TAURINE EFFECT ON GLUCOSE METABOLISM AND BLOOD GLUCOSE LEVEL IN DIABETES MELLITUS

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Abstract

Introduction: Taurine has proved to be involved in a wide range of biological processes and provides several different important health benefits. Its effects have been revealed to be exerted mainly through its antioxidant, osmoregulation and anti-inflammatory effects, among other mechanisms.
Objectives and methods: The present review is aimed to provide a solid body of evidence regarding the beneficial effects of taurine in the context of glucose metabolism in diabetes and its complications, with an special focus on the blood glucose level, cardiovascular health impairments so frequently associated to this disease, so that data from this updated systematic review of the literature, may constitute a base to back up future clinical and epidemiological studies, on the possibilities of taurine supplementation as a useful tool for both prevention and treatment of diabetes complications.
Conclusions: We consider results from the different experimental, in vitro studies as well as some clinical ones reviewed, to provide sufficient evidence as to constitute a solid base to back up future clinical and epidemiological studies on the usefulness of taurine supplementation both in the prevention and treatment of diabetes and its complications with effect on glucose metabolism and level in the blood.

Keywords: Taurine, Diabetes, Glucose, Oxidative damage, Anti-inflammation, Glucose metabolism,Hyperglycemic, Hypoglycemic, etc

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1. Introduction

Diabetes: Diabetes is a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces. Insulin is a hormone that regulates blood glucose. Hyperglycaemia, also called raised blood glucose or raised blood sugar, is a common effect of uncontrolled diabetes and over time leads to serious damage to many of the body's systems, especially the nerves and blood vessels.Taurine β-amino acid that found in very high concentrations in the cells, with levels particularly high in excitable tissues. Although taurine has many functions in mammals, its cytoprotective actions have attracted the most attention, as they dramatically alter the health and nutritional status of various species. Because taurine regulates fundamental events of cells, while altering the balance between life and death, interest in taurine's physiological functions has grown [1]. The International Diabeties Federation (IDF) Diabetes Atlas (2021) reports that 10.5% of the adult population (20-79 years) has diabetes, with almost half unaware that they are living with the condition. By 2045, IDF projections show that 1 in 8 adults, approximately 783 million, will be living with diabetes, an increase of 46% [2]. Diabetes is a prevalent endocrine disease associated with oxidative stress. Taurine appears to ameliorate diabetes 1-related complications in various organs through its antioxidant, anti-inflammatory, and anti-hormonal actions.

In type 2 diabetes, taurine has been positively implicated in glucose homeostasis, exerting potent hypoglycemic, anti-obesity, hypotensive, and hypolipidemic effects. Basically, an interest that taurine protects against renal dysfunction, including hypertension and proteinuria, specific glomerular and tubular disorders, acute and chronic renal conditions, and diabetic cardiomyopathy, nephropathy [3]. The antioxidant properties of taurine have been demonstrated in a wide range of distinct diabetic animal models, where it was shown to protect the stressful signals of insulin resistance or obesity, via various mechanisms: i) The upregulation of antioxidant enzymes, such as superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx); ii) interference with PKC activity; iii) the downregulation of nicotinamide adenine dinucleotide phosphate (NADPH) oxidase/cytochrome P450 2E1 (CYP2E1) expression ratio; iv) the inhibition of protein carbonylated (PC) content accumulation; v) the inhibition of LPO; vi) the disruption of the generation of AGEs (12-15). Based on the above, taurine could be used as an effective therapeutic agent against diabetic complications, mostly due to its anti-oxidant activity [3]. Diabetes has been associated with a decline in the levels of this important endogenous antioxidant in several tissues, which raises the possibility that this decline might negatively contribute to the severity of the oxidant-mediated damage present in the diabetic context [4]. In this paper, we will review experimental, in vitro, and clinical studies on the role of taurine on both type 1 and type 2 diabetes as well as its metabolic effects on glucose metabolism and diabetes complications [5].

