A Brief Insight about Taurine and Its antioxidant Effects

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Abstract

Taurine or 2-aminoethanesulfonic acid, is an organic compound that is widespread in animal tissues. It is a main component of bile and is located in the large intestine, and contributes to 0.1% of the human body weight. The name comes from the Latin word Taurus which means ox, since it was first found in ox bile in 1827 by German scientists Leopold Gmelin and Friedrich Tiedemann. In 1846 it was uncovered in human bile by Edmund Ronalds. Taurine shows neuroprotective activity against hypoxia-induced injury in rats by moderating apoptotic damage. Treatment with taurine (30 mg/kg, i.p., 18 days) rose Bcl-2 expression but decreased Bax and caspase-3 expression. Taurine showed a protective function against anxiety, epilepsy, depression, stroke, neurodegenerative diseases and diabetic neuropathy. It also prevented trauma- and chemical-mediated neuronal injuries. It has displayed ameliorating functions in several models of neurodevelopmental disorders, including Angelman syndrome and Fragile X syndrome, sleep-wake disorders, neural tube defects and attention-deficit hyperactivity disorder. Besides preclinical studies, taurine demonstrated a major therapeutic job against neuroinflammation, SSADH and stroke at the clinical level. Reduced cognitive deficiencies were noticed in Wistar rats given streptozotocin (ICV-STZ) to emulate Alzheimer's disease, this was demonstrated on Morris water maze and in a passive avoidance test when medicated with 60 or 120mg/kg/day taurine.

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Introduction:

Taurine or 2-aminoethanesulfonic acid, is an organic compound that is widespread in animal tissues. It is a main component of bile and is located in the large intestine, and contributes to 0.1% of the human body weight. The name comes from the Latin word Taurus which means ox, since

it was first found in ox bile in 1827 by German scientists Leopold Gmelin and Friedrich Tiedemann. In 1846 it was uncovered in human bile by Edmund Ronalds **(1)**.

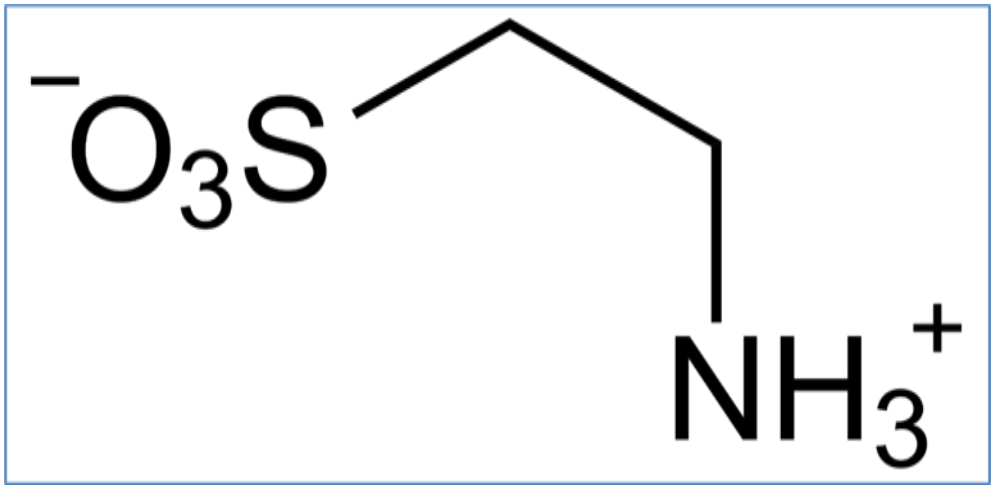

Fig. (1): Chemical structure of Taurine **(1)**.

Taurine is primarily found in the liver and kidney; however, it has been discovered in most other cells and tissues, including: the brain, retina, placenta, muscle, heart and leukocytes. Colostrum, the first milk produced in mammals which plays an important role in developing the brain and retina, consists of a large concentration of taurine. Infant formula and parenteral solutions contain Taurine **(2)**.

