PHARMACOLOGICAL ASPECTS AND POTENTIAL NEW CLINICAL APPLICATIONS OF TAURINE AND BROMOCRIPTINE

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Abstract - Our previous work has shown that high plasma taurine levels was found in hyperprolactinaemic patients; these levels returned to normal after bromocriptine (dopaminergic agonist, D2) treatment for three months. Furthermore we reported that bromocriptine decreased the myometrial PGI2 release in rats; whereas taurine increased the content of the myometrial PGI. It was suggested that the activity of Na (+)-K (+)-ATPase could modulate the production of PGs in several tissues. Bromocriptine is shown to stimulate Na + /K + -ATPase in the liver of rats, while taurine inhibits sperm plasma membrane Na + /K+-ATPase. It is therefore, thought of interest to investigate the effect of bromocriptine, taurine or their combination on the isolated rabbit jejunum and on the rat uterus in vitor and in vivo. Methods, the effect of bromocriptine on isolated tissues and after pretreatment of the tissue with sulpiride, haloperidol, cyproheptadine or taurine were studied in vitro. Rabbit jejunum and rat uterus (in estrus) were obtained and suspended at 37°C in oxygenated Tyrode's and DeJahlon's solutions respectively. Isotonic contractions were measured using Bioscience Isotonic Transducers In vivo treatment was also carried out to study the effects of bromocriptine mesylate 10mg/kg, taurine 200 mg/kg; or bromocriptine mesylate 10mg/kg + taurine 200 mg/kg, compared to a control group, in order to measure uterine Na+, K+-ATPase activity . The drugs were injected intraperitoneally daily for 14 days. Bromocriptine 0.1 - 0.26 mM stimulated the isolated rabbit jejunum and the rat uterus. Sulpiride and haloperidol failed to antagonize the induced contractions. The latter were abolished by pretreating the tissues with cyproheptadine or taurine. ATPase from rat's uterus, pretreated with bromocriptine, showed significantly ($P < 0.01$) higher activity compared to controls. Taurine, on the other hand, caused a significant inhibition of the uterus Na + / K + -ATPase activity. Pretreatment with both taurine and bromocriptine abolished completely the effects of either bromocriptine or taurine alone on the uterus Na +/ K + -ATPase activity. In conclusion, these results showed that bromocriptine and taurine were acting by clearly antagonistic mechanisms in the uterus in vivo and in vitro. The ability of taurine to inhibit uterine Na+, K+-ATPase activity, together with its role as an endogenous regulator of PGs, point to the functional correlations between taurine, PGs and K+-ATPase activity in the uterus. Thus, the result of the present study gives strong evidence for physiological and pharmacological roles of taurine in different clinical fields.