2. Role of Taurine

2.1 Effect of taurine on hyperglycemia in diabetic animal models and its potential mechanisms

Hypoglycemic effect of Taurine on Diabetic animal Model and its potential mechanism. The effect of taurine administration on type 1 diabetes has been well investigated. Treatment of taurine before diabetic onset suppressed hyperglycemia and lowered plasma glycated hemoglobin, cholesterol, and triglyceride in STZ-induced type 1 diabetic rats. Treatment of taurine started from the time-point of diabetic onset failed to improve hyperglycemia in type 1 diabetic animals (Goodman and Shihabi 1990), indicating that the lowering effect of taurine on blood glucose levels in type 1 models may be due to the protection of beta cells from STZ or alloxan. This observation indicates that taurine may confer resistance against some stresses induced by hyperglycemia, which may associate with a beneficial role against the complications [6] (Table 1).

Biological effects of taurine in the context of diabetes[7]

Biological Effect of Taurine	Mechanism
Antioxidant action	By inhibiting ROS generation at mitochondria.
Osmoregulation	By counteracting osmotic imbalance through the cellular membrane due to hyperglycemia.
Anti-inflammatory effects	By interfering with the formation of inflammatory mediators.
Glucose Homeostasis	By interfering with the insulin signaling pathway acting upon the UCP2 protein.

2.2 Effects of Taurine on Glucose Homeostasis and metabolism

In the context of diabetes, taurine provides different beneficial effects which are exerted mainly through four different mechanisms of action:[7]

1. Antioxidant activities, especially relevant when exerted at cellular mitochondria.
2. Anti-inflammatory effects.
3. Osmoregulatory actions.
4. Effects on glucose homeostasis.

2.2.1 Antioxidant activity of Taurine

Although when considering the pathologies derived from diabetes, most studies have focused on the adverse effects of hyperglycemia, it is recently arousing an important number of other studies assessing the role of oxidative stress and damage as the possible link between diabetes and diabetic complications [7]. Taurine has been demonstrated to play a relevant preventive and therapeutic role through its already proven antioxidant effects which are mainly exerted at the mitochondrial level among other cellular and tissular locations, and constitute its most relevant beneficial action in the context of diabetes[8]. It was Brownlee in 2001 who initially explained that the production of reactive oxygen species (ROS) may be the fact that triggers most of the pathological complications frequently associated with diabetes.5 He thus elaborated the "unifying hypothesis of diabetes", which states that "the generation of superoxide anions in the mitochondria of glucose-treated cells, alters key reactions involved in the development of diabetic complications"[9]. On the other hand, it has been proven that diabetes is also associated with a decrease in the levels of endogenous antioxidants, particularly taurine, so oxidative damage may be enhanced by the deficiency of taurine since it frequently becomes depleted in diabetic states[10]. Although taurine by itself cannot directly scavenge classical ROS (Reactive Oxygen Species) such as superoxide anion, hydroxyl radical, and hydrogen peroxide, this amino acid has shown to be capable of inhibiting ROS generation [10].

2.2.2 Anti-inflammatory Action of Taurine

The detoxification of hypochlorous acid used to be considered the only anti-inflammatory action of taurine, but in 2003, subsequent studies by Park et al revealed that taurine-chloramine exerts important anti-inflammatory activities by itself, inhibiting the production of nitric oxide and tumor necrosis factor (TNF-α). This same group had already demonstrated in 1993 that taurine chloramine suppresses the production of IL-6B and IL-8 by polymorphonuclear cells[11]. In this context it is important to remark that type 1 diabetes is an inflammatory disease, triggered by neutrophil-mediated destruction of pancreatic -cells, so it would be of great importance to further investigate the possibility that taurine might lessen the destruction of these cells[12].

2.2.3 Taurine role as an Osmoregulator

Taurine is an important osmoregulator, participating in cell volume regulation together with other low molecular-weighted compounds [13]. In diabetes, the raised levels of extracellular glucose give place to osmotic stress for cells. To counteract the osmotic imbalance across the cellular membrane that occurs in diabetes, either the intracellular production of osmolytes or the transport of

external ones is needed. taurine, betaine, myoinositol, sorbitol, and glycerophosphorylcholine (GPC) are the most relevant intracellular osmolytes[14]. But among them, taurine and betaine have to be transported into the cell since they are not synthesized intracellularly, as occurs with the others. Taurine plays a key role in the so-called "polyol-pathway" (formation of intracellular sorbitol),[15] since this amino acid has to be transported into the cell by an active specific transporter (TauT), a protein whose expression is osmotically induced, and which is coupled to sodium and chloride ions. A study by El-Sherbeny et al provided evidence that hyperosmolarity regulates TauT activity in retinal pigment epithelial cells (RPE) and that TauT is also present in ganglion and Müller cells and it is regulated by hypertonicity. These results are relevant for further studies on the benefits of taurine supplementation in the therapy of retinopathies associated with diabetes, such as macular degeneration, in which retinal cell volume may fluctuate drastically[16].