Taurine is a significant component in different processes such as brain development, osmotic regulation, optical and immune systems, stabilization of membranes, reproduction, inflammation and cardiac muscle regulation. **(2).**

As a promising pharmacological agent, its function to overcome inflammation and oxidative stress has been examined by several studies.

It can be used to prevent numerous diseases and disorders in different organ systems such as the integumentary, muscular, cardiovascular, circulatory respiratory, endocrine systems and skeletal. Taurine has a key job in nervous system disorders, it was proven to have protective activity against toxicity in various neurodegenerative disease models for Alzheimer's, Parkinson's, and Huntington's diseases **(3).**

Molecular investigations have demonstrated that it might be a neuroprotectant against stroke. By activating antioxidative defense signals, it minimized oxidative stress-induced neuropathy in a diabetic mouse model (**4).**

In addition, new studies have demonstrated the pharmacological capability of taurine against neurodevelopmental disorders. It prevented retinoic acid-mediated neural tube defects in a mouse model and improved hyperactive behavior in spontaneously hypertensive rats **(5).**

Taurine can be found in different kinds of food. It can be detected at a low quantity in dairy products, including ice cream and cow's milk, and at a high amount in shellfish, especially mussels, scallops and clams. Taurine can also be found in large amounts in the dark meat of chickens and turkeys. Cooking does not trigger a negative impact on the levels of taurine (**6**)

Due to the fact that Taurine is an amino acid by nature, it can cause the least side effects in the body. According to toxicity studies, it did not generate genotoxic, carcinogenic or teratogenic effects (**7**)

Molecular basis of taurine action against neurological disorders:

Modulation of neurogenesis:

Taurine has a role in progenitor cell proliferation/ neural stem **(8)** during which extracellular signal-controlled kinase (ERK), 1/2 pathways may be linked to the development of synapse. Taurine affects the levels of proteins such as Synapsin 1 and postsynaptic density protein-95, which are pivotal in the development of synapses **(8).** In another study, it showed a direct action on the proliferation of stem/progenitor cells. Indeed, taurine raised newborn neuron survival, resulting in better neurogenesis in the adult (**9).**

Modulation of neuroinflammation

Taurine's anti-neuroinflammatory activity has been reported by various studies. Taurine remarkably improved functional recovery and lessened glial fibrillary acidic protein accumulation and (build up) after induced traumatic brain injury (TBI). It notably protects against growth-related oncogene and interleukin (IL)-1β levels. Moreover, a one-week treatment with taurine significantly decreased levels of 17 cytokines, IL-1α, IL-1β, IL-4, IL-5, IL-6, IL-10, IL-12p70, IL-13, IL-17, tumor necrosis factor (TNF)-α, and vascular endothelial growth factor (VEGF). The treatment with taurine effectively reverted brain injury severity in TBI by ameliorating increased activity of astrocytes, proinflammatory cytokines and brain edema **(10).**

Modulation of endoplasmic reticulum stress

As a regulative mechanism, endoplasmic reticulum (ER) stress is vital for bringing back ER role and restoring an equilibrium between protein degradation and protein biosynthesis/folding. Immoderate ER stress-stimulated cellular pathways leads to cell death. A famous originator of ER stress is the gathering of faulty proteins, whose levels raise following inappropriate protein folding, insufficient protein degradation or weakening of the ER. Three different stress sensors, protein kinase RNA-like endoplasmic reticulum kinase (PERK), activating transcription factor 6 (ATF6) and inositol requiring enzyme-1 (IRE1), are stimulated by misfolded or unfolded proteins. Upon activation, they use the unfolded protein response (UPR) pathways and eventually work to bring back ER function and balance between protein degradation and protein biosynthesis/folding. Collectively, the UPR pathways activate either autophagy or apoptosis. In a stroke model, taurine

lessened glutamate-mediated toxicity by decreasing oxidative stress and an overload of [Ca^{2+}]. It also shut off two of the three UPR pathways. The taurine's role against ER stress and UPR pathways are yet to be explored, however it is a fact that taurine insufficiency is related to the ER stress **(11).**

