Contents lists available at SciOpen

Food Science and Human Wellness

journal homepage: https://www.sciopen.com/journal/2097-0765

China Food Publishing Co.

Taurine: a comprehensive review of its origin, pharmacological properties, potential health benefits, therapeutic applications, and safety profile

Pengfei Zhao[a], Ying Qi[b,*]

[a]Department of Pharmacology, School of Pharmacy, China Medical University, Shenyang 110122, China
[b]Department of Radiology, Shengjing Hospital of China Medical University, Shenyang 110004, China

ARTICLE INFO

Article history:
Received 29 June 2024
Received in revised form 20 September 2024
Accepted 25 October 2024

Keywords:
Health benefits
Anti-tumor
Immunomodulation
Neuroprotection
Cardiovascular protection
Anti-aging

ABSTRACT

Taurine, a multifunctional sulfur-containing amino acid and conditionally essential nutrient for humans, plays a key role in various biological processes and has attracted significant attention for its therapeutic potential. Originally isolated from ox bile, taurine has broad applications, but a comprehensive understanding of its pharmacological properties, health benefits, and safety profile remains incomplete. In this review, we critically evaluate the existing evidence on taurine's effects based on an extensive literature search of multiple databases, including PubMed, Web of Science, Scopus, ScienceDirect, Google Scholar, CNKI, and Baidu Scholar, up to May 2024. Taurine demonstrates a range of beneficial effects, including antioxidant and anti-inflammatory activities, modulation of lipid metabolism, neuroprotection, and cardiovascular protection. It has shown substantial impacts on anti-tumor activity, immune system modulation, blood pressure and lipid regulation, glycemic control, hepatobiliary protection, and potential anti-aging effects. However, the precise regulatory pathways underlying these benefits are not yet fully understood. Epidemiological studies indicate a correlation between high taurine dosage and a reduced risk of diseases. However, direct evidence from interventional studies remains insufficient, and existing clinical trials require further in-depth investigation. Concerns about improper use and potential health risks also highlight the need for thorough safety assessments. To address these gaps, we recommend conducting well-designed, long-term randomized controlled trials to establish effective doses for disease prevention and assess taurine's potential as a primary or adjunct therapy. This review aims to guide future research and support public health efforts, ultimately improving health outcomes.

1. Introduction

Calculus Bovis, a dried gallstone from the gallbladder or bile ducts of *Bos taurus domesticus* Gmelin, is a highly valued component in Traditional Chinese Medicine (TCM) and an integral ingredient in numerous proprietary Chinese medicines[1]. Renowned for its properties of clearing heat, detoxifying, resolving phlegm, and calming convulsions, it has been traditionally used to treat conditions such as delirium caused by phlegm-heat, unconsciousness, acute febrile convulsions in children, sore throat, oral ulcers, and severe infections like carbuncles and abscesses. Due to its high medicinal value and rarity, *Calculus Bovis* is considered a precious Chinese medicinal material[2].

To address the shortage of natural Calculus Bovis, Chinese pharmaceutical researchers have developed Calculus Bovis Artificialis by synthesizing components such as cow bile powder, bile acids, pig deoxycholic acid, taurine, bilirubin, cholesterol, and trace elements[3]. Among these components, taurine—the active ingredient—has

* Corresponding author at : Department of Radiology, Shengjing Hospital of China Medical University, Shenyang 110004, China
E-mail : womanman1982@163.com (Y. Qi)
Peer review under responsibility of Beijing Academy of Food Sciences.

SciOpen Publishing services by Tsinghua University Press

http://doi.org/10.26599/FSHW.2024.9250433

recently attracted extensive research attention and is considered a potential key to unlocking new directions in clinical treatment.

Taurine, chemically known as 2-aminoethanesulfonic acid or β-aminoethanesulfonic acid, with the structural formula $NH_2CH_2CH_2SO_3H$ and a molecular weight of 125.15[4-7]. Please refer to Fig. 1. It is chemically stable and can be stored at room temperature for up to 3 years when kept in a dry, sealed, and light-protected environment. In the animal body, taurine rarely participates in biochemical reactions, predominantly existing in a free form and playing crucial roles in many biological processes.

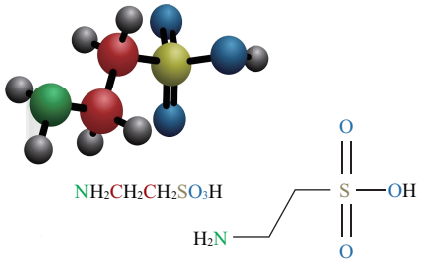

Fig. 1 Taurine spatial structure and molecular formula.

First isolated from ox bile in 1827, taurine derives its name from the Latin word taurus, meaning bull, which is why it is commonly referred to as "taurine" in modern pharmacology[8]. In TCM, Calculus Bovis containing taurine has been used for over 2 000 years[3]. Classified as a non-protein amino acid due to its lack of a genetic codon and non-involvement in protein synthesis, taurine is closely related to the metabolism of cysteine and cystine. The body obtains taurine from 2 primary sources: endogenous synthesis and dietary intake[9]. In mammals, the biosynthesis of taurine primarily occurs through the action of cysteine sulfinic acid decarboxylase (CSAD). Methionine, cystine, and cysteine are converted into hypotaurine via the decarboxylation of cysteine sulfinic acid, which is then further oxidized to form taurine[10]. The liver, brain, and heart are the primary organs involved in taurine synthesis. CSAD is generally considered the rate-limiting enzyme in taurine synthesis in mammals, with pyridoxal phosphate serving as its coenzyme[11]. Its activity reflects the capacity for taurine biosynthesis and varies significantly between different animal species, as well as among different tissues and growth stages within the same species[12]. Young animals are unable to synthesize sufficient amounts of taurine and therefore need to obtain it from their diet. In humans, the capacity for endogenous taurine synthesis is limited, and under certain conditions, such as reduced supply or increased demand, taurine deficiency may occur. Consequently, taurine is regarded as a conditionally essential nutrient for humans[13].

Due to its small molecular weight and lack of antigenicity, taurine is primarily administered orally and is easily absorbed by the digestive tract[14]. After distribution *via* the bloodstream, it is mainly metabolized in the liver and excreted by the kidneys[15]. In the body, taurine undergoes four main hepatic metabolic pathways: it conjugates with bile acids to form taurocholic acid, aiding in the digestion and absorption of fats and fat-soluble vitamins; it forms carbamoyltaurine through transamination, although its specific function remains unclear; it receives a guanidine group from arginine to form taurocyamine under the catalysis of ATP-amidino transferase, which is further phosphorylated to form phosphoryltaurocyamine, serving as a phosphate source for energy metabolism in lower animals; and it is metabolized to form ethionine, which regulates ion transfer across biological membranes[16]. In the kidneys, taurine is primarily (95%) excreted through urine, with approximately 70% excreted in its original form and 25% as sulfate conjugates[17]. Additionally, the kidneys regulate the body's taurine levels based on physiological needs and dietary intake. When taurine levels are excessive, the surplus is excreted in the urine. Conversely, when taurine is deficient, the kidneys reduce its excretion through reabsorption, thereby maintaining taurine balance within the body[18-19].

Taurine is widely distributed in human tissues and has a broad range of biological functions, including maintaining normal visual function, regulating osmotic pressure balance, stabilizing cell membranes, lowering blood glucose levels, modulating immune function, regulating lipid secretion, protecting the cardiovascular system, and regulating the nervous system. Since its significant biological roles were discovered in 1975[20-23], taurine has been the subject of extensive research. In 1989, researchers proposed that taurine is a conditionally essential amino acid for humans[24]. The discovery by Hayes et al.[25] that taurine deficiency caused blindness in young cats established its nutritional importance and prompted widespread research on its biological effects as an essential substance for regulating normal physiological functions. Recent studies have found that many systemic diseases are associated with taurine levels, and research on its potential for disease prevention and treatment is rapidly advancing. There is an urgent need to summarize previous findings to better understand and explore taurine's physiological and pharmacological effects. Therefore, this review provides a detailed overview of taurine's pharmacological properties, mechanisms of action, potential health benefits, and therapeutic applications (Fig. 2). By highlighting current research progress and identifying future research directions, we aim to facilitate the development of taurine-based interventions in clinical practice.

2. Search strategies

To conduct a comprehensive literature review on taurine, we developed a detailed search strategy to explore its multifunctional properties and implications in health and disease. Primary and secondary keywords such as "Taurine" "Anti-tumor" "Immunomodulation" and "Cardiovascular Protection", among others, were systematically searched across a variety of databases including PubMed, Web of Science, Scopus, ScienceDirect, Google Scholar, CNKI, and Baidu Scholar. The search aimed to gather a broad spectrum of peer-reviewed articles, reviews, clinical trials, and experimental studies, filtering for relevance and publications up to May 2024. The information was efficiently organized using reference management tools such as EndNote™. This comprehensive approach enabled the aggregation and evaluation of current research, providing a robust framework for discussing taurine's pharmacological properties, potential health benefits, therapeutic applications, and safety assessments.

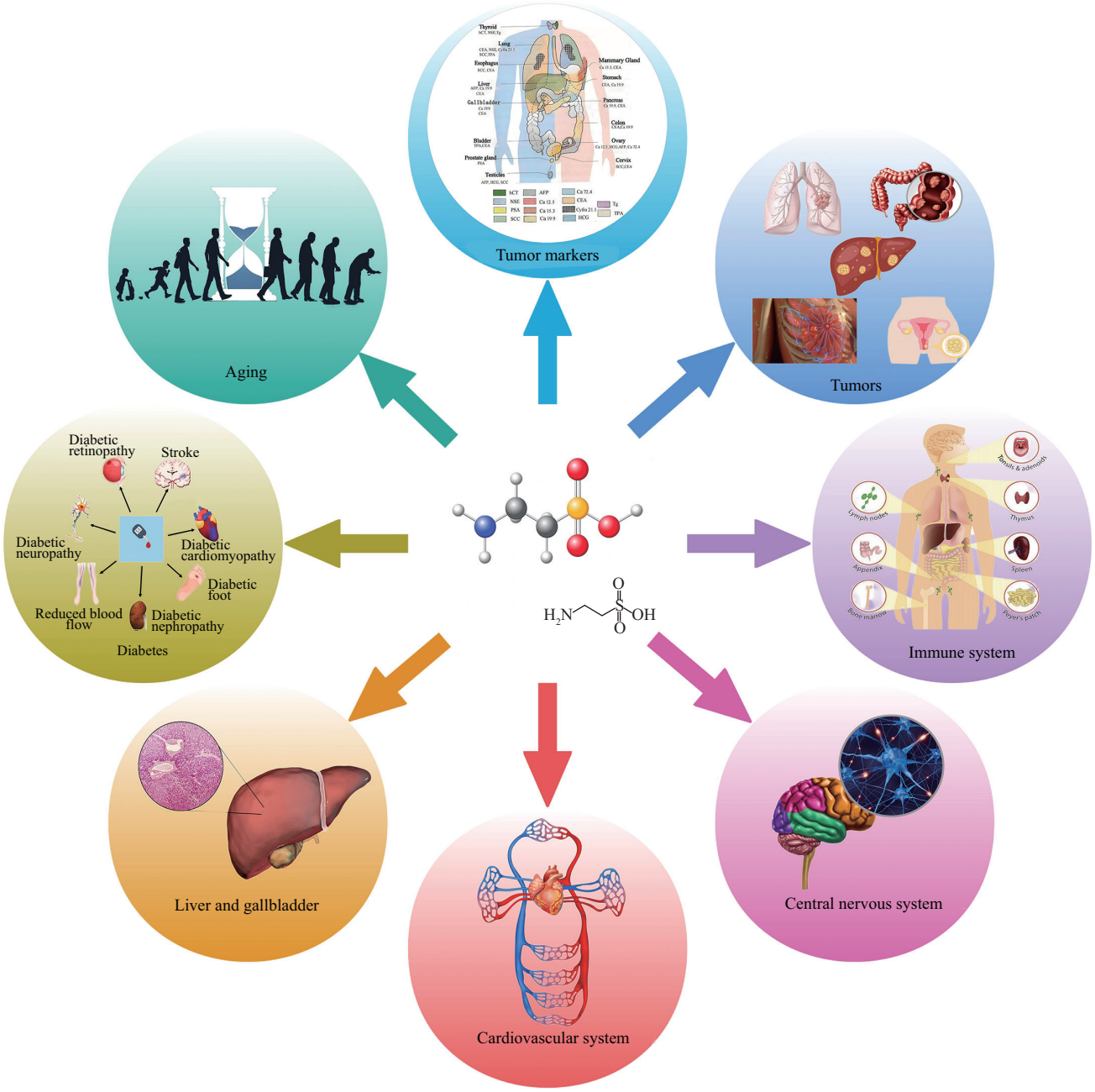

Fig. 2 Pharmacological actions of taurine and its principal clinical applications.

3. Pharmacological properties, potential health benefits, and therapeutic applications

3.1 Role of taurine in cancer prevention and treatment

3.1.1 Biomarkers of malignant tumor occurrence

Tumors represent a critical threat to human health, with both the incidence and mortality rates escalating each year globally. Despite advancements in medical science, the paucity of effective early detection markers for tumors remains a significant barrier to timely intervention and improved patient outcomes. The discovery of novel tumor biomarkers is thus essential for advancing the prevention, diagnosis, and treatment of cancer. In this context, recent research has highlighted potential breakthroughs in biomarker identification. A comparative study of plasma taurine levels between patients diagnosed with esophageal cancer and healthy individuals revealed striking differences. Utilizing high-performance liquid chromatography (HPLC), researchers found that plasma taurine concentrations in 36 patients with esophageal cancer were markedly elevated compared to those in the control group. These findings suggest that taurine levels could serve as a promising biomarker for the early detection

of esophageal cancer, potentially leading to earlier diagnosis and treatment, and ultimately, improved survival rates[26]. Another study found that taurine levels could help predict breast cancer. The serum taurine levels in breast cancer patients were significantly lower compared to high-risk patients and healthy controls. This suggests that assessing serum taurine levels in high-risk individuals could be valuable for the early diagnosis of malignant breast transformations[27]. By facilitating early detection, this biomarker could significantly enhance the clinical management and outcomes of breast cancer, supporting the development of more personalized and timely therapeutic strategies. Further evidence measured serum taurine levels in 50 patients with irregular uterine bleeding. The results indicated that serum taurine levels in patients with functional uterine bleeding, fibroids, cystic endometrial hyperplasia, and endometrial cancer were lower than those in healthy individuals by 8%, 14%, 32%, and 56%, respectively. These significant differences underscore the potential of serum taurine levels as a predictive biomarker for early-stage detection of malignant endometrial lesions[28]. The findings suggest that routine assessment of serum taurine levels in patients with irregular uterine bleeding could play a critical role in the timely diagnosis and intervention in endometrial pathologies, potentially improving patient outcomes through earlier therapeutic engagement. Magnetic resonance spectroscopy has revealed significant differences in urinary taurine levels between bladder cancer patients and healthy individuals. Bladder cancer patients exhibited elevated urinary taurine levels, while taurine was undetectable in the urine of healthy individuals[29]. This stark contrast highlights the potential of urinary taurine levels as a non-invasive and highly specific biomarker for bladder cancerr, potentially facilitating earlier and more targeted interventions. Additionally, magnetic resonance spectroscopy studies have found that taurine is closely associated with the density of apoptotic cells in astrocytomas, independent of the tumor's necrotic state. This suggests that taurine may be a reliable marker of apoptosis in astrocytomas[30]. These findings advocate for the integration of taurine level measurements in the diagnostic and monitoring protocols for astrocytomas, potentially enhancing patient management by providing a clearer picture of tumor behavior and treatment responsiveness. In summary, taurine levels vary across different tumor tissues and detection samples, making it difficult to systematically determine its significance in tumorigenesis. Future studies measuring taurine levels in the same type of samples across various tumors may help elucidate the role of taurine in cancer occurrence.

3.1.2 Enhancing efficacy and reducing toxicity of chemotherapeutic drugs

Despite the often remarkable efficacy of current antitumor drugs, their adverse effects cannot be overlooked. For instance, chemotherapeutic agents like cyclophosphamide (CTX) can cause significant damage to the bone marrow and immune system. Therefore, identifying an adjuvant that can enhance the efficacy of antitumor drugs while also reducing their adverse effects would be highly valuable for cancer treatment. A study on tumor-bearing mice treated with a combination of taurine and CTX found that taurine enhanced the tumor-inhibiting effects of CTX while also mitigating its adverse effects on bone marrow proliferation and the immune system. These findings suggest that taurine can enhance the efficacy of CTX and reduce its toxicity[31]. Additionally, taurine can enhance the antitumor effects of doxorubicin (DOX). Research has shown that while taurine does not alter the uptake of DOX by tumor cells, it significantly inhibits the efflux of DOX, thereby maintaining its concentration within the tumor cells. Moreover, taurine does not increase the concentration of DOX in normal cells. This indicates that taurine can boost the antitumor efficacy of DOX without increasing its adverse effects[32]. The combination of taurine and azelaic acid has been shown to inhibit melanin production in murine melanoma cells more effectively than azelaic acid alone, without exhibiting significant cytotoxicity[33]. The chemotherapeutic drug 5-fluorouracil (5-FU) can cause intestinal mucositis. However, current treatments for mucositis are limited in efficacy and often come with various side effects. Studies have shown that taurine administration alleviates the symptoms of intestinal mucositis, indicating that taurine may be a promising dietary strategy for treating this condition[34]. Additionally, research has shown that the taurine transporter protein SLC6A6 may be a therapeutic target for overcoming chemotherapy resistance. In colorectal cancer cells, SLC6A6 is highly expressed; knocking down *SLC6A6* reduces cell viability and increases sensitivity to 5-FU and DOX. Conversely, overexpressing *SLC6A6* enhances cell viability and multidrug resistance. Treatment with *SLC6A6*-siRNA increases the cytotoxicity of these drugs, indicating that SLC6A6 plays a crucial role in maintaining cancer stem cell characteristics and chemotherapy resistance[35]. Therefore, inhibiting SLC6A6 may be a promising therapeutic strategy for refractory colorectal cancer. Recent studies have also indicated that the taurine transporter protein SLC6A6 is associated with the aggressiveness and poor prognosis of various cancers. SLC6A6-mediated taurine uptake promotes the malignant behavior of tumor cells while enhancing the survival and effector functions of $CD8^+$ T cells. Tumor cells overexpress SLC6A6 to compete for taurine, leading to T cell death and dysfunction, thus promoting tumor progression. Supplementing taurine can rejuvenate exhausted $CD8^+$ T cells and improve the efficacy of cancer treatments[36].

3.1.3 Enhancing antioxidant capacity to inhibit tumor growth

Reactive oxygen species (ROS) are highly reactive intermediates produced during the reduction of molecular oxygen, possessing strong oxidizing capabilities. ROS can exist in both free radical and non-radical forms, and excessive free radicals can damage the body, leading to chronic diseases and aging effects. Therefore, antioxidants in the body, including both enzymatic and non-enzymatic types, play a crucial role in protecting against oxidative damage. Studies have shown that treating melanoma cells with taurine for 24 h enhances the activities of superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), and catalase (CAT). This treatment also dose-dependently reduces ROS levels, thereby inhibiting the growth of tumor cells[37]. Taurine prevents ROS-induced lung damage by enhancing the function of antioxidants, thereby exerting a protective effect against benzo[a]pyrene-induced lung cancer[38]. The mechanisms by which taurine inhibits tumor growth may include the induction of detoxification processes, the scavenging of reactive molecules, and the enhancement of DNA damage repair capabilities.

3.1.4 Enhancing immune response for tumor rejection

The immune organs include the bone marrow, thymus, spleen, and lymph nodes, while immune cells consist of phagocytes and lymphocytes. These components exert immune functions by producing antibodies, lymphokines, and lysozymes. Researchers have discovered that levamisole (Lms) and/or taurine exhibit antitumor and immunomodulatory effects in mice with ascites cancer. The combination treatments of Lms plus taurine or taurine plus CTX altered the immune profiles of $CD3^+$ $CD4^+$, $CD3^+$ $CD8^+$, $CD4^+$ $CD25^+$, and $CD11b^+$ $Ly6G^+$ splenocytes, enhancing immune surveillance against tumor cells[39]. Another study found that taurine can inhibit T cell apoptosis by reducing the expression of fatty acid synthase protein, both *in vivo* and *in vitro*. Additionally, taurine may reverse lymphocyte depletion caused by IL-2 treatment, suggesting its potential to enhance immunotherapy efficacy[40]. Additional research has shown that the functional state of $CD8^+$ T cells determines the therapeutic effectiveness of PD-1 blockade antibodies against tumors. When taurine was combined with immune checkpoint blockade therapy, there was a significant reduction in tumor growth in mouse models and a marked improvement in the function and proliferation of $CD8^+$ T cells[41]. Combining taurine with chemotherapeutic drugs has been shown to enhance peripheral white blood cell counts, bone marrow nucleated cell counts, thymus index, spleen index, splenic lymphocyte proliferation activity, and the phagocytic capacity of peritoneal macrophages in mice. Moreover, this combination reduces the adverse effects on the immune system caused by chemotherapy drugs[31]. In a melanoma lung metastasis model, researchers found that combined treatment with taurine and IL-2 significantly reduced lung nodules, increased host survival rates, and decreased both the lung wet-to-dry weight ratio and lung damage. These findings suggest that this combination enhances the efficacy of immunotherapy while reducing its toxicity[42]. Additionally, researchers have found that taurine regulates B-cell receptor (BCR)-mediated signal transduction and induces B cell activation. Taurine administration also increases IgG production and enhances overall adaptive immune responses[43]. Furthermore, researchers have investigated the positive effects of taurine on dexamethasone-induced immunosuppression in mice. Taurine intervention reversed the reduction in gut microbiota, significantly increased the total number of cells, $CD3^+$ T cells, and $CD19^+$ B cells in Peyer's patches, and restored gut homeostasis in immunosuppressed mice[44].

3.1.5 Inducing tumor cell apoptosis to inhibit tumor growth

Apoptosis is a programmed cell death process that occurs spontaneously in cells. Unlike necrosis, apoptosis does not induce an inflammatory response. Researchers used human lung cancer cell lines and a nude mouse xenograft tumor model and found that taurine significantly inhibited cell proliferation and increased apoptosis rates. Taurine upregulated the expression of PUMA and B-cell lymphoma 2 (Bcl-2)-associated X protein (Bax) while downregulating Bcl-2 expression. When taurine was combined with exogenous PUMA, the inhibition of tumor growth was even more pronounced, indicating that PUMA plays a crucial role in taurine-induced tumor suppression[45]. Researchers have investigated the effects and mechanisms of taurine-induced apoptosis in cervical cancer cells. The results demonstrated that taurine significantly inhibited the proliferation of cervical cancer cells and induced apoptosis. Furthermore, taurine upregulated the expression of mammalian sterile 20-like kinase 1 (MST1) and Bax proteins while downregulating the expression of Bcl-2 protein[46]. Additionally, taurine was found to significantly inhibit the proliferation of human hepatocellular carcinoma (HCC) cells and promote their apoptosis. By overexpressing and silencing the p53-upregulated *PUMA* gene, researchers demonstrated that modulating the *PUMA* gene significantly enhanced taurine's antiproliferative and apoptosis-inducing effects[47]. Currently, research on taurine-induced apoptosis in tumor cells is limited, primarily due to the high doses required, the associated high costs, and concerns about potential adverse effects. These factors have constrained further exploration in this area. Moreover, taurine can inhibit tumor growth through other mechanisms. Studies have shown that taurine inhibits proliferation and induces apoptosis in breast cancer cell lines MCF-7 (p53-normal) and MDA-MB-231 (p53-deficient) in a dose- and time-dependent manner, with particularly pronounced effects in p53-deficient cells. Taurine upregulates PUMA expression, modulates Bax and Bcl-2 protein levels, increases Caspase-3 activity, and promotes apoptosis. These findings suggest that taurine is a potential chemotherapeutic candidate for breast cancer, with mechanisms of action that are independent of p53 status[48].

3.1.6 Antitumor effects of taurine derivatives

Research on the antitumor effects of taurine derivatives began relatively early. Studies have found that taurine derivatives exhibit superior tumor-inhibiting effects compared to taurine itself. Taurolidine, the most extensively studied derivative, demonstrates strong antitumor properties. It inhibits tumor growth through various mechanisms, including promoting tumor cell apoptosis, inhibiting angiogenesis, reducing cell adhesion, downregulating pro-inflammatory factor release, and modulating the immune system[49]. Tauromustine is a taurine-based nitrosourea compound that exhibits high bone marrow toxicity but low liver toxicity. It can inhibit the growth of colorectal cancer and is considered more effective than traditional chemotherapy drugs[50]. Tauroursodeoxycholic acid (TUDCA) is a hydrophilic bile acid that significantly inhibits the NF-κB signaling pathway, reducing tumor cell survival, inflammation, and the expression of pro-cancer proteins. It has potential for treating colitis-associated cancer[51]. In HCC research, TUDCA has been used to investigate the effects of endoplasmic reticulum stress. Studies using a mouse HCC model have shown that TUDCA, during the prevention phase, can reduce liver function markers, decrease hepatocyte apoptosis, and lower tumor burden. TUDCA inhibits pro-apoptotic UPR by reducing eIF2α phosphorylation, lowering C/EBP homologous protein expression, and decreasing Caspase-12 activation. Additionally, it enhances IκBα expression, thereby alleviating liver inflammation. These findings suggest that TUDCA has potential as a chemopreventive agent for liver cancer[52]. chloramine taurine (TauCl) induces apoptosis in human B lymphoblastoma cells through mitochondrial oxidative damage, Caspase-9 activation, and reduction of mitochondrial membrane potential[53]. These findings suggest that taurine derivatives have stronger antitumor activity than taurine itself. Currently, the variety of taurine derivatives is limited. Future research aims to develop a broader range of taurine derivatives with enhanced antitumor effects.

