
Anticholesterolemic and Antiatherogenic Effects of Taurine Supplementation is Model Dependent

Karl-Erik Eilertsen, Rune Larsen,
Hanne K. Mæhre, Ida-Johanne Jensen and Edel O. Elvevoll

Additional information is available at the end of the chapter

<http://dx.doi.org/10.5772/47865>

1. Introduction

Taurine (2-aminoethanesulfonic acid) is a sulphur-containing compound characterized as an amino acid. The presence of a sulfonic group, as opposed to a carboxyl group in other amino acids, gives taurine a pKa value of 1.5 and it is the most acidic amino acid. It is an exclusively free amino acid, i.e. it is not incorporated into proteins, but still widely distributed in most body tissues.

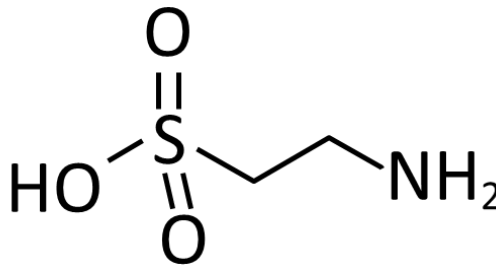


Figure 1. The structure of taurine

Taurine was identified almost two centuries ago and was named after the ox, *Bos taurus*, since it was first isolated from the bile of ox [1]. After its discovery, taurine was considered non-essential and biologically inert, however a multitude of functions have now been identified. Yet, all its physiological roles have not been fully elucidated. The phylogenetically oldest and best documented function of taurine is conjugation with bile acids in bile salt synthesis [2, 3]. In addition, taurine is involved in a variety of physiological processes as extensively reviewed [2], including neuromodulation in the central nervous system [4], energy production [5], protection against oxidation [6, 7] and immunomodulation

[8, 9]. An osmoregulatory role of taurine has also been established, playing a pivotal role in Central nervous system (CNS) cell volume regulation [10-12].

In felines taurine is considered indispensable and dietary deficiency leads to several clinical problems, including retinal degeneration and developmental abnormalities [13]. In humans it is regarded as a conditionally essential amino acid due to a limited ability to synthesize it [14, 15]. Taurine is now thought to play a more important role in human nutrition, and an increased dietary intake of taurine has been linked to several beneficial health outcomes in various diseases and medical conditions [16-18].

2. Taurine and nutrition

Estimates of dietary intake of taurine vary greatly. Although taurine content have been analysed in a variety of foods, it is usually excluded in food and nutrition data banks. Therefore, it is difficult to assess the dietary intake. A diet high in meat and especially seafood will provide a higher intake than a vegetarian diet which will provide very little taurine [19]. Mean \pm SE dietary intake of taurine of 58 ± 19.5 mg/d was reported in omnivores [20], while it was not detected in a vegan diet. Laidlaw et al. [21] analysed taurine content in foods and calculated a taurine intake of less than 200 mg/d for individuals consuming a diet high in meat.

2.1. Taurine biosynthesis

Taurine is the most abundant intracellular free amino acid in the human body, the average amount being approximately 560 mmol (70g). The main organs of distribution are the retina, along with white blood cells, platelets, spleen, heart, muscle and brain [22].

As a product in the metabolism of sulphur-containing amino acids, taurine can be synthesised from its precursors methionine and cysteine, as shown in figure 2. The first step of the synthesis is methionine's reversible conversion to homocysteine by transmethylation and remethylation processes. Homocysteine can then be converted irreversibly to cysteine through the transsulfuration pathway catalyzed by cystathionine β -synthase and cystathionine γ -lyase [23]. Cysteine is, in turn, the origin of several biologically important molecules, including glutathione, inorganic sulphur and taurine [24]. Taurine can be synthesised from cysteine through several pathways, most commonly via cysteine sulfinic acid and hypotaurine, involving the enzymes cysteine dioxygenase (CDO) and cysteine sulfinic decarboxylase (CSAD) mainly present in the liver and brain. The activities of the enzymes involved, in particular the activity of CSAD, are both species and age dependent [25-27], being high in rodents and absent in cats. In addition, taurine synthesis is dependent on an adequate cysteine concentration, as production of glutathione is favoured when cysteine concentration is limited [28].

In humans the CSAD activity is low and the average daily synthesis of taurine ranges from 0.4 to 1.0 mmol (50-125mg). Excretion of taurine is very variable (0.22-1.85 mmol day⁻¹) and affected by several factors such as genetics, age, gender, dietary intake, kidney function and health status [22]. The taurine body pool size is however regulated by the kidneys through renal absorption by the proximal tubule [14, 26, 29, 30].