Keywords - Bromocriptine, Taurine, Rabbit's Jejunum, Rat's Uterus,

I. INTRODUCTION

Dopamine-agonist drugs are the treatment of choice for most patients with hyperprolactinemia [1, 2]. Bromocriptine (2-bromo- α - ergocriptine) has been the reference compound in suppressing prolactin secretion, restoring gonadal function, and shrinking prolactinomas [3]. It has a number of side effects, however, including nausea, dizziness, and headache, that limit the dose and may even necessitate the withdrawal of treatment [4, 5 , 6]. Bromocriptine is be1ieved to decrease plasma prolactin levels by activating central dopaminergic receptors in various mammals [7, 8]. This has been attributed to the accumulation of the compound in the pituitary [9]. It is possible that the compound may affect the synthesis and/or release of some stable endogenous compounds; indeed taurine was found to stimulate prolactin release in rats [10]. Taurine (2-aminoethanesulfonic acid) is a free S-containing amino acid taurine, detected in high concentration in the brain, uterus and some other peripheral organs [11, 12]. Our previous work has shown that high plasma taurine levels were found in hyperprolactinaemic patients; these levels returned to normal after bromocriptine (dopaminergic agonist, D2) treatment for three months [13]. Furthermore, we reported that bromocriptine decreased the myometrial PGI2 release in rats [14], whereas taurine increased the content of the myometrial PGI2, concomitant with the content of the mymetrum TXA2 [15]. It was suggested that the activity of Na (+)-K (+)-ATPase could modulate the production of PGs in several tissues [16]. Bromocriptine is shown to stimulate Na + /K + -ATPase in the liver in the rats [17], meanwhile taurine inhibits sperm plasma membrane Na + /K+-ATPase [18]. Na+K+ ATPase is an enzyme responsible for maintaining the low internal Na+ and high internal K+ concentrations typical of most vertebrate cells. The ion gradients created by the enzyme are important in preserving the volume, pH, and electrical resting potential of cells [19, 20]. It demonstrated that a taurine supplement could stimulate the secretion of LH and T, increase the levels of testicular marker enzymes, elevate testicular antioxidation and improve sperm quality [21]. Further, it was reported that taurine improves impaired memory in animals [22], and treats seizure-associated brain damage [23]. It reported that bromocriptine induced hallucination, which is related to non-dopaminergic action [24], meanwhile some

amino acids implicated in Bromocriptine Induced Schizophrenia [24]. It is therefore thought of interest to investigate the effect of bromocriptine, taurine or their combination on the isolated rabbit jejunum and on the rat uterus in vitro and to compare with their effect on the Na (+)-K (+)-ATPase in the uterus in vivo.

II. MATERIALS AND METHODS

2.1 In Vitro treatment - Isolated Experiments

Preparation of the isolated rabbit jejunum and rat uterus

Young white New Zealand Rabbit weighing 1.5- 2 Kg & Female Sprague–Dawley rats in estrus stage weighing 170 g were utilized in this work. The experiments were carried out with the consent of the Ethical Committee. The animals were subjected to halothane general anaesthesia and after death, rabbit jejunum and rat uterus (in estrus) were obtained by the usual methods [25]; strips 1.5-2 cm long were taken for examination. The strips were placed in 4 automatic bath organs of 20 ml capacity in accordance with the procedure of Alvarez et al [26]. The incubation of strips were suspended at 37°C in oxygenated Tyrode's and DeJahlon's solutions, respectively, and the oxygen and carbon dioxide as mixture (95% O2and 5% CO2) was added. So its pH remained within 7.3-7.5. Rabbit jejunum and rat uterus (in estrus) contractions were recorded by isotonic contractions which were measured using Bioscience Isotonic Transducers. The effect of bromocriptine on the isolated tissues and after pretreatment of the tissue with sulpiride, haloperidol, cyproheptadine or taurine were also studied

2.2 In Vivo treatment

2 .3 Animals:

Female Sprague–Dawley rats weighing 170 g were selected in this work. The rats were housed in groups (three or four in standard polypropylene cage), and maintained under standard laboratory conditions at an ambient temperature of 23±2 °C, relative humidity 50±15% and normal photo period (12 h dark/12 h light). Commercial pellet diet (manufactured by Grani siols and Flour mills Organization Feed Mill) and water were provided ad libitum. Animals were divided into 4 groups, (n=7 each), as follows: group 1, received bromocriptine mesylate 10mg/kg, group 2, received taurine 200 mg/kg; group 3, received bromocriptine mesylate 10mg/kg + taurine 200 mg/kg and group 4: (control group), received a saline solution. The drugs were injected intraperitoneally daily for 14 days. The last dose was injected 1 hr before the sacrifice of the animals.

