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Review Article

# An Update on Taurine: A Review Article

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## Abstract

Taurine chemically known as 2 aminoethanesulfonic acid; NH2CH2CH2SO3H it's a non essential amino acid, due to absence of carboxyl group it does not participate in protein synthesis, it does not metabolized and thus not involved in gluconeogenesis, thereby not constituting a direct energy source, This wonderful molecule was discover in 1827 by two German scientist Tiedemann and Gmelin from bile of ox (Bos taurus), Ten years later, this amino acid got its name as Taurine by Demarcay, and 20 years later Jacobsen and Smith discovered that its structure contains sulfur. In a wide variety of invertebrate and vertebrate tissues the natural occurrence of taurine has been recognized, It is also present in plants algae and fungi. In this review we try to cover all possible beneficial role of taurine..

**Keywords:** Taurine; 2 Aminoethanesulfonic Acid; DED; Sulfur; Gluconeogenesis; Carboxyl Group; Hypotaurine

## Introduction

Taurine chemically known as 2-aminoethane-sulfonic acid, is primarily a free occurring sulfur containing amino acid, As amino acids are the building block of proteins but like other amino acid taurine is not considered as a building block for proteins, yet classifies as a conditionally essential amino acid, this molecule is abundantly present in excitable tissues like brain, retina, heart, and skeletal muscle, where intracellular concentrations range from 20 to 70 mmol/kg. This wonderful molecule was discovered more than 200 years ago, isolated from animal sources i.e., from ox bile in the year 1827, and thus it got it name as Bos taurus [1] that time it was labelled as non-essential, biologically inert, end product of sulfur metabolism. Presence of taurine in living beings were first demonstrated by two great german scientist Tiedemann and Gmelin. It is available in various types of food however it is present in low amount in dairy products including ice cream, and cow's milk. Whereas its concentration is very high in shellfish, particularly mussels, scallops and clams. Dark meat of chicken and turkey is also rich sources of taurine. One of the interesting fact about taurine is that cooking does not produce a negative effect on the levels of taurine [2]. Taurine occupies almost over 50 percent of the total free amino acid pool in the heart, that exerts a positive inotropic action on cardiac tissue, and lowers high BP. Cardiomyocytes are also protected by taurine from the damage caused by either excessive or inadequate calcium ion levels due to its regulatory effect on the activity of the voltagedependent calcium and sodium channels, however at the same time taurine acts on many other ion channels and transporters, even though its mechanism of action is not quite specific, taurine also plays major role in stabilizing membrane potential through its interference with membranebound Na+ K+ ATPase.

According to Srivastava RN., *et al.* [2], taurine concentration in cardiac mitochondria is very high it is estimated approximately 70

nmoL/mg, taurine acts as mitochondrial buffer if there is very high concentration of taurine in heart muscles then it almost suppress mitochondrial apoptosis, oxidative and endoplasmic reticulum stress, Enzyme acyl-CoA dehydrogenases that controls β-oxidation of fatty acids are shown to have satisfactory activity with mitochondrial taurine serving as a mitochondrial buffering agent. One of the study in rat model has shown that if there is deficiency of taurine in heart muscles then the rate of β-oxidation of endogenous fatty acids was 31% lower in comparison to control heart. Environmental factors also helps in inducing accumulation of taurine that also effects epidermal barrier function to water loss, By stimulating epidermal lipid synthesis, taurine also helps in surfactant such as SDS induced dry and scaly skin.

Study by Sturman., *et al*. [3] has proved that when [35S]-labeled taurine is injected intraperitoneally into pregnant rats, it reached both in the brain and liver of the foetus it implies that maternal taurine can be transmitted to the fetus via the placenta as it's a universal truth that taurine is the most abundant free amino acid in the human placenta [4].