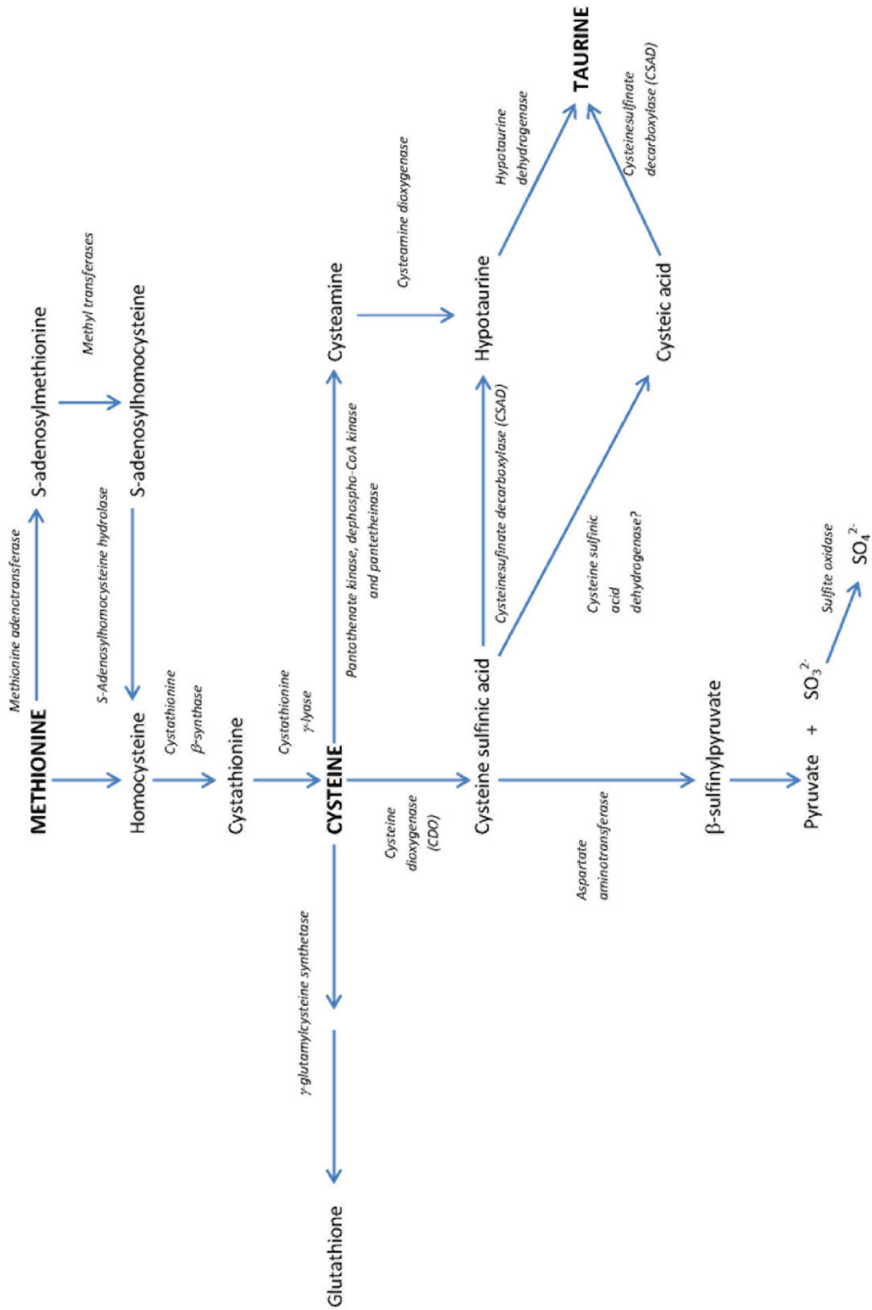


Figure 2. Taurine biosynthesis

2.2. Dietary sources

Taurine is found in most meats used for human consumption, whereas plants including grains, legumes, fruits and vegetables are devoid or contain only negligible amounts [21]. An exception is algae, mainly red algae (*Rhodophyta*), where notable amounts have been found [31, 32].

Taurine concentration has been investigated in a wide range of food products and it varies substantially between different marine and non-marine food items [17, 33]. A comparison of taurine concentrations in various foods is presented in table 1 [21, 34-43]. It is evident that seafood, and especially molluscs are high in taurine. Taurine is a key osmolyte in marine molluscs [44] and the highest taurine concentrations are found in marine bivalves and univalves [45]. Scallops and blue mussels are reported to have a respective taurine content of 827 ± 15 and 510 ± 12 mg per 100g raw muscle [21, 34]. In fact, the univalve abalone was already early in the last century 1918 exploited for preparation of taurine in large quantities [46].

There is also a tendency of taurine being more abundant in fish than in terrestrial animals. Taurine concentrations (mg per 100g raw fillets) of entire muscle of farmed Atlantic salmon (94 ± 16 mg), cod (120 ± 21 mg), saithe (162 ± 25 mg) and haddock (57 ± 6 mg) are reported to be intermediate [34]. Taurine content varies greatly between white and red muscle both in fish, poultry and mammals, with significantly higher levels being present in red muscle [21, 39, 40, 43], probably due to the increased vascularisation of these tissues.

Several studies investigating the retention and losses of taurine during food processing and preparation have been conducted [34, 36, 47-49]. Results indicate that taurine is susceptible to leaching losses similar to or even more than other free amino acids. Data on the oxidative and heat stability of taurine in foods is scarce. In milk, taurine losses seemed to proceed with the same degradation rate as lysine due to browning reactions [50].

2.3. Taurine supplementation

Taurine is maybe most famous for being an ingredient that is added to energy drinks, the concentration being approximately 4.0 g/L. Its physiological effect has been debated, with manufacturers, backed by studies, claiming that taurine in combination with other active ingredients may improve cognitive and muscular performance [51, 52]. The safety of taurine intake has also been investigated, especially in conjunction with its use in energy drinks. The European Food Safety Authority (EFSA) have concluded that taurine do not present any safety concerns with the levels currently used in energy drinks. The no observable adverse effect level (NOAEL) was at least 1000 mg/kg bw/day for pathological and behavioural changes, being much higher than an extreme consumer would be exposed to [53]. In their risk assessment, Shao and Hatchcock [54], found that absence of adverse effects was strong for taurine at supplemental intakes up to 3 g per day.

Food source	Taurine content (mg/100g wet weight) reported range \pm SEM	References
Meat		
Beef, round	36	[38]
Beef (Bos taurus)	43 \pm 8	[21]
Chicken, light meat	18 \pm 3	[21]
Chicken, dark meat	169 \pm 37	[21]
Turkey, light meat	30 \pm 7	[21]
Turkey, dark meat	306 \pm 69	[21]
Pork (loin)	61 \pm 11	[21, 38]
Pork (loin)	50 \pm 11	[21, 38]
Lamb, leg	45 \pm 4	[38]
Veal	40 \pm 13	[21]
Reindeer (loin)	62,4 \pm 12	[42]
Red deer (loin)	28 \pm 13	[37]
Fish		
Plaice	146 \pm 5	[[35]
Cod fillet	120 \pm 21	[34, 48]
Cod roe	365	[34]
Saithe fillet	162 \pm 25	[34]
Haddock fillet	57 \pm 6	[34]
African catfish	201 \pm 32	[36]
Salmon fillet	94 \pm 16	[34]
Mackerel	78	[35]
Bigeye tuna, white muscle	26	[41]
Bigeye tuna, dark muscle	270	[41]
Yellowfin tuna, white muscle	42	[41]
Yellowfin tuna, dark muscle	964	[41]
Bluefin tuna, white muscle	88	[41]
Bluefin tuna, dark muscle	195	[41]
Pacific saury, white muscle	223	[41]
Pacific saury, dark muscle	248	[41]
Milkfish, white muscle	95,7	[39]
Milkfish, dark muscle	309	[39]
Octopus	388 \pm 13	[43]
Squid	356 \pm 95	[21]
Fresh water fish		
Rainbow trout, white muscle	17	[40]
Rainbow trout, dark muscle	206	[40]

Coho salmon, white muscle	23	[40]
Coho salmon, dark muscle	275	[40]
Eel, white muscle	7	[40]
Eel, dark muscle	65	[40]
Catfish, white muscle	193	[40]
Catfish, dark muscle	465	[40]
Tilapia, white muscle	75	[40]
Tilapia, dark muscle	649	[40]
Carp, white muscle	129	[40]
Carp, dark muscle	579	[40]
Char, white muscle	15	[40]
Char, dark muscle	190	[40]
Sweet smelt, white muscle	137	[40]
Sweet smelt, dark muscle	294	[40]
Shellfish		
Peeled shrimps (Northern)	220 ± 2	[34]
Blue mussels	510 ± 12	[34]
Mussel	655 ± 72	[21]
Mussel	349	[43]
Clams	520 ± 97	[21, 43]
Scallops	827 ± 15	[21]
Scallop	332	[43]
Oysters	396 ± 29	[21]

Table 1. Taurine content in various food sources

Another food item where taurine is supplemented is in infant formulas. This practice started in the early 1980s after recognizing that preterm infants fed infant formulas had lower urine and plasma concentrations than infants fed pooled human milk [55]. The necessity of this supplementation remains disputed as clinical studies have not provided evidence of any clinical effects of growth and development in preterm or low birth weight infants [56]. High concentrations of taurine in the developing brain [57], as well as results from various animal studies clearly indicate the importance of taurine in neurodevelopment [58, 59].