3.1.7 Comparison with other agents: taurine's enhancing role in conventional and novel cancer therapies

Chemotherapeutic agents like DOX and CTX are highly effective at targeting cancer cells but are often accompanied by severe side effects, including cardiotoxicity and nephrotoxicity. In contrast, taurine offers a much safer profile and can help mitigate these toxic effects when used alongside traditional chemotherapy. This combination enhances the efficacy of the treatment while reducing the risk of compounding adverse effects, making taurine a valuable adjunct in cancer therapy.

Targeted therapies, such as tyrosine kinase inhibitors, effectively target specific molecular pathways but often lead to resistance over time[54]. In contrast, taurine's broad-spectrum approach may help reduce the likelihood of resistance, offering a more sustainable long-term solution in combination with these therapies.

Immunotherapies, such as IL-2 or PD-1 blockade antibodies, work by enhancing the body's immune response against cancer, but their effectiveness can vary[55]. Taurine complements these therapies by boosting T-cell function and proliferation, potentially leading to improved therapeutic outcomes when used in combination. This synergistic effect makes taurine a valuable adjunct to immunotherapy treatments.

Taurine's versatile approach, characterized by its potential as a biomarker and its capability to alleviate chemotherapy-induced toxicity, offers a more expansive spectrum of action compared to conventional chemotherapies. For details on taurine application in cancer prevention and treatment (Table 1).

Table 1
Applications of taurine in cancer prevention and treatment.

Biomarker or therapeutic effect	Type of research subject	Cancer types	Diagnostic criteria or mechanism of action	Reference
Biomarkers of malignant tumor onset	Human	Esophageal cancer	Plasma taurine levels are significantly elevated in patients with esophageal cancer compared to those in the healthy control group.	[26]
	Human	Breast cancer	Serum taurine levels are significantly reduced in breast cancer patients compared to both high-risk patients and healthy controls.	[27]
	Human	Malignant endometrial lesions	Serum taurine levels are lower in patients with functional uterine bleeding, fibroids, cystic endometrial hyperplasia, and endometrial cancer compared to those in healthy individuals.	[28]
	Human	Bladder cancer	Urinary taurine levels are higher in bladder cancer patients than in healthy individuals.	[29]
	Human	Astrocytoma	Taurine can serve as a biomarker for apoptosis in astrocytoma cells within the human body.	[30]
Enhancing efficacy and reducing toxicity of chemotherapeutic drugs	C57BL/6 mouse	Lung cancer	Taurine enhances the efficacy of cyclophosphamide treatment and reduces its toxicity in mice with Lewis lung cancer.	[31]
	C57BL/6 and BDF1 mouse	Ovarian sarcoma	Taurine enhances the antitumor effect of docetaxel without increasing its adverse reactions.	[32]
	Mouse B16F10 cells	Melanoma	The combined treatment of taurine and azelaic acid inhibits melanin production in mouse melanoma cells, showing a stronger inhibitory effect than azelaic acid alone, without causing significant cytotoxicity.	[33]
	Mouse, human	Colorectal cancer	Taurine can treat intestinal mucositis caused by 5-FU.	[34-35]
	Human colorectal cancer cells	Colorectal cancer	Taurine supplementation can rejuvenate depleted $CD8^+$ T cells and enhance the effectiveness of cancer treatment.	[36]
Enhancing immune response for tumor rejection	Mouse	Breast cancer	Dual therapy with Levamisole and/or taurine modifies the immunological profile of splenic cells, affecting populations such as $CD3^+$ $CD4^+$, $CD3^+$ $CD8^+$, $CD4^+$ $CD25^+$, and $CD11b^+$ $Ly6G^+$ cells.	[39]
	Mouse	Lung cancer	Following treatment with taurine and immune checkpoint inhibitor antibodies, a significant reduction in tumor growth was observed in a mouse tumor model, accompanied by notable improvements in the function and proliferation of $CD8^+$ T cells.	[41]
	Mouse B16 cells, C57BL/6 mouse	Melanoma	The combination of taurine with IL-2 enhanced the efficacy of immunotherapy while reducing the associated dose-limiting toxicity.	[42]
Enhancing antioxidant capacity to inhibit tumor growth	Mouse B16F10 cells	Melanoma	Taurine enhances the activities of SOD, glutathione peroxidase, and catalase, while reducing ROS levels, thereby inhibiting tumor cell growth.	[37]
	Mouse	Lung cancer	Taurine prevents lung damage caused by ROS by enhancing antioxidant functions, providing a protective effect against benzo[a]pyrene-induced lung cancer.	[38]
Inducing tumor cell apoptosis to inhibit tumor growth	Human A549 cells	Lung cancer	Taurine inhibits A549 lung cancer cell proliferation, boosts apoptosis, and enhances tumor suppression with PUMA.	[45]
	Human SiHa cells	Cervical cancer	Taurine suppresses the proliferation of SiHa cervical cancer cells by regulating key apoptosis-related proteins.	[46]
	Human HepG2 cells	Liver cancer	Taurine inhibits HepG2 cell growth and boosts apoptosis *via PUMA* gene regulation.	[47]
Antitumor effects of taurine derivatives	Human cancer cell lines	Multiple types of cancers	Taurolidine inhibits tumor growth by promoting apoptosis, reducing angiogenesis and cell adhesion, and modulating immune response.	[49]
	BALB/C mouse	Colorectal cancer	Tauromustine, based on taurine, exhibits strong myelotoxicity, lesser hepatotoxicity, and effectively inhibits colorectal cancer, surpassing traditional chemotherapy.	[50]
	Mouse	Colorectal cancer	Tauroursodeoxycholic acid, inhibits NF-κB, reduces tumor viability, and suppresses inflammatory proteins, showing promise for treating colorectal cancer through immune modulation.	[51]
	Mouse HCC model, HepG2 cell line, HepG2 xenograft model	Hepatocellular carcinoma	Tauroursodeoxycholic acid reduces liver function markers, hepatocyte apoptosis, and tumor burden in a mouse model of hepatocellular carcinoma. It inhibits pro-apoptotic responses and inflammation, showing potential as a chemopreventive agent without promoting tumor growth.	[52]
	Human B lymphoma cells	B-cell lymphoma	Taurine chloramine induces apoptosis in human B-cell lymphoma through pathways involving mitochondrial oxidative damage, Caspase-9 activation, and the reduction of mitochondrial membrane potential.	[53]

3.2 Immunomodulatory effects of taurine

3.2.1 Impacts on spleen, thymus, and lymph nodes

The spleen and thymus are primary immune organs in animals, playing crucial roles in both humoral and cellular immunity. Taurine is an essential amino acid for cats, making them an ideal model for studying taurine. When cats are deficient in taurine, their spleens become smaller and harder, with thickened, grayish-white capsules. Microscopic examination reveals damage to B cell zones, reduced lymphocytes in follicular germinal centers, amorphous deposits, and positive periodic acid-Schiff staining, indicating impaired B cell function. The spleens show lymphocyte depletion, reticular stroma hyperplasia, and hypertrophy of small blood vessels, with metal ion deposits in the red pulp, which may be associated with extravascular hemolysis. The paracortical areas of the lymph nodes predominantly contain mature small lymphocytes, with occasional immunoblasts and plasma cells, and exhibit postcapillary venule hyperplasia, likely a secondary change[56]. Research has shown that feeding poultry an appropriate amount of taurine can increase the relative mass of immune organs such as the bursa of Fabricius, spleen, and thymus, thereby enhancing the body's immune response[57].

3.2.2 Impacts on lymphocytes

1) Taurine has significant protective effects on lymphocytes. In human peripheral blood, taurine constitutes 50% of the total free amino acids in lymphocytes. The taurine content in peripheral blood lymphocytes is 12 times higher than in plasma, 35 times higher in non-adherent lymphocytes, 20 times higher in adherent lymphocytes, and 8 to 23 times higher in B cells compared to plasma[58]. Lymphocytes have a limited capacity to synthesize taurine and primarily maintain intracellular concentrations through active uptake from plasma. Research indicates that adult lymphocytes possess an active taurine transport system. In taurine-depleted culture media, lymphocyte survival and proliferation rates decline as taurine levels decrease. Adding taurine restores intracellular levels and proliferation rates in a dose-dependent manner, with the highest proliferation rate observed at 0.1 mol/L, a concentration equivalent to that found in normal human plasma[59]. These experiments demonstrate that taurine has protective effects on lymphocytes. It stabilizes cell membranes, protects phospholipids from degradation, counteracts changes in membrane permeability, prevents cell swelling and deformation, and reduces cell death. By interacting with harmful factors through its amino group, taurine maintains the balance of ion and water transfer, thus enhancing cell survival and promoting proliferation[60].

2) Taurine promoting lymphocyte proliferation. Research has shown that taurine can increase DNA synthesis in the spleens of DBA/2 mice by nearly fourfold, thereby promoting lymphocyte proliferation. Additionally, taurine enhances the polyclonal antibody response and exhibits immunoadjuvant activity. However, taurine does not increase DNA synthesis in thymic cells, indicating that its proliferative effects are limited to mature B and T lymphocytes in the spleen[61]. Other studies have found that taurine enhances T lymphocyte proliferation by increasing calcium ion uptake in cells, which in turn boosts T cell activity and proliferation[62]. Additionally, long-term feeding of taurine-deficient diets to cats has been reported to result in numerous immature lymphocytes in B cell zones, lymphocyte depletion around the periarteriolar regions of T cell zones, and mild progressive extravascular hemolysis[63]. Taurine can also mitigate lymphopenia induced by IL-2 immunotherapy, thereby enhancing the potential efficacy of immunotherapy[40]. Furthermore, studies have found that taurine significantly reduces natural killer cell-mediated, rIL-2-activated endothelial cell cytotoxicity without diminishing the antitumor response. It also significantly enhances lymphocyte-mediated lymphokine-activated killer (LAK) cell tumor cytotoxicity. Taurine plays a crucial role in lymphocyte-mediated cytotoxicity by increasing intracellular calcium and promoting calcium-dependent granzyme exocytosis following LAK cell binding to endothelial cells[64]. These findings suggest that taurine protects lymphocytes during rIL-2 immunotherapy while reducing vascular damage and enhancing antitumor activity.

3.2.3 Enhancing neutrophil function

Neutrophils are the primary phagocytic cells in the blood, playing a crucial role in defending against infections and promoting inflammatory responses. Taurine constitutes 76% of the free amino acids in neutrophils, acting as an oxidant scavenger to protect cells. Neutrophils combat pathogens by producing HClO, but excessive HClO can damage cells. Taurine reacts with HClO to form the less toxic TauCl, thereby scavenging HClO and preventing oxidative damage. Additionally, taurine is released into tissue fluid and blood, protecting them from halide oxidants and preventing cell autolysis[65]. Research has shown that a long-term diet lacking taurine can lead to immune system dysfunction and abnormalities in cats. Compared to the taurine-supplemented group, the control group exhibited a significant reduction in total white blood cell count, changes in the proportions of neutrophils and monocytes, and an increase in monocyte numbers. Neutrophil function declined, with disruptions in the respiratory chain, reduced phagocytic and bactericidal capabilities against *Staphylococcus epidermidis*, and increased serum γ-globulin levels. These findings indicate that taurine deficiency broadly affects immune cell function[60]. Recent research has found that taurine, by reacting with HClO produced by neutrophils to form TauCl, plays a crucial role in regulating macrophage function. Moreover, during surgical injury and various pathological conditions, plasma taurine levels decrease, and taurine supplementation supports macrophage function[66]. In studies on hyperlipidemic rats, elevated serum lipid levels were found to potentially reduce the phagocytic and bactericidal capabilities of neutrophils. Taurine treatment enhanced the bactericidal capacity of neutrophils, which was diminished by a cholesterol-rich diet. By day 40, the bactericidal ability in the taurine group was stronger than in the laboratory feed group, indicating that taurine plays a vital role in host defense by enhancing neutrophil function[67].

3.2.4 Therapeutic effects on red blood cell immune function impairment

Research has shown that RBCs not only recognize antigens but also perform various immune functions, such as clearing immune

complexes from the bloodstream and facilitating the immune adhesion of bacteria, viruses, and tumor cells. The C3b receptors on the RBC membrane help attach immune complexes and transport them to the liver and other organs, where they are effectively cleared from the blood through phagocytosis and breakdown by the macrophage system. This process prevents the deposition of immune complexes in sensitive areas, thereby preventing inflammation and other diseases. During inflammatory responses, taurine interacts with the myeloperoxidase-hydrogen peroxide-chloride system to form HClO, which neutralizes hypochlorous acid. This interaction protects IgG and complement C3b from oxidative damage, preserving the ability of red blood cells to clear circulating immune complexs and maintain their immune functions[68].

3.2.5 Impacts on cytokines

Cytokines are hormone-like protein molecules produced by immune cells in response to antigen or mitogen stimulation. These non-antibody, non-complement proteins play essential roles in various aspects of the body's immune response and inflammatory processes. Studies have reported that taurine can significantly reduce rIL-2-activated endothelial cell cytotoxicity mediated by natural killer cells without diminishing the antitumor response of rIL-2. Additionally, taurine decreases LAK cell-mediated endothelial cell lysis[64]. Another study reported that taurine can induce macrophages to produce IL-1, which has biological activity that promotes the proliferation and differentiation of B cells in DBA/2 mice[62]. Furthermore, research has shown that taurine affects the expression of inflammatory cytokines in rats after traumatic brain injury (TBI). Taurine significantly inhibited the levels of growth-related oncogene (*GRO/KC*) and IL-1β while regulating and normalizing T cell expression. Taurine significantly reduced the levels of 17 cytokines: eotaxin, G-CSF, GM-CSF, IFN-γ, IL-1α, IL-1β, IL-4, IL-5, IL-6, IL-10, IL-12p70, IL-13, IL-17, leptin, MCP-1, TNF-α, and VEGF. These results indicate that taurine effectively reduces the severity of brain injury in TBI by decreasing astrocyte activity, edema, and the increase of pro-inflammatory cytokines[69]. Additionally, studies have reported that allergic inflammation may be associated with reduced serum taurine levels. Taurine dose-dependently inhibited the production and mRNA expression of *Tslp* and pro-inflammatory cytokines, reduced the phosphorylation of JNK and p38, and decreased the activity of NF-κB and Caspase-1. In an ovalbumin-induced allergic rhinitis model, taurine significantly reduced nasal itching, histamine, immunoglobulin E, and IL-1β levels. These findings suggest that taurine could be a potential new treatment for allergic inflammation[70].

3.2.6 Impacts on antibodies

Antibodies are crucial products of the immune response generated against antigens. The immune response mediated by antibodies is known as humoral immunity. Research has shown that feeding poultry with taurine significantly enhances immune markers, as well as serum HDL-C and total antioxidant capacity. These findings indicate that taurine has potential applications in promoting animal health and growth[71]. Additionally, other studies have found that taurine can regulate BCR signaling, promote B cell activation, and significantly enhance IgG production in mice immunized with ovalbumin. *In vitro* experiments have shown that taurine specifically binds to the F(ab')2 region of IgG2a-BCR. Molecular docking analysis further revealed the interaction between taurine and the framework regions of variable heavy chain framework regions and variable light chain framework regions in BCR. These findings suggest that taurine, by binding to specific regions of BCR, can significantly enhance B cell-mediated antibody production, demonstrating its potential application in boosting immune responses[72]. Moreover, research has indicated that taurine shows promise as an oral adjuvant for measles and influenza virus vaccines. Individuals vaccinated with influenza vaccines containing taurine exhibited higher influenza virus antibody titers compared to those in the control group without the adjuvant. Additionally, when taurine was combined with lithium and/or parotid gland protein, the increase in influenza antibody titers was greater than with taurine alone, suggesting a significant advantage of combined adjuvants in enhancing vaccine efficacy[73]. This is particularly important for providing protection during the window period following immunization.

3.2.7 Mitigating inflammatory responses in animal models

Extensive research has shown that taurine therapy can prevent tissue damage in various oxidative stress-induced inflammation models, making it an effective protective agent against inflammation. Exogenous taurine can reduce the inflammatory response in colitis induced by trinitrobenzene sulfonic acid[74] and mitigate hypertension and renal dysfunction in mice caused by the immunosuppressant cyclosporine A[75]. These effects are closely related to taurine's antioxidant properties. Taurine also acts as a free radical scavenger, reducing pancreatitis induced by sodium taurocholate in rats[76]. Additionally, taurine can improve tissue oxidative damage caused by chemotherapy, inhibit leukocyte apoptosis, and enhance liver and kidney function. These properties suggest that taurine could be a potential treatment to alleviate systemic side effects caused by chemotherapy[77]. TauCl, a compound formed when taurine reacts with hypochlorous acid, is less toxic and more stable, making it a focal point of immunology and infectious disease research. Studies have shown that TauCl acts as an immunomodulator by downregulating inflammatory mediators such as superoxide anion, nitric oxide, and TNF-α in both rodents and humans. It also enhances the expression of antioxidant proteins in macrophages. Released by neutrophils, TauCl plays a key role in modulating inflammatory responses and protecting macrophages and surrounding tissues from oxidative stress damage, highlighting its potential in combating chronic inflammation[78].

3.2.8 Comparison with immunomodulating agents: taurine as a safer and multi-functional alternative

Immunosuppressants, such as cyclosporine A, are effective at suppressing immune responses but can elevate the risk of infections and cause serious side effects like nephrotoxicity, hypertension, and metabolic disorders[79]. In comparison, taurine gently modulates the immune system, enhancing immune surveillance without causing significant immunosuppression.

Biologics, such as anti-TNF-α antibodies, are highly effective but come with high costs and the risk of adverse reactions, including arthralgia, rheumatoid arthritis, headaches, pneumonia, psoriasis, nausea, diarrhea, pruritus, and dyspnea[80]. In contrast, taurine offers a more affordable and safer alternative or complement, providing comparable therapeutic benefits with fewer side effects.

Nutritional immunomodulators like omega-3 fatty acids are recognized for their anti-inflammatory properties, but their range of effects is somewhat limited[81]. In contrast, taurine not only shares these anti-inflammatory benefits but also provides additional advantages, such as antioxidant activity and cellular protection. This broader therapeutic profile makes taurine a more reliable and effective option for immune modulation, offering benefits beyond those of traditional omega-3 fatty acids.

Unlike conventional broad-spectrum immunosuppressants, taurine selectively boosts beneficial immune functions without substantial suppression, representing a safer option compared to many biologics. Please refer to Table 2 for taurine's immunomodulatory effects.

Table 2
Immunomodulatory effects of taurine.

Components of the immune system	Type of research subject	Pharmacological effects	Reference
Spleen, thymus, and lymph nodes	Cat	Taurine deficiency in cats, used as a model for study, results in hardened, shrunken spleens and B-cell dysfunction, particularly in germinal centers and marrow depletion. Additionally, lymph node alterations and vessel hypertrophy indicate broader systemic effects.	[56]
	Poultry	Feeding poultry taurine enhances immune organ mass and boosts immune response.	[57]
Lymphocytes	Human lymphoblastoid cells	Lymphocyte survival and proliferation are dependent on taurine levels, with optimal effects observed at 0.1 mol/L, which aligns with normal plasma concentrations.	[59]
	Rat, hamster, chimpanzee spermatozoa, neonatal rat cardiomyocytes, human vascular endothelial cells, isolated rat hepatocytes	Taurine stabilizes cell membranes, enhances osmotic balance, and protects against harmful agents, thereby enhancing cell survival and proliferation.	[60]
	Mouse	Taurine boosts spleen lymphocyte proliferation and antibody responses but not in thymic cells.	[61]
	Mouse	Taurine increases T lymphocyte proliferation by boosting calcium ion uptake.	[62]
	Cat	Long-term taurine deficiency in cats leads to immune system changes, affecting white cell count and neutrophil function, indicating broader immune cell impact.	[63]
Lymphocytes	Human Jurkat T cells, $CD4^+$ T cells	Taurine can alleviate lymphocytopenia caused by IL-2 immunotherapy, thereby enhancing the effectiveness of immunotherapeutic treatments.	[40]
	Human cells	Taurine reduces rIL-2 activated NK cell cytotoxicity, boosts LAK cell tumoricidal function, and minimizes vascular damage.	[64]
	Rat	Taurine treatment boosts neutrophil bactericidal capacity in hyperlipidemic rats, enhancing host defense.	[67]
Red blood cells	Rat	Taurine forms hydrophilic chloramines, neutralizing hypochlorous acid to protect IgG and C3b, preserving red blood cells' immune functions.	[68]
	Human cells	Taurine reduces rIL-2-induced NK cell cytotoxicity and LAK cell-mediated endothelial lysis, preserving anti-tumor effects.	[64]
Cytokines	BALB/c Mouse	Taurine induces macrophages to produce IL-1, enhancing the proliferation and differentiation of B cells in BALB/c mice.	[62]
	Rat	Taurine reduces inflammation and cytokine levels in rat traumatic brain injury, mitigating brain injury severity.	[69]
Antibodies	Human mast cell line HMC-1, BALB/c mouse	Taurine reduces allergic inflammation by inhibiting key inflammatory pathways and cytokines.	[70]
	Poultry	Taurine boosts poultry immune markers, HDL-C, and antioxidant capacity.	[71]
	C57BL/6 mouse	Taurine enhances B cell activation and IgG production by binding to specific BCR regions, boosting immune responses.	[72]
	Human	Taurine as an oral adjuvant boosts influenza antibody titers, especially when combined with lithium and parotin, enhancing vaccine efficacy.	[73]
Others	Rat	Exogenous taurine can reduce the inflammatory response of colitis caused by trinitrobenzene sulfonic acid.	[74]
	Rat	Taurine can function as a free radical scavenger, reducing sodium taurocholate-induced pancreatitis in rats.	[76]
	Human	Taurine improves chemotherapy-induced tissue oxidative damage, inhibits leukocyte apoptosis, and enhances liver and kidney function.	[77]
	Human	Taurine chloramine modulates immune responses, downregulates inflammatory mediators like TNF-α, and enhances macrophage antioxidants, offering potential in chronic inflammation treatment.	[78]

3.3 Role of taurine in the nervous system

3.3.1 Taurine and its receptors

Taurine has inhibitory, trophic, and protective effects on the nervous system. It is one of the most abundant free amino acids in the nervous system, particularly in the cerebral cortex, cerebellum, and olfactory bulb of animals. Taurine significantly promotes the growth and development of the nervous system, as well as the proliferation and differentiation of cells. During brain development, it functions as both a neurotrophic and neuroprotective factor[82]. In the nervous system, taurine can function both as a neurotransmitter and as a

neuromodulator. As a neurotransmitter, taurine is first synthesized in the cytoplasm of the presynaptic membrane by taurine synthetase, specifically CSAD. Its release can be either calcium-dependent or calcium-independent. Once released into the synaptic cleft *via* exocytosis, taurine binds to specific receptors on the postsynaptic membrane, causing chloride ion channels to open. This leads to hyperpolarization of the neurons, thereby exerting its physiological effects. Finally, taurine is reabsorbed into cells *via* sodium-dependent taurine transporters, ready to be reused for the next neural impulse[5,83-87]. Research has found that taurine can alleviate depressive behaviors and reduce anxiety and fear in zebrafish. Thus, within the central nervous system, taurine acts as a neurotransmitter involved in the functional activities of nerve cells. In synapses, taurine sometimes serves as an inhibitory neuromodulator, preventing Ca^{2+} influx and counteracting the neurotoxic effects of glutamate[88]. This role makes taurine an important player in the nervous system, potentially involved in various aspects such as mood regulation and cognitive function. Research indicates that taurine acts as a neuromodulator during early neural development, influencing key processes like neurogenesis, neuronal migration, and cell differentiation. By regulating the activity of neurons and neural precursor cells, taurine impacts neural activity during early developmental stages through its action on glycine and gamma-aminobutyric acid (GABA) receptors[89]. The role of taurine in neurotransmission in the central nervous system (Fig. 3).