2. 4. The homogenization medium

To prepare tissue homogenates for determination of Na + K + -ATPase activities, rats were stunned and decapitated; the thorax and abdomen were immediately opened. Uterus tissues were removed from all rats at the end of the experiment; each tissue was quickly excised and washed in the DeJahlon's solution. Tissues were blotted dry on (Whatman) filter paper and weighed. To each sample we added 5 ml of homogenization medium and the tissue was homogenized for 30-120 sec. (HY-Homogenizer, FRG). The homogenization medium Consisted of 0.25 M sucrose, 4 mM EDT A, 30 mM histidine HCI and 20 mM Hepes buffer; pH 6.8. Homogenates were centrifugated at 10,000 rpm (MSE) for 30 min at 4°C [27]. Pellets were washed with the isolation medium, suspended in 0.25 M sucrose containing 1 mM EDTA and 30mM histidine at pH 7.0, and then stored for 14 days at - 5°C. Storage at 5°C was reported to cause destruction of the Mg2 stimulated enzyme, thereby revealing the stimulation due to Na + / K + [27, 28].

2. 5. The incubation medium

Consisted of 3 mM ATP, 3 mM MgCI2, 100mM NaCI, 20mM KCI and 30mM Tris (pH 7.0). Generally 0.1 ml of enzyme suspension was equilibrated for 15 minutes at 37°C, then added to the incubation medium. Incubation continued for 15 min. The reaction was stopped by the addition of 0.1 ml of cold 50% trichloroacetic acid and aliquots of 0.5 ml were assayed for inorganic phosphates by the method of Gomorri [29], using Metal as reducing agent. A TP was added in the form of Tris-A TP, prepared from disodium adenosine triphosphate (Sigma Chemical Co.), according to the procedure of Schwartz et al [30].

2.6. Drugs and Chemicals:

Bromocriptine mesylate was obtained FROM SANDOZ Pharmaceutical Co., sulpiride from Laboratoire Etudes et Development Chimiques. Arpajon. France, Taurine from Fluka.,cyproheptadine from Merck Sharp & Dohme (MSD)., and Haloperidol from Searle Company, G. D. Skokie, IL USA.

2.7. Statistical Analysis:

All the data were subjected to statistical analysis using Student's t-test for non-paired samples [31].

III. RESULTS

3. 1 Results of In Vitro Studies

3. 2 Effect of bromocriptine on the isolated rabbit jejunum:

Bromocriptine 0.26 nM elevated the tonus and induced a sustained contraction of the spontaneously contracting rabbit jejunum. The ED50 of the compound was 0.15 mM. Pretreatment of the tissue with sulpiride 30 µM or halperidol 0.25 µM for 10 min did not antagonize the bromocriptine-induced

contraction. However, pretreatment of the tissue with taurine 4 mM or cyproheptadine 0.5 µM for 5 min completely prevented the effect of bromocriptine (Figures l and 2). The inhibitory concentration IC50 for taurine was 1.8 mM (n = 4).



Figure 1

Figure 1: Effect of bromocriptine (BR 0.26 mM) on the rabbit jejunum. Pretreatment of the tissue with taurine (T 4mM) for 5 min completely prevented the effect of bromocriptine, and the inhibitory dose 50 (LD 50) for taurine was 1.8 mM.

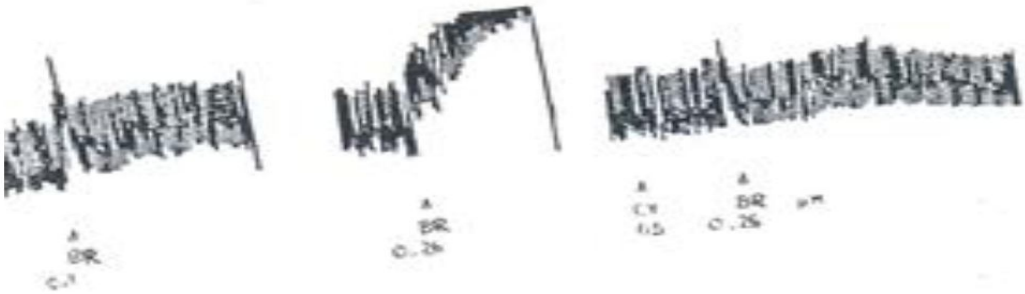


Figure 2: Effect of bromocriptine {BR; 0.26mM} on the rabbit jejunum which was completely antagonized by pretreatment of the tissue with cyproheptadine (CY 0.5 µM) for 5 min.