2.4. Taurine and associated health benefits

An increased dietary intake of taurine has been associated with multiple beneficial health outcomes. Epidemiological data and animal studies suggests that dietary intake of taurine has beneficial effects on cardiovascular disease (CVD) [33, 60-62]. Perhaps the best characterized attribution of taurine is the antihypertensive effect although there are still questions about the exact mechanisms of action [63-66]. A long term effect of hypertension is the development of hypertrophy of the left ventricle, in which Angiotensin II (Ang II) plays an important role. Several studies have shown that taurine

reverses these actions of Ang II [67, 68]. Animal studies have also indicated that taurine may reduce insulin resistance [69, 70], but most of the clinical studies have failed to prove the beneficial role of taurine in insulin resistance and diabetic complications [71, 72]. Taurine have also been found to ameliorate alcoholic steatohepatitis [73-75] in rats. In addition, some evidence have been brought forward of a potential therapeutic use of taurine in nonalcoholic fatty liver disease [76]. Despite taurine being linked to beneficial health outcomes in an increasing number of diseases and medical conditions, the number of studies is relatively small. The effects of taurine on cholesterol and CVD are most studied and documented.

3. Taurine and cholesterol metabolism

Perhaps the best studied function of taurine is its role in cholesterol metabolism. Cholesterol is metabolized and broken down to cholic acids, conjugated to taurine or glycine, and excreted in the bile [77].

3.1. Effects of taurine on circulating cholesterol levels

High blood cholesterol levels is the most pronounced risk factor for developing atherosclerosis, vascular inflammation and hardening of the arteries associated with excess cholesterol deposition in the vasculature. Taurine has generally been associated with a beneficial effect on blood cholesterol levels. Cholesterol is metabolized and broken down to cholic acids, conjugated to taurine or glycine, and excreted in the bile [77]. The conjugation pattern varies considerably across species. In dog and rat bile acids are entirely conjugated to taurine, whereas rabbits have all their bile acids conjugated to glycine. Species where glycine-conjugated bile acids dominate have higher blood cholesterol levels and are more susceptible to dietary induced hypercholesterolemia, and based on these observations it was hypothesized that dietary taurine might counteract dietary induced increase in blood cholesterol [2].

3.1.1. Effects of taurine on cholesterol levels in mice

Several studies have investigated the effect of dietary intake of taurine on lipids in different mice strains. Six months administration of 1% taurine (w/v) to the drinking water given to C57BL/6J mice fed a high-fat diet resulted in reduced serum LDL and VLDL cholesterol and increased serum HDL cholesterol [78]. Similar results were obtained in a small study using the same mouse strain, where 1% taurine (w/w) added to a high cholesterol diet reduced serum triglycerides, total cholesterol and VLDL+LDL cholesterol levels already after 4 weeks treatment [79]. Cholesterol-fed and streptozotocin (STZ)-induced diabetic male ICR mice were given a diet enriched with 2% cholesterol (w/w) and 0.5% cholate (w/w) for 10 weeks [80]. In addition, mice received a daily dose of saline or taurine (50 or 100 mg/kg p.o.). Both taurine-treated groups had lower serum total and LDL cholesterol compared to the STZ/saline group.

In more extreme models such as apolipoprotein E-deficient (apoE^{-/-}) mice fed a normal rodent chow supplemented with 2% taurine (w/w) for 12 weeks, serum VLDL, LDL and total cholesterol levels increased compared to mice without taurine supplementation [81]. Similar results has been reported for extreme spontaneously hyperlipidemic mice (SHL; KOR-Apo^{eshl}), where 12 weeks treatment with 1% taurine (w/v) added to the drinking water increased serum HDL-cholesterol but did not affect serum total cholesterol or VLDL+LDL cholesterol levels [82].

3.1.2. Effects of taurine on cholesterol levels in rats

A large number of studies have investigated the effect of dietary taurine on dietary hypercholesterolemia in various rat models [65]. Rats fed high-fat diets seem to be the model with most consistent antihypercholesterolemic effects of dietary taurine. Rats have a relatively low taurine content in skeletal muscles (10-25 mg/100 g muscle) [83, 84].

Rats are generally not suitable for pharmacologically cholesterol and lipoprotein studies due to their substantially different lipid profile compared to humans.

Male wistar rats. Taurine supplementation does not alter plasma lipids in male wistar rats fed normal chow [85]. However, when these rats were fed high cholesterol diet containing 2% cholesterol and 1% cholic acid, dietary supplementation of 4% taurine significantly counteracted the observed increase in serum cholesterol by 44% [86]. This observation has been confirmed by several studies [87-90]. In Wistar male rats fed a cholesterol-containing diet (0.5% cholesterol w/w) for 40 days, serum cholesterol increased 5 fold compared to chow fed rats. Oral supplementation of 470 mg/kg/day taurine (0.5% w/v) in water lowered the increased serum cholesterol (54%) [91]. When these rats were fed a high-fat diet (11% coconut oil w/w) for 6 months, a daily oral supplementation of 1 mg taurine lowered serum cholesterol (37%), LDL cholesterol (34%), and triglycerides (95%), compared to the high-fat control diet [88]. Already after 14 days intervention, 5% dietary taurine (w/w) supplementation has been indicated to lower high cholesterol (1% cholesterol, 2.5% cholate) induced serum cholesterol (-42%) [90]. In wistar rats, the taurine effect has been indicated to be caused by an increased faecal bile acid excretion, increased hepatic cholesterol 7 α -hydroxylase expression and activity [89, 90]. The rapid effect of taurine supplementation on serum cholesterol has been confirmed recently [92]. When fed a diet containing 60.7% sucrose, 9.0% lard, and 0.5% cholesterol for 14 days, serum cholesteryl ester and free cholesterol were reduced by 39% and 53% compared to rats fed control diet without taurine, respectively. Rats fed taurine also had smaller livers compared to control-fed rats. Hepatic cholesteryl esters were also reduced by approximately 20% in the taurine supplemented rats. This hypocholesterolemic effect was ascribed to a lower hepatic secretion of cholesteryl esters.

Streptozotocin-induced diabetic rats. Male Wistar rats injected with STZ are also used as a diabetic model. In these rats dietary taurine supplementation markedly reduced serum total cholesterol (-50%) induced by cholesterol-containing diet (1% cholesterol w/w) for 4 weeks [93].

Fructose-induced rat insulin resistance model. Male wistar rats fed a diet containing 60% fructose developed impaired glucose tolerance and insulin resistance [85]. Taurine administration (300 mg/kg/day *i.p.*) counteracted the fructose induced plasma total cholesterol, LDL cholesterol, and triglycerides by 11%, 21%, and 23%, respectively.

Spontaneously hypertensive rats (SHR). The effect of taurine supplementation on blood pressure in SHR rats was investigated already in the 1970ies [94]. How dietary administration of taurine affects cholesterol metabolism has not been reported in these studies. However, in a stroke-prone substrain of the SHR rats, taurine supplementation has been indicated to prevent high-fat/high cholesterol induced elevation of serum cholesterol in SHR rats [95].

Sprague-Dawley rats. Also in male Sprague-Dawley rats fed a high-fat, high cholesterol diet (HFCD; 10% corn oil, 1.5% cholesterol) supplemented with taurine (1.5% w/w) plasma cholesterol was lowered by 31% compared to HFCD control rats [87]. LDL+VLDL cholesterol (-38%) and triglycerides (-43%) were also lower in rats supplemented with taurine compared to HFCD control rats. These results have been confirmed with an identical experimental setup for 5 weeks reporting a 20% and 25% reduction in serum total cholesterol and triglycerides, respectively [96]. In this model, plasma total cholesterol, LDL cholesterol and triglycerides were reduced in rats fed taurine supplemented cholesterol free diet compared the cholesterol free control diet [87].

