

Forms and Functional Repertoire of Acetylcholinesterase

Chavan Jiteesha V.¹, Donde S. B.²

¹PhD Scholar, Department of Zoology, Kirti M. Doongursee College (Autonomous), Dadar -400028, Mumbai Maharashtra India.

²Associate Professor, Department of Zoology, Kirti M. Doongursee College (Autonomous), Dadar -400028, Mumbai Maharashtra India.

Email: ¹jitchavan26@gmail.com, ²dsubhash40@gmail.com

Cite this paper as: Chavan Jiteesha V., Donde S. B., (2025). Forms and Functional Repertoire of Acetylcholinesterase.. *Journal of Neonatal Surgery*, 14 (21s), 962-965.

ABSTRACT

Acetylcholinesterase is an enzyme that breaks down the bridge made in between the synaptic cleft by acetylcholine. This enzyme has neuronal as well as neuronal activity. Initially in this enzyme was known to be found only in invertebrates and vertebrates but in recent times we have found this in bacteria, algae, protozoa and primitive plants, suggesting its extremely early appearance in the course of evolution and a widespread expression in non-neuronal cells. There are two fractions when it comes to acetylcholinesterase one being a salt soluble form also called as a cytoplasmic form and a detergent soluble form can also be called as membrane bound form. The primary function ascribed to membrane bound fraction of AChE is pertaining to hydrolysis of acetylcholine at the cholinergic synapses as well as myoneural junctions, while salt-soluble or cytoplasmic fraction of enzyme is supposed to be involved in either cationic permeability or utilization of acetyl groups by excitable cells and therefore it is believed that this fraction of AChE might be associated with energy metabolism facets of cholinergic neurotransmission process. But the equally bountiful functional repertoire of its marker enzyme called acetylcholinesterase is in the light of pioneering research findings are reported from all the world over.

Keywords: *Acetylcholinesterase, Acetylcholine, Cytoplasmic, Membrane Bound, Hydrolysis, Protozoa, Plants, Algae, Bacteria, Mammals, Human, Marker Enzyme, Invertebrates, Vertebrates.*

INTRODUCTION

Acetylcholine is an ester of acetic acid and choline. Being a neurotransmitter mostly found in the neuro-muscular junctions of the body; its work is to relay the signals passed in-between these junctions. This molecule is not just working in motor neurons but also a part of autonomic nervous system where it works in sympathetic as well as parasympathetic neurons.^{1,2} Acetylcholine is found at the inception stage of the ectodermal system to be exact the neural plate formation wherein it acts as the foundational enzyme for neural cells differentiation.¹

The functions of the said neurotransmitter include triggering muscle contractions primarily at the neuromuscular junctions, regulating the heart rate from minute to minute via muscarinic receptors antagonistic to the sympathetic nervous system.^{3,4} The said molecule has also shown its non-neuronal role. A study conducted in the year 2011 has shown the role of ACh in regulating insulin secretion.⁵ The regulatory part played by this non-neuronal ACh, where in they are secreted not just by the macrophages, B-cells etc.^{6,7} Observing the varied functions of Acetylcholine. The presence is vast.

The principal function of Acetylcholinesterase is to terminate the synapse made by Acetylcholine via hydrolysis and converting it to the acetic acid and choline.⁸ In muscles, AChE is known for its very important contractile function ensuring the proper contraction and relaxation of the muscles.^{9,10} AChE is also found in two types the membrane bound form and a soluble form.¹¹

The disruption or alteration of membrane bound and soluble form AChE can lead to Alzheimer's and Parkinson's disease^{11,12,13,14}, Myasthenia Gravis^{1,15} etc. As AChE plays such a major role in these neurodegenerative diseases the exact role is still not known in many diseases. Wherein, AChE is known to be involved in influencing factors like apoptosis, oxidative stress, inflammation, and protein aggregation.^{16,17,18} Acetylcholinesterase [E.C.3.1.17] were discovered in the year 1914 which was first isolated from Pacific electric ray.^{15,19}

1. METHODOLOGY

A review was done on the role of Acetylcholinesterase by using the keywords acetylcholinesterase + organism. Recent articles were chosen for this purpose.

