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Original Article

Huperzinea: Pharmacological and Therapeutic Potential

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ABSTRACT

Introduction: Huperzine A (HupA) is derived from a club moss (*Huperzia serrata*). It is a potent and reversible inhibitor of acetyl cholinesterase (AChE). Chemically, it is a sesquiterpene alkaloid. It has been used for the treatment of swelling, fever and blood disorders for centuries in China. **Methodology:** The literature available on Huperzine was thoroughly studied. It has shown much beneficial effect since ages. It is a established Nootropic agent and widely used in the treatment of Alzheimer's disease. The plant has shown promising results *in vivo* and *in vitro* studies. **Results and Conclusion:** The present review highlights the pharmacological potential of Huperzine with its pharmacokinetic and pharmacokinetic studies and it's rational for future prospective.

Key words: Huperzine, Pharmacology, Neuroprotective agent, Pharmacokinetics.

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INTRODUCTION

Huperzine A: A Chinese Traditional Drug

Traditional Chinese medicine often aims to raise the natural defenses of the organism instead of trying to restore its natural functions and it offers a vast repertory for pharmaceutical research. The experience accumulated during many centuries inspires the search for new drugs in modern times. Huperzine A (HupA) is a good example of this continuum. HupA is a plant-based alkaloid. In China, the folk medicine Qian Ceng Ta (*Huperzia serrata*), a source of HupA, has been used for centuries to treat fever, inflammation, blood disorders and schizophrenia.[1] HupA acts as a potent, highly specific and reversible inhibitor of acetyl cholinesterase that crosses the blood brain barrier. Its potency of acetyl cholinesterase (AChE) inhibition is similar or superior to that of physostigmine, galantamine,[2] donepezil and tacrine. The latter three are acetyl cholinesterase inhibitors (AChEIs) approved for Alzheimer's disease (AD) in the United States and some European countries.[3] Cholinesterase inhibitors increase the amount of ACh (Acetylcholine) at the neuronal synaptic cleft by inhibiting the enzyme responsible for the hydrolysis of Ach and consequently improve neuronal transmission.

Huperzine A in Alzheimer's disease

HupA reverses or weakens cognitive deficits in some animal models, such as passive foot shock avoidance,[4] water maze,[5] spatial radial arm maze discrimination and delayed response performance.[6] Likewise, cognition enhancement was seen in aged monkeys in a delayed recognition task.[7] In China, where it has been approved and clinically used as a symptomatic agent for AD after many clinical trials, HupA exhibited considerable improvement in memory of aged subjects and patients with AD, with less peripheral cholinergic side effects typical of other AChEIs in use, particularly without the dose-limiting hepatotoxicity induced by tacrine[8]. Adverse effects (mainly cholinergic) are low, including dizziness, nausea, gastro enteric symptoms, headaches and depressed heart rate. "Huperzine A appears to be strongly specific for AChE, which suggests that it can be effective without the adverse effects that have been caused by drugs used to treat memory loss and dementia" as stated by The Journal of the American Medical Association (JAMA) in March of 1997.[9]

HupA as a neuroprotective agent

HupA also reduces neuronal cell death due to increased amount of glutamate[10] It is used for prophylaxis of drug against the irreversible AchE Isoman and other nerve gases.[11] It is also powerful neuroprotective and antioxidant agent[11] and a protective against amyloid beta peptide-induced apoptosis.

Phytobiology of Hup A

Huperzine occurs in many chemical species, with similar properties and different strengths. The average content of HupA in plants is 0.011%.[12] Recently, huprine X, a hybrid which combines the carbobicyclic substructure of HupA with the 4-amino- quinoline substructure of tacrine, has been synthesized with one of the highest affinities reported (Ki of 26 nM) for human AChE.[13] Under equivalent assay conditions, this affinity was 180 times more than HupA, 1200 times that of tacrine and 40 times that of donepezil. Compared with other classes of drug for the treatment of AD, it provides more symptomatic treatment.