In basic antagonist research, inhibitory amino acids are classified into two groups: the glycine group and the GABA group, each with its specific receptors. Taurine does not belong to either of these groups and has its specific receptors. However, taurine can also activate GABA and glycine receptors. Specific taurine receptors have been identified, with dissociation constants in the nmol/L range, distinct from GABA and glycine receptors, as the agonists or antagonists of these receptors have little effect on taurine binding to its receptors[90]. Similar observations have been reported by other researchers[91]. Research has found that endogenous taurine can activate glycine receptors in rat hippocampal neurons[92]. During ischemia-reperfusion, taurine at concentrations of 0.3, 1.0, and 3.0 mmol/L exhibited effects similar to glycine, with the optimal effect observed at 1 mmol/L. This indicates that the neuroprotective effect of taurine is mediated by strychnine-sensitive glycine receptors[93]. Further studies have shown that taurine acts on GABA receptors in the rat hippocampus. Taurine activates $GABA_A$ receptors, but not $GABA_B$ receptors, in the CA1 region of the rat hippocampus[94]. Additionally, taurine has a higher affinity for α4β2δ $GABA_A$ receptors than for α1β2γ2 $GABA_A$ receptors[95]. GABA receptors and glycine receptors coexist in the ventral posterolateral nucleus of the thalamus, close to inhibitory amino acid release sites[96]. Similarly, taurine and GABA coexist in certain nerve terminals, where they can be co-released or exhibit "coactivation and cotransport" characteristics in close proximity. Taurine interacts with GABA, activating both GABA and glycine receptors, thereby enhancing the inhibitory effects on neurons[97].

3.3.2 *Neurotrophic and anti-Alzheimer's effects*

Taurine promotes brain neural growth and development, enhances synaptic connections, facilitates nerve repair, and combats neuronal aging. Firstly, in neonatal animals, taurine plays a crucial role in neural development by engaging in signaling pathways related to neurogenesis and mediating the proliferation and differentiation of neurons[98]. In calcium ion-related signaling pathways, taurine influences brain neural growth and development by maintaining calcium homeostasis. Supplementing pregnant rats with taurine has been found to upregulate the PKA-CaMKII/c-fos signaling pathway and promote neuronal proliferation. This indicates that taurine promotes the development of fetal rat brains under restricted conditions by stabilizing calcium homeostasis[99]. Additionally, taurine supplementation can activate the PKA-CREB-BDNF signaling

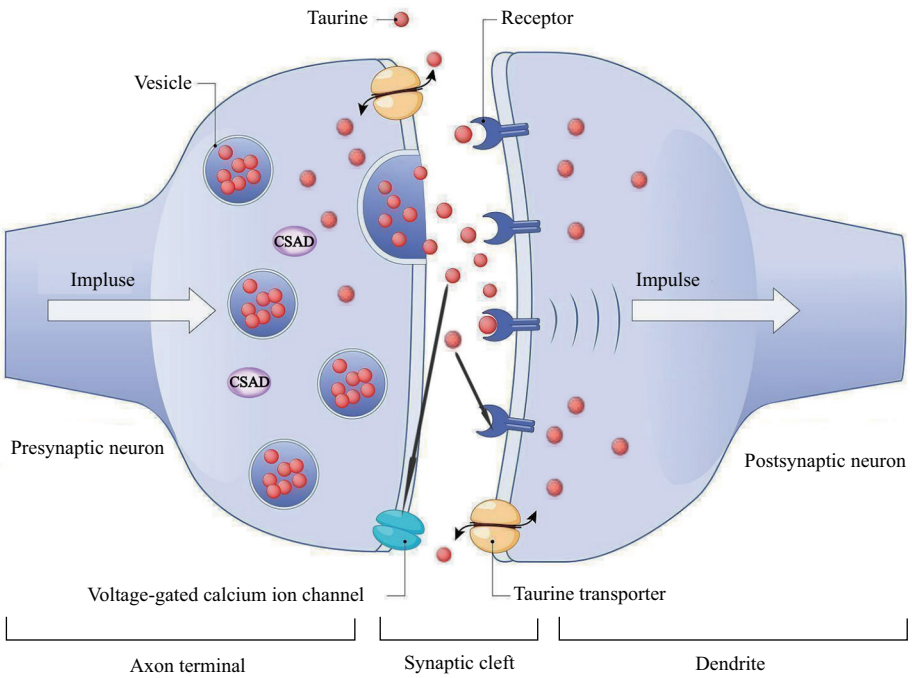

Fig. 3 Diagram illustrating taurine's role as a neurotransmitter and a neuromodulator in neural signal transmission.

pathway, increasing the ratio of neurons to glial cells in fetal rats and preventing gliosis during the differentiation of neural stem cells[100]. Furthermore, studies have indicated that taurine can upregulate the cAMP-PKA signaling pathway and *Gdnf* mRNA expression in the fetal rat brain. This suggests that taurine can enhance neurogenesis in the central nervous system and improve the neuronal environment by increasing the secretion of neurotrophic factors[101]. Other research has reported that prenatal taurine supplementation can improve neural stem cell proliferation in rats by inhibiting the activity of Rho family factors[102]. Secondly, taurine can activate ion-gated channels, enhancing synaptic plasticity between neurons and stimulating neuronal activity[103]. Studies have found that taurine can promote the growth of hippocampal neuron axons, thereby participating in the neural growth process[104]. Additionally, *in vitro* cultivation of hippocampal neural stem cells revealed that the group supplemented with a certain concentration of taurine exhibited a significant increase in stem cells, with more dendrites and axons, and enhanced network connections between them[105].

Recent studies have found that taurine not only promotes the growth and development of the nervous system in neonatal animals but also acts as a neurotrophic factor in adult animals, enhancing learning and memory abilities. Research indicates that taurine supplementation in rats leads to improved learning and memory capabilities[106]. As animals age, their learning and memory abilities decline, and their nervous systems degenerate, a process closely related to a decrease in taurine levels. Supplementing taurine has been shown to enhance the learning, memory, and stress resilience of elderly mice, with a corresponding increase in GABA levels. Taurine may exert compensatory effects by mediating GABA to delay aging[107].

Alzheimer's disease (AD) is a highly age-related eurodegenerative disorder of the central nervous system, primarily characterized by progressive cognitive impairment and memory loss. It manifests as a decline in general intellectual abilities, including memory, judgment, and abstract thinking, while vision and motor skills remain unaffected[108]. A characteristic histopathological change in AD is the deposition of Aβ plaques in the brain, consisting of 39–43 amino acid residues[109]. Early studies have demonstrated that Aβ exhibits neurotoxicity both *in vivo* and *in vitro*. Reports indicate that Aβ's neurotoxicity is mediated through glutamate receptors and that blocking ionotropic or metabotropic glutamate receptors can prevent the neuronal damage caused by Aβ[110]. In the presence of Aβ, taurine levels in the cerebral cortex, hippocampus, and striatum are significantly reduced[111]. Taurine has been shown to protect chick retinal neurons from the neurotoxicity of amyloid-beta (Aβ) peptides and glutamate receptor agonists. The GABA receptor antagonist picrotoxin can completely block taurine's protective effects, indicating that taurine inhibits neurodegeneration by activating GABA receptors[112]. Furthermore, studies have found that taurine can inhibit neurotoxicity induced by Aβ and high concentrations of glutamate in rat hippocampal and cortical neurons. This effect depends on the activation of $GABA_A$ receptors, as the $GABA_A$ receptor antagonist picrotoxin abolishes taurine's protective effect. This suggests that taurine, by modulating GABAergic neurotransmission, has potential in treating Alzheimer's disease and other excitotoxicity-related neurodegenerative diseases[113], such as Parkinson's disease[114] and epilepsy[115]. In summary, taurine, as a neurotrophic factor, promotes neural regeneration, enhances synaptic connections between neurons, and improves the microenvironment for neuronal survival.

3.3.3 Neuroprotective effects

Taurine's primary physiological role is neuroprotection, reducing damage and death of nerve cells under stress conditions. Research shows that taurine can downregulate the expression of various apoptotic proteins. In models of glutamate-induced neuronal death, taurine prevents apoptosis by maintaining the balance of Bcl-2 and Bax proteins and inhibiting calpain activation. This process prevents Bax mitochondrial translocation and cytochrome C release, thereby inhibiting the caspase cascade reaction and avoiding cell death. These findings highlight taurine's potential therapeutic value in treating neurodegenerative diseases caused by glutamate toxicity[116]. Furthermore, experiments on brain slices under simulated hypoxic conditions observed that the addition of 20 mmol/L taurine significantly reduced the expression of Caspase-8 and Caspase-9 in the supraoptic and paraventricular nuclei of the hypothalamus[117]. These 2 Caspase enzymes are critical inducers of apoptosis, with their overactivation closely linked to receptor-mediated and mitochondrial pathways of cell death. Therefore, taurine's protective effects are significant not only for reducing cell damage in these critical regions but also for maintaining the functional integrity of the brain's response to stress. This highlights taurine's potential application in preventing and treating neurodegenerative diseases and other conditions associated with brain hypoxia. Additionally, research has explored taurine's multifaceted role in combating TBI, particularly its effects in reducing inflammation, apoptosis, and oxidative stress[118]. Studies have found that taurine significantly lowers the expression of oxidative stress markers, inflammatory factors, and apoptosis-related proteins. Through its antioxidant and neuroprotective properties, taurine helps restore the physiological state of damaged brain cells, demonstrating its potential for treating TBI. Furthermore, taurine also exhibits neuroprotective effects in cerebral ischemic injury. Taurine has been found to improve cognitive dysfunction by acting on *N*-methyl-*D*-aspartic acid (NMDA) receptor binding sites and alleviate anxiety symptoms through $GABA_A$ receptor binding sites. This effectively counteracts the neurotoxicity of lead, providing preventive and therapeutic strategies for lead exposure[119].

3.3.4 Preventing disruption of mitochondrial structure and function

Mitochondria are highly sensitive to oxidative damage; incompletely reduced oxygen within the respiratory chain can generate superoxides that disrupt cellular structures and functions. Taurine regulates the production of mitochondrial superoxides and oxidative phosphorylation, preserving mitochondrial functionality. Studies have demonstrated that taurine supplementation reduces superoxide generation and maintains electron transport within the respiratory chain[120]. Additionally, mutations in mitochondrial genes are a major cause of functional disruption. Research has shown that these mutations result from the lack of taurine-dependent post-transcriptional modifications, leading to mitochondrial-related diseases such as mitochondrial myopathy, encephalopathy, stroke-

like episodes, and myoclonic epilepsy[121-122]. Furthermore, researchers have discovered that taurine's neuroprotective effects are linked to the enhancement of NADH dehydrogenase activity. In a rat stroke model, it was found that taurine helps maintain normal mitochondrial function post-stroke, prevents cell death mediated by the mitochondrial pathway, and increases cell survival, thereby exerting protective effects[123].

3.3.5 Improving endoplasmic reticulum stress

Accumulation of the UPR leads to endoplasmic reticulum stress, which disrupts neural signal transmission and ultimately causes neuronal death. Misfolded proteins can activate three ER transmembrane proteins: PERK, IRE-1, and activating transcription factor-6 (ATF-6). Under normal conditions, these proteins are bound to the ER chaperone GRP78, which regulates transcription and protein synthesis to restore ER function. However, under stress conditions, GRP78 dissociates and becomes a pathological marker of ER stress. When the stress is severe or prolonged, the UPR activates apoptotic signaling pathways mediated by C/EBP homologous protein (CHOP), Caspase-12, and JNK[124]. Research has found that taurine's protective effects on the ER are achieved by maintaining the stability of ER-associated proteins. Taurine significantly reduces the activation of ATF-6 and IRE-1 within the ER stress pathway, thereby diminishing apoptotic signaling and exerting its protective effects[125]. Additionally, researchers have found that supplementing taurine in stroke model groups can downregulate the expression of molecules associated with the JNK signaling pathway, thereby inhibiting ER stress-induced apoptosis[126].

3.3.6 Maintaining calcium homeostasis

When neurons are stimulated by glutamate, extracellular calcium ions rapidly flow in and activate NMDA receptors. Subsequently, the excess intracellular calcium ions are released *via* the reverse action of the Na^+/Ca^{2+} exchanger. In the presence of taurine, the glutamate-mediated increase in calcium ions is significantly reduced, preventing glutamate-induced membrane depolarization and counteracting the neurotoxic effects of glutamate. This suggests that taurine's protective effects on the central nervous system can be achieved by regulating intracellular calcium homeostasis[127]. As an antioxidant, taurine secretion increases in brain ischemia models, participating in numerous pathophysiological processes. It can counteract the neurotoxicity of excitatory amino acids, regulate Ca^{2+} homeostasis, reduce the production of NO and free radicals, inhibit lipid peroxidation, decrease cell apoptosis, and influence the expression of hypoxia-inducible factors. These actions provide neuroprotective effects against neuronal damage during cerebral ischemia-reperfusion injury[128].

3.3.7 Comparison with neuroprotective agents: taurine's multi-pathway advantages and safety profile

Neuroprotective drugs like Memantine, which target NMDA receptors to prevent excitotoxicity, can cause side effects such as dizziness and confusion[129]. In contrast, taurine offers a more comprehensive approach to neuroprotection by activating multiple protective pathways with a much better safety profile, delivering broad-spectrum benefits without the associated risks.

Antioxidants like vitamin E primarily work to combat oxidative stress, but they offer limited scope in terms of overall cellular support[130]. In contrast, taurine provides a more comprehensive solution by not only reducing oxidative damage but also regulating neurotransmission and calcium homeostasis. This broader approach enhances cellular health with a much better safety profile, making taurine a superior option for neurological care.

Nootropics like piracetam are known to enhance cognitive function, but their mechanisms remain unclear, and their safety profiles are not fully established, leading to inconsistent efficacy[131-132]. In contrast, taurine's mechanisms are well-documented, offering comprehensive support for neuronal health. This makes taurine a more reliable and effective option for cognitive enhancement without the uncertainties associated with traditional nootropics.

Taurine surpasses traditional neuroprotective agents by offering a wide range of protective mechanisms that cover neurotransmission, neurotrophic support, and cellular defense. Its well-characterized properties and extensive biological activities establish it as a leading candidate in neuroprotection, outperforming many specialized pharmaceuticals and antioxidants. For further details on taurine's impact on the nervous system, please refer to Table 3.

3.4 The role of taurine in the cardiovascular system

3.4.1 Inhibiting cardiomyocyte apoptosis and protecting myocardial injury

Cardiac ischemia and reperfusion injury not only cause myocardial cell necrosis but also lead to apoptosis. Taurine can effectively inhibit cardiomyocyte apoptosis. During ischemia/reperfusion, oxygen free radicals damage membrane structures, resulting in calcium overload and mitochondrial damage. Taurine protects ischemic myocardium by inhibiting calcium overload, membrane lipid peroxidation, and apoptosis. Studies have shown that in a simulated ischemic environment with low oxygen and nutrients, taurine significantly inhibits cardiomyocyte apoptosis. This effect is linked to the inhibition of the apoptotic protease activating factor 1/Caspase-9 apoptosome[133-134]. Studies have shown that in a hypoxia/reoxygenation injury model of neonatal rat cardiomyocytes, taurine significantly reduces the apoptosis rate of myocardial cells. The mechanisms include reducing PUMA expression, lowering Bax and Caspase-3 levels, and increasing Bcl-2 expression. Taurine also decreases GRP78 and CHOP expression, alleviating endoplasmic reticulum stress, and regulates calcium homeostasis to prevent calcium overload, thereby protecting cell survival[135]. Other studies have shown that taurine prevents ischemia-induced apoptosis in cultured neonatal rat cardiomyocytes through the Akt/Caspase-9 pathway[136]. Studies have found that while taurine does not affect the expression of Bcl-2 in mitochondria or the release of cytochrome C, it effectively inhibits the activation of Caspase-9 and Caspase-3. When a dominant-negative form of Akt was introduced to inhibit Akt function, the protective effect of taurine was negated, confirming the central role of the Akt pathway in taurine's anti-apoptotic effect on ischemic cardiomyocytes. Furthermore, both *in vivo* and *in vitro* experiments

Table 3
Effects of taurine on the nervous system.

Pharmacological effects	Type of research subject	Common mechanisms of action	Reference
Neurotrophic Effects	Rat, lymnaea stagnalis	In calcium ion-involved signaling pathways, taurine can influence the process of brain neuronal growth and development by maintaining calcium homeostasis.	[98]
Effects	Rat	Supplementing pregnant rats with taurine was found to upregulate the PKA-CaMKII/c-fos signaling pathway and promote neuronal proliferation, indicating that taurine promotes the development of the restricted fetal rat brain by stabilizing calcium homeostasis.	[99]
	Rat	Supplementing taurine can activate the PKA-CREB-BDNF signaling pathway, increasing the ratio of neurons to glial cells in fetal rats and preventing glial proliferation during the differentiation of neural stem cells.	[100]
	Rat	Taurine can upregulate the PKA-CREB signaling pathway and the expression of glial cell-derived neurotrophic factor mRNA in the fetal rat brain.	[101]
	Rat	Prenatal taurine supplementation can improve neural stem cell proliferation in rats by inhibiting the activity of Rho family factors.	[102]
	Rat, mouse, ferret, monkey, human	Taurine can activate ion-gated channels, enhance synaptic plasticity connections between nerve cells, and stimulate neuronal activity.	[103]
	Rat	Taurine can promote axonal growth in hippocampal neurons, participating in the process of neural growth.	[104]
	Mouse	Taurine boosts hippocampal stem cells, dendrites, and axons, enhancing neural connectivity.	[105]
	C57BL/6J mouse	Taurine enhances neural growth and memory in both young and adult mice.	[106]
	Mouse	Taurine supplementation in elderly mice boosts memory and stress resistance, potentially delaying aging *via* GABA mediation.	[107]
Anti-Alzheimer's effects	Chick	Taurine protects chick retinal neurons from Aβ toxicity by activating GABA receptors, not through direct glutamate receptor interaction.	[112]
	Rat	Taurine prevents Aβ and glutamate toxicity in rat neurons *via* $GABA_A$ receptor activation, suggesting potential as an AD therapy.	[113]
Neuroprotective effects	Rat	Taurine inhibits glutamate-induced apoptosis, regulating Bcl-2/Bax and blocking cytochrome C release, offering potential for neuroprotection.	[116]
	Mouse	Taurine reduces Caspase-8 and -9 in hypothalamic nuclei under hypoxia, suggesting neuroprotection.	[117]
	Rat	Taurine reduces oxidative stress and apoptosis markers in neural cells, enhancing recovery in brain injury.	[118]
	Human	Taurine mitigates lead-induced neurodevelopmental damage *via* NMDA and $GABA_A$ receptors, enhancing cognition and reducing anxiety.	[119]
Preventing disruption of mitochondrial structure and function	Rat, dog, cat, human	Taurine aids mitochondrial protein synthesis by binding tRNALeu(UUR) and tRNALys(UUU), reducing dysfunction and oxidative stress.	[120]
	Human, yeast	Lack of taurine-dependent modifications in mitochondrial genes leads to severe mitochondrial diseases.	[121-122]
	Rat	Taurine enhances NADH dehydrogenase activity, maintains mitochondrial function post-stroke, and prevents cell death, increasing cell survival.	[123]
Improving endoplasmic reticulum stress	Rat	Taurine protects the endoplasmic reticulum by stabilizing ER-associated proteins, reducing ATF-6 and IRE-1 activation in the ER stress pathway, and attenuating apoptotic signaling.	[125]
	Rat	Supplementing taurine in a stroke model downregulates JNK signaling pathway-related molecules and inhibits cell apoptosis due to endoplasmic reticulum stress.	[126]
Maintaining calcium homeostasis	Rat	Taurine regulates calcium, reducing glutamate-induced neurotoxicity and membrane depolarization, protecting the central nervous system.	[127]
	Vertebrates	Taurine counters neurotoxicity, regulates Ca^{2+}, reduces NO and free radicals, and protects neurons in cerebral ischemia-reperfusion.	[128]

demonstrate that taurine reduces ischemia-induced myocardial injury by increasing taurine concentrations in the heart[137]. Taurine exerts anti-apoptotic effects by upregulating the expression of SLC6A6, cysteine deoxyase, and cysteine sulfinate decarboxylase (CSD), which enhances transport and synthesis, and by increasing Bcl-2 levels while decreasing BAX levels and inhibiting calcium overload. These findings offer new insights and a theoretical basis for taurine's therapeutic potential in myocardial ischemia. Other studies have also explored the signaling mechanisms through which taurine combats DOX-induced cardiac oxidative stress[138]. In rats injected with DOX, both body weight and heart growth were impaired, and the heart sustained damage due to oxidative stress. DOX caused a decrease in cardiomyocyte viability, an increase in ROS and intracellular calcium ions, DNA fragmentation, disruption of mitochondrial membrane potential, and apoptosis. It also increased the phosphorylation of p53, JNK, p38, and NFκB while reducing the phosphorylation of ERK and Akt. This disrupted the balance of Bcl-2 proteins, activated Caspases-12, 9, and 3, and induced PARP cleavage. Taurine treatment mitigated these adverse effects by activating survival signals and the PI3-K/Akt pathway, while inhibiting p53, JNK, p38, and NFκB, demonstrating its potential to prevent DOX-induced cardiac oxidative stress.

3.4.2 Protection of vascular endothelial function

In cardiovascular events,atherosclerosis (AS), hypercholestero lemia, and hypertension have been identified as risk factors, all of which are associated with impaired vascular endothelial function. Researchers developed models of vascular endothelial dysfunction in hypercholesterolemic mice and streptozotocin-induced diabetic mice to evaluate the effects of taurine on vascular endothelium. The results showed that the vasodilation response in the hypercholesterolemic and diabetic groups was lower than in the control group. However, after taurine supplementation, the vasodilation response in these groups

was restored to levels similar to those of the control group, indicating that taurine can improve vascular endothelial dysfunction[139]. Research has shown that high concentrations of glucose and oxLDL significantly increase apoptosis, Caspase-3 activity, and the expression of VCAM-1 and ICAM-1 in human umbilical vein endothelial cells. Taurine can effectively reverse these changes, reducing cell apoptosis and the expression of inflammatory markers. Notably, under the combined influence of high glucose and oxLDL, taurine significantly lowers the apoptosis rate to near-normal levels. This indicates that taurine protects endothelial cell function from damage induced by high glucose and oxLDL by modulating apoptotic pathways and inflammatory responses[140]. Researchers conducted an experiment on healthy smokers who smoked at least one pack per day for over 2 years. The participants took 1 500 mg of taurine orally each day for 5 consecutive days. The results showed that taurine restored the vasodilation response impaired by smoking to the level of non-smokers. Blood sample tests indicated that taurine increased levels of NO and eNOS and decreased levels of ET-1. Additionally, taurine improved endothelial dysfunction by regulating monocyte activity factors and inhibiting the interaction between monocytes and endothelial cells[141]. In recent years, HHcy has been recognized as an independent risk factor for vascular injury-related diseases. Research has shown that HHcy causes vascular damage by enhancing oxidative stress, activating inflammatory signaling pathways, inducing endoplasmic reticulum stress, altering DNA methylation, and promoting protein homocysteinylation. Furthermore, HHcy indirectly causes damage to other organs by activating the sympathetic nervous system and impairing adipose tissue. As a potential treatment, taurine may counteract the vascular and other tissue damage caused by HHcy by influencing these pathological pathways, providing an effective therapeutic strategy[142].

3.4.3 Effect on vascular smooth muscle cells (VSMCs)

Analysis of atherosclerotic (AS) lesions reveals that the primary constituent cells are macrophages and VSMCs, indicating that VSMCs proliferation is involved in the AS process[143]. Studies have shown that taurine can inhibit the proliferation of rat VSMCs even at low concentrations, primarily by reducing cell count and DNA synthesis. At a concentration of 30 mmol/L, taurine significantly extends the cell doubling time and reduces total protein content without affecting protein synthesis. Compared to other amino acids like alanine, taurine significantly inhibits VSMCs proliferation and DNA synthesis without impacting protein synthesis or cell viability[144]. Additionally, other researchers have reported that taurine can inhibit VSMCs proliferation, suggesting that taurine may effectively slow the progression of AS[145].

Vascular tissue calcification is a significant risk factor for cardiovascular diseases. Research indicates that taurine can inhibit the proliferation and calcification of VSMCs. In an experiment where rat VSMCs were induced to calcify using β-glycerophosphate, it was found that the calcified cells exhibited significantly increased alkaline phosphatase activity, calcium content, and ^{45}Ca accumulation. Taurine significantly reduced these indicators in a dose-dependent manner and effectively reversed calcification when added at both early and late stages. This suggests that taurine is highly effective in inhibiting and reversing VSMCs calcification[146].