2. CONCLUSION

Recent advances in evolutionary biology have suggested that Acetylcholinesterase has a role beyond the neuronal cells. Initially, it was noted that AChE has its presence only in invertebrate and vertebrate. With current scenario it is observed that AChE has a role in non-neuronal cell, including the single-celled organisms.²⁰

As the role of AChE in archaeobacteria is seldomly understood; Yamada *et al* (2005) conducted a study on 7 strains of archaea where in the expression of AChE has been established.²¹ Study conducted on *P. aeruginosa* concluded that ChoE was required by the said for the use of acetylcholine as a carbon and nitrogen source to grow.²² Currently, most of the studies for the said enzyme is targeted onto eukaryotes leading to the dearth of data available in these archae bacteria. As the role at present relating to archaea is just the use of ACh as a source of nutrient, discussed above not much of evidences available as compared to the neuronal cells and role in eukaryote.²³ A study conducted by screening 887 bacteria. The prevalence of AChE in bacteria is well established under this study.²⁴

In plants, it is observed that they contain both ChAT and AChE which decomposes ACh leading to an evidence that the role might be same like animals.²⁵ ACh is synthesized by roots in plants²⁶, AChE and ACh are involved in plant morphogenesis.^{27,28,29} In case of viruses no such suggestions were available stating the presence of the said enzyme but the viruses were known to cause the alterations in the level of the enzyme. Currently, viruses do not encode for the said enzyme.^{30,31,32} Presence of ACh in fungi indirectly vouches for presence of AChE in fungi.³³

The difference at present in invertebrate AChE and mammalian suggests a 2 gene encoding for invertebrates whereas, 3 genes encoding for mammals.³⁴ The invertebrate AChE plays similar roles to mammalian one's^{35,36}. As far as sponges are concerned they lack a nervous system but they might secrete the said enzyme but does secrete inhibitors of it to tackle their predators and prey with AChE.^{37,38} The role in Cnidaria is not fully understood.³⁹ In helminths, secretion is observed of the said enzymes not just as a function similar to mammals but in host-parasite interactions too.^{40,41,42}

As far as Annelida and Arthropoda are concerned, there is a well-established presence of AChE and also functions which are specified in pesticide effects as they are used widely in agriculture.^{43,44,45,46} The echinoderms and tunicates also other protochordates, show the presence of AChE stating a similar role and adding to AChE's evolutionary significance.^{47,48,49}

In vertebrata, role of AChE is defined comparatively well. Two types of cholinesterase's are observed here the acetylcholinesterase and the butylcholinesterase.⁵⁰ The presence of AChE in amphibian, reptiles, birds and mainly mammals is observed.^{51,52,53}

The review suggests a more research in the lower organisms in-order to be able to establish a more phylogenetic connection and evolve the understanding towards AChE to understand the eldress of the enzyme and understand the evolution of its function from non-neuronal to neuronal cells.

