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Can This Molecule Boost Fertility and Longevity in Aging Humans?

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STORY AT-A-GLANCE

- Spermidine, a polyamine compound originally isolated from semen, encourages autophagy, a cellular 'self-eating' process known to positively affect aging and longevity
- Spermidine, an antiaging molecule, has the potential to reverse declining fertility in older mice, with potential ramifications for humans as well
- Older mice not only had less spermidine in their ovaries compared to young and middle-aged mice, but they also had more degraded oocytes and follicles
- When the older mice received spermidine, their oocytes developed faster and with fewer defects compared to untreated mice of the same age
- Spermidine is found in common foods, including aged cheese and fermented soy products, as well as mushrooms, pears and potatoes

Fertility declines in women as they age, in part due to decreases in the quality of developing eggs, or oocytes. Little is known, however, about how this process occurs — and whether it could be prevented or slowed. A study on mice suggests it's possible to improve oocyte quality with spermidine supplementation.[1]

It found that spermidine, an antiaging molecule, has the potential to reverse declining fertility in older mice, with potential ramifications for humans as well.[2] Spermidine, a polyamine compound originally isolated from semen, encourages autophagy, a cellular 'self-eating' process known to positively affect aging and longevity.[3]

Why Spermidine Is Considered a Fountain of Youth

While spermidine was first found in semen, it has various metabolic functions in many types of cells and is naturally found in all living organisms.[4] It's also found in common foods, including aged cheese and fermented soy products, as well as mushrooms, pears and potatoes. A review published in the journal Autophagy details some of spermidine's benefits:[5]

> *"This chemical affects numerous biological processes, including cell growth and proliferation, tissue regeneration, DNA and RNA stabilization, enzymatic modulation, and regulation of translation, among others. Furthermore, spermidine exhibits anti-inflammatory and antioxidant properties, enhances mitochondrial metabolic function and respiration, promotes chaperone activity and improves proteostasis."*

Spermidine also appears to act as a fountain of youth, offering longevity benefits in a number of species. In addition to extending lifespan, studies show spermidine offers cardio- and neuroprotection, stimulates anticancer immune response and may decrease immunosenescence[6] — the gradual deterioration of your immune system — which is a leading cause of death in the elderly.[7]

Many of spermidine's antiaging effects are believed to be linked to its stimulation of cytoprotective macroautophagy. According to the Autophagy review, "Age-associated conditions including cancer, neurodegeneration and cardiovascular diseases are directly connected to the intracellular accumulation of toxic debris, and its removal by autophagy constitutes a well-documented avenue for protection against age and disease."[8]

In fact, spermidine's potency is equivalent to that of rapamycin,[9] a prescription immunosuppressant drug with autophagy-stimulating properties that's used in cancer treatment.

Spermidine Boosts Fertility in Older Mice

Research published in Nature Aging suggests spermidine may have a role to play in helping fertility issues. In humans, spermidine levels decline with aging, and researchers have suggested the molecule may act as an "antiaging vitamin."[10] This may include turning back the reproductive clock.

Researchers with Nanjing Agricultural University in China found that older mice not only had less spermidine in their ovaries compared to young and middle-aged mice, but they also had more degraded oocytes and follicles. When the older mice received spermidine, however, their oocytes developed faster and with fewer defects compared to untreated mice of the same age.[11]

The number of follicles also increased. In humans, the number of follicles, which hold and release oocytes, is often used to measure the quantity and quality of oocytes. "Even when the researchers delivered spermidine in drinking water instead of with an injection, it still reversed signs of oocyte ageing," according to a news release in Nature.[12]

And the benefits didn't end there. The formation of blastocysts, the early stage of an embryo, also improved after spermidine exposure. Older mice given the compound also produced about double the number of young per litter compared to older mice not given spermidine.[13] It's possible that it works to boost fertility by improving mitochondrial function and helping clear away damaged cell components.

"Genes linked to cell energy production and processes that clean up cellular debris had different expression patterns in young mice, older mice and older mice that had received spermidine," the Nature release noted. "In spermidine-enriched mice, oocytes recovered their ability to clear out broken components. The compound also seemed to enhance the function of healthy mitochondria in ageing mice."[14]

What's more, when the team applied spermidine to aged pig oocytes in a lab that were under stress, similar beneficial effects occurred, suggesting its fertility-boosting effects may apply to multiple species[15] — possibly even humans. Next, the team plans to test spermidine on human oocytes in a lab.