3.4.4 Effects on lipid metabolism

Hyperlipidemia is a well-recognized major cause of cardiovascular diseases. Taurine counteracts lipid peroxidation, scavenges free radicals, and participates in the absorption of fats and fat-soluble substances. Taurine deficiency exacerbates hyperlipidemia. Furthermore, recent meta-analyses demonstrate that long-term taurine supplementation in overweight or obese adults results in significant reductions in total cholesterol and atherogenic risk, along with weight loss[147]. Researchers conducted a study on mice fed a high-cholesterol diet while simultaneously administering taurine to observe its effects on cholesterol metabolism and accumulation in the aorta. The results showed that, compared to the control group, the taurine group experienced a 44% reduction in serum low-density lipoprotein (LDL) and a 20% decrease in cholesterol accumulation in the aorta[148]. Another study indicated that rats fed a high-cholesterol diet without taurine supplementation experienced increased serum total cholesterol and decreased HDL cholesterol. However, after taurine supplementation, serum total cholesterol significantly decreased, and HDL cholesterol levels were restored. Taurine enhances CYP7A1 activity and its mRNA expression, promoting the conversion of cholesterol to bile acids and their excretion while inhibiting the rise of very-low-density lipoprotein (VLDL). This demonstrates taurine's potential protective role in lowering cholesterol[149]. Further research has shown that taurine can effectively reduce plasma cholesterol and triglyceride levels in rabbits fed a high-cholesterol diet, alleviate oxidative stress, and decrease cholesterol accumulation in the aorta. These findings indicate taurine's potential application in preventing and improving AS[150].

LDL is a protein in the blood primarily responsible for transporting cholesterol. Elevated LDL levels typically indicate an increase in cholesterol. When LDL receptors are defective or dysfunctional, cholesterol tends to accumulate in the vessel walls, leading to AS. Watanabe heritable hyperlipidemic rabbits, which develop AS even on a regular diet, are commonly used in AS research. Studies have found that taurine supplementation, while not significantly affecting plasma cholesterol and LDL levels, significantly reduces cholesterol accumulation (by 50%) and macrophage aggregation in the aortic intima. This reduction helps inhibit the formation of atherosclerotic plaques[151]. Taurine can lower blood lipids in animal models and influence lipid metabolism in humans. In a study involving non-diabetic, overweight or obese young adults, 30 college students were randomly assigned to either a taurine group or a placebo group. The taurine group received 3 g of taurine daily for 7 weeks. The results showed significant improvements in triglycerides (TG), atherogenic index (AI), and body weight in the taurine group compared to the placebo group, indicating that taurine positively affects lipid metabolism and may help prevent cardiovascular diseases[147].

3.4.5 Antioxidant and anti-atherosclerotic actions

AS lesions contain monocytes and macrophages, which are absent in normal blood vessel walls. In diseased vessels, macrophages coexist with oxLDL, indicating that macrophages play a crucial role in LDL oxidation. In experiments, when LDL was added to macrophage culture media, it was rapidly oxidized to oxLDL[152-153]. Studies have

shown that myeloperoxidase (MPO) produced by macrophages plays a significant role in the development of AS and coronary heart disease (CHD). MPO levels in the plasma of CHD patients are higher than those in non-CHD patients[154]. HClO produced by MPO has strong oxidative properties, and taurine, which is abundant in leukocytes, reacts with hypochlorous acid to form TauCl. TauCl is not only a reaction product but also inhibits various cytokines. During the formation of AS, leukocytes, platelets, endothelial cells, and VSMCs regulate cell proliferation, migration, differentiation, and adhesion by secreting cytokines, chemokines, and growth factors. TauCl plays a regulatory role in these processes[155]. Research has found that TauCl can enhance the ability of the macrophage cell line RAW264.7 to phagocytose apoptotic neutrophils. TauCl achieves this by binding to Keap1, thereby preventing its degradation of Nrf2, which enhances the translocation of Nrf2 into the nucleus and the expression of HO-1. This process increases the production of CO, significantly boosting the phagocytic activity of macrophages. Additionally, TauCl increases the expression of scavenger receptors, which recognize and bind to phosphatidylserine on apoptotic cells, promoting their clearance and helping to alleviate inflammation[156]. A study created a myocardial infarction rat model and treated it with taurine. Myocardial infarction activates the NLRP3 inflammasome, induces the maturation of Caspase-1 and IL-1β, and affects NGF synthesis, which in turn impacts cardiac sympathetic innervation. Taurine significantly reduced the expression of NF-κB, NLRP3 inflammasome, Caspase-1, and IL-1β in the myocardium, alleviating excessive sympathetic innervation and improving arrhythmia vulnerability. The conversion of taurine to TauCl played a key role in this process. These findings enhance the understanding of taurine's anti-inflammatory effects and offer new strategies for clinical management post-myocardial infarction[157].

3.4.6 Abnormal taurine transport in pathological cardiomyocytes and vascular tissue cells

Taurine is abundant in mammalian tissues, particularly in cardiomyocytes, where its concentration is approximately 100 times higher than in plasma. This high intracellular concentration is achieved through the active transport of taurine from the plasma against its concentration gradient[158]. The biological effects of taurine largely depend on its ability to be transported across cell membranes *via* the TAUT. Various TAUT isoforms have been cloned. In pathological cardiomyocytes and vascular cells, taurine transport is impaired, and cardiovascular disease risk factors, such as Hcy, can also inhibit its transport[159–161]. Researchers have observed changes in taurine transport and *Taut* mRNA in the myocardial and aortic vascular tissues of spontaneously hypertensive rats. The results showed an increase in plasma taurine levels and release, while taurine levels and *Taut* mRNA content in myocardial and vascular tissues decreased. The maximum transport rate of taurine decreased by 24% and 35%, respectively. This suggests that the impaired taurine transport in myocardial and vascular tissues is related to reduced TAUT activity, decreased affinity, and downregulation of the *Taut* gene[162]. Cardiovascular disease patients and the elderly often experience myocardial and vascular calcification, which is related to the occurrence and prognosis of cardiovascular diseases. Researchers cultured and induced calcification in rat VSMCs to study the expression and function of Taut during the calcification process. The results showed that calcified VSMCs had increased calcium content, reduced taurine levels, decreased transport rates, and significantly reduced *Taut* mRNA levels. This suggests that the reduced taurine binding to TAUT is associated with the downregulation of *Taut* gene transcription[163]. Moreover, researchers found that Hcy inhibits taurine transport in VSMCs in a concentration-dependent manner, while exogenous taurine supplementation can effectively counteract this inhibitory effect. These findings provide a potential biological basis for the use of taurine in the treatment of cardiovascular diseases[164]. The function and expression of TAUT are inhibited by pathological conditions such as inflammation, type 2 diabetes, hyperglycemia, and oxidative stress. TAUT is regulated through phosphorylation by PKC and PKA, and its activity is directly influenced by the concentrations of sodium and chloride ions. As well, age, nutritional status, high-fat diets, and liver diseases significantly affect TAUT expression and function. These factors collectively determine the intracellular taurine homeostasis and the cell's ability to adapt to environmental changes[159], all of which are directly or indirectly related to cardiovascular diseases.

3.4.7 Hypotensive activity

Hypertension is a common chronic condition characterized by a systolic blood pressure of ≥ 140 mmHg or a diastolic blood pressure of ≥ 90 mmHg. It is a major risk factor for cardiovascular and cerebrovascular diseases, and if left uncontrolled, can lead to severe consequences such as heart disease, stroke, and kidney failure[165]. Researchers have reported that taurine can prevent fructose-induced hypertension in rats. The study showed that taurine effectively inhibits the rise in blood pressure and the increase in platelet Ca^{2+} levels by regulating intracellular Ca^{2+} and Mg^{2+}. It also reduces triglyceride levels and platelet Mg^{2+}, although it may exacerbate hyperinsulinemia. These findings suggest that taurine has a potential protective role in regulating electrolytes and blood pressure[166]. Researchers have studied the effects of taurine and *L*-arginine on blood pressure in fructose-fed rats. The results showed that 3% fructose significantly increased the rats' systolic blood pressure and blood glucose levels. However, the combination of taurine and *L*-arginine effectively prevented these increases, reversed the thickening of the blood vessels, and maintained normal levels of serum NO, cyclic guanosine monophosphate, and endothelin. This demonstrated significant antihypertensive and antidiabetic effects[167].

3.4.8 Antithrombotic activity

Taurine is highly concentrated in platelets, at levels over 400 times greater than in plasma. Taurine in platelets can inhibit platelet aggregation and prevent embolism caused by collagen-induced platelet clumping[168]. Studies have found that insulin-dependent diabetes mellitus patients have significantly lower plasma and platelet taurine concentrations compared to healthy individuals. After supplementing with 1.5 g taurine for 90 days, patients' taurine levels increased significantly to normal levels and platelet aggregation was inhibited, suggesting that taurine may help reduce diabetes-related platelet hyperactivity[169]. Additionally, numerous studies have

confirmed that taurine can inhibit platelet activation and aggregation. This effect has been demonstrated in both animal and human *in vivo* and *in vitro* experiments. Due to its higher stability and selectivity for platelet receptors, taurine's chloramine derivatives are considered potential future antithrombotic agents[170].

3.4.9 Antiarrhythmic activity

Arrhythmias include both bradyarrhythmias and tachyarrhythmias, with taurine and *L*-arginine deficiencies potentially leading to premature beats, atrial fibrillation, and sinus arrest. Supplementing with 10–20 g taurine daily can reduce atrial premature beats by 50% and prevent ventricular premature beats, but it does not prevent sinus arrest. Supplementing with 4–6 g *L*-arginine can quickly terminate pauses and atrial premature beats, maintaining normal heart rhythm with continued use. Taurine helps prevent arrhythmias by regulating electrolyte levels and protecting against free radical damage, as well as restoring energy and endurance. As a precursor to NO, *L*-arginine stabilizes the sinoatrial node, preventing arrhythmias. With age, levels of taurine and *L*-arginine decrease, necessitating supplementation to prevent related diseases[171]. Researchers have also studied the effects of a taurine-magnesium complex (TMCC) on ouabain-induced arrhythmias in rat ventricular myocytes. The results showed that TMCC blocked sodium current and transient outward potassium current in a concentration-dependent manner, with effects comparable to amiodarone at 400 μmol/L. Unlike amiodarone, which reduces *L*-type calcium current, TMCC moderately increased *L*-type calcium current. Ouabain significantly reduced sodium current, *L*-type calcium current, and transient outward potassium current. TMCC alleviated ouabain-induced abnormalities in sodium and *L*-type calcium currents by improving ion channel inactivation and activation properties, demonstrating its potential as an antiarrhythmic agent[172].

3.4.10 Other functions

Iron overload refers to a condition where the body's iron content exceeds its needs, commonly seen in hereditary hemochromatosis, long-term blood transfusions, or excessive iron supplementation. This condition can lead to liver and heart damage, endocrine disorders, and is positively associated with the incidence and mortality of cardiovascular diseases[173]. When cardiac iron levels increase, the heart's systolic and diastolic functions are reduced, and lipid peroxidation is exacerbated. Taurine, which constitutes 25% to 50% of the total amino acids in the myocardium, has anti-lipid peroxidation properties and can inhibit *L*-type Ca^{2+} channels. Researchers created an iron overload model by injecting iron into mice and found that iron overload increased mortality, oxidative stress, and cardiac dysfunction in mice. Supplementing with taurine raised myocardial taurine levels by 45%, effectively reducing mortality, improving cardiac function and blood pressure, and mitigating myocardial damage. The study suggests that taurine can alleviate myocardial oxidative stress and cardiovascular damage caused by iron overload, making it a potential supplement for treating iron overload symptoms[174]. Another study explored the effects of taurine on liver oxidative stress and damage caused by iron overload. Mice were administered iron injections intraperitoneally for 13 consecutive weeks, resulting in increased liver dysfunction, apoptosis, and oxidative stress. Taurine supplementation raised liver taurine levels by 40%, effectively improving liver function, reducing apoptosis and ROS production, alleviating mitochondrial swelling and membrane potential loss, decreasing liver lipid peroxidation, enhancing antioxidant enzyme activity, and maintaining glutathione levels. This indicates that taurine can mitigate liver oxidative stress induced by iron overload, protect liver function, and may serve as a potential therapeutic agent for iron overload-induced liver damage[175].

Ventricular remodeling is a pathological process caused by myocardial injury or load changes, potentially leading to heart failure or sudden death. Studies have shown that reduced taurine levels are associated with cardiovascular changes, while taurine supplementation can mitigate cardiac remodeling. Taurine protects the heart through multiple mechanisms: promoting sodium and water excretion, regulating key ions, protecting lipid membranes, counteracting angiotensin II, and reducing oxidative stress. These actions make taurine a crucial player in the ventricular remodeling process[176]. One study investigated the effects of taurine on cardiac remodeling after myocardial infarction. Rats underwent coronary artery occlusion and were divided into 3 groups: control, myocardial infarction (MI), and myocardial infarction with taurine treatment (MI-T). The results showed that taurine levels were higher in the hearts of the MI-T group. While there was no difference in the infarct size between groups, taurine treatment alleviated structural and functional changes in the heart, such as the thickening of the left atrium and left ventricular posterior wall. Taurine significantly improved diastolic dysfunction, reduced myocardial cell apoptosis and oxidative stress, regulated the activities of matrix metalloproteinases-2 and -9, and improved cardiac energy metabolism[177]. These findings suggest that taurine may be a potential therapeutic agent beneficial for the recovery of cardiac function after remodeling. For details on the effects of taurine on the cardiovascular system, please refer to Table 4.

3.5 Hepatobiliary protective effects of taurine

In liver diseases, hepatocyte damage encompasses necrosis, apoptosis, steatosis, inflammation, and fibrosis. Taurine protects the liver through mechanisms including lipid-lowering, hepatocyte membrane protection, apoptosis inhibition, antioxidation, and antifibrosis. Taurine combines with bile acids to form taurocholic acid, promoting fat emulsification, increasing lipase activity, and aiding the digestion and absorption of neutral fats, cholesterol, fat-soluble vitamins, and other lipophilic substances[178]. Researchers have investigated the effects of taurine on non-alcoholic fatty liver disease (NAFLD) in rats fed a high-fat diet. The results showed that the taurine-treated group had significantly lower serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), and triglyceride levels, and reduced expression of inflammatory markers TGF-β and IL-9 in the liver and small intestinal mucosa. Tissue damage was also mitigated. Histological analysis indicated that liver steatosis and inflammatory cell infiltration were less severe in the taurine-treated group, and the structure of the small intestinal mucosal villi was preserved. These findings suggest that taurine has potential in preventing and treating NAFLD, possibly by regulating the expression of TGF-β and IL-9[179]. Furthermore, researchers

Table 4
Effects of taurine on the cardiovascular system.

Components and functions of the circulatory system	Type of research subject	Pharmacological effects	Reference
Inhibiting cardiomyocyte apoptosis and protecting myocardial injury	Neonatal rat cardiomyocytes	Taurine inhibits myocardial apoptosis in an ischemic-like model by targeting the Apaf-1/Caspase-9 apoptosome.	[133-134]
	Neonatal rat cardiomyocytes	Taurine reduces cardiomyocyte apoptosis by regulating PUMA, Bax, Caspase-3, Bcl-2, and endoplasmic reticulum stress, and maintaining calcium homeostasis.	[135]
	Neonatal rat cardiomyocytes	Taurine prevents ischemia-induced cardiomyocyte apoptosis *via* the Akt/Caspase-9 pathway, inhibiting Caspase-9 and Caspase-3 activation.	[136]
	Primary rat cardiomyocytes	Taurine alleviates myocardial ischemia damage by increasing taurine levels, enhancing transport and synthesis, and exerting anti-apoptotic effects.	[137]
	Neonatal rat cardiomyocytes	Taurine mitigates doxorubicin-induced cardiac oxidative stress by activating PI3-K/Akt survival signals and inhibiting p53, JNK, p38, and NFκB pathways.	[138]
Vascular endothelial cell	Mouse	Taurine improves endothelial dysfunction in hypercholesterolemic and diabetic mice by restoring the vascular dilation response to acetylcholine stimulation.	[139]
	Mouse	Taurine significantly mitigated the adverse effects of hyperglycemia and oxLDL by reducing apoptosis and the expression of adhesion molecules like VCAM-1 and ICAM-1.	[140]
	Human	Taurine restores vasodilation in smokers to non-smoker levels, increases NO and eNOS, and decreases ET-1, improving endothelial dysfunction.	[141]
	Human	Taurine counteracts vascular and tissue damage caused by hyperhomocysteinemia by affecting oxidative stress, inflammation, and other pathological pathways.	[142]
Vascular smooth muscle cell	Rat vascular smooth muscle cell	Taurine and its analogs inhibit vascular smooth muscle cell proliferation without affecting normal protein synthesis or cell viability.	[144]
	Rat vascular smooth muscle cell	Taurine inhibits and reverses vascular smooth muscle cell proliferation and calcification, especially with early treatment.	[146]
Effects on lipid metabolism	Human	Taurine significantly improved triglycerides, atherogenic index, and body weight, suggesting benefits for lipid metabolism and cardiovascular health.	[147]
	Mouse	Taurine reduced serum LDL levels by 44% and decreased cholesterol accumulation in the aorta by 20% in mice fed a high-cholesterol diet.	[148]
	Rat	Taurine lowers serum total cholesterol and restores HDL cholesterol in high-cholesterol diet rats by enhancing CYP7A1 activity and promoting cholesterol conversion to bile acids.	[149]
	Rabbit	Taurine reduces cholesterol, triglycerides, and oxidative stress in high-cholesterol diet rabbits, suggesting its potential in preventing atherosclerosis.	[150]
	Rabbit	Taurine reduces aortic cholesterol accumulation and macrophage aggregation by 50% in WHHL rabbits, inhibiting atherosclerotic plaque formation.	[151]
Antioxidant and anti-atherosclerotic actions	Mouse	Taurine chloramine enhances macrophages' ability to engulf apoptotic neutrophils by stabilizing nuclear factor E2-related factor 2, increasing heme oxygenase-1expression, and promoting inflammation resolution.	[156]
	Rat	Taurine significantly reduced the expression levels of NF-κB, NLRP3 inflammasome, mature Caspase-1, and IL-1β in the myocardium, thereby alleviating the overactivation of sympathetic nerve innervation.	[157]
Taurine transporter	Rat	In spontaneously hypertensive rats, myocardial and vascular taurine transport is impaired, with reduced *Taut* mRNA and activity, suggesting *Taut* gene downregulation.	[162]

studied taurine's antioxidative effects and its impact on HSCs in a liver fibrosis model. The results showed that taurine treatment significantly reduced malondialdehyde levels and oxidative stress markers, while increasing the activity of SOD and GSHpx, and promoting HSCs apoptosis. Moreover, taurine-treated rats exhibited elevated levels of MMP-13 and reduced levels of tissue inhibitor of TIMP-1. By reducing oxidative stress and modulating the expression of related proteins, taurine effectively inhibited liver fibrosis[180]. In another study, researchers investigated the effects of taurine on vitamin A toxicity in rats. The rats were divided into six groups, each fed diets containing different doses of vitamin A, with some groups also receiving 5% taurine supplementation for 2 months. The results showed that as the vitamin A dose increased, the rats experienced weight loss, decreased liver and kidney weight ratios, reduced hepatic glutathione levels, and increased levels of vitamin A, TBARS, AST, ALT, BUN, and creatinine, indicating significant hepatorenal toxicity. However, taurine supplementation significantly alleviated these toxic effects. The combined treatment groups had higher serum vitamin A levels than the vitamin A-only groups, suggesting that taurine reduces the toxic side effects by enhancing vitamin A stability and decreasing its toxic metabolism[181]. Taurine also exhibits choleretic effects and can inhibit gallstone formation. Studies have shown that adding taurine under TPN conditions increased bile flow in guinea pigs, bringing the bile acid secretion rate (BASR) close to normal control levels. Taurine supplementation also increased the levels of secondary bile acid 7-ketolithocholic acid, reduced chenodeoxycholic acid

(CDC), and promoted the secretion of bicarbonates and cholesterol. Under high-dose CDC challenge, the BASR in the TPN taurine group further increased, indicating that taurine can prevent TPN-associated biliary function changes, improve bile flow and composition, and reduce the risk of gallstone formation[182].

3.6 Role of taurine in diabetes and its complications

3.6.1 Changes in tissue and plasma taurine levels in diabetes and underlying mechanisms

Diabetes is a group of heterogeneous diseases primarily characterized by hyperglycemia resulting from insufficient insulin secretion or weakened insulin action. This chronic hyperglycemic state is associated with damage, dysfunction, and failure of various organs, including the retina, kidneys, nervous system, heart, and blood vessels[183]. Taurine can be synthesized intracellularly or transported into cells from plasma *via* TAUT on the cell membrane. However, under pathological conditions, the levels of taurine in tissues and plasma can change. Research has found that diabetes is associated with decreased taurine concentration in tissues[184]. For example, in diabetic rats without taurine supplementation, the retinal taurine levels were significantly lower than those in normal control rats. However, taurine supplementation restored the retinal taurine levels, indicating that the retinal taurine concentration progressively declines during diabetes progression[185]. Additionally, studies have shown that in diabetic animal models, both plasma and kidney taurine levels are lower than in normal rats, and taurine supplementation significantly increases these levels[186]. Furthermore, both insulin-dependent and non-insulin-dependent diabetes patients exhibit significantly reduced taurine levels in plasma and platelets[187]. The underlying mechanism is believed to be linked to organ damage in the kidneys and liver caused by diabetes and its complications, leading to decreased expression of CSD and subsequently reduced taurine synthesis. This results in overall lower taurine levels in the body. Additionally, hyperglycemia has been shown to inhibit the function and expression of TAUT, impeding taurine transport into cells and significantly lowering intracellular taurine levels[188]. High glucose concentrations markedly reduce *Taut* mRNA and protein expression, an effect that can be reversed by blocking the aldose reductase pathway, thereby increasing intracellular taurine levels. Taurine supplementation can upregulate TAUT expression, improving taurine levels reduced by diabetes, indicating its therapeutic potential. In another study, rats were injected with IH containing heparin for 48 h to simulate decreased insulin sensitivity, with some rats also receiving taurine injections. The results showed that IH injection increased oxidative stress markers and JNK-1 activity in the liver, impairing insulin signaling and causing hepatic insulin resistance. Taurine improved hepatic insulin sensitivity by preventing oxidative stress, inhibiting JNK-1 activity, and enhancing insulin signaling, highlighting its potential to protect the liver from insulin resistance[189]. Researchers have also explored the effects of taurine on insulin resistance and type 2 diabetes in rat models. Male rats at 16 weeks old were divided into taurine-supplemented and non-supplemented groups. Glucose tolerance tests and hyperinsulinemic-euglycemic clamp tests were conducted at 23 and 25 weeks old. The results showed that rats without taurine supplementation exhibited hyperglycemia, insulin resistance, and abdominal fat accumulation, whereas taurine-supplemented rats showed significant improvements in these parameters[190]. Another study found that a high-fructose diet altered insulin signaling enzyme activity and glucose metabolism in rats, characterized by decreased glycolytic enzyme activity and increased gluconeogenic enzyme activity. Taurine supplementation improved insulin sensitivity, controlled blood glucose and insulin levels, and restored impaired glucose metabolism enzyme activity. Therefore, taurine effectively counteracts insulin resistance and metabolic abnormalities induced by a high-fructose diet[191].

3.6.2 Mechanisms of blood glucose reduction

1) Taurine facilitates insulin release from pancreatic β-cells and improves insulin resistance. Dysfunction of β-cells and insulin resistance are primary mechanisms in the development of diabetes[192]. Studies indicate that β-cell dysfunction caused by metabolic syndrome is critical in the progression of type 2 diabetes. Excess nutrition leads to insulin secretion failure, with hypoxia and oxidative stress playing significant roles. Enhanced mitochondrial respiration in a high-glucose environment increases oxidative stress, and low antioxidant gene expression makes β-cells more susceptible to damage[193]. On one hand, taurine can protect diabetic β-cells by reducing oxidative stress and upregulating the expression of PDX-1 and NeuroD1, thereby promoting insulin release[194]. On the other hand, taurine enters β-cells through the taurine transporter and binds to the SUR, causing the ATP-sensitive K^+ channels to inactivate. This leads to the opening of voltage-gated calcium channels, allowing extracellular Ca^{2+} to enter the β-cells. When the intracellular Ca^{2+} concentration reaches a certain level, exocytosis is triggered, resulting in the release of insulin[195].

2) Antioxidant effects. Diabetic complications pathways (such as the polyol pathway, AGE pathway, PKC pathway, and hexosamine pathway) generate excessive mitochondrial ROS in a hyperglycemic environment. This leads to oxidative stress, which damages pancreatic β-cells, impairs their function, and exacerbates the progression of diabetes, creating a vicious cycle[196]. Taurine, as an antioxidant, can enhance the intracellular antioxidant defense system and scavenge ROS. In a fructose-fed insulin-resistant rat model, fructose feeding resulted in a high HOMA index, increased lipid peroxidation, and decreased antioxidant enzyme activity. Taurine supplementation reduced lipid peroxidation levels and increased antioxidant enzyme activity, improving insulin sensitivity. Additionally, taurine improved oxidative stress induced by a high-fructose diet by enhancing the antioxidant capacity of the heart and kidneys[197]. Taurine can also inhibit the production of ROS. Studies have shown that diabetic rats exhibit increased expression of p47phox protein and CYP2E1, both of which are key inducers of ROS generation. Taurine supplementation significantly suppressed the expression of p47phox and CYP2E1, thereby reducing ROS production and alleviating oxidative stress[198].

