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Dietary taurine supplementation: hypolipidemic and antiatherogenic effects

Julius D. Militante[a], John B. Lombardini[a,b,*]

[a]*Department of Pharmacology, Texas Tech University Health Sciences Center, 3601 4th Street, Lubbock, TX 79430, USA*

[b]*Department of Ophthalmology and Visual Sciences, Texas Tech University Health Sciences Center, Lubbock, TX 79430, USA*

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Abstract

Taurine supplementation may prove to be a safe and convenient method to reverse high blood cholesterol and the associated rise in atherosclerosis. Although human studies are limited, experiments using animal models provide extensive proof of the hypolipidemic and antiatherogenic effects of taurine. Examples of these animal models involve feeding with high-fat diets, genetically determined or heritable disease conditions, and artificially induced or genetic diabetes. Most importantly, the addition of taurine to the diet clearly has effects against pathological increases in serum and liver cholesterol and triglycerides. Another consistent and noteworthy effect of taurine is the simulation of cholesterol 7α-hydroxylase activity, the enzyme that is responsible for the catabolism of cholesterol into bile acids. Taurine also exhibited considerable effects on atherosclerotic lipid accumulation, perhaps through an antioxidative mechanism and through the elevation of HDL cholesterol levels. Data from animal model systems support the specific cardiovascular benefits of taurine, and hopefully, this research will be continued in human studies in the future.

Keywords: Dietary taurine; Hypercholesterolemia; Hyperlipidemia; Acyl CoA:cholesterol acyltransferase; Antioxidation

* Corresponding author. Tel.: (806) 743-2425; Fax: (806) 743-2744.
E-mail address: jbarry.lombardini@ttmc.ttuhsc.edu. (J.B. Lombardini).

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1. Introduction

Taurine (2-aminoethanesulfonic acid) is a free acid amino that is found in high concentrations in most types of animal tissues (reviewed in [1]). The main source of taurine for most mammals is the diet, although some species are capable of surviving severe taurine diet restrictions without much harm. Various physiological functions have been attributed to taurine, among them, osmoregulation, calcium modulation and antioxidation. However, much still has to be understood about the role that taurine plays in the maintenance of life and normal function.

Dietary intake of taurine is well tolerated in humans and presents as an interesting nutritional regimen for the wide number of positive effects that it seems to have. The benefits of taurine supplementation have been reviewed with respect to diabetes, cardiomyopathy, and hypertension [2–4]. Taurine also has significant effects in alleviating dyslipidemic and atherosclerotic states, thus rounding off the benefits of what truly is a protective and restorative molecule for the whole cardiovascular system. This review aims to describe the hypolipidemic and antiatherosclerotic effects of taurine, mostly in pathological or abnormal conditions that involve hypercholesterolemia, and to suggest some possible mechanisms of action for these effects.

Early studies in humans who exhibited normal lipid metabolism appeared to show that taurine supplementation had no effect on serum lipids [5]. It was suggested that inasmuch as humans conjugate cholesterol mostly with glycine instead of taurine, increased intake of taurine would not affect serum lipid levels to a significant extent. Few studies have appeared since then examining the effects of taurine in humans, specifically on serum lipid metabolism. Most studies have been correlative [6], evaluating regional diets and eating behavior relative to general health and the incidence of disease, and not truly experimental in nature. There have been some reports on the effects of taurine supplementation on bile metabolism in infants; there were no apparent benefits with taurine (reviewed in [7]). Sadly, the paucity of human studies contribute heavily to the lack of knowledge and familiarity with taurine among the general population.

In 1983, however, a study in Japan demonstrated significant correlations between daily urinary taurine excretion and serum high-density lipoprotein (HDL) [8]. The data suggested that taurine may be involved in serum lipid metabolism, albeit in an indirect manner. A more recent study, also in Japan, studied 22 healthy male volunteers after they were given a high-fat diet designed to increase serum cholesterol levels within the 3-week period of the experiment [9]. Taurine attenuated the increase in serum total cholesterol, low-density lipoprotein (LDL), and LDL-cholesterol brought about by increased cholesterol intake. However, taurine also increased very–low-density lipoprotein (VLDL) cholesterol and serum triglycerides. The significance of these effects have yet to be explained and given practical and scientific meaning. However, the data strongly suggest that taurine modulates serum lipid levels in humans.