In case of Osteoporosis, one of the musculoskeletal disorder in which bones become fragile, One of the study by Berry TM., *et al*. [5], connect a common relation between dysregulation of the transsulfuration pathway to bone dysregulations, In case of osteoporosis, fracture risk increases due to increase level of homocysteine (Hcy), transsulfuration pathway is responsible for metabolizing Hcy to L-cysteine, if there is increased concentration of homocysteine (Hcy), then its an indication of dysregulation of the transsulfuration pathway, with the dysregulation of this pathway there will be decreased in the level of both L-cysteine and taurine as taurine is synthesized from L-cysteine, thus level of taurine declines in osteoporotic Subjects. Intracellular calcium homeostasis is regulated by taurine, it assist bile acids when conjugated with it in absorption of fats and fat-soluble vitamins like vitamin D and vitamin K. Thus when there is low content of taurine then it negatively affects bone Mineral Density leading to osteoporosis and fractures as there is dysregulation in calcium homeostasis, decreased calcium, Vitamin K and Vitamin D absorption. Thus from this study we can conclude that combination of four neutraceuticals i.e. taurine, calcium, vitamin D and vitamin K, could help in improving BMD and thus helps in reducing number of years spent in disability and reducing deaths due to fractures in patients with osteoporosis. In bone cells, taurine is found in high amount, taurine also stimulates bone formation and suppress bone resorption. In bone forming cells i.e. Osteoblast cells taurine transporters are present, both osteoblast cells and taurine transporters together plays role in bone homeostasis, taurine also stimulates osteoblast formation, Increase in osteoblast cells due to taurine is because of the stimulation of the extracellular signal-regulated kinase (ERK) pathway, Activity of Alkaline phosphatase is a marker of bone formation, So studies have shown that in a concentration dependent manner by taurine, activity of Alkaline phosphatase and bone mineralization were increased, taurine also induced the expression of osteogenic growth factors, Osteoclast activity or bone resorption is inhibited by taurine, By inhibiting the reverse mode of the Na+/Ca+2 exchanger (NCX),as it exports calcium from cells while importing Na; however, in reverse mode the Na+Ca+2 exchanger imports Ca+2 and exports Na+, thus taurine inhibits the reverse mode of sodium calcium exchanger,NCX is expressed by osteoblast cells where NCX is located on the mineralizing side of osteoblasts, In forming Bones Osteoblasts exports calcium via NCX into the growing bone matrix, Thus by inhibiting the reverse mode of NCX exchanger taurine contributes in the formation of bones. NCX variant is also expressed by Osteoclasts where NCX mediate calcium transport during bone resorption, so inhibition of reverse mode of NCX by taurine contributes in increase of bone growth by osteoblast cells and helps in preventing bone resorption by osteoclasts [5]. It is true to say taurine a wonderful molecule as studies has shown that taurine is very effective against toxic mediated insults, taurine plays major role in inhibiting oxidative stressinduced lung damage. Study by Higuchi., *et al*. [6]. showed in Japanese eel, that taurine and its transporter TAUT are mainly involved in the initiation of germ cell meiosis, whereas many studies have shown that adding taurine to culture medium can effectively improve quality of sperm and promotes early embryo development in many species such as mouse and human embryos [7], Study by Lewandowski., *et al*. [8], has demonstrated in his study that if taurine-upregulated gene 1 (*Tug1*) is knockout in male mice then it leads to infertility, characterized by reduced epididymal sperm count and increased sperm deformity. According to Srivastava RN., *et al*. [2] concentration of taurine gradually decreases in subjects with chronic kidney disease, whereas in absence of CKD, plasma taurine concentration gradually increases when subject is supplemented with L-glutamine, whereas one of the study on animal model has shown that in case CKD continuous depletion of taurine can be rectified if supplemented with L-glutamine. Role of taurine in case of Spinal cord injury is still a hot topic of debate as more research need to be conducted on human as according to Ara Z., *et al.* [9], SCI is a life threatning process and it greatly effects subjects' quality of life and families, According to Srivastava RN., *et al*. [2],action of taurine in the case of spinal cord injury has been demonstrated since many years before as in case of SCI it acts as neurotransmitter, this interpretation also focuses the possible involvement of taurine in the anti-epileptic action on the spinal cord, in case of SCI high content of taurine is found in the neutrophils that migrate to the site of injury. One of the study on spinal cord compression model, it was shown that taurine treatment inhibit expression of the proinflammatory cytokine IL-6 and also decrease phosphorylation of STAT3

and expression of COX2.Study by Ruan Y., *et al.* 2016 demonstrated that in diabetes, erectile dysfunction (ED) is more common when supplemented with taurine for 4 weeks, improvement in erectile function by potential antifibrotic activity was obeserved.

Minsu PA., *et al*. [10], in his study demonstrated that Activity of alkaline phosphatase and mineralization in a concentration-dependent manner is improved by taurine supplementation, as taurine supplementation helps in inducing the expression of osteogenic growth factors such as bone morphogenetic protein-2 (BMP-2), runt-related transcription factor 2 (RUNX2), small mothers against decapentaplegic 1/5/8 (SMAD1/5/8), wingless-type MMTV integration site family member 3A (Wnt3a), and collagen type 1 (COL-1) via mitogen-activated protein kinase (MAPK) and serine/threonine protein kinase (Akt). Moreover, the RUNX2 activity of the taurine-treated group was enhanced by protein–protein interactions such as Wnt3a-induced p-AKT/RUNX2 and BMP-mediated SMADs/MAPK/RUNX2 interactions.