3) Anti-inflammatory effects. Inflammation and oxidative stress are interconnected, making diabetes not only a hyperglycemic condition but also an inflammatory disease. As a hypochlorous acid scavenger, taurine can reduce the formation of inflammatory mediators and exert anti-inflammatory effects. Research has shown

that taurine supplementation significantly improves the morphology and biochemical characteristics of mouse islet cells, increasing the total cell count, promoting DNA synthesis, reducing cell apoptosis, and improving the cellular growth environment. Taurine delays the onset of diabetes, particularly in female mice, postponing it from 10 to 18 weeks. By altering islet cell development and regulating immune function, taurine delays or prevents the onset of type 1 diabetes, offering new insights for prevention and treatment[199]. Another study explored the impact of taurine on oxidative stress and inflammatory biomarkers in patients with type 2 diabetes mellitus (T2DM). Fifty T2DM patients were divided into a taurine group and a placebo group. The taurine group took 1 000 mg of taurine 3 times daily for eight weeks. The results showed that the taurine group had significantly increased activities of SOD and CAT, and significantly decreased levels of malondialdehyde, high-sensitivity C-reactive protein, and TNF-α, while the placebo group showed no significant changes. This indicates that taurine supplementation can improve oxidative stress and inflammatory markers in T2DM patients, alleviating oxidative stress and inflammation caused by diabetes, and providing scientific evidence for taurine as a potential treatment option for T2DM[200].

3.6.3 Prevention and treatment of diabetes complications

A range of clinical complications of diabetes, including eye disease, nephropathy, neuropathy, and cardiomyopathy, are often attributed to endothelial or vascular dysfunction[201]. As an antioxidant and osmotic regulator, taurine helps prevent and treat cellular and vascular dysfunction through multiple pathways. Diabetic nephropathy (DN) is a significant complication of diabetes and a leading cause of chronic renal failure. Hyperglycemia-induced non-enzymatic glycation results in the accumulation of advanced glycation end products (AGEs) in the glomerular basement membrane, promoting the progression of DN[202]. A study investigated serum taurine as a potential biomarker for the early detection and prevention of DN[203]. The study found that serum taurine levels were related to the severity of nephropathy in 90 diabetic patients. Serum taurine levels were generally lower in diabetic patients, particularly in those with severe nephropathy. Another study indicated that hyperglycemia-induced apoptosis is a key factor in DN. In diabetic kidneys, *Caspase-3* and *Caspase-9* mRNA expression decreased, Caspase-3 activity increased, Bax and Bcl-2 expression became dysregulated, and p-Akt levels declined. Taurine treatment restored the expression of *Caspase-3* and *Caspase-9*, reduced Caspase-3 activity, reversed the dysregulation of Bax and Bcl-2 expression, and prevented the decline in p-Akt levels. These findings suggest that taurine improves apoptosis in diabetic kidney cells by activating the Akt signaling pathway[204]. Another study explored the renoprotective effects of taurine in DN rats. The rats were divided into control, taurine, diabetes, and diabetes + taurine groups, with diabetes induced by STZ injection and taurine administered via drinking water. After 12 weeks, taurine reduced MDA, TOS, and NOX4 protein levels in diabetic kidney tissue, increased SOD activity, decreased fibronectin mRNA and protein levels, enhanced MMP-2 and MMP-9 activity, reduced *Emmprin* mRNA expression, and inhibited the expression and activation of TGF-β and Smad2/3. This indicates that taurine may effectively prevent diabetic kidney damage[205].

Diabetic retinopathy (DR) is one of the complications of diabetes, which can lead to vision impairment and even blindness in severe cases. Retinal tissue is rich in free taurine, and retinal cells have a high concentration of taurine transport proteins, allowing taurine to quickly enter retinal cells and exert various biological effects. Taurine plays a crucial role in the development, differentiation, structure, and function of retinal neural tissue[206]. Taurine protects Müller cells under diabetic conditions, especially in terms of antioxidation, maintaining glutamate balance, and neuroprotection. In a high-glucose environment, taurine reduces TBARS, ROS, and NO levels while increasing antioxidant enzyme activity. It also inhibits the reduction in Müller cell glutamate uptake capacity, glutamine synthetase activity, and related protein expression induced by high glucose, thus protecting retinal neural cells from damage[207]. These results highlight the potential of taurine in DR treatment, particularly its role in inhibiting oxidative stress and preserving retinal cell function. Taurine can also dose-dependently inhibit high-glucose-induced apoptosis of retinal Müller cells[208]. Dysfunction of Müller cells due to retinal oxidative stress is a key mechanism in DR. Researchers used a high-glucose culture medium to simulate diabetic cataracts and found that while taurine did not significantly affect lens weight or transparency, taurine pretreatment significantly reduced protein oxidation and increased glutathione levels. This indicates that taurine can protect the lens from oxidative stress induced by high glucose[209].

Diabetic peripheral neuropathy (DPN) is a common complication caused by metabolic disorders and nerve ischemia, affecting about 50% of diabetes patients. Under hyperglycemic conditions, glucose undergoes non-enzymatic glycation with proteins to produce AGEs, which are key factors in microvascular and axonal damage[210]. Studies have shown that taurine can reduce Schwann cell apoptosis in the sciatic nerve of diabetic rats and improve nerve myelin sheath damage by regulating the NGF/Akt/GSK3β signaling pathway. This indicates that taurine has potential applications in the prevention and treatment of DPN[211]. Additionally, researchers have found that taurine significantly lowers blood glucose levels, improves insulin resistance, enhances nerve conduction function, repairs axonal degeneration in the sciatic nerve of diabetic rats, and promotes axonal growth in neurons under high glucose conditions. These benefits are associated with the activation of the PI3K/Akt/mTOR signaling pathway. Taurine is considered a potential candidate for the treatment of diabetic axonopathy[212]. Diabetes is a chronic metabolic disease caused by a combination of genetic and environmental factors. While insulin can control blood glucose levels, it cannot cure diabetes or its complications. Taurine influences the development of diabetes and its complications through mechanisms such as osmotic regulation, free radical scavenging, and anti-inflammatory effects. Given its lack of antigenicity and side effects, taurine holds significant potential for the prevention and treatment of diabetes and its complications in clinical applications.

3.7 Role of taurine in anti-aging

Research shows that taurine levels in the human body decline with age. Supplementing taurine may counteract this loss and slow the progression of age-related health issues, potentially offering a

positive preventive effect against age-related diseases[213]. Studies have indicated that taurine concentrations decrease with age in mice, monkeys, and humans. Supplementing taurine can extend the healthy lifespan of worms and mice and prolong the healthspan of monkeys. These effects are achieved by reducing cellular senescence, protecting telomeres, inhibiting mitochondrial dysfunction, decreasing DNA damage, and alleviating inflammation. The deficiency of taurine may drive aging, and reversing this deficiency could increase healthy lifespan, thus justifying related clinical trials in humans[214]. Duchenne muscular dystrophy (DMD) is a severe muscle-wasting disease. Researchers have studied the effects of taurine on the symptoms of DMD in MDX mice. The results show that taurine improves muscle function and reduces inflammation, while also enhancing muscle antioxidant capacity and decreasing protein oxidation[215]. The study suggests that increasing dietary taurine intake may be a promising strategy for treating DMD. Additionally, taurine significantly regulates the gut microbiota in mice, increasing the abundance of lactobacilli, enhancing gut immunity, combating pathogenic bacteria, and increasing microbial diversity. These effects help restore a healthy gut microenvironment, highlighting taurine's potential for treating or preventing gut microbiota imbalances[216].

3.7.1 Taurine and cellular senescence: exploring the connection

Cellular senescence was first described in 1961 and is characterized by the permanent cessation of cell proliferation in response to internal and external stressors such as telomere dysfunction, oncogene activation, and DNA damage. While senescence can prevent cancer formation, limit tissue damage, and inhibit tumorigenesis, the accumulation of senescent cells and their secretory phenotype can negatively impact surrounding tissues. This process promotes chronic inflammation and tissue dysfunction, ultimately affecting health and lifespan[217]. As we age, the concentration of taurine in the brain decreases, potentially leading to reduced neurogenesis. Research has shown that taurine can activate dormant stem cells, increase cell proliferation, and improve the survival rate of new neurons, thereby enhancing neurogenesis in the hippocampus during brain aging[218]. With aging, the physiological concentration of taurine in the kidneys of rats decreases, which may contribute to kidney fibrosis[219]. Research has found that aging increases the expression of mRNA for type I and IV collagen and fibronectin in rat kidneys. Taurine treatment significantly reduced the levels of these proteins and *Tgfb1* mRNA, thereby mitigating age-related kidney sclerosis. Taurine promotes the formation and proliferation of fibroblast colonies from multipotent stromal cells, shortens doubling time, inhibits senescence-associated β-galactosidase activity, and slows the loss of differentiation potential, demonstrating its anti-replicative aging effects[220]. Additionally, taurine promotes the formation and proliferation of fibroblast colonies from bone marrow-derived multipotent stromal cells, shortens doubling time, significantly inhibits senescence-associated β-galactosidase activity, and slows the loss of differentiation potential, demonstrating its anti-replicative aging effects[221]. Studies have shown that taurine transporter knockout mice exhibit a significant deficiency of taurine in their tissues, which not only shortens their lifespan but also accelerates skeletal muscle aging. Signs of aging include an increase in central nuclei, decreased activity of mitochondrial complex I, and elevated expression of $p16^{INK4a}$. This indicates that taurine plays an important role in regulating tissue aging and extending lifespan[222]. Another research has shown that taurine transporter knockout mice suffer from premature death due to cardiomyopathy. The absence of taurine weakens cardiac contractility, disrupts the electron transport chain, and affects ventricular remodeling by altering protein phosphatase and CaMKII activity. Furthermore, taurine deficiency increases mitochondrial ROS, DNA damage, and chronic inflammation, which accelerates premature aging. This is driven by enhanced NFκB signaling and reduced TauCl levels[223]. In a family with consanguineous marriage in Pakistan, 2 patients with a homozygous mutation (Gly399Val) in the *SLC6A6* gene exhibited severe retinal degeneration and cardiomyopathy, with extremely low plasma taurine levels. Long-term oral taurine supplementation restored their plasma taurine levels to normal. After 24 months, significant improvements in cardiomyopathy and retinal health were observed. This case underscores the potential therapeutic role of taurine supplementation in similar genetic disorders[224]. In Addition, research has shown that taurine depletion accelerates skeletal muscle aging in mice. Transcriptomic analysis revealed activation of SMAD3 and β-catenin signaling pathways, which are associated with the aging gene *CDKN2A*. Western blot analysis confirmed the activation of these pathways in the muscles of taurine transporter knockout mice, indicating that the knockout directly accelerates skeletal muscle aging[225].

3.7.2 Impact of taurine on the unfolded protein response

Loss of protein homeostasis is one of the hallmarks of aging, particularly the accumulation of misfolded proteins in the ER, which triggers the unfolded protein response (UPR) and ER stress. Misfolded proteins increase due to somatic mutations, splicing dysregulation, loss of chaperone activity, and autophagy dysfunction, ultimately leading to cell death and significantly impacting the aging process[226]. Research has found that taurine can inhibit the excessive proliferation of intestinal stem cells in adult fruit flies and prevent the decline in intestinal function associated with aging. This mechanism is achieved by activating UPRER target genes in the ER and inhibiting JNK signaling[227]. Other studies indicate that taurine has potential in delaying stem cell aging and treating age-related intestinal dysfunction. Research using a mouse model lacking the taurine transporter found that taurine deficiency significantly reduces GRP78 expression and inhibits the activation of the PERK-eIF2α-ATF4 pathway in the UPR, underscoring the importance of taurine in maintaining endoplasmic reticulum homeostasis[228].

3.7.3 Regulation of telomere length by taurine

Telomeres are tandem nucleotide repeat sequences located at the ends of chromosomes, serving to protect chromosome termini and maintain genomic integrity. Due to the constraints of DNA replication and the inhibition of telomerase in most somatic cells, telomeres gradually shorten with age, leading to cellular replicative senescence[229]. Telomerase reverse transcriptase (TERT) can stably bind with telomeric RNA and repeatedly reverse transcribe the RNA template, preventing excessive telomere shortening and maintaining telomere stability. This function distinguishes it from

other reverse transcriptases, as it preserves chromosome end integrity and prevents genomic instability[230]. Research has found that taurine significantly enhances the expression of cartilage markers and glycosaminoglycan production in dental pulp-derived stem cells, promoting chondrogenesis. By increasing the expression of the TERT gene and protein, taurine enhances cell proliferation and reverses the effects of telomerase inhibitors, demonstrating its potential in cartilage regeneration and other fields of regenerative medicine[231]. Additionally, studies have shown that higher levels of taurine are associated with longer telomere length, suggesting that taurine may influence telomere maintenance and the aging process through its antioxidant properties[232].

3.7.4 Regulation of sirtuin activity by taurine

Sirtuins are a group of NAD^+-dependent deacetylases that play a critical role in cellular regulation, particularly important in metabolism and aging processes[233]. Sirtuins act as metabolic sensors, regulating cellular functions in response to energy status. Their activation as deacetylases is associated with improved metabolic health and extended lifespan. The seven sirtuins in mammals have distinct locations and functions. SIRT1 is located in the nucleus and can move to the cytoplasm, regulating energy metabolism, DNA repair, and inflammation. SIRT2 is on cytoplasmic microtubules, regulating the cell cycle and mitosis. SIRT3, SIRT4, and SIRT5 are in the mitochondria, enhancing mitochondrial function, regulating insulin secretion and amino acid metabolism, and controlling amino acid metabolism and the urea cycle, respectively. SIRT6, found in the nucleus, is involved in DNA repair, gene expression, and inflammation, and its overexpression can extend the lifespan of male mice. SIRT7, located in the nucleolus, is involved in ribosomal RNA transcription and protein synthesis regulation. Sirtuins depend on NAD^+ for their activity regulation, responding to energy and redox states. SIRT1 interacts with adenosine monophosphate (AMP)-activated protein kinase to activate energy production pathways, enhancing the cell's response to energy stress. Sirtuins also regulate fatty acid metabolism, optimize mitochondrial function, and participate in antioxidant defense mechanisms. This ensures that cells adapt to environmental stress, maintaining metabolic health and physiological balance[234]. Some researchers have pointed out that the decreased expression of sirtuins with age is associated with a decline in cellular function. Increasing the activity or expression of sirtuins can extend lifespan, particularly in studies involving calorie restriction. Upregulation of sirtuins extends lifespan by regulating insulin and insulin-like growth factor signaling, reducing cellular demand for these factors[235]. These findings suggest that sirtuins have the potential to extend healthspan, and activating these proteins may offer new strategies for treating age-related diseases. Taurine can activate SIRT1 in the urinary, digestive, circulatory, and nervous systems[236-239]. Taurine-activated SIRT1 improves mitochondrial function, enhances antioxidant capacity, and inhibits inflammation. This prevents dysfunction in the heart, liver, and nervous system, reducing the risk of age-related diseases and improving overall health.

3.7.5 Impact of taurine on stem cells

The aging and depletion of stem cell reservoirs lead to a decline in organ function and a reduced capacity for healing. As age increases, the replicative ability of stem cells diminishes, resulting in organ function degradation. Stem cell aging is influenced by factors such as levels of ROS and changes in mitochondrial function, which affect their quiescence, self-renewal, and differentiation capabilities[240]. Increasing research demonstrates that taurine can enhance the survival and regenerative capabilities of neural stem cells, while also preserving their stem cell characteristics[241]. Further research has revealed that taurine treatment has a beneficial impact on stem cells related to the development of bone and cartilage[242].

3.7.6 Taurine's unique contributions to anti-aging compared to established compounds

Taurine stands out among established anti-aging compounds such as resveratrol, metformin, nicotinamide mononucleotide (NMN), and Coenzyme Q10 (CoQ10) due to its unique mechanisms and significant contributions to longevity and healthspan enhancement. Resveratrol, a polyphenol in red wine, activates the sirtuin pathway—particularly SIRT1—improving mitochondrial functions and boosting both antioxidant capabilities and stress resistance[243]. Metformin, widely used for diabetes management, extends lifespan across species by enhancing insulin sensitivity, reducing oxidative stress, and activating AMP-activated protein kinase (AMPK)[244]. NMN, as a precursor to NAD^+, raises cellular NAD^+ levels, thereby activating sirtuins, enhancing mitochondrial functionality, and promoting cellular metabolism to delay aging processes[245]. CoQ10, a vital component of the mitochondrial electron transport chain, plays an essential role in ATP synthesis. It effectively counters oxidative damage within mitochondria, providing powerful antioxidant protection and guarding cells against aging-associated oxidative stress[246].

In contrast, taurine not only shares similar antioxidant and anti-inflammatory properties but also uniquely influences calcium homeostasis, mitochondrial function, and endoplasmic reticulum stress. Taurine's anti-aging effects include reducing cellular aging by lowering the expression of aging-related genes, protecting telomeres through the enhanced activity of telomerase reverse transcriptase (hTERT), alleviating DNA damage, maintaining protein homeostasis in the endoplasmic reticulum to prevent the accumulation of misfolded proteins, and modulating cellular metabolism and anti-inflammatory responses *via* activation of sirtuin proteins like SIRT1. Furthermore, taurine positively affects the gut microbiota and strengthens immune function, offering a holistic approach to healthy aging that is distinct from the capabilities of other anti-aging agents. As an endogenous amino acid, taurine boasts high bioavailability and safety, minimizing the potential side effects often associated with synthetic compounds. This blend of extensive biological activities and a strong safety profile positions taurine as an exceptionally promising candidate in anti-aging research, providing a broader spectrum of health benefits than many well-known anti-aging compounds.

4. Assessing toxicity and safety

Taurine is a natural β-amino acid obtained mainly through dietary intake and internal synthesis, though its synthesis capacity is limited, rendering it a conditionally essential amino acid under certain conditions. It is found in high concentrations in meat,

dairy, poultry, fish, and infant formula, while being nearly absent in plant-based foods. Typically, based on a standard weight of 70 kg, omnivores consume approximately 123 mg of taurine per day, lacto-ovo vegetarians about 17 mg, and vegans consume almost none[247]. Taurine is predominantly found in animal-derived foods, with significant variations in content. Seafood has the highest levels, with scallops containing up to 800 mg/100 g. Meat has lower levels, with raw beef containing 40 mg/100 g and raw turkey 300 mg/100 g. Red algae have the highest content among non-animal sources, with some subspecies containing up to 12.49 mg/100 g. Cooking methods like roasting and grilling better preserve taurine compared to boiling[248]. Currently, there is no established dietary reference intake for taurine, primarily due to a lack of consensus within the scientific community regarding its necessary consumption levels[249]. Taurine supplements come in several forms, such as powders, capsules, tablets, and liquids. The recommended dosage varies depending on the product and its intended use, generally ranging from 500 to 2 000 mg per serving[250]. The appropriate intake of taurine supplements varies among individuals, and it is advised to adjust the dosage based on the product label or professional guidance. Numerous human clinical trials have indicated that taurine is a very safe supplement to use[251]. Additionally, caution is warranted when using taurine supplements due to potential interactions with certain medications. Taurine may interact indirectly with cardiovascular drugs by affecting various mechanisms in the cardiovascular system. It is believed to lower blood pressure primarily by reducing adrenaline activity and lessening the effects of angiotensin II, both targets of many antihypertensive medications. This could lead to a synergistic blood pressure-lowering effect. Furthermore, taurine can regulate heart contractility and heart rate, potentially impacting the efficacy of some cardiovascular therapies[252]. Taurine may interact with ethanol by modulating $GABA_A$ and glycine receptors, jointly suppressing central nervous system functions. Additionally, taurine and ethanol can inhibit the function of NMDA receptors and calcium channels, further enhancing their inhibitory impact[253]. Before taking taurine supplements, vulnerable groups including the elderly, children, pregnant and nursing women, as well as individuals with bipolar disorder, epilepsy, liver or kidney diseases, cardiovascular diseases, or diabetes should consult with a healthcare provider. This consultation allows for an evaluation of potential risks, personalized advice, and monitored usage to ensure safety.

A double-blind, crossover study evaluated the therapeutic effects of taurine at a dosage of 100–150 mg/kg body weight on patients with myotonic dystrophy, confirming its effectiveness. In a 6-month trial with doses up to 7–10 g/day, no significant adverse reactions were observed apart from mild gastrointestinal discomfort[254]. A clinical trial assessed the effects and tolerability of intravenous taurine in 37 epilepsy patients. Participants received daily treatments of 200 mg/kg of taurine for the first 15 days, followed by weekly treatments for 6 weeks. The results showed a reduction in seizures by approximately 30% during the first 10 days; however, seizure frequency returned to baseline levels between days 30 and 60. Around 50% of patients experienced improvements in skin appearance, attention, and memory, with no significant adverse reactions reported, indicating that this dosage is well-tolerated[255]. A study conducted at the University of Turin evaluated the antiepileptic effects of taurine in 15 patients with refractory epilepsy. The treatment regimen involved intravenous infusions of 150–200 mg/kg taurine every 12 h for 5 days, followed by once every 24 h for the next 5 days, and then twice a week for the following 50 days. The results indicated that most patients experienced seizure cessation and EEG improvements early in the treatment, although symptoms gradually returned later. Only 4 young patients maintained improvement by the end of the follow-up period. The only side effect observed was a slight reduction in arterial pressure, demonstrating good tolerability of taurine treatment[256]. In another study, a daily dose of 6 g taurine was administered to 14 patients with congestive heart failure over a period of 4 weeks. Compared to the placebo, taurine significantly improved heart function classification, pulmonary rales, and chest X-ray abnormalities. Based on clinical examinations, the overall treatment response assessment for each patient showed a significant advantage for taurine. During taurine treatment, no patients experienced worsening of their condition, whereas four patients in the placebo group did. No side effects were observed in the treatment group, indicating that taurine supplementation is both safe and effective for treating patients with congestive heart failure[257]. In a double-blind, placebo-controlled study, 10 out of 19 patients with borderline hypertension were administered 6 g taurine orally each day for 7 days. The results showed a significant reduction in both systolic and diastolic blood pressure in the taurine group, while no significant changes were observed in the placebo group. Taurine also reduced baseline plasma adrenaline levels and attenuated the adrenaline response to glucagon stimulation, confirming its antihypertensive effects. In individuals with normal blood pressure, taurine did not significantly alter blood pressure or adrenaline levels, and no adverse reactions were reported[258]. In a study, 22 healthy men were randomly divided into 2 groups and subjected to a high-fat, high-cholesterol diet for three weeks. One group received a daily supplement of 6 g taurine, while the other group received a placebo. The results showed that taurine reduced the increase in total cholesterol and LDL cholesterol but increased VLDL cholesterol, VLDL, and TG. Additionally, taurine significantly lowered urinary norepinephrine excretion, suggesting an inhibitory effect on the sympathetic nervous system. No adverse reactions were reported[259]. A study evaluated the effects of taurine on serum lipids in overweight or obese young adults. A total of 30 college students were randomly assigned to either a taurine group or a placebo group, receiving 3 g taurine or a placebo daily for 7 weeks. The results showed that taurine significantly reduced TG, lowered the AI, and led to notable weight loss, with no adverse reactions reported[260]. Based on currently published human clinical trial data, some researchers have used a new method called the Observed Safety Level or Highest Observed Intake to assess taurine's safety. They concluded that daily supplementation of taurine up to 3 g has not been associated with any adverse effects, and this intake level is considered safe for healthy adults[261]. For insights into the safety

Table 5
Safety and toxicity observations of taurine in medical use.

Study subjects	Dosage	Administration schedule	Key observational findings	Reference
Eighteen cases of myotonic dystrophy patients	100–150 mg/(kg·day)	Administered orally daily for 6 consecutive months.	Studies have shown that with the use of supplements, taurine levels in serum and urine increased. Throughout the study period, no significant adverse reactions were observed, with only occasional reports of mild gastrointestinal discomfort.	[254]
Thirty seven cases of epilepsy patients	200 mg/(kg·day)	Treatment was administered intravenously daily for the initial 15 days, followed by once weekly for the subsequent 6 weeks.	The study did not report any significant adverse reactions related to the dosage, indicating that the doses administered were well tolerated by the participants in this research setting.	[255]
Fifteen cases of epilepsy patients	150–200 mg/(kg·12 h)	Administered intravenously 150 , 200 mg/kg of taurine every 12 h for 5 days, followed by once every 24 h for another 5 days, and then twice weekly for the next 50 days.	The only side effect observed was a slight decrease in arterial pressure in most patients, indicating that the taurine treatment is well tolerated.	[256]
Fourteen cases of congestive heart failure patients	6 g/(day·person)	Administered orally for 4 weeks.	No side effects were observed in the treatment group, demonstrating that the addition of taurine is both safe and effective for treating patients with congestive heart failure.	[257]
Ninteen cases of borderline hypertensive patients	6 g/(day·person)	Administered orally for 7 days.	In patients treated with taurine, both systolic and diastolic blood pressures showed significant reductions, whereas the decreases were not significant in the placebo group. No adverse reactions were reported.	[258]
Twenty two healthy individuals	6 g/(day·person)	Administered orally for 3 weeks.	Taurine supplementation effectively mitigated the increases in total cholesterol, LDL cholesterol, and LDL observed in a high-fat, high-cholesterol diet, but led to significant increases in VLDL cholesterol, VLDL, and triglycerides. Additionally, it significantly reduced the urinary excretion of norepinephrine, indicating an inhibitory effect on the sympathetic nervous system. No adverse reactions were reported.	[259]
Thirty healthy individuals	3 g/(day·person)	Administered orally for 7 weeks.	Before and after supplementation, levels of TG, total cholesterol TC, HDL-C, and plasma glucose were measured. The AI was calculated using the formula (TC-HDL-C)/HDL-C. There were no significant differences in baseline parameters between the 2 groups. Supplementation with taurine significantly lowered TG and AI, and also led to a significant reduction in body weight in the taurine group. No adverse reactions were reported.	[260]

and toxicity of taurine in medical applications, please refer to Table 5.