3. 3.The Effect on the isolated rat uterus:

Addition of bromocriptine 0.1 - 0.5 mM to the quiescent uterus induced a contraction in a concentration dependent manner.Furthermore, when bromocriptine was added to induce a sustained contraction, addition of tau¬rine 5 mM induced rapid relaxation of the tissue (Figure 3).

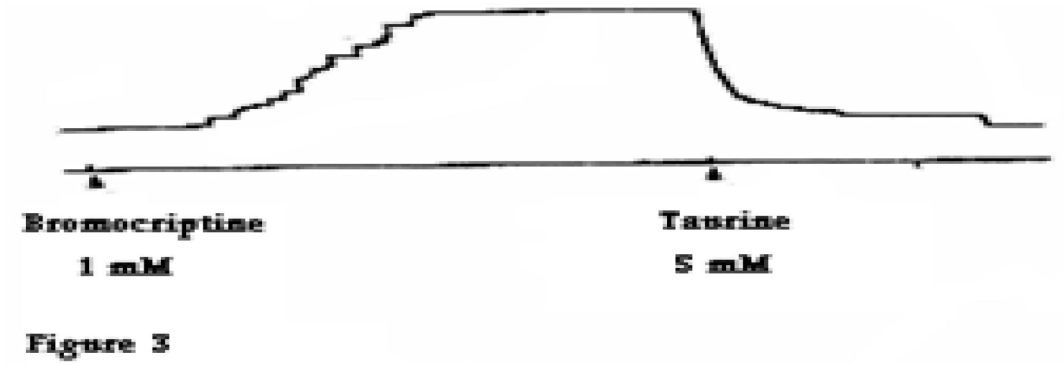


Figure 3

Figure 3: Effect of bromocriptine on rat uterus, treatment with taurine (T 5 mM) completely antagonized the sustained contraction induced by bromocriptine (BR 1mM

3.4. Results of In Vivo treatment

Uterus Na + / K + -ATPase activity from rats pretreated with bromocriptine showed significantly ($P < 0.01$) higher activity compared to controls (Table 1). Taurine, on the other hand, caused a significant inhibition of the uterus Na + / K + -ATPase activity (Table 1). Pretreatment with both taurine and bromocriptine abolished completely the effects of either bromocriptine or sulpiride alone on the uterus Na + K + -ATPase activity (Table 1 & Figure 4).

Table1: Effects of bromocriptine, taurine or their combinations on the Na + K + -ATPase activities of rat uterus. Mean ± SEM

Treatment	ATPase µ moles/100mg tissue/hr
Control	310 ± 8.25
Bromocriptine	521 ± 10.4*
Taurine	212 ± 6.56*
Brom + Tau	307 ± 7.72

Samples were run in duplicates, N (number of rats) = 7.
For isolation and incubation medium, see text. Value is mean ±SEM.

I. Bromocriptine mesylate, l0 mg/kg, i.p. for 14 days.
2. Taurine 200 mg/kg, i.p for 14 days.
* Significantly (P < 0.001) different from control group.