Another Study by Bian Y., *et al*. [11] on Osteoarthritis in rat models, showed that after surgery in rat models, they were given taurine injections in a dose dependent manner and major improvements regarding the symptoms of OA was observed such as reduction of secondary mechanical allodynia, decrease in hind limb weight-bearing alterations, reduction in swelling of Knee whereas on the knee joint cartilage at 14 weeks, histopathological analysis was conducted by western blotting that showed taurine supplementation in a dose dependent manner suppressed cartilage degeneration, matrix loss and suppressed the expression of matrix metalloproteinase-3 (MMP-3) and CHOP. In bone tissues significant amount of taurine is transported in bone tissue, thus taurine plays major role in bone metabolism, Experimental Bone resorption and osteoclast formation and survival, has been inhibited by taurine [12]. Taurine has also inhibitory effects on bacteria-stimulated osteoclast formation *in vitro*.

## Properties of taurine

Acute inflammation is a physiological reaction of tissues to harmful stimuli such infections, damaged cells, cancer cells, and irritants. This response, which is primarily handled by innate immunity, is in charge of removing these harmful stimuli and initiating the healing process. Neutrophils, phagocytic cells that destroy microbes and produce a variety of proinflammatory mediators, are the main cells involved in acute inflammation. Pathogens that are phagocytosed by neutrophils are killed by a unique system The myeloperoxidase-halide system [13], by the generation of a potent microbicidal and cytotoxic oxidant i.e., hypochlorous acid (HOCl).The uniquiness of Enzyme MPO is that it is the only mammalian enzyme that oxidizes $Cl^-$ into HOCl [14], and also oxidize $Br^-$ to produce hypobromous acid (HOBr) [15]. When any pathogen comes into touch with neutrophils or macrophages, they both create an intensive oxygen absorption respiratory burst. The process of producing oxidants starts when a membrane-associated NADPH oxidase converts molecule oxygen into superoxide, which subsequently produces H2O2. Myeloperoxidase (MPO), a component of neutrophil phagolysosomes, is employed to change chloride ions into HOCl or bromide ions into HOBr. [16], both HOCl,and HOBr are components of innate immunity that help in protecting the host from getting infection by using their oxidizing potential to kill pathogens, but host tissues might get damaged by these components. The microbicidal effects of HOCl have been linked to oxidation of methionine residues in bacterial cytosolic and inner membrane proteins [17]. Overproduction of these antioxidants and insufficient neutralization by antioxidants may lead to the development of oxidative stress and chronic inflammation [18]. This scenario may contribute in the pathogenesis of inflammatory diseases, so in this situation neutrophil MPO–halide system is involved, it clearly suggests that in maintaining homeostasis and in amelioration of the harmful effect of oxidative stress, antioxidants plays major role. Now the question arises that is taurine plays role against inflammatory responses however levels of taurine is high in phagocytes and accumulation in taurine inflammatory lesions that suggests its role in innate immunity [19]. As mentioned above that concentration of taurine is very high in leukocytes, activated phagocytes generate a variety of microbicidal and toxic oxidants produced by the peroxidase system in these cells, thus we can hypothesize that immune system will be effected by the deficiency of taurine, whereas studies have shown that in cats prolonged deficiency of taurine may lead to profound abnormalities in the immune system including significant leukopenia, a decreased respiratory burst in neutrophils and depletion of cells from B cell areas of lymph nodes and spleen [19]. But in case of human there is still no clear evidence concerning the association between taurine deficiency and a defect of the immune system in humans. But it is commonly accepted by some studies that due to its antioxidant properties taurine has major protective role in cells like leukocytes from oxidative stress [19]. Thus taurines immense role such as antioxidant property, cytoprotection, maintaining homeostasis of cell is mainly involved in acute and chronic inflammatory/oxidative stress. Taurine haloamines such as TauCl and TauBr inhibits the production of proinflammatory cytokines such as TNF-α, IL-1β and IL-6 [19]. Whereas beneficial role of TauCl has been investigated as it reduces the production of nitric oxide (NO) and prostaglandin $E_2$ ($PGE_2$) as well decrease the activity of matrix metalloproteinases [19], The above-mentioned anti-inflammatory properties together with the capacity of TauCl to induce leukocyte apoptosis suggest that TauCl may be involved

