Agmatine Sulfate

Researchers have known about agmatine since 1910, but it has taken over 100 years to appreciate how much this simple nutrient can do. Scientists have only recently discovered that agmatine may improve cognition and memory, reduce anxiety, and improve depression.¹

What is Agmatine?
Agmatine is a small molecule that the body makes naturally from arginine, an amino acid. While the total concentration of agmatine in the body is low, it shows up in concentrated pockets throughout the body. In fact, agmatine has effects on many different organs such as the kidneys, heart and blood vessels. Likewise, agmatine has many roles in health and disease, such as drug addiction, diabetes, anxiety disorder, depression, and even cancer.¹ Some diseases may be linked to deficiencies in agmatine levels and activity, while performance may be enhanced by agmatine supplementation.

Agmatine Effects on the Kidney
Kidney function can decrease as part of certain disease processes. Diabetes and high blood pressure are known to wreak havoc on the kidneys, for example. Moreover, kidney function declines simply as a person grows older. If left untreated, kidney disease can lead to kidney failure and may require dialysis or kidney transplant.

Recent research has revealed that agmatine has a number of beneficial effects on the kidney. Agmatine protects the kidney from injury that is caused by blood vessel disease² and by inflammatory diseases.³ Agmatine also improves kidney function.⁴,⁵ Specifically, agmatine increases the rate at which the kidney filters the blood.⁵ The filtration rate of the kidney (GFR) is one of the main indicators of kidney health and function. In fact, measuring GFR is the main way that doctors determine the health of your kidney.

A Role for Agmatine Sulfate in Type 2 Diabetes
In type 2 diabetes, cells in the body become less sensitive to the effects of insulin. Some treatments for type 2 diabetes, like Avandia (rosiglitazone) and Actos (pioglitazone), work by increasing how cells respond to insulin. Other drugs, like glyburide and glipizide, stimulate the pancreas to secrete more insulin. Indeed, people with more advanced diabetes may need injections of insulin to treat the disease.

Amazingly, agmatine has been shown to have all three anti-diabetic effects. It sensitizes cells to the effects of insulin in at least two different ways.⁶ Agmatine acts on the pancreas, causing it to release insulin.⁷,⁸ Agmatine even acts like insulin itself on cells.⁹ Taken together, this strongly suggests that agmatine sulfate may be a useful addition in the treatment of type 2 diabetes.

Agmatine Sulfate’s Actions on the Heart and Blood Vessels
Historically, agmatine generated the most interest among researchers for its ability to beneficially affect the cardiovascular system by reducing the heart rate and blood pressure.¹⁰ It is important to note, however, that this blood pressure lowering effect is considered mild compared to today’s blood pressure medications. In other words, agmatine only modestly decreases blood pressure and heart rate compared to prescription drugs like lisinopril and metoprolol. Nevertheless, agmatine is a natural molecule that the body produces (see Safety of Agmatine below) while prescription medications carry the risk of certain side effects.
Also, because of agmatine’s effects on the kidney, the supplement may be helpful in people with congestive heart failure. Specifically, agmatine increases urinary flow and filtration. Agmatine sulfate also enhances a phenomenon called natriuresis, which is the body's way of getting rid of excess sodium. People with congestive heart failure must reduce their intake of fluid and salt to prevent exacerbations of their disease. Therefore, agmatine may be a useful addition to the treatment of congestive heart failure.

**Agmatine’s Role in the Brain and in Brain Diseases**
Perhaps the most exciting effects that agmatine exerts are those that occur in the brain. Agmatine is a neurotransmitter, which means it is a chemical that allows nerve cells to communicate with one another. As a neurotransmitter, agmatine interacts with several types of nerve cell receptors including the NMDA receptor, which is important for epilepsy, learning and memory. This receptor also plays a key role in schizophrenia and other diseases.

**Anxiety and Depression**
Most of the research on agmatine in anxiety and depression has been conducted on animals. Nevertheless, agmatine appears to reduce anxiety and improve depression in various laboratory studies. Some of the reports in anxiety have been mixed, but agmatine clearly and consistently improves depression in animal models of this condition. Clinical studies are needed, however, to conclusively show if this effect also occurs in humans.