REFERENCES

- [1] Sam C, Bordoni B. Physiology, Acetylcholine. [Updated 2023 Apr 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK557825/>
- [2] Waxenbaum, J. A., Reddy, V., & Varacallo, M. A. (2023). Anatomy, Autonomic Nervous System. In *StatPearls*. StatPearls Publishing.
- [3] Purves D, Augustine GJ, Fitzpatrick D, et al., editors. Neuroscience. 2nd edition. Sunderland (MA): Sinauer Associates; 2001. Acetylcholine. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK11143/>
- [4] Levy M. N. (1997). Neural control of cardiac function. *Bailliere's clinical neurology*, 6(2), 227–244.
- [5] Rodriguez-Diaz, R., Dando, R., Jacques-Silva, M. C., Fachado, A., Molina, J., Abdulreda, M. H., Ricordi, C., Roper, S. D., Berggren, P. O., & Caicedo, A. (2011). Alpha cells secrete acetylcholine as a non-neuronal paracrine signal priming beta cell function in humans. *Nature medicine*, 17(7), 888–892. <https://doi.org/10.1038/nm.2371>
- [6] Mashimo, M., Moriwaki, Y., Misawa, H., Kawashima, K., & Fujii, T. (2021). Regulation of Immune Functions by Non-Neuronal Acetylcholine (ACh) via Muscarinic and Nicotinic ACh Receptors. *International Journal of Molecular Sciences*, 22(13), 6818. <https://doi.org/10.3390/ijms22136818>
- [7] Fujii, T., & Kawashima, K. (2000). Ca²⁺ oscillation and c-fos gene expression induced via muscarinic acetylcholine receptor in human T- and B-cell lines. *Naunyn-Schmiedeberg's Archives of Pharmacology*, 362, 14–21.
- [8] McHardy, S. F., Wang, H. L., McCowen, S. V., & Valdez, M. C. (2017). Recent advances in acetylcholinesterase Inhibitors and Reactivators: an update on the patent literature (2012–2015). *Expert opinion on therapeutic patents*, 27(4), 455–476. <https://doi.org/10.1080/13543776.2017.1272571>
- [9] Walker, C. R., & Wilson, B. W. (1975). Control of acetylcholinesterase by contractile activity of cultured muscle cells. *Nature*, 256(5514), 215–216. <https://doi.org/10.1038/256215a0>
- [10] Blotnick, E., & Anglister, L. (2016). Exercise modulates synaptic acetylcholinesterase at neuromuscular junctions. *Neuroscience*, 319, 221–232. <https://doi.org/10.1016/j.neuroscience.2016.01.044>
- [11] Fishman, E. B., Siek, G. C., MacCallum, R. D., Bird, E. D., Volicer, L., & Marquis, J. K. (1986). Distribution of the molecular forms of acetylcholinesterase in human brain: alterations in dementia of the Alzheimer type. *Annals of neurology*, 19(3), 246–252. <https://doi.org/10.1002/ana.410190305>
- [12] García-Ayllón, M. (2011). Revisiting the role of acetylcholinesterase in Alzheimer's disease: cross-talk with P-tau and β -amyloid. *Frontiers in Molecular Neuroscience*, 4. <https://doi.org/10.3389/fnmol.2011.00022>
- [13] Schegg, K. M., Harrington, L. S., Neilsen, S., Zweig, R. M., & Peacock, J. H. (1992). Soluble and membrane-bound forms of brain acetylcholinesterase in Alzheimer's disease. *Neurobiology of Aging*, 13(6), 697–704. [https://doi.org/10.1016/0197-4580\(92\)90092-c](https://doi.org/10.1016/0197-4580(92)90092-c)