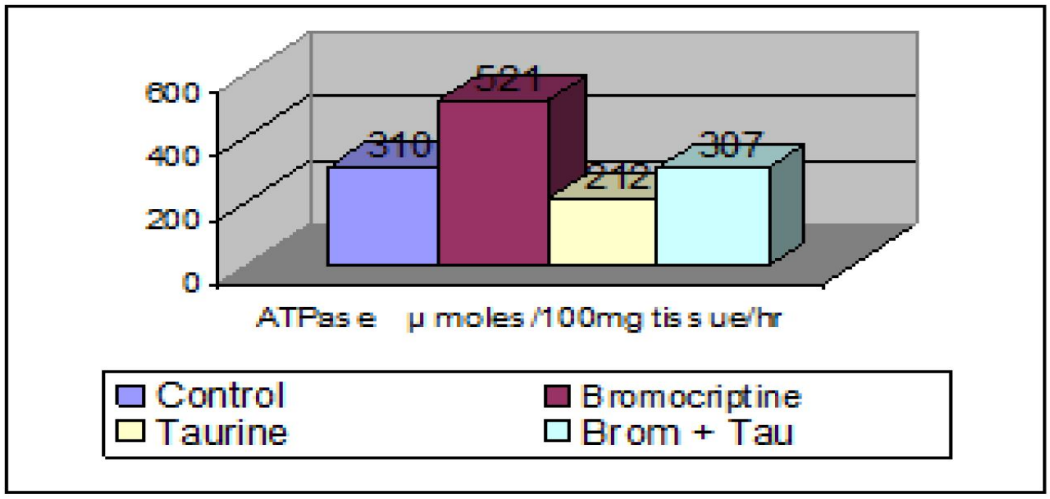


Figure 4: Effect of bromocriptine, taurine or their combination on uterine Na + K + -ATPase activities of rat uterus. in the rats (Values are mean ± S.E.M. , n = 7). µ moles/100mg tissue/hr * Significantly (P < 0.001) different from control group.

DISCUSSION

The results of the present study indicated that addition of bromocriptine 0.1 - 0.5 mM to the quiescent uterus induced a contraction in a concentration dependent manner. The stimulating effect of bromocriptine, a selective D2 agonist, on uterus contractility in vitro might be related to the fact that it decreases the concentration of PGI2, in the uterus, which blocks its contractility. [14]. Since, Bromocriptine can displace d- H-1ysergic acid diethylamide LSD from its binding sites in the brain [32], and that LSD can acti¬vate central postsynaptic 5-HT receptors [33]. Thus, the results of this investigation suggested antagonism between taurine and bromocriptine, which may probably involve activation of 5-HT receptors. It would be reasonable to suggest that co-administration of taurine with bromocriptine may suppress the hallucinations that could accompany high doses of bromocriptine used during the management of Parkinson's disease patients. Several functions have been postulated for taurine, such as osmoregulation, membrane stabilization of electrical activity of the cell membrane, metabolism, transport, detoxification, antioxidation, modulation of ion channels flux or calcium ion storage capacity, and as an inhibitory neurotransmitter or neuromodulator [34-37]. Our present study also indicated that taurine induced inhibition Na+-K -ATPase in uterus. This result is in agreement with the findings that there is association between Ca2+ transport and the concentration of Na+ and K+ , which has been demonstrated in vitro [38] and in vivo [39], and in agreement with the study, which indicated that taurine inhibits sperm plasma membrane Na + /K+-ATPase [18]. Further, our result may explain the study demonstrated that a taurine supplement could stimulate the secretion of LH and T, increase the levels of testicular marker enzymes, elevate testicular antioxidation and improve sperm quality [21]. On other side it reported that taurine can suppress testicular function deterioration by increasing antioxidant ability and inhibiting apoptosis [40]. Thus, these results with our present results imply that taurine plays important roles in the reproduction system.

On the other hand, taurine was found to protect the embryo from high potassium concentrations; the impairment of mouse embryo development in the presence of high potassium concentrations can be reversed if taurine is added to the culture medium & it