3.1.3. *Effects of taurine on cholesterol levels in rabbits*

Different rabbit strains have been used to investigate the effects of dietary taurine supplementation on dietary induced hypercholesterolemia [86, 97, 98]. The results from the administration of taurine to rabbits have been ambiguous. In *Male New Zealand white rabbits*, fed a high cholesterol (1% w/w) diet, addition of 2.5% taurine (w/w) for 2.5 month reduced the serum total cholesterol and triglyceride levels by 22% and 38%, respectively, compared to high cholesterol diet alone [99]. In this study similar reductions were observed for hepatic and aorta lipid levels in these rabbits. However, when the same rabbit strain were given normal chow supplemented with 0.5% cholesterol (w/w) for 4 weeks no effect of dietary taurine (2.5% w/w) supplementation was observed [100]. Also when given a normal diet supplemented with 2% cholesterol (w/w), taurine added to the drinking water (0.1 or 0.5% w/v) for 14 weeks had no influence on serum cholesterol and triglycerides [97].

3.1.4. *Effects of taurine on cholesterol levels in hamsters*

Hamsters (Male Golden Syrian hamsters) have also been used as model for studying cholesterol metabolism. The rationale for this is that hamsters and humans have comparable blood cholesterol levels, hamsters use both taurine and glycine for bile acid conjugation and the lipoprotein profile in response to dietary cholesterol is comparable [101]. When Male Golden Syrian hamsters were fed a normal chow supplemented with 0.05% cholesterol or a 10% coconut oil, high-fat diet (0.05% cholesterol) for two weeks, taurine dissolved in

drinking water (1% w/v) reduced serum total cholesterol in chow- (15% reduction) as well as high-fat diet-fed (42% reduction) hamsters [102]. A similar effect was observed for non-HDL (LDL+VLDL) cholesterol.

Recently, lipid metabolism has been closely studied in Male Golden Syrian Hamsters fed different diets with or without taurine for 4 weeks [103]. The groups received a high fat diet (chow mixed with 7% butter [w/w] and 0.2% cholesterol [w/w]) and drinking water without or supplemented with either 0.35% or 0.7% taurine (w/v). Hamsters given taurine was smaller, had less visceral fat and smaller livers after 4 weeks. Both taurine concentrations resulted in significant lower serum triglycerides, total cholesterol, and LDL+VLDL cholesterol. Up-regulated gene expression of the low-density lipoprotein receptor and CYP7A1 genes, paralleled by increased faecal cholesterol and bile acid concentrations in the taurine treated hamsters, indicated that the taurine effect on the cholesterol and lipid profiles is due to increased cholesterol metabolism.

3.1.5. *Effects of taurine on cholesterol levels in humans*

Historically, taurine has been believed to decrease blood cholesterol levels in adults. Only a limited number of studies have investigated the effect of oral taurine supplementation on blood cholesterol or lipoprotein levels in humans and ambiguous results have arisen from these. Early studies found no effect on serum cholesterol after incidental treatment of patients with 1.5 to 3 g taurine/day for up to 2 months [77, 104, 105]. To our knowledge there has been no well-designed random controlled clinical trial assessing the dose-response effect of oral taurine supplementation on blood lipids in healthy humans. However, the effect of taurine in relation to development of CVD has been documented through a human clinical trial. Results of a 7 week human intervention trial revealed that supplementation with 0.4 g taurine/day in combination with omega-3 fatty acids (1 g EPA+DHA/day) significantly improved the lipid profiles by reducing serum total and LDL cholesterol levels compared to supplementation with omega-3 fatty acids alone [106]. In another study the effects of oral supplementation with taurine (3 g/day) or placebo for 7 weeks was assessed in young obese healthy subjects [107]. In this study, taurine had no effect on serum cholesterol, but triglycerides and bodyweight was significantly reduced compared to placebo effect. Finally, a daily 6 g taurine supplementation to human healthy volunteers receiving a cholesterol-inducing diet for 3 weeks attenuated the expected increase of serum total cholesterol and LDL-cholesterol, whereas serum VLDL-cholesterol and triglyceride levels compared to the control group [108]. In insulin-dependent diabetes mellitus patients intake of taurine (1 g/day) reduced serum triglyceride levels, but no effect was observed on serum cholesterol [109]. Finally, in a randomized, double-blinded, crossover intervention, overweight non-diabetic men given a daily dose of 1.5 g taurine or placebo, no effect was reported on blood lipids [71]. In summary, results from oral taurine supplementation to humans are ambiguous, and further adequately designed interventions are warranted to further investigate the potential of taurine as a hypocholesterolemic agent.

4. Effects of taurine on atherogenesis/development of atherosclerosis

High blood cholesterol levels is the most pronounced risk factor for developing atherosclerosis, vascular inflammation and hardening of the arteries associated with excess cholesterol deposition in the vasculature. Apart from humans and monkeys, wild animals normally do not develop substantial atherosclerosis. There is however, an array of laboratory animal models in common use for studying the effects of pharmacological substances and dietary modifications on lesion formation. The effect of taurine has been investigated in several of these models.

4.1. Effects of taurine on atherosclerosis in mice

In the hyperlipidemic apoE^{-/-} mice, taurine has been reported to delay atherogenesis by decreasing oxidized substances that cause inflammation, as well as increasing HDL-cholesterol [82]. Also in apoE^{-/-} mice fed a normal rodent chow supplemented with 2% taurine (w/w) for 12 weeks, formation of atherosclerotic lesions were significantly reduced [81]. However this effect was independent of serum cholesterol as VLDL, LDL, and total cholesterol were increased.

Moreover, in spontaneously hyperlipidemic mice, taurine (1% w/v) provided through drinking water, was reported to suppress the development of lesion formation without affecting the levels of serum VLDL and LDL [82].

In our lab, apoE^{-/-}-mice were given Western diets (WD) containing 20% fat (w/w), 0.2% cholesterol (w/w) for 13 weeks [110]. The mice received WD, WD supplemented with 0.5% taurine (w/w) or WD supplemented with 0.5% taurine (w/w) in combination with a daily dose of marine long-chain omega-3 polyunsaturated fatty acids (n-3 PUFA) recommend in the dietary guidelines for humans. In these studies, taurine did not affect serum cholesterol or triglyceride levels alone or combination with n-3 PUFA. This may indicate that a larger supplementary dose of taurine is needed to prevent dietary induced hypercholesterolemia in apoE^{-/-}-mice.

4.2. Effects of taurine on lipid lesion formation in rats

Rats are generally not a suitable animal model for atherosclerosis as they do not develop lesion deposits resembling the early phase of human atherogenesis. However, in a rat model of balloon induced vascular neointima formation, supplementation with taurine (3% in drinking water) from 2 days before the surgical procedure and 14 days after, reduced vascular smooth muscle cell proliferation [111]. This key step in the initiation of atherogenesis was reduced by 28% compared to control fed rats. Taurine was located immunohistochemically mainly to the surface of the exposed media and adventitia of the injured carotid artery and higher levels were observed in the taurine treated rats. This corresponded to a lower vascular production of superoxide anion compared to the control animals. From these experiments it was concluded that the preventive effect of taurine towards neointima formation was attributable to anti-oxidative effects.