in the resolution and termination of acute inflammation [19]. It is interesting to note that in contrast to TauCl, taurine also protects cells from apoptosis as it is proved by many *in vitro* studies [20]. The other important role of these above mentioned analoges is their antioxidant properties as TauCl and TauBr mostly reduces the activity of phagocytic cells, thus suppress the ability of phagocytic cells to consume oxygen and induce respiratory burst. In addition production of ROS is suppressed by TauCl as it elevates the expression of antioxidant enzymes peroxyredoxin-1 and thioredoxin-1, normally induced by the activation of NF-E2-related factor-2 (Nrf2) [21-22]. Whereas *in vitro* in various cells the expression of heme-oxygenase-1 (HO-1) is significantly enhanced by TauCl and TauBr, in a similar, dose-dependent manner [23]. Heme-oxygenase-1 (HO-1) is essential for tissue homeostasis because it inhibits the synthesis of pro-inflammatory heme proteins including COX-2 and iNOS. Heme-oxygenase-1 (HO-1)-mediated heme degradation also regulates crucial biological processes like oxidative stress and inflammation. [25]. Therefore its another assumption or logic that needs further research to proved that at site of inflammation, applying TauCl and/or TauBr will induce HO-1 in neighboring non-activated cells to protect them against oxidative stress.

$Cl^- + H_2O_2 + H^+ \rightarrow HOCl + H_2O$, $Cl^- + H_2O_2 + H^+ \rightarrow HOCl + H_2O$,

$Br^- + H_2O_2 + H^+ \rightarrow HOBr + H_2O$.$Br^- + H_2O_2 + H^+ \rightarrow HOBr + H_2O$.

## Role in brain and spinal cord

SCI is a life threatning neurological condition that changes ones life completely, Synthesis of taurine is well recorded in brain and after Spinal cord injury its concentration is very high mostly in glia and synaptosomes. However its presence in brain is proved by many studies but in spinal cord its presence is not well documented but presence of taurine precursor i.e. cysteine in spinal cord of cat and enzyme Cysteine sulfinate presence in rats spinal cord is recorded thus it provides some clue for taurine synthesis in spinal cord injury, yet a detailed study behind this is needed whereas studies have shown that taurine concentration is highest in dorsal horn and lowest in ventral horn [26,27].

Taurine modulates various neurological activities and it exerts neuroprotective effect, some studies have shown that increased levels of taurine is involved in neuroprotection and axonal regeneration after SCI, thus it is true to say taurine a beneficial therapeutic agent for SCI [28]. Study by Nakajima, Y., *et al*. [29] states in his study in SCI rat model, that taurine administration suppressed IL-6, COX-2, and MPO concentrations.

Taurine exhibits strong hydrophilic and lipophobic nature and a rapid extraction rate, One of the taurine analoges such as N-chlorotaurine (NCT), also exerts best therapeutic properties as it helps in downregulating the action of various cytokines and oxidative stress markers such as TNF-α, IL-1β, IL-6, IL-8, ROS and MPO.

According to Srivastava RN., *et al.* [2] ,some studies have proved that the combined treatment of taurine along with Ascorbic acid proved very beneficial against SCI-induced rats, when this animal model was treated with both of the combined drug for 45 consecutive days then certain changes were notified such as suppressed level of caspase-3, Bax, pro-NGF, and p53 mRNA expression by more than 30% compared to individual treatment of both drugs in addition changes in antioxidant markers along with recovery in altered antioxidant markers and induced lipid peroxidant to normal level in SCI induced rats when treated with combination of taurine and Ascorbic acid.

Latest study by Abud GF., *et al*. [30] demonstrated the antiaging property of taurine as their study suggested that due to its antioxidant nature it prevents the decrease in the antioxidant enzyme SOD, in women 55 to 70 y of age thus prevent aging. Iwegbulem O., *et al*. [31], demonstrated that one of the analogues of taurine i.e., Taurolidine (TRD) is a taurine *N*-methylol derivative has broad spectrum bactericidal activity and is mostly used in Europe and the USA as adjunct therapy in a variety of infections in humans. It metabolizes into taurine as the active metabolite with *N*-methylol derivatives taurultam (TRLT) and taurinamide, that block the component of gram-negative bacterial cell wall, lipopolysaccharide (LPS) irreversibly, and downregulates inflammation through inhibition of proinflammatory cytokines TNF-α, IL-1β, IL-6, and IL-8 in peripheral blood mononuclear cells (PBMCs).Type 1 muscle fibres have high roughly four times higher Taurine concentration in comparison to type II muscle fibres, taurine maintains whole-body homeostasis, Compared to glutamate, alanine and glycine, taurine is one of the most abundant organic osmolytes, In the treatment of myotonia, fatigue and alcoholism taurine is proved to be a potent negotiator as shown by many studies [2], Some of the published studies have demonstrated that in the epidermis of skin especially in the epidermal granular layer concentration of taurine is very high, and with advancing age, concentration of taurine declines, taurine has immense role as it protects skin from harmful UV rays helps in moisture retention by by exerting osmoregulatory and anti-inflammatory effects [2].