has a positive effect on preimplantation development of mouse embryos in vitro [41]. Thus our results may explain the taurine induced-protection action of embryo from high potassium, which is likely mediated through the inhibition of the Na+K+ ATPase enzyme, a plasma membrane enzyme that controls the intracellular content of potassium. Both taurine and potassium are found in high concentrations in oviduct and uterine fluid [19]. On a wider basis, these results showed that bromocriptine and taurine were acting by clearly antagonistic mechanisms in the uterus in vivo and in vitro The ability of taurine to inhibit uterine Na+K+ ATPase activity together with its role as an endogenous regulator of PGs [14], [42], and given that the activity of Na +K+ ATPase modulates the production of PGs in several tissues [15], there may be a physiological correlations between taurine, PGs and K+-ATPase activities in the uterus. The results of the present study also suggest a functional role of taurine in the protection and the implantation of embryo In conclusion, these results showed that bromocriptine and taurine were acting by clearly antagonistic mechanisms in the uterus in vivo and in vitro. The ability of taurine to inhibit uterine Na +K+ ATPase activity, the role of taurine as endogenous regulator of PGs, and the activity of Na (+)-K(+)-ATPase modulate the production of PGs in several tissues point to the functional correlations between taurine, PGs and Na +K+ ATPase activity in the uterus. Thus, the results of the present study gives strong evidence for physiological and pharmacological roles of taurine in protection and implantation of embryo.

Therefore, on the base of these results of the present study 1) Bromocriptine could be used as postcoital contraceptive. 2) Where taurine could be clinically used for protection and implantation the embryo especially in vitro fertilization. 3) It would be reasonable to suggest that co-administration of taurine with bromocriptine may suppress the hallucinations that could associated with bromocriptine used during the management of Parkinson's disease patients

CONCLUSION

A conclusion these results showed that bromocriptine and taurine were acting by clearly antagonistic mechanisms in the uterus in vivo and in vitro Thus, the results of the present study gives strong evidence for physiological and pharmacological roles of taurine in protection and implantation of embryo.

RECOMMENDATION

Therefore, on the base of these results of the present study 1) Bromocriptine could be used as postcoital contraceptive. 2) Where taurine could be clinically used for protection and implantation the embryo especially in vitro fertilization. 3) It would be reasonable to suggest that co-administration of taurine with bromocriptine may suppress the hallucinations that could associated with bromocriptine used during the management of Parkinson's disease patients.

REFERENCES

[1] K. Y. Ho and M.O. Thorner, Therapeutic applications of bromocriptine in endocrine and neurological diseases, Drugs, Vol. 36, pp. 67-82, 1988.

[2] P. G. Crosignani and C. Ferrari, Dopaminergic treatments for hyperprolactinaemia, Baillieres Clin Obstet Gynaecol, Vol. 4, pp. 441- 455, 1990.

[3] M. L. Vance, W. S. Evans, and M. O. Thorner, Drugs five years later: bromocriptine, Ann Intern Med, Vol. 100, pp. 78-91, 1984.

[4] R. Homburg, C. West, J. Brownell, H. S. Jacobs, A double-blind study comparing a new non-ergot, long-acting dopamine agonist, CV 205-502, with bromocriptine in women with hyperprolactinaemia, Clin Endocrinol, Oxford, Vol. 32, pp. 565-571, 1990.

[5] J. A. Verhelst, A. L. Froud, R. Touzel, et al, Acute and long-term effects of once-daily oral bromocriptine and a new long-acting non-ergot dopamine agonist, quinagolide, in the treatment of hyperprolactinemia: a double-blind study, Acta Endocrinol, Copenh, Vol. 125, pp. 385-391, 1991.

[6] P. F. M. Van der Heijden, W. de Wit, J. Brownell, J. Shoemaker and R. Rolland, A new dopamine agonist, versus bromocriptine in the treatment of hyperprolactinaemia, Eur. J. Obstet. Gynecol. Reprod.Biol, 40, pp. 111-118, 1991.

[7] C. L. Brooks, and C. W. Welsch, Reduction of serum prolactin in rats by 2 ergot alkaloids and 2 ergo1ine derivatives: a comparison, Proc. Soc. Exp.Biol. Med,Vol 146, No, 3, pp. 863-867, 1974.

[8] G. Anlezark, C. Pycock, and B. Meldrum, Ergot alkaloids as dopamine agonists: a comparison in two rodent models, Eur. J. Pharmacol, Vol. 37 , pp. 295-302,1976.