4.3. Effects of taurine on atherosclerosis in rabbits

The effect of dietary taurine on development of atherosclerosis has been investigated in different rabbit strains. Taurine has been indicated to prevent progression of atherosclerotic lesions in rabbits without affecting serum cholesterol in two different models. In New-Zealand white male rabbits given a diet containing 2% cholesterol (w/w), taurine added to the drinking water (0.1 or 0.5% w/v) for 14 weeks reduced the aortic deposition of fat [97]. This so-called anti-atherosclerotic effect was only significant for the highest taurine dose tested. Recently, it was indicated that the taurine antiatherosclerotic effect was evident in these rabbits after only 4 weeks on the atherogenic diet [100]. *Watanabe heritable hyperlipidemic (WHHL) rabbits* carries an inheritable mutation in the LDL receptor and is hence a typical genetically hyperlipidemic animal model. When WHHL rabbits were given drinking water containing 1% taurine (w/v) for 6 months they developed significantly less atherosclerotic lesion formation compared to rabbits not supplemented with taurine [112].

4.4. Effects of taurine on atherosclerosis in humans

Results on the effects of dietary taurine in humans are mainly from prospective studies. It is evident that individuals with high urinary excretion of taurine and high dietary intake of food high in taurine in general have fewer incidences of cardiovascular diseases compared to individuals with low dietary intake of taurine [33]. In addition, increased dietary intake of taurine either alone or in the combination with omega-3 fatty acids, has also been suggested to reduce MCP-1, an important risk factor of CVD [106]. No further randomised clinical trials on the effects of dietary supplementation of taurine on CVD disease markers has been reported.

5. Conclusion

Taurine appears to be able to prevent hypercholesterolemia and hepatic steatosis induced by high-fat and high-cholesterol diets in most animal models. The major mechanism by which taurine lowers serum cholesterol levels is by increased utilization of cholesterol for bile acid synthesis. In mice, rats, and hamsters, dietary intake of taurine cause reduction in diet-induced serum cholesterol accompanied by enhanced mRNA expression and enzymatic activity of 7 α -hydroxylase, the rate-limiting enzyme of bile acid synthesis. In normal diets taurine does not appear to modify serum and liver cholesterol levels.

Dietary supplementation with taurine is indicated to have cardiovascular benefits. The effect on atherosclerosis appears to be highly dose- and model-dependent. In animal experiments using high-fat diets to induce increased levels of lipids, taurine has been demonstrated to significantly alleviate atherosclerotic lesions. The effects of taurine appear to be related to increased degradation and excretion of cholesterol as bile in the feces and the most common feature is that taurine increases expression and activity of cholesterol 7 α -hydroxylase. Only a few studies have evaluated the effects of taurine in human subjects.

From the available data it is not possible to conclude about the proposed antihyperlipidemic and antiatherosclerotic, therefore more basic and clinical research on the effects of taurine supplementation on hypercholesterolemic and atherosclerotic effects are warranted. Randomized clinical trials of dietary taurine and taurine sources may provide further knowledge about the potential hypocholesterolemic and antiatherogenic effects of long-term dietary taurine supplementation in healthy volunteers and humans with hyperlipidemia, metabolic syndrome and cardiovascular diseases.

Author details

Karl-Erik Eilertsen, Rune Larsen,
Hanne K. Mæhre, Ida-Johanne Jensen and Edel O. Elvevoll
University of Tromsø, Norway

6. References

- [1] Demarcay H. Ueber die Natur der Galle. *Annalen der Pharmacie*. 1938;27(3):270-291.
- [2] Huxtable RJ. Physiological actions of taurine. *Physiological Reviews*. 1992;72(1):101-163.
- [3] Jacobsen JG, Smith LH. Biochemistry and physiology of taurine and taurine derivatives. *Physiological Reviews*. 1968;48(2):424-.
- [4] Belluzzi O, Puopolo M, Benedusi M, Kratskin I. Selective neuroinhibitory effects of taurine in slices of rat main olfactory bulb. *Neuroscience*. 2004;124(4):929-944.
- [5] Giehl TJ, Qoronfle MW, Wilkinson BJ. Transport, nutritional and metabolic studies of taurine in staphylococci. *Journal of General Microbiology*. 1987;133:849-856.
- [6] Atmaca G. Antioxidant effects of sulfur-containing amino acids. *Yonsei Medical Journal*. 2004;45(5):776-788.
- [7] Schaffer S, Azuma J, Takahashi K, Mozaffari M. Why is taurine cytoprotective? In: Lombardini JB, Schaffer SW, Azuma J, editors. *Taurine 5: Beginning the 21st Century*2003. p. 307-321.
- [8] Schuller-Levis GB, Park E. Taurine and its chloramine: Modulators of immunity. *Neurochemical Research*. 2004;29(1):117-126.
- [9] Wojtecka-Lukasik E, Czuprynska K, Maslinska D, Gajewski M, Gujski M, Maslinski S. Taurine - chloramine is a potent antiinflammatory substance. *Inflammation Research*. 2006;55:17-18.
- [10] Lambert IH. Regulation of the cellular content of the organic osmolyte taurine in mammalian cells. *Neurochemical Research*. 2004;29(1):27-63.
- [11] Oja SS, Saransaari P. Taurine as osmoregulator and neuromodulator in the brain. *Metab Brain Dis*. 1996;11(2):153-164.
- [12] Olson JE, Martinho E. Regulation of taurine transport in rat hippocampal neurons by hypo-osmotic swelling. *Journal of Neurochemistry*. 2006;96(5):1375-89.
- [13] Markwell PJ, Earle KE. Taurine - an essential nutrient for the cat - a brief review of the biochemistry of its requirement and the clinical consequences of deficiency. *Nutrition Research*. 1995;15(1):53-8.

