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Review

Protective and therapeutic effectiveness of taurine in diabetes mellitus: A rationale for antioxidant supplementation

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ABSTRACT

Taurine, 2-amino ethanesulfonic acid, is a conditionally essential β amino acid which is not utilized in protein synthesis. Taurine is one of the most abundant free amino acids in mammals tissues and is one of the three well-known sulfur-containing amino acids; the others are methionine and cysteine which are considered as the precursors for taurine synthesis. Different scientific studies emphasize on the cytoprotective properties of taurine which included antioxidation, antiapoptosis, membrane stabilization, osmoregulation, and neurotransmission. Protective and therapeutic ameliorations of oxidative stress-induced pathologies were also attributed to taurine both in experimental and human models. Data demonstrating the beneficial effectiveness of taurine against type 1 and type 2 diabetes mellitus and their complications are growing and providing a better understanding of the underlying molecular mechanisms. Although the clinical studies are limited compared to the experimental ones, the present updated systematic review of the literature is set up to provide experimental and clinical evidences regarding the effectiveness of taurine in the context of diabetes mellitus and its complications. Gathering these scientific effects of taurine on diabetes mellitus could provide the physicians and specially the endocrinologists with a comprehensive overview on possible trends in the prevention and management of the disease and its complications through antioxidant supplementation.

Contents

1. Introduction

Taurine (2-aminoethanesulfonic acid $NH_2CH_2CH_2SO_3H$) is a naturally occurring β-sulphonated amino acid. Taurine is a conditionally essential amino acid which is not utilized in protein synthesis and never incorporated into muscle proteins, and hence, occurs in the body as a free molecule or in simple peptides. Along with methionine and cysteine, taurine is a sulfur containing amino acid (Fig. 1) with a molecular weight of 125.2 and two pK_a values (at 25 °C) of 1.5 and 8.82. Biosynthesis and dietary intake are the only sources of taurine in our bodies. The precursors of taurine biosynthesis are methionine and cysteine which occurs mainly in liver. However, consumption of sea foods, very rich in taurine, and

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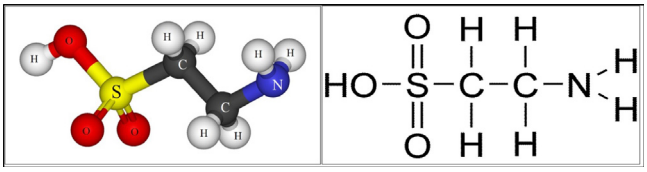

Fig. 1. Taurine three dimensional structure.

meat are almost the only sources of dietary taurine as it is reported to be very scarce in the plant kingdom. In 1827, the German professors Friedrich Tiedemann and Leopold Gmelin were the first who isolated the currently known taurine from Ox bile and they named it Gallen-Asparagin [1]. Later, it was named taurus, after the Latin *Bos taurus* which means Ox. However, the currently used name (taurine) first appeared in the literature in 1838 by von H. Demarcay [2]. Even though taurine was discovered since about two centuries, it is only in the past four decades that the clinical and nutritional magnitudes of taurine have really been examined and recognized.

Taurine is one of the most abundant free amino acid in the human body, and a 70 kg person can contain up to 70 g of taurine. In mammals, taurine is almost ubiquitous in distribution, with high concentration in electrically excitable tissues (heart and brain), retina, platelets and secretary structures [3]. Although taurine is one of the lesser-known amino acids, data from scientific studies revealed many important and beneficial effects of taurine on the human body. Depleted serum levels of taurine have been associated with many oxidative stress-induced pathologies, while taurine supplementation was found to ameliorate the picture of these pathologies and their complications. Different physiological functions and roles are modulated by taurine (Fig. 2); among these are: antioxidation; osmoregulation; membrane stabilization; conjugation of bile acids; neuromodulation; detoxification; and regulation of calcium homeostasis. Clinically, prophylactic and therapeutic taurine supplementation showed a beneficial effectiveness in a broad spectrum of oxidative stress-induced pathologies and clinical conditions including: hepatotoxicity and hepatic disorders; renal disorders; epilepsy and other seizure disorders; cardiomyopathy; cystic fibrosis; alcoholism; Alzheimer's disease; growth retardation; retinal degeneration; and diabetes mellitus [3–13].