## Taurine and bone healing

In the presence of fractures or other bone abnormalities, bone healing is a phenomena of tissue reconstitution. The three main metabolic phases of fracture healing are inflammation, endochondral ossification, and linked remodelling. When taurine is given orally to rabbits with osteotomies, early bone healing is seen to

include the production of a callus rich in osseous components as opposed to the control group, which produced a callus rich in fibrous components [32].In another animal model i.e. glucocorticoid-induced rabbit osteonecrosis, when this model was administered with taurine then it was demonstrated that expression of mitochondrial transcription factor A and the complex responsible for the synthesis of ATP got normalized thus, mitochondrial function prevented the development of osteonecrosis, In addition tauroursodeoxycholic acid, it's a common bile acid that plays role in inducing new blood vessel formation and bone formation after implantation is enhanced by it as revealed by a three-dimensional micro-computed tomographic analysis of rabbit calvarial defects. Finally incorporation of taurine biomaterials to improve the osseointegration of bioactive scaffolds for bone defect regeneration has been explored, Recently three -dimensional combination of polylactic acid, polycaprolactone, gelatin nanofibers, and taurine was found to be suitable for cell growth and proliferation, studies have shown that bone defect treated with this scaffold resulted in higher bone formation in comparison to controls, demonstrating the potential use of taurine in biomaterials. UVtreated cells when treated with taurine they get protected from oxidative stress, as taurine downregulates the p53Chk1 pathway, this antiapoptotic property of taurine has been seen in injuries mediated by toxic insults or drugs, where taurine apparently reverses doxorubicin (DOX)mediated liver damage, Experiments have shown the antiapoptotic ability of taurine may ameliorate oxidized lowdensity lipoprotein (oxLDL)induced cytotoxicity, In human renal proximal tubular epithelial (HK2) cells [33].

## Role in infants

Taurine is transported via human placenta by an active process via mother to the foetus as the concentration of taurine is higher in foetal blood in comparison to maternal blood [34]. Tochitani S., *et al*. [35], states that Syncytiotrophoblast (STB) cells in the placenta possess an active transport system for taurine. Certain growth factors and principal nutrients that helps in facilitating fetal growth and provide mechanical cushioning are present in Amniotic fluid (AF),these Amniotic fluid (AF) also contains taurine and in this fluid greater quantity of taurine is present in comparison to maternal serum. At the same time concentration of other amino acids are present in lower concentration in AF in comparison to maternal and foetal blood, indicating the activity of an unidentified mechanism by which taurine is enriched in AF. In Milk of many species taurine is a significant component and is second in concentration to glutamate, Concentration of taurine in some animals like chimpanzees, rhesus monkeys, sheep, and rats were found to be the highest during the first days of lactation, and after the first week it decreased to a particular constant concentration[35].Study by Sturman., *et al*. [36], states that after parturition, injecting [35S]taurine intraperitoneally into lactating dams observed that taurine was transferred to pups via milk and get accumulated in brains to greater extent in comparison to liver. Production of milk in in the mammary gland of animals including human depends on the milk synthesis and the proliferation abilities of mammary epithelial cells (MECs), synthesis of milk is the combined result of several intracellular processes within MECs, In the endoplasmic reticulum of MECs, proteins that are synthesized are packaged into vesicles within the Golgi apparatus and then released by exocytosis. whereas Some vesicles containing other proteins, such as IgA, are transported across the apical membrane, Some monosaccharides, sodium, potassium, chloride, and water can directly pass through the apical membrane. MECs get differentiated into the lobuloalveolar complex, Under the influence of progesterone and prolactin, lobuloalveolar complex is single layer of polarized MECs surrounding a lumen connected to the central duct system. At the end of pregnancy there is a fall of progesterone and tight junctions are formed between MECs, milk comes to be contained within the lumen of the lobuloalveolar complex, and it becomes available for secretion, studies have shown that taurine transporters are present in mammary glands, and during pregnancy TauT mRNA is abundant in mammary glands of rats, however the expression levels decreased after the onset of lactation and stabilized around the levels observed in virgin rats [34], Similarly another study in rats found lower transcription levels of TauT during lactation in comparison to the levels in pregnancy, the mRNA transcription level for cysteine sulfinic acid decarboxylase (CSAD), a rate-limiting enzyme for taurine synthesis, was higher during early stage of lactation (day 1 and 6 of lactation) than in the later lactational stage (day 14) in rat mammary glands. In MECs of rat mammary glands, CSAD mRNA was observed to be expressed, whereas the expression level of cysteine dioxygenase (CDO),protein was found to be present preferentially, in the ductal cells of pregnant rats but not in other MECs or the ductal cells of nonpregnant rats [35], In rats during the early lactation period and right after birth, milk taurine concentration were highest, and it gradually declines rapidly after the onset of lactation, During lactation process the expression levels of CDO proteins in the mammary tissue increases, whereas expression of CSAD protein decreases slightly through out the lactation period [36]. The above mentioned results suggested that in addition to taurine transported by MECs from maternal blood, mother's milk also contained a significant amount of taurine that might be synthesized de novo in MECs.