Modulation of apoptosis

Taurine shows neuroprotective activity against hypoxia-induced injury in rats by moderating apoptotic damage. Treatment with taurine (30 mg/kg, i.p., 18 days) rose Bcl-2 expression but decreased Bax and caspase-3 expression **(12).**

Furthermore, the anti-apoptotic function of taurine was explored in a very recent study in a traumatic brain injury model. Apoptosis-mediated brain injury can be treated by Taurine. Beside the anti-apoptotic activity, it showed an effect against inflammation and oxidative stress in injured brain cells **(13).**

Regulatory role in gene and protein expressions

The genetic modifications that are stimulated by Taurine were studied for the first time by **Park et al. (2).** Four enzymes such as branched-chain amino acid aminotransferases 2, branched-chain aminotransferase 1, cytosolic and mitochondrial branched-chain keto acid dehydrogenase, and 3-hydroxy-3-methylglutaryl-CoA lyase are upregulated by taurine. These enzymes are involved in branched-chain amino acid catabolism. Lombardini (1992) found inhibitory actions of taurine on the phosphorylation of specific proteins in the brain, retina and heart **(3).**

Role in neuromodulation

Upon binding the particular taurine receptors (TauR), taurine stimulated neuronal hyperpolarization through the opening of chloride channels. Additionally, working especially on $GABA_A$, $GABA_B$ and/or the glycine receptor, it resulted in depressive activity **(3).** The impact of taurine on $GABA_A$ receptors reverts seizures triggered by a $GABA_A$ antagonist (picrotoxin) **(14).**

Taurine showed a protective function against anxiety, epilepsy, depression, stroke, neurodegenerative diseases and diabetic neuropathy. It also prevented trauma- and chemical-mediated neuronal injuries. It has displayed ameliorating functions in several models of neurodevelopmental disorders, including Angelman syndrome and Fragile X syndrome, sleep-wake disorders, neural tube defects and attention-deficit hyperactivity disorder. Besides preclinical studies, taurine demonstrated a major therapeutic job against neuroinflammation, SSADH and stroke at the clinical level.

Protecting against brain aging

Kim et al. (15) studied the impacts of taurine supplementation in mice with Alzheimer's Disease (AD). In the study a number of mice were given the six-week taurine supplementation, while

another group was given a placebo. The results showed that the Mice that were given the taurine appeared to have enhancements in Alzheimer-like learning and memory deficits. More research is required to find out if these same advantages are applicable to humans.

Salimaki et al. (16) showed that a cumulative dose of 45 mmol/kg of taurine (i.p. injection) remarkably reduced extracellular dopamine in the striatum of Wistar rats, the levels decreased even more on the day following treatment.

Interestingly, the levels of taurine in the brain were reduced significantly with age, which resulted in numerous studies investigating the possible neuroprotective effects of supplemental taurine in some different experimental models **(17)**.

Pharmacology

Taurine travels across the blood–brain barrier and has been involved in a wide array of physiological phenomena including inhibitory neuro-transmission, long-term potentiation in the striatum/hippocampus, protection against glutamate excitotoxicity, prevention of epileptic seizures, feedback inhibition of neutrophil/macrophage respiratory burst, membrane stabilization, adipose tissue regulation, possible prevention of obesity, calcium homeostasis and recovery from osmotic shock. **(17)**.

Insights from animal studies:

Evidence for neuroprotection

Reduced cognitive deficiencies were noticed in Wistar rats given streptozotocin (ICV-STZ) to emulate Alzheimer's disease, this was demonstrated on Morris water maze and in a passive avoidance test when medicated with 60 or 120mg/kg/day taurine **(18)**.

