Drug Review

Huperzine

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What is Huperzine A

Huperzine-A is a plant alkaloid derived from Club moss plant, Huperzine serrata, which is a member or the Lycopodium species. Huperzine-A is in phase III clinical trial in the USA and is available as a dietary supplement.¹

Huperzine A, has been studied extensively for its potential in treating memory loss. It reversibly inhibits the enzyme acetylcholinesterase. In addition, huperzine A has antioxidant and neuroprotective properties.²

Several effects of Huperzine A helps preserve or even restore memory. Several studies of memory-impaired humans have shown that taking Huperzine A may help to enhance memory. Additionally, in a study of teenagers, Huperzine A appeared to enhance general mental functioning when it was taken consistently for as little as one month.³

Mechanisms by which Huperazine Acts

• Selectively and reversibly inhibits acetylcholinesterase and increases Acetylcholine concentrations.
• Huperzine A is also a NMDA receptor antagonist which protects the brain against glutamate induced damage, and it increases nerve growth factor levels.

Additional Effects of Huperzine

• These protective effects are related to its ability to attenuate oxidative stress, regulate the expression of apoptotic proteins Bcl-2, Bax, P53, and caspase-3, protect mitochondria, upregulate nerve growth factor and its receptors, and interfere with amyloid precursor protein metabolism.

Effects on the Mitochondria

• Preserves mitochondrial membrane integrity and improves energy metabolism.
• Prevents mitochondrial swelling, reactive oxygen species increase, and cytochrome c release due to neuronal or cellular damage.
• Promotes the rate of ATP production and blocked mitochondrial swelling caused by normal osmosis.

Huperzine-A Capsules Enhance Memory and Learning Performance in Adolescent Students

To study the efficacy of huperzine-A capsules (Hup) on memory and learning performance of adolescent students.

Methods

Using double-blind and matched pair method, 34 pairs of junior middle school students complaining of memory inadequacy were divided into two groups by normal psychological health inventory (PHI), similar memory quotient (MQ), same sex and class. The Hup group was administrated orally 2 capsules of Hup (each contains Hup 50 micrograms) b.i.d., and the placebo group was given 2 capsules of placebo (starch and lactose inside) b.i.d., for 4 wk.
Results

At the end of trial, the Hup group’s MQ (115+/ -6) was more than that of the placebo group (104+/ - 9, p < 0.01), and the scores of Chinese language lesson in the Hup group were elevated markedly too.

Safety Assessment

BP, HR, ECG, ALT, AKP, BUN, Cr, Hb, WBC, and urine routine.

Observations

• About 58% (29/50) of patients treated with Hup showed improvements in their memory (P < 0.01), cognitive (P < 0.01), and behavioral P < 0.01 functions.
• The efficacy of Hup was better than placebo (P < 0.05).
• No severe side effect was found.

Conclusion

The Hup capsules enhance the memory and learning performance of adolescent students. Huperzine A is a promising drug for symptomatic treatment of Alzheimer’s disease.4
• Activity of daily scale
• Treatment emergency symptom scale

Pharmacokinetics of Huperzine

The in vivo pharmacokinetics of Huperzine Alpha has been studied in healthy human volunteers. Huperzine A was administered in tablet form at a single dose of 0.4 mg.5,6

Absorption: Huperzine Alpha is absorbed rapidly, distributed widely in the body, and eliminated at a moderate rate.3 Following oral administration, the presence of Huperzine Alpha started to appear in the plasma at 5-10 min.

Peak Concentrations: Huperzine Alpha reached the peak concentrations with a Cmax of 2.59 +/- 0.37 ng/ml at 58.33 +/- 3.89 min (time to reach peak level), Tmax.3

Bioavailability: The area under plasma vs time curve (AUC(0-t)) and the area under plasma from zero to infinity (AUC(0-infinity)) for Huperzine Alpha were found to be 1986.96 +/- 164.57 microg/ 1.min and 2450.34 +/- 233.32 microg/1.min, respectively.5,7

Metabolism: In the liver.

Excretion: In the urine.

Half Life: The mean values of alpha and the beta half-life were 21.13 +/- 7.28 min and 716.25 +/- 130.18 min respectively, and showed a biphasic profile with rapid distribution followed by a slower elimination rate.

Indications

• Improving Memory, Mental Function, and Behaviour in elderly patients with Dementia, Alzheimer’s Disease.3,4
• Improving memory in healthy adolescents.

Additionally Helpful in

Increasing alertness and energy, protection from organophosphate poisoning causing neuronal apoptosis, and other conditions.

Huperzine Dosage Information

In clinical trials Huperzine A has been given to patients with memory impairment due to Dementia and Alzheimer’s disease, doses from 100 mcg to 400 mcg in single or divided doses. Huperzine A should only be used with a physician’s recommendation and monitoring.

Huperzine versus Donepezil, Rivastigmine and Tacrine

Huperzine Alpha is a patent, highly specific and reversible inhibitor of acetylcholinesterase (AChE).

Compared with tacrine, donepezil, and rivastigmine, HupA has better penetration through the blood barrier, higher oral bioavailability, and longer duration of AChE inhibitory action.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Huperzine Alpha</th>
<th>Tacrine</th>
<th>Donepezil</th>
<th>Rivastigmine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penetration the blood-brain barrier</td>
<td>Better</td>
<td>Lower</td>
<td>Lower</td>
<td>Lower</td>
</tr>
<tr>
<td>Oral bioavailability</td>
<td>Higher</td>
<td>Lower</td>
<td>Lower</td>
<td>Lower</td>
</tr>
<tr>
<td>Duration of AChE inhibitory action</td>
<td>Longer</td>
<td>Shorter</td>
<td>Shorter</td>
<td>Shorter</td>
</tr>
</tbody>
</table>

In molar terms, huperzine A had similar potency on increasing mPFC ACh and DA levels as compared to the 11-and 2-fold dosages of donepezil and rivastigmine, respectively, and had longer lasting effects after oral dosing.6,8,9
HupA is a potent, reversible and selective inhibitor of AChE with a rapid absorption and penetration into the brain in animal tests. It exhibits memory-enhancing activities in animal and clinical trials. Compared to tacrine and donepezil, HupA possesses a longer duration of action and higher therapeutic index, and the peripheral cholinergic side effects are minimal at therapeutic doses.10

References