Biochemistry of HupA

HupA is an unsaturated sesquiterpene alkaloid with a pyridone moiety and primary amino group. Its empirical formula is $C_{15}H_{18}N_2O$ and molecular weight 242. Chemically, HupA is 9-amino-13-ethylidene-11-methyl-4-azatri-cyclo[7.3.1.0(3.8)]trideca-3(8),6,11-trien-5-one . It is optically active and in the plant is present only in its enantiomer.[14] It is a very stable molecule, with a white-crystal appearance. HupA is a potent reversible inhibitor of AChE over Butyrylcholinesterase (BuChE).[15]

Pharmacology of HupA

AChE inhibition

HupA is a strong reversible inhibitor of AChE (Ki = 20–40 nM), which combines with aromatic residues in the active site of AChE, situated between Trp86 and Tyr337 in the enzyme. The formation of the AChE –HupA complex is very fast and the dissociation isslow[16] (Xu *et al.* 2017). This complex was examined using kinetic, computer-aided docking and X-ray crystallography methods. The X-ray structures of AChE from the Torpedo California fish (one of the richest sources of

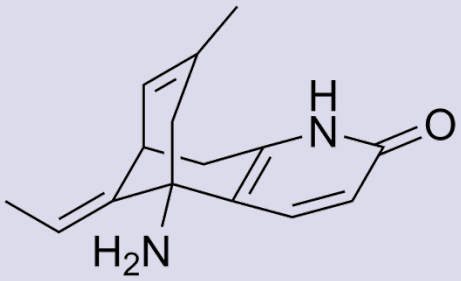

Figure 1: Leave and fruit of *Acronychia acidula* (lemon aspen).

this enzyme) complexed with HupA showed a high affinity for AChE. The Structural analysis exposes no similarity of HupA to ACh. Only one strong hydrogen bond is occurs and few hydrophobic interactions are evident within the crystalline complex. The 3-D computer image of AChE–HupA binding in the Raves study showed how the HupA blocks the enzyme by sliding smoothly into the active site of AChE where acetylcholine (ACh) is broken down and latches onto this site via a large number of subtle chemical links. It was also revealed that HupA can form an extra hydrogen bond with Tyr 337 within the choline site that exists only in mammalian AChE, but not in Torpedo enzyme and BuChE.[17] The cholinesterase inhibition activity of HupA has been assessed *in vitro* and *in vivo* using spectrophotometric methods.[18]

In vitro Studies on Huperzine

The inhibition of AChE activity of HupA was more efficient than tacrine and galantamine, but less than donepezil. The pattern of inhibition is consistent with mixed competitive type. The inhibition on BuChE showed a different report: HupA inhibited BuChE at a greater concentration than required for AChE compared with donepezil. The Ki values (inhibition constants, in nM) showed that HupA was more powerful than tacrine and galantamine, but about two times less potent than donepezil. Compared to AChE in animals such as horse and rat, HupA is a weaker inhibitor of human serum BuChE. This selectivity for AChE as opposed to BuChE (similar to that of galantamine) may imply a better side-effects profile.[19] However, a stronger inhibition of BuChE could be significant in the later stage of AD and give more protection over A-beta amyloid plaque deposition.[20] In contrast to isoflurophate (DFP), the AChE activity did not reduce with the prolongation of incubation with HupA *in vitro* and the AChE activity returned to 94% of the control after being washed five times, showing a reversible inhibitory action.[21]

In vivo studies on Huperzine

In contrast to the AChE inhibition *in vitro*, the comparative inhibitory result of oral HupA over AChE was 24- and 180-times greater on an equimolar basis more powerful than donepezil and tacrine respectively. In rats, HupA injected intraperitoneally (ip) showed the same efficacy of AChE inhibition as displayed following oral administration, althoughip administration of tacrine and donepezil showed higher inhibition on both AChE activity and serum BuChE.[22] The inhibitory action of HupA on brain AChE was not as much as that of donepezil after the intraventricular injection, but more efficient than tacrine.[23] Maximal AChE inhibition in rat cortex and whole brain was reached at 30–60 min and maintained for 360 min following oral administration of 0.36 mg/kg HupA. The oral administration of HupA yielded higher AChE inhibition as compared to donepezil and tacrine, which denoted its greater bioavailability and easy penetration the blood brain barrier.[24]