- [14] Schuller-Levis G, Park E. Is taurine a biomarker? *Advances in Clinical Chemistry*. 2006;41:1-21.
- [15] Stapleton PP, Charles RP, Redmond HP, Bouchier-Hayes DJ. Taurine and human nutrition. *Clinical Nutrition*. 1997;16(3):103-108.
- [16] Bouckennooghe T, Remacle C, Reusens B. Is taurine a functional nutrient? *Current Opinion in Clinical Nutrition and Metabolic Care*. 2006;9(6):728-733.
- [17] Wojcik OP, Koenig KL, Zeleniuch-Jacquotte A, Costa M, Chen Y. The potential protective effects of taurine on coronary heart disease. *Atherosclerosis*. 2010;208(1):19-25.
- [18] Zulli A. Taurine in cardiovascular disease. *Current Opinion in Clinical Nutrition and Metabolic Care*. 2011;14(1):57-60.
- [19] Laidlaw SA, Shultz TD, Cecchino JT, Kopple JD. Plasma and urine taurine levels in vegans. *American Journal of Clinical Nutrition*. 1988;47(4):660-663. Epub 1988/04/01.
- [20] Rana SK, Sanders TA. Taurine concentrations in the diet, plasma, urine and breast milk of vegans compared with omnivores. *British Journal of Nutrition*. 1986;56(1):17-27. Epub 1986/07/01.
- [21] Laidlaw SA, Grosvenor M, Kopple JD. The taurine content of common foodstuffs. *Journal of Parenteral and Enteral Nutrition*. 1990;14(2):183-188.
- [22] Lourenco R, Camilo ME. Taurine: a conditionally essential amino acid in humans? An overview in health and disease. 2002;17:262-270.
- [23] Brosnan JT, Brosnan ME. The sulfur-containing amino acids: An overview. *Journal of Nutrition*. 2006;136(6):1636S-1640S.
- [24] Stipanuk MH, Dominy JE, Lee JI, Coloso RM. Mammalian cysteine metabolism: New insights into regulation of cysteine metabolism. *Journal of Nutrition*. 2006;136(6):1652S-1659S.
- [25] Delarosa J, Stipanuk MH. Evidence for a rate-limiting role of cysteinesulfinate decarboxylase activity in taurine biosynthesis *in vivo*. *Comparative Biochemistry and Physiology B-Biochemistry & Molecular Biology*. 1985;81(3):565-571.
- [26] Jacobsen JG, Smith LH. Comparison of decarboxylation of cysteine sulphinic acid-1-14C and cysteic acid-1-14C by human, dog, and rat liver and brain. *Nature*. 1963;200(490):575-577.
- [27] Worden JA, Stipanuk MH. A comparison by species, age and sex of cysteinesulfinate decarboxylase activity and taurine concentration in liver and brain of animals. *Comparative Biochemistry and Physiology B-Biochemistry & Molecular Biology*. 1985;82(2):233-239.
- [28] Stipanuk MH. Role of the liver in regulation of body cysteine and taurine levels: A brief review. *Neurochemical Research*. 2004;29(1):105-110.
- [29] Lourenco R, Camilo ME. Taurine: a conditionally essential amino acid in humans? An overview in health and disease. *Nutricion hospitalaria : organo oficial de la Sociedad Espanola de Nutricion Parenteral y Enteral*. 2002;17(6):262-270. Epub 2003/01/08.
- [30] Tappaz ML. Taurine biosynthetic enzymes and taurine transporter: Molecular identification and regulations. *Neurochemical Research*. 2004;29(1):83-96.
- [31] Dawczynski C, Schubert R, Jahreis G. Amino acids, fatty acids, and dietary fibre in edible seaweed products. *Food Chemistry*. 2007;103(3):891-839.

- [32] Kataoka H, Ohnishi N. Occurrence of Taurine in Plants. *Agricultural and Biological Chemistry*. 1986;50(7):1887-1888.
- [33] Yamori Y, Taguchi T, Hamada A, Kunimasa K, Mori H, Mori M. Taurine in health and diseases: consistent evidence from experimental and epidemiological studies. *Journal of Biomedical Science*. 2010;17:S6
- [34] Dragnes BT, Larsen R, Ernstsens MH, Maehre H, Elvevoll EO. Impact of processing on the taurine content in processed seafood and their corresponding unprocessed raw materials. *International Journal of Food Sciences and Nutrition*. 2009;60(2):143-152.
- [35] Gormley TR, Neumann T, Fagan JD, Brunton NP. Taurine content of raw and processed fish fillets/portions. *European Food Research and Technology*. 2007;225(5-6):837-842.
- [36] Mierke-Klemeyer S, Larsen R, Oehlenschlager J, Maehre H, Elvevoll EO, Bandarra NM, et al. Retention of health-related beneficial components during household preparation of selenium-enriched African catfish (*Clarias gariepinus*) fillets. *European Food Research and Technology*. 2008;227(3):827-833.
- [37] Purchas RW, Triumf EC, Egelandsdal B. Quality characteristics and composition of the longissimus muscle in the short-loin from male and female farmed red deer in New Zealand. *Meat Science*. 2010;86(2):505-510.
- [38] Roe DA, Weston MO. Potential significance of free taurine in the diet. *Nature*. 1965;205:287-288.
- [39] Shiau CY, Pong YJ, Chiou TK, Chai TY. Free amino acids and nucleotide-related compounds in milkfish (*Chanos chanos*) muscles and viscera. *Journal of Agricultural and Food Chemistry*. 1996;44(9):2650-2553.
- [40] Suzuki T, Hirano T, Shirai T. Distribution of Extractive Nitrogenous Constituents in White and Dark Muscles of Fresh-Water Fish. *Comparative Biochemistry and Physiology B-Biochemistry & Molecular Biology*. 1990;96(1):107-111.
- [41] Suzuki T, Hirano T, Suyama M. Free Imidazole Compounds in White and Dark Muscles of Migratory Marine Fish. *Comparative Biochemistry and Physiology B-Biochemistry & Molecular Biology*. 1987;87(3):615-619.
- [42] Triumf EC, Purchas RW, Mielnik M, Maehre HK, Elvevoll E, Slinde E, et al. Composition and some quality characteristics of the longissimus muscle of reindeer in Norway compared to farmed New Zealand red deer. *Meat Science*. 2012;90(1):122-129.
- [43] Zhao XH, Jia JB, Lin Y. Taurine content in Chinese food and daily taurine intake of Chinese men. *Taurine*. 1998;442:501-505.
- [44] Lange R. Osmotic function of amino acids and taurine in mussel, *mytilus edulis*. *Comparative Biochemistry and Physiology*. 1963;10(2):173-179.
- [45] Bradley HC. The occurrence of taurine in invertebrate muscle. *Science*. 1904;20:25.
- [46] Schmidt CLA, Watson T. A method for the preparation of taurine in large quantities. *Journal of Biological Chemistry*. 1918;33(3):499-500.
- [47] Larsen R, Elvevoll EO. Water uptake, drip losses and retention of free amino acids and minerals in cod (*Gadus morhua*) fillet immersed in NaCl or KCl. *Food Chemistry*. 2008;107(1):369-376.
- [48] Larsen R, Stormo SK, Dragnes BT, Elvevoll EO. Losses of taurine, creatine, glycine and alanine from cod (*Gadus morhua* L.) fillet during processing. *Journal of Food Composition and Analysis*. 2007;20(5):396-402.