With animal experimental models, the effects of taurine have been studied more and are easier to demonstrate. It is worthwhile to note that with data from the rat model, the hypolipidemic effects of taurine were demonstrated in control rats given normal diets and not

high-fat chow. Serum total cholesterol, LDL cholesterol, triglyceride, and hepatic cholesterol, triglyceride, and free fatty acid were effectively decreased by taurine in animals fed a normal diet [10–12]. HDL cholesterol, the antiatherogenic form of serum cholesterol, was found to be decreased by taurine in one study [10] but elevated in another [13]. Some of the hypolipidemic effects of taurine may be attributed to an increase in bile acid synthesis and in the activity of the cholesterol 7α-hydroxylase enzyme, the rate-limiting enzyme in the catabolism of cholesterol into bile acids (enzyme biochemistry reviewed in [14]). The stimulatory effect of taurine on this enzyme was observed in the rat [11], as well as in the guinea pig [15], with both model system using normal diets and no other treatments.

It was also found that taurine decreased serum and hepatic cholesterol levels in hamsters fed a normal diet [16], although this same effect was not observed in another hamster study [17]. Taurine treatment increased bile acid output and bile acid pool size while decreasing cholesterol secretion from the liver [17]. These effects would necessarily lead to the lowering of blood cholesterol levels. The positive effects of taurine are not limited to the lowering of lipid levels. Taurine increased the proportion of HDL, considered to be antiatherogenic in comparison to LDL and VLDL, which are considered to be atherogenic, in mice that were given a control diet [18]. The ratio between HDL and LDL+VLDL is known as the atherogenic index, and taurine is known to improve this index as noted in other reports. Indeed, the hypolipidemic effects of taurine lead inevitably to its antiatherogenic effects. This review hopefully will shed light and understanding on the link between taurine, hyperlipidemia, and atherosclerosis.

The human and animal data suggest that even in cases of normal fat intake, taurine supplementation may still provide some cardiovascular benefit. Available data, however, lean heavily on abnormal conditions or pathological lesions that increase lipid levels and induce atherosclerosis. The following sections describe various conditions that induce hypercholesterolemia and atherosclerosis, and the beneficial effects that taurine exhibits.

2. The hypercholesterolemic effects of high-fat diets can be reduced

Dietary fat intake is the most important factor that modulates serum levels of cholesterol, and this modulation figured prominently in the early scientific study of cholesterol metabolism. Portman and Stare [19] wrote a review that evaluated dietary factors in the regulation of serum cholesterol and described how every species studied exhibited a rise in serum cholesterol levels after a high-fat dietary challenge. Thus, fat intake has always been considered key in the control of blood lipid levels and associated cardiovascular diseases. Diets with increased lipid content, loosely termed high-fat diets, have been used successfully to increase serum cholesterol levels experimentally and have become valuable tools in the study of hypercholesterolemia. Various recipes for these diets have been reported and are described throughout this review article (e.g., see Table 1). Indeed, the use of high-fat diets to stimulate hypercholesterolemic conditions has become quite routine and widespread in experimental work.

Although taurine supplementation may not always exhibit significant effects on blood cholesterol levels in control animals, early studies clearly suggested that taurine is strongly