Effects on neurotransmitters

HupA causes a considerable increase in ACh levels in rat brain. Rats treated with HupA at doses of 0.3, 0.5 or 2 mg/kg showed increased brain ACh 6 h after administration. HupA induces delayed increases of ACh levels in whole brain than seen for tacrine, heptylphysostigmine, physostigmine and metrifonate.[25] The degree of Achrise was regionally selective: the maximum increase was at 60 min in the frontal and parietal cortex, intermediate at 30 min in the hippocampus and at 5 min in the medulla oblongata and little increases at 30 min in the striatum. Considering that the level of ACh is considerably lower in the cerebral cortex of patients with AD,[25] the regional specificity by HupA may give therapeutic advantages. The biosynthesis of ACh was not changed, which was shown by unaltered choline levels or choline acetyltransferase level in any region of rat's brain.[26] This rise was sustained for 6 h. Systemic HupA considerably enhanced ACh levels above baseline at doses of 0.1, 0.3 and 0.5 mg/kg by 54%, 129% and 220% respectively. NE and DA levels were enhanced more than 100%after administration of the 0.3 and 0.5 mg/kg doses. No changes at the 5-HT (5-hydroxytryptamine receptor) levels were seen. These effects suggest cognitive enhancing effects of HupA and also demonstrate interaction between cholinergic and Monoaminergic systems in the control of cognitive function and the clinical effect of AChE linked to the stimulation of cholinergic as well as Monoaminergic systems.[26]

Cholinergic receptors

Studies on displacement of [3H] QNB and [3H] nicotine binding have revealed effects of HupA on cholinergic receptors compared to other AChEIs including galantamine and tacrine.[27] HupA lacks an effect on muscarinic receptors, whereas huprine X, a hybrid between tacrine and HupA, exhibited micro molar activity at M(1) and M(2) receptors, mostly agonistic. This additional muscarinic activity of huprineX is significant and offers therapeutic advantages in dementia therapy.[28]

Protective properties of Huperzine

In nerve gas poisoning

Other properties of HupA pharmacology include its protective actions. HupA has been verified as a prophylactic drug against soman and other nerve gas poisoning with notable results.[29] It functions by shielding cortical AChE from soman inhibition and avoiding following seizures. Hence, HupA a powerful protective agent against chemical weapons.[30]

Huperzine and glutamate toxicity

HupA also protects primary neuronal cell cultures and animals from glutamate toxicity. Glutamate activates N-methyl-D-aspartate receptors and increases the flux of calcium ions into the neurons. Pretreatment of primary neuronal cells with HupA reduced glutamate- and OP-induced toxicity and reduced neuronal death. HupA is more potent in protecting mature neurons, then comes donepezil, physostigmine and tacrine. HupA was mainly efficient in protecting more mature neurons against neurotoxicity because of more functional NMDA receptors in mature neurons.[31] Additionally, loss of cholinergic function in patients with AD, glutamatergic and GABAergic neurotransmitter systems may also be compromised.[8] Therefore, HupA is used in treatment of dementia and also as a preventive agent as it slows down or blocks the pathogenesis of AD in early stage because it attenuates glutamate-mediated toxicity.

Antioxidant effects

Increased oxidative stress due to free radical damages the cellular function which can lead to AD. This damage are also associated with lesions called tangles and plaques. Plaques are formed by the deposition of amyloid beta-peptide (Abeta) and seen in brains of AD patients.[32] HupA and

tacrine were tested comparatively for protection against A beta-induced cell lesion, levels of lipid peroxidation and antioxidant enzyme activities in rat PC12 and primary cultured cortical neurons.[33] Both drugs have similar protective actions against A beta toxicity, causing decrement of cell survival and glutathione peroxidase (GSH-Px) and catalase (CAT) activity, increasing the production of malondialdehyde (MDA) and superoxide dismutase (SOD). Administration of HupA decreased apoptosis (programmed cell death), which is followed by beta-amyloid injection thereby regulating expression of apoptosis-related genes.[34] The neuroprotective properties of HupA enantiomers have no relation to anticholinesterase activity: preincubation with (+) HupA or (-)HupA (0.1–10 mM) protected cells with similar potency against Abeta toxicity (toxicity in AD) and considerably increased survival.[7]

Free radical level

In a study Hup A showed decreased level of abnormal free radical in hippocampus, cerebral cortex and serum of aged rats. Huperzine B demonstrated neuroprotective properties same as HupA and other AChEIs (donepezil, galantamine, tacrine), attenuating the hydrogen-peroxide-induced injury.[35]