[9] E. Fluckiger, In: Bromocriptine: A Clinical and Pharmacological review. Eds. M. Thorner, E. Fluckiger and D. B. Calne, New York, Raven Press, pp. 42, 1980.

[10] J. Schibel, J. Elasser, and J.G. Ondo, Stimulation of prolactin secretion by taurine, a neutrally depressant amino acid, Neuroendocrinology, Vol. 30, pp. 350-354, 1980.

[11] B. G. Casslén, Free amino acids in human uterine fluid. Possible role of high taurine concentration. J. Reprod. Med, Vol. 32, pp. 181–184, 1987.

[12] R. J. Huxtable, Physiological actions of taurine, Physiol Rev, Vol. 72, pp. 101-163, 1992.

[13] R. Abu-Jayyab, and A. Bekairi, Plasma prolactin, insulin and amino acid levels in hyperprolactinaemic patients: Pre- and Post - treatment with bromocriptine, Med. Sci. Res. Vol, 15, pp. 639-640, 1987.

[14] M. Ageel., K. E. H. El Tahir, and A. R. Abu-Jayyab, Effect of bromocriptine on prostacyclin release and cyclic nucleotides on rat aortic and uterine tissues, Prostaglandins, Vol. 30 , pp. 369-381, 1985

[15] R. Abu-Jayyab, Effect of taurine and bromocriptine on uterine PGI2 and TXA2 contents in the rats, Med. Sci. Res, Vol. 15, pp. 713-714, 1987.

[16] M. Franchi, A. Motta, A. L. Gimeno, and M. A. Gimeno, Relationship between factors influencing Na (+)-K(+)-ATPase activity and eicosanoid production from 14C- arachidonic acid in spayed rat uterus, Prostaglandins Leukot Essent Fatty Acids, Vol. 48, No. 3, pp. 273-275, 1993.

[17] R. Abu-Jayyab, and A. Mahgoub, A role of Na+/K+ -stimulated odenosine triphosphatase in the action of dopaminergic D2 receptors of the liver in rats, Bioscience Reports, Vol. 7, No. 11, pp. 839-842, 1987.

[18] R. J. Mrsny, and S. Meizel, Inhibition of hamster sperm Na+, K+-ATPase activity by taurine and hypotaurine, Life Sci, Vol. 36, pp. 271-275, 1985.

[19] M. Glynn, The Na,K-transporting adenosine triphosphatase. In: The Enzymes of Biological Membranes edited by A. Martonosi, New York, Plenum, Vol. 3, pp. 35 -114, 1992.