2.2.4 Glucose homeostasis: effects of taurine on insulin secretion and action

Several studies have revealed that taurine is involved in glucose homeostasis, but the specific molecular mechanisms are [17]. Taurine exerts effects on glucose homeostasis through two known mechanisms:

a) By its effects upon β-cell insulin secretion.
b) By interfering with the insulin signaling pathway and post-receptor events.

a) In an experimental study with mice fed with a diet supplemented with and without taurine for 30 days, Carneiro et al obtained results that indicate that taurine controls glucose homeostasis by two mechanisms: by regulating the expression of genes required for the glucose-stimulated insulin secretion and by enhancing peripheral insulin sensitivity. In this study, islets were isolated from taurine-supplemented mice and control ones, and islet cell gene expression and translocation were examined. Islets from taurine-supplemented mice presented: a)-higher insulin content; b)-increased insulin secretion at stimulatory glucose concentrations; c)-slowed cytosolic Ca+2 oscillations in response to stimulatory glucose concentration; d)-increased expression of genes of insulin, sulfonylurea receptor-1, glucokinase, Glut-2, proconverstase and pancreas duodenum homeobox (PDX-1). Besides, mice supplemented with taurine had a significantly increased tyrosine phosphorylation of the insulin receptor in skeletal muscle, both at basal and insulin-stimulated states[18]. Other studies also indicate that taurine exerts hypoglycemic effects by enhancing insulin action[19], as well as by facilitating the interaction of insulin with its receptor. On the other hand, taurine increases glycogen synthesis, glycolysis, and glucose uptake in the liver and heart of adult rats. These effects were shown to be dependent of insulin concentration. In addition, taurine has been shown to better ameliorate insulin sensitivity in type 2 diabetes when compared to N-acetylcysteine in a study with humans[20].

b) Taurine interference with insulin signaling pathway.

In addition to all these studies, results from other ones show that taurine acts on several stages of the so-called stimulus-secretion coupling process. Going back to the potential role of taurine in the mitochondria of cells overexposed to glucose: oxidative mitochondrial metabolism plays a key role in the generation of the signaling cascade that couples glucose recognition to insulin secretion, in pancreatic -cells. Prolonged exposure of these cells to high concentrations of glucose generates oxidative stress, which ends up in -cell dysfunction and in some cases even in cell death[21]. Within the mitochondrial inner membrane carrier family, there is a key protein called "Uncoupling protein 2" (UCP2) which catalyzes a proton leak and subsequently hyperpolarized the mitochondrial membrane potential and reduces the cellular content. UCP2 is upregulated in pancreatic beta cells when exposed to prolonged high glucose or free fatty acids, which results in impaired glucose-induced insulin secretion (GIIS). On the other hand, GIIS, which is critical for maintaining normal blood glucose, becomes suppressed when UCP2 is overexpressed. In this study by Han et al, the effects of taurine on impaired glucose responses of diabetic rat-cell adenoviral overexpressing UCP2 were studied, which on

the other hand is also upregulated in obesity-related type 2 diabetes[21].

There is a study by Brons et al with the opposite results. The authors assessed the effect of taurine treatment on both insulin secretion and action and on plasma lipid levels, in overweight men with a positive history of type 2 diabetes. In this study, 20 nondiabetic subjects were included in a double-blinded, randomized, crossover study, receiving a daily supplementation of 1.5 g of taurine or placebo, for 8 weeks. Subjects were overweight ones and first-degree relatives of type 2 diabetes patients. An intravenous glucose tolerance test (IVGTT) was used to measure first-phase insulin secretory response, and a euglycemic hyperinsulinemic clamp was used to determine peripheral insulin action. There was no significant difference after the taurine intervention compared to the placebo in incremental insulin response, neither during IVGTT nor in insulin-stimulated glucose disposal during the clamp. Insulin secretion adjusted for insulin sensitivity was also unchanged, and there was no difference in blood lipid levels between the group receiving a placebo and the one which was supplemented with taurine.[22]