Other studies demonstrated distinguishing or additional processes of neuroprotection. **Adedara et al. (19)** studied taurine's efficacy against sodium fluoride toxicity. Drinking water was administered with doses of 100 or 200 mg/kg/day taurine, this helped to reduce lipid peroxidation and contributed to the re-establishment of acetylcholinesterase activity in male Wistar rats, as well as re initiating the activity of the antioxidant enzymes superoxide dismutase (SOD) and catalase. Taurine intake in fluoride-treated rats also reduced deficiencies in negative geotaxis and re-established normal locomotor activity.

Lu et al. (20) also demonstrated the restoration of choline acetyltransferase activity as well as the acetylcholinesterase activity in male Sprague-Dawley rats exposed to 15 mg/kg manganese chloride during puberty and adolescence. Rats medicated with 200 mg/kg/day (i.p. injection) of taurine achieved the same results as control rats in Morris water maze test, which illustrates the potential role of taurine against manganese neurotoxicity.

Taurine effect as antioxidants

The general terms "antioxidant systems" or "antioxidant system network" merge these various mechanisms, aiming at the prevention of the deleterious actions of ROS and RNS. They also have a vital role in providing optimum conditions for cell signaling and adaptation to different stresses.

The extracellular space, major organelles, as well as the subcellular compartments contain these beneficial antioxidant compounds. The antioxidant defense network is implicated in various crucial mechanisms, including (21):

- reducing the oxygen concentration
- decreasing pro oxidant enzymes process
- enhancing the effectiveness of the mitochondria function and reducing the leakage of electrons
- promoting different transcription factors (e.g., Nrf2, NF-κB, etc.) with increased synthesis of different antioxidants
- Acting as metal chelating and metal-binding proteins
- destroying peroxides
- binding 4-hydroxynonenal, MDA, etc (reactive products of peroxidation)
- getting rid of damaged molecules
- supporting optimal redox status
- contributing to antioxidant recycling mechanisms, that involve the recycling of vitamin E
- preventing of irreversible protein oxidation by the induction of its glutathionylation
- restricting mutagenesis by activating apoptosis/ferroptosis.

References:

1. Ronalds BF. (2019): "Bringing Together Academic and Industrial Chemistry: Edmund Ronalds' Contribution". Substantia.; 3(1): 139–152.
2. Park, E., Park, S. Y., Dobkin, C., & Schuller-Levis, G. (2014): Development of a novel cysteine sulfinic acid decarboxylase knockout mouse: dietary taurine reduces neonatal mortality. Journal of amino acids, 2014.
3. Jakaria, M., Azam, S., Haque, M. E., Jo, S. H., Uddin, M. S., Kim, I. S., & Choi, D. K. (2019): Taurine and its analogs in neurological disorders: Focus on therapeutic potential and molecular mechanisms. Redox biology, 24, 101223.