Table 1
Rat models of dietary hypercholesterolemia treated with taurine

Year [Citation]	Animals	High-Fat Diet	Taurine Treatment
1986 [56]	Male Wistar rats (110–120 g)	0.5% cholesterol + 1.0% cholic acid for 10 days	Dissolved in water and administered orally (500 mg/kg/day)
1986 [35]	Male Wistar rats (~120 g)	0.5% cholesterol	0.5% taurine in drinking water
1989 [57]	Male Wistar	(1% cholesterol + 0.25% sodium cholate) ± (0.8% L-methionine or choline chloride)	5% in chow
1992 [58]	Haffkine Wistar rats (~57 g)	1% cholesterol + 0.2% cholic acid for 8 weeks	1% or 2% in chow
1996 [59]	Male Wistar rats (~100 g)	1% cholesterol + 0.25% sodium cholate	5% in chow
1998 [10]	Male Sprague-Dawley (110–130 g)	15 g/kg cholesterol for 5 weeks	15 g/kg in chow
1999 [11]	Male Wistar rats (~100 g)	10 g/kg cholesterol + 2.5 g/kg sodium cholate for 2 weeks	0.25–50 g/kg in chow
2000 [60]	Male Wistar and Sprague-Dawley rats (100–110 g)	0.5% cholesterol + 0.15% sodium cholate	5% taurine in chow
2002 [34]	Male Wistar rats (225–250 g)	10% coconut oil for 4 months	Administered orally (0.5 mL of 2% w/v in water)
2003 [37]	Ovariectomized female Wistar rat (6 months old)	50 g/kg com oil or 50 g/kg coconut oil for 28 days	50 g/kg in chow

and universally potent in counteracting the rise in cholesterol levels induced specifically by a high-fat diet. Rats were fed a hypercholesterolemic diet (2% cholesterol and 1% cholic acid for 11 weeks), which raised serum cholesterol (~320%), liver cholesterol (~2840%), and aortic cholesterol (~340%) [20]. The addition of 4% taurine significantly reduced the effects of the hypercholesterolemic diet, although control levels were not achieved. Similar results were observed in Cebus monkeys [21] and in Japanese quail [22].

However, the hypolipidemic effects of taurine appears to be species-specific, inasmuch as high-cholesterol intake experiments in rabbits did not demonstrate the same effects [20,23]. Indeed, in humans, there is great controversy as to whether cholesterol intake bears any impact on blood cholesterol levels at all. A survey of 128 reports spanning 30 years revealed that modest changes in cholesterol intake produce little if any effect on serum cholesterol levels [24]. Humans may adapt to the increased cholesterol intake by decreasing cholesterol fractional absorption and/or endogenous cholesterol synthesis [25]. At the very least, there is considerable variation in the response to increased cholesterol intake, with two thirds of human subjects exhibiting apparent insensitivity. On the other hand, there is evidence suggesting that the increased intake of saturated fat increases all serum lipid levels. In fact,

it has become a dietary principle that calories from saturated fatty acid be substituted with polyunsaturated fatty acid calories in cases in which a hypocholesterolemic effect is desired (reviewed in [26]).

Regardless, the specific lipid-lowering effect of taurine in cases of diet-induced hypercholesterolemia has great significance in the face of the increasing consumption of high-fat fast food and the associated increase in the incidence of obesity in the general population of Western countries. The simple reduction or elimination of cholesterol and saturated fat in the diet is considered to be unwise for the most part, as this regimen alters the serum lipoprotein levels toward a greater atherogenic profile [27]. Thus, there is good scientific rationale for the regular inclusion of these lipids in the diet. Taurine may provide a normolipidemic if not a hypolipidemic effect, even with continued intake of cholesterol and saturated fat. The following sections describe the hypolipidemic effects of taurine in more recent reports featuring high-fat intake in experimental animals.

2.1. Taurine improves cholesterol metabolism and prevents gallstone formation and atherogenesis in mice fed a high-fat diet

The effects of taurine on blood lipid levels after high-fat treatment has been studied in several animal species. Among others, the effects of taurine in mice [18,28–30] have been reported. Moreover, these effects were linked to the prevention of gallstone formation and to the retardation of atherosclerosis.

