

## Hydergine

Hydergine (pronounced hi-der-gene) an ergoloid mesylate (derived from rye) is one of the most popular and widely used smart-drugs that have been in use for over 40-years. Hydergine stimulates oxygen flow to the brain, relieving symptoms of deteriorating mental capacity.

Hydergine has received only 'mild' reviews whilst being used to treat senile dementias, (although it is widely regarded to have been used in dosages that were far too small for those purposes). However, hydergine presents itself as a remarkable anti-aging medicine and an adjunct for the treatment of age-related mental decline.

Hydergine is known to have all the following effects:

1. Increase blood supply to the brain.
2. Increase oxygen delivered to the brain.
3. Enhance metabolism of brain cells.
4. Protect the brain from insufficient oxygen supply.
5. Slow the deposit of the age pigment lipofuscin in the brain.
6. Prevent free radical damage to brain cells.
7. Increase intelligence, memory, learning and recall.

### *Oxygen and the brain*

Oxygen is unique in that it is both a free radical generator and a free radical scavenger. At optimum concentrations, oxygen neutralizes more free radicals than it produces. Either too much or too little can upset the balance and generate the production of free radicals, which in turn can lead to aging. One of the major ways in which oxygen generates free radicals is its reaction with unsaturated fats, a process called peroxidation. Brain cells contain more unsaturated fats than any other part of the body; therefore it is our brains that are most susceptible to peroxidation.

Peroxidation and the formation of massive amounts of potent free radicals can occur during heart attacks, strokes and through the effects of smoking and pollution.

Consequently, many countries use Hydergine for emergencies and accidents that involve heart attacks and strokes. Hospitals give Hydergine to patients before an operation in order to gain time in case of any ensuing crises. This is because Hydergine helps to stabilize brain oxygen levels, if they are too high Hydergine lowers them, if they are too low then Hydergine improves them.

Here are some conditions that can cause major peroxidation and the formation of massive amounts of potent free radicals:

- Heart attack
- Stroke
- Pollution (Carbon monoxide greatly reduces the oxygen carrying ability of the blood).
- Smoking cigarettes (Nicotine constricts blood vessels and decreases oxygen supply to the brain. It is estimated that those who smoke more than 20 cigarettes a day lose at least 7% of the normal blood flow to the brain).
- Some European countries use hydergine for emergencies and accidents that involve shock, haemorrhage, strokes, heart attacks, drowning, electrocution and drug overdose.
- Hospitals give hydergine to patients before an operation in order to gain time in case of any ensuing crises. This is because hydergine helps to stabilize brain oxygen levels, if they are too high hydergine lowers them, if they are too low then hydergine improves them.
- Hydergine has also been shown to increase the level of neurotransmitters in the brain, whilst this may not be significant enough for the treatment of senile dementia,

such action has implications and benefits for the treatment and prevention of age related mental decline.

There is also evidence that hydergine stimulates the growth of dendrite nerve fibres. Dendrites can normally be expected to decline with aging and some scientists have associated the number and density of dendrites with intelligence.

This decrease in brain cell connection has been hypothesized to be due to impairment in the energy supply at synaptic regions. Because of hydergine's known ability to improve nerve cell metabolism, a group of Italian scientists studied the ultra-cellular features of synaptic mitochondria to see if long-term hydergine treatment could delay or prevent the loss of synaptic connections.

The mitochondria are the 'intracellular powerhouses' where the universal energy molecule-ATP (adenosine triphosphate) is produced. The scientists found that the number of mitochondria is greatest at about 12-months of age in rats (equivalent to a 25-year old in human terms) and then progressively decreases. However, the size of the mitochondria increased progressively after 12 months. Thus in young adult rats, the energy required at synaptic regions are provided by a large number of small, highly efficient mitochondria, whereas in old rats, energy is produced by a smaller number of larger, less efficient mitochondria. But, astonishingly after treatment with hydergine, it can be seen that the total mitochondrial volume of old rats was nearly the same as the young rats. Furthermore, the mitochondrial size was altered to a more youthful direction.

Like its ergot relatives, hydergine has also shown itself to be a mild vasodilator (it enhances brain blood flow) and improves the uptake of the brain energy molecule – glucose. Hydergine also reduces the accumulation of age-related toxin, lipofuscin.