2.2.4 *Taurine and diabetes associated pathologies: the cardiovascular complications*

As it is well known, a series of pathological complications are associated with diabetes, especially when this disease has been of long-term development. According to the unifying hypothesis of diabetes, the main pathological complications associated with this are due to the oxidative damage that accompanies this pathology, thus, the possible therapeutical and/or preventive effects of taurine are based mainly on its antioxidant properties, although other actions exerted by this aminoacid also contribute to provide health benefits to diabetes patients.[7] Although we count on very few clinical trials to back up in vitro and experimental findings, a handful of them have reported that taurine supplementation has beneficial effects on platelet aggregation, nephropathy, and retinopathy, as well as on vascular dysfunction and cardiomyopathies, all of them being considered as the main clinical complications of diabetes.[13] In addition, recent studies have attributed an important role to taurine in fetal development, particularly in the case of diabetic mothers, since taurine might block the transfer of diabetes from these mothers to their offspring.[23]

Taurine has been reported to have nephroprotective properties. These may occur as a result of diminished renal NADPH oxidase activity, which is produced by the increased presence of taurine. Thus, this amino acid seems to be beneficial for the therapy of both diabetes and diabetic nephropathy: in a study by Winiarska et al,[24] the potential benefits of taurine on nephropathy associated with diabetes was investigated in alloxan diabetic rabbits. Animals were fed for three weeks with 1% taurine in their daily drinking water. Histological studies of kidneys were performed in addition to the measurement of several blood parameters. Taurine administration to diabetic rabbits resulted in a 30% decrease in serum glucose level and the normalization of diabetes elevated the rate of renal gluconeogenesis. It also diminished serum urea and creatinine concentrations and abolished hydroxyl free radicals accumulation in serum, liver, and kidney cortex. In addition, animals supplemented with taurine exhibited elevated activities of gamma-glutamylcysteine synthetase and renal glutathione reductase, and catalase. Taurine treatment evoked the normalization of the diabetes-stimulated activity of renal NADPH oxidase. Besides, taurine treatment attenuated both albuminuria and glomerulopathy which are characteristic of diabetes. The authors concluded that taurine seems to be beneficial for the therapy of both diabetes and diabetic nephropathy. These results suggest that taurine can suppress the progression of diabetic nephropathy through its antioxidant effects. Besides, Higo S. et al have referred that the development of proteinuria and the expansion of the mesangial extracellular matrix expansion were both efficiently reduced after taurine supplementation in diabetic rats.26 To view of these results, taurine administration was potentially expected to be applied in the clinical field to retard the development of nephropathy in diagnosed diabetic patients.[24] In the context of diabetic retinopathy, Yu et al have reported a decrease in the severity of this diabetic complication due to taurine supplementation, which

hypothetically exerts this beneficial effect by the inhibition of glutamate toxicity. The study was performed in rats with induced diabetes, which were fed with and without supplementation of taurine during 4-12 weeks. The supplementation did not lower plasma glucose concentration but produced an elevation in taurine content and a decline in the levels of glutamate and gamma-aminobutyric acid (GABA) in the diabetic retina ($p < 0.05$).35 Of all diabetes complications, cardiopathies, and vascular dysfunctions are among the most relevant and prevalent ones, if we take into account that 80% of deaths among diabetic patients are due to Cardiovascular Diseases (CVD).[25,26,27] Although further clinical trials are needed, we already count on some studies which demonstrate that taurine benefits cardiovascular health in diabetes patients. Some mechanisms have been proposed to explain how taurine exerts protection against CVD, namely, through the formation of bile acid conjugates to produce bile salts, which constitute the main via of excretion of cholesterol, and also through its demonstrated ability to reduce oxidative stress and inflammation.[28]