The inhibitory effect of taurine on gallstone formation was studied in male Jcl:ICR mice [28,29]. Gallstone formation was stimulated by providing the animals with a lithogenic diet consisting of 0.5% cholesterol and 0.25% sodium cholate. All animals exhibited gallstone formation by week 5 of treatment, but taurine treatment (5% in food) inhibited this effect completely. Total serum cholesterol was significantly increased by the lithogenic diet but was lowered to normal levels with taurine after 2 weeks of exposure. Similarly, taurine treatment lowered liver and gallbladder cholesterol levels, which were increased by the cholesterol + sodium cholate diet, albeit, taurine did not lower these levels to those of controls. The effect of taurine to lower cholesterol levels and prevent gallstone formation was attributed to the stimulatory effect of taurine on cholesterol 7α-hydroxylase, the rate-limiting enzyme responsible for the synthesis of bile acid from cholesterol in the liver [31]. The increase in bile synthesis was correlated to the increased degradation of cholesterol and is an important mechanism behind the hypolipidemic effects of taurine.

Similar to the Jcl:ICR mice, ICR mice have been used to study the hypercholesterolemia associated with high-fat diet and the beneficial effects of taurine [32]. ICR mice received a diet supplemented with 2% cholesterol (w/w) and 0.5% cholate (w/w) for 10 weeks [32]. Taurine was also administered orally at the rate of 50 or 100 mg/kg weight daily. The cholesterol diet significantly increased total and LDL cholesterol, and this effect was reduced by chronic taurine treatment. Cholesterol treatment was also associated with a decrease in endothelium-dependent aortic relaxation, and again this effect was reversed by taurine treatment.

The C57BL/6J mice are inbred mice that were found to be particularly susceptible to atherosclerosis if treated with a high-fat diet [33]. These mice were given a high-fat (30%

cocoa butter), high-cholesterol (5%), sodium cholate (2%) diet with or without taurine (1% in drinking water) for 6 months [18]. This diet decreased cholesterol 7α-hydroxylase activity, and increased total liver cholesterol by ~500% and serum cholesterol levels by almost 100%. Even more significantly, the proportion of the atherogenic lipoproteins LDL+VLDL cholesterol increased whereas the antiatherogenic lipoprotein HDL cholesterol decreased. The atherogenic index, which is the ratio of HDL to LDL+VLDL, thus increased and predicted greater propensity for atherosclerotic lesions. Indeed, lipid accumulation was found to be increased in the aortic valve.

Taurine was found to decrease serum LDL+VLDL cholesterol and increase HDL cholesterol in these mice, without changing total cholesterol levels [18,30]. These data contrast with the data generated by the study in Jcl:ICR and ICR mice, which exhibited a decrease in total cholesterol levels [28,29,32]. Nevertheless, the effects of taurine represented a major improvement in the atherogenic index, and indeed taurine produced a 20% decrease in lipid accumulation in the aortic valve. The cholesterol levels of the liver were also decreased with taurine treatment, and this effect was associated with the normalized function of the otherwise reduced activity of the cholesterol 7α-hydroxylase enzyme.

2.2. The rat high-fat diet model provides the most extensive proof of the ameliorating effects of taurine

The use of taurine to counteract the hypercholesterolemic effects of a high-fat diet is most extensively described in rat animal models. Table 1 describes the various conditions used to induce hypercholesterolemia and to supplement the diet with taurine. Table 2 summarizes the deleterious effects of high-fat diet and the ameliorative effects of taurine treatment. The prominent effects were the increases in serum and liver lipid levels, and the reversal of these increases with taurine treatment. Increased cholesterol metabolism and removal through the upregulation of cholesterol 7α-hydroxylase activity and bile secretion were also observed with taurine treatment. Taurine may prove beneficial even in cases in which cholesterol levels do not diminish, as taurine also increases the levels of the antiatherogenic lipoprotein HDL thereby improving the atherogenic index. It must be noted, however, that some of the effects observed in one study may not have been observed in another. Although the data may be viewed as conflicting, for the most part the differences are minor, and in general the table summary presents what is in our judgment a reasonable and reliable assessment of the experimental effects of high-fat and taurine treatments.