Time and again, clinical trials indicate that hydergine can improve cognitive functions, mental alertness, clarity and mood. This effect

was demonstrated when two groups of cats were anaesthetized and their brains electronically monitored. The scientists reduced the brain's blood supply (and therefore oxygen supply). The cats in the control group (with no Hydergine) had brain damage within 5 minutes and died within 15 minutes. However, the cats in the pre-Hydergine treated group had strong brain wave patterns up to 45 minutes later. This experiment proved two things:

- Firstly, that a decrease in the normal oxygen balance results in tremendous free radical damage;
- Hydergine protects against this free radical damage when the oxygen level is upset.

### *Rejuvenation properties*

A group of Italian scientists have studied the ultra-cellular features of synaptic mitochondria (contains enzymes for respiration and energy production) to see if long-term Hydergine treatment could delay or prevent the loss of synaptic connections. The scientists found that the number of mitochondria is greatest at about 12-months of age in rats (equivalent to a 25-year old in human terms) and then progressively decreases. However, the size of the mitochondria increased progressively after 12 months. Thus in young adult rats, the energy required at synaptic regions are provided by a large number of small, highly efficient mitochondria, whereas in old rats, energy is produced by a smaller number of larger, less efficient mitochondria. After treatment with Hydergine, it was seen that the total mitochondrial volume of old rats was nearly the same as the young rats. Furthermore, the mitochondrial was altered to a size more youthful.

Hydergine and the other ergot-derived cognitive enhancers help to reverse many of the effects of age-related cognitive decline.

### *Dosages, Side effects and Contradictions*

Usual dosages are 2.25mg to 9mg daily, but always build up the doses slowly. There is also a more easily absorbed liquid hydergine, which provides precise titration because dosages of 0.5mg increments can be taken. Liquid hydergine is also less likely to cause any stomach upset. Most people do well at dosages of around 2.25 mg to 4.5mg per day with occasional breaks.

With literally thousands of published clinical research papers and hydergine's decades of use around the world, it has proven itself to be non-toxic and relatively safe. Side effects even at quite high dosages are few as long as the dose is gradually built up. Otherwise side effect of nausea and headaches may occur.

Its potential side effects include mild nausea, gastric disturbances and bradycardia. It should be avoided by people who suffer from psychosis, or those with low blood pressure or abnormally slow heartbeat. The most common side effect of stomach upset can be avoided with the use of specially coated tablets (known as FAS) or sublingual liquid versions.

Seek a health professional's advice if combining hydergine (at dosages in excess of 9mg per day) with other ergot derivatives or vasodilators.

With its beneficial affects, mild side effects and few contraindications, hydergine is ranked as one of the most important and safe anti-aging medicines available today.

### *History*

When Dr. Hofmann began working for Sandoz Pharmaceuticals (now Novartis) in Switzerland during the 1930s his research goal was to work towards the isolation of active principles in known medicinal plants.

Dr. Hofmann developed Hydergine in the 1940s, while researching the chemistry of ergot, a fungus that grows on rye and was traditionally used by midwives in Europe to lower blood pressure

with birthing mothers. While purifying the ergot-derived substance ergotoxine, Dr. Hofmann had the intuition that this alkaloidal preparation was not homogenous. Dr. Hofmann's intuition proved correct. Upon further analysis ergotoxine turned out to mixture of three different components.

During testing by Professor Rothlin at Sandoz, medicinally useful properties were discovered, and from these three substances, two pharmaceutical preparations were developed: the blood-pressure-stabilizing compound Dihyergot and the cognitive enhancer Hydergine.

Although Sandoz was initially interested in new blood-pressure medications, they began devoting a great deal of resources into researching Hydergine, after studies started to uncover its cognition-enhancing effects. Hydergine was developed because of its ability to improve peripheral circulation and cerebral function in the control of geriatric disorders, and it has proven to be an effective treatment for these indications. Hydergine was the first drug to show efficacy as a treatment for Alzheimer's disease and dementias. (2)

Today Hydergine is widely used around the world as a treatment for senility, age-related cognitive decline, and as a treatment for a number of other problems. Extensive research has revealed a plethora of brain-boosting and anti-aging benefits that Hydergine has to offer. Hydergine is one of the most tested pharmaceuticals ever developed and it still remains one of Novartis' most important pharmaceutical products. It has proven to be beneficial and nontoxic in numerous studies. Dr. Hofmann has periodically used Hydergine himself over the years, and I suspect that his use of this cognitive enhancer may play a significant role in his extraordinary mental clarity at the age of a hundred. (3)

### **The many benefits of Hydergine**

Studies indicate that Hydergine has the ability to enhance memory and learning. It improves a range of cognitive abilities, such as concentration and recall (4,5,6) and helps to prevent damage to brain cells from insufficient oxygen. (7) A number of studies even suggest that Hydergine may be able to help reverse existing damage to brain cells. (8)

