When the drug called deprenyl was first developed in the early 1960’s, the Hungarian doctor who synthesized it could hardly have foreseen its widespread therapeutic potential.

Over the past half century, deprenyl has gained recognition not only as a clinically proven antidepressant and Parkinson’s treatment, but also as a mental energizer, physical and cognitive performance booster, generalized mood-lifter, sex enhancer, brain protector, and longevity tonic. The age-retarding and performance-enhancing effects of deprenyl have been clearly demonstrated in animal studies, and humans can benefit from these intriguing findings. The drug is not just beneficial in cases of neurodegenerative diseases; the general healthy but aging population can employ low-dose deprenyl to improve quality of life in their middle to late years, fend off physiological and cognitive decline, boost physical, sexual, and mental vigor, and promote longevity.

Deprenyl Preserves the Essential Neurotransmitter Dopamine

Deprenyl (also known by trade names Selegiline, Jumex, and Eldepryl) exhibits a wide spectrum of pharmacological activity. The first one, for which it is most well-known, is inhibition of an enzyme that breaks down neurotransmitters such as dopamine. (1-5) Let’s take a quick look at the operation of the brain’s circuitry, which depends on the continuous regulation of neurotransmitter levels. In a healthy brain, this achieved by a fine balance between neurotransmitter manufacture from amino acids and breakdown by enzymes. Any disruption of either neurotransmitter synthesis or degradation (or both) can upset the brain’s delicate equilibrium, resulting in mood, psychiatric, or neurological disorders. Here we’re focused on neurotransmitter breakdown, specifically by MAO-B, a member of the monoamine oxidase family of enzymes that degrades dopamine (as well as other brain chemicals such as phenylethylamine (PEA)). Enzymatic degradation is a biochemical pathway necessary for the elimination of used neurotransmitters. MAO-B is essential to brain metabolism, but if its over-activity exceeds the rate of dopamine synthesis, the brain’s dopamine stores become depleted, with disastrous consequences. That’s
where deprenyl comes to the rescue: by blocking MAO-B, it prevents the breakdown of dopamine, replenishing the neurotransmitter’s levels in the brain — the crucial mechanism that underlies deprenyl’s success in treating depression and neurodegenerative diseases. Dopamine is central to movement, coordination, sex drive, and cognition, and its production is hindered in these diseases, and also, as we’ll see below, as a consequence of aging.

**Deprenyl Treats Depression and Neurodegenerative Diseases by Blocking MAO-B**

MAO-B inhibitors were among the first antidepressants before the advent of tricyclics, SSRI’s, and other newer generation drugs, but their use was limited due to the “cheese” effect, a hypertensive reaction brought on by ingestion of foods rich in tyramine, a natural substance found in aged cheeses, cured meats, and other foods. Deprenyl was the first MAO-B inhibitor shown to effectively treat depression without the danger of elevated blood pressure or other side effects. (6-10) Recently, the drug was approved in a transdermal patch formulation (Emsam) for the treatment of major depressive disorder. (6,11)

MAO-B inhibition is also key to deprenyl’s use in Parkinson’s, a disease characterized by a dramatic decline in brain dopamine due to the destruction of dopamine-producing neurons in the substantia nigra region of the brain. Symptoms include impaired cognition, tremors, rigid muscles, loss of coordination, progressive disability, and shortened lifespan. Clinical studies beginning in the 1980’s suggesting that deprenyl slows disease progression in early Parkinson’s disease (12,13) led to its FDA approval in 1989. In advanced cases, deprenyl is often used as an adjunct treatment to L-dopa, another Parkinson’s treatment, but one riddled with serious side effects. (14) Besides its dopamine-potentiating capacity, deprenyl has a protective effect on dopaminergic neurons, as we’ll see below, and delays the need for L-dopa therapy if initiated early in the progression of the disease. (2) Many physicians report that their Parkinson’s patients taking deprenyl demonstrate physical improvements, enhanced memory and concentration, and increased life expectancy.