The data from the rat model present many interesting ramifications for the hypolipidemic effects of taurine. Aside from the obvious effects of taurine on lipid levels in both the serum and the liver, the data in Table 2 suggest that the antiatherosclerotic effects of taurine are quite significant, specifically with respect to lipid accumulation in blood vessels [34]. These effects may be a result of the antioxidative benefits of taurine supplementation as much as it is a result of its lipid-lowering effects. Oxidative activity in the serum and in the aorta was assayed using the thiobarbituric acid reactive substances (TBARS) test (Table 2) and was found to be increased in this rat model. This lesion was linked to increased atherogenesis as a contributing factor. Because TBARS levels were shown to be reversed with taurine supplementation, an antioxidative component to the effects of taurine was suggested.

Table 2
Observed effects of high-fat diet and of taurine treatment in rat models of hypercholesterolemia

High-Fat diet	Citation	Taurine Treatment	[Citation]
(+) Serum total cholesterol, LDL-cholesterol, VLDL protein, triglyceride	[10,11,34,59]	(−) serum total cholesterol, LDL cholesterol, VLDL protein, triglyceride	[10,11,34,35,37,56–59]
(−) Serum HDL cholesterol	[10]	(+) serum HDL cholesterol	[11,37,57]
(+) Liver total cholesterol, triglyceride, phospholipids, free fatty acids	[10,11,60]	(−) liver total cholesterol, triglyceride, phospholipids	[10,11,57,58,60]
(+) Fecal bile acids, fecal cholesterol	[11]	(+) taurine-conjugated biliary and fecal bile, fecal bile acid; fecal sterol excretion	[11,37,56–58]
		(−) glycine/taurine bile ratio	
		(−) cholesterol ester secretion from perfused liver	[60]
Liver and kidney fatty vacuolation	[58]	amelioration of fatty vacuolation	[58]
		(+) 7α-hydroxylase activity and mRNA levels	[11,37,38,57]
(+) Serum and aortic TBARS levels; aortic cholesterol, triglyceride, phospholipid; aortic lipid accumulation	[34]	(−) serum and aortic TBARS levels; aortic cholesterol, triglyceride, phospholipid; aortic lipid accumulation	[34]
(−) Aortic GSH levels	[34]	(+) aortic GSH levels	[34]

GSH = reduced glutathione; TBARS = thiobarbituric acid reactive substances; + = increase; − = decrease.

Another benefit that the hypolipidemic properties of taurine appears to produce in the rat is the restoration of the bactericidal activity of neutrophils, which was found to be inhibited specifically by hyperlipidemia [35]. This study studied the effects of high-fat diet on neutrophil activity. Apparently, the elevated levels of lipids interferes with the neutrophil membrane and prevent its phagocytotic activity. Taurine supplementation lowered blood lipid levels and resulted in normalization of neutrophil activity, presenting a functional benefit of its hypolipidemic effects.

Hypercholesterolemia could also be induced in female rats through the removal of the ovary [36–38]. Ovariectomy simulates menopause, and the ovariectomized (OVX) rat model may be used to study postmenopausal hypercholesterolemia [39]. Plasma cholesterol concentrations increased in aged OVX rats and this effect was antagonized by taurine treatment. The positive effect of taurine was observed whether the animals were fed normal chow or high-fat chow [36–38]. The effects of taurine could be attributed to increased cholesterol 7α-hydroxylase activity, bile acid synthesis, and fecal bile excretion. Taurine also increase LDL receptor expression and HDL levels in these animals. These effects mirror most data observed from other animal models that made use of high-fat diets.

A most interesting finding in rats given a high-fat diet is the reduction of taurine levels in

the serum, kidney, liver, and heart [11]. The high-fat diet was given for 2 weeks and the decrease in hepatic taurine levels was specifically dramatic (~90% decrease). Taurine decreased about 50% in the other tissues. How this occurs is not clear, but it may be due to increased synthesis and excretion of taurine conjugated bile acid produced by the excess cholesterol flooding the liver. Inasmuch as taurine reverses many of the effects of a high-fat diet (Table 2), we may surmise that these effects of a high-fat diet have been caused, at least in part, by the reduction in taurine levels and that there may exist some vicious cycle of hypercholesterolemia and taurine depletion that can only be broken by increased taurine intake.