[20] M. Glynn, All hands to the sodium pump, J. Physiol, London, Vol. 462, pp. 1-30, 1993.
[21] I Yang, G. Wu, Y. Feng, Q. Lv, S. Lin, J. Hu, Effects of taurine on male reproduction in rats of different ages, J. Biomed. Sci. Suppl 1:S9, doi: 10.1186/1423-0127-17-S1-S9, 2010.
[22] B. P. Vohra, and X. Hui, Improvement of impaired memory in mice by taurine.., Neural. Plast, Vol. 7, pp. 245-259, 2000.
[23] A, El Idrissi, J. Messing, J. Scalia and E. Trenkner, Prevention of epileptic seizures by taurine. Adv. Exp. Med. Biol, Vol. 526, pp. 515-525, 2003.
[24] Abdulrahim Abu Jayyab, Taurine Implicated in Bromocriptine Induced Hallucination: Glycine-Glutamic-Aspartic Implicated in Bromocriptine Induced Schizophrenia, American Journal of Pharmacology and Toxicology, Vol. 5, no. 1, pp. 34-41, 2010.
[25] Kitchen, Textbook of in vitro Practical Pharmacology (Blackwell Scientific Publications), Oxford, 1984).
[26] F. J. Alvarez, A. Valasco and J. L. Palomares, Blockada of muscarinic, histamine H1 and histamine H2 receptors by antidepressants, Pharmacology, 15, pp. 177-184, 1988.A. Schwartz, A Na K-stimulated adenosine triphosphatase in "microsomal" fractions from rat liver, Biochem. Biophys. Acta, Vol. 67, pp. 329-331, 1963.J. C. Skou, Preparation from mammallian brain and kidney of the enzyme system involved in active transport of Na ions and K ions, Biochem. Biophys. Acta, Vol 58, pp. 314-325, 1962.
[27] G. A. Gomori, modification of the colorimetric phosphorus determination for use with photoelectric colorimeter, J. Clin. Lab. Med, Vol. 27, pp. 955–960, 1942.
[28] Schwartz, H. S. Bachelard and H. McIL, The sodium-stimulated adenosine-triphosphatase activity and other properties of cerebral microsomal fractions and
[29] subfractions, Biochem. J, Vol 84, pp. 626-637, 1962.
[30] R. R. Sokal and F. J. Rholf, Biometry: The principles and practice of statistics in Biological Research, 2nd edn, W.H. Freeman, San Francisco, pp. 128-175, 1981.
[31] P. M. Whitaker and P. Seeman, SelectIve labelling of serotonin receptors by d- H-1ysergic acid diethylamide in calf caudate, Proc. Natl. Acad. Sci, U.S.A, Vol. 75, pp. 5783-5787, 1987.
[32] U. R. Burth, I. Creese and S. H. Snyder, Binding interactions of lysergic acid diethylamide and related agents with dopa¬mine receptors of the brain, Mol. Pharmacol, Vol 12, pp. 631-638, 1976.
[33] M. Solís, A. S. Herranz, O. Herreras , J. Lerma , and R. Martín Del Río, Does taurine act as an osmoregulatory substance in the rat brain?, Neurosci. Lett, Vol. 91, pp. 53-55, 1988.
[34] R. Martín del Río, A. S. Herranz, O. Herreras, N. Menéndez, and J. M. Solís, Possible osmoregulatory role of taurine in the cellular swelling evoked by weak organic acids in the rat hippocampus, Prog Clin Biol Res, Vol. 351, pp. 357-368, 1990.
[35] Galarreta, J. Bustamante, R. Martín Del Río and J. M. Solís, Taurine induces a long-lasting increase of synaptic efficacy and axon excitability in the hippocampus, J Neurosci, Vol. 16, pp. 92-102, 1996.
[36] R. J. Huxtable, Taurine in the central nervous system and the mammalian actions of taurine, Prog Neurobiol, Vol. 32, pp. 471-533, 1989.
[37] E. Lundholm, Relation between Ca metabolism and ATPase activities in the subcellular fractions from duck eggshell gland mucosa after DDE administration during different stages of eggshell formation, Comp. Biochem. Physiol. Pharmacol. Toxicol. Endocrinol, Vol. 82, pp. 1-16, 1985.
[38] W. C. Jr. Eastin and E. Spaziani, On the mechanism of calcium secretion in the avian shell gland (uterus), Biol Reprod, Vol. 19, pp. 505-518, 1987.
[39] I. Yang, X. Zong, G. Wu, S. Lin, Y. Feng, J.Hu, Taurine increases testicular function in aged rats by inhibiting oxidative stress and apoptosis, Amino Acids, Vol. 47, no. 8, pp. 1549-58, 2015.
[40] C. M. Dumoulin, J. L. H. Evers, M. Bras, et al. Positive effect of taurine on preimplantation development of mouse embryos in vitro, J. Reprod. Fertil, Vol. 94a, pp. 373–380, 1992b.
[41] E. H. El-Tahir, A. M. Ageel and A. R. Abu-Jayyab, Effect on taurine on arterial uterine and cardiac PGI2 and TXA2 synthetis in the rat, Prostaglandin, Vol. 33, pp. 17-24, 1987.

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