Spermidine May Lower Mortality, Support Brain Health

Beyond offering a potential option to stave off declining fertility, spermidine is also linked to increased survival in humans. Consuming spermidine-rich food lowers mortality associated with cardiovascular diseases and cancer.[16] Further, a study published in The American Journal of Clinical Nutrition found a diet rich in spermidine, at levels commonly found in the Western diet, lowers the risk of all-cause mortality:[17]

> *"Spermidine showed the strongest inverse relation with mortality among 146 nutrients studied. The reduction in mortality risk related to a diet rich in spermidine (top compared with bottom third of spermidine intake) was comparable to that associated with a 5.7-y younger age. All of the findings apply to spermidine from dietary sources and to amounts characteristically found in the Western diet …"*

Cognitive benefits are also possible. In fruit flies, spermidine slows age-induced memory impairment,[18] while also delaying brain aging and improving cognitive dysfunction in mice with age-related cognitive decline. Spermidine helped to decrease malondialdehyde levels, an indication of an overproduction of reactive oxygen species, while improving superoxide dismutase, which defends against oxidative stress.[19]

In humans, higher dietary intake of spermidine is also linked with a reduced risk of cognitive impairment.[20]

A research team with Manipal College of Pharmaceutical Sciences in India further suggested spermidine could be a useful therapeutic strategy for neurological disorders due to its autophagy-inducing properties. They noted that a healthy brain is dependent on its concentration of polyamines:[21]

> *"Polyamines interact with the opioid system, glutamatergic signaling and neuroinflammation in the neuronal and glial compartments. Among the polyamines, spermidine is found highest in the human brain. Age-linked fluctuations in the spermidine levels may possibly contribute to the impairments in neural network and neurogenesis."*

Protection for Your Heart and Liver, Obesity Benefits

Spermidine also offers cardioprotective properties, even when simply added to drinking water. One study on mice found feeding spermidine:[22]

- Enhanced cardiac autophagy, mitophagy and mitochondrial respiration
- Improved the mechano-elastic properties of cardiomyocytes, which coincided with increased titin phosphorylation and suppressed subclinical inflammation
- Preserved diastolic function
- Reduced systemic blood pressure
- Reduced cardiac hypertrophy

In humans, a diet high in spermidine is associated with reduced blood pressure and lower incidence of cardiovascular disease.[23] It also reverses arterial aging, which is characterized by stiffening of large arteries and the development of arterial endothelial dysfunction, which increases the risk of cardiovascular disease (CVD).

This benefit may be due to its interactions with nitric oxide (NO) and other factors, according to researchers with the University of Colorado, Boulder:[24]

> *"Our results indicate that spermidine exerts a potent anti-aging influence on arteries by increasing NO bioavailability, reducing oxidative stress, modifying structural factors and enhancing autophagy. Spermidine may be a promising nutraceutical treatment for arterial aging and prevention of age-associated CVD."*

Research published in the journal Cancer Research also demonstrated how spermidine can be used to prevent liver fibrosis and hepatocellular carcinoma (HCC), a common type of liver cancer, in lab mice.[25] Researchers noted the mice lived longer after receiving a 3 millimolar (mM) spermidine supplement in their drinking water.

The spermidine-treated mice were also less likely than their untreated counterparts to develop liver fibrosis and cancerous liver tumors, even if they were predisposed to those

conditions. Whereas the mice groups treated lifelong with spermidine achieved a 25% greater life extension, those treated at older ages saw a 10% increase in longevity.

The team explained, "Consuming spermidine over the lifetime of humans provides a novel paradigm to prevent, change, or reverse the pathogenic course of liver fibrosis and HCC in a safe and cost-effective way for patients with chronic liver diseases or with high risk for developing HCC, and patients already developing HCC."[26] They further suggested that spermidine's wide-reach health benefits may significantly impact human health for the better:

> *"As spermidine is a natural component … plentiful in a variety of food and agricultural products such as wheat germ, grapefruit, and Natto (a Japanese product of fermented soy), and can be chemically synthesized and developed as a drink or a dietary supplement to serve with normal diets, it will be a promising safe and cost-effective intervention that will be readily adopted for long-term intervention by the general human population to extend lifespans."*

Indeed, spermidine also alters the composition and function of gut microbiota, and intake is linked with a lower risk of obesity. The compound leads to significant weight loss and improved insulin resistance in obese mice, which may be related to alleviation of metabolic endotoxemia, which causes low-grade inflammation, and its ability to enhance intestinal barrier function.[27]

Spermidine-Rich Foods to Add to Your Diet

If you're interested in harnessing spermidine's health potential, it may be as simple as increasing spermidine-rich foods in your diet. According to The American Journal of Clinical Nutrition study:[28]

> *"Spermidine is the polyamine most readily absorbed from the human gut. A broad and diverse palette of foods contain high amounts of spermidine, such as fresh green pepper, wheat germ, cauliflower, broccoli, mushrooms, and a variety*

of cheeses, whereas even higher amounts are found in soybean products such as natto, shitake mushrooms, amaranth grain, and durian."

Polyamines like spermidine are also present in aged (fermented) cheese, including blue cheese, Brie, cheddar, Swiss, Gouda, Gruyere, Manchego and Parmesan. Intake of spermidine-rich foods is important at any age but may be particularly useful as you get older, when spermidine levels tend to decline.

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