**Seizures and Epilepsy**
As with anxiety and depression, most research on agmatine in epilepsy has been done on laboratory animals. Agmatine increases seizure threshold, which means that the natural substance makes it less likely for a seizure to occur in response to an inciting factor. Agmatine also shortens the length of seizures once they occur. In separate work, agmatine was a successful remedy for the treatment of seizures in mice. Agmatine may also help other antiepileptic drugs work better, such as phenobarbital and valproate. While clinical studies are needed, agmatine clearly appears to be a promising natural substance in the treatment of epilepsy and seizures.

**Pain and Addiction**
Agmatine appears to be a potent analgesic. In other words, agmatine sulfate can reduce several types of pain including those caused by inflammation, spinal cord injury, heat, noxious chemicals, mechanical injury, and neuropathic pain. Importantly, agmatine does not block pain signals by binding to the opioid receptor. This is important because it means that agmatine does not carry the same risk of opioid dependence and addiction that opioid pain medications like morphine and oxycodone do. In fact, agmatine appears to reduce the body’s dependence on morphine and reduce withdrawal symptoms in those taking opioids chronically. Therefore, agmatine sulfate may be helpful in pain control and as a way to prevent or treat dependence on opioids.

**Learning, Memory, and Cognition**
Agmatine concentrations in the brain decline with aging, and this correlates with the ability to learn and remember new information. Amazingly, agmatine specifically and profoundly improves tests of learning and memory in aged rats. Agmatine has also been shown to improve memory deficits caused by diabetes and toxic Alzheimer's disease proteins in rats. Studies suggest that agmatine sulfate may be able to improve cognitive function, learning, and memory in older individuals and in those with certain diseases. Furthermore, agmatine appears to improve learning and memory performance even in younger animals, which means the supplement could improve cognition at all ages.
**Parkinson’s Disease**
A toxin called MPTP causes Parkinson's disease-like damage in the brain. Agmatine sulfate protected mice from developing Parkinson's disease symptoms after they were injected with MPTP. 24

**Alzheimer’s Disease**
Researchers have discovered that there are abnormalities with the system that produces agmatine in patients with Alzheimer's disease. 25, 26

**Stroke**
Agmatine blocks the effects of nitric oxide and glutamate, both of which are released in dangerous quantities during a stroke. 27

**Spinal Cord Injury**
When mice were subjected to a spinal cord injury, agmatine improved recovery by reducing the scar that occurs at the site of the injury. 28 Likewise, agmatine reduced the negative effects of 35 days of spinal cord compression in animals. 29

**Safety of Agmatine**
Agmatine is a natural substance produced by various areas of the body. Thus, within normal circulating levels, there is no inherent danger of agmatine. Indeed, several disease states seem to be associated with abnormally low levels of agmatine in various locations in the body. 1

Researchers have shown that adult rats can consume large amounts of agmatine sulfate over three months without negative effects in behavior or in their organs. 30 The only noticeable effects were slight but significant reductions in body weight and blood pressure. While clinical trials in humans have shown that taking 3.5 grams of Agmatine sulfate each day is safe over 21 days 31, two researchers consumed 2.6 grams of Agmatine sulfate each day for five years and had no adverse events. 32 Thus, agmatine sulfate is likely to be safe when taken in 2 to 3 grams doses each day for up to five years or longer in healthy individuals.

**Conclusions**
Laboratory and clinical studies show that agmatine is a natural substance that exerts a wide array of impressive health benefits. The supplement has a number of interesting effects on the heart, kidneys, and brain. Agmatine sulfate lowers blood pressure and heart rate while helping the kidney to get rid of excess salt and fluid. This may be particularly useful in people with congestive heart failure. The supplement improves kidney function by increasing the filtration rate and protects the kidney from blood vessel disease and inflammation. In addition to protective effects on the kidney, agmatine sulfate improves insulin sensitivity, increases insulin secretion, and can act like insulin itself. These findings strongly suggest that the agmatine may be helpful in people with type 2 diabetes.

Agmatine lowers the seizure threshold, making seizures less likely to occur.

At the same time, agmatine sulfate may improve learning, memory, and cognition in both young and (especially) older individuals. The supplement may improve symptoms of anxiety but almost certainly improves symptoms of depression. Finally, agmatine sulfate may represent a new type of painkiller (analgesic) that controls pain without directly affecting the opioid receptor. This means it can block pain without addiction and may even help those who have become addicted to opioids like morphine and Vicodin.
The potential benefits of Agmatine sulfate to support numerous complex systems simultaneously, combined with its low risk profile, make this compound an attractive addition to any supplementation program.

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

References