2.2.5 ***Taurine benefits cardiovascular health of diabetes patients in different aspects***

a*) Taurine protects from atherosclerosis in diabetic patients*. Some of the experimental and in vitro studies have suggested that taurine when used as a nutritional supplement, might play a relevant role as a protector against oxidative stress and atherosclerosis development.[26,27] In humans, taurine, as well as glycine, forms conjugates with bile acids (mainly cholic acid) giving place to the bile salts taurocholate and glycocholate respectively. The first one is the major bile salt that extracts cholesterol from plasma.[27] On the other hand, oral administration of taurine has been shown to increase relative amounts of taurocholic acid in the bile, whereas no effect on bile acid composition was observed when the dietary supplement administered was glycine.[28] Between 5% and 10 % of the bile acids are excreted via feces, thus bile salts are only partially reabsorbed. Due to all these facts, we can consider taurine as a relevant player in cholesterol metabolism, since the excretion of bile salts via feces, constitutes the only excretion route of cholesterol from the body, with a daily output of bile acids of about 200-1,000 mg.40 This means that low levels of taurine in the diet might give place to lower cholesterol extraction and subsequently to its accumulation in plasma, a fact that is well known to substantially increase the risk of developing atherosclerosis.[17]

b) *Taurine supplementation gives place to an improved lipidic profile*. In a study by M. Zhang et al in which the effects of taurine supplementation on the lipidic profile of overweighted subjects were studied. Thirty participants, with a Body Mass Index (BMI) $\geq$ 25 kg/ m2 were supplemented with 3g/day of taurine for 7 weeks, while the control group received a placebo. Measurements of triacylglycerol (TG), total cholesterol (TC), and high-density lipoprotein cholesterol (HDLC) were taken, before and after the intervention period, existing no difference at baseline in these parameter levels between groups. The group that received taurine supplementation presented a significant decrease in TG (of 8 mg/dl) while the group that had placebo presented an increase of 3g/dl in this parameter. These changes were statistically significantly different between the two groups (taurine and placebo), $p = 0.04$.41 These results suggest that taurine does produce an improvement in lipidic profile after supplementation. In another study with twenty-two healthy male Japanese, aged 18-25, the effects of 6g/day taurine supplementation during 3 weeks versus placebo were assessed. Participants were placed on a diet specially designed to increase their cholesterol levels. This parameter was significantly increased in the group that received a placebo, as well as their LDL-cholesterol, and LDL plasma levels, while the group receiving the taurine supplementation suffered significantly smaller increases in these parameters.[29] Nevertheless, we must remark that results from these studies, although participant subjects were obese or overweight, were neither diabetes patients nor had any evidence of diabetes at all. But results show the beneficial effects of taurine on lipidic profile and subsequently upon cardiovascular health, being both key facts in the development of diabetes complications.[7,8]