Some of Hydergine's cognitive enhancement may be due to the fact that it increases oxygen and blood flow to the brain because it's a mild vasodilator. (9) It also enhances brain cell metabolism and mitochondrial metabolism. Hydergine's ability to improve cell metabolism inspired a team of Italian researchers to study how it affects the intracellular features of rat mitochondria, structures within cells that produce energy in the form of ATP (adenosine triphosphate) by respiratory metabolism. In these studies Hydergine not only increased the volume of the mitochondria, it also reduced their size, which is similar to the more efficient mitochondria in younger animals. (10)

Hydergine is an extremely powerful antioxidant. When I spoke with life extension researcher Durk Pearson he said, “We suspected that Hydergine might be a powerful antioxidant due to its structure, so we suggested an experiment that was done at NYU. Every time vitamin C is oxidized and then reduced by the iron in redox cycles, you produce a hydroxyl radical. And the hydroxyl radical is tremendously chemically reactive. It’s about as reactive as fluorine is at eight hundred degrees Fahrenheit--so it can rip up anything. What they found is that Hydergine was the most powerful antioxidant that they tested.”

Hydergine stimulates new interconnective growth between neurons. It causes the release of brain-derived neurotrophic factor (BDNF), which is involved in the repair of damaged neurons and the growth of neurons and neurites. (11) According to Pearson, “If you deprive the brain of BDNF the neurites die back and eventually the cell bodies connected to them die. The brain normally produces BDNF, but as you get older you produce less and less. You end up with some neurites dying back and your brain sort of gets disconnected. The neurons get disconnected from each other.”

This is an important mechanism by which Hydergine may enhance learning and memory in the elderly. Hydergine mimics the effect of a substance found in the brain called nerve growth factor, which stimulates protein synthesis that results in the growth of new dendrites (tiny tree-like branches at the receiving ends of brain cells). (12) Many neuroscientists believe that intelligence is correlated with the number of interneural connections in the brain. Studies have demonstrated that Hydergine actually increases cortical thickness in the brain through this process and that it also raises levels of the neurotransmitter dopamine. (13)

Studies have shown that Hydergine helps to stabilize brain oxygen levels. (14) If brain oxygen levels are too low then Hydergine raises them, and if they’re too high then Hydergine lowers them. This is why some European countries use Hydergine preoperatively in surgery and after strokes, hemorrhages, and heart attacks to gain precious time. It is also sometimes used to gain more time after certain types of accidents, such as drowning, electrocution and drug overdoses.

Hydergine reduces deposits of the age-related toxin lipofuscin in the brain (15), and normalizes systolic blood pressure. (16) It has also been shown to reduce symptoms of lethargy and, in some cases, even lower abnormally high levels of cholesterol. (17) Many people report that their brain simply feels more awake and more lucid on Hydergine.

Some studies on Hydergine have demonstrated only mild effects, leading some people to believe that it’s not very effective. (18) However many European physicians believe that these studies were less dramatic than others simply because the dosages used were too low, and studies comparing the effects of a 3 mg daily dose to a 6 mg daily dose support this notion. (19) The U.S. recommended dose is 3 mg. per day, while the European recommended dose is 9 mg. per day in 3 divided doses. Some people need to take Hydergine for several months before they notice any significant effects.

Hydergine is extremely nontoxic and has very few side-effects. Initially, Hydergine may cause some mild nausea, gastric disturbances, and bradycardia. It is contraindicated for people who are allergic to it, who suffer from psychosis, or who have an abnormally slow heartbeat or low blood pressure. (20)

Combining Hydergine with other ergot derivatives or other cognitive enhancers may have a synergistic effect, so you may need to scale down the dosages of all the drugs. One should seek the advice of a physician when combining Hydergine with other cognitive enhancers in excess of 9 mg. per day. Most people do well at dosages of around 3 mg. to 9 mg. per day, in divided doses, with occasional breaks. The most common side effect is stomach upset. This can be avoided by using specially coated (FAS) tablets or by using a sublingual liquid preparation.

### *Conclusion*

Fungi's from rye were used by our ancestors for many different reasons, some of them as rites of passage into adulthood, most were considered to be 'mind-expanding.' Now we know many of the pharmacological actions and roles they play in mental and memory enhancement and in the slowing of age-related brain disorders.

Today, we understand that brain protection and enhancement is a most important factor- if not the most important factor for anti-aging medicine and successful longevity.