5. Discussion

In modern medicine, taurine is recognized for its distinct pharmacological properties, playing significant roles in antitumor activity, immune regulation, neuroprotection, cardiovascular health, and providing protective benefits for the liver and gallbladder. It is known for its ability to reduce blood pressure, lipid levels, and blood sugar levels, and offers anti-aging properties, making it a valuable compound in medical research and therapy.

TCM advocates a holistic approach that emphasizes syndrome differentiation and individualized treatment, suggesting that diseases are systemic and treatments should address both specific symptoms and overall body wellness[262]. This philosophy also stems from dietary therapy, as the majority of medicinal materials used in TCM are derived from plants and animals in the natural environment[263]. Within this framework, taurine's broad biological regulatory effects are exceptionally beneficial. It enhances immune clearance in individuals with compromised immunity, offers neuroprotective benefits by modulating neurotransmission, inhibits neuronal overexcitation, and exhibits antithrombotic properties in hypercoagulable states. Moreover, taurine aids in regulating heart rate, protecting myocardial cells during arrhythmias or ischemic events, and normalizing metabolic anomalies such as abnormal blood glucose and lipid levels. Consequently, taurine represents a dietary supplement or medication with significant therapeutic potential, exerting regulatory effects that can both stimulate and inhibit physiological processes as needed, aligning with the principles of TCM. In this context, TCM and modern medicine find common ground, both recognizing the functional and pharmacological properties of taurine in remarkably similar ways. Additionally, taurine is a valuable component of various TCM—such as bezoar, pearl, snake bile, cordyceps, and scorpion—underscoring its importance in these often expensive remedies.

As a dietary supplement, taurine is cost-effective and widely available, making it a popular choice in nutritional regimens aimed at health maintenance and disease prevention. However, its utility extends beyond traditional and modern medical applications into the realm of functional foods, where it can be harnessed for its comprehensive biological impacts on human health. In summary, the functional properties and pharmacological characteristics of taurine, whether utilized as a dietary supplement or medication, align seamlessly with the fundamental principles of TCM and the evidence-based outcomes of modern medicine.

Regarding the safety and toxicology of taurine, the literature consistently highlights its widespread use and robust safety profile in foods, dietary supplements, and pharmaceuticals. Taurine is primarily obtained from dietary sources and internal synthesis, being abundant in meat, dairy, poultry, fish, and infant formulas, but scarcely found in plant-based foods. Although there is no established recommended daily intake, rigorous safety assessments have confirmed that daily dosages up to 3 g are considered safe and risk-free for healthy adults. Taurine has demonstrated excellent tolerability and significant therapeutic effectiveness in clinical trials involving patients with myotonic dystrophy, epilepsy, and heart failure, with minimal side effects. Nevertheless, taurine may interact with certain cardiovascular medications, potentially enhancing their effects on lowering blood pressure and regulating heart contractility due to its influence on

multiple mechanisms within the cardiovascular system. Additionally, some studies suggest that taurine may interact with alcohol, potentially affecting central nervous system activity; therefore, caution is advised when combining taurine supplements with alcohol. Caution is also advised before using taurine supplements, especially for vulnerable groups such as the elderly, children, pregnant and nursing women, and individuals with conditions like bipolar disorder, epilepsy, liver or kidney disease, cardiovascular diseases, or diabetes. Consultation with a healthcare professional is recommended for these individuals. Understanding the safety and potential drug interactions of taurine is essential for its further research and application, which could optimize therapeutic regimens and ensure patient safety. Future research should continue to focus on safety assessments of taurine and its potential application across diverse populations and complex diseases. This interdisciplinary approach will advance the use of taurine in functional foods and medical applications, offering safer and more effective solutions for preventing and treating various health issues.

6. Conclusion and future perspectives

Given its wide-ranging benefits, taurine has demonstrated substantial potential in both the prevention and adjunct treatment of various diseases, and is a crucial component in the development of functional foods aimed at enhancing physiological functions and health outcomes. As research progresses, the application of taurine in clinical and nutritional domains appears increasingly promising. Given its capacity to manage complex pathological conditions such as cancer, cardiovascular diseases, and neurological disorders, it is imperative to further pursue in-depth research into taurine-based pharmaceuticals, derivatives, and its inclusion in cost-effective, health-promoting dietary strategies. This exploration, by merging food science with pharmacology, is poised to yield innovative solutions that enhance health and functional nutrition.

Conflicts of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgement

This work was supported by was supported by the Medical Education Research Project of Liaoning (2024-N005-01), Key Project of the Second Clinical College of China Medical University's Institutional Teaching Reform Project 'Teacher Teaching Ability Construction' (SJJG-2025ZXZD04), Postgraduate Education Reform Project of Liaoning Province (LNYJG2023209), and the Second Clinical College of China Medical University 14th Five-Year Plan Institutional Teaching Reform Project Open Topic (SJJG-2024YB07).

References

[1] M. Cooley, Bezoar: medicine in the belly of the beast, in natural things in early modern worlds, Routledge (2023) 52-84. https://doi.org/10.4324/9781003351054.

[2] D.Q. Wang, M.C. Carey, Therapeutic uses of animal biles in traditional chinese medicine: an ethnopharmacological, biophysical chemical and medicinal review, World J. Gastroenterol. 20(29) (2014) 9952-9975. https://doi.org/10.3748/wjg.v20.i29.9952.

[3] Z.J. Yu, Y. Xu, W. Peng, et al., Calculus bovis: a review of the traditional usages, origin, chemistry, pharmacological activities and toxicology, J. Ethnopharmacol. 254 (2020) 112649. https://doi.org/10.1016/j.jep.2020.112649.

[4] National Center for Biotechnology Information, PubChem Compound Summary for CID 1123, Taurine, PubChem Database (2024). https://pubchem.ncbi.nlm.nih.gov/compound/Taurine.

[5] H. Ripps, W. Shen, Taurine: a 'very essential' amino acid, Mol. Vis. 18 (2012) 2673-2686. https://doi.org/10.1186/1476-4598-18-275.

[6] H.H. Sutherland, D.W. Young, The crystal and molecular structure of taurine, Acta Crystallogr. 16(9) (1963) 897-901. https://doi.org/10.1107/S0365110X63002413.

[7] D.E. Hibbs, C.J. Austin-Woods, J.A. Platts, et al., Experimental and theoretical charge density study of the neurotransmitter taurine, Chemistry 9(5) (2003) 1075-1084. https://doi.org/10.1002/chem.200390100.

[8] A.O.H. Ahmed, A brief insight about taurine and its antioxidant effects, Tobacco Regulatory Science (2023) 2929-2936.

[9] N. Rais, A. Ved, M. Shadab, et al., Taurine, a non-proteinous essential amino acid for human body systems: an overview, Arab. Gulf. J. Sci. Res. 41(1) (2023) 48-66. https://doi.org/10.1108/AGJSR-04-2022-0019.

[10] M.L. Tappaz, Taurine biosynthetic enzymes and taurine transporter: molecular identification and regulations, Neurochem. Res. 29 (2004) 83-96. https://doi.org/10.1023/b.0000010436.44223.f8.

[11] J. De la Rosa, M.H. Stipanuk, Evidence for a rate-limiting role of cysteinesulfinate decarboxylase activity in taurine biosynthesis *in vivo*, Comp. Biochem. Physiol. B 81(3) (1985) 565-571. https://doi.org/10.1016/0305-0491(85)90367-0.

[12] J.A. Sturman, Taurine in development, Physiol. Rev. 73(1) (1993) 119-147. https://doi.org/10.1152/physrev.1993.73.1.119.

[13] P.P. Stapleton, R.P. Charles, H.P. Redmond, et al., Taurine and human nutrition, Clin. Nutr. 16(3) (1997) 103-108. https://doi.org/10.1016/s0261-5614(97)80234-8.

[14] M. Shimizu, H. Satsu, Physiological significance of taurine and the taurine transporter in intestinal epithelial cells, Amino Acids 19(3-4) (2000) 605-614. https://doi.org/10.1007/s007260070010.

[15] K.C. Hayes, J. A. Sturman, Taurine in metabolism, Ann. Rev. Nutr. 1 (1981) 401-425. https://doi.org/10.1146/annurev.nu.01.070181.002153.

[16] T. Miyazaki, Y. Matsuzaki, Taurine and liver diseases: a focus on the heterogeneous protective properties of taurine, Amino Acids 46(1) (2014) 101-110. https://doi.org/10.1007/s00726-012-1381-0.

[17] J.A. Sturman, G.W. Hepner, A.F. Hofmann, et al., Metabolism of [35S]taurine in man, J. Nutr. 105(9) (1975) 1206-1214. https://doi.org/10.1093/jn/105.9.1206.

[18] R.W. Chesney, I. Zelikovic, D.P. Jones, et al., The renal transport of taurine and the regulation of renal sodium-chloride-dependent transporter activity, Pediatric Nephrology 4(4) (1990) 399-407. https://doi.org/10.1007/BF00862526.

[19] R.C. Gupta, Taurine analogues and taurine transport: therapeutic advantages, Adv. Exp. Med. Biol. 583 (2006) 449-467. https://doi.org/10.1007/978-0-387-33504-9_52.

[20] A. Barbeau, N. Inoue, Y. Tsukada, et al., The neuropharmacology of taurine, Life Sci. 17(5) (1975) 669-677. https://doi.org/10.1016/0024-3205(75)90520-2.

[21] J.A. Sturman, G.E. Gaull, Taurine in the brain and liver of the developing human and monkey, J. Neurochem. 25(6) (1975) 831-835. https://doi.org/10.1111/j.1471-4159.1975.tb04414.x.

[22] T.L. Perry, P.J. Bratty, S. Hansen, et al., Hereditary mental depression and Parkinsonism with taurine deficiency, Arch. Neurol. 32(2) (1975) 108-113. https://doi.org/10.1001/archneur.1975.00490440058009.

[23] A.G. Goodridge, E.G. Ball, Taurine involvement in retinal and heart muscle function, Nutr. Rev. 33(11) (1975) 343-347. https://doi.org/10.1111/j.1753-4887.1975.tb05205.x.

[24] G.E. Gaull, Taurine in pediatric nutrition: review and update, Pediatrics 83(3) (1989) 433-442. https://doi.org/10.1542/peds.83.3.433.

[25] K.C. Hayes, A. Pronczuk, A.E. Addesa, et al., Taurine modulates platelet aggregation in cats and humans, Am. J. Clin. Nutr. 49(6) (1989) 1211-1216. https://doi.org/10.1093/ajcn/49.6.1211.

[26] M. Taherizadeh, M. Khoshnia, S. Shams, et al., Comparison of plasma taurine levels between patients with esophageal cancer and healthy controls, Medical Laboratory Journal 11(2) (2017). https://doi.org/10.18869/acadpub.mlj.11.2.1.

[27] I.M. El Agouza, S.S. Eissa, M.M. El Houseini, et al., Taurine: a novel tumor marker for enhanced detection of breast cancer among female patients, Angiogenesis 14(3) (2011) 321-330. https://doi.org/10.1007/s10456-011-9215-3.

[28] I.M.A.E.L. Agouza, D.E.E.L. Nashar, Serum taurine as a marker of endometrial cancer, Open Women's Health Journal 5 (2011) 1-6. https://doi.org/10.2174/1874291201105010001.

[29] S. Srivastava, R. Roy, S. Singh, et al., Taurine - a possible fingerprint biomarker in non-muscle invasive bladder cancer: a pilot study by 1H NMR spectroscopy, Cancer Biomark 6(1) (2010) 11-20. https://doi.org/10.3233/CBM-2009-0115.

[30] K.S. Opstad, B.A. Bell, J.R. Griffiths, et al., Taurine: a potential marker of apoptosis in gliomas, Br. J. Cancer 100(5) (2009) 789-794. https://doi.org/10.1038/sj.bjc.6604933.

[31] L. Wang, N. Zhao, F. Zhang, et al., Effect of taurine on leucocyte function, Eur. J. Pharm. 616(1-3) (2009) 275-280. https://doi.org/10.1016/j.ejphar.2009.05.027.

[32] Y. Sadzuka, M. Matsuura, T. Sonobe, The effect of taurine, a novel biochemical modulator, on the antitumor activity of doxorubicin, Biol. Pharm. Bull. 32(9) (2009) 1584-1587. https://doi.org/10.1248/bpb.32.1584.

[33] J.S. Yu, A.K. Kim, Effect of combination of taurine and azelaic acid on antimelanogenesis in murine melanoma cells, J. Biomed. Sci. 17(Suppl 1) (2010) S45. https://doi.org/10.1186/1423-0127-17-S1-S45.

[34] J. Wang, L. Wei, C. Liu, et al., Taurine treatment alleviates intestinal mucositis induced by 5-fluorouracil in mice, Plant Food Hum. Nutr. 77(3) (2022) 399-404. https://doi.org/10.1007/s11130-022-00980-5.

[35] M. Yasunaga, Y. Matsumura, Role of SLC6A6 in promoting the survival and multidrug resistance of colorectal cancer, Sci. Rep. 4 (2014) 4852. https://doi.org/10.1038/srep04852.

[36] T. Cao, W. Zhang, Q. Wang, et al., Cancer SLC6A6-mediated taurine uptake transactivates immune checkpoint genes and induces exhaustion in $CD8^+$ T cells, Cell (2024). https://doi.org/10.1016/j.cell.2024.03.011.

[37] J. Yu, A.K. Kim, Effect of taurine on antioxidant enzyme system in B16F10 melanoma cells, Adv. Exp. Med. Bio. 643 (2009) 491-499. https://doi.org/10.1007/978-0-387-75681-3_51.

[38] S. Venkatachalam, P. Kuppusamy, B. Kuppusamy, et al., The potency of essential nutrient taurine on boosting the antioxidant status and chemopreventive effect against benzo(a)pyrene induced experimental lung cancer, Biomed. Preventive Nutr. 4(2) (2014) 251-255. https://doi.org/10.1016/j.bionut.2013.09.006.

[39] H.M. Ibrahim, F.R. Abdel Ghaffar, I.A. El-Elaimy, et al., Antitumor and immune-modulatory efficacy of dual-treatment based on levamisole and/or taurine in Ehrlich ascites carcinoma-bearing mice, Biomed. Pharmacother. 106 (2018) 43-49. https://doi.org/10.1016/j.biopha.2018.06.113.

[40] S.G. Maher, C.E. Condron, D.J. Bouchier-Hayes, et al., Taurine attenuates CD3/interleukin-2-induced T cell apoptosis in an *in vitro* model of activation-induced cell death (AICD), Clin. Exp. Immun. 139(2) (2005) 279-286. https://doi.org/10.1111/j.1365-2249.2005.02694.x.

[41] Y. Ping, J. Shan, Y. Liu, et al., Taurine enhances the antitumor efficacy of PD-1 antibody by boosting $CD8^+$ T cell function, Cancer Immunol. Immun. 72(4) (2023) 1015-1027. https://doi.org/10.1007/s00262-022-03308-z.

[42] N. Finnegan, D. Toomey, C. Condron, et al., Potentiation of the therapeutic index of interleukin-2 immunotherapy by combination with taurine in a syngeneic murine tumour model, Irish J. Med. Sci. 171(2) (2002) 85-88. https://doi.org/10.1007/BF03168959.

[43] Z. Liang, F. Nong, Z. Li, et al., Taurine-mediated metabolic immune crosstalk indicates and promotes immunosuppression with anti-PD-1 resistance in bladder cancer, Front. Immunol. 16 (2025) 1618439. https://doi.org/10.3389/fimmu.2025.1618439.

[44] H. Fang, F. Meng, F. Piao, et al., Effect of taurine on intestinal microbiota and immune cells in Peyer's patches of immunosuppressive mice, Adv. Exp. Med. Bio. 1155 (2019) 13-24. https://doi.org/10.1007/978-981-13-8023-5_2.

[45] S. Tu, X.L. Zhang, H.F. Wan, et al., Effect of taurine on cell proliferation and apoptosis in human lung cancer A549 cells, Oncol. Lett. 15(4) (2018) 5473-5480. https://doi.org/10.3892/ol.2018.8036.

[46] H. Li, W.J. Ruan, L.Q. Liu, et al., Impact of taurine on the proliferation and apoptosis of human cervical carcinoma cells and its mechanism, Chinese Med. Jo. 132(8) (2019) 948-956. https://doi.org/10.1097/CM9.0000000000000162.

[47] S. Tu, X. Zhang, D. Luo, et al., Effect of taurine on the proliferation and apoptosis of human hepatocellular carcinoma HepG2 cells, Exp. Therap. Med. 10(1) (2015) 193-200. https://doi.org/10.3892/etm.2015.2476.

[48] X. Zhang, H. Lu, Y. Wang, et al., Taurine induces the apoptosis of breast cancer cells by regulating apoptosis-related proteins of mitochondria, Intern. J. Mol. Med. 35(1) (2015) 218-226. https://doi.org/10.3892/ijmm.2014.2002.

[49] P.M. Neary, P. Hallihan, J.H. Wang, et al., The evolving role of taurolidine in cancer therapy, Ann. Surg. Oncol 17(4) (2010) 1135-1143. https://doi.org/10.1245/s10434-009-0867-9.

[50] G. Singh, H.O. Graffner, J.W. Milsom, et al., Tauromustine is more effective than conventional chemotherapy in the treatment of colonic tumors, Dis. Colon Rectum 36(4) (1993) 394-399. https://doi.org/10.1007/BF02053946.

[51] Y.H. Kim, J.H. Kim, B.G. Kim, et al., Tauroursodeoxycholic acid attenuates colitis-associated colon cancer by inhibiting nuclear factor kappaB signaling, J. Gas. Hepat. 34(3) (2019) 544-551. https://doi.org/10.1111/jgh.14526.

[52] Y.P. Vandewynckel, D. Laukens, L. Devisscher, et al., Tauroursodeoxycholic acid dampens oncogenic apoptosis induced by endoplasmic reticulum stress during hepatocarcinogen exposure, Oncotarget 6(29) (2015) 28011-28025. https://doi.org/10.18632/oncotarget.4377.

[53] F. Klamt, E. Shacter, Taurine chloramine, an oxidant derived from neutrophils, induces apoptosis in human B lymphoma cells through mitochondrial damage, J. Biol. Chem. 280(22) (2005) 21346-21352. https://doi.org/10.1074/jbc.M501170200.

[54] X. Ou, G. Gao, I.A. Habaz, et al., Mechanisms of resistance to tyrosine kinase inhibitor-targeted therapy and overcoming strategies, MedComm. 5(9) (2024) e694. https://doi.org/10.1002/mco2.694.

[55] M. Sambi, L. Bagheri, M.R. Szewczuk, Current challenges in cancer immunotherapy: multimodal approaches to improve efficacy and patient response rates, J. Oncol. 2019 (2019) 4508794. https://doi.org/10.1155/2019/4508794.

[56] J.G. Morris, Q.R. Rogers, Taurine: an essential nutrient for cats, J. Small Anim. Pract. 31(10) (1990). https://doi.org/10.1111/j.1748-5827.1990.tb00672.x.

[57] P.F. Surai, I.I. Kochish, M.T. Kidd, Taurine in poultry nutrition, Anim. Feed Sci. Technol. 260 (2020) 114339. https://doi.org/10.1016/j.anifeedsci.2019.114339.

[58] L. Lima, F. Obregón, M. Urbina, et al., Taurine concentration in human blood peripheral lymphocytes: major depression and treatment with the antidepressant mirtazapine, Adv. Exp. Med. Biol. 526 (2003) 297-304. https://doi.org/10.1007/978-1-4615-0077-3_38.

[59] H.H. Tallan, E. Jacobson, C.E. Wright, et al., Taurine uptake by cultured human lymphoblastoid cells, Life Sci. 33(19) (1983) 1853-1860. https://doi.org/10.1016/0024-3205(83)90669-0.

[60] S. Roysommuti, J. Azuma, K. Takahashi, et al., Taurine cytoprotection: from cell to system, J. Physiol. Sci. 16(2) (2003) 17-27.

[61] S. Kuriyama, T. Tsujii, S. Ishizaka, et al., Enhancing effects of oral adjuvants on anti-HBs responses induced by hepatitis B vaccine, Clin. Exp. Immunol. 72(3) (1988) 383-389.

[62] S. Nishio, S. Negoro, T. Hosokawa, et al., The effect of taurine on age-related immune decline in mice: the effect of taurine on T cell and B cell proliferative response under costimulation with ionomycin and phorbol myristate acetate, Mech. Ageing Dev. 52(2-3) (1990) 125-139. https://doi.org/10.1016/0047-6374(90)90119-z.

[63] G. Schuller-Levis, P.D. Mehta, R. Rudelli, et al., Immunologic consequences of taurine deficiency in cats, J. Leukoc. Biol. 47(4) (1990) 321-331. https://doi.org/10.1002/jlb.47.4.321.

[64] N.M. Finnegan, H.P. Redmond, D.J. Bouchier-Hayes, et al., Taurine attenuates recombinant interleukin-2-activated, lymphocyte-mediated endothelial cell injury, Cancer 82(1) (1998) 186-199.

[65] H.P. Redmond, P.P. Stapleton, P. Neary, et al., Immunonutrition: the role of taurine, Nutrition 14(7-8) (1998) 599-604. https://doi.org/10.1016/s0899-9007(98)00097-5.

[66] P.P. Stapleton, L. O'Flaherty, H.P. Redmond, et al., Host defense—a role for the amino acid taurine? JPEN J. Parenter Enteral. Nutr. 22(1) (1998) 42-48. https://doi.org/10.1177/014860719802200142.

[67] M. Masuda, K. Horisaka, T. Koeda, Effects of taurine on neutrophil function in hyperlipidemic rats, Jpn. J. Pharmacol. 40(3) (1986) 478-480. https://doi.org/10.1254/jjp.40.478.

[68] M.E. Medof, T. Lam, G.M. Prince, et al., Requirement for human red blood cells in inactivation of C3b in immune complexes and enhancement of binding to spleen cells, J. Immunol. 130(3) (1983) 1336-1340. https://doi.org/10.4049/jimmunol.130.3.1336.

[69] Y. Su, W. Fan, Z. Ma, et al., Taurine improves functional and histological outcomes and reduces inflammation in traumatic brain injury, Neuroscience 266 (2014) 56-65. https://doi.org/10.1016/j.neuroscience.2014.02.006.

[70] S.Y. Nam, H.M. Kim, H.J. Jeong, The potential protective role of taurine against experimental allergic inflammation, Life Sci. 184 (2017) 18-24. https://doi.org/10.1016/j.lfs.2017.07.007.

[71] Q. Lv, L. Sun, Y. Cui, et al., Effects of replacement of methionine in diets with taurine on growth performance and blood index in broilers, Adv. Exp. Med. Biol. 975 Pt 2 (2017) 989-1000. https://doi.org/10.1007/978-94-024-1079-2_78.

[72] W. Song, X. Li, H. Cao, et al., Taurine promotes B-cell activation by interaction with the VH/VL framework regions of B-cell receptor, Immunology 169(2) (2023) 141-156. https://doi.org/10.1111/imm.13617.

[73] S. Ishizaka, M. Yoshikawa, K. Kitagami, et al., Oral adjuvants for viral vaccines in humans, Vaccine. 8(4) (1990) 337-341. https://doi.org/10.1016/0264-410x(90)90091-y.

[74] M. Giriş, B. Depboylu, S. Doğru-Abbasoğlu, et al., Effect of taurine on oxidative stress and apoptosis-related protein expression in trinitrobenzene sulphonic acid-induced colitis, Clin. Exp. Immunol. 152(1) (2008) 102-110. https://doi.org/10.1111/j.1365-2249.2008.03599.x.

[75] H.H. Hagar, E. El Etter, M. Arafa, Taurine attenuates hypertension and renal dysfunction induced by cyclosporine A in rats, Clin. Exp. Pharmacol. Physiol. 33(3) (2006) 189-196. https://doi.org/10.1111/j.1440-1681.2006.04345.x.