- [14] Walczak-Nowicka, Ł. J., & Herbet, M. (2021). Acetylcholinesterase Inhibitors in the Treatment of Neurodegenerative Diseases and the Role of Acetylcholinesterase in their Pathogenesis. *International Journal of Molecular Sciences*, 22(17), 9290. <https://doi.org/10.3390/ijms22179290>
- [15] Haroon Khan, Marya, Surriya Amin, Mohammad Amjad Kamal, Seema Patel, Flavonoids as acetylcholinesterase inhibitors: Current therapeutic standing and future prospects, *Biomedicine & Pharmacotherapy*, Volume 101, 2018, Pages 860-870, ISSN 07533322, <https://doi.org/10.1016/j.biopha.2018.03.007>. (<https://www.sciencedirect.com/science/article/pii/S0753332217356998>)
- [16] Sternfeld, M., Shoham, S., Klein, O., Flores-Flores, C., Evron, T., Idelson, G. H., ... & Soreq, H. (2000). Excess “read-through” acetylcholinesterase attenuates but the “synaptic” variant intensifies neurodeterioration correlates. *Proceedings of the National Academy of Sciences*, 97(15), 8647-8652.
- [17] Meshorer, E., & Soreq, H. (2006). Virtues and woes of AChE alternative splicing in stress-related neuropathologies. *Trends in neurosciences*, 29(4), 216-224.
- [18] Walczak-Nowicka, Ł. J., & Herbet, M. (2021). Acetylcholinesterase Inhibitors in the Treatment of Neurodegenerative Diseases and the Role of Acetylcholinesterase in their Pathogenesis. *International journal of molecular sciences*, 22(17), 9290. <https://doi.org/10.3390/ijms22179290>
- [19] Dale, H. (1914). THE ACTION OF CERTAIN ESTERS AND ETHERS OF CHOLINE, AND THEIR RELATION TO MUSCARINE. *Journal of Pharmacology and Experimental Therapeutics*, 6(2), 147–190. [https://doi.org/10.1016/s0022-3565\(25\)08268-0](https://doi.org/10.1016/s0022-3565(25)08268-0)
- [20] Cox, M. A., Bassi, C., Saunders, M. E., Nechanitzky, R., Morgado-Palacin, I., Zheng, C., & Mak, T. W. (2020). Beyond neurotransmission: acetylcholine in immunity and inflammation. *Journal of internal medicine*, 287(2), 120–133. <https://doi.org/10.1111/joim.13006>
- [21] Yamada, T., Fujii, T., Kanai, T., Amo, T., Imanaka, T., Nishimasu, H., Wakagi, T., Shoun, H., Kamekura, M., Kamagata, Y., Kato, T., & Kawashima, K. (2005). Expression of acetylcholine (ACh) and ACh-synthesizing activity in Archaea. *Life Sciences*, 77(16), 1935–1944. <https://doi.org/10.1016/j.lfs.2005.01.026>
- [22] Pham, V. D., To, T. A., Gagné-Thivierge, C., Couture, M., Lagüe, P., Yao, D., Picard, M., Lortie, L., Attéré, S. A., Zhu, X., Levesque, R. C., Charette, S. J., & Shi, R. (2020). Structural insights into the putative bacterial acetylcholinesterase ChoE and its substrate inhibition mechanism. *Journal of Biological Chemistry*, 295(26), 8708–8724. <https://doi.org/10.1074/jbc.ra119.011809>