Pharmacokinetics of Huperzine

An auto radiographic study in mice after intravenous (IV) injection of a dose of 183 mg/kg demonstrated the presence of HupA in all regions of brain, with higher concentration in the frontal parietal cortex, striatal cortex, hippocampus and nucleus accumbens.[36] In another study, radio labeled HupA was found highest in kidney and liver 15 min after iv administration. After 12 h, no radioactivity was found in any part of the body.[37] In pregnant mice, a small amount of radioactivity was detected in the fetus. HupA was (73%) excreted in the urine 24 h after iv injections and only 2.4% of radioactivity was seen in the feaces.[38] HupA removed from the kidney was part metabolites and part prototype. In six young healthy volunteers, oral HupA was absorbed quickly, distributed widely in body and eliminated at moderate rate.[39]

Toxicity Study

Toxicological studies performed in various animal species showed less severe undesirable side effects in association with cholinergic activation for HupA compared to other than AChEIs such as physostigmine and tacrine.[40] In mice, the LD_{50} doses were 4.6 mg po, 3.0 mg sc, 1.8 mg ip and 0.63 mg IV. Histopathological examinations demonstrated no changes in liver, kidney, heart, lung and brain after administration of HupA for 180 days, in dogs (0.6 mg/kg im) and in rats (1.5 mg/kg po). No mutagenicity was found in rats and no teratogenic effect in mice or rabbits.[41]

CONCLUSION

HupA has been recognized to have strong and long-lasting effects on the brain, with lower side effects. It has suitable pharmacological and rational enhancing profile for AD and age-related memory loss. Also, it can decrease neuronal cell death characteristic to glutamate. However, there is room for more research to explore its action as alkaloid and its analogues. There are many benefits with low side effects, making HupA reliable for treatment of AD and a very effective and safe for the pretreatment against nerve gases and other chemical weapons.

CONFLICT OF INTEREST

The authors declare no Conflict of interest.

ABBREVIATIONS

Hup-A: (Huperzine _a); **Ach:** Acetyl choline; **Bch:** Butylcholine; **Ache:** Acetylcholinesterase; **Bche:** Butylcholinesterase.