[76] C. Akay, H. Yaman, M. Oztosun, et al., The protective effects of taurine on experimental acute pancreatitis in a rat model, Hum. Exp. Toxicol. 32(5) (2013) 522-529. https://doi.org/10.1177/0960327113482692.

[77] M. Islambulchilar, I. Asvadi, Z. Sanaat, et al., Effect of taurine on attenuating chemotherapy-induced adverse effects in acute lymphoblastic leukemia, J. Cancer Res. Ther. 11(2) (2015) 426-432. https://doi.org/10.4103/0973-1482.151933.

[78] C. Kim, Y.N. Cha, Taurine chloramine produced from taurine under inflammation provides anti-inflammatory and cytoprotective effects, Amino Acids 46(1) (2014) 89-100. https://doi.org/10.1007/s00726-013-1545-6.

[79] J. Hoosain, E. Hamad, Adverse effects of immunosuppression: nephrotoxicity, hypertension, and metabolic disease, Handbook of Experimental Pharmacology 272 (2022) 337-348. https://doi.org/10.1007/164_2021_547.

[80] M. Li, R. You, Y. Su, et al., Characteristic analysis of adverse reactions of 5 anti-TNFα agents: a descriptive analysis from WHO-VigiAccess, Front. Pharmacol. 14 (2023) 1169327. https://doi.org/10.3389/fphar.2023.1169327.

[81] Z. Kavyani, V. Musazadeh, S. Fathi, et al., Efficacy of the omega-3 fatty acids supplementation on inflammatory biomarkers: an umbrella meta-analysis, Int. Immunopharmacol. 111 (2022) 109104. https://doi.org/10.1016/j.intimp.2022.109104.

[82] J. Menzie, C. Pan, H. Prentice, et al., Taurine and central nervous system disorders, Amino Acids 46(1) (2014) 31-46. https://doi.org/10.1007/s00726-012-1382-z.

[83] J.Y. Wu, H. Prentice, Role of taurine in the central nervous system, J. Biomed. Sci. 17 Suppl 1 (2010) S1. https://doi.org/10.1186/1423-0127-17-S1-S1.

[84] H. Pasantes-Morales, J. Morán, Taurine as a neuromodulator: its action on calcium fluxes and neurotransmitter release, in R. Tapia, C.W. Cotman (Eds.), Regulatory Mechanisms of Synaptic Transmission, Springer, Boston, MA, 1981. https://doi.org/10.1007/978-1-4684-3968-7_7.

[85] R.E. Haskew-Layton, A. Rudkouskaya, Y. Jin, et al., Two distinct modes of hypoosmotic medium-induced release of excitatory amino acids and taurine in the rat brain *in vivo*, PLoS One 3(10) (2008) e3543. https://doi.org/10.1371/journal.pone.0003543.

[86] P. Kontro, K.M. Marnela, S.S. Oja, Free amino acids in the synaptosome and synaptic vesicle fractions of different bovine brain areas, Brain Res. 184(1) (1980) 129-141. https://doi.org/10.1016/0006-8993(80)90592-2.

[87] A.M. López-Colomé, Taurine receptors in CNS membranes: binding studies, Adv. Exp. Med. Biol. 139 (1981) 293-310. https://doi.org/10.1007/978-1-4757-0402-0_19.

[88] A. El Idrissi, E. Trenkner, Taurine as a modulator of excitatory and inhibitory neurotransmission, Neurochem. Res. 29(1) (2004) 189-197. https://doi.org/10.1023/b.0000010448.17740.6e.

[89] W. Kilb, A. Fukuda, Taurine as an essential neuromodulator during perinatal cortical development, Front. Cell. Neurosci. 11 (2017) 328. https://doi.org/10.3389/fncel.2017.00328.

[90] J.Y. Wu, X.W. Tang, W.H. Tsai, Taurine receptor: kinetic analysis and pharmacological studies, Adv. Exp. Med. Biol. 315 (1992) 263-268. https://doi.org/10.1007/978-1-4615-3436-5_31.

[91] M. Frosini, C. Sesti, S. Dragoni, et al., Interactions of taurine and structurally related analogues with the GABAergic system and taurine binding sites of rabbit brain, Br. J. Pharmacol. 138(6) (2003) 1163-1171. https://doi.org/10.1038/sj.bjp.0705134.

[92] M. Mori, B.H. Gähwiler, U. Gerber, Beta-alanine and taurine as endogenous agonists at glycine receptors in rat hippocampus *in vitro*, J. Physiol. 539(Pt 1) (2002) 191-200. https://doi.org/10.1113/jphysiol.2001.013147.

[93] G.H. Wang, Z.L. Jiang, X.J. Fan, et al., Neuroprotective effect of taurine against focal cerebral ischemia in rats possibly mediated by activation of both $GABA_A$ and glycine receptors, Neuropharmacology 52(5) (2007) 1199-1209. https://doi.org/10.1016/j.neuropharm.2006.10.022.

[94] N. Del Olmo, J. Bustamante, R.M. del Río, et al., Taurine activates $GABA_A$ but not $GABA_B$ receptors in rat hippocampal CA1 area, Brain Res. 864(2) (2000) 298-307. https://doi.org/10.1016/s0006-8993(00)02211-3.

[95] F. Jia, M. Yue, D. Chandra, et al., Taurine is a potent activator of extrasynaptic GABA(A) receptors in the thalamus, J. Neurosci. 28(1) (2008) 106-115. https://doi.org/10.1523/JNEUROSCI.3996-07.2008.

[96] A. Popratiloff, J.G. Valtschanoff, A. Rustioni, et al., Colocalization of GABA and glycine in the rat dorsal column nuclei, Brain Res. 706(2) (1996) 308-312. https://doi.org/10.1016/0006-8993(95)01280-x.

[97] K. Kuriyama, T. Hashimoto, Interrelationship between taurine and GABA, Adv. Exp. Med. Biol. 442 (1998) 329-337. https://doi.org/10.1007/978-1-4899-0117-0_41.

[98] B. Mersman, W. Zaidi, N.I. Syed, et al., Taurine promotes neurite outgrowth and synapse development of both vertebrate and invertebrate central neurons, Front. Synaptic Neurosci. 12 (2020) 29. https://doi.org/10.3389/fnsyn.2020.00029.

[99] F. Liu, Y. Liu, L.Y. Ma, et al., Antenatal taurine improves intrauterine growth-restricted fetal rat brain development which is associated with increasing the activity of PKA-CaMKII/c-fos signal pathway, Neuropediatrics 46(5) (2015) 299-306. https://doi.org/10.1055/s-0035-1558434.

[100] Q. Fang, J. Liu, L. Chen, et al., Taurine improves the differentiation of neural stem cells in fetal rats with intrauterine growth restriction *via* activation of the PKA-CREB-BDNF signaling pathway, Metab. Brain Dis. 36(5) (2021) 969-981. https://doi.org/10.1007/s11011-021-00672-0.

[101] H. Chen, J. Li, J. Liu, et al., Effects of prenatal taurine on mRNA expression of PKA CREB signal pathway and glial cell line derived neurotrophic factor in fetal rat brains of intrauterine growth restriction, Chin. J. Contemp. Pediatr. 11(11) (2009) 923-926.

[102] Y. Wang, X.W. Li, J. Liu, et al., Antenatal taurine supplementation in fetal rats with growth restriction improves neural stem cell proliferation by inhibiting the activities of Rho family factors, J. Matern. Fetal Neonatal Med. 31(11) (2018) 1454-1461. https://doi.org/10.1080/14767058.2017.1319353.

[103] H.J. Luhmann, A. Sinning, J.W. Yang, et al., Spontaneous neuronal activity in developing neocortical networks: from single cells to large-scale interactions, Front. Neural Circuits 10 (2016) 40. https://doi.org/10.3389/fncir.2016.00040.

[104] M. Mohibbullah, M.M. Bhuiyan, M.A. Hannan, et al., The edible red alga Porphyra yezoensis promotes neuronal survival and cytoarchitecture in primary hippocampal neurons, Cell. Mol. Neurobiol. 36(5) (2016) 669-682. https://doi.org/10.1007/s10571-015-0247-x.

[105] M.C. Shivaraj, G. Marcy, G. Low, et al., Taurine induces proliferation of neural stem cells and synapse development in the developing mouse brain, PLoS One 7(8) (2012) e42935. https://doi.org/10.1371/journal.pone.0042935.

[106] J. Brown, Y. Villalona, J. Weimer, et al., Supplemental taurine during adolescence and early adulthood has sex-specific effects on cognition, behavior and neurotransmitter levels in C57BL/6J mice dependent on exposure window, Neurotoxicol. Teratol. 79 (2020) 106883. https://doi.org/10.1016/j.ntt.2020.106883.

[107] A. El Idrissi, Taurine improves learning and retention in aged mice, Neurosci. Lett. 436(1) (2008) 19-22. https://doi.org/10.1016/j.neulet.2008.02.070.

[108] P. Scheltens, B. De Strooper, M. Kivipelto, et al., Alzheimer's disease, Lancet. 397(10284) (2021) 1577-1590. https://doi.org/10.1016/S0140-6736(20)32205-4.

[109] K. Terai, A. Iwai, S. Kawabata, et al., Beta-amyloid deposits in transgenic mice expressing human beta-amyloid precursor protein have the same characteristics as those in Alzheimer's disease, Neuroscience 104(2) (2001) 299-310. https://doi.org/10.1016/s0306-4522(01)00095-1.

[110] W. Danysz, C.G. Parsons, Alzheimer's disease, β-amyloid, glutamate, NMDA receptors and memantine—searching for the connections, Br. J. Pharmacol. 167(2) (2012) 324-352. https://doi.org/10.1111/j.1476-5381.2012.02057.x.

[111] K. Yenkoyan, K. Safaryan, G. Navasardyan, et al., Effects of beta-amyloid on behavioral and amino acids spectrum in rats' brain and their modulation by embryonic proteins, Neurochem. Int. 54(5-6) (2009) 292-298. https://doi.org/10.1016/j.neuint.2009.01.020.

[112] P.R. Louzada, A.C. Paula Lima, D.L. Mendonca-Silva, et al., Taurine prevents the neurotoxicity of beta-amyloid and glutamate receptor agonists: activation of GABA receptors and possible implications for Alzheimer's disease and other neurological disorders, FASEB J. 18(3) (2004) 511-518. https://doi.org/10.1096/fj.03-0739com.

[113] A.C. Paula-Lima, F.G. De Felice, J. Brito-Moreira, et al., Activation of GABA(A) receptors by taurine and muscimol blocks the neurotoxicity of beta-amyloid in rat hippocampal and cortical neurons, Neuropharmacology 49(8) (2005) 1140-1148. https://doi.org/10.1016/j.neuropharm.2005.06.015.

[114] Y. Che, L. Hou, F. Sun, et al., Taurine protects dopaminergic neurons in a mouse Parkinson's disease model through inhibition of microglial M1 polarization, Cell Death & Disease 9(4) (2018) 435. https://doi.org/10.1038/s41419-018-0468-2.

[115] S. Shukurova, R. Sadek, N. Mekawy, et al., Electrophysiological evidence for anti-epileptic property of taurine, Adv. Exp. Med. Biol. 1370 (2022) 333-340. https://doi.org/10.1007/978-3-030-93337-1_32.

[116] R. Leon, H. Wu, Y. Jin, et al., Protective function of taurine in glutamate-induced apoptosis in cultured neurons, J. Neurosci. Res. 87(5) (2009) 1185-1194. https://doi.org/10.1002/jnr.21926.

[117] A.G. Taranukhin, E.Y. Taranukhina, P. Saransaari, et al., Taurine reduces Caspase-8 and Caspase-9 expression induced by ischemia in the mouse hypothalamic nuclei, Amino Acids 34(1) (2008) 169-174. https://doi.org/10.1007/s00726-006-0405-z.

[118] X. Niu, S. Zheng, H. Liu, et al., Protective effects of taurine against inflammation, apoptosis, and oxidative stress in brain injury, Mol. Med. Rep. 18(5) (2018) 4516-4522. https://doi.org/10.3892/mmr.2018.9465.

[119] L.S. Neuwirth, B.U. Emenike, Taurine in symptom amelioration and recovery in lead-induced neurotoxicity, in: Treatments, nutraceuticals, supplements, and herbal medicine in neurological disorders, Academic Press, 2023, pp.267-284. https://doi.org/10.1016/B978-0-323-90052-2.00013-5.

[120] C.J. Jong, P. Sandal, S.W. Schaffer, The role of taurine in mitochondria health: more than just an antioxidant, Molecules 26(16) (2021) 4913. https://doi.org/10.3390/molecules26164913.

[121] M. Fakruddin, F.Y. Wei, T. Suzuki, et al., Defective mitochondrial tRNA taurine modification activates global proteostress and leads to mitochondrial disease, Cell Reports 22(2) (2018) 482-496. https://doi.org/10.1016/j.celrep.2017.12.051.

[122] S.W. Schaffer, T. Ito, J. Azuma, Clinical significance of taurine, Amino Acids 46(1) (2014) 1-5. https://doi.org/10.1007/s00726-013-1632-8.

[123] Q. Wang, W. Fan, Y. Cai, et al., Protective effects of taurine in traumatic brain injury via mitochondria and cerebral blood flow, Amino Acids. 48(9) (2016) 2169-2177. https://doi.org/10.1007/s00726-016-2244-x.

[124] L. Wang, Y. Liu, X. Zhang, et al., Endoplasmic reticulum stress and the unfolded protein response in cerebral ischemia/reperfusion injury, Front. Cell. Neurosci. 16 (2022) 864426. https://doi.org/10.3389/fncel.2022.864426.

[125] H. Prentice, P.M. Gharibani, Z. Ma, et al., Neuroprotective functions through inhibition of ER stress by taurine or taurine combination treatments in a rat stroke model, Adv. Exp. Med. Biol. 975 Pt 1 (2017) 193-205. https://doi.org/10.1007/978-94-024-1079-2_17.

[126] J. Menzie, H. Prentice, J.Y. Wu, Neuroprotective mechanisms of taurine against ischemic stroke, Brain Sci. 3(2) (2013) 877-907. https://doi.org/10.3390/brainsci3020877.

[127] T.M. Foos, J.Y. Wu, The role of taurine in the central nervous system and the modulation of intracellular calcium homeostasis, Neurochem. Res. 27(1-2) (2002) 21-26. https://doi.org/10.1023/a:1014890219513.

[128] M. Jakaria, S. Azam, M.E. Haque, et al., Taurine and its analogs in neurological disorders: focus on therapeutic potential and molecular mechanisms, Redox. Biol. 24 (2019) 101223. https://doi.org/10.1016/j.redox.2019.101223.

[129] W. Zhang, M. Chen, X. Cai, et al., Detection and analysis of signals of adverse events of memantine based on the US food and drug administration adverse event reporting system, Expert Opin. Drug Saf. 23(5) (2024) 617-625. https://doi.org/10.1080/14740338.2024.2338251.

[130] S. Liao, S.O. Omage, L. Börmel, et al., Vitamin E and metabolic health: relevance of interactions with other micronutrients, Antioxidants 11(9) (2022) 1785. https://doi.org/10.3390/antiox11091785.

[131] A. Kumar, G. Mishra, N. Dhama, et al., Piracetam pharmacological effects: a review, IJBPAS 11(12) (2022) 5648-5661. https://doi.org/10.31032/IJBPAS/2022/11.12.6612.

[132] C. Liu, C. Wu, T. Wang, Risks of piracetam preparations to safety, Chin. J. Pharmacovigilance 21(5) (2024) 563-566. https://doi.org/10.19803/j.1672-8629.20230381.

[133] K. Takahashi, Y. Ohyabu, S.W. Schaffer, et al., Cellular characterization of an *in-vitro* cell culture model of seal-induced cardiac ischemia, J. Pharm. Pharmacol. 53(3) (2001) 379-386. https://doi.org/10.1211/0022357011775433.

[134] K. Takahashi, Y. Ohyabu, K. Takahashi, et al., Taurine renders the cell resistant to ischemia-induced injury in cultured neonatal rat cardiomyocytes, J. Cardiovasc. Pharmacol. 41(5) (2003) 726-733. https://doi.org/10.1097/00005344-200305000-00009.

[135] X. Yang, J. Fu, H. Wan, et al., Protective roles and mechanisms of taurine on myocardial hypoxia/reoxygenation-induced apoptosis, Acta Cardiol. Sin. 35(4) (2019) 415-424. https://doi.org/10.6515/ACS.201907_35(4).20181218A.

[136] T. Takatani, K. Takahashi, Y. Uozumi, et al., Taurine prevents the ischemia-induced apoptosis in cultured neonatal rat cardiomyocytes through Akt/Caspase-9 pathway, Biochem. Biophys. Res. Commun. 316(2) (2004) 484-489. https://doi.org/10.1016/j.bbrc.2004.02.066.

[137] F. Ren, X. Liu, X. Liu, et al., In vitro and *in vivo* study on prevention of myocardial ischemic injury by taurine, Ann. Transl. Med. 9(12) (2021) 984. https://doi.org/10.21037/atm-21-2481.

[138] J. Das, J. Ghosh, P. Manna, et al., Taurine suppresses doxorubicin-triggered oxidative stress and cardiac apoptosis in rat *via* up-regulation of PI3-K/Akt and inhibition of p53, p38-JNK, Biochem. Pharmacol. 81(7) (2011) 891-909. https://doi.org/10.1016/j.bcp.2011.01.008.

[139] K. Kamata, M. Sugiura, S. Kojima, et al., Restoration of endothelium-dependent relaxation in both hypercholesterolemia and diabetes by chronic taurine, Eur. J. Pharmacol. 303(1-2) (1996) 47-53. https://doi.org/10.1016/0014-2999(96)00094-5.

[140] G. Ulrich-Merzenich, H. Zeitler, H. Vetter, et al., Protective effects of taurine on endothelial cells impaired by high glucose and oxidized low density lipoproteins, Eur. J. Nutr. 46(8) (2007) 431-438. https://doi.org/10.1007/s00394-007-0682-7.

[141] F.M. Fennessy, D.S. Moneley, J.H. Wang, et al., Taurine and vitamin C modify monocyte and endothelial dysfunction in young smokers, Circulation 107(3) (2003) 410-415. https://doi.org/10.1161/01.cir.0000046447.72402.47.

[142] Y. Fu, X. Wang, W. Kong, Hyperhomocysteinaemia and vascular injury: advances in mechanisms and drug targets, Br. J. Pharmacol. 175(8) (2018) 1173-1189. https://doi.org/10.1111/bph.13988.

[143] G.L. Basatemur, H.F. Jørgensen, M.C.H. Clarke, et al., Vascular smooth muscle cells in atherosclerosis, Nat. Rev. Cardiol. 16(12) (2019) 727-744. https://doi.org/10.1038/s41569-019-0227-9.

[144] X. Zhang, T.E. Tenner Jr, J.B. Lombardini, Inhibition of rat vascular smooth muscle cell proliferation by taurine and taurine analogues, Biochem. Pharmacol. 57(11) (1999) 1331-1339. https://doi.org/10.1016/s0006-2952(99)00037-4.

[145] S. Murakami, Taurine and atherosclerosis, Amino Acids. 46(1) (2014) 73-80. https://doi.org/10.1007/s00726-012-1432-6.

[146] J. Li, B. Zhang, Z. Huang, et al., Taurine prevents beta-glycerophosphate-induced calcification in cultured rat vascular smooth muscle cells, Heart Vessels 19(3) (2004) 125-131. https://doi.org/10.1007/s00380-003-0744-6.

[147] Q. Sun, J. Wang, H. Wang, et al., Effect of long-term taurine supplementation on the lipid and glycaemic profile in adults with overweight or obesity: a systematic review and meta-analysis, Nutrients 17(1) (2024) 55. https://doi.org/10.3390/nu17010055.

[148] S. Murakami, Y. Kondo, K. Tomisawa, et al., Prevention of atherosclerotic lesion development in mice by taurine, Drugs Exp. Clin. Res. 25(5) (1999) 227-234.

[149] H. Yokogoshi, H. Oda, Dietary taurine enhances cholesterol degradation and reduces serum and liver cholesterol concentrations in rats fed a high-cholesterol diet, Amino Acids 23(4) (2002) 433-439. https://doi.org/10.1007/s00726-002-0211-1.

[150] J. Balkan, O. Kanbağli, A. Hatipoğlu, et al., 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, Biosci. Biotechnol. Biochem. 66(8) (2002) 1755-1758. https://doi.org/10.1271/bbb.66.1755.

[151] S. Murakami, Y. Kondo, T. Sakurai, et al., Taurine suppresses development of atherosclerosis in Watanabe heritable hyperlipidemic (WHHL) rabbits, Atherosclerosis 163(1) (2002) 79-87. https://doi.org/10.1016/s0021-9150(01)00764-x.

[152] W. Jessup, P. Wilson, K. Gaus, et al., Oxidized lipoproteins and macrophages, Vasc. Pharmacol. 38(4) (2002) 239-248. https://doi.org/10.1016/s1537-1891(02)00174-x.

[153] J.W. Heinecke, Oxidative stress: new approaches to diagnosis and prognosis in atherosclerosis, Am. J. Cardiol. 91(3A) (2003) 12A-16A. https://doi.org/10.1016/s0002-9149(02)03145-4.

[154] M. Karakas, W. Koenig, A. Zierer, et al., Myeloperoxidase is associated with incident coronary heart disease independently of traditional risk factors: results from the MONICA/KORA Augsburg study, J. Intern. Med. 271(1) (2012) 43-50. https://doi.org/10.1111/j.1365-2796.2011.02397.x.

[155] J. Marcinkiewicz, E. Kontny, Taurine and inflammatory diseases, Amino Acids 46(1) (2014) 7-20. https://doi.org/10.1007/s00726-012-1361-4.

[156] W. Kim, H.U. Kim, H.N. Lee, et al., Taurine chloramine stimulates efferocytosis through upregulation of Nrf2-mediated heme oxygenase-1 expression in murine macrophages: possible involvement of carbon monoxide, Antioxid. Redox Signal. 23(2) (2015) 163-177. https://doi.org/10.1089/ars.2013.5825.

[157] C.C. Lee, W.T. Chen, S.Y. Chen, et al., Taurine alleviates sympathetic innervation by inhibiting NLRP3 inflammasome in postinfarcted rats, J. Cardiovasc. Pharmacol. 77(6) (2021) 745-755. https://doi.org/10.1097/FJC.0000000000001005.

[158] T. Ito, S. Murakami, Taurine deficiency associated with dilated cardiomyopathy and aging, J. Pharmacol. Sci. 154(3) (2024) 175-181. https://doi.org/10.1016/j.jphs.2023.12.006.

[159] S. Baliou, A.M. Kyriakopoulos, M. Goulielmaki, et al., Significance of taurine transporter (*TauT*) in homeostasis and its layers of regulation, Mol. Med. Rep. 22(3) (2020) 2163-2173. https://doi.org/10.3892/mmr.2020.11321.

[160] I.H. Lambert, D.M. Kristensen, J.B. Holm, et al., Physiological role of taurine from organism to organelle, Acta Physiol. 213(1) (2015) 191-212. https://doi.org/10.1111/apha.12365.

[161] W. Abebe, M.S. Mozaffari, Role of taurine in the vasculature: an overview of experimental and human studies, Am. J. Cardiovasc. Dis. 1(3) (2011) 293-311.

[162] Y.R. Shi, Y.F. Qi, D.F. Bu, et al., Dysfunction of myocardial and vascular taurine transport in spontaneously hypertensive rats, Acta Physiol. Sin. 54(5) (2002) 359-364.

[163] Y.R. Shi, S.H. Wang, D.F. Bu, et al., An observation of taurine transport alterations in calcification of myocardial cells *in vitro*, Acta Acad. Med. Sin. 24(4) (2002) 359-363.

[164] Y.R. Shi, D.D. Niu, S.H. Wang, et al., Homocysteine inhibits taurine transport in rat vascular smooth muscle cells, Chin. J. Arterioscler. 10(3) (2002) 203-205.

[165] T. Unger, C. Borghi, F. Charchar, et al., International society of hypertension global hypertension practice guidelines, Hypertension 75(6) (2020) 1334-1357. https://doi.org/10.1161/HYPERTENSIONAHA.120.15026.

[166] H. Harada, T. Tsujino, Y. Watari, et al., Oral taurine supplementation prevents fructose-induced hypertension in rats, Heart Vessels 19(3) (2004) 132-136. https://doi.org/10.1007/s00380-003-0757-1.

[167] Y. Feng, J. Li, J. Yang, et al., Synergistic effects of taurine and *L*-arginine on attenuating insulin resistance hypertension, Adv. Exp. Med. Biol. 775 (2013) 427-435. https://doi.org/10.1007/978-1-4614-6130-2_32.

[168] L. Ahtee, D.J. Boullin, M.K. Paasonen, Transport of taurine by normal human blood platelets, Br. J. Pharmacol. 52(2) (1974) 245-251. https://doi.org/10.1111/j.1476-5381.1974.tb09707.x.