- [23] Zhu, J., Li, W., Zhou, Y., Pei, L., Liu, J., Xia, X., Che, R., & Li, H. (2021). Molecular characterization, expression and functional analysis of acyl-CoA-binding protein gene family in maize (*Zea mays*). *BMC plant biology*, 21(1), 94. <https://doi.org/10.1186/s12870-021-02863-4>
- [24] Pandey, S., Sree, A., Sethi, D., Kumar, C., Kakollu, S., Chowdhury, L., & Dash, S. (2014). A marine sponge associated strain of *Bacillus subtilis* and other marine bacteria can produce anticholinesterase compounds. *Microbial Cell Factories*, 13(1), 24. <https://doi.org/10.1186/1475-2859-13-24>
- [25] Tretyn, A., & Kendrick, R. E. (1991). Acetylcholine in plants: Presence, metabolism and mechanism of action. *The Botanical Review*, 57(1), 33–73. <https://doi.org/10.1007/bf02858764>
- [26] Jia, W., & Zhang, J. (2008). Stomatal movements and long-distance signaling in plants. *Plant signaling & behavior*, 3(10), 772-777.
- [27] Bamel, K., Gupta, S. C., & Gupta, R. (2007). Acetylcholine causes rooting in leaf explants of in vitro raised tomato (*Lycopersicon esculentum* Miller) seedlings. *Life sciences*, 80(24-25), 2393-2396.
- [28] Hartmann E, Gupta R. (1989) 11. Acetylcholine as a signaling system in plants.
- [29] Sarangle, Y., Bamel, K., & Purty, R. S. (2024). Role of acetylcholine and acetylcholinesterase in improving abiotic stress resistance/tolerance. *Communicative & integrative biology*, 17(1), 2353200. <https://doi.org/10.1080/19420889.2024.2353200>
- [30] Rubenstein, R., & Price, R. W. (1984). Early inhibition of acetylcholinesterase and choline acetyltransferase activity in herpes simplex virus type 1 infection of PC12 cells. *Journal of neurochemistry*, 42(1), 142–150. <https://doi.org/10.1111/j.1471-4159.1984.tb09710.x>
- [31] Horkowitz, A. P., Schwartz, A. V., Alvarez, C. A., Herrera, E. B., Thoman, M. L., Chatfield, D. A., Osborn, K. G., Feuer, R., George, U. Z., & Phillips, J. A. (2020). Acetylcholine Regulates Pulmonary Pathology During Viral Infection and Recovery. *ImmunoTargets and therapy*, 9, 333–350. <https://doi.org/10.2147/ITT.S279228>
- [32] Neu, C., Tremblay, R. E., Baumbach, P., Engelmann, M., Gebhardt, C., Götze, J., & Coldewey, S. M. (2024). Activités des cholinestérases et encéphalopathie associée au sepsis dans le sepsis viral versus non viral. *Canadian Journal of Anesthesia/Journal Canadien D Anesthésie*, 71(3), 378–389. <https://doi.org/10.1007/s12630-024-02692-7>
- [33] Horiuchi, Y., Kimura, R., Kato, N., Fujii, T., Seki, M., Endo, T., Kato, T., & Kawashima, K. (2003). Evolutional study on acetylcholine expression. *Life Sciences*, 72(15), 1745–1756. [https://doi.org/10.1016/s0024-3205\(02\)02478-5](https://doi.org/10.1016/s0024-3205(02)02478-5)
- [34] Knorr, D. Y., Georges, N. S., Pauls, S., & Heinrich, R. (2020). Acetylcholinesterase promotes apoptosis in insect neurons. *APOPTOSIS*, 25(9–10), 730–746. <https://doi.org/10.1007/s10495-020-01630-4>