Nishigawa, T., *et al*. [38], demonstrated that in breast milk of lactating mouse dams, taurine's concentration does not get affected when they received Intraperitoneal injection of taurine but its concentration decreases when they received the injection of β-alanine, administration of β-alanine affect the concentration of taurine in brains of offspring, and concentration of taurine in

brain is negatively correlated with the total distance traveled in the open field test at postnatal day 15, suggesting that a decreased concentration of taurine in the mother's milk can alter offspring behavior. Offspring that survive from the taurine-depleted mothers they possess various neurological abnormalities, and these off springs have reduced concentrations of taurine in body tissues and fluids, Neuringer, M., *et al*. [39] suggest that when they fed rhesus monkeys a taurine-free, soy protein-based infant formula from birth till 3 months of age, that resulted in impaired visual acuity on the other hand Hayes, K.C., *et al*. [40], also raised infant monkeys from birth on taurine deficient diet i.e. on soyabean infant milk formula and observed significant growth depression, it suggests that dietry taurine is essential for development of infants. In infants low birth rate is closely related with increased chances of Coronary heart disease and related disorders like hypertension, stroke and adult-onset diabetes. A new 'developmental' hypothesis for the etiology considers specifically how development in early life affects the development of chronic diseases later in life, this theory was proposed by Barker and now developed to the concepts of *developmental programming* or *the developmental origins of the health and disease hypothesis (DOHaD). IUGR exerts its long term effect on disease suspectibility later in life. Reduced activity of* TauT is associated with IUGR, and it is important to note that in IUGR foetus reduced plasma taurine concentration is found, whereas reduced acivity of TauT in placenta is associated with maternal obesity and PE. thus these above mentioned data suggest that reduced taurine levels have very high impact on Foetal and infant development [35].

## Role in toxicity

Study by Venkatachalam S., *et al*. [41] observed that taurine supplementation is effective as it elevates the activity of antioxidant enzymes in the lungs.In case of bleomycin, induced lung injury and in addition amiodarone, paraquat or sumatriptan mediated lipid peroxidation (LPO), and mitochondrial injury taurine exerts protective effect due to its antioxidant property [33], Whereas Oral taurine supplementation is effective against damaged caused due to nitrogen dioxide [42]. Treatment of cell line MRC5 fibroblasts with 20mM concentration of taurine has found to be effective against lipopolysaccharide (LPS)induced ROS formation and the activation of the MAPK signaling pathway [43]. Against testicular toxicity also taurine seems to act as protecting agent due to its antioxidant capacity [44]. According to Ara Z., *et al*. [26], Spinal cord injury is the most disabling condition affecting an individual's life, in most of the cases SCI leads to paralysis, studies have proved that nutritional supplementation may be considered as a boon in this life threatning disease as many studies on animal model like lampreys and rats have shown that taurine supplementation helps in axonal regeneration in complete spinal cord injury model and in addition it helps in the reduction in the level of IL-6 and myeloperoxidase in a dose-dependent manner, taurine treatment also helps in reducing neutrophil accumulation exclusively in the subarachnoid spaces and induced secondary degenerative deviations in the gray matter [26].