2.3. Taurine decreases acyl CoA:cholesterol acyltransferase activity and increases LDL receptors in the hamster model of hypercholsterolemia

The hypolipidemic effects of taurine have also been demonstrated in the hamster [16,40]. Male Golden Syrian hamster were used and given high-fat diets featuring coconut oil (10%). The hyperlipidemia associated with the diet was partially reversed by taurine treatment. The effect on serum cholesterol was characterized by a decrease in non-HDL (LDL+VLDL) cholesterol and the overall decrease in cholesterol was probably caused by the observed increase in cholesterol 7α-hydroxylase activity in the liver. This effect is significant and similar to the beneficial effect of taurine on the atherogenic index in mice fed a normal diet [18].

In this specific hamster model, other hypolipidemic mechanisms were attributed to taurine: the decreased in CoA:cholesterol acyltransferase (ACAT) activity, the up-regulation of the LDL receptors in the liver, and the associated acceleration of LDL turnover [16]. ACAT is a hepatic enzyme that is involved in the esterification of cholesterol inside the cell and the assembly and eventual secretion of VLDL cholesterol [41]. Thus, the decreased activity of ACAT is associated with decreased secretion VLDL cholesterol into the blood. LDL cholesterol, on the other hand, needs to bind to its receptors in order for LDL cholesterol to be internalized by the liver cells and metabolized. Thus, an increase in LDL receptors is associated with faster turnover of LDL cholesterol and faster removal of cholesterol from the blood. Male Golden Syrian hamsters were given free access to rodent chow containing 0.05% cholesterol for 1 week [16]. The diet was then changed to a high-fat version containing 10% coconut oil for 14 days with or without taurine (1% in drinking water). Serum cholesterol (HDL and non-HDL), triglyceride and phospholipid levels were higher with the high-fat diet, as were liver cholesterol levels. Taurine effectively reversed these changes, although not to the levels of controls. These effects were associated with elevated cholesterol 7α-hydroxylase activity and diminished ACAT activity.

LDL receptor binding activity was also determined in liver membrane samples through the use of ^{125}I-labeled LDL, and the maximal binding of LDL was found to exhibit an apparent increase. Similar effects were observed in cultured liver cells. The enhancement of LDL binding with taurine treatment has been demonstrated in Hep G2 cells, a human hepatoblastoma cell line [42]. Finally, the fractional catabolic rate for radiolabeled LDL was also measured to determine the removal rate of LDL. These studies demonstrated faster receptor-mediated removal of LDL with taurine treatment [16].

2.4. The hypolipidemic effect of taurine in the rabbit is inconsistent

As mentioned before, results in experiments in rabbits suggested that taurine has no significant effect on hypercholesterolemia induced by a cholesterol diet [20,23]. The rabbits (1–1.5 kg) were fed a diet that was 2% cholesterol by weight, but the increase in serum cholesterol levels varied greatly from 440% [20] to 2270% [23]. Taurine was given as a food additive (4% w/w) for the former, or as part of the drinking water (0.5%) for the latter, for at least 11 weeks, and was found to have no effect on total cholesterol levels in the blood.

More recently, however, another experiment using larger rabbits (2–2.5 kg) demonstrated the hypolipidemic effects of taurine in the rabbit fed a high-fat diet [43]. The rabbits were fed a diet consisting of 1% cholesterol (w/w) for 2 months with or without taurine in the food (2.5% w/w). Cholesterol treatment increased plasma cholesterol tremendously. Plasma cholesterol increased by almost 1300%, whereas plasma triglyceride levels rose almost 300%. Taurine treatment reversed the effects of cholesterol treatment on total plasma cholesterol (39.9–31.1 mmol/L) and on plasma triglyceride levels (1.92–1.20 mmol/L). It must noted, however, that lipid levels were not restored to control values. The discrepancy between the above-mentioned experiments is yet to be fully understood.

3. There is a genetic predisposition for hyperlipidemia and the effects of taurine

Hypercholesterolemia may be determined more by the genes that we have than by our dietary behavior [44,45]. This idea is indirectly suggested by the great variation in the response of human subjects to a high-fat diet [24]. There are several animal models of genetic or inherited hypercholesterolemia that may be used to study the effects of taurine. These experimental models may be more applicable to the human condition than the more popular models involving high-fat dietary intake.