REFERENCES

1. Ma X, Tan C, Zhu D, Gang DR, Xiao P. Huperzine A from Huperzia species: An ethnopharmacolgical review. J Ethnopharmacol. 2007;113(1):15-34.
2. Upadhyay SD, Ahmad Y, Kohli S. A Review on Pharmacological Potential of Galantamine. Pharm Commun. 2020;10(2):63-6.
3. Csernansky JG, Martin M, Shah R, Bertchume A, Colvin J, Dong H. Cholinesterase inhibitors ameliorate behavioral deficits induced by MK-801 in mice. Neuropsychopharm. 2005;30(12):2135-43.
4. Ou LY, Tang XC, Cai JX. Effect of huperzine: A on working memory in reserpine- or yohimbine-treated monkeys. Europ J Pharm. 2001 Dec 21;433(2-3):151-6.
5. Cai Y, Huang P, Xie Y. Effects of huperzine: A on hippocampal inflammatory response and neurotrophic factors in aged rats after anesthesia. Acta Cirurgica Brasileira. 2019;34(12).
6. Ou LY, Tang XC, Cai JX. Effect of Huperzine A on working memory in reserpine- or yohimbine-treated monkeys. Europ J Pharm. 2001;433(2-3):151-6.
7. Auti ST, Kulkarni YA. A systematic review on the role of natural products in modulating the pathways in Alzheimer's disease. Int J VitamNutr Res. 2017;87(1-2):99-116.
8. Damar U, Gersner R, Johnstone JT, Schachter S, Rotenberg A. Huperzine A: A promising anticonvulsant, disease modifying and memory enhancing treatment option in Alzheimer's disease. Med Hyp. 2017;99:57-62.
9. Zangara A. The psychopharmacology of Huperzine A: An alkaloid with cognitive enhancing and neuroprotective properties of interest in the treatment of Alzheimer's disease. Pharma Biochem Beha. 2003;75(3):675-86.
10. Mao XY, Zhou HH, Li X, Liu ZQ. Huperzine A alleviates oxidative glutamate toxicity in hippocampal HT22 cells via activating BDNF/TrkB-dependent PI3K/Akt/mTOR signaling pathway. Cellmol Neurob. 2016;36(6):915-25.
11. Yang X, Wei HM, Hu GY, Zhao J, Long LN, Li CJ, *et al.* Combining antioxidant astaxantin and cholinesterase inhibitor huperzine A boosts neuroprotection. Mol Med Rep. 2020;21(3):1043-50.
12. Ferreira A, Rodrigues M, Fortuna A, Falcão A, Alves G. Huperzine A from *Huperzia serrata*: A review of its sources, chemistry, pharmacology and toxicology. Phytochem Rev. 2016;15(1):51-85.
13. Zhang S, Hou B, Yang H, Zuo Z. Design and prediction of new acetylcholinesterase inhibitor via quantitative structure activity relationship of huprines derivatives. Archives of Pharmacal Research. 2016;39(5):591-602.
14. Lian WW, Liu AL, Du GH, Huperzine A. In Natural Small Molecule. Drugs from Plants Springer, Singapore. 2018;271-5.
15. Davletshina R, Ivanov A, Evtugyn G. Acetylcholinesterase Sensor Based on Polyelectrolyte Complexes with DNA inclusion for the Determination of Reversible Inhibitors. Electroan. 2020;32(2):308-16.
16. Xu M, Heidmarsson S, Thorsteinsdottir M, Wasowicz P, Sun H, Deng T, *et al.* Infraspecific Variation of Huperzine A and B in Icelandic Huperziaselago Complex. Planta Medica. 2019;85(02):160-8.
17. Upadhyay SD, Ahmad Y, Kohli S, Sharma RK. Evaluation of acetylcholinesterase and butyrylcholinesterase inhibitory activity of Huperzine-A; *in silico* and *in vitro* studies. Ind Jol Biochem Bioph. 2019;56(3):224-9.
18. Tung BT, Hai NT, Thu DK. Antioxidant and acetylcholinesterase inhibitory activities *in vitro* of different fraction of *Huperzia squarrosa* (Forst.) Trevis extract and attenuation of scopolamine-induced cognitive impairment in mice. Jol Ethnopharm. 2017;198:24-32.
19. García MV, Poser GLV, Apel M, Tlatilpa RC, Mendoza-Ruiz A, Villarreal ML, *et al.* Anticholinesterase activity and identification of huperzine A in three Mexican lycopods: *Huperzia cuernavacensis*, *Huperzia dichotoma* and *Huperzia linifolia* (Lycopodiaceae). Pak J Pharm Sci. 2017;30(1):235-9.
20. Sharma R, Kuca K, Nepovimova E, Kabra A, Rao MM, Prajapati PK. Traditional Ayurvedic and herbal remedies for Alzheimer's disease: From bench to bedside. Expt Rev Neurotherap. 2019;19(5):359-74.
21. Ye LN, Tu YS, Huang Q, Yu X, Yuan HH, Lu SM. Studies on H_2O_2 Induced Effect on *Huperzia serrata in vitro*. Jol Trop Subtrop Bot. 2017(6):9.
22. Chen Y, Cheng G, Hu R, Chen S, Lu W, Gao S, *et al.* A nasal temperature and pH dual-responsive *in situ* gel delivery system based on microemulsion of huperzine A: Formulation, evaluation and *in vivo* pharmacokinetic study. AAPS Pharm Sci Tech. 2019;20(7):301.
23. Shih CC, Chen PY, Chen MF, Lee TJ. Differential blockade by huperzine A and donepezil of sympathetic nicotinic acetylcholine receptor-mediated nitrergic neurogenic dilations in porcine basilar arteries. Europ Jol Pharmacol. 2020;868:172851.
24. Damar U, Gersner R, Johnstone JT, Schachter S, Rotenberg A. Huperzine A as a neuroprotective and antiepileptic drug: A review of preclinical research. Expt Rev Neurotherap. 2016;16(6):671-80.
25. Mei Z, Zheng P, Tan X, Wang Y, Situ B. Huperzine A alleviates neuroinflammation,