## Synthesis of taurine

It is true to say that its content relies on cysteine/methionine metabolism, two different routes are involved in biosynthesis of taurine, firstly oxidation of cysteine to cysteine sulfinic acid occurs due to involvement of enzyme cysteine dioxygenase (CDO) after that enzyme cysteine sulfinic acid decarboxylase (CSAD) converts cysteine sulfinic acid to hypotaurine, and finally oxidation of hypotaurine converts into taurine. The importance of the enzyme cysteine sulfinic acid decarboxylase (CSAD) is established by one of the study in which it was seen that death of third generation (G3) CSAD KO (knockout) mouse models occurs within 24 h from their birth. Whereas second biosynthetic pathway of taurine synthesis occurs via cysteine, which can be conjugated to coenzyme A (CoA),and thus during CoA turnover cyste amine is released, In this whole procedure enzyme 2-aminoethomethiol dioxygenase (ADO) actively participate in converting cysteamine to hypotaurine. However during prenatal life its biosynthetic capacity is very high and starts to decline as we entered in adulthood, and taurine concentration is very lowest in the elderly stage and during certain pathological conditions such as trauma, sepsis, Whereas commercially it is synthesized from ethylene oxide or monoethanolamine. Taurine is an antioxidant as it scavenges reactive oxygen species (ROS), thus reduces the generation of reactive oxygen species,and suppress the harmful effects of oxidative stress. Presence of taurine concentration decides its ability to scavenging away of free radicals, however taurine is very effective against peroxyl radicals (ROO•), superoxide anion (O2•-), nitric oxide (NO•), and peroxynitrite (ONOO-),but hydrogen peroxide is not scavenge away by taurine, It exerts protective effect to mitochondria which blocks ROS generation. Upon reaction with mitochondrial tRNAs and form 5-taurinomethyluridine (τm5U) and 5-taurinomethyl-2-thiouridine,thus contributes in improving codon-anticodon interaction between the uridine-uridine-guanosine (UUG) codon and taurine-modified adenosine-adenosine-uridine, optimizing the translation of encoded proteins that are rich in UUG regions of subunits 5 (mt-ND5) and 6 (mt-ND6) of the respiratory chain complex I, Presence of taurine is recorded in glia and synaptosomes, synthesis of taurine is well recorded in brain, however its presence in spinal cord is still contridactory but presence of its precursor amino acid, cysteine is reported in spinal cord of cat [44],whereas presence of Cystein sulfinate is also reported in spinal cord of mouse [45]. As we know cysteine and methionine are precursors of taurine so it can provide a logic that presence of these amino acid in spinal cord may help in taurine synthesis, yet a detailed study is needed to proved this hypothesis. Though initial

findings favor a uniform distribution of taurine in spinal cord [47], Enzyme cysteine sulfinate decarboxylase (CSD) is highly active in superficial part, the dorsal horn, it suggests increased synthesis of taurine in superficial dorsal horn region.