c) *Taurine exerts a protective effect on endothelial dysfunction*. As it is well known, endothelial dysfunction is a precursor of atherosclerosis. On the other hand, negative changes in the vascular endothelium are very frequently associated with diabetes, where both hyperglycemia and dyslipidemia contribute to altering this tissue.[30] More specifically, hyperglycemia is considered to be the major causal factor in the development of endothelial dysfunction in diabetes patients, mainly through the formation of advanced glycation end products (AGEs), a biochemical situation that usually appears accompanying diabetes,[31] but also through a series of other mechanisms, such as the impairment of the nitric oxide (NO) production cells: in this case, taurine has demonstrated to exert an anti-inflammatory action through the previous formation of the compound taurine-chloramine, which inhibits the production of NO and prostaglandin E2 (PGE2), by suppressing inducible nitric oxide synthase and cyclooxygenase, two enzymes which become activated by hyperglycemia.[32] Other mechanisms through which hyperglycemia leads to endothelial dysfunction are an increase in the production of vasoconstrictor prostaglandins, platelet, and vascular growth factors, among other cardiovascular phenomena, all of them leading to the onset and development of subsequent atherosclerosis.[30] In this context, a study with rats showed that microvascular inflammatory injuries caused by hyperglycemia became reverted after supplementation with taurine, which suggests that this amino acid may play a role in reducing these effects, by attenuating excess leucocyte activity through the induction of the formation of less toxic inflammatory mediators.[31] As we have stated above, antioxidation is the most relevant biological action through which taurine exerts beneficial effects on diabetes patient health. In the context of cardiopathies associated with diabetes, since taurine is considered to be an effective endogenous antioxidant, it can improve vascular endothelial dysfunction caused by oxidative stress. In a study by Wang et al. in the context of induced experimental type 1 diabetes in rats, authors showed that this effect might be associated with the downregulation of the expression of genes that encode for LOX-1 (a novel endothelial receptor for oxidized low-density lipoprotein which might mediate endothelial dysfunction) as well as those for soluble intracellular adhesion molecule-1 (sICAM-1) on aortic vascular endothelium via taurine antioxidative properties.[32,33] This study aimed to investigate the protective effect of taurine on early vascular endothelial dysfunction and its possible mechanism, by detecting the changes of oxidized-Low Density lipoprotein (oxLDL)/LOX-1 system, in young STZ-induced diabetic rats. In this, rats were divided into three groups (CN group, n = 8), diabetes mellitus group (DM group, n = 8), and taurine supplemented group (DM+TAU group, n = 8). Diabetes was induced in the rats by intraperitoneal injection of streptozotocin (STZ), (60 mg/kg) and after the onset of diabetes, the rats in the DM+TAU group were given free access to drinking water containing 1% taurine. At the end of 4 weeks, blood glucose, serum total cholesterol (TC), triglyceride (TG), low-density lipoprotein (LDL) and high-density lipoprotein (HDL), oxidized low-density lipoprotein (oxLDL), and sICAM-1 level was determined, meanwhile LOX-1 and ICAM-1 expression on abdominal aortas were examined by immunostaining, Western blotting and reverse transcription PCR, respectively. Compared to normal control, in STZ-induced diabetic rats, the levels of serum TC, TG, LDL, oxLDL, and sICAM-1 were all increased ($p < 0.01$) meanwhile LOX-1 and ICAM-1 expression (protein and mRNA) in the endothelium layers of abdominal aortas were also markedly enhanced ($p < 0.01$ for all); while in taurine supplemented rats, were all markedly lower than those of untreated diabetic rats ($p < 0.05$ for all). Also, the level of LOX-1 protein expression was positively correlated with levels of serum oxLDL ($r = 0.922$, $p = 0.001$), sICAM-1 ($r = 0.753$, $p = 0.031$), and ICAM-1 expression on abdominal aorta ($r = 0.849$, $p = 0.008$). The authors concluded that vascular endothelial dysfunction was present in the early stage of young diabetic rats and that taurine supplement could protect against this early endothelial dysfunction by its antioxidant action, consisting of the inhibition of the role of oxLDL/LOX-1 system in young rats with diabetes mellitus.[34] Another study using human umbilical cord venous endothelial cells,