- [35] Gaitonde, D., Sarkar, A., Kaisary, S., Silva, C. D., Dias, C., Rao, D. P., Ray, D., Nagarajan, R., De Sousa, S. N., Sarker, S., & Patill, D. (2006). Acetylcholinesterase activities in marine snail (*Cronia contracta*) as a biomarker of neurotoxic contaminants along the Goa coast, West coast of India. *Ecotoxicology*, 15(4), 353–358. <https://doi.org/10.1007/s10646-006-0075-3>
- [36] Nie, Y., Yang, W., Liu, Y., Yang, J., Lei, X., Gerwick, W. H., & Zhang, Y. (2020). Acetylcholinesterase inhibitors and antioxidants mining from marine fungi: bioassays, bioactivity coupled LC–MS/MS analyses and molecular networking. *Marine Life Science & Technology*, 2(4), 386–397. <https://doi.org/10.1007/s42995-020-00065-9>
- [37] Xu, F., Chen, W., Ye, Y., Qi, X., Zhao, K., Long, J., ... Wang, J. (2022). A new quinolone and acetylcholinesterase inhibitors from a sponge-associated fungus *Penicillium* sp. SCSIO41033. *Natural Product Research*, 37(17), 2871–2877. <https://doi.org/10.1080/14786419.2022.2139694>
- [38] Gardères, J., Wang, X., & Müller, W. E. (2016). Molecular Evolution of Defense Pathways in Sponges: Self–Self-recognition and Fight against the Nonself. In Elsevier eBooks (pp. 407–416). <https://doi.org/10.1016/b978-0-12-374279-7.12003-x>
- [39] Scemes, E. (1989). Rethinking the role of cholinergic neurotransmission in the CNidaria. In Springer eBooks (pp. 157–166). https://doi.org/10.1007/978-1-4899-0921-3_11
- [40] Selkirk, M. E., Lazari, O., & Matthews, J. B. (2005). Functional genomics of nematode acetylcholinesterases. *Parasitology*, 131 Suppl, S3–S18. <https://doi.org/10.1017/S0031182005008206>
- [41] de Lange, A., Prodjinotho, U. F., Tomes, H., Hagen, J., Jacobs, B. A., Smith, K., Horsnell, W., Sikasunge, C., Hockman, D., Selkirk, M. E., Prazeres da Costa, C., & Raimondo, J. V. (2020). Taenia larvae possess distinct acetylcholinesterase profiles with implications for host cholinergic signalling. *PLoS neglected tropical diseases*, 14(12), e0008966. <https://doi.org/10.1371/journal.pntd.0008966>
- [42] Skelly, P. J., & Da'dara, A. A. (2023). A novel, non-neuronal acetylcholinesterase of schistosome parasites is essential for definitive host infection. *Frontiers in immunology*, 14, 1056469. <https://doi.org/10.3389/fimmu.2023.1056469>
- [43] Scaps, P., Demuynck, S., Descamps, M., & Dhainaut, A. (1996). Biochemical and Enzymatic Characterization of an Acetylcholinesterase From *Nereis diversicolor* (Annelida, Polychaeta): Comparison With the Cholinesterases of *Eisenia fetida* (Annelida, Oligochaeta). *The Biological bulletin*, 190(3), 396–402. <https://doi.org/10.2307/1543032>
- [44] Gambi, N., Pasteris, A., & Fabbri, E. (2007). Acetylcholinesterase activity in the earthworm *Eisenia andrei* at different conditions of carbaryl exposure. *Comparative biochemistry and physiology. Toxicology & pharmacology : CBP*, 145(4), 678–685. <https://doi.org/10.1016/j.cbpc.2007.03.002>
- [45] López, M., & Pascual-Villalobos, M. (2009). Mode of inhibition of acetylcholinesterase by monoterpenoids and implications for pest control. *Industrial Crops and Products*, 31(2), 284–288. <https://doi.org/10.1016/j.indcrop.2009.11.005>
- [46] Choi, I., Kim, S., Lee, J., Chang, Y., Na, J. H., & Han, J. (2022). Analysis of the insect-repelling mechanism of star anise extract and its major active compounds against *Plodia interpunctella*. *Food Science and Biotechnology*, 31(4), 451–462. <https://doi.org/10.1007/s10068-022-01053-8>
- [47] Sköld, H. N., Baden, S. P., Looström, J., Eriksson, S. P., & Hernroth, B. E. (2015). Motoric impairment following manganese exposure in asteroid echinoderms. *Aquatic Toxicology*, 167, 31–37. <https://doi.org/10.1016/j.aquatox.2015.07.016>
- [48] Frederick, A., Tsigelny, I., Cohenour, F., Spiker, C., Krejci, E., Chatonnet, A., Bourgoin, S., Richards, G., Allen, T., Whitlock, M. H., & Pezzementi, L. (2008). Acetylcholinesterase from the invertebrate *Ciona intestinalis* is capable of assembling into asymmetric forms when co-expressed with vertebrate collagenic tail peptide. *FEBS Journal*, 275(6), 1309–1322. <https://doi.org/10.1111/j.1742-4658.2008.06292.x>
- [49] Flood, P. R. (1974). Histochemistry of cholinesterase in amphioxus (*Branchiostoma lanceolatum*, pallas). *The Journal of Comparative Neurology*, 157(4), 407–437. <https://doi.org/10.1002/cne.901570405>
- [50] Nicolet, M., Pinçon-Raymond, M., & Rieger, F. (1986). Globular and asymmetric acetylcholinesterase in frog muscle basal lamina sheaths. *The Journal of cell biology*, 102(3), 762–768. <https://doi.org/10.1083/jcb.102.3.762>
- [51] Cousin, X., & Bon, C. (1997). L'acétylcholinestérase des venins de serpents [Acetylcholinesterase from snake venoms]. *Comptes rendus des seances de la Societe de biologie et de ses filiales*, 191(3), 381–400.
- [52] Wilson, B., & Viola, G. (1972). Multiple forms of acetylcholinesterase in nutritional and inherited muscular dystrophy of the chicken. *Journal of the Neurological Sciences*, 16(2), 183–192. [https://doi.org/10.1016/0022-510x\(72\)90087-1](https://doi.org/10.1016/0022-510x(72)90087-1)
- [53] Bon, S., Vigny, M., & Massoulié, J. (1979). Asymmetric and globular forms of acetylcholinesterase in mammals and birds. *Proceedings of the National Academy of Sciences of the United States of America*, 76(6), 2546–2550. <https://doi.org/10.1073/pnas.76.6.2546>