Study by Palkovits., *et al*. [48], proved this observation with one of his finding that presence of higher level of taurine in dorsal horn and lower level in ventral horn. Blood brain barrier is responsible for carrying taurine including hypotaurine, β-alanine, and other β-amino acids, into the brain by a high-affinity, low-capacity Na+ - and Cl−- dependent transport system, whereas passive diffusion of taurine across the blood-brain barrier is negligible, Taurine transporter known as SLC6A6 transporter or Tau T transporter is mainly responsible for both taurine uptake and efflux at both luminal and albumen membranes, GABA transporter SLC6A13 also called as GAT-2, responsible for transporting taurine across membranes is represented by blood-brain barrier. Both these mentioned transporters i.e. TauT and GAT-2 are also involved in efficiently carrying hypotaurine. One of the study on mice model had shown that genetic deletion of taurine transporter (TauT), suppress the taurine concentration in plasma and tissues, including the brain. In contrast studies have proved that in brain taurine concentration increases in mice with genetic deletion of GAT-2, suggesting that GAT-2 is mainly functioning as a brain-to-blood efflux system for taurine. Mainly taurine transporter Tau T is expressed in astrocytes and to a very lesser extent in neurons, and expression of GAT-2 is restricted to leptomeninges and blood vessels. Volume -sensitive organic osmolyte–anion channels, commonly called volume-regulated anion channels (VRACs),that are mainly activated at time of cell swelling, they also plays major role in taurine transportation ubiquitously. Taurine transporter Tau T is mainly proposed to be responsible for taurine uptake in brain parenchyma, while taurine release is mostly mediated by VRACs. Schmid, R and Lähdesmäki, P., *et al*. [49], in their studies reported uptake of taurine into synaptosomes and its release upon electrical stimulation, as well as binding of taurine to synaptosomal membranes. These observations from mentioned studies proved that taurine acts as a neurotransmitter in the central nervous system (CNS); in fact, taurine turned out to be a modulator of inhibitory neurotransmission. Intracellular taurine concentration is estimated to be 400-fold higher than the concentration in the extracellular space, Using microdialysis when extracellularly taurine concentration is measured in brain it is recorded below 10 μmol/L, and increases by at least one order of magnitude upon depolarization. After its release taurine began to act on GABA and glycine receptors and is cleared through sodium-dependent transport whereas taurine does not exclusively release at synapses but can be of glial origin, and mediate astrocyte-to-neuron communication. Abundance of taurine is also recorded in semen, the concentration of which (679 μM) is reported to be maintained at levels 10-fold higher than in the blood, this evidence suggest the importance of taurine in the testis including germ cells (50). Study by Alahmar, A.T., *et al*. [51], proved that abnormalities in the form and motility of sperm are caused by oxidative stress and due to low expression of antioxidant enzymes such as superoxide dismutase (SOD) in the testis, one of the study by Das, J., *et al*. [44], on mouse model showed that oral administration of taurine exerts protective effect against arsenic-induced oxidative stress in rats, this evidence supports that taurine administration plays significant role in the development of testis, whereas another study by Tsounapi, P., *et al*. [52] again in streptozotocin-induced diabetic rats model showed the antioxidant property of taurine, their study showed that administration of taurine in diabetic rats acts as an antioxidant in the seminiferous tubules harboring germ cells, and this proves that dietry intake of taurine improves the sperm characteristics, its motility and number that are closely linked to male infertility. Due to taurine deficiency there may be dysregulation in Intracellular calcium homeostasis, though there are near normal calcium serum levels or normal calcium serum levels. Taurine deficiency there is occurrence of dysregulation of intracellular calcium in osteoblast and osteoclast cells leading to decreased bone growth and increased bone resorption, Studies have shown that in bone high level of taurine is found, as it promotes bone formation and suppress bone resorption, as in osteoblast i.e. bone forming cells taurine transporters are present that play role in bone homeostasis [26], its beneficial role is explained by Sturman et al.in developing foetus, when [35S]-labeled taurine, is injected intraperitoneally into pregnant rats, then it can be delivered to both the brain and liver of the fetus, this suggests that maternal taurine can be transmitted to the fetus via the placenta, Human placenta is abundant source of taurine as high content of taurine is found in placenta, Through active transport taurine is transported via placenta from mother to the fetus as the concentration of taurine is higher in fetal blood in comparison to maternal blood. Mottaghi S., *et al*. [53], in his recent randomized control trial on Subjects with Post Liver Transplantation Delirium in Abu-Ali Sina transplantation center in Shiraz, Iran from September 2020 to June 2021, demonstrated that when these subjects were administered 2g/d taurine from the first day post-LT till 30 days then they had reduced Delirium symptoms thus they concluded that taurine can prevent post-LT delirium, dramatically. In conclusion we can say that the newest insights regarding various biological roles of taurine its biosynthesis etc has been covered in this issue.

Whereas another study by Li L., *et al*. [54], demonstrated the impact of taurine in regulating effect of estrogen synthesis in ovary in their study on animal model they observed that taurine treatment enhances the expression of miR-7a and *Cyp19a1* in ovaries of mouse and increased serum 17β-estradiol ($E_2$) concentration whereas

miR-7a2 knockout mouse have reversed effect of taurine on $E_2$,and taurine also downregulates the expression of Golgi apparatus protein 1 (Glg1), a downstream target gene of miR-7a2,similarly reverse phenomenon was observed in Glg1 knockdown mice with increased expression of the *Cyp19a1* and E2 synthesis, thus their study concluded that by activating p38/miR-7a/Glg1/ Cyp19a1 signaling pathway taurine promotes the synthesis of $E_2$. The major reason behind its various roles could be its simple and specific structure that is very similar to the structures of other β-amino acids with amino and sulfo groups.More and more research is still going on taurine to proves its efficacy in every field.

## Conclusion

Taurine is a cytoprotective molecule having immense role such as energy production, neuromodulation, calcium homeostasis, osmoregulation and its oxidative properties. The efficacy of taurine is well established by most studies on animal model, but it needs more human trials to examine taurine's therapeutic efficacy. If more clinical trials will be conducted then, we will acquire information about taurine's duration and dose administration in patients bearing various oxidative stressrelated diseases. In this we have tried to cover all beneficial properties of taurine.

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