- [49] Purchas RW, Busboom JR, Wilkinson BHP. Changes in the forms of iron and in concentrations of taurine, carnosine, coenzyme Q(10), and creatine in beef longissimus muscle with cooking and simulated stomach and duodenal digestion. *Meat Science*. 2006;74(3):443-449.
- [50] Saidi B, Warthesen JJ. Analysis and Heat-Stability of Taurine in Milk. *Journal of Dairy Science*. 1990;73(7):1700-1706.
- [51] Geiss KR, Jester I, Falke W, Hamm M, Waag KL. The Effect of a Taurine-Containing Drink on Performance in 10 Endurance-Athletes. *Amino Acids*. 1994;7(1):45-56.
- [52] Seidl R, Peyrl A, Nicham R, Hauser E. A taurine and caffeine-containing drink stimulates cognitive performance and well-being. *Amino Acids*. 2000;19(3-4):635-642.
- [53] Authority EFS. Scientific Opinion of the Panel on Food Additives and Nutrient Sources added to Food on a request from the Commission on the use of taurine and D-glucurono-g-lactone as constituents of the so-called "energy" drinks. 2009;935: 1-31. *The EFSA Journal*. 2009;935:1-31.
- [54] Shao A, Hathcock JN. Risk assessment for the amino acids taurine, l-glutamine and l-arginine. *Regulatory Toxicology and Pharmacology*. 2008;50(3):376-399.
- [55] Chesney RW. Taurine - Is It Required for Infant Nutrition. *Journal of Nutrition*. 1988;118(1):6-10.
- [56] Verner A, Craig S, McGuire W. Effect of taurine supplementation on growth and development in preterm or low birth weight infants. *Cochrane Database of Systematic Reviews*. 2007(4).
- [57] Sturman JA, Gaull GE. Taurine in the Brain and Liver of Developing Human and Monkey. *Journal of Neurochemistry*. 1975;25(6):831-835.
- [58] Chapman GE, Greenwood CE. Taurine in nutrition and brain development. *Nutrition Research*. 1988;8(8):955-968.
- [59] Gaull GE. Taurine in pediatric nutrition: review and update. *Pediatrics*. 1989;83(3):433-442. Epub 1989/03/01.
- [60] Yamauchitakahara K, Azuma J, Kishimoto S. Taurine protection against experimental arterial calcinosis in mice. *Biochemical and Biophysical Research Communications*. 1986;140(2):679-683.
- [61] Yamori Y, Liu L, Mizushima S, Ikeda K, Nara Y, Group CS. Male cardiovascular mortality and dietary markers in 25 population samples of 16 countries. *Journal of Hypertension*. 2006;24(8):1499-1505.
- [62] Yamori Y, Liu LJ, Ikeda K, Miura A, Mizushima S, Miki T, et al. Distribution of twenty-four hour urinary taurine excretion and association with ischemic heart disease mortality in 24 populations of 16 countries: Results from the WHO-CARDIAC Study. *Hypertension Research*. 2001;24(4):453-457.
- [63] Hagar HH, El Etter E, Arafa M. Taurine attenuates hypertension and renal dysfunction induced by cyclosporine A in rats. *Clinical and Experimental Pharmacology and Physiology*. 2006;33(3):189-196.
- [64] Hu JM, Xu XL, Yang JC, Wu GF, Sun CM, Lv QF. Antihypertensive Effect of Taurine in Rat. In: Azuma J, Schaffer SW, Ito T, editors. *Advances in Experimental and Medical Biology*. 2009. p. 75-84.
- [65] Militante JD, Lombardini JB. Treatment of hypertension with oral taurine: experimental and clinical studies. *Amino Acids*. 2002;23(4):381-393.

- [66] Nandhini AT, Thirunavukkarasu V, Anuradha CV. Potential role of kinins in the effects of taurine in high-fructose-fed rats. *Canadian Journal of Physiology and Pharmacology*. 2004;82(1):1-8.
- [67] Azuma M, Takahashi K, Fukuda T, Ohyabu Y, Yamamoto I, Kim S, Iwao H, Schaffer SW, Azuma J. Taurine attenuates hypertrophy induced by angiotensin II in cultured neonatal rat cardiac myocytes. *European Journal of Pharmacology*. 2000;403(3):181-188.
- [68] Rao MR, Tao L. Effects of taurine on signal transduction steps induced during hypertrophy of rat heart myocytes. In: Schaffer S, Lombardini JB, Huxtable RJ, editors. *Taurine 3: Cellular and Regulatory Mechanisms*1998. p. 137-143.
- [69] Franconi F, Di Leo MAS, Bennardini F, Ghirlanda G. Is taurine beneficial in reducing risk factors for diabetes mellitus? *Neurochemical Research*. 2004;29(1):143-150.
- [70] Franconi F, Loizzo A, Ghirlanda G, Seghieri G. Taurine supplementation and diabetes mellitus. *Current Opinion in Clinical Nutrition and Metabolic Care*. 2006;9(1):32-36.
- [71] Brons C, Spohr C, Storgaard H, Dyerberg J, Vaag A. Effect of taurine treatment on insulin secretion and action, and on serum lipid levels in overweight men with a genetic predisposition for type II diabetes mellitus. *European Journal of Clinical Nutrition*. 2004;58(9):1239-1247.
- [72] Ito T, Schaffer SW, Azuma J. The potential usefulness of taurine on diabetes mellitus and its complications. *Amino Acids*. 2012;42(5):1529-1539.
- [73] Fang YJ, Chiu CH, Chang YY, Chou CH, Lin HW, Chen MF, Chen YC. Taurine ameliorates alcoholic steatohepatitis via enhancing self-antioxidant capacity and alcohol metabolism. *Food Research International*. 2011;44(9):3105-3110.
- [74] Kerai MDJ, Waterfield CJ, Kenyon SH, Asker DS, Timbrell JA. Reversal of ethanol-induced hepatic steatosis and lipid peroxidation by taurine: A study in rats. *Alcohol and Alcoholism*. 1999;34(4):529-541.
- [75] Wu GF, Yang JC, Sun CM, Luan XH, Shi J, Hu JM. Effect of Taurine on Alcoholic Liver Disease in Rats. *Advances in Experimental and Medical Biology*. 2009;643:313-22.
- [76] Gentile CL, Nivala AM, Gonzales JC, Pfaffenbach KT, Wang D, Wei YR, Jiang H, Orlicky DJ, Petersen DR, Pagliassotti MJ, Maclean KN. Experimental evidence for therapeutic potential of taurine in the treatment of nonalcoholic fatty liver disease. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*. 2011;301(6):R1710-R722.
- [77] Truswell AS, Mcveigh S, Mitchell WD, Brontest.B. Effect in Man of Feeding Taurine on Bile Acid Conjugation and Serum Cholesterol Levels. *Journal of Atherosclerosis Research*. 1965;5(5):526-529.
- [78] Murakami S, Kondo-Ohta Y, Tomisawa K. Improvement in cholesterol metabolism in mice given chronic treatment of taurine and fed a high-fat diet. *Life Sciences*. 1998;64(1):83-91.
- [79] Chen W, Matuda K, Nishimura N, Yokogoshi H. The effect of taurine on cholesterol degradation in mice fed a high-cholesterol diet. *Life Sciences*. 2004;74(15):1889-1898.
- [80] Kamata K, Sugiura M, Kojima S, Kasuya Y. Restoration of endothelium-dependent relaxation in both hypercholesterolemia and diabetes by chronic taurine. *European Journal of Pharmacology*. 1996;303(1-2):47-53.

