LOX-1 in animal models of vascular disease (Gokce et al. 2011) and diabetes (Wang et al. 2008). The effects of taurine on LOX-1 expression in hypertensive salt-loaded Dahl salt-sensitive rats have also been reported (Chiba et al. 2002). In that study, taurine supplementation prevented renal damage and reduced the expression of LOX-1.

Therefore, both in vitro and in vivo studies show preventive effects of taurine on endothelial dysfunction. Several molecules and mechanisms, including osmoregulation, anti-oxidation, anti-inflammation and suppression of LOX-1, may be associated with the beneficial effects of taurine in endothelial cells.

## Effects of taurine on vascular tone

Endothelial dysfunction is defined as the impairment of physiologic endothelium-dependent relaxation, which is associated with the decreased bioavailability of NO, an endothelial-derived relaxant factor. This is an early event in the pathophysiology of atherosclerosis. Taurine supplementation has been shown to attenuate the inhibition of endothelium-dependent vasorelaxation and the reduction of plasma level of NO (Tan et al. 2007). Taurine has been shown to affect vascular tone in both endothelium-dependent and independent manner. Abebe and Mozaffari (2000) reported that taurine treatment attenuates vascular contractility nonspecifically in rats, and this effect is partly mediated via the endothelium. Conversely, both norepinephrine- and potassium-chloride-induced maximum contractile responses of endothelium-denuded aortae are enhanced in taurine-depleted rats (Abebe and Mozaffari 2003). Taurine exerts either a vasodilation or vasoconstriction depending on cellular $Ca^{2+}$ concentrations (Nishida and Satoh 2009). A study using porcine coronary arteries showed that taurine antagonizes and relaxes the contractions of arteries, associated with the activation of potassium channel including $K_{IR}$, $K_{ATP}$ and $K_{Ca}$ (Liu et al. 2009). Taurine supplementation has been shown to normalize impaired endothelium-dependent vasodilation in mice fed with a high-cholesterol diet and in streptozotocin-induced diabetic mice (Kamata et al. 1996). These observations suggest that taurine may have a physiological role in the maintenance of vascular tone under both normal and pathological conditions.

## Effects of taurine on vascular smooth muscle cells (SMCs)

The presence of taurine has been immunocytochemically detected in rat aortic SMCs (Lobo et al. 2000). Cultured SMCs prepared from rat aortae express taurine transporter, which takes up [$^3$H]taurine (Liao et al. 2007). An immunohistochemical study revealed that taurine transporter is located in rat thoracic aortae (Liao et al. 2007). These data indicate the existence of functional taurine transporter in vascular SMCs. Kempf et al. (1970) reported that taurine levels in the arterial intima and media are 40–50 times

higher than those in plasma, which is characteristic of taurine. Abnormal vascular SMC proliferation is thought to play an important role in the pathogenesis of both atherosclerosis and restenosis. Taurine has been shown to attenuate the proliferation of vascular SMCs and to reduce subsequent neointimal hyperplasia in the balloon-injured carotid arteries of rats (Murakami et al. 2010b). The inhibition of vascular SMC proliferation by taurine is associated with a reduced production of ROS.

The direct effects of taurine on the proliferation of rat aortic SMCs has been studied by measuring cell numbers and [$^3$H]thymidine incorporation into cellular DNA (Zhang et al. 1999). Taurine at 0.3 mM was found to inhibit SMC proliferation without affecting protein synthesis. Yoshimura et al. (2005) showed that the suppression of platelet-derived growth factor (PDGF)-BB-induced phosphorylation of PDGF-β receptor may be a mechanism responsible for the anti-proliferative effects of taurine. They suggested that taurine promotes PDGF-β receptor dephosphorylation, thereby restoring PDGF-BB-induced suppression of protein tyrosine phosphatase (PTPase) activity, which leads to the inhibition of downstream signaling molecules such as Ras, MAPK/ERK kinase (MEK) 1/2 and Akt. Thus, taurine may affect vascular SMCs in both direct and indirect manners.

## Effects of taurine on platelets

Platelets are central mediators of hemostasis at sites of vascular injury. Activated platelets stimulate thrombus formation in response to the rupture of an atherosclerotic plaque, and this process promotes atherothrombotic disease. Platelets also interact with endothelial cells and leukocytes to promote inflammation, which contributes to the pathogenesis of atherosclerosis (Libby 2002). Platelets as well as monocytes and leukocytes contain millimolar concentrations of taurine (Learn et al. 1990).

Changes in platelet taurine content have been reported in some diseases such as diabetes. Patients with diabetes have significantly lower taurine concentrations than control subjects (Franconi et al. 1995). The reduced platelet content observed in diabetic patients is associated with reduced taurine uptake and increased taurine release (De Luca et al. 2001). After oral taurine supplementation, increased platelet aggregation is returned to healthy control levels. Hayes et al. (1989) showed that platelets from taurine-depleted cats were twice as sensitive to aggregation as platelets from cats receiving taurine. Welles et al. (1993) also noted that taurine deficiency affects platelet aggregation in cats. The effects of taurine on platelet function may be partly related to intracellular $Ca^{2+}$ concentrations (Atahanov and Elizarova 1992). Taurine seems to modulate platelet function by $Ca^{2+}$ and osmoregulatory mechanisms. However, 8 weeks of supplementation with taurine was found to have no effects on ADP-induced platelet aggregation in overweight prediabetic men (Spohr et al. 2005).