4. **Agca, C. A., Tuzcu, M., Hayirli, A., & Sahin, K. (2014):** Taurine ameliorates neuropathy via regulating NF-κB and Nrf2/HO-1 signaling cascades in diabetic rats. Food and chemical toxicology, 71, 116-121.
5. **Chen, V. C. H., Hsu, T. C., Chen, L. J., Chou, H. C., Weng, J. C., & Tzang, B. S. (2017):** Effects of taurine on resting-state fMRI activity in spontaneously hypertensive rats. Plos one, 12(7), e0181122.
6. **Wójcik, O. P., Koenig, K. L., Zeleniuch-Jacquotte, A., Costa, M., & Chen, Y. (2010):** The potential protective effects of taurine on coronary heart disease. Atherosclerosis, 208(1), 19-25.
7. **Menzie, J., Prentice, H., & Wu, J.-Y. (2013):** Neuroprotective Mechanisms of Taurine against Ischemic Stroke. Brain Sciences, 3(4), 877–907. MDPI AG.
8. **Shivaraj MC, Marcy G, Low G, Ryu JR, Zhao X, Rosales FJ, Goh ELK. (2012):** Taurine induces proliferation of neural stem cells and synapse development in the developing mouse brain. PLoS ONE; 7: e42935.
9. **Gebara, E., Udry, F., Sultan, S., & Toni, N. (2015):** Taurine increases hippocampal neurogenesis in aging mice. Stem Cell Research, 14(3), 369-379.Grujičić, R. (2022): Prefrontal cortex. Kenhub.
10. **Su, Y., Fan, W., Ma, Z., Wen, X., Wang, W., Wu, Q., & Huang, H. (2014):** Taurine improves functional and histological outcomes and reduces inflammation in traumatic brain injury. Neuroscience, 266, 56-65.
11. **Prentice, H., Modi, J. P., & Wu, J. Y. (2015):** Mechanisms of neuronal protection against excitotoxicity, endoplasmic reticulum stress, and mitochondrial dysfunction in stroke and neurodegenerative diseases. Oxidative medicine and cellular longevity, 2015.
12. **Jeong, J. E., Kim, T. Y., Park, H. J., Lee, K. H., Lee, K. H., Choi, E. J., ... & Kim, W. T. (2009):** Taurine exerts neuroprotective effects via anti-apoptosis in hypoxic-ischemic brain injury in neonatal rats. Clinical and Experimental Pediatrics, 52(12), 1337-1347.
13. **Niu, X., Zheng, S., Liu, H., & Li, S. (2018):** Protective effects of taurine against inflammation, apoptosis, and oxidative stress in brain injury. Molecular medicine reports, 18(5), 4516-4522.
14. **L'Amoreaux, W. J., Marsillo, A., & El Idrissi, A. (2010):** Pharmacological characterization of GABAA receptors in taurine-fed mice. Journal of Biomedical Science, 17(1), 1-5.
15. **Kim H, Kim H, Yoon J, et al. (2014):** Taurine in drinking water recovers learning and memory in the adult APP/PS1 mouse model of Alzheimer's disease. Sci Rep; 4: 7467.
16. **Salimäki J, Scriba G, Piepponen TP, Rautolahti N, Ahtee L. (2003):** The effects of systemically administered taurine and N-pivaloyltaurine on striatal extracellular dopamine and taurine in freely moving rats. Naunyn Schmiedebergs Arch Pharmacol.; 368: 134–141.
17. **Zhang, Q., Liu, Y., Wang, H., Ma, L., Xia, H., Niu, J., ... & Zhang, L. (2017):** The preventive effects of taurine on neural tube defects through the Wnt/PCP-Jnk-dependent pathway. Amino Acids, 49(9), 1633-1640.

18. **Reeta KH, Singh D, Gupta YK. (2017):** Chronic treatment with taurine after intracerebroventricular streptozotocin injection improves cognitive dysfunction in rats by modulating oxidative stress, cholinergic functions and neuroinflammation. Neurochem Int.; 108: 146–156.
19. **Adedara IA, Olabiyi BF, Ojuade TD, Idris UF, Onibiyo EM, Farombi EO. (2017):** Taurine reverses sodium fluoride-mediated increase in inflammation, caspase-3 activity, and oxidative damage along the brain-pituitary-gonadal axis in male rats. Can J Physiol Pharmacol.; 95(9): 1019-1029.
20. **Lu CL, Tang S, Meng ZJ, He YY, Song LY, Liu YP, Ma N, Li XY, Guo SC. (2014)**: Taurine improves the spatial learning and memory ability impaired by sub-chronic manganese exposure. J Biomed Sci.; 21(5): 51.
21. **Surai PF. (2020):** Vitagenes in Avian Biology and Poultry Health. Wageningen Academic Publishers; Wageningen, The Netherlands.
22. **Barrett, K., Barman, S., Boitano, S., & Brooks,H (2015):** Ganong's Review of Medical Physiology, 25th Edition(Lange Medical Book) : Learning, Memory, Language, & Speech p 283 McGraw Hill Professional.