- [81] Kondo Y, Toda Y, Kitajima H, Oda H, Nagate T, Kameo K, Murakami S. Taurine inhibits development of atherosclerotic lesions in apolipoprotein E-deficient mice. *Clinical and Experimental Pharmacology and Physiology*. 2001;28(10):809-815.
- [82] Matsushima Y, Sekine T, Kondo Y, Sakurai T, Kameo K, Tachibana M, Murakami S. Effects of taurine on serum cholesterol levels and development of atherosclerosis in spontaneously hyperlipidaemic mice. *Clinical and Experimental Pharmacology and Physiology*. 2003;30(4):295-299.
- [83] Matsuzaki Y, Miyazaki T, Miyakawa S, Bouscarel B, Ikegami T, Tanaka N. Decreased taurine concentration in skeletal muscles after exercise for various durations. *Medicine and Science in Sports and Exercise*. 2002;34(5):793-797.
- [84] Yatabe Y, Miyakawa S, Miyazaki T, Matsuzaki Y, Ochiai N. Effects of taurine administration in rat skeletal muscles on exercise. *Journal of Orthopaedic Science* 2003;8(3):415-419.
- [85] El Mesallamy HO, El-Demerdash E, Hammad LN, El Magdoub HM. Effect of taurine supplementation on hyperhomocysteinemia and markers of oxidative stress in high fructose diet induced insulin resistance. *Diabetology & Metabolic Syndrome*. 2010;2:46. Epub 2010/07/02.
- [86] Herrmann RG. Effect of taurine, glycine and beta-sitosterols on serum and tissue cholesterol in the rat and rabbit. *Circulation Research*. 1959;7(2):224-227.
- [87] Park T, Lee K, Um Y. Dietary taurine supplementation reduces plasma and liver cholesterol and triglyceride concentrations in rats fed a high-cholesterol diet. *Nutrition Research*. 1998;18(9):1559-1571.
- [88] Sethupathy S, Elanchezhiyan C, Vasudevan K, Rajagopal G. Antiatherogenic effect of taurine in high fat diet fed rats. *Indian Journal of Experimental Biology*. 2002;40(10):1169-1172.
- [89] Sugiyama K, Ohishi A, Muramatsu K. Comparison between the plasma cholesterol-elevating effects of caffeine and methionine in rats on a high cholesterol diet. *Agricultural and Biological Chemistry*. 1989;53(11):3101-3103.
- [90] Yokogoshi H, Mochizuki H, Nanami K, Hida Y, Miyachi F, Oda H. Dietary taurine enhances cholesterol degradation and reduces serum and liver cholesterol concentrations in rats fed a high-cholesterol diet. *Journal of Nutrition*. 1999;129(9):1705-1712.
- [91] Masuda M, Horisaka K. Effect of taurine and homotaurine on bile acid metabolism in dietary hyperlipidemic rats. *Journal of pharmacobio-dynamics*. 1986;9(11):934-940. Epub 1986/11/01.
- [92] Fukuda N, Yoshitama A, Sugita S, Fujita M, Murakami S. Dietary Taurine Reduces Hepatic Secretion of Cholesteryl Ester and Enhances Fatty Acid Oxidation in Rats Fed a High-Cholesterol Diet. *Journal of Nutritional Science and Vitaminology*. 2011;57(2):144-149.
- [93] Mochizuki H, Takido J, Oda H, Yokogoshi H. Improving effect of dietary taurine on marked hypercholesterolemia induced by a high-cholesterol diet in streptozotocin-induced diabetic rats. *Bioscience Biotechnology and Biochemistry*. 1999;63(11):1984-1987.
- [94] Nara Y, Yamori Y, Lovenberg W. Effect of Dietary Taurine on Blood-Pressure in Spontaneously Hypertensive Rats. *Biochemical Pharmacology*. 1978;27(23):2689-2692.

- [95] Murakami S, Yamagishi I, Asami Y, Ohta Y, Toda Y, Nara Y, Yamori Y. Hypolipidemic effect of taurine in stroke-prone spontaneously hypertensive rats. *Pharmacology*. 1996;52(5):303-313.
- [96] Choi MJ, Kim JH, Chang KJ. The effect of dietary taurine supplementation on plasma and liver lipid concentrations and free amino acid concentrations in rats fed a high-cholesterol diet. In: Oja SS, Saransaari P, editors. *Taurine 62006*. p. 235-242.
- [97] Petty MA, Kintz J, Difrancesco GF. The effects of taurine on atherosclerosis development in cholesterol-fed rabbits. *European Journal of Pharmacology*. 1990;180(1):119-127.
- [98] Takenaga T, Imada K, Otomo S. Hypolipidemic effect of taurine in golden Syrian hamsters. *Taurine 4: Taurine and Excitable Tissues*. 2000;483:187-192.
- [99] Balkan J, Kanbagli O, Hatipoglu A, Kucuk M, Cevikbas U, Aykac-Toker G, Uysal M. Improving effect of dietary taurine supplementation on the oxidative stress and lipid levels in the plasma, liver and aorta of rabbits fed on a high-cholesterol diet. *Bioscience Biotechnology and Biochemistry*. 2002;66(8):1755-1758.
- [100] Zulli A, Lau E, Wijaya BPP, Jin X, Sutarga K, Schwartz GD, Learmont J, Wookey PJ, Zinellu A, Carru C, Hare DL. High Dietary Taurine Reduces Apoptosis and Atherosclerosis in the Left Main Coronary Artery Association With Reduced CCAAT/Enhancer Binding Protein Homologous Protein and Total Plasma Homocysteine but not Lipidemia. *Hypertension*. 2009;53(6):1017-1022.
- [101] Nistor A, Bulla A, Filip DA, Radu A. The hyperlipidemic hamster as a model of experimental atherosclerosis. *Atherosclerosis*. 1987;68(1-2):159-173.
- [102] Murakami S, Kondo Y, Toda Y, Kitajima H, Kameo K, Sakono M, Fukuda N. Effect of taurine on cholesterol metabolism in hamsters: Up-regulation of low density lipoprotein (LDL) receptor by taurine. *Life Sciences*. 2002;70(20):2355-2366.
- [103] Chang YY, Chou CH, Chiu CH, Yang KT, Lin YL, Weng WL, Chen YC. Preventive Effects of Taurine on Development of Hepatic Steatosis Induced by a High-Fat/Cholesterol Dietary Habit. *Journal of Agricultural and Food Chemistry*. 2011;59(1):450-457.
- [104] Failey RB, Childress RH. Effect of Para-Aminobenzoic Acid on Serum Cholesterol Level in Man. *American Journal of Clinical Nutrition*. 1962;10(2):158-162.
- [105] Hellstrom K, Sjovall J. Conjugation of Bile Acids in Patients with Hypothyroidism (Bile Acids and Steroids, 105). *Journal of Atherosclerosis Research*. 1961;1(3):205-210.
- [106] Elvevoll EO, Eilertsen KE, Brox J, Dragnes BT, Falkenberg P, Olsen JO, Kirkhus B, Lamglait A, Østerud B. Seafood diets: Hypolipidemic and antiatherogenic effects of taurine and n-3 fatty acids. *Atherosclerosis*. 2008;200(2):396-402.
- [107] Zhang M, Bi LF, Fang JH, Su XL, Da GL, Kuwamori T, Kagamimori S. Beneficial effects of taurine on serum lipids in overweight or obese non-diabetic subjects. *Amino Acids*. 2004;26(3):267-271.
- [108] Mizushima S, Nara Y, Sawamura M, Yamori Y. Effects of oral taurine supplementation on lipids and sympathetic nerve tone. *Taurine 2*. 1996;403:615-622.
- [109] Elizarova EP, Nedosugova LV. First experiments in taurine administration for diabetes mellitus - The effect on erythrocyte membranes. In: Huxtable RJ, Azuma J, Kuriyama K, Nakagawa M, Baba A, editors. *Taurine 2: Basic and Clinical Aspects* 1996. p. 583-588.

- [110] Eilertsen KE. Manuscript in preparation.
- [111] Murakami S, Sakurai T, Toda Y, Morito A, Sakono M, Fukuda N. Prevention of neointima formation by taurine ingestion after carotid balloon injury. *Vascular Pharmacology*. 2010;53(3-4):177-184.
- [112] Murakami S, Kondo Y, Sakurai T, Kitajima H, Nagate T. Taurine suppresses development of atherosclerosis in Watanabe heritable hyperlipidemic (WHHL) rabbits. *Atherosclerosis*. 2002;163(1):79-87.