More recently, the drug has also showed promise in treating Alzheimer’s disease, which involves the impairment of several neurotransmitter systems, including dopamine. The dysfunction of the dopaminergic system is associated with an increase in MAO-B, and interestingly, the extent of this rise is proportional to the severity of dementia. (3) As in Parkinson’s, deprenyl has demonstrated positive effects on cognitive performance and memory in Alzheimer’s patients, (3,15,16) as a result of enhanced function of the prefrontal areas of the brain that are rich in dopamine receptors. (3)

**Deprenyl Combats Brain Aging**

While deprenyl is a successful treatment for neurodegenerative diseases, its medicinal value is even more far-reaching: it can also benefit the healthy but aging population by countering the increase in MAO-B activity and resulting dopamine deficits that go hand in hand with growing older. After age 45, the brain’s dopaminergic neurons age rapidly, causing a decline in dopamine levels of 13% per decade. (17) A drop in brain dopamine to 30% of the normal level leads to Parkinson’s, and a plummet to 10% results in death. (17) But levels don’t have to drop precipitously to upset normal functioning — just a modest dip in dopamine as a result of aging can produce lowered sex drive, impaired cognitive function, or loss of coordination. Obviously, we want to keep the dopaminergic system functioning optimally as we age by keeping rising MAO-B levels and falling dopamine production in check, and thankfully this is possible. We’ll see below how to use low-dose deprenyl to preserve youthful neurotransmitter levels and brain function, slow cognitive and physical decline, and promote longevity.

**Deprenyl Protects the Brain**

Besides its dopamine-potentiating ability, deprenyl displays multiple neuro-protective properties. It boosts levels of endogenous antioxidant enzymes such as superoxide dismutase and catalase in the brain, (1,5,7,8,18) while also scavenging free radicals and other reactive oxygens. (1,3,5) This dual antioxidant defense is another way that deprenyl slows down the aging process and ameliorates neurodegenerative diseases, both of which are associated with cumulative oxidative damage. Deprenyl also neutralizes dangerous neurotoxins, such as MPTP, (1,2,5) which has been shown experimentally to produce Parkinson’s symptoms, (2) and protects against glutamate-receptor-mediated toxicity. (3,4) Glutamate is an excitatory neurotransmitter that can be lethal to brain cells. Furthermore, deprenyl has been shown to rescue damaged neurons. (3,4) Because deprenyl is such a powerful brain defender, researchers have labeled it one of the “most promising neuroprotective agents to date.” (4,19).
Deprenyl Extends Life Span by Unique “Enhancer” Mechanism

We’ve just seen deprenyl’s potent effects in slowing cognitive and physical deterioration and protecting the brain; but perhaps even more compelling is its age-retarding effect, which has been demonstrated in rats, mice, hamsters and dogs. (15,18;20-23) In one of numerous experiments evaluating the drug’s impact on life span, female rats treated with deprenyl lived longer than placebo-treated rats, in some cases twice as long (36 months versus 15 months). (21) In another trial, immunosuppressed mice fed a deprenyl-spiked diet lived up to three times longer than the control mice (14.5 months versus 5 months). (22) Joszef Knoll, the Hungarian doctor who discovered deprenyl, performed several fascinating experiments on rodent longevity including one in which he tested the effects of deprenyl on 94 sexually inactive and 99 highly active rats. Knoll observed that the group of highly active rats lived longer (153 weeks) than the “under-sexed” rats (135 weeks), and that medication with deprenyl enabled the underachievers to reach an equivalent level of sexual activity and longevity as their unmedicated high-performing peers. And when this latter group of already highly lively animals was treated with deprenyl, they became “super” rats, with even greater libido, increased learning capacity, and longer life span (185 weeks), with many living longer than the estimated technical life span! (23)

Knoll determined that the mechanism responsible for these remarkable improvements is enhancement of catecholaminergic activity in the brain. (7,24) The catecholamines are the inter-related neurotransmitters dopamine, noradrenaline, and adrenaline. Deprenyl acts as a “neuroamplifier,” boosting the brain’s catecholaminergic circuitry to a higher level of activity. Even though deprenyl is an analogue of methamphetamine and PEA (we’ll see more on this later), the enhancer action is independent of amphetamine-like activity: instead of inducing a continuous release of neurotransmitters from neuronal storage in an uncontrolled manner, deprenyl selectively stimulates and boosts catecholaminergic neurons. (17,24) This mechanism is also unrelated to MAO-B inhibition. (8,25,26) Knoll’s experiments demonstrated that these performance, cognitive, and longevity gains can be achieved by repeated, low-dose administration of deprenyl. (8,25,26) These findings have profound implications for humans in enhancing the quality of their middle and late years of life (i.e., improved sexual, physical, and mental function) and increasing the quantity of those years. Indeed, Knoll postulated that the same mechanism that extends life span and improves sexual and learning performance in rats also operates in humans who incorporate low-dose deprenyl into their anti-aging regimen beginning in their forties. Specifically, Knoll recommends the “prophylactic” administration of deprenyl as a general anti-aging tonic at a dose of 1 mg/day (one-tenth the dose used in Parkinson’s and Alzheimer’s) to slow brain aging and the decline of cognitive and physiological functions, prolong life, and prevent or delay the onset of neurodegenerative diseases. (7,24,27) According to Knoll, this low-dose life extension technique “will work for decades. It will improve the quality of life in the latter period of life, hopefully shifting the time of natural death.”