oxidative stress and improves cognitive function after repetitive traumatic brain injury. Metabolic Brain Disease. 2017;32(6):1861-9.
26. Du Y, Liang H, Zhang L, Fu F. Administration of Huperzine A exerts antidepressant-like activity in a rat model of post-stroke depression. Pharmacol Biochem and Behavr. 2017;158:32-8.
27. Upadhyay SD, Ahmad Y, Kohli S. A Review on Pharmacological Potential of Galantamine. Pharmacog Comm. 2020;10(2):63-6.
28. Katsuki H, Matsumoto K. Nicotinic Acetylcholine Receptors in Regulation of Pathology of Cerebrovascular Disorders. In Nicotinic Acetylcholine Receptor Signaling in Neuroprotection Springer, Singapore. ;
29. Lallement G, Baille V, Baubichon D, Carpentier P, Collombet JM, Filliat P, *et al.* Review of the value of huperzine as pretreatment of organophosphate poisoning. Neurotoxicol. 2002;23(1):1-5.
30. Bajgar J, Kassa J, Kucera T, Musilek K, Jun D, Kuca K. Some possibilities to study new prophylactics against nerve agents. Mini Revi Med Chem. 2019;19(12):970-9.
31. Ved HS, Koenig ML, Dave JR, Doctor BP. Huperzine A, a potential therapeutic agent for dementia, reduces neuronal cell death caused by glutamate. Neuroreport. 1997;8(4):963-7.
32. Zhang S, Xiao T, Yu Y, Qiao Y, Xu Z, Geng J, *et al.* The extracellular matrix enriched with membrane metalloendopeptidase and insulin-degrading enzyme suppresses the deposition of amyloid-beta peptide in Alzheimer's disease cell models. Jol Tis Engg Reg Med. 2019;13(10):1759-69.
33. Chand K, Alsoghier HM, Chaves S, Santos MA. Tacrine-(hydroxybenzoyl-pyridone) hybrids as potential multifunctional anti-Alzheimer's agents: AChE inhibition, antioxidant activity and metal chelating capacity. Jol Inorg Biochem. 2016;163:266-77.
34. Giménez-Llort L, Ratia M, Pérez B, Camps P, Muñoz-Torrero D, Badia A, *et al.* Behavioural effects of novel multitarget anticholinesterasic derivatives in Alzheimer's disease. Behav Pharmacol. 2017;28(2):124-31.
35. Gao X, Tang XC. Huperzine a attenuates mitochondrial dysfunction in β-amyloid-treated PC12 cells by reducing oxygen free radicals accumulation and improving mitochondrial energy metabolism. Jol Neurosci Res. 2006;83(6):1048-57.
36. Zhu HF, Yan PW, Wang LJ, Liu YT, Wen J, Zhang Q, *et al.* Protective properties of Huperzine A through activation Nrf2/ARE-mediated transcriptional response in X-rays radiation-induced NIH3T3 cells. Jol Cell Biochem. 2018;119(10):8359-67.
37. Chen H, Xiang S, Huang L, Lin J, Hu S, Mak SH, *et al.* Tacrine (10)-hupyridone, a dual-binding acetylcholinesterase inhibitor, potently attenuates scopolamine-induced impairments of cognition in mice. Metab Brain Dis. 2018;33(4):1131-9.
38. Zafonte RD, Fregni F, Bergin MJ, Goldstein R, Boudreau N, Monge I, *et al.* Huperzine A for the treatment of cognitive, mood and functional deficits after moderate and severe TBI (HUP-TBI): results of a Phase II randomized controlled pilot study: Implications for understanding the placebo effect. Brn Inj. 2020;34(1):34-41.
39. Peng T, Shi Y, Zhu C, Feng D, Ma X, Yang P, *et al.* Huperzine A loaded multiparticulate disintegrating tablet: Drug release mechanism of ethyl cellulose microparticles and pharmacokinetic study. Pow Tech. 2019;355:649-56.
40. Lian WW, Liu AL, Du GH. Huperzine A. In Natural Small Molecule Drugs from Plants Spri, Singapore. 2019;355:649-56;
41. Lallement G, Demoncheaux JP, Foquin A, Baubichon D, Galonnier M, Clarençon D, *et al.* Subchronic administration of pyridostigmine or huperzine to primates: Compared efficacy against soman toxicity. Drug Chem Toxicol. 2002;25(3):309-20.

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SUMMARY

Hup-A is established nootropic agent with many established effects like antioxidant, in nevere gas poisioning etc. Huperzine has been a drug of choice in Alzheimer's disease. The has shown its promising effects on brain cholinergic system. The drug has influential effect brain associated neurotransmitters. Owing to the above facts it can be summarized that Huperzine can be preferably used for brain health in day today life.