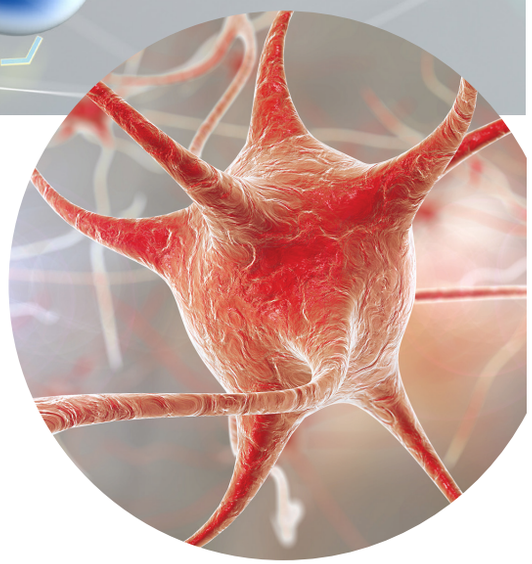
CogniUp™

A Neuroprotective and Antioxidative combination of *Huperzia serrata*, *Convolvulus pluricaulis* and *Celastrus paniculatus*+

Physical, environmental and work stress in conjunction with hectic lifestyle and unhealthy food habits are the major cause of diverse neurodegenerative disorders including cognitive decline & memory impairment.

Oxidative neuronal injury and acetylcholine deficiency have a major impact on learning and memory. The majority of the neuro supportive strategies are based on the improvement of cholinergic function in the brain and one of the emerging therapeutic targets is to enhance the acetylcholine level in the brain. Standardized botanical extracts including Huperzia serrata (CP), Convolvulus pluricaulis (Shankhapushpi; SP) and Celastrus paniculatus (Jyotismati; JY) have been demonstrated to attenuate brain function by serving as a natural acetylcholinesterase (AChE) inhibitor and exhibited their efficacy in the management of neurological impairment & dementia. We have developed a novel combination of CP, SP & JY named CogniUP®.



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Cepham Inc. | 142 Belmont Drive, Unit 14, Somerset NJ 08873
Tel: (201) 255-6011 | Fax: (201) 255-6012 | info@cepham.com | www.cepham.com

We have carried out a study with CogniUP® which demonstrates effective and synergistic inhibition of AChE and attenuation of oxidative stress as reflected in reduced glutathione (GSH) values. Concentration-dependent AChE inhibition kinetics was assessed individually using 0, 3.0, 6.0, 9.0, 12.0 and 24.0 mg SP/ml, and 0, 0.5, 1.0, 2.0, 4.0 and 8.0 mg JY/ml, and 0, 0.0625, 0.125, 0.25 and 0.5 µg CP/ml. It was observed that a combination of SP, JY and CP (12 mg/ml, 4 mg/ml and 0.125 µg/ml) provided the most efficacious and synergistic AChE inhibition. In another independent study, cultured pheochromocytoma PC-12 cells were pre-incubated with CP (0, 0.0625, 0.125, 0.25 and 0.5 µg/ml) and a combination of SP, JY and CP (12 mg/ml, 4 mg/ml and 0.125 µg/ml) (MZ001) followed by an oxidative exposure to 200 mM of H2O2 over the period 0-48 hours. Pretreatment of these cells with CogniUp® prior to H2O2 exposure significantly elevated the cell survival, increased the levels of reduced glutathione. Our results indicate that CogniUp® exhibited dramatic neuroprotective effect against H2O2-induced oxidative damage, which may be important for clinical efficacy for the treatment of neuronal injury. Further studies are in progress to establish the therapeutic efficacy of CogniUp® in neuroprotection.

Based on our studies and published literature we found that the unique combination of CogniUp® can provide:

- **Neuroprotection***
- **Cognitive enhancement***
- **Increased focus***

The components of CogniUp® are standardized herbs:

1. Convolvulus pluricaulis (JY): Standardized for glycosides, flavonoids, coumarins & alkaloids.
2. Celastrus Paniculatus (SP): Standardized for alkaloids, saponins & terpenoids.
3. Huperzia serrata (CP): Standardized for sesquiterpene alkaloid Huperzine A 1%

Following are the summary results of the study we have carried out:

Table 1: Comparative Protective Effects of SP, JY and CP on AChE Inhibition (%)

SP (12 mg/ml)	JY (4 mg/ml)	CP (Ø.25 mg/ml)	CP (0.125 mg/ml)	SP (12 mg/ml) + JY (4 mg/ml) + CP (0.25 mg/ml)	SP (12 mg/ml) + JY (4 mg/ml) + CP (0.125 mg/ml)
27.63%	25.86%	28.24%	30.18%	33.84%	37.30%

Table 2: Comparative Protective Effects of SP, JY and CP on GSH Depletion (mM)

Control	H_2O_2	SP (12 mg/ml) + H_2O_2	JY (4 mg/ml) + H_2O_2	CP (0.25 mg/ml) + H_2O_2	SP + JY + CP + H_2O_2	SP (12 mg/ml) Alone	JY (4 mg/ml) Alone	CP (0.25 mg/ml) Alone	SP + JY + CP
327 ± 18.6	88.5 ± 7.5	250.5 ± 21.2	284.4 ± 24.3	308.3 ± 26.7	328.5 ± 30.7	328.9 ± 20.5	339.1 ± 31.2	347 ± 18.7	337.5 ± 24.8

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