reports that taurine supplementation reduces the expression of molecules such as vascular cell adhesion molecule-1 (VCAM-1), ICAM-1, and its soluble form sICAM-1 also caused by hyperglycemia In this study, cells were cultivated and exposed to a high glucose concentration medium (60 μ/ml) alone, and in the presence of taurine (0.5-2.5 mg/ml) for 20 hours. Results were given as a percentage of the low glucose medium used as a control. As expected, hyperglycemia increased cell-surface expression of VCAM1, ICAM-1, and sICAM-1, while endothelial cells cultured with added taurine, presented values restored to normal levels in the expression of these molecules, as well as those of oxidized-LDL.[35] d) Taurine has been demonstrated to lower homocysteine plasma levels: an independent marker of cardiovascular risk. Plasma Homocysteine (Hcy) has lately been used as an independent cardiovascular risk predictor.[36] On the other hand, a study by Ahn et al evidenced that taurine supplementation affects Hcy levels. The participants were 22 healthy middle-aged women (33- 54 years). After 4 weeks of supplementation with 3 g of taurine per day, plasma taurine concentration was significantly higher ($p < 001$) while the levels of plasma Hcy significantly decreased after supplementation ($p < 0.05$). [37] These results provide more data to support the idea that taurine might be a beneficial nutrient in preventing cardiovascular diseases which on the other hand, are so frequently associated with diabetes mellitus. e) Taurine exerts antiaggregant effects in the diabetic patient. It is known that diabetes mellitus patients present an increased platelet activity, which contributes to the development of diabetic complications.18 On the other hand, plasma and platelet taurine concentrations are frequently depleted in these patients.9 Taurine supplementation reduces platelet aggregation in diabetes patients, as demonstrated by Franconi et al in a study of 39 patients with insulin-dependent diabetes, and 34 control ones which were all matched for age, sex, and protein-derived daily energy intake. Patients were all supplemented with 1.5 g of Taurine for 90 days. Platelet aggregation induced by arachidonic acid was assayed in vitro at baseline, resulting to be lower in diabetic patients than in the control ones ($p < 0.01$). After the period of taurine supplementation, plasma, and platelet taurine concentration resulted significantly increased in the diabetic patients, reaching the normal values of the control group. Besides, the dose of arachidonic acid necessary to provoke platelet aggregation was significantly lower in the diabetic patients than in the control ones.[38] Nevertheless, Spohr et al did not observe any beneficial effect of taurine supplements on platelet aggregation in type 2 diabetic patients.[39] f) Taurine has positive effects on Blood Pressure. Taurine is considered to decrease blood pressure (BP) through a mechanism consisting of interference with the angiotensin II signaling, which is in charge of causing vasoconstriction and the subsequent increase in blood pressure.[40] We count on a study by the World Health Organization (WHO), the so-called WHOCARDIAC study,[41] a multicenter cross-sectional study in which an inverse correlation between 24-hour-urinary excretion of taurine and BP was found in 755 Han participants and 125 Tibetan ones. In the first population group, a correlation was found between urinary excretion of taurine and diastolic pressure, while in the second, this inverse correlation was present with both the diastolic and the systolic one. In a double-blind placebo-controlled trial, 19 borderline hypertensive patients were supplemented with 6 g. of taurine a day, which resulted in a significant decrease of systolic and diastolic BP, while the placebo group suffered no changes in this parameter.[42] To all these, we can add a study on platelets from both cats and humans, in which it was shown that platelet aggregation was associated with increased platelet levels of taurine and glutathione.[43,44] Besides, an in vitro study shows another mechanism that may explain the action through which taurine exerts a hypotensive effect, by inhibiting the production of nitric oxide and prostaglandin E2 [32]

3. Conclusions

Taurine health benefits are based mainly on its antioxidant and anti-inflammatory power as well as on its osmoregulator activity in the occurrence of hyperglycemia, on one hand, and on is participation in the formation of bile-acid conjugates (taurocholate) which helps

excrete cholesterol, and thus improves the metabolic profile of diabetes patients, both type 1 and type 2. Nevertheless, we must remark that the above-mentioned health benefits of taurine have been demonstrated mainly through animal and in vitro studies, so up to date we count on too scarce clinical studies to evidence that taurine supplementation does provide important health benefits in diabetes patients, not only in preventive perspective, but also as a coadjuvant therapeutic tool. Many more clinical studies are needed. It is important to remark though, that the use of these supplements constitutes the opening of promising therapeutic and preventive possibilities but that the efficacy and safety of such supplements, the adequate dose to be utilized, still needs much further investigation in clinical trials. Nevertheless, taurine seems to be especially useful as a coadjuvant in the therapy of diabetic complications such as retinopathy, nephropathy and particularly in the field of cardiovascular health alterations associated with diabetes. In addition to all this, studies on aminoacid formulas for PN, supplemented with taurine are in the course, to assess its potential in preventing and/or ameliorating metabolic and inflammatory alterations in patients requiring PN.

List of abbreviation

ACE--angiotensin-converting enzyme
ADA--American Diabetes Association
AUC--area under curve
BMI--body mass index
BP--blood pressure
CHD--coronary health disease
CI--confidence interval
CRS--Cambridge Risk Score
CVD--cardiovascular disease
DBP--diastolic blood pressure
FBG--fasting blood glucose
GABA-- gamma-aminobutyric acid
GTT--glucose tolerance test
HbA_{1c}--glycated haemoglobin
HDL--high-density lipoprotein
PGE-Prostaglandins
ROS—reactive oxygen species
SOD-superoxide dimutase
T2DM--type 2 diabetes mellitus
UKPDS--UK Prospective Diabetes Study
VADT--Veterans Affairs Diabetes Trial
WHO--World Health Organization

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