## Effects of taurine chloramines: anti-inflammatory effects of taurine

Myeloperoxidase (MPO) derived from neutrophils, monocytes, and macrophages plays an important role in the defense of organisms by producing highly cytotoxic hypochlorous acid (HOCl). However, excessive or misplaced production of HOCl can cause tissue damage and has been implicated in the pathogenesis of inflammatory vascular diseases (Podrez et al. 2000). MPO- and HOCl-modified LDL have been shown to be present in animal and human atherosclerotic lesions (Malle et al. 2000, 2001). Similar to oxidized LDL, HOCl-modifed LDL is easily taken up by macrophages, a process which results in the stimulation of arterial lipid accumulation (Marsche et al. 2003).

Taurine reacts with the HOCl produced by neutrophils and macrophages to form taurine chloramines, a less toxic substance (Weiss et al. 1982). Under physiological conditions, HOCl is detoxified via this process (Schuller-Levis and Park 2004). Therefore, it is plausible that taurine neutralizes HOCl and thereby reduces the levels of HOCl-modified LDL and other molecules, leading to the suppression of inflammatory response and lipid accumulation in the aorta.

It is of interest that generated taurine chloramines (TauCl) inhibit the production of superoxide and pro-inflammatory mediators, including tumor necrosis factor-α (TNF-α), NO, prostaglandin $E_2$ ($PGE_2$) and monocyte chemotactic protein-1 (MCP-1) in activated macrophages (Park et al. 1995) and neutrophils (Marcinkiewicz et al. 1998a). TauCl also modulates the functions of T cells (Marcinkiewicz et al. 1998b). The inhibition of nuclear factor-κB (NF-κB) activation associated with inhibitor of nuclear factor κB (IkBα) oxidation has been postulated to be a mechanism responsible for the anti-inflammatory effects of TauCl (Kanayama et al. 2002). Thus, it has been suggested that TauCl is produced at sites of inflammation to function as a modulator of inflammatory reaction (Schuller-Levis and Park 2004).

It has been reported that the locally activated renin-angiotensin system contributes to vascular damage by increasing oxidative stress and activating immune response (Schmieder et al. 2007). Blocking the actions of angiotensin II have been shown to suppress the development of atherosclerosis (Rosenson 2003). Taurine has been shown to antagonize the actions of angiotensin II (Takahashi et al. 1997; Schaffer et al. 2000), which may be partly responsible for the anti-inflammatory effects of taurine.

These findings suggest that taurine may reduce the HOCl-mediated modification of LDL and other proteins in

atherosclerotic lesions by neutralizing HOCl produced by neutrophils and macrophages. In addition, TauCl modulates inflammation and affects the development of atherosclerosis. Considering that atherosclerosis is a chronic inflammatory disease, TauCl may play a role as a local modulator of inflammation.

### Anti-oxidative effects of taurine

Increased production of ROS, such as superoxide and $H_2O_2$ contributes to the pathogenesis of cardiovascular diseases, including atherosclerosis (Madamanchi et al. 2005). The major sources of ROS in the arterial wall are NADP oxidase, xanthine oxidase and myeloperoxidase. ROS can induce endothelial dysfunction and macrophage activation, leading to the release of cytokines and growth factors that stimulate smooth muscle proliferation and matrix remodeling.

Although taurine itself is not an anti-oxidant and little to no anti-oxidative effects of taurine are seen in vitro, taurine has been widely shown to reduce oxidative stress and increase biological anti-oxidation defense systems under pathological conditions in vivo. For example, taurine supplementation prevents oxidative stress induced by toxic substance (Waters et al. 2001), alcohol (Chen et al. 2009), exercise (Silva et al. 2011), ischemic reperfusion (Guz et al. 2007) and mechanical injury (Murakami et al. 2010b). It has been suggested that reduced oxidative stress is important for anti-atherosclerotic effect of taurine.

The oxidation of LDL is thought to be pivotal for the initiation and development of atherosclerosis. Oxidized LDL is a ligand for scavenger receptors including LOX-1 (Murphy et al. 2005). Oxidized LDL stimulates the cellular production of chemokines, leading to the recruitment of inflammatory cells into arterial walls. In addition, oxidized LDL produces both cellular dysfunction and death, two phenomena that further promote the atherogenic process. The anti-oxidative actions of taurine may reduce the formation of oxidized and MPO-/HOCl-modified LDL and thereby affect the initiation and progression of atherosclerosis.

## Conclusion and perspectives

Taurine seems to affect vascular function via multiple mechanisms, including osmoregulatory, anti-oxidant, anti-inflammatory and $Ca^{2+}$ modulating effects. The protective effects of taurine on the endothelial cells may be important, since dysfunction of the endothelium is pivotal for the initiation and progression of atherosclerosis. In addition, abundant levels of taurine in leukocytes may play important roles in the direct detoxification of cytotoxic hypochlorous acid. The taurine chloramines generated at sites of inflammation may contribute to the modulation of the immune response in vascular walls. Although the anti-oxidative effects of taurine are widely recognized, the mechanisms underlying the actions of taurine, other than the neutralization of hypochlorous acid, remain unclear. Further studies are necessary to reveal the details regarding the anti-oxidative actions of taurine.

Studies in animal models have demonstrated anti-atherosclerotic effects of taurine. Worldwide epidemiological studies have also revealed beneficial effects of taurine intake on cardiovascular disease prevention. However, the effects of taurine ingestion on humans remain unclear. A large-scale interventional study is needed to elucidate the roles of taurine in the pathogenesis of atherosclerosis.

**Conflict of interest** The authors declare that there are no conflicts of interest associated with this study.

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