Diabetes mellitus is a complex of metabolic syndromes due to deficiency or diminished effectiveness of insulin. Diabetes mellitus is categorized according to the pathogenic process into two main classes: Type 1 or insulin-dependent diabetes mellitus (IDDM), formerly known as juvenile diabetes and type 2 or non-insulin-dependent diabetes mellitus (NIDDM), formerly known as adult diabetes. Both types of diabetes mellitus are preceded by a period of altered glucose homeostasis as the pathogenic processes progress. Other minor classes of diabetes exist (gestational diabetes, protein-deficient pancreatic diabetes, impaired glucose tolerance and drug-induced diabetes); nevertheless, type 1 and type 2 are most likely the most dangerous forms of the disease and are certainly the most widely investigated and studied [14–16]. Both type 1 and type 2 diabetes have been associated with an increased level of oxidative stress [17] concomitant to decline in the levels of endogenous antioxidant taurine in several tissues, which might negatively contribute to the severity of the oxidant-mediated damage present in the diabetic context [18–20].

This work presents updated systematic review of the literature and emphasizes on experimental and clinical protective and therapeutic evidences regarding the effectiveness of taurine in the context of diabetes mellitus and its complications, which could offer a comprehensive overview on possible trends in the prevention and management of the disease and its complications.

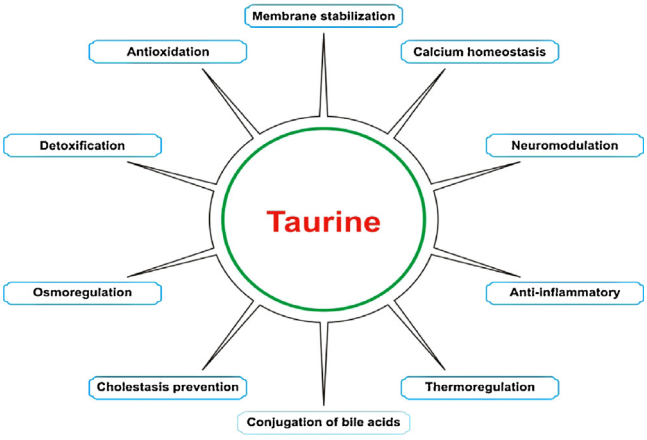

Fig. 2. Taurine physiological functions and roles.

2. Diabetes mellitus

Diabetes mellitus has been described as a heterogeneous group of disorders characterized by persistent hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Although different classes of diabetes have been proposed, type 1 and type 2 are the commonest forms of diabetes, and could be caused by a combination of genetic and environmental risk factors [16]. In addition to hyperlipidemia and glycosylation as consequences of abnormal metabolism of glucose in diabetes, the hyperglycemic state in diabetes gives rise to high risk of microvascular damages that involve retinopathy, nephropathy and neuropathy which are responsible for significant morbidity, disability, reduced life expectancy, and increased risk of macrovascular complications [21,22]. Moreover, diabetes is associated with sexual disabilities and sexual dissatisfaction which diminishes the quality of life [23–25].

In their 2006 report, the International Diabetes Foundation (IDF) and the World Health Organization (WHO) provided an estimate (171 million in the year 2000) for the prevalence worldwide, which is expected to increase to 366 million by 2030 [26]. Although controlling the hyperglycemic state in diabetes, through diets and medications, ameliorates the clinical condition, diabetes remains a very significant disorder leading to social and psychological troubles meanwhile increasing economic burden on national health care systems worldwide [27].

2.1. Oxidative stress and taurine level in diabetes mellitus

The association between diabetes mellitus and oxidative stress is well documented in the literature for both experimental and human models. Different studies assessed the role of the oxidative stress in the prognosis of diabetes and diabetic complications [28–31]. Generally, these studies attribute the high oxidative stress level in diabetes due to the imbalance between the production of the reactive oxygen species and the decline in the endogenous antioxidants in different tissues. The magnitude of such imbalance contributes to the severity of the oxidant-mediated damage present in the diabetic context [32].

The model that reactive oxygen species initiate the development of diabetic complications was suggested by Brownlee in his unifying hypothesis of diabetes. He hypothesized that the overproduction of the reactive oxygen species (ROS), superoxide anion $O_2^{\bullet-}$, in the mitochondrial electron-transport chain of glucose treated cells may alter important biochemical reactions

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