Professor Knoll’s animal experiments highlight a considerable increase in longevity for the deprenyl treated rats over their non-treated counterparts. In fact, the first deprenyl treated rat to die only did so after all the non-treated rats had died.

It’s important to recognize that the mechanism of catecholamine enhancement, or “neuroamplification,” is one of a kind, and unrelated to any other life extension method that we know of today, such as calorie restriction (CR) and CR mimetics, restoring mitochondrial bioenergetics, telomere-lengthening, hormone restoration, etc. It should also be noted that deprenyl’s longevity effects are also a result of its ability to counteract oxidative damage to the brain’s dopaminergic system during aging. (18)

Reported Effects of Deprenyl in Healthy People

Some doctors, including Dr. Dharma Singh Khalsa, an anti-aging physician and Alzheimer’s researcher, report that deprenyl exhibits a cognitive-boosting power in their Alzheimer’s and Parkinson’s patients that is even more dramatic in their disease-free patients who suffer from only mild to moderate age-related memory impairment. Even though these relatively healthy patients take doses recommended for anti-aging purposes (1 mg three times/week to 1-3 mg/day, depending on age and symptoms), a fraction of the dose used for neurodegenerative diseases (10 mg/day), they exhibit not only better recall, but also improved concentration, cognitive processing speed, and ability to process complex information, with the added benefits of enhanced sex drive, mood, and energy levels. (On a personal note, this author, while writing this article, sampled a 1.25 mg dose (one quarter of a 5-mg tablet) on three separate occasions, and can attest to deprenyl’s...
brain-energizing effects.) All of these marked improvements are similar to those observed in Knoll’s experiments with deprenyl-medicated rats, which supports the view that the “enhancer effect” does indeed operate in humans.

It should also be noted that a couple of other mechanisms besides catecholamine enhancement may contribute to, or compound, these positive outcomes. For example, the increase in libido may also be mediated by MAO-B inhibition, which increases levels of dopamine and PEA, both of which influence sex drive. (PEA, sometimes called the “love hormone,” is a stimulating brain chemical that acts as a neurotransmitter.) Enhanced levels of both of these neurotransmitters may also contribute to the heightened mood, energy, and youthful vitality reported by those on low-dose deprenyl. In addition, deprenyl’s metabolites also play a role in its complex pharmacology. (28) Two of its three main metabolites, methamphetamine and amphetamine, (28) likely add to its brain stimulatory and cognitive effects, including improvements in learning, memory, and concentration. Keep in mind that at the low doses used for life extension purposes, blood levels of these metabolites would likely be relatively minor. Also, in contrast to amphetamines, deprenyl has been shown over the past 50 years to be an extremely safe drug, free of toxic side effects, and without the risks associated with amphetamine use.

What Dose Should You Take?

Knoll recommends a universal 1 mg daily dose for anti-aging purposes, but some experts suggest a graduated dosing scheme based on age. For example, a reasonable guideline would be: 1 mg daily, or every other day, for ages 40-45; 2 mg daily for ages 45-50; 3 mg daily for ages 50-55, etc., with dose proportional to age. The best rule of thumb is to start low and increase as desired; cut back if over-stimulation or insomnia occurs. Dep-Pro Liquid is a low-dose liquid deprenyl formulation that delivers 1 mg per drop, making it easy and convenient to dispense the desired amount (i.e., between 1 and 4 mg). For those desiring higher dosages, 5 mg tablets (Jumex) are also available.

Note: Consult your healthcare professional before using deprenyl if you are taking other antidepressants or any other neurologically active medication.

Summary

Deprenyl is an intriguing and pharmacologically diverse drug with a wide range of applications. The drug’s enzyme-inhibitory action makes it a powerful anti-depressant, anti-Parkinson’s, and anti-Alzheimer’s agent that is also of value to those without neurological disorders who wish to optimize and preserve the health and functioning of their dopaminergic nervous system as they enter their middle to senior years. Additionally, deprenyl offers potent antioxidant and neuroprotective properties to further support a healthy and youthful brain. Deprenyl’s life extension properties are equally, if not more compelling. Aging humans can take advantage of this safe and unique therapy to extend lifespan while improving cognitive function, physical performance, and general quality of life in the latter decades.

References


www.antiaging-systems.com // Order hotline: 1-866-800-4677 // e-mail: ias@antiaging-systems.com