[169] F. Franconi, F. Bennardini, A. Mattana, et al., Plasma and platelet taurine are reduced in subjects with insulin-dependent diabetes mellitus: effects of taurine supplementation, Am. J. Clin. Nutr. 61(5) (1995) 1115-1119. https://doi.org/10.1093/ajcn/61.4.1115.

[170] A.E. Roşca, A.M. Vlădăreanu, R. Mirica, et al., Taurine and its derivatives: analysis of the inhibitory effect on platelet function and their antithrombotic potential, J. Clin. Med. 11(3) (2022) 666. https://doi.org/10.3390/jcm11030666.

[171] G. Eby, W.W. Halcomb, Elimination of cardiac arrhythmias using oral taurine with *L*-arginine with case histories: hypothesis for nitric oxide stabilization of the sinus node, Med. Hypotheses 67(5) (2006) 1200-1204. https://doi.org/10.1016/j.mehy.2006.04.055.

[172] L. Zhao, J. Lou, H. Wu, et al., Effects of taurine-magnesium coordination compound on ionic channels in rat ventricular myocytes of arrhythmia induced by ouabain, Biol. Trace Elem. Res. 147(1-3) (2012) 275-284. https://doi.org/10.1007/s12011-011-9317-1.

[173] C.C. Hsu, N.H. Senussi, K.Y. Fertrin, et al., Iron overload disorders, Hepatol. Commun. 6(8) (2022) 1842-1854. https://doi.org/10.1002/hep4.2012.

[174] G.Y. Oudit, M.G. Trivieri, N. Khaper, et al., Taurine supplementation reduces oxidative stress and improves cardiovascular function in an iron-overload murine model, Circulation 109(15) (2004) 1877-1885. https://doi.org/10.1161/01.CIR.0000124229.40424.80.

[175] Z. Zhang, D. Liu, B. Yi, et al., Taurine supplementation reduces oxidative stress and protects the liver in an iron-overload murine model, Mol. Med. Rep. 10(5) (2014) 2255-2262. https://doi.org/10.3892/mmr.2014.2544.

[176] F.G. Denipote, S.A.R. Paiva, L.A.M. Zornoff, Influence of taurine on cardiac remodeling, Nutrire-Rev. Soc. Bras. Aliment. Nutr. 34(1) (2009) 211-223.

[177] L.P. Ardisson, B.P. Rafacho, P.P. Santos, et al., Taurine attenuates cardiac remodeling after myocardial infarction, Int. J. Cardiol. 168(5) (2013) 4925-4926. https://doi.org/10.1016/j.ijcard.2013.07.091.

[178] E. Nikkhah, K. Shirani, R. Rezaee, et al., Protective effects of taurine against hepatotoxicity induced by pharmaceuticals and environmental chemicals, Toxicol. Environ. Chem. 103(1) (2021) 56-84.

[179] Z. Yao, G. Liang, Z.L. Lv, et al., Taurine reduces liver damage in non-alcoholic fatty liver disease model in rats by down-regulating IL-9 and tumor growth factor TGF-β, Bull. Exp. Biol. Med. 171(5) (2021) 638-643. https://doi.org/10.1007/s10517-021-05285-2.

[180] M.R. Mas, B. Comert, K. Oncu, et al., The effect of taurine treatment on oxidative stress in experimental liver fibrosis, Hepatol. Res. 28(4) (2004) 207-215. https://doi.org/10.1016/j.hepres.2003.11.012.

[181] Y.H. Yeh, Y.T. Lee, H.S. Hsieh, et al., Effect of taurine on toxicity of vitamin A in rats, Food Chem. 106(1) (2008) 260-268. https://doi.org/10.1016/j.foodchem.2007.05.084.

[182] F. Guertin, C.C. Roy, G. Lepage, et al., Effect of taurine on total parenteral nutrition-associated cholestasis, JPEN J. Parenter. Enteral. Nutr. 15(3) (1991) 247-251. https://doi.org/10.1177/0148607191015003247.

[183] U. Alam, O. Asghar, S. Azmi, et al., General aspects of diabetes mellitus, Handb. Clin. Neurol. 126 (2014) 211-222. https://doi.org/10.1016/B978-0-444-53480-4.00015-1.

[184] S.W. Schaffer, J. Azuma, M. Mozaffari, Role of antioxidant activity of taurine in diabetes, Can. J. Physiol. Pharmacol. 87(2) (2009) 91-99. https://doi.org/10.1139/Y08-110.

[185] K. Zeng, H. Xu, M. Mi, et al., Dietary taurine supplementation prevents glial alterations in retina of diabetic rats, Neurochem. Res. 34(2) (2009) 244-254. https://doi.org/10.1007/s11064-008-9763-0.

[186] S. Baliou, M. Adamaki, P. Ioannou, et al., Ameliorative effect of taurine against diabetes and renal-associated disorders, Med. Int. 1(2) (2021) 3. https://doi.org/10.3892/mi.2021.3.

[187] F. Franconi, F. Bennardini, A. Mattana, et al., Taurine levels in plasma and platelets in insulin-dependent and non-insulin-dependent diabetes mellitus: correlation with platelet aggregation, Adv. Exp. Med. Biol. 359 (1994) 419-424. https://doi.org/10.1007/978-1-4899-1471-2_45.

[188] T. Askwith, W. Zeng, M.C. Eggo, et al., Oxidative stress and dysregulation of the taurine transporter in high-glucose-exposed human Schwann cells: implications for pathogenesis of diabetic neuropathy, Am. J. Physiol. Endocrinol. Metab. 297(3) (2009) E620-E628. https://doi.org/10.1152/ajpendo.00287.2009.

[189] N. Wu, Y. Lu, B. He, et al., Taurine prevents free fatty acid-induced hepatic insulin resistance in association with inhibiting JNK1 activation and improving insulin signaling *in vivo*, Diabetes Res. Clin. Pract. 90(3) (2010) 288-296. https://doi.org/10.1016/j.diabres.2010.08.020.

[190] Y. Nakaya, A. Minami, N. Harada, et al., Taurine improves insulin sensitivity in the Otsuka Long-Evans Tokushima Fatty rat, a model of spontaneous type 2 diabetes, Am. J. Clin. Nutr. 71(1) (2000) 54-58. https://doi.org/10.1093/ajcn/71.1.54.

[191] A.T. Nandhini, V. Thirunavukkarasu, C.V. Anuradha, Taurine modifies insulin signaling enzymes in the fructose-fed insulin resistant rats, Diabetes Metab. 31(4 Pt 1) (2005) 337-344. https://doi.org/10.1016/s1262-3636(07)70202-1.

[192] G. Paolisso, B.V. Howard, Role of non-esterified fatty acids in the pathogenesis of type 2 diabetes mellitus, Diabet. Med. 15(5) (1998) 360-366.

[193] P.A. Gerber, G.A. Rutter, The role of oxidative stress and hypoxia in pancreatic beta-cell dysfunction in diabetes mellitus, Antioxid. Redox Signal. 26(10) (2017) 501-518. https://doi.org/10.1089/ars.2016.6755.

[194] S. Lin, G. Wu, D. Zhao, et al., Taurine increases insulin expression in STZ-treated rat islet cells in vitro, Adv. Exp. Med. Biol. 975 Pt 1 (2017) 319-328. https://doi.org/10.1007/978-94-024-1079-2_28.

[195] G. Drews, P. Krippeit-Drews, M. Düfer, Oxidative stress and beta-cell dysfunction, Pflugers Arch. Eur. J. Physiol. 460(4) (2010) 703-718. https://doi.org/10.1007/s00424-010-0862-9.

[196] S. Dinić, J. Arambašić Jovanović, A. Uskoković, et al., Oxidative stress-mediated beta cell death and dysfunction as a target for diabetes management, Front. Endocrinol. 13 (2022) 1006376. https://doi.org/10.3389/fendo.2022.1006376.

[197] A.T. Nandhini, V. Thirunavukkarasu, M.K. Ravichandran, et al., Effect of taurine on biomarkers of oxidative stress in tissues of fructose-fed insulin-resistant rats, Singapore Med. J. 46(2) (2005) 82-87.

[198] J. Das, P.C. Sil, Taurine ameliorates alloxan-induced diabetic renal injury, oxidative stress-related signaling pathways and apoptosis in rats, Amino Acids 43(4) (2012) 1509-1523. https://doi.org/10.1007/s00726-012-1225-y.

[199] E. Arany, B. Strutt, P. Romanus, et al., Taurine supplement in early life altered islet morphology, decreased insulitis and delayed the onset of diabetes in non-obese diabetic mice, Diabetologia 47(10) (2004) 1831-1837. https://doi.org/10.1007/s00125-004-1535-z.

[200] V. Maleki, R. Mahdavi, F. Hajizadeh-Sharafabad, et al., The effects of taurine supplementation on oxidative stress indices and inflammation biomarkers in patients with type 2 diabetes: a randomized, double-blind, placebo-controlled trial, Diabetol. Metab. Syndr. 12 (2020) 9. https://doi.org/10.1186/s13098-020-0518-7.

[201] J.M. Forbes, M.E. Cooper, Mechanisms of diabetic complications, Physiol. Rev. 93(1) (2013) 137-188. https://doi.org/10.1152/physrev.00045.2011.

[202] M.K. Sagoo, L. Gnudi, Diabetic nephropathy: an overview, Methods Mol. Biol. 2067 (2020) 3-7. https://doi.org/10.1007/978-1-4939-9841-8_1.

[203] A.M. Mostafa, I.M. El Agouza, H.F. Hafez, et al., Assessment of serum taurine level as a potential biomarker for early diagnosis of diabetic nephropathy, GSC Biol. Pharm. Sci. 22(1) (2023) 312-320. https://doi.org/10.30574/gscbps.2023.22.1.0035.

[204] S. Li, D. Wang, M. Zhang, et al., Taurine ameliorates apoptosis *via* AKT pathway in the kidney of diabetic rats, Adv. Exp. Med. Biol. 1370 (2022) 227-233. https://doi.org/10.1007/978-3-030-93337-1_22.

[205] C. Ural, A. Celik, S. Ozbal, et al., The renoprotective effects of taurine against diabetic nephropathy *via* the p38 MAPK and TGF-β/Smad2/3 signaling pathways, Amino Acids 55(11) (2023) 1665-1677. https://doi.org/10.1007/s00726-023-03342-w.

[206] S.H. Hansen, The role of taurine in diabetes and the development of diabetic complications, Diabetes Metab. Res. Rev. 17(5) (2001) 330-346. https://doi.org/10.1002/dmrr.229.

[207] K. Zeng, H. Xu, K. Chen, et al., Effects of taurine on glutamate uptake and degradation in Müller cells under diabetic conditions *via* antioxidant mechanism, Mol. Cell. Neurosci. 45(2) (2010) 192-199. https://doi.org/10.1016/j.mcn.2010.06.010.

[208] X. Yu, Z. Xu, M. Mi, et al., Dietary taurine supplementation ameliorates diabetic retinopathy via anti-excitotoxicity of glutamate in streptozotocin-induced Sprague-Dawley rats, Neurochem. Res. 33(3) (2008) 500-507. https://doi.org/10.1007/s11064-007-9465-z.

[209] H.Y. Son, H. Kim, Y.H. Kwon, Taurine prevents oxidative damage of high glucose-induced cataractogenesis in isolated rat lenses, J. Nutr. Sci. Vitaminol. 53(4) (2007) 324-330. https://doi.org/10.3177/jnsv.53.324.

[210] K. Juster-Switlyk, A.G. Smith, Updates in diabetic peripheral neuropathy, F1000Research 5 (2016) F1000 Faculty Rev-738. https://doi.org/10.12688/f1000research.7898.1.

[211] K. Li, X. Shi, M. Luo, et al., Taurine protects against myelin damage of sciatic nerve in diabetic peripheral neuropathy rats by controlling apoptosis of Schwann cells *via* NGF/Akt/GSK3β pathway, Exp. Cell Res. 383(2) (2019) 111557. https://doi.org/10.1016/j.yexcr.2019.111557.

[212] M. Zhang, X. Shi, M. Luo, et al., Taurine ameliorates axonal damage in sciatic nerve of diabetic rats and high glucose exposed DRG neuron by PI3K/Akt/mTOR-dependent pathway, Amino Acids 53(3) (2021) 395-406. https://doi.org/10.1007/s00726-021-02957-1.

[213] G.F. Abud, F.G. De Carvalho, G. Batitucci, et al., Taurine as a possible antiaging therapy: a controlled clinical trial on taurine antioxidant activity in women ages 55 to 70, Nutrition 101 (2022) 111706. https://doi.org/10.1016/j.nut.2022.111706.

[214] P. Singh, K. Gollapalli, S. Mangiola, et al., Taurine deficiency as a driver of aging, Science 380(6649) (2023) eabn9257. https://doi.org/10.1126/science.abn9257.

[215] J.R. Terrill, G.J. Pinniger, J.A. Graves, et al., Increasing taurine intake and taurine synthesis improves skeletal muscle function in the mdx mouse model for Duchenne muscular dystrophy, J. Physiol. 594(11) (2016) 3095-3110. https://doi.org/10.1113/JP271418.

[216] W. Qian, M. Li, L. Yu, et al., Effects of taurine on gut microbiota homeostasis: an evaluation based on two models of gut dysbiosis, Biomedicines 11(4) (2023) 1048. https://doi.org/10.3390/biomedicines11041048.

[217] R. Di Micco, V. Krizhanovsky, D. Baker, et al., Cellular senescence in ageing: from mechanisms to therapeutic opportunities, Nat. Rev. Mol. Cell Biol. 22(2) (2021) 75-95. https://doi.org/10.1038/s41580-020-00314-w.

[218] E. Gebara, F. Udry, S. Sultan, et al., Taurine increases hippocampal neurogenesis in aging mice, Stem Cell Res. 14(3) (2015) 369-379. https://doi.org/10.1016/j.scr.2015.04.001.

[219] R. Dawson Jr, B. Eppler, T.A. Patterson, et al., The effects of taurine in a rodent model of aging, Adv. Exp. Med. Biol. 403 (1996) 37-50. https://doi.org/10.1007/978-1-4899-0182-8_4.

[220] C.I. Cruz, P. Ruiz-Torres, R.G. del Moral, et al., Age-related progressive renal fibrosis in rats and its prevention with ACE inhibitors and taurine, Am. J. Physiol. Renal Physiol. 278(1) (2000) F122-F129. https://doi.org/10.1152/ajprenal.2000.278.1.F122.

[221] H. Ji, G. Zhao, J. Luo, et al., Taurine postponed the replicative senescence of rat bone marrow-derived multipotent stromal cells *in vitro*, Mol. Cell. Biochem. 366(1-2) (2012) 259-267. https://doi.org/10.1007/s11010-012-1304-0.

[222] T. Ito, N. Yoshikawa, T. Inui, et al., Tissue depletion of taurine accelerates skeletal muscle senescence and leads to early death in mice, PLoS One 9(9)

(2014) e107409. https://doi.org/10.1371/journal.pone.0107409.
[223] S.W. Schaffer, K.C. Ramila, C.J. Jong, et al., Does taurine prolong lifespan by improving heart function? Adv. Exp. Med. Biol. 803 (2015) 555-570. https://doi.org/10.1007/978-3-319-15126-7_45.
[224] M. Ansar, E. Ranza, M. Shetty, et al., Taurine treatment of retinal degeneration and cardiomyopathy in a consanguineous family with SLC6A6 taurine transporter deficiency, Hum. Mol. Genet. 29(4) (2020) 618-623. https://doi.org/10.1093/hmg/ddz303.
[225] T. Ito, N. Yamamoto, S. Nakajima, et al., Beta-Catenin and SMAD3 are associated with skeletal muscle aging in the taurine transporter knockout mouse, Adv. Exp. Med. Biol. 975(Pt 1) (2017) 497-502. https://doi.org/10.1007/978-94-024-1079-2_39.
[226] S. Kaushik, A.M. Cuervo, Proteostasis and aging, Nat. Med. 21(12) (2015) 1406-1415. https://doi.org/10.1038/nm.4001.
[227] G. Du, Z. Liu, Z. Yu, et al., Taurine represses age-associated gut hyperplasia in Drosophila via counteracting endoplasmic reticulum stress, Aging Cell 20(3) (2021) e13319. https://doi.org/10.1111/acel.13319.
[228] S. Chowdhury, K. Sinha, S. Banerjee, et al., Taurine protects cisplatin induced cardiotoxicity by modulating inflammatory and endoplasmic reticulum stress responses, BioFactors 42(6) (2016) 647-664. https://doi.org/10.1002/biof.1301.
[229] N. Srinivas, S. Rachakonda, R. Kumar, Telomeres and telomere length: a general overview, Cancers. 12(3) (2020) 558. https://doi.org/10.3390/cancers12030558.
[230] C. Autexier, N.F. Lue, The structure and function of telomerase reverse transcriptase, Annu. Rev. Biochem. 75 (2006) 493-517. https://doi.org/10.1146/annurev.biochem.75.103004.142412.
[231] M. Mashyakhy, A. Alkahtani, A.S. Abumelha, et al., Taurine augments telomerase activity and promotes chondrogenesis in dental pulp stem cells, J. Pers. Med. 11(6) (2021) 491. https://doi.org/10.3390/jpm11060491.
[232] R. Gokarn, S. Solon-Biet, N.A. Youngson, et al., The relationship between dietary macronutrients and hepatic telomere length in aging mice, J. Gerontol. A Biol. Sci. Med. Sci. 73(4) (2018) 446-449. https://doi.org/10.1093/gerona/glx186.
[233] R.H. Houtkooper, E. Pirinen, J. Auwerx, Sirtuins as regulators of metabolism and healthspan, Nat. Rev. Mol. Cell Biol. 13(4) (2012) 225-238. https://doi.org/10.1038/nrm3293.
[234] B.J. Morris, Seven sirtuins for seven deadly diseases of aging, Free Radic. Biol. Med. 56 (2013) 133-171. https://doi.org/10.1016/j.freeradbiomed.2012.10.525.
[235] M. Wątroba, D. Szukiewicz, The role of sirtuins in aging and age-related diseases, Adv. Med. Sci. 61(1) (2016) 52-62. https://doi.org/10.1016/j.advms.2015.09.003.
[236] A.J. Clark, S.M. Parikh, Targeting energy pathways in kidney disease: the roles of sirtuins, AMPK, and PGC1α, Kidney Int. 99(4) (2021) 828-840. https://doi.org/10.1016/j.kint.2020.09.037.
[237] A. H. Abd Elwahab, B. K. Ramadan, M. F. Schaalan, et al., A novel role of SIRT1/FGF-21 in taurine protection against cafeteria diet-induced steatohepatitis in rats, Cell Physiol. Biochem. 43(2) (2017) 644-659. https://doi.org/10.1159/000480649.
[238] Y. Wang, R. Zhao, C. Wu, et al., Activation of the sirtuin silent information regulator 1 pathway inhibits pathological myocardial remodeling, Front. Pharmacol. 14 (2023) 1111320. https://doi.org/10.3389/fphar.2023.1111320.
[239] A. Jangra, P. Gola, J. Singh, et al., Emergence of taurine as a therapeutic agent for neurological disorders, Neural Regen. Res. 19(1) (2024) 62-68. https://doi.org/10.4103/1673-5374.374139.
[240] D. De, P. Karmakar, D. Bhattacharya, Stem cell aging and regenerative medicine, Adv. Exp. Med. Biol. 1326 (2021) 11-37. https://doi.org/10.1007/5584_2020_577.
[241] X.W. Li, H.Y. Gao, J. Liu, The role of taurine in improving neural stem cells proliferation and differentiation, Nutr. Neurosci. 20(7) (2017) 409-415. https://doi.org/10.1080/1028415X.2016.1152004.
[242] E. Pérez-Hernández, J.J. Pastrana-Carballo, F. Gómez-Chávez, et al., A key metabolic regulator of bone and cartilage health, Endocrinol. Metab. 37(4) (2022) 559-574. https://doi.org/10.3803/EnM.2022.1443.
[243] L.X. Zhang, C.X. Li, M.U. Kakar, et al., Resveratrol (RV): a pharmacological review and call for further research, Biomed. Pharmacother. 143 (2021) 112164. https://doi.org/10.1016/j.biopha.2021.112164.
[244] A.S. Kulkarni, S. Gubbi, N. Barzilai, Benefits of metformin in attenuating the hallmarks of aging, Cell Metab. 32(1) (2020) 15-30. https://doi.org/10.1016/j.cmet.2020.04.001.
[245] M. Soma, S.K. Lalam, The role of nicotinamide mononucleotide (NMN) in anti-aging, longevity, and its potential for treating chronic conditions, Mol. Biol. Rep. 49(10) (2022) 9737-9748. https://doi.org/10.1007/s11033-022-07459-1.
[246] J.D. Hernández-Camacho, M. Bernier, G. López-Lluch, et al., Coenzyme Q10 supplementation in aging and disease, Front. Physiol. 9 (2018) 44. https://doi.org/10.3389/fphys.2018.00044.
[247] S.A. Laidlaw, M. Grosvenor, J.D. Kopple, The taurine content of common foodstuffs, JPEN J. Parenter. Enteral Nutr. 14(2) (1990) 183-188. https://doi.org/10.1177/0148607190014002183.
[248] U. Seidel, P. Huebbe, G. Rimbach, Taurine: a regulator of cellular redox homeostasis and skeletal muscle function, Mol. Nutr. Food Res. 63(16) (2019) e1800569. https://doi.org/10.1002/mnfr.201800569.
[249] R. Elango, Tolerable upper intake level for individual amino acids in humans: a narrative review of recent clinical studies, Adv. Nutr. 14(4) (2023) 885-894. https://doi.org/10.1016/j.advnut.2023.04.004.
[250] G. Santulli, U. Kansakar, F. Varzideh, et al., Functional role of taurine in aging and cardiovascular health: an updated overview, Nutrients 15(19) (2023) 4236. https://doi.org/10.3390/nu15194236.
[251] A. De Luca, S. Pierno, D.C. Camerino, Taurine: the appeal of a safe amino acid for skeletal muscle disorders, J. Transl. Med. 13 (2015) 243. https://doi.org/10.1186/s12967-015-0610-1.
[252] S.W. Schaffer, K. Shimada, C.J. Jong, et al., Effect of taurine and potential interactions with caffeine on cardiovascular function, Amino Acids 46(5) (2014) 1147-1157. https://doi.org/10.1007/s00726-014-1708-0.
[253] M. Olive, Interactions between taurine and ethanol in the central nervous system, Amino Acids. 23 (2002) 345-357. https://doi.org/10.1007/s00726-002-0203-1.
[254] L. Durelli, R. Mutani, F. Fassio, The treatment of myotonia: evaluation of chronic oral taurine therapy, Neurology 33(5) (1983) 599-603. https://doi.org/10.1212/wnl.33.5.599-a.
[255] G.F. Marchesi, A. Quattrini, O. Scarpino, et al., Therapeutic effects of taurine in epilepsy: a clinical and polyphysiographic study, Riv. Patol. Nerv. Ment. 96(3) (1975) 166-184.
[256] L. Bergamini, R. Mutani, M. Delsedime, et al., First clinical experience on the antiepileptic action of taurine, Eur. Neurol. 11(5) (1974) 261-269. https://doi.org/10.1159/000114324.
[257] J. Azuma, A. Sawamura, N. Awata, et al., Therapeutic effect of taurine in congestive heart failure: a double-blind crossover trial, Clin. Cardiol. 8(5) (1985) 276-282. https://doi.org/10.1002/clc.4960080507.
[258] T. Fujita, K. Ando, H. Noda, et al., Effects of increased adrenomedullary activity and taurine in young patients with borderline hypertension, Circulation 75(3) (1987) 525-532. https://doi.org/10.1161/01.cir.75.3.525.
[259] M. Mizushima, Y. Nara, M. Sawamura, et al., Effects of oral taurine supplementation on lipids and sympathetic nerve tone, Adv. Exp. Med. Biol. 403 (1996) 615-622. https://doi.org/10.1007/978-1-4899-0182-8_68.
[260] M. Zhang, L.F. Bi, J.H. Fang, et al., Beneficial effects of taurine on serum lipids in overweight or obese non-diabetic subjects, Amino Acids 26(3) (2004) 267-271. https://doi.org/10.1007/s00726-003-0059-z.
[261] A. Shao, J.N. Hathcock, Risk assessment for the amino acids taurine, *L*-glutamine and *L*-arginine, Regul. Toxicol. Pharmacol. 50(3) (2008) 376-399. https://doi.org/10.1016/j.yrtph.2008.01.004.
[262] Z. Wang, D. Wang, W. Liu, et al., Traditional Chinese medicine diagnosis and treatment based on systematics, iLIVER 2(4) (2023) 181-187. https://doi.org/10.1016/j.iliver.2023.08.004.
[263] Q.Wu, X. Liang, Food therapy and medical diet therapy of Traditional Chinese Medicine, Clin. Nutr. Exp. 18 (2018) 1-5. https://doi.org/10.1016/j.yclnex.2018.01.001.