Cognitive Vitality Reports® are reports written by neuroscientists at the Alzheimer's Drug Discovery Foundation (ADDF). These scientific reports include analysis of drugs, drugs-in-development, drug targets, supplements, nutraceuticals, food/drink, non-pharmacologic interventions, and risk factors. Neuroscientists evaluate the potential benefit (or harm) for brain health, as well as for age-related health concerns that can affect brain health (e.g., cardiovascular diseases, cancers, diabetes/metabolic syndrome). In addition, these reports include evaluation of safety data, from clinical trials if available, and from preclinical models.

Semax

Evidence Summary

Semax is used in Russia as a neuroprotective drug for stroke; however, there is little evidence whether it would improve cognition in healthy patients and no evidence for Alzheimer's disease.

Neuroprotective Benefit: Semax may be beneficial in stroke patients (and is used for stroke in Russia), but published literature of well-conducted studies is lacking.

Aging and related health concerns: There is not a strong rationale (and little evidence) that intranasal semax is useful for age-related indications.

Safety: Little human evidence exists for potential side effects.

What is it?

Semax is a heptapeptide (Met-Glu-His-Phe-Pro-Gly-Pro) which is a derivative of the adrenocorticotrophic hormone (ACTH) that possesses ACTH's neurotrophic effects and lacks its hormonal activity. It was first recognized in the 1950's that ACTH may have cognitive effects in addition to its hormonal effects. Several derivatives were developed around the N-terminal of ACTH to isolate the cognitive effects of the peptide. Although there is no consensus on the exact mechanism behind the cognitive effects of the ACTH fragments, they are believed to increase circulation of monoamines in the brain. The peptides have a short half-life, and in the 1970s a modification to the C-terminal with Pro-Gly-Pro increased its effects to 20-24hrs in animal models (Kolomin et al, 2013).

Semax was developed at the Russian Academy of Sciences, and is used in Russia for stroke, dyscirculatory encephalopathy, Parkinson's, ocular nerve atrophy, and for newborns with neurological deficits (Kolomin et al, 2013). Unfortunately, there are few published English-language studies in humans.

Semax is usually taken intranasally (by a dropper).

Neuroprotective benefit: Semax may be beneficial in stroke patients (and is used for stroke in Russia), but published literature of well-conducted studies is lacking.

Types of evidence:

- Two pilot studies in healthy individuals
- Two studies in stroke patients
- Several preclinical studies in different models

Human research to suggest prevention of dementia and cognitive aging

In one pilot study in 24 healthy subjects, intranasal 1% semax solution (total dose 1.2 mg) increased resting fMRI signal in the default mode network rostral subcomponent relative to placebo (Lebedeva et al, 2018). Another study in healthy patients reported that semax (250-1000ug/kg) improved attention and short-term memory and caused EEG changes that were similar to other neuroprotective drugs (cannot access, in Russian, referenced in Kolomin et al, 2013). Another study reported that semax improved neurological function in stroke patients when added to the standard of care (Gusev et al, 1997 – abstract only, article in Russian). Another study in 110 patients with stroke reported that treatment with semax (2 courses – 6000 µg/day for 10 days with 20-day interval) increased plasma BDNF levels.

Treated patients with high BDNF levels had an improved timing of rehabilitation (Gusev et al, 2017 – abstract only, article in Russian).

Clinical research to suggest benefits to patients with dementia or cognitive aging
None

Mechanisms of action from preclinical research
Intranasal semax was reported to bind in the rat basal forebrain and increase BDNF levels 3 hours, but not 24 hours, after administration (Dolotov et al, 2006). It was also reported to increase BDNF in the hippocampus (Dolotov et al, 2003) and BDNF and NGF in the frontal cortex and hippocampus 8 hours after administration (Shadrina et al, 2010). Intranasal semax also increased serotonin, but not dopamine, levels. However, it did potentiate the stimulatory effects of d-amphetamine (Eremin et al, 2005).

In healthy rats, intranasal and intraperitoneal (I.P.) semax improved cognition (passive avoidance test) 15 minutes after treatment (Manchenko et al, 2012). In a rat model of photothrombosis, six daily treatments with semax (250ug/kg) after injury reduced infarction size and improved performance on a passive avoidance task (Romanova et al, 2006). Semax also reduced neurological damage and improved performance on a passive avoidance test in a model of cerebral ischemia cause by gravitation overload (Iasnetsov and Voronina, 2009 – article in Russian), reduced the increase in nitric oxide generation post-ischemia (Bashkatova et al, 2001), and improved cognition in a rat model of postresuscitation after clinical death (Kolomin et al, 2013).

In a rat model of Parkinson's disease (MPTP injection), four daily treatments with intranasal semax improved some behavioral aspects, but not others (Levitskaya et al, 2004). Another study of intranasal semax in a Parkinson's disease model (MPTP) suggested that treatment increased anxiety and did not change motor behavior (Slominsky et al, 2017).

Aging and related health concerns: There is not a strong rationale (and little evidence) that intranasal semax is useful for age-related indications.

Types of evidence:

- One preclinical study in a model of ischemia/reperfusion

In a rat model of myocardial ischemia/reperfusion (I/R), semax (I.P. before, during, and after I/R) had no effect on lesion size. It reduced the increase of sympathetic innervation of the ventricular septum after I/R but had no effect on the density of β_2 adrenoceptors in the ventricular septum (Gavrilova et al, 2017).

Safety: Little human evidence exists for potential side effects.

Types of evidence:

- Little human evidence
- Many preclinical studies

Although I am unable to access the original data from published studies in humans using semax, as reported in a review the most common adverse events are discoloration of the nasal cavity (~10% of patients) and an increase in blood glucose levels in diabetics (~7.4% of patients) (Kolomin et al, 2013). Long-term side effects are unknown. It is reportedly commonly used in Russia, so presumably there are not many serious adverse effects.

Drug interactions:
Not known

Sources and dosing:
In healthy individuals, 1-2 drops of the 0.1% solution are used two times per day. For stroke, 2-4 drops of the 1% solution are used 3-4 times per day. It is available in Russia.

Research underway:
None in the US, though possibly some research is ongoing in Russia.

Search terms:

- Semax

Websites:

- Clinicaltrials.gov
- Pubmed

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If you have suggestions for drugs, drugs-in-development, supplements, nutraceuticals, or food/drink with neuroprotective properties that warrant in-depth reviews by ADDF's Aging and Alzheimer's Prevention Program, please contact INFO@alzdiscovery.org. To view our official ratings, visit Cognitive Vitality's Rating page.