The spontaneously hyperlipidemic (SHL) mouse was generated by genetically targeting the apolipoprotein E (apoE), a structural component of all non-LDL lipoproteins [46]. The homozygous progeny is known to exhibit serum total cholesterol and triglyceride levels ~500% and ~70% times higher than controls, respectively, while displaying a ~45% decrease in HDL cholesterol levels. LDL and VLDL cholesterol also increase significantly in these mice. The animal develops foam cell–rich depositions in the aorta, and the lesions progress with age. These effects occur without any changes from the normal diet or any drug treatments, and thus the SHL mouse is used as a model for spontaneous atherosclerosis. Taurine treatment of these mice (1% w/v in drinking water) did not lower serum total cholesterol but significantly increased the HDL cholesterol fraction, thereby improving the atherogenic index [47]. Sure enough, atherosclerotic lesions in the aorta were found to be decreased by 29%.

Another genetic model for hypercholesterolemia is the SHRSP rat (stroke-prone spontaneously hypertensive rat), which exhibits elevated blood pressure spontaneously and atherosclerotic lesions if given a high-fat diet. Serum total and free cholesterol, cholesteryl ester, LDL+VLDL cholesterol and triglycerides, as well as liver lipids, increased dramatically in

Table 3
Diabetic animal models and the effects of taurine treatment

Diabetic Model	Effect of Taurine Treatment	Year [Citation]
STZ-treated Sprague-Dawley rats	Reduced diabetic hypercholesterolemia and hypertriglyceridemia	1990 [61]
STZ-treated male ICR mice	Reduced diabetic hypercholesterolemia	1996 [32]
STZ-treated male Wistar rats	Reduced diabetic hypercholesterolemia (total and LDL + VLDL) and diabetic increases in hepatic cholesterol content	1996 [59]
STZ-treated male Sprague-Dawley rats	Reduced diabetic increase in plasma triglyceride levels	1998 [62]
STZ-treated male Wistar rats	Reduced the effects of a high-fat diet to increase plasma cholesterol and VLDL levels	1999 [63]
Otsuka Long-Evans Tokushima Fatty rat	Reduced the levels of serum and liver cholesterol and triglycerides; increased secretion of bile	2000 [64]
Genetically diabetic GK rats	Reduced the effects of a high-fat diet to increase plasma cholesterol levels; Increased fecal bile excretion; improved the atherogenic index	2002 [65]
STZ-treated male Wistar rats	Reduced the increase in plasma cholesterol and triglyceride levels produced by STZ treatment	2003 [66]

STZ = streptozotocin.

these rats after the diet was changed to a high-cholesterol version [48,49]. At the same time, HDL cholesterol levels were decreased. These lesions were reversed to a significant degree by taurine treatment. Serum levels of cholesterol increase and decrease through time with the commencement and the termination of a high-fat diet, respectively. Taurine treatment retarded the increase and accelerated the decrease. Moreover, taurine improved the atherogenic index and indeed reduced the fat deposition in the mesenteric arteries that was stimulated by the high-fat diet. Taurine had no positive effects on serum cholesterol in the absence of high-fat intake, however.

The effects of taurine on hyperlipidemia were much less pronounced in another genetic model, the Watanabe heritable hyperlipidemic (WHHL) rabbit [50,51]. These rabbits exhibit a 55% increase in serum total cholesterol after 7 months of age. Aortic fibrosis, intimal thickening, fatty streaks, and plaques were observed, among other things, and indicated a predisposition to atherosclerosis. Taurine treatment had no effect on all serum cholesterol levels in WHHL rabbits studied from age 2–8 months [52]. The absence of an obvious effect may result from the relatively young age of the rabbit. Hypercholesterolemia in these animals is age-dependent and may not have fully developed in these young rabbits [50]. On the other hand, aortic cholesterol and ACAT activity were decreased, along with the aortic oxidative index, providing a strong antiatherogenic effect.

Table 4
Antiatherogenic effects of taurine

Atherogenic Model	Effect of Taurine	Year [Citation]
SHRSP rats fed a high-fat diet	Reduced serum, liver and aortic cholesterol levels; decreased fat deposition in mesenteric arteries	1996 [49]
C57BL/6J mice fed a high-fat diet	Reduced LDL + VLDL cholesterol levels; improved arterial lipid accumulation; increased cholesterol 7α-hydroxylase activity; lowered serum TBARS levels	1999 [30]
apo E–Deficient mice	Increased serum total cholesterol levels; reduced arterial lipid accumulation; reduced serum TBARS levels	2001 [67]
WHHL rabbits	Decreased aortic lesions; reduced aortic cholesterol levels; decreased serum and aortic TBARS levels	2002 [52]
Male Wistar rats fed a high-fat diet	Reduced serum LDL cholesterol and triglyceride levels, and aortic cholesterol levels; decreased serum and aortic TBARS levels; increased aortic GSH; reduced arterial lipid accumulation	2002 [34]
SHL mice	Increased HDL cholesterol levels; reduced aortic lipid accumulation; decreased serum TBARS levels	2003 [47]

GSH = reduced glutathione; SHL = spontaneously hyperlipidemic; SHRSP = stroke-prone spontaneously hypertensive rat; TBARS = thiobarbituric acid reactive substances; WHHL = Watanabe heritable hyperlipidemic.

4. Taurine provides beneficial effects in cases of diabetic hyperlipidemia

Cardiovascular diseases are the most prevalent and most fatal complications in diabetes. Thus, a major risk factor and medical concern in the diabetic patient is hypercholesterolemia [53]. Patients usually have elevated plasma triglycerides and VLDL, and decreased HDL levels. Studies with diabetic rats suggest that these changes may be due, in part, to decreased bile and lipid output from the liver [54]. Taurine supplementation is well tolerated in diabetic patients [55], and is known to produce hypolipidemic effects in animal models of diabetes (Table 3). In general, diabetes produced significant elevation of both serum and liver lipid levels, and taurine supplementation of the diet reversed these lesions. The beneficial effects of taurine apparently were a result of increased bile excretion. The data suggest quite strongly that taurine may be a potential hypolipidemic agent for diabetics.

5. The anti-atherosclerotic effects of taurine cannot be separated from its effects on blood lipid levels

Much of the above-mentioned studies included the evaluation of taurine as an antiatherogenic agent. It is clear that the hypolipidemic effects of taurine cannot be separated from its

ability to prevent the formation of atherosclerotic lesions. Most of the studies attribute the beneficial effects of taurine to its antioxidant effects (e.g., TBARS levels) in addition to its ability to lower lipid levels. Table 4 summarizes the findings that link taurine to the reduction of atherosclerosis, most of which have been mentioned in the previous sections.

6. Conclusions

The supplementation of the diet with taurine is known to have many cardiovascular benefits. In these experiments, increased levels of lipid substances were induced in experimental animals through the use of high-fat diets, or were associated with genetic abnormalities or diabetes. Taurine was found to have significant effects in terms of alleviating dyslipidemic lesions. Examples of the lesions that are reversed to a certain degree by taurine are as follows: 1) increased serum total cholesterol and triglyceride levels; 2) specific increase in atherogenic LDL+VLDL cholesterol; 3) specific decrease in antiatherogenic HDL cholesterol; 4) increased liver lipid levels; 5) increased serum and liver oxidation reactions; 6) increased arterial fat deposition; and 7) formation of gallstones.

The effects of taurine were mostly related to increased degradation and excretion of cholesterol as bile in the feces. Specific hypolipidemic mechanisms include increased activity of cholesterol 7α-hydroxylase activity, increased LDL receptor binding, and turnover of LDL, among others. Unfortunately, very few studies have been done to evaluate these effects of taurine in human subjects. Regardless, the available data should encourage more basic and clinical research on the effects of taurine supplementation on hypercholesterolemic and atherosclerotic states.

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